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Management of epithelial precancerous conditions and early neoplasia of the stomach (MAPS III): European Society of Gastrointestinal Endoscopy (ESGE), European Helicobacter and Microbiota Study Group (EHMSG) and European Society of Pathology (ESP) Guideline update 2025

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MAIN RECOMMENDATIONS

At a population level, the European Society of Gastrointestinal Endoscopy (ESGE), the European *Helicobacter* and Microbiota Study Group (EHMSG), and the European Society of Pathology (ESP) suggest endoscopic screening for gastric cancer (and precancerous conditions) in high-risk regions (age-standardized rate [ASR] >20 per 100 000 person-years) every 2 to 3 years or, if cost–effectiveness has been proven, in intermediate risk regions (ASR 10–20 per 100 000 person-years) every 5 years, but not in low-risk regions (ASR <10).

ESGE/EHMSG/ESP recommend that irrespective of country of origin, individual gastric risk assessment and stratification of precancerous conditions is recommended for first-time gastroscopy.

ESGE/EHMSG/ESP suggest that gastric cancer screening or surveillance in asymptomatic individuals over 80 should be discontinued or not started, and that patients' comorbidities should be considered when treatment of superficial lesions is planned.

ESGE/EHMSG/ESP recommend that a high quality endoscopy including the use of virtual chromoendoscopy (VCE), after proper training, is performed for screening, diagnosis, and staging of precancerous conditions (atrophy and intestinal metaplasia) and lesions (dysplasia or cancer), as well as after endoscopic therapy. VCE should be used to guide the sampling site for biopsies in the case of suspected neoplastic lesions as well as to guide biopsies for diagnosis and staging of gastric precancerous conditions, with random biopsies to be taken in the absence of endoscopically suspected changes. When there is a suspected early gastric

neoplastic lesion, it should be properly described (location, size, Paris classification, vascular and mucosal pattern), photodocumented, and two targeted biopsies taken.

ESGE/EHMSG/ESP do not recommend routine performance of endoscopic ultrasonography (EUS), computed tomography (CT), magnetic resonance imaging (MRI), or positron emission tomography (PET)-CT prior to endoscopic resection unless there are signs of deep submucosal invasion or if the lesion is not considered suitable for endoscopic resection.

ESGE/EHMSG/ESP recommend endoscopic submucosal dissection (ESD) for differentiated gastric lesions clinically staged as dysplastic (low grade and high grade) or as intramucosal carcinoma (of any size if not ulcerated or ≤ 30 mm if ulcerated), with EMR being an alternative for Paris 0-IIa lesions of size ≤ 10 mm with low likelihood of malignancy.

ESGE/EHMSG/ESP suggest that a decision about ESD can be considered for malignant lesions clinically staged as having minimal submucosal invasion if differentiated and ≤ 30 mm; or for malignant lesions clinically staged as intramucosal, undifferentiated and ≤ 20 mm; and in both cases with no ulcerative findings.

ESGE/EHMSG/ESP recommends patient management based on the following histological risk after endoscopic resection:

Curative/very low-risk resection (lymph node metastasis [LNM] risk < 0.5 %–1 %): en bloc R0 resection; dysplastic/pT1a, differentiated lesion, no lymphovascular invasion, independent of size if no ulceration and ≤ 30 mm if ulcerated. No further staging procedure or treatment is recommended.

Curative/low-risk resection (LNM risk < 3 %): en bloc R0 resection; lesion with no lymphovascular invasion and: a) pT1b, invasion ≤ 500 µm, differentiated, size ≤ 30 mm; or b) pT1a, undifferentiated, size ≤ 20 mm and no ulceration. Staging should be completed, and further treatment is generally not necessary, but a multidisciplinary discussion is required.

Local-risk resection (very low risk of LNM but increased risk of local persistence/recurrence): Piecemeal resection or tumor-positive horizontal margin of a lesion otherwise meeting curative/very low-risk criteria (or meeting low-risk criteria provided that there is no submucosal invasive tumor at the resection margin in the case of piecemeal resection or tumor-positive horizontal margin for pT1b lesions [invasion ≤ 500 µm; well-differentiated; size ≤ 30 mm, and VM0]). Endoscopic surveillance/re-treatment is recommended rather than other additional treatment.

High-risk resection (noncurative): Any lesion with any of the following: (a) a positive vertical margin (if carcinoma) or lymphovascular invasion or deep submucosal invasion (> 500 µm from the muscularis mucosae); (b) poorly differentiated lesions if ulceration or size > 20 mm; (c) pT1b differentiated lesions with submucosal invasion ≤ 500 µm with size > 30 mm; or (d) intramucosal ulcerative lesion with size > 30 mm. Complete staging and strong consideration for additional treatments (surgery) in multidisciplinary discussion.

ESGE/EHMSG/ESP suggest the use of validated endoscopic classifications of atrophy (e. g. Kimura–Takemoto) or intestinal metaplasia (e. g. endoscopic grading of gastric intestinal metaplasia [EGGIM]) to endoscopically stage precancerous conditions and stratify the risk for gastric cancer.

ESGE/EHMSG/ESP recommend that biopsies should be taken from at least two topographic sites (2 biopsies from the antrum/incisura and 2 from the corpus, guided by VCE) in two separate, clearly labeled vials. Additional biopsy from the incisura is optional.

ESGE/EHMSG/ESP recommend that patients with extensive endoscopic changes (Kimura C3 + or EGGIM 5 +) or advanced histological stages of atrophic gastritis (severe atrophic changes or intestinal metaplasia, or changes in both antrum and corpus, operative link on gastritis assessment/operative link on gastric intestinal metaplasia [OLGA/OLGIM] III/IV) should be followed up with high quality endoscopy every 3 years, irrespective of the individual's country of origin.

ESGE/EHMSG/ESP recommend that no surveillance is proposed for patients with mild to moderate atrophy or intestinal metaplasia restricted to the antrum, in the absence of endoscopic signs of extensive lesions or other risk factors (family history, incomplete intestinal metaplasia, persistent *H. pylori* infection). This group constitutes most individuals found in clinical practice.

ESGE/EHMSG/ESP recommend *H. pylori* eradication for patients with precancerous conditions and after endoscopic or surgical therapy.

ESGE/EHMSG/ESP recommend that patients should be advised to stop smoking and low-dose daily aspirin use may be considered for the prevention of gastric cancer in selected individuals with high risk for cardiovascular events.

ABBREVIATIONS

AGREE	Appraisal of Guidelines for Research and Evaluation
AI	artificial intelligence
ASR	age-standardized rate
AUC	area under the curve
BLI	blue-laser imaging
BSG	British Society of Gastroenterology
CAG	chronic atrophic gastritis
COX-2	cyclo-oxygenase 2
CI	confidence interval
CT	computed tomography
CVID	common variable immunodeficiency
DALY	disability-adjusted life-year
EGD	esophagogastroduodenoscopy
EGGIM	endoscopic grading of gastric intestinal metaplasia
EHMS	European *Helicobacter* and Microbiota Study Group
EMR	endoscopic mucosal resection
ER	endoscopic resection
ESD	endoscopic submucosal dissection
ESDII	2022 update of the ESGE guideline on ESD
ESGE	European Society of Gastrointestinal Endoscopy
ESP	European Society of Pathology (ESP)
EUS	endoscopic ultrasonography
GC	gastric cancer
GIM	gastric intestinal metaplasia
GML	gastric MALT (mucosa-associated lymphoid tissue) lymphoma
GRADE	Grading of Recommendations, Assessment, Development, and Evaluation
HGD	high grade dysplasia
HM	horizontal margin
IM	intestinal metaplasia
KT	Kimura–Takemoto
LCI	linked-color imaging
LGD	low grade dysplasia
LNM	lymph node metastasis
MAPS	management of epithelial precancerous conditions and early neoplasia of the stomach
MDT	multidisciplinary team
MRI	magnetic resonance imaging
NBI	narrow-band imaging
NPV	negative predictive value
OLGA	operative link on gastritis assessment
OLGIM	operative link on gastric intestinal metaplasia
OR	odds ratio
PET	positron emission tomography
PG	pepsinogen
PICO	patient/population, intervention, comparison, outcomes
PPV	positive predictive value
RCT	randomized controlled trial
RR	relative risk
QALY	quality-adjusted life-year
VM	vertical margin
WHO	World Health Organization
WLI	white-light imaging

SOURCE AND SCOPE

This is an official statement of the European Society of Gastrointestinal Endoscopy (ESGE), the European *Helicobacter* and Microbiota Study Group (EHMSG), and the European Society of Pathology (ESP). Gastric adenocarcinoma (GC) represents a significant burden on patients, health systems, and society in general. Well-known risk factors and a slow stepwise pathway of carcinogenesis allow GC to be considered a potentially preventable disease. However, interventions should also be cost-effective including in their environmental impact. This Guideline provides the update of recommendations on screening, diagnosis, and management of precancerous conditions and early neoplasia of the stomach, namely the 2019 MAPS II Guideline and 2022 ESD Guideline.

Introduction

Gastric cancer (GC) represents a significant burden on patients, health systems, and society in general. In 2017, more than one million incident cases of GC occurred worldwide, and nearly 865 000 people died of stomach cancer, contributing to 19 million disability-adjusted life-years (DALYs) [1].

Given the several well-known risk factors and the slow stepwise pathway of carcinogenesis (the "Correa cascade"), the intestinal type of GC can be considered as a potentially preventable disease. Primary prevention of a proportion of cases can be achieved by eradication of *Helicobacter pylori*, promotion of healthy dietary habits, and smoking cessation [1]. The Correa cascade describes the progression of precancerous conditions, leading from the initial chronic mucosal inflammation to atrophy and gastric intestinal metaplasia (GIM), followed by subsequent dysplasia and intestinal-subtype carcinoma. Awareness of this sequence may permit measures that detect early cancerous lesions curable by resection or by the surveillance of individuals with precancerous conditions at risk of GC. Endoscopy with histology is the mainstay for the care of individuals harboring these mucosal changes [2]. Recommendations must be cost-effective and feasible and should have the minimum possible environmental impact [3].

No specific guidelines existed for the management of precancerous conditions until 2012 (MAPS I [4]). In 2015, the first guidelines concerning the role of endoscopy in the treatment of early GC were published in Europe [5]. Subsequently, various

position statements, guidelines, and quality metrics adopted or incorporated concepts expressed in those texts [6]. In 2024, the RE.GA.IN. (Real-world Gastritis Initiative) consensus, a legacy of the updated Sydney–Houston and Kyoto consensus, updated the diagnosis of gastritis emphasizing a reconciled message about the endoscopy–histology crosstalk [2]. Furthermore, a recent systematic review of all guidelines on the management of gastric precancerous conditions addressed the management of GIM, the need to deliver high quality endoscopy and pathology, the role of *H. pylori* eradication, and the means of stratification to determine which high-risk phenotypes should be considered for surveillance [6]. While the risk of precancerous conditions and cancer varies according to geography/ethnicity, there are no differences in the management between patient groups once a patient develops high-risk mucosal changes. The review also pointed out gaps and areas for improvement that we attempt to address and incorporate in this updated guideline, including the clarification of endoscopic and histological protocols and the management of specific situations and conditions. In line with guidelines for other organs (e. g., esophagus and Barrett's mucosa [7]), we decided to incorporate the management of early neoplastic lesions in the same document.

In 2023, the European Society of Gastrointestinal Endoscopy (ESGE), the European *Helicobacter* and Microbiota Study Group (EHMSG) and the European Society of Pathology (ESP) joined forces to review the new evidence and to provide a comprehensive modular guideline (MAPS III) on the management of epithelial precancerous conditions and early neoplasia of the stomach, updating both MAPS II and the ESGE endoscopic submucosal dissection (ESD) Guideline. MAPS III aims to provide guidance on: (a) screening criteria for early neoplasia and precancerous conditions; (b) diagnosis of early gastric neoplasia and relevant precancerous conditions; (c) endoscopic management of early cancerous lesions; (d) the role of endoscopy in the follow-up of precancerous conditions; (e) role of *H. pylori* eradication and (f) other nonendoscopic interventions for individuals diagnosed with early cancer lesions and precancerous conditions; and (g) management of precancerous conditions within specific situations. All modules can be individually updated without the need for a full revision of the Guideline. Finally, a perspective for uptake by ESGE national societies was incorporated. Moreover, three additional sections provide data on previous uptake of guidelines, on sustainability (the "green box"), and on a future research agenda.

Methods

The MAPS III recommendations were developed according to the Appraisal of Guidelines for Research and Evaluation (AGREE) process for the development of clinical practice guidelines [8]. In the last quarter of 2023, after an open call to ESGE individual members and national societies, ESGE, EHMSG, and ESP assembled a panel of European gastroenterologists and pathologists to update the previous MAPS II Guideline [9] and the updated 2022 ESGE Guideline on the role of ESD (ESDII) [10]. If applicable, other ESGE publications were used to provide a comprehensive manuscript. No specific national society was involved.

Working groups were formed according to the following topics (see Topics and Working groups, available online-only in **Supplementary Material**): **1** Screening and cost–effectiveness of interventions; **2** Diagnosis of precancerous conditions and early neoplasias of the stomach; **3** Endoscopic resection and management of superficial early cancer lesions; **4** Endoscopic follow-up of individuals with precancerous conditions; **5** Role of *H. pylori* eradication in the management of precancerous conditions and after early neoplasia resection; **6** Role of other non-*H. pylori* interventions; **7** Management of individuals in specific settings that also harbor precancerous conditions.

The evidence-based Delphi process was applied to develop consensus statements. First, key questions were agreed, and statements were proposed by guideline leaders, considering previous MAPS II and ESD Guideline statements and subsequent changes to previous recommendations. Secondly, each working group edited their statements and modified them according to the evidence if necessary. A literature search up till March 2024 was done using a PICO (patient/population, intervention, comparison, outcome) structure and PubMed queries (see **Supplementary Material**), with a focus on articles published after the production of previous guidelines. M.D.R. and T.G. rated the quality level of the available evidence and the strength of recommendations by using the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) process [11, 12]. The coordinators evaluated and grouped every statement and the evidence in a document with the relevant bibliography. They then sent the document to every participant for online voting on each statement. At this stage, changes were made if necessary, and any statement with less than 80 % agreement was excluded. Every author then approved a final version with recommendations. Finally, a summary of previous uptake of MAPS guidelines and a "green section" was added and the manuscript was reviewed by two members of the ESGE Governing Board. It was then sent for further comments to the ESP and EHMSG boards and ESGE national societies and individual members. Suggestions were considered, and after agreement was reached on a final version, the manuscript was submitted for publication.

For each statement/recommendation, the Guideline records the strength of the recommendation and the quality of the evidence (and provides suggestions or recommendations accordingly) and the percentage agreement among participants; it is shown whether the statement/recommendation is unchanged, modified, or new, compared to the previous guidelines (MAPS II, ESDII). See ▶ **Table 1**.

The reader should consider these recommendations with the understanding that this guidance does not apply to diffuse cancer of the stomach (including the related hereditary syndromes) where the precancerous sequence of events in the Correa cascade is not observed [13]. Also, no recommendations will be made regarding primary prevention measures, screening in the context of diffuse hereditary cancer, management of advanced forms of GC [14], or training both for endoscopic recognition of lesions or ESD or regarding specific technical components of endoscopic classifications for ESD [15].

▶ **Table 1** Management of epithelial precancerous conditions and early neoplasia of the stomach (MAPS III) recommendations: updated from MAPS II [9] and previous endoscopic submucosal dissection (ESD) guideline [5].

MAPS II/ESDII		**MAPS III**	
Module **Recommendation**	**Strength of recommendation/ Quality of evidence**	***Module*** **Recommendation**	**Strength of recommendation/ Quality of evidence**
Screening for early gastric neoplasia and gastric precancerous conditions			
		1 ESGE/EHMSG/ESP suggest population-based endoscopic screening for gastric cancer (and precancerous conditions) every 2 to 3 years in high-risk regions (age-standardized rate [ASR] > 20 per 100 000 person-years) or every 5 years in intermediate-risk regions (ASR 10–20 per 100 000 person-years), if cost–effectiveness has been proven and resources are available. **New**	Conditional/Low
		2 ESGE/EHMSG/ESP suggest against population-based endoscopic screening for gastric cancer (and precancerous conditions) in low-risk regions (ASR < 10 per 100 000 person-years). **New**	Conditional/Low
(MAPS II) **8** For adequate staging of gastric precancerous conditions, a first-time diagnostic upper gastrointestinal endoscopy should include gastric biopsies both for *Helicobacter pylori* infection diagnosis and for identification of advanced stages of atrophic gastritis.	Strong/Moderate	**3** ESGE/EHMSG/ESP recommend that a diagnostic upper gastrointestinal endoscopy (endoscopic opportunistic diagnosis) should include screening for gastric cancer as well as the diagnosis and stratification of risk of precancerous conditions, irrespective of country of origin. **New**	Strong/Moderate
		4 ESGE/EHMSG/ESP suggest *H. pylori* non-invasive screening and eradication between the ages of 20 and 30 for first-degree relatives of patients with gastric cancer. **New**	Conditional/ Moderate
		5 ESGE/EHMSG/ESP suggest endoscopic screening for gastric cancer in first-degree relatives of patients with gastric cancer at the age of 45 years or 10 years before the age of diagnosis of the affected relative. **New**	Conditional/ Moderate
		6 ESGE/EHMSG/ESP suggest that gastric cancer screening or surveillance of precancerous conditions in asymptomatic individuals over 80 should be discontinued or not started. **New**	Conditional/Low
(MAPS II) **11** Low pepsinogen I serum levels or/ and low pepsinogen I/II ratio identify patients with advanced stages of atrophic gastritis and endoscopy is recommended for these patients, particularly if *H. pylori* serology is negative.	Strong/Moderate	**7** ESGE/EHMSG/ESP recommend endoscopic screening for precancerous conditions in individuals with low pepsinogen (PG) I serum levels or/and a low PG I/II ratio, particularly if *H. pylori* serology is negative. **Modified**	Strong/Moderate
Diagnosis of early neoplasia and precancerous conditions			
(MAPS II) **6** High definition endoscopy with chromoendoscopy (CE) is better than high definition white-light endoscopy alone for the diagnosis of gastric precancerous conditions and early neoplastic lesions.	High	**8** ESGE/EHMSG/ESP recommend a high quality endoscopy including virtual chromoendoscopy (VCE), for screening, diagnosis, and surveillance of gastric precancerous conditions and lesions. **Modified**	Strong/Moderate

▶ **Table 1** (Continuation)

MAPS II/ESDII		MAPS III	
Module **Recommendation**	**Strength of recommendation/ Quality of evidence**	***Module*** **Recommendation**	**Strength of recommendation/ Quality of evidence**
(MAPS II) **7** Whenever available and after proper training, virtual CE, with or without magnification, should be used for the diagnosis of gastric precancerous conditions, by guiding biopsy for staging atrophic and metaplastic changes and by helping to target neoplastic lesions.	Strong/Moderate	**9** ESGE/EHMSG/ESP recommend that VCE should be used to guide biopsies in the case of suspected neoplastic lesions. **Modified**	Conditional/ Moderate
		10 ESGE/EHMSG/ESP recommend guided biopsies with VCE for diagnosis and staging of gastric precancerous conditions, and random biopsies in the absence of endoscopically suspected precancerous conditions. **Modified**	Strong/Moderate
(MAPS II) **7** Whenever available and after proper training, virtual CE, with or without magnification, should be used for the diagnosis of gastric precancerous conditions, by guiding biopsy for staging atrophic and metaplastic changes and by helping to target neoplastic lesions.	Strong/Moderate	**11** ESGE/EHMSG/ESP recommend training in the endoscopic diagnosis of gastric precancerous conditions and lesions. **New**	Strong/Moderate
		12 ESGE/EHMSG/ESP suggest that real-time artificial intelligence (AI)-assisted detection and localization of gastric neoplastic lesions or staging of precancerous conditions may be used whenever available. **New**	Conditional/Low
(ESDII) **1** ESGE recommends that the evaluation of superficial gastrointestinal lesions should be made by an experienced endoscopist, using high definition white-light and chromoendoscopy (virtual or dye-based), and validated classifications when available.	Strong/High	**13** ESGE/EHMSG/ESP recommend that when there is suspicion of a neoplastic lesion, the lesion should be ▪ properly described (size, morphology according to Paris classification [namely, ulceration], location, vascular and mucosal patterns); ▪ photodocumented; and ▪ 2 targeted biopsies should be taken. **Modified**	Conditional/ Moderate
(ESDII) **3** ESGE suggests that when suspicious features for deep submucosal invasion are present, complete staging should be considered in order to exclude stage T2/T3 or lymph node metastasis (LNM).	Weak/Low		
(ESDII) **2** ESGE does not recommend routine performance of endoscopic ultrasonography (EUS), computed tomography (CT), magnetic resonance imaging (MRI), or positron emission tomography (PET)-CT prior to endoscopic resection except if there are signs suspicious of deep submucosal invasion or the lesion is not considered suitable for endoscopic resection.	Strong/Moderate	**14** ESGE/EHMSG/ESP do not recommend routine performance of endoscopic ultrasonography (EUS), computed tomography (CT), magnetic resonance imaging (MRI), or positron emission tomography (PET)-CT prior to endoscopic resection unless there are signs suspicious of deep submucosal invasion or the lesion is not considered suitable for endoscopic resection. **Unchanged**	Strong/Moderate
		15 ESGE/EHMSG/ESP suggest the use of validated endoscopic classifications of atrophy (e. g. Kimura–Takemoto) or gastric intestinal metaplasia (e. g. endoscopic grading of gastric intestinal metaplasia [EGGIM]) to endoscopically stage precancerous conditions and stratify risk for gastric cancer. **New**	Conditional/Low
(MAPS II) **9** Biopsies of at least two topographic sites (from both the antrum and the corpus, at the lesser and greater curvature of each) should be taken and clearly labelled in two separate vials. Additional biopsies of visible neoplastic suspicious lesions should be taken.	Strong/Moderate	**16** ESGE/EHMSG/ESP recommend biopsy of 2 fragments from the antrum/incisura and 2 from the corpus, guided by virtual chromoendoscopy (VCE), clearly labeled in two separate vials. Additional biopsy from the incisura is optional. **Modified**	Strong/Moderate

▶ **Table 1** (Continuation)

MAPS II/ESDII		MAPS III	
Module **Recommendation**	**Strength of recommendation/ Quality of evidence**	***Module*** **Recommendation**	**Strength of recommendation/ Quality of evidence**
(MAPS II) 2. Histologically confirmed intestinal metaplasia is the most reliable marker of atrophy in gastric mucosa.	High	**17** ESGE/EHMSG/ESP recommend high quality histopathologic reporting for all endoscopic biopsies that should include: ▪ presence and grade of dysplasia; ▪ presence and subtype of adenocarcinoma (Lauren and WHO classifications); ▪ presence and severity of atrophy; ▪ presence and severity of intestinal metaplasia; ▪ subtyping as complete or incomplete intestinal metaplasia; ▪ presence of *H. pylori* infection. **Modified**	Strong/Moderate
(MAPS II) **1** Patients with chronic atrophic gastritis or intestinal metaplasia are at risk for gastric adenocarcinoma.	High		
(MAPS II) **3** Patients with advanced stages of gastritis, that is atrophy and/or intestinal metaplasia affecting both antral and corpus mucosa, should be identified as they are considered to be at higher risk for gastric adenocarcinoma.	Strong/Moderate		
(MAPS II) **4** High grade dysplasia and invasive carcinoma should be regarded as the outcomes to be prevented when patients with chronic atrophic gastritis or intestinal metaplasia are managed.	Strong/Moderate		
(MAPS II) **10** Systems for histopathological staging (e. g. operative link on gastritis assessment [OLGA] and operative link on gastric intestinal metaplasia [OLGIM] assessment) can be used to identify patients with advanced stages of gastritis. If these systems are used to stratify patients, additional biopsy of the incisura should be considered	Weak/Moderate	**18** ESGE/EHMSG/ESP suggest that systems for histopathological staging of atrophy (operative link on gastritis assessment [OLGA]) or, preferably, intestinal metaplasia (operative link on gastric intestinal metaplasia [OLGIM]) can be used and integrated with endoscopic information in the management of patients. **Modified**	Conditional/ Moderate
		19 ESGE/EHMSG/ESP recommend against further subtyping intestinal metaplasia as type I to III because of risks to health care professionals. **New**	Strong/Moderate
		20 ESGE/EHMSG/ESP suggest that biopsies revealing dysplasia are reviewed by an expert gastrointestinal (GI) pathologist. **New**	Conditional/Low
Management of individuals with nonvisible dysplasia and those with superficial lesions with dysplasia/cancer			
(MAPS II) **13** In patients with dysplasia in the absence of an endoscopically defined lesion immediate high quality endoscopic reassessment with CE (virtual or dye-based) is recommended. If no lesion is detected in this high quality endoscopy, biopsies for staging of gastritis (if not previously done) and endoscopic surveillance within 6 months (if high grade dysplasia) to 12 months (if low grade dysplasia) are recommended.	Strong/Low	**21** ESGE/EHMSG/ESP suggest that patients with dysplasia (or indefinite for dysplasia) but no lesions seen on gastroscopy, are referred for a high-quality endoscopy (namely, high definition white-light endoscopy with virtual chromoendoscopy [VCE]), staging of precancerous conditions, and *H. pylori* testing if not previously performed. If no endoscopic lesions are again not seen, a follow-up high quality endoscopy is then needed, in 6 months for high grade dysplasia, or 12 months for low grade dysplasia/indefinite for dysplasia. **Modified**	Conditional/ Moderate
		22 ESGE/EHMSG/ESP suggest that patients with a diagnosis of indefinite for dysplasia (confirmed by an expert GI pathologist) and an endoscopic lesion are referred for a high quality endoscopy and, according to endoscopic findings, consideration for guided biopsies or resection. **New**	Conditional/Low

▶ **Table 1** (Continuation)

MAPS II/ESDII		MAPS III	
Module **Recommendation**	**Strength of recommendation/ Quality of evidence**	***Module*** **Recommendation**	**Strength of recommendation/ Quality of evidence**
		23 ESGE/EHMSG/ESP suggest that age and comorbidities should be taken into account when selecting patients for endoscopic treatment of an early gastric lesion. **New**	Conditional/Low
(MAPS II) **5** Patients with an endoscopically visible lesion harboring low or high grade dysplasia or carcinoma should undergo staging and treatment.	Strong/High	**24** ESGE/EHMSG/ESP recommend that patients with an endoscopically visible lesion harboring dysplasia (low grade or high grade) or carcinoma should undergo staging and treatment. **Unchanged**	Strong/Moderate
(ESDII) **4** ESGE recommends ESD as the treatment of choice for most gastric superficial lesions, mainly to provide an en bloc potentially curative resection with accurate pathologic staging	Strong/Moderate	**25** ESGE/EHMSG/ESP recommend endoscopic submucosal dissection (ESD) as the treatment of choice for most superficial gastric lesions. **Unchanged**	Strong/Moderate
(ESDII) **8** ESGE recommends ESD for differentiated gastric lesions clinically staged as dysplastic or as intramucosal carcinoma (of any size if not ulcerated and ≤ 30 mm if ulcerated), with EMR being an alternative for Paris 0-IIa lesions of size ≤ 10 mm with low likelihood of malignancy.	Strong/Moderate	**26** ESGE/EHMSG/ESP recommend ESD for differentiated gastric lesions clinically staged as dysplastic (low and high grade) or as intramucosal carcinoma (of any size if not ulcerated and ≤ 30 mm if ulcerated), with endoscopic mucosal resection (EMR) being an alternative for Paris 0-IIa lesions with size ≤ 10 mm with low likelihood of malignancy. **Unchanged**	Strong/Moderate
(ESDII) **9** ESGE suggests that gastric adenocarcinoma that are ≤ 30 mm, submucosal (sm1), and well differentiated, or ≤ 20 mm, intramucosal, and poorly differentiated type, both without ulcerative findings, can be considered for ESD, although decision should be individualized.	Weak/Low	**27** ESGE/EHMSG/ESP suggest that a decision about ESD can be considered for malignant lesions clinically staged as having minimal submucosal invasion if differentiated and ≤ 30 mm, or for lesions clinically staged as intramucosal, when undifferentiated and ≤ 20 mm; and in both cases with no ulcerative findings. **Unchanged**	Conditional/Low

▶ **Table 1** continuation on next page.

▶ **Table 1** (Continuation)

MAPS II/ESDII		MAPS III	
Module **Recommendation**	**Strength of recommendation/ Quality of evidence**	***Module*** **Recommendation**	**Strength of recommendation/ Quality of evidence**
(ESDII) **20** ESGE recommends that as en bloc R0 resection of a superficial gastric lesion with histology no more advanced than intramucosal cancer, well to moderately differentiated, with no lymphovascular invasion, should be considered a very low-risk (curative) resection, independently of size if without ulceration or of lesions ≤ 30 mm if ulcerated, and no further staging procedure or treatment is generally recommended.	Strong/Moderate	**28** ESGE/EHMSG/ESP recommends patient management based on the following histological risk after endoscopic resection: *Curative/very low-risk resection (LNM risk < 0.5 %–1 %)* En bloc R0 resection; dysplastic/pT1a, differentiated lesion, no lymphovascular invasion, independent of size if no ulceration and ≤ 30 mm if ulcerated: No further staging procedure or treatment is recommended. *Curative/low-risk resection (LNM risk < 3 %)* En bloc R0 resection; lesion with no lymphovascular invasion, and: a) pT1b, submucosal invasion ≤ 500 µm, differentiated, size ≤ 30 mm; or b) pT1a, undifferentiated, size ≤ 20 mm and no ulceration: Staging should be completed, and further treatment is generally not necessary after a multidisciplinary discussion. *Local-risk resection (very low risk of LNM but increased risk of persistence/recurrence*) ▪ Piecemeal resection or tumor-positive horizontal margin of a lesion otherwise meeting curative/very low-risk criteria; or ▪ Provided there is no submucosally invasive tumor at the resection margin in the case of piecemeal resection or tumor-positive horizontal margin, for otherwise low-risk pT1b lesion (submucosal invasion ≤ 500 µm, well-differentiated, size ≤ 30 mm, and VM0). Endoscopic surveillance/re-treatment is recommended rather than other additional treatment. *High-risk resection* (noncurative): Any lesion with any of the following: a) a positive vertical margin (if carcinoma) or lymphovascular invasion or deep submucosal invasion (> 500 µm from the muscularis mucosae); b) poorly differentiated lesions if ulceration or size > 20 mm; c) in pT1b differentiated lesions with submucosal invasion ≤ 500 µm with size > 30 mm d) in intramucosal ulcerative lesion with size > 30 mm. Complete staging and strong consideration for additional treatments (surgery) in multidisciplinary discussion. **Unchanged**	Strong/Moderate
(ESDII) **21** ESGE suggests that an en bloc R0 resection of a ≤ 30 mm gastric adenocarcinoma, with superficial submucosal invasion (sm1), that is well to moderately differentiated and with no lymphovascular invasion and no ulcer, should be considered a low-risk (curative) resection and no further treatment is generally recommended. [...]	Weak/Moderate		
(ESDII) **22** ESGE suggests that an en bloc R0 resection of a ≤ 20 mm gastric intramucosal poorly differentiated carcinoma, with no lymphovascular invasion or ulcer, should be considered a low-risk (curative) resection and no further treatment is generally recommended.	Weak/Moderate		
(ESDII) **23** ESGE recommends that a resection of a > 30 mm gastric adenocarcinoma with superficial submucosal invasion (sm1) or with ulceration should be considered a high-risk (noncurative) resection and complete staging should be done and strong consideration for additional treatments (surgery) should be given on an individual basis in a multidisciplinary discussion.	Strong/Moderate		

▶ **Table 1** (Continuation)

MAPS II/ESDII		MAPS III	
Module **Recommendation**	**Strength of recommendation/ Quality of evidence**	***Module*** **Recommendation**	**Strength of recommendation/ Quality of evidence**
(ESDII) **30** ESGE recommends scheduled endoscopic surveillance with high definition white-light and chromoendoscopy (virtual or dye-based) with biopsies of only the suspicious areas after a curative ESD.	Strong/Moderate	**29** ESGE/EHMSG/ESP suggest a surveillance high quality endoscopy at 3–6 months and then annually after a very low- or low-risk ESD resection or after a local-risk ESD resection without recurrence. Routine use of EUS, MRI, CT, or PET in the follow-up after very low-risk resections is not suggested but could be considered for higher-risk lesions. **Modified**	Conditional/Low
(ESDII) **32** ESGE suggested endoscopy at 3–6 months and then annually after a curative ESD resection or after a local-risk ESD resection without recurrence.	Weak/Low		
(ESDII) **34** ESGE does not suggest routine use of EUS, MRI, CT, or PET in the follow-up after a very low- or low-risk (curative) endoscopic resection [...]	Weak/Low		
(ESDII) **23** ESGE recommends that a resection of a > 30 mm gastric adenocarcinoma with superficial submucosal invasion (sm1) or with ulceration should be considered a high-risk (noncurative) resection and complete staging should be done and strong consideration for additional treatments (surgery) should be given on an individual basis in a multidisciplinary discussion.	Strong/Moderate	**30** ESGE/EHMSG/ESP recommend that after a high-risk resection the need for additional treatment is decided in a multidisciplinary team (MDT) discussion taking into account LNM risk, age, comorbidities, and life expectancy. **Modified**	Strong/Moderate
Surveillance of individuals with precancerous conditions			
(MAPS II) **17** Patients with advanced stages of atrophic gastritis (severe atrophic changes or intestinal metaplasia in both antrum and corpus, OLGA/OLGIM III/IV) should be followed up with a high quality endoscopy every 3 years.	Strong/Low	**31** ESGE/EHMSG/ESP recommend that patients with extensive endoscopic changes (C3 + or EGGIM 5 +) or advanced histological stages of atrophic gastritis (severe CAG or GIM and/or significant changes in both antrum and corpus, OLGA/OLGIM III/IV) should be followed up with high quality endoscopy every 3 years. **Unchanged**	Strong/Moderate
(MAPS II) **25** In intermediate- to high-risk regions, identifications and surveillance of patients with precancerous gastric conditions is cost-effective.	Moderate	**32** ESGE/EHMSG/ESP recommend opportunistic risk stratification of precancerous conditions in all endoscopies, because endoscopic surveillance every 3 years in patients with high-risk premalignant conditions is cost-effective irrespective of country. **Modified**	Strong/Moderate
(MAPS II) **18** Patients with advanced stages of atrophic gastritis and with a family history of gastric cancer may benefit from a more intensive follow-up (e. g. every 1–2 years after diagnosis).	Weak/Low	**33** ESGE/EHMSG/ESP suggest that endoscopic features of extensive changes (C3 + or EGGIM 5 +) or histologically advanced stages of atrophic gastritis (severe atrophic changes or intestinal metaplasia in both antrum and corpus, OLGA/OLGIM III/IV) and with a first-degree relative with gastric cancer may benefit from a more intensive follow-up (e. g. every 1 to 2 years after diagnosis). **Modified**	Conditional/Low

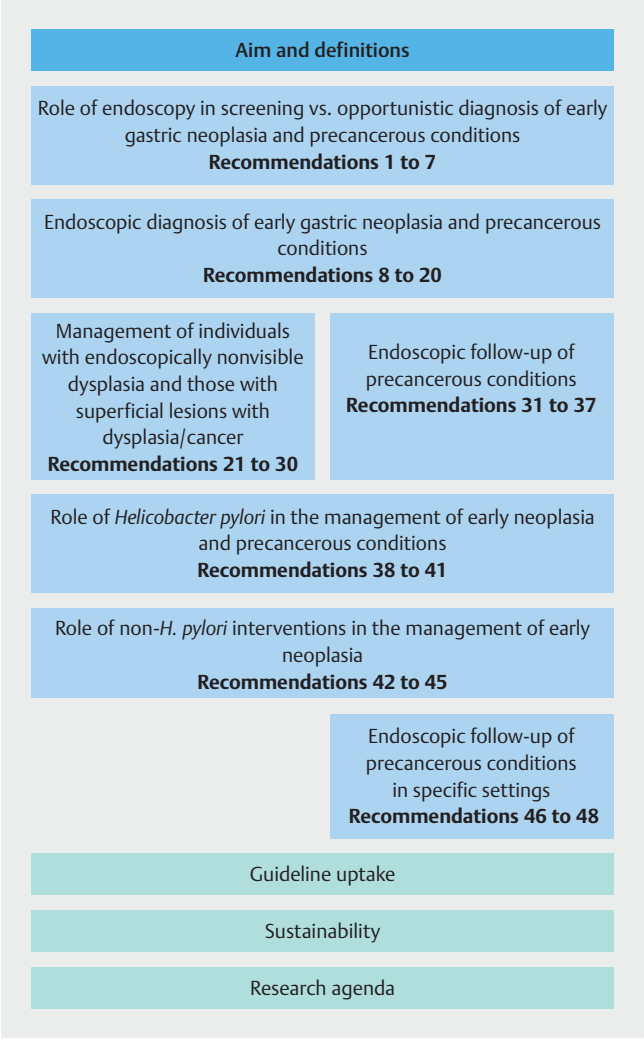
▶ **Table 1** (Continuation)

MAPS II/ESDII		MAPS III	
Module **Recommendation**	**Strength of recommendation/ Quality of evidence**	***Module*** **Recommendation**	**Strength of recommendation/ Quality of evidence**
(MAPS II) **14** For patients with mild to moderate atrophy restricted to the antrum there is no evidence to recommend surveillance.	Strong/Moderate	**34** ESGE/EHMSG/ESP recommend no surveillance endoscopy to patients with mild to moderate chronic atrophic gastritis (CAG) or gastric intestinal metaplasia (GIM) restricted to the antrum, in the absence of endoscopic signs of extensive lesions or other risk factors (family history, incomplete intestinal metaplasia or persistent *H. pylori* infection). This group constitutes most individuals found in clinical practice. **Modified**	Strong/Moderate
(MAPS II) **15** Patients with IM at a single location have a higher risk of gastric cancer. However, this increased risk does not justify surveillance in most cases, particularly if a high quality endoscopy with biopsies has excluded advanced stages of atrophic gastritis.	Strong/moderate		
(MAPS II) **16** In patients with IM at a single location but with a family history of gastric cancer, or with incomplete IM, or with persistent *H. pylori* gastritis, endoscopic surveillance with chromoendoscopy and guided biopsies in 3 years' time may be considered.	Weak/Low	**35** ESGE/EHMSG/ESP suggest that in patients with gastric intestinal metaplasia at a single location but with a family history of gastric cancer, or with incomplete intestinal metaplasia, or with persistent *H. pylori* gastritis, high quality endoscopic surveillance every 3 years may be considered. **Unchanged**	Conditional/Low
(MAPS II) **12** Even though diverse studies assessed age, gender, and *H. pylori* virulence factors, as well as host genetic variations, no clinical recommendation regarding diagnosis and surveillance can be made for targeted management based on these factors.	Weak/Low	**36** ESGE/EHMSG/ESP recommend against any tailored surveillance strategy based on genetic status, birthplace, or ethnicity in patients with gastric precancerous conditions. **Modified**	Conditional/Low
		37 ESGE/EHMSG/ESP suggest that random biopsies are not required during surveillance of cases with advanced OLGA/OLGIM stages at baseline endoscopy once no superficial lesions are observed. **New**	Conditional/Low
Role of H. pylori in patients with precancerous conditions and cancer			
(MAPS II) **20** *H. pylori* eradication heals nonatrophic chronic gastritis, may lead to regression of atrophic gastritis, and reduces the risk of gastric cancer in patients with nonatrophic and atrophic gastritis, and, therefore, it is recommended in patients with these conditions.	Strong/High	**38** ESGE/EHMSG/ESP recommend *H. pylori* eradication in individuals with nonatrophic chronic gastritis and atrophic gastritis to reduce the risk of gastric cancer. **Modified**	Strong/High
(MAPS II) **21** In patients with established IM, *H. pylori* eradication does not appear to significantly reduce the risk of gastric cancer, at least in the short term, but reduces inflammation and atrophy and, therefore, it should be considered.	Weak/Low	**39** ESGE /EHMSG/ESP recommend that *H. pylori* eradication should be considered in patients with established gastric intestinal metaplasia. **Unchanged**	Conditional/ Moderate
(MAPS II) **22** *H. pylori* eradication is recommended for patients with gastric neoplasia after endoscopic therapy.	Strong/High	**40** ESGE/EHMSG/ESP recommend *H. pylori* eradication for patients with gastric neoplasia after endoscopic or surgical therapy. **Modified**	Strong/Moderate
		41 ESGE/EHMSG/ESP recommend against testing for microbiota other than *H. pylori* for preventing or treating gastric precancerous conditions. **New**	Strong/Moderate

▶ **Table 1** (Continuation)

MAPS II/ESDII		MAPS III	
Module **Recommendation**	**Strength of recommendation/ Quality of evidence**	***Module*** **Recommendation**	**Strength of recommendation/ Quality of evidence**
Role of non H. pylori interventions			
		42 ESGE/EHMSG/ESP recommend smoking cessation in individuals with precancerous conditions or after endoscopic treatment of superficial lesions. **New**	Strong/Low
		43 ESGE/EHMSG/ESP suggest that patients with an appropriate indication for proton pump inhibitors (PPIs) or histamine (H2) receptor antagonists (H2RAs) should not discontinue the medication. **New**	Conditional/Low
(MAPS II) **24** Low dose daily aspirin may be considered for prevention of various cancers, including gastric cancer, in selected patients.	Weak/Moderate	**44** ESGE/EHMSG/ESP suggest that low-dose daily aspirin can be considered for prevention of gastric cancer in selected individuals with high risk for cardiovascular events. **Unchanged**	Conditional/Low
(MAPS II) **23** Even though cyclo-oxygenase (COX)-1 or COX-2 inhibitors may slow progression of gastric precancerous conditions, they cannot be recommended specifically for this purpose.	Weak/Low	**45** ESGE/EHMSG/ESP recommend against the use of other specific drugs or supplements (including probiotics) for chemoprevention in any clinical setting outside of clinical studies. **Modified**	Conditional/Low
Special situations			
		46 ESGE/EHMSG/ESP suggest that in individuals with hereditary syndromes with increased risk of gastric cancer, endoscopic surveillance should follow recommendations for the specific syndrome or according to the gastric mucosal changes, whichever interval is shorter. **New**	Conditional/Very low
(MAPS II) **19** Patients with autoimmune gastritis may benefit from endoscopic follow-up every 3–5 years	Weak/Low	**47** ESGE/EHMSG/ESP suggest that patients with autoimmune gastritis should have high quality endoscopic follow-up every 3 years to detect gastric cancer and neuroendocrine tumors. **New**	Conditional/Low
		48 ESGE/EHMSG/ESP suggest that patients with common variable immunodeficiency (CVID) should have a high quality endoscopy at the time of diagnosis and then should be followed up according to staging of precancerous conditions and/or presence of autoimmune gastritis. **New**	Conditional/Very Low

EHMSG, European *Helicobacter* and Microbiota Study Group; ESGE, European Society of Gastrointestinal Endoscopy; ESP, European Society of Pathology; GC, gastric cancer; WHO, World Health Organization



▶ **Fig. 1** Schematic outline of guideline on endoscopic management of epithelial precancerous conditions and early neoplasia of the stomach: the MAPS III Guideline.

This Guideline was issued in 2025 and will be considered for review and update in 2030, or sooner if new and relevant evidence becomes available. Any updates to the Guideline in the interim will be noted on the ESGE website: https://www.esge.com/esge-guidelines.html.

Outline, aim, and definitions

Outline of the Guideline

Following the presentation of the aim and scope of the guideline, definitions are provided before the main sections are presented. The sequence of topics is as follows: (a) indications for screening in general populations and on an individual basis; (b) the endoscopic diagnosis of both early gastric neoplasia and precancerous conditions; (c) management of early gastric neoplasia if diagnosed; (d) endoscopic follow-up and surveillance of precancerous conditions; (e) the role of *H. pylori* eradication; (f) the role of other nonendoscopic interventions for individuals with early gastric neoplasia and precancerous conditions; and (g) management of precancerous conditions in the context of specific situations (▶ **Fig. 1**).

Aim

A cascade of mucosal changes towards the intestinal subtype of gastric adenocarcinoma occurs multifocally in the stomach, comprising progression from normal mucosa to chronic inflammation, atrophy and GIM, dysplasia, and adenocarcinoma. This progressive nature permits potential interventions for early diagnosis and management of cancer, thus improving GC survival rates and, in addition, action to prevent gastric high grade dysplasia and invasive adenocarcinoma by intervention at the precancerous stages. Therefore, the present Guideline is organized (a) to provide guidance on the potential use of endoscopy to screen for precancerous conditions or early neoplasia, in the general population and also by targeted or opportunistic diagnosis, and (b) to provide recommendations on the diagnosis of patients identified with precancerous conditions or early neoplasia of the stomach, and their management, including *H. pylori* and non-*H. pylori* interventions.

Population-based versus targeted versus opportunistic screening for GC and precancerous conditions

Population-based screening for GC or precancerous conditions and lesions should be interpreted as their identification in the asymptomatic general population, whereas *targeted screening* of GC or precancerous conditions and lesions is their identification in specific subsets of the general population defined by a priori high-risk variables (e. g., family history, hereditary syndromes). *Opportunistic screening* refers to the individual GC risk stratification of each patient undergoing an esophagogastroduodenoscopy (EGD), by the careful assessment of the presence and stage of precancerous conditions. The management of superficial GC or precancerous conditions comprises the guidance on endoscopic and nonendoscopic interventions for the care of patients with diagnosed superficial GC or precancerous lesions or conditions. It should be assumed that endoscopic GC screening always includes the endoscopic assessment of precancerous conditions. *Surveillance* refers to the scheduled care using endoscopic assessment, after treatment of a superficial lesion or if precancerous conditions merit that specific care.

Endoscopic versus histological definitions

Fundamental to the application of this Guideline is the assumption that both the endoscopy performed and pathological examination provided are of high quality. The term *endoscopic superficial lesions* refers to lesions in the digestive tract in which the endoscopic appearance predicts that neoplastic changes are limited to the mucosa and submucosa [16]. Endoscopic descriptors can be used to predict lymph node metastasis and to make decisions about cancer management.

These endoscopic lesions when biopsied often reveal the so-called gastric precancerous conditions (chronic atrophic gastritis [CAG] and/or gastric intestinal metaplasia [IM]), precancerous lesions (*intraepithelial neoplasia/dysplasia*), or even cancer. In this paper the designation of early neoplasia of the stomach

▶ **Table 2** Correspondences between common classification systems for gastric cancer histology. This table summarizes the common gastric cancer histology classifications. In the endoscopic pre-therapy and post-therapy approach for early gastric cancer, we use the differentiated or undifferentiated types (Nakamura et al. [17]) for risk evaluation according to pathology, in alignment with other guidelines. (Modified from reference [18].)

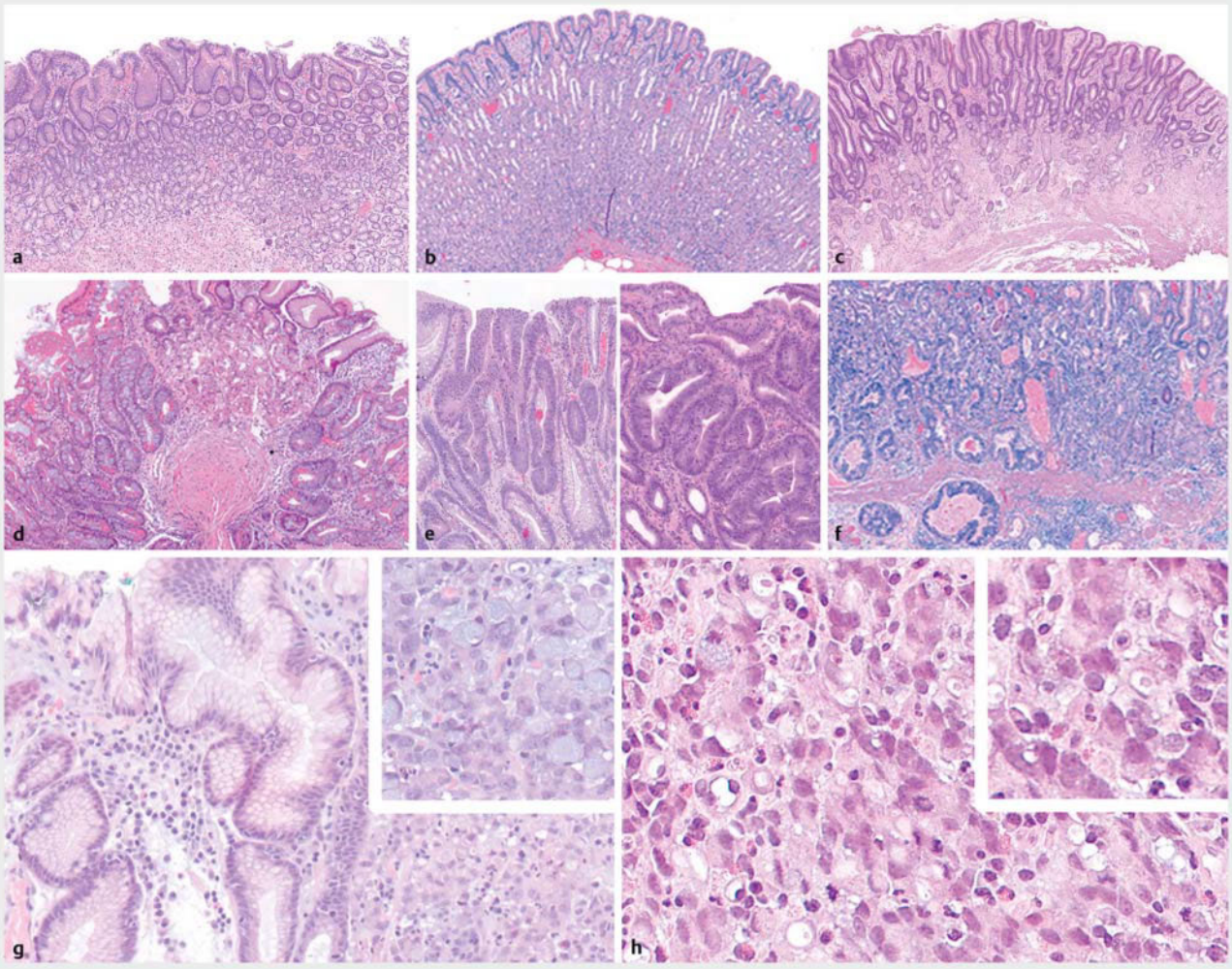
Nakamura et al. (1968) [17]	World Health Organization (WHO) (2019) [19]	Japanese Gastric Cancer Association (2017) [20]	Laurén (1965) [21]
Differentiated	Papillary	Papillary: pap	Intestinal
	Tubular, well differentiated	Tubular 1, well diferentiated: tub1	
	Tubular, moderately differentiated	Tubular 2, moderately differentiated: tub2	
Undifferentiated	Tubular (solid), poorly differentiated	Poorly 1 (solid type): por1	Indeterminate
Undifferentiated	Poorly cohesive, signet ring cell phenotype	Signet ring cell: sig	Diffuse
	Poorly cohesive, other cell types	Poorly 2 (non-solid type): por2	
Differentiated/ undifferentiated	Mucinous	Mucinous	Intestinal/diffuse/ indeterminate
	Mixed	Description according to the proportion (e. g., por2 > sig > tub2)	Mixed
Not defined	Other subtypes: Undifferentiated carcinoma[1]	Special type: Undifferentiated carcinoma[1]	Not defined
	Adenosquamous carcinoma	Adenosquamous carcinoma	
	Squamous cell carcinoma	Squamous cell carcinoma	
	Carcinoma with lymphoid stroma	Carcinoma with lymphoid stroma	
	Hepatoid adenocarcinoma	Hepatoid adenocarcinoma	
	Adenocarcinoma with enteroblastic differentiation	Adenocarcinoma with enteroblastic differentiation	
	Adenocarcinoma of fundic gland type	Adenocarcinoma of fundic gland type	
	Micropapillary adenocarcinoma		

[1] Undifferentiated carcinoma of the stomach is a very rare entity of a highly aggressive nature, constituted by malignant cells without evidence of differentiation, and frequently driven by various components of the SWI/SNF chromatin-remodelling complex.

applies to early gastric cancer and dysplasia/intraepithelial neoplasia. The World Health Organization (WHO) classifies gastric dysplasia or intraepithelial neoplasia as histologically unequivocal neoplastic epithelium characterized by variable cellular and architectural atypia without evidence of stromal invasion. It encompasses *low grade intraepithelial neoplasia/dysplasia* and *high grade intraepithelial neoplasia/dysplasia*, that are precursors of *intramucosal invasive neoplasia/intramucosal carcinoma*. *Low grade dysplasia* shows minimal or mild architectural disarray and mild to moderate cytological atypia. *High grade intraepithelial neoplasia/dysplasia* comprises neoplastic cells that are often cuboidal, rather than columnar, with a high nucleus-to-cytoplasm ratio and prominent amphophilic nucleoli. The nuclei frequently extend into the luminal half of the cell, and nuclear polarity is usually lost. Mitotic figures are more numerous than in low grade dysplasia and may be atypical. There is more pronounced architectural disarray. *Intramucosal invasive neoplasia/intramucosal carcinoma* shows unequivocal invasion of the lamina propria or muscularis mucosae (mucosa). Features that help to distinguish it from intraepithelial neoplasia/dysplasia include stromal desmoplastic changes (that can be minimal or absent), marked glandular crowding, excessive branching, budding, and fused or cribriform glands. The diagnosis of intramucosal carcinoma means that there is an increased risk of lymphatic invasion and lymph node metastasis, although with certain features this risk is absent or minimal (described later).

The above definitions refer to conventional (adenomatous/intestinal) type dysplasia, which is by far the most likely type to occur in the setting of chronic atrophic gastritis (CAG) with GIM. Other types of dysplasia can also occur in the stomach and, in comparison with conventional dysplasia, have different morphological features and, often, have different criteria for classification as low grade or high grade.

Sometimes, superficial lesions harbor a carcinoma that invades beyond the mucosa into the submucosa. Diverse



▶ **Fig. 2** **a** Normal antral mucosa. **b** Normal oxyntic mucosa. **c** Antral mucosa: mild glandular atrophy. **d** Oxyntic mucosa: severe glandular atrophy and extensive intestinal metaplasia. **e** Left: Low grade dysplasia. Right: High grade dysplasia. **f** Gastric adenocarcinoma: tubular type (WHO)/intestinal type (Laurén). **g** Gastric adenocarcinoma: poorly cohesive carcinoma, signet ring cell (WHO)/diffuse carcinoma (Laurén). **h** Gastric adenocarcinoma: poorly cohesive carcinoma, not otherwise specified (WHO)/diffuse carcinoma (Laurén).

features may be related to the risk of lymph node metastasis and, therefore, the need for further surgery, and the risk of death.

Moreover, for managing early GC, in the pre- and post-therapy approaches, we will refer to the Nakamura classification, as most studies evaluating the risk of lymph node metastasis and the guidelines concerning the endoscopic management of early GC use this classification. It divides GC into two types: differentiated (corresponding to well or moderately differentiated tubular or papillary adenocarcinoma) and undifferentiated (corresponding to poorly differentiated tubular adenocarcinoma or poorly cohesive carcinoma including the signet ring cell phenotype) (▶ **Table 2** [17–21]).

Precancerous conditions should be considered as CAG and/or GIM because these constitute the main background in which dysplasia and intestinal subtype adenocarcinoma may occur, and they independently confer an increased risk of development of GC. CAG should be diagnosed and graded based on the presence of chronic inflammatory cells, including lymphocytes and plasma cells that expand the lamina propria, and the disappearance of the normal glands. In the gastric body and fundus, this is associated with a loss of specialized cells and thus a reduction of gastric secretory functions. The severity of gland loss (atrophy) should be graded. *Intestinal metaplasia* may be classified as "complete" or "incomplete" as this has management relevance. Complete intestinal metaplasia displays goblet and absorptive cells, decreased expression of gastric mucins (MUC1, MUC5AC, and MUC6), and expression of MUC2, an intestinal mucin. Incomplete intestinal metaplasia displays goblet and columnar nonabsorptive cells, in which gastric mucins (MUC1, MUC5AC, and MUC6) are co-expressed with MUC2. Further classification into types I, II, and III was based on the detection of sialomucin and sulphomucin by high iron diamine–alcian blue staining but was discontinued because of

the toxicity of the reagents. Specific guidelines for diagnosis of intestinal metaplasia have been published [2], supporting a comprehensive approach that includes both endoscopy and endoscopic biopsies, and risk stratification that takes account of the endoscopic and histological extension of the changes to different gastric compartments (antrum and corpus).

▶ **Fig. 2** presents in brief the histological appearances representing the spectrum of changes from normal gastric mucosa to adenocarcinoma.

Screening for early gastric neoplasia and gastric precancerous conditions

RECOMMENDATION

1 ESGE/EHMSG/ESP suggest population-based endoscopic screening for GC (and precancerous conditions) every 2 to 3 years in high-risk regions (age-standardized rate [ASR] > 20 per 100 000 person-years) or every 5 years in intermediate-risk regions (ASR 10–20 per 100 000 person-years), if cost–effectiveness has been proven and resources are available. [New]

Conditional recommendation/Low quality; 96 % agreement.

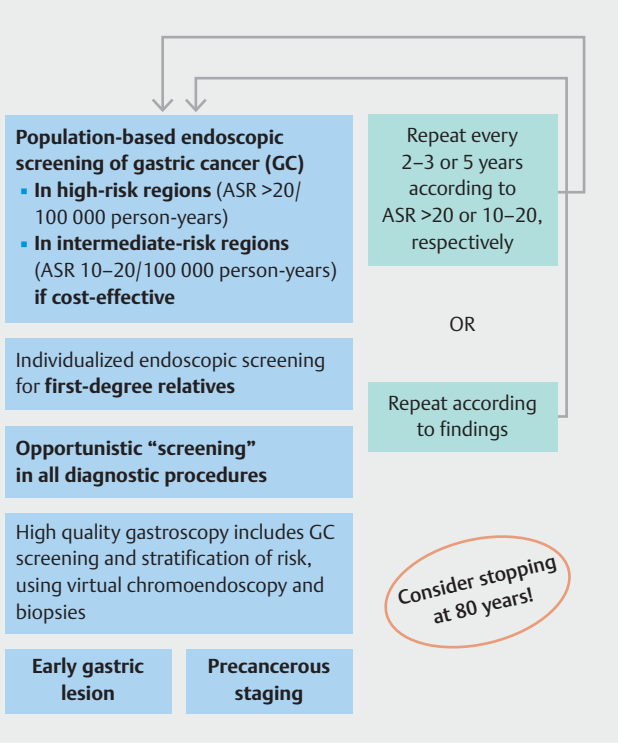
RECOMMENDATION

2 ESGE/EHMSG/ESP suggest against population-based endoscopic screening for gastric cancer (and precancerous conditions) in low-risk regions (ASR < 10 per 100 000 person-years). [New]

Conditional recommendation/Low quality; 96 % agreement.

Population-based screening for GC is only performed in high-risk areas. In a meta-analysis, it was shown that a 40 % risk reduction in GC mortality can be achieved by endoscopic screening in the high-risk Asian population [22]. Data from the South Korean National Screening Program showed a > 20 % reduction in GC mortality in the screened population. This was mostly seen in those screened by endoscopy compared to upper gastrointestinal series with barium meal, which did not show any benefit [23]. Currently, in Asia, the intervals for endoscopic GC screening programs are every 2–3 years at a starting age of 40 or 50 years [24]. The cost–effectiveness of these programs depends mainly on the costs of an upper endoscopy [24–27] (▶ **Fig. 3**).

Although the benefit of GC screening in intermediate-risk regions is still unknown, there is some evidence that GC screening is cost-effective if combined with colonoscopy screening in individuals between 50 to 75 years [24, 28]. Introduction of AI-assisted upper endoscopy may even improve cost–effectiveness in low–intermediate-risk areas by lowering the miss rate for detection of early GC and precancerous gastric lesions. This



▶ **Fig. 3** Overview of indications for screening for gastric cancer and precancerous conditions. ASR, age-standardized rate; VCE, virtual chromoendoscopy.

was shown in an effectiveness analysis using a Markov model, indicating that screening colonoscopy combined with AI-assisted upper endoscopy may improve the cost–effectiveness of GC screening in low–intermediate-risk countries in Europe [29]. As well as cost–effectiveness, other parameters such as participation rate, accuracy of the screening test, and endoscopic capacity should be included to assure the effectiveness of a GC screening program in an intermediate-risk region. In a recent ESGE Position Statement on the role of gastrointestinal endoscopy in the screening of digestive cancers it was stated that endoscopy may have a GC screening role in intermediate-risk regions if cost–effectiveness is proven and local settings and availability of endoscopic resources are taken into account [27]. Although this Position Statement suggests an interval of every 5 years after a negative exam, no data are yet available on the optimal interval for GC screening in intermediate-risk regions.

Population-based endoscopic screening for GC is not recommended in low-risk regions, because of the low prevalence of *H. pylori* and GC. However, no data are available on the efficacy of population-based screening in low-risk regions [24, 30, 31]. There is some evidence that endoscopic GC screening might be cost-effective for high-risk populations within low-risk regions. In two Markov model studies endoscopic noncardia GC screening was combined with colonoscopy screening for high-risk groups and appeared to be cost-effective in the United States [32, 33].

RECOMMENDATION

3 ESGE/EHMSG/ESP recommend that a diagnostic upper gastrointestinal endoscopy (endoscopic opportunistic diagnosis) should include screening for gastric cancer as well as the diagnosis and stratification of risk of precancerous conditions, irrespective of country of origin. [New]

Strong recommendation/Moderate quality; 92 % agreement.

Although the overall incidence of GC in low-risk countries is low, the diagnosis of early gastric neoplasia represents a significant benefit at an individual level. Even though some patients are at high risk of GC development and endoscopists may also consider pre-endoscopically determining the GC risk for that specific individual, the opportunity to impact significantly on an individual's life by diagnosing GC or precancerous conditions that warrant further surveillance should be considered in all endoscopies. In British Society of Gastroenterology (BSG) guidelines, the term "endoscopic GC screening" (including the stratification of precancerous conditions) is used, and it is suggested for patients aged ≥ 50 years and with other high-risk features such as pernicious anemia, male sex, smoking, and/or a positive family history of GC (i. e., targeted screening) [30]. In the Maastricht VI/Florence consensus, endoscopic gastric screening at the age of 45 years is suggested for asymptomatic individuals with a family history of GC [31]. Besides these risk factors, ethnicity in combination with *H. pylori* infection may add information to identify individuals with a high pretest probability of GC, contributing to a cost-effective approach to endoscopic GC screening in intermediate- and low-risk countries [32]. Although most of the data on the identification of the high-risk population in low-risk regions comes from the US, the risk factors found may also apply for other low-risk regions [33]. Therefore, individuals at an increased risk for GC development include those ≥ 50 years of age with at least one of the following additional risk factors: pernicious anemia, ethnic propensity, *H. pylori* infection, and/or a positive family history of GC.

Worldwide, estimates of the prevalence of gastric precancerous conditions are highly variable [34–37]. A systematic review and meta-analysis incorporating data exclusively from European countries found an overall pooled prevalence of gastric precancerous conditions of 20.1 % (95 % confidence intervals [95 %CI] 15.6 %–24.6 %), with the prevalence being higher in selected versus unselected populations (22.3 %, 95 %CI 17.3 %–27.3 % vs. 17.0 %, 95 %CI 11.1 %–22.9 %), and in endoscopic versus serology-based studies (23.4 %, 95 %CI 19.3 %–27.4 % vs. 9.2 %, 95 %CI 4.6 %–13.9 %). Prevalence of CAG and GIM was 12.2 %–22.0 % and 17.6 %–36.8 %, respectively. Of note, the estimated prevalence of extensive gastric precancerous conditions was previously reported to be 16.2 % for CAG and 13.2 % for GIM, respectively [37]. This shows that precancerous conditions are frequent in Europe, and thus, opportunistic screening of precancerous conditions should be considered.

In almost all international guidelines, endoscopic surveillance every 3 years is recommended in those with extensive GIM/CAG. This strategy appeared to be cost-effective [32, 38, 39]. In a recent Markov analysis from the US [40] different surveillance intervals in patients with GIM were compared. Intervals of 5 years, 3 years, 2 years, and 1 year were compared with surveillance at 10 years. All modeled surveillance intervals yielded a greater life expectancy (87–190 undiscounted life-years gained per 1000) than surveillance at 10 years. The 5-year surveillance interval was associated with the greatest number of life-years gained and was the most cost-effective strategy ($40 706/quality-adjusted life-year [QALY]) in all patients with GIM. In individuals with a family history of GC or extensive, incomplete-type GIM, a 3-year surveillance was cost-effective (incremental cost–effectiveness ratio $28 156/QALY and $87 020/QALY, respectively). The consequence of this is that stratification of individuals with precancerous conditions according to GC risk must be performed in all gastroscopies to identify individuals who benefit from surveillance.

RECOMMENDATION

4 ESGE/EHMSG/ESP suggest *H. pylori* noninvasive screening and eradication between the ages of 20 and 30 for first-degree relatives of patients with gastric cancer. [New]

Conditional recommendation/Moderate quality; 100 % agreement.

RECOMMENDATION

5 ESGE/EHMSG/ESP suggest endoscopic screening for GC in first-degree relatives of patients with gastric cancer, at the age of 45 years or at 10 years before the age of diagnosis of the affected relative. [New]

Conditional recommendation/Moderate quality; 100 % agreement.

Patients with first-degree relatives with GC have a higher risk of developing GC. Indeed, a recent meta-analysis of 21 studies underscores a substantial correlation between GC risk and first-degree relatives with GC, with odds ratio (OR) of 2.92 (95 %CI 2.402–3.552, $P < 0.001$; $I^2 = 81.85\%$, $P < 0.001$) [41]. This risk is further substantiated by earlier meta-analyses indicating a doubled risk of GC among individuals with a family history of GC without specifying the degree of relationship (relative risk [RR] 2.00, 95 %CI 1.83–2.20, $P < 0.001$; OR 2.35, 95 %CI 1.96–2.81; and OR 1.84, 95 %CI 1.64–2.04, $P < 0.001$) [42–44]. Despite significant heterogeneity among studies, of approximately 80 %–90 %, these consistent findings advocate for a proactive endoscopic screening approach. It could prove pivotal to conduct noninvasive screening and eradication of *H. pylori* at the age of 20–30 and endoscopy at the age of 45 years to identify precancerous gastric conditions or lesions or early-stage GC in first-

degree relatives of GC patients. This proactive approach remains significant even in regions with low GC incidence, as it facilitates timely detection and intervention to reduce the mortality associated with GC. After screening, the management and follow-up will be according to mucosal status and *H. pylori* infection persistence (see later sections of this Guideline).

RECOMMENDATION

6 ESGE/EHMSG/ESP suggest that gastric cancer screening or surveillance of precancerous conditions in asymptomatic individuals over 80 should be discontinued or not started. [New]

Conditional recommendation/Low quality; 96% agreement.

The benefit of screening the general population may be limited by age and comorbidities, both of which reduce the life expectancy of the patient and increase the risks and complications of invasive procedures. Screening is unlikely to significantly modify life expectancy when this is less than 10 years due to an individual's underlying disease. For all these reasons, it is suggested that GC screening be discontinued, i. e., surveillance stopped or not started, at 80 years of age or when the individual's life expectancy is clearly less than 10 years [45, 46]. The age cutoff of 80 is arbitrary and is based on average life expectancy and the lifetime likelihood of further progression of precancerous conditions, according to current data on average life expectancy.

RECOMMENDATION

7 ESGE/EHMSG/ESP recommend endoscopic screening for precancerous conditions in individuals with low pepsinogen (PG) I serum levels or/and a low PG I/II ratio, particularly if *H. pylori* serology is negative. [Modified]

Strong recommendation/Moderate quality; 92% agreement.

There are no new data suggesting modification of the approach proposed in MAPS II. Most of the studies show similar results regarding the performance of pepsinogens (PGs) in atrophic gastritis prediction, and a meta-analysis published in 2019 found a high specificity (0.89, 95%CI 0.70–0.97) but a modest sensitivity (0.59, 95%CI 0.38–0.78) [47] for CAG. For GC, pooled specificity was 0.73 (95%CI 0.64–0.81) and pooled sensitivity was 0.59 (95%CI 0.50–0.670 [47–64]. Hence, given the high specificity for CAG and moderate for GC, endoscopy is recommended for patients with low PG I serum levels (≤ 70 ng/mL) or low PG I/II ratio (≤ 3).

Regarding combined testing (combination of PG I, PG II, gastrin-17, *H. pylori* serology), a recent meta-analysis showed a pooled sensitivity of 0.70 (95%CI 0.64–0.76) and pooled specificity of 0.93 (95%CI 0.90–0.95) for the diagnosis of corpus atrophic gastritis. However, there was significant heterogeneity, and thus endoscopy is also recommended in the case of positive noninvasive testing (positive predictive value [PPV] 72% at population level) [64].

Diagnosis of early gastric neoplasia and precancerous conditions

RECOMMENDATION

8 ESGE/EHMSG/ESP recommend a high quality endoscopy, including virtual chromoendoscopy (VCE), for screening, diagnosis, and surveillance of gastric precancerous conditions and lesions. [Modified]

Strong recommendation/Moderate quality; 100% agreement.

RECOMMENDATION

9 ESGE/EHMSG/ESP recommend that VCE should be used to guide biopsies in the case of suspected neoplastic lesions. [Modified]

Conditional recommendation/Moderate quality; 100% agreement.

RECOMMENDATION

10 ESGE/EHMSG/ESP recommend guided biopsies with VCE for diagnosis and staging of gastric precancerous conditions, and random biopsies in the absence of endoscopically suspected precancerous conditions. [Modified]

Strong recommendation/Moderate quality; 100% agreement.

RECOMMENDATION

11 ESGE/EHMSG/ESP recommend training in the endoscopic diagnosis of gastric precancerous conditions and lesions. [New]

Strong recommendation/Moderate quality; 96% agreement.

Because of a significant gastric neoplasia miss rate (6%–10%), various quality indicators for EGD have been identified [65–67]. Despite different thresholds, several studies found that longer EGD duration was associated with higher detection rates [68–78]. Three recent meta-analyses also found that preprocedural use of simethicone (with or without N-acetyl cysteine) is associated with better visibility [79–81] and with a higher detection rate for upper gastrointestinal pathology, namely precancerous conditions and neoplasia [81–83]. In a single study, premedication with cimetropium bromide increased detection of gastric neoplastic lesions [13]. Several scales have been proposed to classify mucosal visibility [84–

88]. Of note, dedicated training in gastric neoplasia detection has also been shown to improve detection rates [71, 89–92].

Since the last revision of the MAPS guidelines, there has been new evidence supporting use of VCE (particularly narrow-band imaging [NBI], blue-laser imaging [BLI] and linked-color imaging [LCI]) for the detection of early lesions and precancerous conditions. NBI and BLI showed superiority over white-light imaging (WLI) in a meta-analysis for the diagnosis of early GC, without significant differences between NBI and BLI [93]. Some studies, including two randomized controlled trials (RCTs), also showed the superiority of LCI over WLI for the detection of gastric neoplastic lesions [94–97]. Two single-arm meta-analyses showed that NBI has a sensitivity of 79 %–80 % and a specificity of 91 %–93 % for the diagnosis of GIM [98, 99], and a meta-analysis including 6 studies showed that LCI has high accuracy for diagnosis of GIM, with sensitivity and specificity of 87 % and 86 %, respectively [100]. A meta-analysis of comparative studies also confirmed the superiority of NBI versus WLI for GIM detection [101]. Although the evidence is more limited, some studies also showed superiority of BLI, i-scan optical enhancement [102], and LCI [103] for GIM diagnosis when compared with WLI.

Previous studies showed that guided biopsies are useful for the identification and staging of gastric precancerous conditions in combination with random mapping biopsies [104, 105]. However, mapping biopsies still have a role since chromoendoscopy-targeted biopsies plus mapping biopsies have been shown to be superior to targeted biopsies alone in some studies [104, 106, 107]. Thus, VCE should guide the biopsies for suspicious areas, but additional random biopsies may increase the identification of patients with GIM at least in less experienced operators.

However, the strategy of targeted biopsy alone with chromoendoscopy (resulting in fewer specimens and vials) may be considered as an alternative if there is experience with VCE. According to the ESGE curriculum for optical diagnosis training [108], endoscopists are encouraged to participate in training courses that utilize validated classifications, such as the vessel plus surface classification system (VSCS) for VCE with magnification [109, 110] or the simplified NBI classification for high definition NBI endoscopy [111], since there is some evidence that training (namely using online models) increases the accuracy of optical diagnosis [89, 112–117].

RECOMMENDATION

12 ESGE/EHMSG/ESP suggest that real-time artificial intelligence (AI)-assisted detection and localization of gastric neoplastic lesions or staging of precancerous conditions may be used whenever available. [New]

Conditional recommendation/Low quality; 96 % agreement.

Despite the increasing number of EGDs performed annually, the rate of missed GC is constant [65, 66]. In recent years AI in gastrointestinal endoscopy has also been developed for detection of early neoplasia in the stomach [118–141]. Most of the studies are retrospective and rely on the assessment of still images. In the meta-analysis by Arribas et al., AI systems had 88 % sensitivity and 89 % specificity in gastric adenocarcinoma detection [140]. In another recent meta-analysis including 17 studies, the pooled area under the curve (AUC) was 0.94 with 87 % sensitivity and 88 % specificity [134]. The real-time use of the Endoangel system resulted in sensitivity and specificity of 91.8 % and 92.4 %, respectively [124]. This system was also shown to significantly decrease blind spots during EGD, in a single RCT [126], and to decrease the neoplasia miss rate (RR 0.224, 95 %CI 0.068–0.744; $P = 0.015$) [141]. Several systems have also been developed for the diagnosis of CAG and GIM with promising results [142–152]. In a recent meta-analysis, assessment of images by AI resulted in 94 %, 96 %, and 0.98 for sensitivity, specificity, and AUC, respectively [150]. ESGE recommends that the threshold of 90 % should be achieved for detection of both cancer and precancerous conditions [153] and therefore, whenever available, AI-assisted systems may be used.

RECOMMENDATION

13 ESGE/EHMSG/ESP recommend that when there is suspicion of a neoplastic lesion, the lesion should be:

- properly described (size, morphology according to Paris classification [namely, ulceration], location, vascular and mucosal patterns);
- photodocumented; and
- 2 targeted biopsies should be taken.

[Modified]

Conditional recommendation/Moderate quality; 100 % agreement.

Successful endoscopic resection (ER) of gastric neoplasia depends on proper characterization and assessment of the indication for ER (▶ **Fig. 3**). This includes evaluation of the size (characterization of the horizontal extent of the lesion with VCE) and morphology (Paris classification) of the lesion, and prediction of invasion depth and differentiation [10, 16].

Although there are some Eastern studies showing that VCE can predict differentiation, in our (European) setting, biopsies are needed to assess differentiation and to confirm the neoplastic nature of a lesion before ER [10]. Although a 95 % accuracy was found in a multicenter prospective study [154], biopsies may underestimate the final histology of a lesion, with a reported 10 % discrepancy rate between biopsy and histology of the resection specimen [155, 156].

The ESGE tissue sampling guideline recommends only 1–2 targeted biopsies of a lesion [157]. However, a large retrospective study showed that the diagnostic accuracy was significantly higher when 2 biopsies were performed (92.5 % vs. 83.9 % with 1 biopsy, $P < 0.001$) [158]. Since there is no evidence that 1–2 biopsies before ER compromise subsequent ER, we recommend

performing 2 biopsies in early lesions (prior to ER) and 6 biopsies in the case of advanced lesions [157, 159].

When a lesion is found the endoscopist should also evaluate whether there are endoscopic signs of deep submucosal invasion or risk factors for noncurative resection (in addition to size, morphology, and differentiation). Risk factors for noncurative resection confirmed in meta-analyses include poor differentiation [160–165], greater tumor size (≥20 mm, OR 3.66–3.94; ≥30 mm, OR 5.01) [160, 166], ulceration (OR 2.69–3.92) [160, 166], depressed-type morphology (OR 1.49), and tumor location in the upper third of the stomach (OR 1.49) [160]. Other observational studies have shown other findings for noncurative resection of early GC, including: convergence, clubbing, or abrupt cutting of gastric folds; absence of mucosal nodularity; and spontaneous bleeding/friability [167–169].

Risk factors for submucosal invasion include lesion size >30 mm [170], tumor location in the upper third of the stomach, marked margin elevation [170], uneven surface/nodularity [170], remarkable redness [170], fusion of converging folds [162, 171], irregular/nodular surface depression with fusion of converging folds [171], enlarged gastric folds [172], and the nonextension sign [173, 174].

A proforma endoscopy report is suggested in ▶ **Appendix A**.

RECOMMENDATION

14 ESGE/EHMSG/ESP do not recommend routine performance of endoscopic ultrasonography (EUS), computed tomography (CT), magnetic resonance imaging (MRI), or positron emission tomography (PET)-CT prior to endoscopic resection unless there are signs suspicious of deep submucosal invasion or the lesion is not considered suitable for endoscopic resection. [Unchanged]

Strong recommendation/Moderate quality; 100 % agreement.

The risk of lymph node metastasis (a priori risk) is low in early gastric lesions considered for ER. Given that the curative resection rate after ESD is around 80 %, there is interest in improving lesion selection and in more accurate staging. Only a few studies have evaluated the role of CT or PET-CT in the prediction of invasion depth/lymph node metastasis/curability of early GC by ER. The accuracy of CT for early GC stage (early 0-IA vs. advanced IB-IIIC) was 60 %. The sensitivity for advanced GC was 61.1 % and specificity for N + was 75 % (PPV 62.5 %), corresponding to overstaging rates of 16.6 % and understaging rates of 36.8 % [175]. CT using a gastric window has been later found to improve the accuracy for T1/T2 differentiation and to decrease the rates of overstaging (7 %–8 % in T1), but the accuracy for differentiating T1a and T1b was modest (67 %–69 %) [176].

Concerning PET-CT, a study by Chung et al. [177] published in 2019 found that PET-CT had an accuracy of 85 % regarding endoscopic curability, with a sensitivity of 79 %, specificity of 91 %, PPV of 81 %, and negative predictive value (NPV) of 89 % for noncurative resection.

Regarding the role of EUS, a meta-analysis was published by Shi et al. [178], analyzing the accuracy of invasion depth prediction by EUS with a sensitivity of 87 % and specificity of 67 %. The overall overstaging rate of mucosa/submucosa 1 (M/SM1) was 13.3 % and for submucosa (SM) it was 32.8 %, while the overall understaging for SM was 29.7 %. Lee et al. [179] described an EUS overestimation rate in early GC of 26.5 % and underestimation of 6.9 %. In a similar study, Li et al. [180] described overestimation in 33.6 % and underestimation in 10.4 %, respectively.

Many studies described the risk factors for EUS misdiagnosis [178, 180–182]. Kim et al. [182] demonstrated risk factors for lower EUS accuracy including lesion size, presence of ulceration, and non-flat lesion (lesion size >20 mm and ≤30 mm, OR 3.59, $P = 0.001$; lesion size >30 mm, OR 5.47, $P = 0.001$; ulceration, OR 6.62, $P = 0.003$; non-flat lesion, OR 2.94, $P = 0.029$).

The overall EUS accuracy for invasion depth of early GC varies from 55.9 % to 95 % [173, 175, 179–186]; however, the results from the studies range mostly from around 66 % to 79 % [173, 175, 179, 182, 184, 186].

It should be noted that endoscopy alone (even without chromoendoscopy) has almost 80 % accuracy in determining curability by ER, with several prediction models described to decide between ESD or surgery, with good results published in the literature [163, 168, 187]. Moreover, ESD does not preclude the possibility of subsequent surgery and should be seen as the most definitive T-staging modality.

To conclude, EUS, CT, or PET-CT do not significantly add to endoscopic evaluation alone: they have significant rates of over- and understaging, and cannot be recommended routinely, particularly for lesions that are considered endoscopically resectable. Although the accuracy of PET-CT is in line with that of endoscopic prediction (~80 %), in lesions with suspicion of submucosal invasion/noncurative resection, its high PPV for noncurative resection may be helpful and aid the decision between endoscopic or surgical treatment.

RECOMMENDATION

15 ESGE/EHMSG/ESP suggest the use of validated endoscopic classifications of atrophy (e. g. Kimura–Takemoto) or gastric intestinal metaplasia (e. g. endoscopic grading of gastric intestinal metaplasia [EGGIM]) to endoscopically stage precancerous conditions and stratify risk for gastric cancer. [New]

Conditional recommendation/Low quality; 96 % agreement.

The EGGIM scoring system has been shown to stratify GC risk during endoscopy based on nonmagnified VCE without the need of routine biopsies, achieving high concordance with the gold standard for high-risk GIM phenotypes (operative link on gastritis assessment [OLGIM] III–IV) [188]. A meta-analysis of comparative studies (4 diagnostic studies and 3 case–control) showed that EGGIM accurately identifies OLGIM III/IV with pooled sensitivity and specificity of 92 % (95 %CI 86 %–96 %) and 90 % (95 %CI 88 %–93 %), and an AUC of 0.9702. Moreover,

patients with higher EGGIM scores (5–10) were found to be at higher risk for early GC (OR 7.46, 95 %CI 3.41–16.310 [189]. In another meta-analysis assessing the role of VCE in prediction of GIM severity, EGGIM achieved a high predictive value for the severity of GIM under different modes of digital chromoendoscopy. Moreover, for high-risk GIM, the combined endoscopic prediction sensitivity of this method was 93 % (95 %CI 87–96, specificity 91 % (95 %CI 88%–93%), and AUC 0.9728 [190].

Similarly, grading endoscopic atrophy using white-light endoscopy (WLE) according to the Kimura–Takemoto classification can accurately assess the risk of gastric neoplasia development. In a meta-analysis of 14 retrospective studies, the pooled risk ratio (RR) for developing gastric neoplasms was 3.89 (95 %CI 2.92–5.17) among unselected patients with severe endoscopic atrophy (O2–O3), and 7.27 (95 %CI 1.64–32.33) among those with open-type endoscopic atrophy [191].

In summary, patients with endoscopic identification of extensive precancerous conditions (EGGIM ≥ 5 and/or Kimura–Takemoto open-type) are at higher risk of GC and the endoscopic staging may also guide management.

A proforma endoscopy report is suggested in ▶ **Appendix A**.

RECOMMENDATION

16 ESGE/EHMSG/ESP recommend biopsy of 2 fragments from the antrum/incisura and 2 from the corpus, guided by VCE, clearly labeled in two separate vials. Additional biopsy from the incisura is optional. [Modified]

Strong recommendation/Moderate quality; 96 % agreement.

Previous European guidelines for the management of epithelial precancerous conditions in the stomach (MAPS II) advocated biopsies of at least two topographic sites (from both the antrum and corpus, at lesser and greater curvature) to enable histopathological assessment according to the updated Sydney system. Although the incisura is the anatomical location where the highest incidence and severity of IM has been traditionally noted, addition of an incisura biopsy has shown small additional diagnostic yield in identifying patients in high-risk stages (OLGA/OLGIM III/IV) [192–194]. Ten prospective studies evaluated the role of the incisura angularis biopsy in the staging of precancerous conditions including further GC risk stratification [192–201]. Addition of an incisura angularis biopsy did not increase the identification of high-risk OLGA stages (OR 1.15, 95 %CI 0.99–1.34; I^2 0 %), but significantly increased the detection of high-risk OLGIM stages (OR 1.46, 95 %CI 1.17–1.84; I^2 0 %). However, subgroup analysis including of studies originating exclusively from Europe showed that – for Europe – addition of an incisura angularis biopsy changed neither grading from low- to high-risk OLGA nor from low- to high-risk OLGIM stages.

In other terms, the absolute increase in the proportion of patients with OLGA/OLGIM III/IV due to the additional incisura biopsy is small, with a number needed to treat (NNT) of 59 overall (and a NNT of 70 if only studies performed in unselected populations are considered) [193, 197], meaning that fewer than 1 of 59 patients will not be correctly included in a high-risk group if the incisura biopsy is not taken. Moreover, in the era of high definition endoscopy and VCE, the chance of missing IM at the incisura is even lower. Our literature search on this topic revealed no data regarding biopsy-related costs and workload. Based on these considerations, we recommend taking at least 2 biopsies from the antrum/incisura and 2 biopsies from the corpus, guided by VCE. Addition of the incisura angularis biopsy can be considered on a case-by-case basis to potentially increase the detection rate of precancerous conditions or when VCE is not available, and OLGA and OLGIM grading systems are implemented.

Regarding the number of vials, in the absence of a typical endoscopic pattern of severe atrophy/IM using VCE, use of a single vial to place all biopsy specimens (for *H. pylori* diagnosis) or even complete abstinence from biopsies can be applied (if *H. pylori* status is known or not considered clinically relevant) if expertise exists regarding both endoscopists and pathologists involved [198].

RECOMMENDATION

17 ESGE/EHMSG/ESP recommend high quality histopathological reporting for all endoscopic biopsies, that should include:

- presence and grade of dysplasia;
- presence and subtype of adenocarcinoma (Laurén and WHO classifications);
- presence and severity of atrophy;
- presence and severity of intestinal metaplasia;
- subtyping as complete or incomplete intestinal metaplasia;
- presence of *H. pylori* infection.

[Modified]

Strong recommendation/Moderate quality; 100 % agreement.

RECOMMENDATION

18 ESGE/EHMSG/ESP suggest that systems for histopathological staging of atrophy (operative link on gastritis assessment [OLGA]) or, preferably, intestinal metaplasia (operative link on gastric intestinal metaplasia [OLGIM]) can be used and integrated with endoscopic information in the management of patients. [Modified]

Conditional recommendation/Moderate quality; 100 % agreement.

RECOMMENDATION

19 ESGE/EHMSG/ESP recommend against further subtyping intestinal metaplasia as type I to III because of risks to health care professionals. [New]

Strong recommendation/Moderate quality; 100 % agreement.

RECOMMENDATION

20 ESGE/EHMSG/ESP suggest that biopsies revealing dysplasia are reviewed by an expert gastrointestinal pathologist. [New]

Conditional recommendation/Low quality; 96 % agreement.

All superficial lesions harboring dysplasia or more severe changes should be staged and managed by resecting them. ESGE/EHMSG/ESP recommends that patients who undergo resection of malignant lesions are treated by multidisciplinary teams (MDTs), with the recommendations for management based on endoscopic and pathology reports as detailed. Thus, handling of specimens must follow rigorous standards (see ▶ **Appendix B**). In some cases, biopsy findings are "indeterminate/indefinite for dysplasia" (IND). This refers to a borderline lesion that presents a challenge for definitive histopathological diagnosis as either regenerative or neoplastic from endoscopic forceps biopsy samples. Limited data indicate a relatively high frequency of high grade dysplasia (5 %) or invasive carcinoma (23 %–29 %) [202–204], with about 40 % being histologically upgraded upon review. Only 9 % of cases show recurrent gastric IND upon repeat biopsy [204]. Thus, it may be reasonable for reassessment of the diagnosis by a pathologist expert in GI pathology and to repeat endoscopic assessment.

Precancerous conditions. The risk for developing cancer seems to be related to the extent (particularly when affecting both antrum and corpus), severity, and subtype of IM. In MAPS I and MAPS II, the OLGA and OLGIM systems were proposed for staging of atrophy and IM, respectively. A meta-analysis of comparative studies (6 case–control studies and 2 cohort studies) including 2700 patients demonstrated a significant association between advanced OLGA and OLGIM stages III/IV and the risk of GC (both intestinal and diffuse type: OR for OLGA 2.64, 95 %CI 1.84–3.79, I^2 60 %; OR for OLGIM 3.99, 95 %CI 3.05–5.21, I^2 0 %) [205, 206]. We identified 18 observational studies [207–224]. Meta-analyses comprising data exclusively from 8 prospective studies with long-term follow up [209, 210, 216, 218–222] showed that OLGA/OLGIM stages III/IV are associated with the development of not only GC (OR 44.21, 95 %CI 8.32–235.01; I^2 63 %) but also low grade dysplasia (OR 14.49, 95 %CI 1.91–109.26; I^2 92 %) and high grade dysplasia (OR 16.57, 95 %CI 5.71–48.07; I^2 21 %). Based on these predictive properties, OLGA and OLGIM systems can be used to histologically assess GC risk. However, the diagnosis of atrophic gastritis needs grading of severity of gland loss – which shows poor inter- and intraobserver agreement. Therefore, we suggest that OLGIM could be preferred whenever the aim is staging of mucosal transformation. OLGIM has lower technical requirements regarding orientation of biopsy samples (compared with the assessment of atrophy for OLGA). However, the concept of extensive precancerous conditions (their presence in the antrum and body, independently of severity) is easier to use in clinical practice, widely available, and also correlates with GC risk. In fact, RE.GA.IN. suggested that OLGIM III/IV be regarded as equivalent to changes being present both in antrum and corpus, in line with the recommendations from MAPS I and II [2].

Extent of the mucosal changes seems also to be more relevant and easier to apply than subtyping of GIM. One exception may be the classification of GIM as complete or incomplete. Some studies indicate a positive correlation between the degree of incomplete GIM and the extent of GIM, which should be considered when managing these patients. However, the approach of subtyping GIM into types I, II and III was discontinued because of the toxicity of the reagents used for the necessary staining.

An example of completeness of reporting is provided in ▶ **Appendix B**. Also ▶ **Fig. 4** shows a general approach. ▶ **Fig. 5** and ▶ **Fig. 6** provide endoscopic images of superficial lesions and ▶ **Fig. 7** shows gastric images with no neoplastic lesions present but different stages of suspected precancerous conditions.

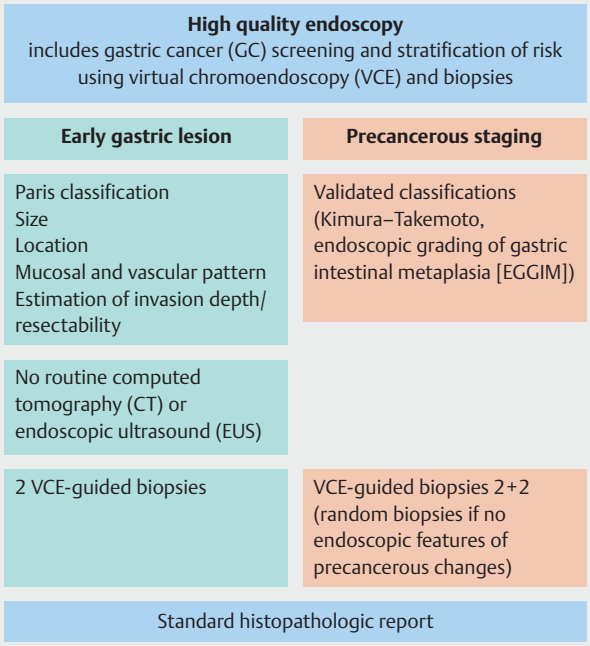
Management of individuals with endoscopically nonvisible dysplasia and those with superficial lesions with dysplasia/cancer

RECOMMENDATION

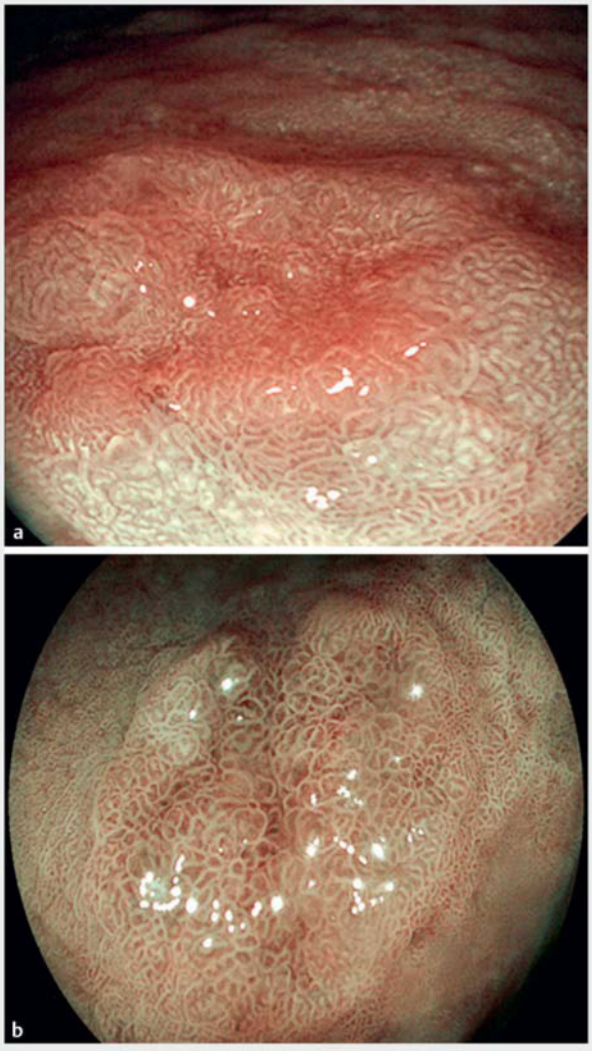
21 ESGE/EHMSG/ESP suggest that patients with dysplasia (or indefinite for dysplasia) but no lesions seen on gastroscopy, are referred for a high quality endoscopy (namely, high definition white-light endoscopy with virtual chromoendoscopy [VCE]), staging of precancerous conditions, and *H. pylori* testing if not previously performed. If endoscopic lesions are again not seen, a follow-up high quality endoscopy is then needed, in 6 months for high grade dysplasia, or 12 months for low grade dysplasia/indefinite for dysplasia. [Modified]

Conditional recommendation/Moderate quality; 100 % agreement.

High quality endoscopy (high definition WLE with VCE or conventional dye-based chromoendoscopy) improves the detection and demarcation of early GC or premalignant lesions in comparison with standard definition WLE [99, 225–227]. Some studies have questioned the added value of VCE compared to high definition WLE [228], but due to its widespread and easy use in the detection of premalignant lesions and early GC, it is preferentially recommended. Conventional chromoendos-



▶ **Fig. 4** General diagnostic approach to gastric cancer and precancerous conditions.



▶ **Fig. 5** Superficial lesions submitted to curative resection: **a** Paris 0-IIa, no ulceration, 8 mm, antrum; en bloc resection with endoscopic submucosal dissection (ESD); low grade dysplasia (LGD), R0. **b** Paris 0-Is, no ulceration,12 mm, incisura; en bloc resection with ESD; well-differentiated, HM0, VM0, Ly neg, R0.

copy improves the detection of precancerous and malignant lesions, and is clinically equivalent to magnifying NBI [229].

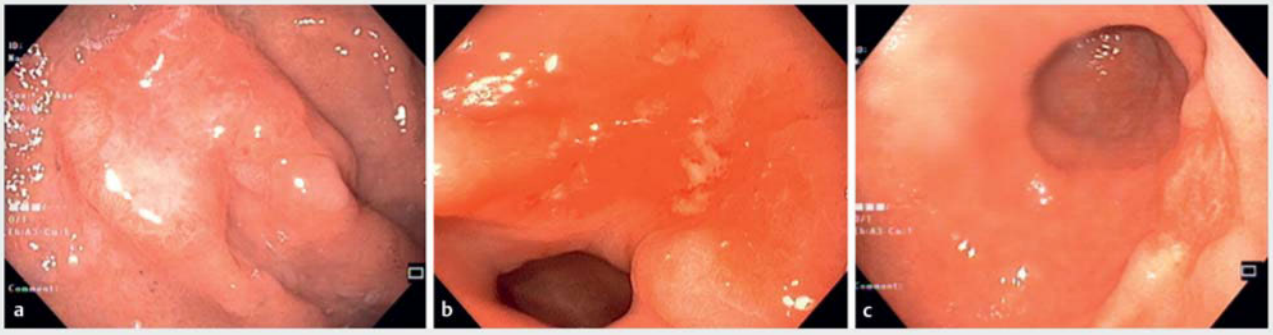
The presence of GC or HGD carries a substantial risk of other synchronous tumors being overlooked, and the risk of development of other early GCs over time with these metachronous lesions emerging only 15 months after the primary lesion [230, 231]. Given these findings, it seems reasonable to conduct a follow-up high quality endoscopy 6 to 12 months after histologically confirmed dysplasia (or indefinite for dysplasia) that does not present with an endoscopically visible lesion.

RECOMMENDATION

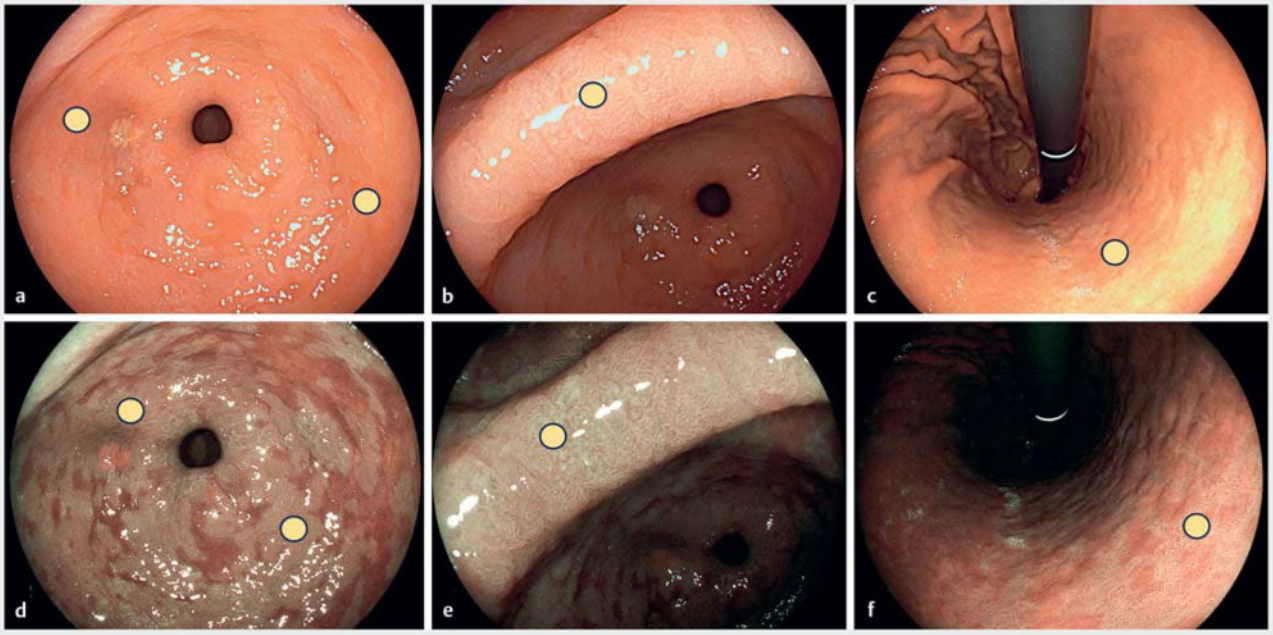
22 ESGE/EHMSG/ESP suggest that patients with a diagnosis of indefinite for dysplasia (confirmed by an expert GI pathologist) and an endoscopic lesion are referred for a high quality endoscopy and, according to endoscopic findings, consideration for guided biopsies or resection. [New]

Conditional recommendation/Low quality; 100 % agreement.

As described above, limited data indicate a relatively high frequency of low grade dysplasia (LGD) (7 %), HGD (5 %), or invasive carcinoma (23 %–29 %) among patients with the diagnosis of indefinite for dysplasia by forceps biopsy [202–204]. Up to 40 % of these patients had a histological upgrade – established through subsequent repeat biopsy, endoscopic resection, or surgical samples – and only 9 % of cases showed recurrent gastric indefinite for dysplasia lesions upon repeat biopsy [204]. Certain risk factors such as surface erythema, nodularity, spontaneous bleeding, lesion size ≥ 10 mm, and depressed morphology are significant predictors of HGD or adenocarcinoma, especially when present in combination [204, 232–234]. In these cases, ER of the lesion can be considered. On the other hand, small tumors and a low sampling ratio are associated with benign pathological findings after endoscopic resection [235]. Diagnostic delays shorter than 1 year were not associated with worse prognoses. Extremely well-differentiated adenocarcinomas accounted for half of the repeated indeterminate cases [203].



▶ **Fig. 6** Superficial lesions sent for surgical treatment because of suspected invasion. **a** Proximal corpus, 0-Is, 20 mm, ulcerated (Ulc +), fold convergences and elevated margins; deep submucosal invasion suspected. Surgery revealed differentiated carcinoma, pT2N + Mo lesion. **b** Distal antrum, 0-IIc-IIa, 23 mm, Ulc + , fold convergences; submucosal invasion suspected. Surgery revealed undifferentiated, pT1b N0 lesion. **c** Antrum, IIc + IIa, 25 mm, fold convergence. Surgery revealed differentiated, pT1b Ly + N0 lesion.



▶ **Fig. 7** Images reflecting absence of significant changes with random biopsies (upper panel) versus significant changes and targeted biopsies (lower panel).

RECOMMENDATION

23 ESGE/EHMSG/ESP suggest that age and comorbidities should be taken into account when selecting patients for endoscopic treatment of an early gastric lesion. [New] Conditional recommendation/Low quality; 96 % agreement.

Gastric ESD has good results in elderly and patients with comorbidities [236–244], but the decision for ER should consider overall survival benefits versus risks, especially in fragile patients with severe comorbidities and multiple risk factors of early mortality or short life expectancy [245–248]. Limited evidence suggests potential survival improvement in very elderly patients with cT1N0 early GC [241], but the impact of conservative management without intervention versus ESD in fragile patients remains unclear. For instance, it is possible that ER may not help to prolong survival in very elderly patients with severe comorbidities such as cardiovascular disease [242]. On the other hand, ER could be a reasonable alternative to surgery for the management of early GC cT1N0 beyond standard indi-

cations for local excision in elderly patients or those with severe comorbidities, or can be considered as definitive treatment with conservative management after noncurative ESD with low and intermediate risk [238, 239, 244, 249–251]. Thus, the indication for ESD should be discussed in a multidisciplinary team taking into account age and comorbidities, especially for fragile patients, and considering assessment of predictors of early and late mortality in high-risk patients; surveillance after ESD should also be discussed.

RECOMMENDATION

24 ESGE/EHMSG/ESP recommend that patients with an endoscopically visible lesion harboring dysplasia (low grade or high grade) or carcinoma should undergo staging and treatment. [Unchanged]

Strong recommendation/Moderate quality; 92 % agreement.

For most superficial lesions when endoscopic features do not predict noncurative resection (see ▶ **Fig. 8**), resection should be proposed. Several studies have shown discrepancies between pretreatment endoscopic biopsies and final diagnosis after resection [252, 253]. A European study demonstrated that histology was upgraded following ESD in 33 % of cases [254]. A meta-analysis conducted by Zhao et al. [255], which included 16 studies and assessed 3033 lesions, also revealed upstaging of gastric LGD occurred in 25.0 % of cases (specifically, LGD to HGD in 16.7 %, and HGD to carcinoma in 6.9 %). Three more recent studies also confirmed the abovementioned findings. A study published in 2021 reported upgrades from LGD to HGD in 17 % and from HGD to carcinoma in 11 %, and a study published in 2023 by Shin et al. reported an overall upgrade rate of 26 % (LGD to HGD in 19 %, and HGD to carcinoma in 7 %) [256, 257]. Another study focusing on 2150 lesions with LGD on biopsies indicated an even higher risk of upgrade to carcinoma (27.4 %) [258]. Thus, biopsy sampling is important to confirm neoplasia but insufficient for staging and correct diagnosis concerning invasion depth, and thus, any endoscopically visible lesion with any neoplastic change should be considered for treatment.

Despite the limitations of biopsies, their results can have prognostic implications. Libânio et al. found that carcinoma in pre-resection biopsies is a significant risk factor for noncurative resection (noncurative resection 29 % vs. 10 %–13 % with dysplasia biopsies, $P<0.01$). This was confirmed as an independent risk factor in multivariable analysis (adjusted OR 3.04) [169].

RECOMMENDATION

25 ESGE/EHMSG/ESP recommend endoscopic submucosal dissection (ESD) as the treatment of choice for most superficial gastric lesions. [Unchanged]

Strong recommendation/Moderate quality; 96 % agreement.

No new evidence.

RECOMMENDATION

26 ESGE/EHMSG/ESP recommend ESD for differentiated gastric lesions clinically staged as dysplastic (low and high grade) or as intramucosal carcinoma (of any size if not ulcerated and ≤ 30 mm if ulcerated), with endoscopic mucosal resection (EMR) being an alternative for Paris 0-IIa lesions with size ≤ 10 mm, with low likelihood of malignancy. [Unchanged]

Strong recommendation/Moderate quality; 96 % agreement.

No new evidence.

RECOMMENDATION

27 ESGE/EHMSG/ESP suggest that a decision about ESD can be considered for malignant lesions clinically staged as having minimal submucosal invasion if differentiated and ≤ 30 mm; or for malignant lesions clinically staged as intramucosal, when undifferentiated and ≤ 20 mm; and in both cases with no ulcerative findings. [Unchanged]

Conditional recommendation/Low quality; 100 % agreement.

ESD is considered safe for expanded indications [259]. Mixed- or undifferentiated-type ECGs with any submucosal invasion have a high risk (36 %) of lymph node metastasis (LNM) [260] and should not be considered for ER. A meta-analysis showed that ESD for undifferentiated early GC is associated with a higher risk of recurrence, but similar adjusted all-cause mortality during follow-up compared to surgery [261].

RECOMMENDATION

28 ESGE/EHMSG/ESP recommends patient management based on the following histological risk after endoscopic resection:

- *Curative/very low-risk resection (LNM risk < 0.5 %–1 %)* En bloc R0 resection; dysplastic/pT1a, differentiated lesion, no lymphovascular invasion, independent of size if no ulceration and ≤ 30 mm if ulcerated. No further staging procedure or treatment is recommended.
- *Curative/low-risk resection (LNM risk < 3 %)* En bloc R0 resection; lesion with no lymphovascular invasion, and:
  a) pT1b, submucosal invasion ≤ 500 µm, differentiated, size ≤ 30 mm; or
  b) pT1a, undifferentiated, size ≤ 20 mm and no ulceration.

Staging should be completed, and further treatment is generally not necessary after a multidisciplinary discussion.

- *Local-risk resection (very low risk of LNM but increased risk of persistence/recurrence)*
  – Piecemeal resection or tumor-positive horizontal margin of a lesion otherwise meeting curative/very low-risk criteria; or
  – Provided there is no submucosally invasive tumor at the resection margin in the case of piecemeal resection or tumor-positive horizontal margin, for otherwise low-risk pT1b lesion (submucosal invasion ≤ 500 µm, well-differentiated, size ≤ 30 mm, and VM0).

Endoscopic surveillance/re-treatment is recommended rather than other additional treatment.

- *High-risk resection* (noncurative): Any lesion with any of the following:
  a) a positive vertical margin (if carcinoma) or lymphovascular invasion or deep submucosal invasion (> 500 µm from the muscularis mucosae);
  b) poorly differentiated lesion if ulceration or size > 20 mm;
  c) in pT1b differentiated lesion with submucosal invasion < 500 µm with size > 30 mm;
  d) or in intramucosal ulcerative lesion with size > 30 mm.

Complete staging and strong consideration for additional treatments (surgery) in multidisciplinary discussion.

[Unchanged]
Strong recommendation/Moderate quality; 100 % agreement.

There are some histological factors that help to predict a minimal risk of LNM. When these criteria are met, the 5-year overall survival of around 90 % and disease-specific survival are similar to surgical outcomes [262]. See also ▶ **Table 3**.

RECOMMENDATION

29 ESGE/EHMSG/ESP suggest a surveillance high quality endoscopy at 3–6 months and then annually after a very low- or low-risk ESD resection or after a local-risk ESD resection without recurrence. Routine use of EUS, MRI, CT, or PET in the follow-up after very low-risk resections is not suggested but could be considered for higher-risk lesions. [Modified]
Conditional recommendation/Low quality; 100 % agreement.

Surveillance after a local-risk ER should include close observation with biopsies from the scar, taken at least at the first follow-up endoscopy, or interventions such as coagulation or ablation, or repeat ESD, which includes resection of the ESD scar and/or coagulation of the scar to prevent recurrence (▶ **Fig. 4**).

In the case of finding a metachronous lesion, the treatment is the same as for any primary gastric lesion. In a recent systematic review ESD showed better outcomes regarding complete resection compared with EMR, and similar outcomes compared with surgery, for metachronous lesions or recurrences [263].

Based on a recent meta-analysis that identified risk factors for metachronous lesions after ER or subtotal gastrectomy [264], the FAMISH score was developed to predict the risk for metachronous lesions after gastric ESD. It identified a low-risk group that could benefit from extended surveillance intervals (contributing to a “greener” surveillance).

RECOMMENDATION

30 ESGE/ EHMSG/ESP recommend that after a high-risk resection, the need for additional treatment is decided in a multidisciplinary team (MDT) discussion taking into account LNM risk, age, comorbidities, and life expectancy. [Modified]
Strong recommendation/Moderate quality; 100 % agreement.

A recent study created a nomogram based on lesion features predicting noncurative resection, externally validated with an AUC of 0.8675 [162]. Other nomograms and AI-based scores exist.

Lymphovascular invasion is a key risk factor for LNM. The eCura system classifies patients based on a scoring system of tumor-related histological risk factors to predict the likelihood of LNM after a high-risk resection, categorizing them into low-, intermediate-, or high-risk groups. Recent evidence shows that surgery is better than observation regarding 5-year overall survival only in the eCura high-risk group, with similar results in the low and intermediate groups, despite a higher recurrence-free survival rate in all groups [265]. The eCura system was validated in the West, with a new W-eCura score proposed, showing improved accuracy in LNM prediction [266]. If surgery is

necessary, a previous noncurative ESD does not negatively impact results [267], and one study suggested that delaying the surgery more than 30 days after the ESD may improve safety without compromising the oncological outcomes [268].

Close surveillance, including endoscopy and CT every 6–12 months, could be considered when surgery is not an option because of age or severe comorbidities, when the surgical risk surpasses the risk of LNM (e. g., eCura low-risk), or based on the patient's choice. In this scenario, patients should be informed of their risk for local or distant recurrence, considering that such recurrences have a poor prognosis with treatment often limited to palliative care.

Overall management algorithms are shown in ▶ **Fig. 8** and ▶ **Fig. 9**.

Surveillance of individuals with precancerous conditions

RECOMMENDATION

31 ESGE/EHMSG/ESP recommend that patients with extensive endoscopic changes (C3 + or EGGIM 5 +) or advanced histological stages of atrophic gastritis (severe CAG or GIM and/or significant changes in both antrum and corpus, OLGA/OLGIM III/IV) should be followed up with high quality endoscopy every 3 years. [Unchanged]
Strong recommendation/Moderate quality; 100 % agreement.

RECOMMENDATION

32 ESGE/EHMSG/ESP recommend opportunistic risk stratification of precancerous conditions in all endoscopies, because endoscopic surveillance every 3 years in patients with high-risk premalignant conditions is cost-effective irrespective of country. [Modified]
Strong recommendation/Moderate quality; 87 % agreement.

Studies published since 2018 have confirmed that patients with significant atrophy and/or IM in both antrum and corpus (OLGA/OLGIM III/IV) are at increased risk of gastric adenocarcinoma [205, 216, 219, 221, 223, 269–271]. A 2– to 3-year surveillance interval may facilitate early detection of dysplasia or early gastric carcinoma in those patients [269, 272]. In the diverse guidelines, surveillance every 3 years is recommended and, as stated above, this strategy is cost-effective in different settings including in low-prevalence countries (e. g. USA). Thus, stratifying of risk among individuals with precancerous conditions must be performed in all gastroscopies.

RECOMMENDATION

33 ESGE/EHMSG/ESP suggest that individuals with endoscopic features of extensive changes (C3 + or EGGIM 5 +) or histologically advanced stages of atrophic gastritis (severe atrophic changes or intestinal metaplasia in both antrum and corpus, OLGA/OLGIM III/IV), and with a first-degree relative with gastric cancer may benefit from a more intensive follow-up (e. g. every 1 to 2 years after diagnosis). [Modified]
Conditional recommendation/Low quality; 100 % agreement.

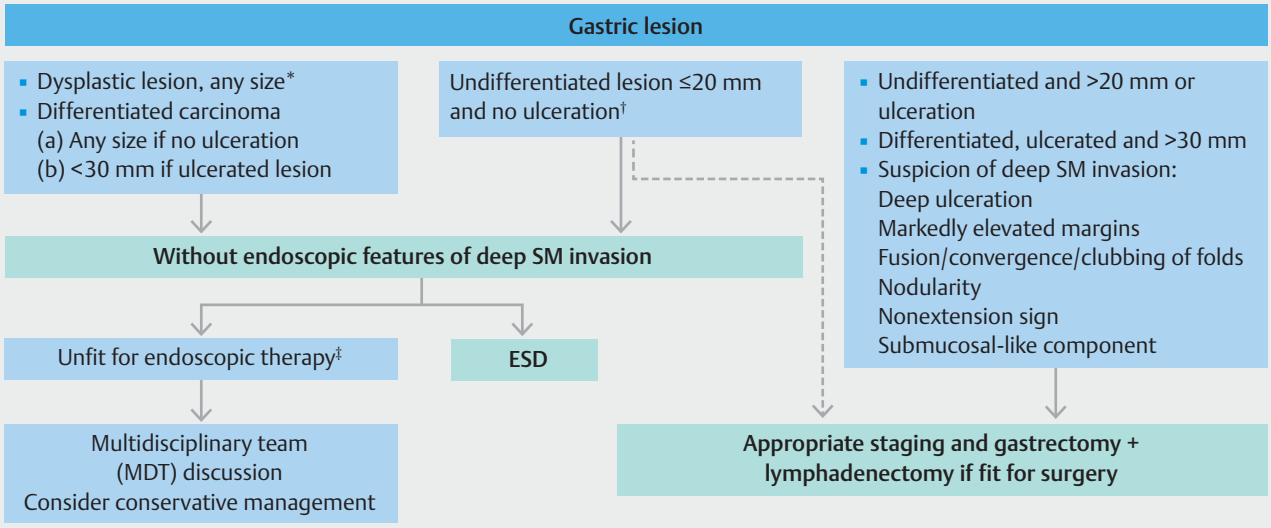
Since 2019, two cross-sectional studies have confirmed that there is a high prevalence of gastric precancerous conditions in first-degree relatives of patients with GC [273, 274]. Two case–control studies have also reinforced family history of GC (first- and/or second-degree relatives) as an independent risk factor for gastric neoplasia development [223, 275]. Considering the new data, there is no reason to change the statement.

RECOMMENDATION

34 ESGE/EHMSG/ESP recommend no surveillance endoscopy in patients with mild to moderate chronic atrophic gastritis (CAG) or gastric intestinal metaplasia (GIM) restricted to the antrum, in the absence of endoscopic signs of extensive lesions or of other risk factors (family history, incomplete intestinal metaplasia, or persistent *H. pylori* infection). This group constitutes most individuals found in clinical practice. [Modified]
Strong recommendation/Moderate quality; 100 % agreement.

There is no evidence in the literature for increased risk of GC in patients with mild to moderate atrophy localized to the gastric antrum. A family history of GC is an independent and significant risk factor for GC, and atrophic gastritis is significantly more prevalent in first-degree relatives than controls [195, 212, 223, 274–277]. Persistent *H. pylori* infection is an independent risk factor for gastric neoplastic lesions [270].

Even though several studies have reaffirmed IM as an important risk factor for dysplasia and gastric adenocarcinoma, the increase in the risk of gastric adenocarcinoma is progressive, being observed with increasing OLGIM stages, with the risk for OLGIM I being negligible [206, 212, 221, 223, 271, 278–287].

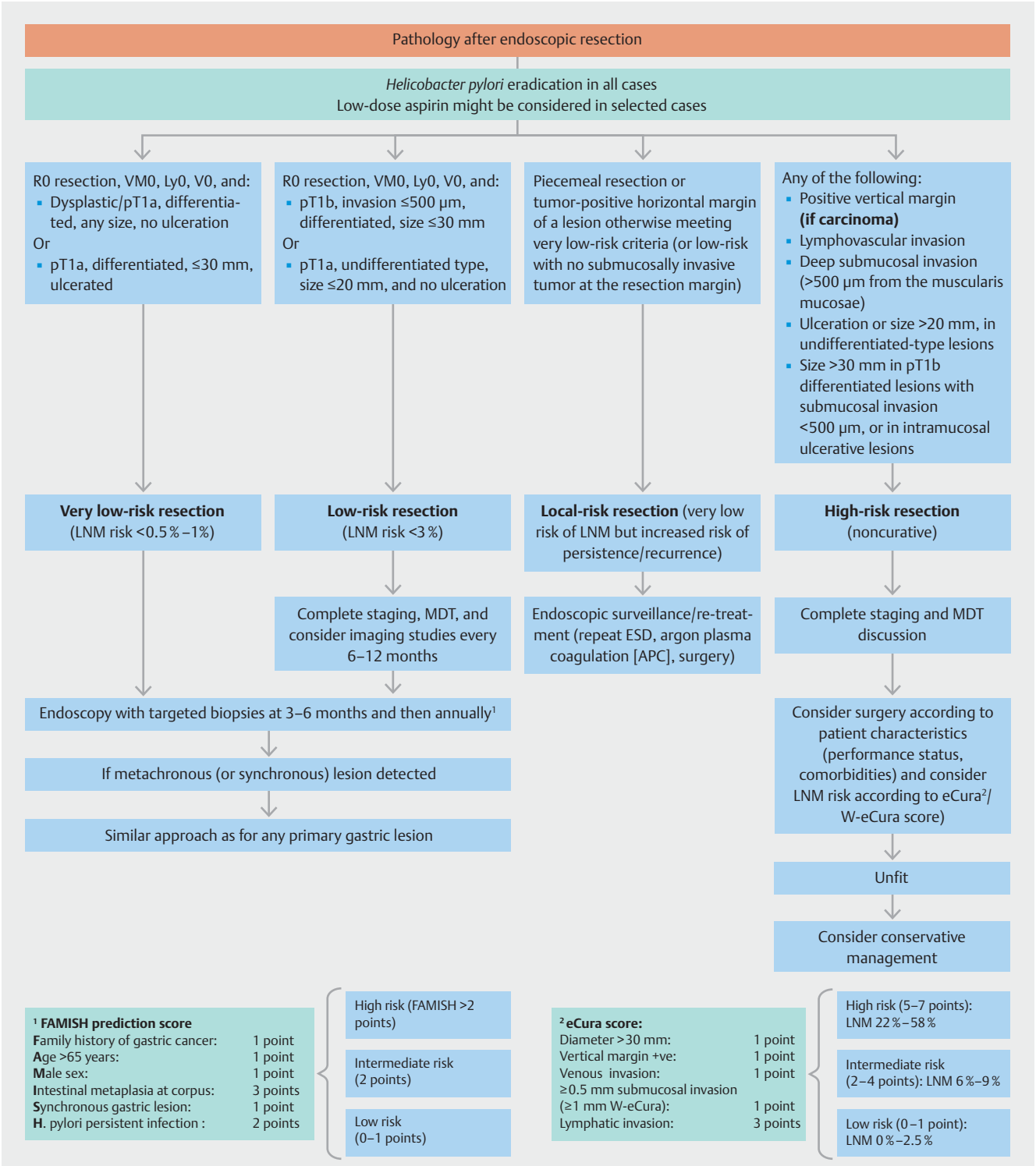


* Consider en bloc EMR if Paris 0–IIa, <10 mm, and predicted dysplasia/no suspicion of carcinoma
† Expanded indication – individualized decision
‡ Fragile patients with short life expectancy

▶ **Fig. 8** Algorithm for pre-therapy allocation and treatment decision for gastric lesions. SM, submucosal; ESD, endscopic submucosal dissection; EMR, endoscopic mucosal resection.

▶ **Table 3** Definitions for risk levels and associated risks: summary of definitions of different risk levels for gastric lesions and the associated risk for lymph node metastasis and gastric cancer death.

Risk according to pathology	Pathology	Risk for lymph node metastasis (LNM)	Gastric cancer-related mortality
Very low risk	En bloc R0 resection; dysplastic/pT1a, differentiated lesion; no lymphovascular invasion, independent of size if no ulceration and ≤ 30 mm if ulcerated	0.5 %–1 %	Very low
Low risk	En bloc R0 resection; lesion with no lymphovascular invasion, and a) pT1b, invasion ≤ 500 µm, differentiated, size ≤ 30 mm, or b) pT1a, predominant type is undifferentiated, size ≤ 20 mm, no ulceration;	< 3 %	Low
Local risk	Piecemeal resection or positive horizontal margin of a lesion otherwise meeting very low-risk criteria; no submucosal invasive tumor at the resection margin or tumor-positive horizontal margin for low-risk pT1b lesion (invasion ≤ 500 µm; well-differentiated; size ≤ 30 mm and VM0)	Very low	Low (Increased risk of persistence/local recurrence)
High risk	Any of: ▪ Positive vertical margin (if carcinoma); ▪ Lymphovascular invasion; ▪ Deep submucosal invasion (> 500 µm from the muscularis mucosae); ▪ Ulceration or size > 20 mm in undifferentiated lesions; ▪ Size > 30 mm in pT1b differentiated lesions with submucosal invasion < 500 µm or in intramucosal ulcerated lesions	Higher than 3 % eCura: ▪ High risk: 22 %–58 % ▪ Intermediate risk: 6 %–9 % ▪ Low risk: 2.5 %	Higher 5-year overall survival 85 %



▶ **Fig. 9** Algorithm for post-therapy care of gastric lesions considering risk profiles**.** LNM, lymph node metastasis; Ly0, no lymphatic invasion; MDT, multidisciplinary team; VM0, negative vertical margin; V0, no venous invasion.
[1]FAMISH score may be used to individualize surveillance; [2]eCURA may define risk for LNM.

RECOMMENDATION

35 ESGE/EHMSG/ESP suggest that in patients with gastric intestinal metaplasia (GIM) at a single location but with a family history of gastric cancer, or with incomplete intestinal metaplasia, or with persistent *H. pylori* gastritis, high quality endoscopic surveillance every 3 years may be considered. [Unchanged]

Conditional recommendation/Low quality; 96 % agreement.

Since 2019, several studies, including two meta-analyses, have shown that incomplete IM is an independent risk factor for gastric adenocarcinoma, even when IM is present at a single location [220, 288, 289]. Additionally, having a family history of GC in first- or second-degree relatives has also been identified as an independent risk factor for gastric adenocarcinoma [223, 275]. Lastly, persistent *H. pylori* infection is a known class I carcinogen for gastric adenocarcinoma and is an independent risk factor for gastritis progression and carcinogenesis.

RECOMMENDATION

36 ESGE/EHMSG/ESP recommend against any tailored surveillance strategy based on genetic status, birthplace, or ethnicity in patients with gastric precancerous conditions. [Unchanged]

Conditional recommendation/Low quality; 96 % agreement.

The American Gastroenterological Association's Technical Review on the natural history and outcomes in patients with GIM showed no significant differences in progression according to ethnicity, based on a meta-analysis of 3 studies [290]. Another systematic review and meta-analysis reported no significant differences in the odds ratio for progression to GC of gastric precancerous conditions according to area (East Asia pooled OR 3.99, 95 %CI 2.78–5.73; Western countries pooled OR 2.95, 95 %CI 1.91–4.57) [291]. A study published in 2020 found no increased risk according to race/ethnicity for progression of gastric precancerous conditions to dysplasia or cancer [292]. Another recent study was not informative because of the absence of progression in the included cohort (because of relative sample size and follow-up duration) [293]. On the other hand, a systematic review and meta-analysis dedicated to the natural course of GIM published in 2019 showed higher GC incidence in patients with IM in studies (n = 21) conducted in Asia (7.58 [95 %CI 4.10–11.91] per 1000 person-years) as compared to Europe (n = 25) (1.72 [95 %CI 0.36–3.70] per 1000 person-years; $P < 0.029$) but information at individual level was not provided [286]. A retrospective study by Dhingra et al. [272], not included in that meta-analysis, suggested a higher progression rate in patients of Asian ethnicity of 3.07 (95 %CI 1.02–9.19). Controversial findings reported in the literature preclude any robust recommendation.

Regarding genetic susceptibility, several studies show divergent trends for progression toward GC in patients with *H. pylori* infection or precancerous conditions [294, 295]. However, no tool is available in routine practice to provide tailored surveillance. This is of course different for specific situations such as hereditary syndromes.

RECOMMENDATION

37 ESGE/EHMSG/ESP suggest that random biopsies are not required during surveillance of cases with advanced OLGA/OLGIM stages at baseline endoscopy once no superficial lesions are observed. [New]

Conditional recommendation/Low quality; 100 % agreement.

Previous studies reveal conflicting evidence whether IM can progress or regress over a period of time [296–299], and disease-associated risk may be underestimated in one third of patients classified as low-risk by the index endoscopy [222]. Therefore, endoscopic reassessment with nontargeted biopsies in patients with an initial low-risk stage can help to redefine the surveillance program. Contrarily, in cases of already known advanced stages of precancerous conditions at baseline endoscopy in which no regression is expected, the follow-up could be performed without random biopsies but with a high quality endoscopy including chromoendoscopy to detect visible lesions. In this case, the assessment of the extent of IM could be performed with the EGGIM endoscopic system that has demonstrated a good correlation with the pathological score [300]. Notably, this may be an opportunity to reassess *H. pylori* status. See ▶ **Fig. 10** and ▶ **Fig. 11**.

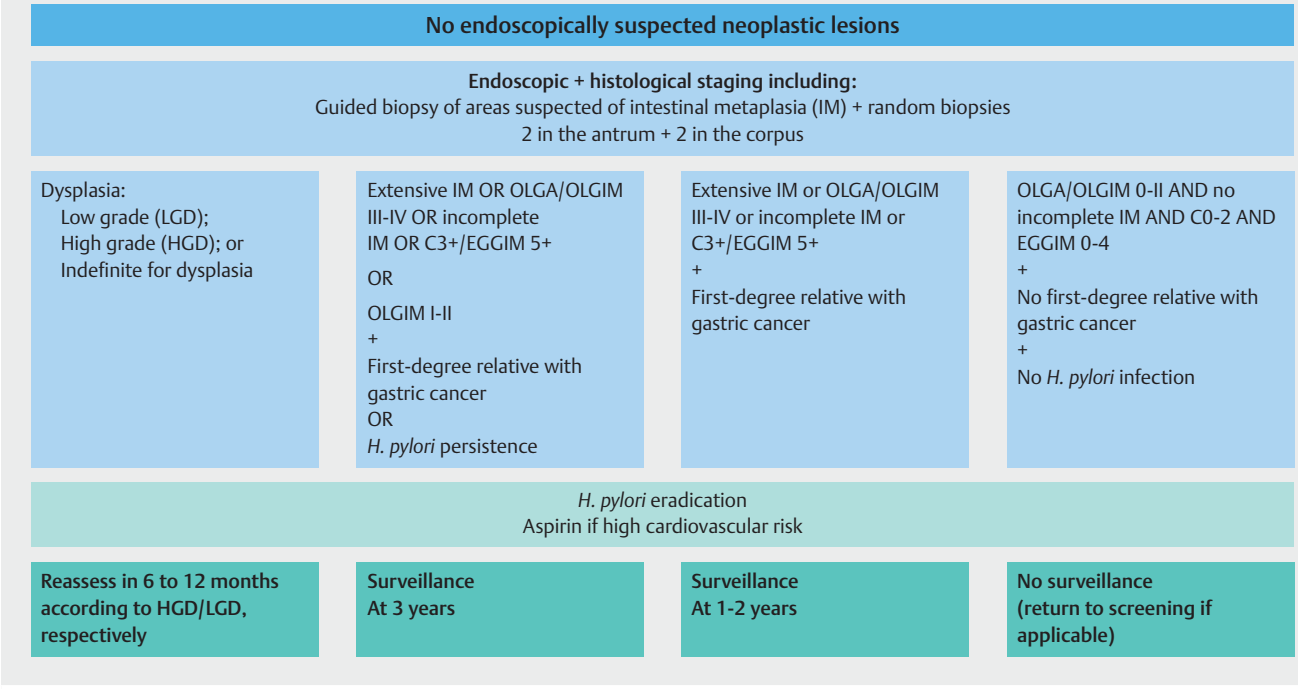
Role of *H. pylori* in patients with precancerous conditions and early gastric neoplasia

RECOMMENDATION

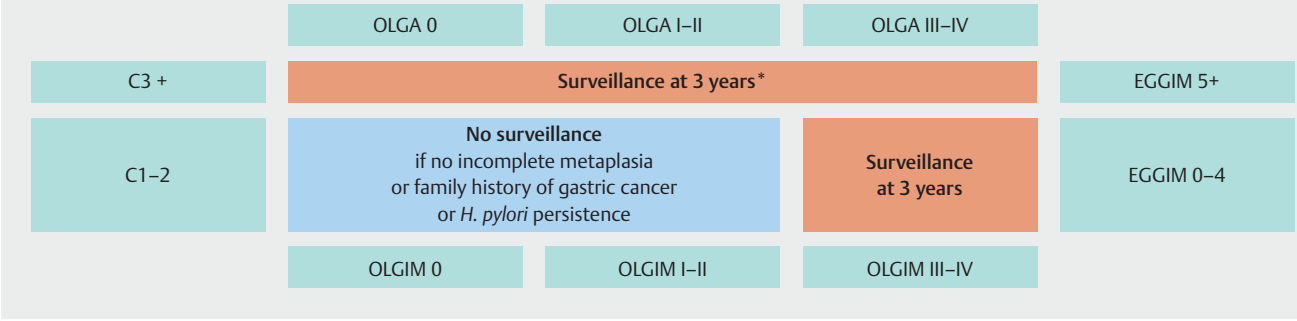
38 ESGE/EHMSG/ESP recommend *H. pylori* eradication in individuals with nonatrophic chronic gastritis and atrophic gastritis, to reduce the risk of gastric cancer. [Modified]

Strong recommendation/High quality; 100 % agreement.

The reduction of GC risk after *H. pylori* eradication is more obvious in individuals without baseline premalignant conditions, before the development of CAG or GIM (hazard ratio [HR] 0.37, 95 %CI 0.15–0.95) [301, 302], and also in the long term (8–10 years after the treatment) [303]. Even after CAG had been established, a Turkish study including 40 060 patients observed a significant improvement in the grade of CAG in the corpus and antrum after *H. pylori* eradication [304]. Also, a recent meta-analysis (15 studies included) showed that, compared with placebo or no treatment, *H. pylori* eradication improved CAG (RR 1.84, 95 %CI 1.30–2.61, $P < 0–01$) [305]. In



▶ **Fig. 10** Management of precancerous conditions (and nonvisible dysplasia or indefined). C3 + , C0–2, Kimura–Takemoto classification; EGGIM, endoscopic grading of gastric intestinal metaplasia; OLGA, operative link on gastritis assessment; OLGIM, operative link on gastric intestinal metaplasia.



▶ **Fig. 11** Comprehensive approach: both endoscopic and histological information must be considered for stratification of risk and allocation of individuals to different surveillance regimes (if no autoimmune gastritis is diagnosed). C3 + , C1–2, Kimura–Takemoto classification; EGGIM, endoscopic grading of gastric intestinal metaplasia; OLGA, operative link on gastritis assessment; OLGIM, operative link on gastric intestinal metaplasia. *Adjust to 1–2 years if first-degree relatives with gastric cancer.

a 20-year follow-up study in a high GC risk Hispanic population, treatment of *H. pylori* led to a significant regression of CAG to nonatrophic gastritis after 6 years [284]. The current evidence supports that *H. pylori* eradication therapy impacts on preventing the progression and improving the severity of preneoplastic conditions, such as chronic gastritis, especially in the earliest phases [306].

RECOMMENDATION

39 ESGE /EHMSG/ESP recommend that *H. pylori* eradication should be considered in patients with established gastric intestinal metaplasia. [Unchanged]

Conditional recommendation/Moderate quality; 100 % agreement.

H. pylori is the major etiological and risk factor for GC development [31,306]. It is largely accepted that *H. pylori* eradication is associated with decreased GC risk and incidence in healthy individuals [307,308]. However, the effects of *H. pylori* eradication on precancerous conditions were not consistently seen previously, emphasizing the concept of "point of no return" in the Correa cascade. One systematic review and one meta-analysis from 2020 found no decreased risk or incidence of GC in patients with precancerous conditions after *H. pylori* treatment [309,310]. Despite these data, *H. pylori* eradication induced improvement and regression in established atrophic gastritis and IM in two meta-analyses [305,310]. However, when the authors explored RCTs conducted outside China, the precancerous regression was not observed [305]. In both meta-analyses the authors only observed this association in RCTs with a follow-up greater than 5 years, suggesting slow reduction of inflammation after elimination of *H. pylori* infection because of the chronic inflammatory effects in gastric mucosa. A prospective study found a significant improvement in atrophy and inflammation after *H. pylori* eradication, highlighting the need for treatment of this infection [311]. These data are in line with the most recent international guidelines, which recommend *H. pylori* eradication in patients with GIM [30,31,312].

To conclude, new evidence was published after MAPS II regarding the impact of *H. pylori* eradication in patients with established precancerous conditions. Although a reduction in GC risk was not seen after *H. pylori* eradication in patients with established GIM, a regression of precancerous conditions was seen in long-term follow-up. It is important to mention that most of the RCTs were conducted in Asian populations, emphasizing the importance of conducting more studies on Western populations to validate these data.

RECOMMENDATION

40 ESGE/EHMSG/ESP recommend *H. pylori* eradication for patients with gastric neoplasia after endoscopic or surgical therapy. [Modified]

Strong recommendation/Moderate quality; 100% agreement.

New evidence strengthens recommendations for *H. pylori* eradication after endoscopic treatment of gastric precancerous or neoplastic lesions or subtotal surgical treatment of malignant lesions with remaining gastric mucosa [313,314].

In a randomized trial, it was shown that risk of metachronous GC was significantly reduced after successful eradication compared to placebo after 5.9 years' follow-up (HR 0.50, 95%CI 0.26–0.94; $P=0.03$) and even an improvement in atrophic changes was observed (in 48.4% vs. 15.0%, $P<0.001$) [303]. Another randomized trial reported comparable data about metachronous GC after endoscopic resection (4.1% vs. 8.2%, $P=0.01$) after 71.6 months' follow-up with an adjusted HR of 2.02 (95%CI 1.14–3.56; $P=0.02$) for the control group without *H. pylori* treatment [315]. The improvement of atrophy was confirmed in another study after 60 months of follow-up, when compared to persistent *H. pylori* infection ($P=0.029$) [316]. A systematic review and meta-analysis combining nine cohort studies with 2755 patients included, concluded a lower effect of *H. pylori* eradication in patients with severe atrophic gastritis and IM (RR 1.18, 95%CI 0.88–1.59, I^2 10%) [317].

RECOMMENDATION

41 ESGE/EHMSG/ESP recommend against testing for microbiota other than *H. pylori* for preventing or treating gastric precancerous conditions. [New]

Strong recommendation/Moderate quality; 100% agreement.

There is increasing evidence that microbiota other than *H. pylori* might play a role in gastric carcinogenesis [318–327]. Changes in the physiological environment along the carcinogenic cascade lead to altered microbial profiles [319,320,323]. Dysbiotic bacterial communities have been identified both in gastric precancerous conditions and even in gastric adenocarcinoma [319,320,323]. Animal studies demonstrated accelerated development of gastric precancerous conditions in germ-free mice infected with *H. pylori* and colonized with intestinal bacteria compared with *H. pylori*-infected mice, suggesting additional effects on gastric carcinogenesis [328,329].

Up to the present, there is no evidence to support the concept of analyzing gastric microbiota with the objective of stratifying individual risk or intervening to reduce the risk for the development of gastric precancerous conditions [330].

Role of non-*H. pylori* interventions in the management of early gastric neoplasia and precancerous conditions

RECOMMENDATION

42 ESGE/EHMSG/ESP recommend smoking cessation in individuals with precancerous conditions or after endoscopic treatment of superficial lesions. [New]

Strong recommendation/Low quality; 100% agreement.

Most data on the impact of lifestyle factors on the risk for metachronous or synchronous GC after ESD for early gastric cancer originate from East Asia. In a multicenter prospective study from Japan including 850 patients, current smoking status remained an independent risk factor for synchronous lesions (within 1 year of treatment) in the multivariate analysis (OR 2.33). In contrast, alcohol intake, salt consumption, as well as diet content of yellow or green vegetables and fruit, and consumption of green tea as protective factor, did not reveal a significant risk effect in univariate analysis [331]. This confirmed the data of an earlier study of the same group, following 439 patients for 53.6 months, which also showed a dose–

response relationship for smokers with >20 pack-years [332]. Similar results were reported for a cohort of elderly patients >75 years of age. Patients who stopped smoking after ESD of early GC have also been shown to have a lower incidence of metachronous lesions [333].

European data on a Portuguese cohort of 230 patients who were followed for a median of 33 months after ESD also found that both current and former smoking status represented an independent risk factor for synchronous lesions [334]. As mentioned above, alcohol intake was not confirmed as an independent risk factor in these studies.

While some studies suggest an impact of smoking on both the development and progression of precancerous conditions of the stomach [335,336], a meta-analysis from 2014 could not confirm this issue [337]. Thus, there are no comprehensive studies that highlight an impact of smoking or dietary factors on the progression of precancerous conditions. Nevertheless it seems reasonable, as an intervention with further impact, to recommend stopping smoking.

RECOMMENDATION

43 ESGE/EHMSG/ESP suggest that patients with an appropriate indication for proton pump inhibitors (PPIs) or histamine (H2) receptor antagonists (H2RAs) should not discontinue the medication. [New]

Conditional recommendation/Low quality; 100% agreement.

An increasing body of literature suggests a positive association of long-term PPI intake and individual GC risk, but results of individual studies remain highly variable and there is no evidence for a causal link. A hypothesis states that the increased gastrin secretion with PPI intake has a trophic effect on the gastric mucosa, also resulting in enterochromaffin-like (ECL) cell hyperplasia and the possibility of type 1 gastric neuroendocrine tumors [338]. Several recent meta-analyses have reported a 1.5– to 2-fold increased risk for individuals on PPI [339–350]. These referred almost universally to noncardia GC. The data on the effect on the incidence of cardia cancer are heterogeneous [339,341]. Most of these publications include data from Western and, in particular, European cohorts, but only a few of the authors include a dedicated analysis of these cohorts. Some of these report a maintained effect, although weaker than for Asian cohorts [342,348], others do not confirm this [343]. Zhang et al. published an overview on the meta-analyses that have been published up to 2022 [351]. All analyses share similar limitations, including significant heterogeneity of the studies as well as a high likelihood of publication bias. There is lack of adjustment for relevant confounding factors which can be seen across most of these studies, including *H. pylori* status, tobacco consumption, family history, and previous treatment or co-medication. Given these limitations, and in view of a lack of evidence for a causal relationship, PPI use should not be restricted for patients with a clear indication for use. Long-term use is feasible in the right clinical context, that is, at low dose for the correct indication.

Several studies on the impact of long-term PPI intake on the incidence of gastric atrophy or IM are suggestive of a positive association, but most meta-analyses fail to confirm a significantly increased risk [338,352–354]. In a meta-analysis by Lv et al., only a subanalysis of four studies with a follow-up of at least 12 months demonstrated a twofold risk increase (RR 2.21, 95%CI 1.47–3.33) [355]. This remained significant only for cases with IM (RR 1.93, 95%CI 1.03–3.63), not for atrophy (RR 1.50, 95%CI 0.91–2.47). The authors note a high likelihood of publication bias and significant study heterogeneity. There remains an unaccounted variation regarding the type of PPI used as well as dose and treatment duration. About half of the studies compare PPI intake with the effect of antireflux surgery which is also likely to have an impact on gastric physiology. Furthermore, most studies are not well controlled for *H. pylori* status which remains a major confounding factor. There are no good quality data suggesting an increased risk of progression of precancerous conditions on PPI [352].

Data on the impact on the recurrence of endoscopically treated cancer or of metachronous lesions are scarce. Oura et al. published data on one cohort of 418 patients with various durations of PPI treatment and could not show an effect (HR 1.04, 95%CI 0.10–1.09) [356]. The results were not adjusted for smoking status, family history of GC, or *H. pylori* eradication status. Randomized controlled trials on this issue are needed.

There is no clear evidence to suggest that long-term intake of H2RA has an effect on individual GC risk. The majority of studies investigate the intake of H2RAs in comparison to PPIs. Only a few studies analyzed the risk of H2RA alone. A detailed meta-analysis on the effect of long-term intake of acid-suppressive medication by Ahn et al. suggests that long-term H2RA intake is also associated with an increased risk for GC (OR 1.39, 95%CI 1.19–1.64) [340]. This is further supported by other analyses that do not confirm the risk attributed to PPI intake, when comparison is made with individuals on H2RA [339,346]. While there are more abundant data on the association of gastric neoplasia with PPI, H2RAs should also be used with caution.

For these patients, with a need for long-term PPI therapy, it may be reasonable to test and treat for *H. pylori*.

RECOMMENDATION

44 ESGE/EHMSG/ESP suggest that low-dose daily aspirin can be considered for prevention of gastric cancer in selected individuals with high risk for cardiovascular events. [Unchanged]

Conditional recommendation/Low quality; 100% agreement.

Since the MAPS II guideline, five new meta-analyses on mostly observational studies have been published exploring the chemopreventive effects of aspirin and other nonsteroidal anti-inflammatory drugs (NSAIDs) against GC [357–361]. The

most recent meta-analysis, including 18 studies, was preceded by a nationwide Korean cohort study with a total of 63 678 participants after large-scale propensity score-matching. A lower risk for GC was reported for regular aspirin users during a median 4.7-year observation period (HR 0.72, 95 %CI 0.60–0.85) [357]. The pooled analysis further corroborated the beneficial effect of aspirin use for at least 365 days in GC protection, although with significant heterogeneity noticed according to study design (HR 0.77, 95 %CI 0.70–0.86, I^2 87 %; and HR 0.73, 95 %CI 0.59–0.90, I^2 61 %; for case–control and cohort studies, respectively) [357]. Furthermore, no difference in effect size was observed between Eastern and Western populations (OR 0.79, 95 %CI 0.70–0.89; and OR 0.73, 95 %CI 0.56–0.95; respectively) [357]. In a meta-analysis by Niikura et al. the daily use of aspirin was associated with the highest preventive benefit against GC (daily, RR 0.65, 95 %CI 0.52–0.83, vs. monthly, RR 0.77, 95 %CI 0.55–1.07, vs. occasionally, RR 1.09, 95 %CI 0.77–1.54), and reduced noncardiac GC incidence was observed (RR 0.74, 95 %CI 0.58–0.94, vs. RR 0.84; 95 %CI 0.54–1.23 for cardiac GC) [361]. Considering that NSAIDs and aspirin have a potential for serious adverse events it is the opinion of the present authors that they cannot be recommended specifically for this purpose. The exception may be low-dose aspirin since it has a better safety profile and its beneficial effects are more generalized, reducing also cardiovascular death risk and the risk of development of other cancers, and therefore it could be considered in selected patients.

Thus far, there is no conclusive evidence confirming a protective effect of long-term use of aspirin against the development of metachronous lesions after endoscopic resection of early gastric cancer. Data on this topic originate mostly from retrospective cohort studies and while the results are suggestive of a trend towards reduced incidence, the difference from the control group was not significant in any of the studies [362, 363].

RECOMMENDATION

45 ESGE/EHMSG/ESP recommend against the use of other specific drugs or supplements (including probiotics) for chemoprevention in any clinical setting outside of clinical studies. [Modified]

Conditional recommendation/Low quality; 96 % agreement.

Statins There is no adequate evidence from RCTs, but observational studies suggest a lower risk for GC in individuals on statin treatment. Several meta-analyses report a risk reduction of 30 %–40 % [364–370]. However, publications that included a distinct analysis of data from Western populations show less of an impact (10 %–20 % risk reduction) compared to Asian cohorts [366–368, 370]. There is a general agreement across these publications that there is broad heterogeneity between studies and a high likelihood of publication bias. There are no good data on the impact of statin intake on the risk for precancerous conditions of the stomach, but one Korean study addressed the risk of metachronous lesions after endoscopic resection of early GC [371]; statin intake resulted in a risk reduction of over 80 % in the multivariate analysis (HR 0.17, 95 % CI 0.13–0.24).

COX-2 inhibitors Meta-analyses have highlighted the role of COX-2 inhibition as an effective approach in GC prevention [372–374]. Nevertheless, more recent studies on this topic remain mostly elusive [375]. A 2013 prospective nonrandomized study on the role of selective COX-2 inhibitor treatment in patients with precancerous gastric conditions demonstrated intestinal metaplasia regression was more frequent in patients on celecoxib after *H. pylori* eradication after 1 year (44.3 % vs. 14.3 %) [376]. Other studies suggest that inhibition of COX may slow progression of gastric precancerous conditions. A double-blind RCT, including 1024 participants who received *H. pylori* eradication treatment or placebo followed by celecoxib or placebo showed that regression of gastric precancerous conditions significantly increased both in the eradication group (59 % vs. 41 % placebo) and in the celecoxib group (53 % vs. 41 % placebo) [377]. However, in this study no statistically significant benefit was observed for celecoxib after *H. pylori* eradication.

Metformin It remains controversial as to whether metformin is associated with a reduced risk of GC in patients with diabetes. Up to the present, four systematic reviews and meta-analyses have looked at this issue. Franciosi et al. analyzed the results of 12 randomized controlled trials and 41 observational studies [378]. While no significant difference was observed in the randomized trials, the evidence from the observational studies shows an overall reduced risk of all-cause and cancer-related mortality (in particular GC) for patients on metformin (OR 0.83, 95 %CI 0.76–0.91). A systematic review by Li et al. does not report a significant difference in GC incidence, but an association of metformin intake with better prognosis [379]. Shuai et al. reviewed 11 nonrandomized studies and concluded that metformin was associated with reduced GC recurrence (HR 0.79, 95 %CI 0.62–1.0], but the effect was particularly evident in Asian populations [380]. The data from a Korean nationwide population-based cohort study did not show a significant association between metformin use and GC development, although the data from a linked meta-analysis confirmed an effect (0.84; 95 %CI 0.73–0.96) [357].

Supplements Vitamin and nutritional supplements are proposed for prevention or improved prognosis of GC [381, 382]. The prospective long-term interventional Linxians trial evaluated multiple interventions including retinol/zinc, riboflavin/niacin, vitamin C/molybdenum, selenium, and vitamin E/beta-carotene compared to placebo [383, 384]. Nutritional intervention for 6 years with more than 20 years of post-intervention follow-up showed no effect on mortality. The Shandong Interventional Trial showed that vitamin but not garlic supplementation (for 7 years) was associated with a reduced incidence of GC within 22 years of long-term follow-up after *H. pylori* treatment [385–388]. The Nutrition Intervention NIH study evaluated several supplements, including iron, zinc, selenium, calcium, folic acid, vitamin A, beta-carotene, vitamin C, and vitamin E [389]. The study provided evidence that multivitamin supplementation was associated with a reduced risk of upper GI

cancers in general, but an increased risk of gastric noncardia cancer (HR 1.59, 95 %CI 1.24–2.05]. According to two systematic reviews and meta-analyses of nonrandomized trials, vitamin D intake is not associated with a reduced incidence of GC [370, 390]. A randomized controlled trial from Japan showed no impact on GC recurrence in patients on vitamin D supplementation [391, 392]. Selenium is not associated with a beneficial effect and a reduction in cancer risk according to a Cochrane review and meta-analysis [393].

Probiotics There are no high quality prospective randomized controlled trials addressing the effect of probiotics on GC incidence, progression of precancerous conditions, or effect on the development of metachronous cancers.

Special settings

Hereditary syndromes with increased risk of GC

RECOMMENDATION

46 ESGE/EHMSG/ESP suggest that in individuals with hereditary syndromes with increased risk of gastric cancer, endoscopic surveillance should follow recommendations for the specific syndrome or according to the gastric mucosal changes, whichever interval is shorter. [New]

Conditional recommendation/Very low quality; 100 % agreement.

Although most GCs are sporadic, approximately 1 %–3 % are related to known cancer susceptibility syndromes and/or genetic causes [394]. Patients with hereditary diffuse GC, gastric adenocarcinoma and proximal polyposis of the stomach, familial intestinal GC, classic and attenuated familial polyposis, MUTYH-associated polyposis, Peutz–Jeghers syndrome, juvenile polyposis syndrome, Lynch syndrome, and Li–Fraumeni syndrome are at increased risk of GC [394]. Detailed gastric surveillance protocols for each of these syndromes are outside the scope of this Guideline. However, some evidence exists for Lynch syndrome [395–397] and limited evidence for FAP patients [398], identifying *H. pylori*, advanced stages of gastritis, and family history of GC as additional risk factors for GC in these groups of individuals. Thus, we do suggest that surveillance intervals be tailored to individual patient characteristics and follow the shortest interval.

Autoimmune gastritis

RECOMMENDATION

47 ESGE/EHMSG/ESP suggest that patients with autoimmune gastritis should have high quality endoscopic follow-up every 3 years to detect gastric cancer and neuroendocrine tumors. [New]

Conditional recommendation/Low quality; 96 % agreement.

Autoimmune gastritis is a chronic condition at risk for the development of neuroendocrine tumors and GC [399]. An advanced stage of autoimmune gastritis, when gastric intrinsic factor and vitamin B12 deficit occur, is represented by pernicious anemia [400], a condition associated with a higher risk of GC. In a case–control study, 5 % of patients with GC presented autoimmune gastritis and pernicious anemia was the leading clinical sign (OR 22.0) [401], whilst in a retrospective study on patients with autoimmune gastritis, 5.9 % of patients presented high grade dysplasia or adenocarcinoma [402]. In another retrospective study, the incidence rate of GC in patients with autoimmune gastritis was 14.2 cases per 1000 person-years [403], and a very recent meta-analysis conducted on 13 studies, showed an incidence rate of GC of 0.14 % per person-year [404].

Regarding endoscopic follow-up, in a longitudinal cohort study on 160 patients (76 % had autoimmune gastritis), 3 GCs were found at a 3-year follow-up and all the patients had autoimmune gastritis and 1 of them presented pernicious anemia [405].

Common variable immunodeficiency

RECOMMENDATION

48 ESGE/EHMSG/ESP suggest that patients with common variable immunodeficiency (CVID) should have a high quality endoscopy at the time of diagnosis and then should be followed up according to staging of precancerous conditions and/or presence of autoimmune gastritis. [New]

Conditional recommendation/Very low quality; 100 % agreement.

GC seems more prevalent [406–410], and develops earlier [407, 411–414] in patients with CVID compared to the general population, but large sample or population-based studies are missing. An association between CVID and autoimmune gastritis/pernicious anemia has been described in several studies [411, 414–417]. Because of the Ig defect, endoscopic screening or breath-test for *H. pylori* and for gastric precancerous conditions including autoimmune gastritis diagnosis should be recommended.

Other situations

Autoimmune diseases Several autoimmune diseases have been studied for the risk of developing GC. In a recent meta-analysis [418], 52 studies were included and 24 different types of autoimmune diseases having at least two studies, were considered. Dermatomyositis showed the highest relative risk (RR 3.69, 95 %CI 1.74–7.79), followed by pernicious anemia (RR 2.84 95 %CI 2.30–3.50), and Addison disease (RR 2.11, 95 %CI 1.26–3.53). Dermatitis herpetiformis, IgG4-related disease, primary biliary cirrhosis, diabetes mellitus type 1, systematic lupus erythematosus, and celiac disease showed RRs between 1.36 and 1.74.

Other autoimmune diseases showed a slight increase in the risk of developing GC.

ESGE does not recommend systematic surveillance in these patients but an upper endoscopy with gastric mapping or non-invasive tests for the presence of *H. pylori* could be useful, in particular for the detection of associated autoimmune gastritis.

Immunosuppressive therapies Regarding the risk of GC in patients receiving immunosuppressive therapies, the scarce data available in the literature do not allow provision of specific recommendations on surveillance in this context [419–422]. Most of the studies are retrospective and concern mainly transplant recipients and their risk of malignancies in general, rather than specifically focusing on GC [423–430].

According to certain studies, patients who received renal transplants had a higher incidence of GC than the overall population. As a result, the authors suggested regular endoscopic surveillance [423,424]. A meta-analysis showed that the incidence of GC (among other types of cancers) is significantly increased in patients with a diagnosis of HIV/AIDS and who underwent transplants, underlining the importance of immunosuppression in the development of malignancies [430]. Nevertheless, the paucity and the weakness of the supporting data do not allow definition of a standardized surveillance program.

Undoubtedly, further studies are needed to better understand the correlation between immunosuppressive therapy and the risk of GC.

Gastric MALT lymphoma (GML) Patients with gastric MALT (mucosa-associated lymphoid tissue) lymphoma present a higher incidence of GC than the general population as reflected by a population-based study (RR 4.32, 95%CI 2.64–6.67) [431], and a nationwide study (6-fold increase as compared with the general population) [432]. In a multicenter retrospective study including 474 patients with primary gastric lymphoma between 2010 and 2020, 24 cases of gastric adenocarcinoma (5.1%) were identified [433]. In a long-term (median 122 months) follow-up study of 120 patients with GML after *H. pylori* eradication, a significantly higher incidence of GC (8.567; 95%CI 3.566–20.582) was observed as compared to the general population [434]. One systematic review of the literature has been reported on synchronous GML and gastric adenocarcinoma [435]. Patients with GML present a higher rate of gastric precancerous conditions (68% [436], 33% [437], 46% [438], and 57.9% [439]) than nonlymphoma patients (22% [219] and 3.2% [219]; historical comparisons).

Gastric precancerous conditions in patients with GML seem to progress more rapidly than in nonlymphoma patients (historical comparisons): with progression to dysplasia/cancer in 13.5% of patients during 5 years [438], progression to more severe intestinal metaplasia in 21.2% of patients during a median 30.5-month follow-up [439,440], and frequent and rapid progression of atrophy and GIM [439,440], as compared to 4%–14% in patients without lymphoma [218,220]. In the presence of residual GML, the risk of GC appears even higher and gastric precancerous conditions may progress even after remission of GML [441]. Moreover, data coming from several fundamental studies indicate several common pathways in gastric carcinogenesis and lymphomagenesis [442,443]. Therefore, ESGE/EHMSG/ESP recommends that after remission patients with gastric MALT lymphoma should be followed up according to the stage of precancerous conditions, and in the absence of precancerous conditions, every 5 years (expert opinion).

Uptake of guideline recommendations

It has been over a decade since the first international guideline on the diagnostic assessment and management of individuals with atrophic gastritis, GIM, and dysplasia of the stomach was published [4]. However, to our knowledge, few studies have explored the extent of adherence to this guideline [444–447].

In the same year that the first MAPS guideline was published, a nationwide survey was conducted by two Italian national gastroenterology societies: the Italian Association of Hospital Gastroenterologists and Digestive Endoscopists and the Italian Society of Digestive Endoscopy. This survey included 24 endoscopy units across Italy and a total of 979 patients with dyspeptic symptoms. The results showed that separate descriptions of antral and corporal biopsies were included in 69% of the pathology reports, while the Sydney system was applied in only one third of the histology reports [446]. In 2018, the Italian Society of Digestive Endoscopy conducted a new survey among its endoscopist members. The results indicated that approximately nine out of ten gastroscopists applied the biopsy protocol according to MAPS guidelines for diagnosing and staging atrophic gastritis and intestinal metaplasia [445].

A retrospective study was conducted on patients diagnosed with GIM or gastric atrophy at three centers in the Netherlands and the UK between 2012 and 2019. The authors analyzed the adequacy of surveillance, following histological diagnosis at the index endoscopy, based on the 2012 ESGE guidelines [447]. According to their results, surveillance was adequately performed in 54.3% of patients.

In a study conducted in the USA, 50 patients with newly diagnosed GIM based on gastric biopsy histopathology performed between 2016 and 2019 were included. The study assessed adherence to GIM management recommendations as defined by the American Gastroenterological Association [312] and ESGE [9], including: (a) ordering *H. pylori* testing after GIM diagnosis; (b) obtaining subsequent gastric mapping biopsies if gastric biopsy location, and thus extent of GIM, was not initially specified; (c) recording the family history of GC in the medical record by the gastroenterologist; and (d) including a recommendation on interval for surveillance endoscopy in the procedure note following GIM diagnosis by biopsy. The results showed that 42.3% of GIM patients had a *H. pylori* test recommended after GIM was detected, 22.0% had antrum and gastric body biopsies separated into labeled specimen jars, 14.0% had gastric mapping biopsies recommended or performed, 2.0% had surveillance endoscopy interval recommended, and 32.0% had documentation of family history of GC in the medical record [444].

From January 2010 to February 2023, at least 15 guidelines or consensus statements addressing the diagnosis and management of GIM have been issued, emphasizing the importance

of GIM as a precancerous condition and the need for a risk-stratified approach to endoscopic surveillance [6]. Future studies are needed that evaluate the uptake of these guidelines in clinical practice.

The "green box"

How might MAPS III strategies improve green sustainability in endoscopy practice?

- ***Appropriate diagnostic and follow-up examinations*** Inappropriate digestive endoscopy results in increased overall carbon footprint (in Europe estimated to be 30 804 CO_2 metric tons). The MAPS III guides clinical practice on indications namely gastric cancer or gastric precancerous conditions and screening and surveillance endoscopy, reducing the number of inappropriate diagnostic examinations as well as inappropriate endoscopic follow-up (e. g. for atrophic gastritis restricted to the antrum without dysplasia and no additional risk factors). Additionally, noninvasive biomarkers (e. g., PG I serum levels or/and PG I/II ratio) may allow screening, potentially avoiding endoscopy.
- ***Application of virtual chromoendoscopy (VCE)*** Application of an endoscopy-led staging system (incorporating the Kimura–Takemoto classification for CAG and EGGIM for intestinal metaplasia) as recommended by the MAPS III Guideline will result in fewer endoscopies, reducing the environmental impact of unnecessary follow-up procedures. Developments in AI with computer-aided characterization may also allow a further gain in optical diagnosis, further limiting the need for histology.
- ***Biopsy sampling and histology*** Biopsy sample processing, including production and transport of chemical reagents, waste, and electricity consumption, accounts for a large proportion of endoscopy-related greenhouse gas emission. MAPS III advocates the use of advanced optical diagnosis via implementation of virtual chromoendoscopy, limiting histological examination only to necessary cases, thus reducing the number of samples and consequently the environmental impact, without affecting diagnostic accuracy even in non-expert hands. Absence of an endoscopic pattern suggestive of severe atrophy/intestinal metaplasia could result in the use of a single vial for biopsy specimens (for *H. pylori* diagnosis) or completely preclude biopsy (when the *H. pylori* status is known), saving 0.29 kg of CO_2e (carbon dioxide equivalent) per sample container avoided.
- ***Energy optimization*** The energy consumption of radiology examinations, for example, MRI and contrast-enhanced CT scanning, makes a significant contribution to overall energy usage of radiology departments. The carbon footprint of MRI (including both in-hospital process energy at 29 kWh per patient and off-hospital energy at about 75 kWh per patient), required not only for electricity consumed during use but also for manufacturing the scanner itself and disposable and reusable products, may reach up to a maximum of 22.4 kg of CO_2e. The MAPS III Guideline does not recommend routine performance of three modalities, contributing to an environmentally friendly aspect.

Research agenda

The first cohort studies on the clinical relevance of atrophic gastritis and gastric intestinal metaplasia date back to the 1960 s. Since then, our understanding of these conditions has markedly progressed. This knowledge was first translated into a clinical guideline in 2012 with the publication of the first MAPS Guideline (MAPS I). That Guideline not only aimed to improve and standardize clinical practice, but also to identify a research agenda to allow further improvement of our management of patients with gastric atrophy and metaplasia. With this MAPS III Guideline, an updated research agenda remains as relevant as before.

Our future research should aim to address the following issues.

We need to improve our understanding of determinants of disease progression and move beyond the current phenotyping of severity and extent of gastric IM. The latter details are helpful in excluding patients at low risk for development of cancer, but are insufficiently selective in identifying patients at high risk.

Further, we also need to align endoscopic protocols, and improve training of endoscopists in the use of these protocols. When doing so, AI-based tools are likely to be helpful. To improve clinical practice, these tools should help to increase selectivity, rather than merely expand clinical demand for endoscopic surveillance. Next, to allow clinicians to understand their performance, we need appropriate, simple, and reproducible quality assurance measures and standards.

Finally, we need to understand the clinical efficacy and cost–effectiveness of therapies that aim to alter the natural course, both of gastric IM and after treatment of early cancer.

▶ **Appendix A** Components to be included in endoscopic report

Report	Required data
Endoscopy (pre-endoscopic submucosal dissection [ESD])	▪ Paris classification ▪ Ulceration (Y/N) ▪ Size (mm) ▪ Inclusion of images is mandatory, preferably within the endoscopic report; they should be clear and well-labeled
Endoscopy (ESD)	▪ Exact location ▪ Paris classification ▪ Ulceration (Y/N) ▪ Size (mm) ▪ En bloc versus piecemeal ▪ Inclusion of images is mandatory, preferably within the endoscopic report
Report	Required data
Stage of precancerous conditions	▪ Refer to the system used (eg. Kimura–Takemoto [KT], or endoscopic grading of gastric intestinal metaplasia [EGGIM]) ▪ Inclusion of images is mandatory

▶ **Appendix B** Components to be included in histology report

Pathology of endoscopic submucosal dissection (ESD) specimens	▪ Most severe histology observed and differentiation ▪ Size [mm] ▪ Horizontal margin – negative, HM0 (preferably >1 mm) – positive for carcinoma, HM1c, or dysplasia, HM1dh (for high grade dysplasia), HM1 dl (for low grade dysplasia) ▪ Vertical margin – negative, VM0 (preferably > 1 mm) – positive, VM1; only applicable for carcinoma ▪ Maximum depth of invasion sm (taken from the lowest fibre of the muscularis mucosae) ▪ Lymphatic and/or venous infiltration (L0, L1; V0, V1) ▪ R0 if en bloc, and horizontal and vertical margins negative ▪ RX (nonassessable), if en bloc or piecemeal, and horizontal margin positive (HM1) and vertical margin negative (VM0) ▪ R1 if vertical margin positive (VM1)
Pathology of precancerous conditions	▪ Chronic gastritis (Y/N; severity) ▪ Activity (Y/N; severity) ▪ Glandular atrophy (none, mild, moderate, severe) ▪ Intestinal metaplasia (none, mild, moderate, severe; ideally complete vs. incomplete) ▪ Dysplasia (no; low grade; high grade) ▪ *H. pylori* (Y/N; method of detecion (Giemsa, immunohistochemical [IHC]) ▪ Pathological diagnosis

Disclaimer

The legal disclaimer for ESGE guidelines [448] applies to this Guideline.

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Competing interests

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Supplementary material:

Management of epithelial precancerous conditions and early neoplasia of the stomach (MAPS III): European Society of Gastrointestinal Endoscopy (ESGE), European Helicobacter and Microbiota Study Group (EHMSG) and European Society of Pathology (ESP) Guideline update 2025

Topics and Working groups

Topics	Working groups
1. Screening and cost–effectiveness of interventions	Manon Spaander Miguel Areia
2. Diagnosis of precancerous conditions and early neoplasias of the stomach	Diogo Libânio Marcin Romańczyk Georgios Tziatzios Lumir Kunovsky
3. Endoscopic resection and management of superficial early cancer lesions	Hugo Ikuo Uchima Koecklin Pedro Pimentel-Nunes João Santos-Antunes
4. Endoscopic follow-up of individuals with precancerous conditions	Mário Dinis-Ribeiro Nicolas Chapelle Gloria Fernández Esparrach Ilja Tacheci Pedro Marcos
5. Role of *H. pylori* eradication in the management of precancerous conditions and after early neoplasia resection	Christian Schulz Leticia Moreira Ricardo Marcos-Pinto
6. Role of other non-*H. pylori* interventions	Jan Borschein Alexander Link Carina Pereira
7. Management of individuals in specific settings that also harbor precancerous conditions	Tamara Matysiak-Budnik Gianluca Esposito Mónica Garrido

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MAPS III | PICO & Queries & Evidence Tables
Version 2.0 | October 7th 2024

Section	**SCREENING FOR GC AND GASTRIC PRECANCEROUS CONDITIONS**										
Sentence	**ESGE/EHMSG/ESP suggest population based endoscopic screening for gastric cancer (and precancerous conditions) every 2 to 3 years in high-risk regions (ASR >20 per 100,000 p-y) or every 5 years in intermediate-risk regions (ASR 10-20 per 100,000 p-y), if cost-effectiveness has been proven and resources are available.**										
GRADE	**Strength of recommendation: Conditional**	**Quality of evidence: Low**									
Sentence	**ESGE/EHMSG/ESP suggest against population-based endoscopic screening for gastric cancer (and precancerous conditions) in low-risk regions (ASR <10 per 100,000 p-y).**										
GRADE	**Strength of recommendation: Conditional**	**Quality of evidence: Low**									
PICO	How are low-, intermediate-, and high-risk areas for gastric cancer defines? And is screening recommended? Is there an indication for case finding for GC in low- and intermediate-risk areas? P: Regions with low, intermediate, and high risk for gastric cancer. I: Definition and criteria for risk categorization and recommendations for screening. C: No specific definitions or guidelines for screening in these areas. O: Defining regional risk for gastric cancer and the appropriateness of screening.										
Query(ies) and databases searched	Search: ((cost-effectiveness) AND (early detection gastric cancer)) AND (gastric cancer screening) Filters: Meta-Analysis, Randomized Controlled Trial, Systematic Review. (("cost effectiveness analysis"[MeSH Terms] OR ("cost effectiveness"[All Fields] AND "analysis"[All Fields]) OR "cost effectiveness analysis"[All Fields] OR ("cost"[All Fields] AND "effectiveness"[All Fields]) OR "cost effectiveness"[All Fields]) AND (("early diagnosis"[MeSH Terms] OR ("early"[All Fields] AND "diagnosis"[All Fields]) OR "early diagnosis"[All Fields] OR ("early"[All Fields] AND "detection"[All Fields]) OR "early detection"[All Fields]) AND ("stomach neoplasms"[MeSH Terms] OR ("stomach"[All Fields] AND "neoplasms"[All Fields]) OR "stomach neoplasms"[All Fields] OR ("gastric"[All Fields] AND "cancer"[All Fields]) OR "gastric cancer"[All Fields])) AND (("stomach neoplasms"[MeSH Terms] OR ("stomach"[All Fields] AND "neoplasms"[All Fields]) OR "stomach neoplasms"[All Fields] OR ("gastric"[All Fields] AND "cancer"[All Fields]) OR "gastric cancer"[All Fields]) AND ("diagnosis"[MeSH Subheading] OR "diagnosis"[All Fields] OR "screening"[All Fields] OR "mass screening"[MeSH Terms] OR ("mass"[All Fields] AND "screening"[All Fields]) OR "mass screening"[All Fields] OR "early detection of cancer"[MeSH Terms] OR ("early"[All Fields] AND "detection"[All Fields] AND "cancer"[All Fields]) OR "early detection of cancer"[All Fields] OR "screen"[All Fields] OR "screenings"[All Fields] OR "screened"[All Fields] OR "screens"[All Fields]))) AND Search: ((cost-effectiveness) AND (early detection gastric cancer)) AND (gastric cancer screening) Filters: in the last 10 years (("cost effectiveness analysis"[MeSH Terms] OR ("cost effectiveness"[All Fields] AND "analysis"[All Fields]) OR "cost effectiveness analysis"[All Fields] OR ("cost"[All Fields] AND "effectiveness"[All Fields]) OR "cost effectiveness"[All Fields]) AND (("early diagnosis"[MeSH Terms] OR ("early"[All Fields] AND "diagnosis"[All Fields]) OR "early diagnosis"[All Fields] OR ("early"[All Fields] AND "detection"[All Fields]) OR "early detection"[All Fields]) AND ("stomach neoplasms"[MeSH Terms] OR ("stomach"[All Fields] AND "neoplasms"[All Fields]) OR "stomach neoplasms"[All Fields] OR ("gastric"[All Fields] AND "cancer"[All Fields]) OR "gastric cancer"[All Fields])) AND (("stomach neoplasms"[MeSH Terms] OR ("stomach"[All Fields] AND "neoplasms"[All Fields]) OR "stomach neoplasms"[All Fields] OR ("gastric"[All Fields] AND "cancer"[All Fields]) OR "gastric cancer"[All Fields]) AND ("diagnosis"[MeSH Subheading] OR "diagnosis"[All Fields] OR "screening"[All Fields] OR "mass screening"[MeSH Terms] OR ("mass"[All Fields] AND "screening"[All Fields]) OR "mass screening"[All Fields] OR "early detection of cancer"[MeSH Terms] OR ("early"[All Fields] AND "detection"[All Fields] AND "cancer"[All Fields]) OR "early detection of cancer"[All Fields] OR "screen"[All Fields] OR "screenings"[All Fields] OR "screened"[All Fields] OR "screens"[All Fields]))) AND (y_10[Filter])										
Table of evidence											

Study ID	Study design	Risk of Bias (alinea(s)) *	Quality Score	Consistency Score	Directness Score	Publication bias †	Reported ICER	Effect size Score **(0 to**	Evidence Level¶	Type of study according to SIGN	Recommendation SIGN

	Score		(0 to -2) **	(-1 to 1) #	(0 to -2) @	(0: No, 1: Yes)		2) §															
									High	Mod	Low	Very Low	1++	1+	1-	2++	2+	2-	3	4	A	B	C	D
36765621 Januszewicz, W (2023)	2	Review to provide update on existing screening programs in high-risk countries and potentially applicable gastric cancer-screening options in intermediate- and low-risk regions.	-1	1	0	n/a	n/a	n/a	x				x									x		
38131423 Libanio, D (2017)	2	Markov model to assess the cost-effectiveness of AI for GC detection in settings with different GC incidence and different accuracies of AI systems Compared no screening versus single EGD at 50 years versus stand-alone EGD every 5/10 years versus combined EGD and screening colonoscopy once or twice per decade in Netherlands, Italy and Portugal.	-1	0	-1	n/a	n/a	n/a		x				x								x		
32052404 Sa̧ftoiu, A (2020)	2	ESGE position statement on the role of gastrointestinal endoscopy in the screening of digestive tract cancers in Europe using a structured PICO framework. Individuals with known precancerous gastric lesions were excluded.	-1	0	0	n/a	n/a	n/a	x											x				x
32728390 Canakis, A. (2020)	2	Systematic review, decision model analyses of upper endoscopy for gastric cancer screening and preneoplasia	0	1	0	n/a	n/a	n.a	x					x								x		

Sentence	**ESGE/EHMSG/ESP recommend that a diagnostic gastrointestinal endoscopy (endoscopic opportunistic diagnosis) should include screening for GC as well as the diagnosis and stratification of risk of precancerous conditions irrespective of country of origin.**	
GRADE	**Strength of recommendation: Strong**	**Quality of evidence: Moderate**
PICO	Is there an indication for case finding for GC in low- and intermediate-risk areas? Is endoscopic screening/surveillance of premalignant gastric lesions/gastric cancer cost-effective in low/intermediate risk areas? P: Individuals in low- and intermediate-risk areas for gastric cancer. I: Case finding for gastric cancer. C: No case finding or standard care. O: Indication for case finding.	
Query(ies) and databases searched	Search: (risk assesment) AND (early detection gastric cancer) Database: PubMed Filters: Meta-Analysis, Randomized Controlled Trial, Systematic Review (("risk"[MeSH Terms] OR "risk"[All Fields]) AND ("assesed"[All Fields] OR "assesment"[All Fields] OR "assesments"[All Fields]) AND (("early diagnosis"[MeSH Terms] OR ("early"[All Fields] AND "diagnosis"[All Fields]) OR "early diagnosis"[All Fields] OR ("early"[All Fields] AND "detection"[All Fields]) OR "early detection"[All Fields]) AND ("stomach neoplasms"[MeSH Terms] OR ("stomach"[All Fields] AND "neoplasms"[All Fields]) OR "stomach neoplasms"[All Fields] OR ("gastric"[All Fields] AND "cancer"[All Fields]) OR "gastric cancer"[All Fields]))) AND Search: (risk assesment) AND (early detection gastric cancer) - Spellcheck off Filters: in the last 5 years, Meta-Analysis, Randomized Controlled Trial, Systematic Review (("risk"[MeSH Terms] OR "risk"[All Fields]) AND ("assesed"[All Fields] OR "assesment"[All Fields] OR "assesments"[All Fields]) AND (("early diagnosis"[MeSH Terms] OR ("early"[All Fields] AND "diagnosis"[All Fields]) OR "early diagnosis"[All Fields] OR ("early"[All Fields] AND "detection"[All Fields]) OR "early detection"[All Fields]) AND ("stomach neoplasms"[MeSH Terms] OR ("stomach"[All Fields] AND "neoplasms"[All Fields]) OR "stomach neoplasms"[All Fields] OR ("gastric"[All Fields] AND "cancer"[All Fields]) OR "gastric cancer"[All Fields]))) AND ((y_5[Filter]) AND (meta-analysis[Filter] OR randomizedcontrolledtrial[Filter] OR systematicreview[Filter])) AND	

	(("ieee int conf automation sci eng case"[Journal] OR "case phila"[Journal] OR "case"[All Fields]) AND ("diagnosis"[MeSH Subheading] OR "diagnosis"[All Fields] OR "findings"[All Fields] OR "diagnosis"[MeSH Terms] OR "finds"[All Fields] OR "signs and symptoms"[MeSH Terms] OR ("signs"[All Fields] AND "symptoms"[All Fields]) OR "signs and symptoms"[All Fields] OR "finding"[All Fields]) AND (("early diagnosis"[MeSH Terms] OR ("early"[All Fields] AND "diagnosis"[All Fields]) OR "early diagnosis"[All Fields] OR ("early"[All Fields] AND "detection"[All Fields]) OR "early detection"[All Fields]) AND ("stomach neoplasms"[MeSH Terms] OR ("stomach"[All Fields] AND "neoplasms"[All Fields]) OR "stomach neoplasms"[All Fields] OR ("gastric"[All Fields] AND "cancer"[All Fields]) OR "gastric cancer"[All Fields])) AND (("stomach neoplasms"[MeSH Terms] OR ("stomach"[All Fields] AND "neoplasms"[All Fields]) OR "stomach neoplasms"[All Fields] OR ("gastric"[All Fields] AND "cancer"[All Fields]) OR "gastric cancer"[All Fields]) AND ("diagnosis"[MeSH Subheading] OR "diagnosis"[All Fields] OR "screening"[All Fields] OR "mass screening"[MeSH Terms] OR ("mass"[All Fields] AND "screening"[All Fields]) OR "mass screening"[All Fields] OR "early detection of cancer"[MeSH Terms] OR ("early"[All Fields] AND "detection"[All Fields] AND "cancer"[All Fields]) OR "early detection of cancer"[All Fields] OR "screen"[All Fields] OR "screenings"[All Fields] OR "screened"[All Fields] OR "screens"[All Fields]))) AND (meta-analysis[Filter] OR randomizedcontrolledtrial[Filter] OR systematicreview[Filter]) AND Search: (case finding) AND (early detection gastric cancer)) AND (gastric cancer screening) Filters: in the last 5 years, Meta-Analysis, Randomized Controlled Trial, Systematic Review (("ieee int conf automation sci eng case"[Journal] OR "case phila"[Journal] OR "case"[All Fields]) AND ("diagnosis"[MeSH Subheading] OR "diagnosis"[All Fields] OR "findings"[All Fields] OR "diagnosis"[MeSH Terms] OR "finds"[All Fields] OR "signs and symptoms"[MeSH Terms] OR ("signs"[All Fields] AND "symptoms"[All Fields]) OR "signs and symptoms"[All Fields] OR "finding"[All Fields]) AND (("early diagnosis"[MeSH Terms] OR ("early"[All Fields] AND "diagnosis"[All Fields]) OR "early diagnosis"[All Fields] OR ("early"[All Fields] AND "detection"[All Fields]) OR "early detection"[All Fields]) AND ("stomach neoplasms"[MeSH Terms] OR ("stomach"[All Fields] AND "neoplasms"[All Fields]) OR "stomach neoplasms"[All Fields] OR ("gastric"[All Fields] AND "cancer"[All Fields]) OR "gastric cancer"[All Fields])) AND (("stomach neoplasms"[MeSH Terms] OR ("stomach"[All Fields] AND "neoplasms"[All Fields]) OR "stomach neoplasms"[All Fields] OR ("gastric"[All Fields] AND "cancer"[All Fields]) OR "gastric cancer"[All Fields]) AND ("diagnosis"[MeSH Subheading] OR "diagnosis"[All Fields] OR "screening"[All Fields] OR "mass screening"[MeSH Terms] OR ("mass"[All Fields] AND "screening"[All Fields]) OR "mass screening"[All Fields] OR "early detection of cancer"[MeSH Terms] OR ("early"[All Fields] AND "detection"[All Fields] AND "cancer"[All Fields]) OR "early detection of cancer"[All Fields] OR "screen"[All Fields] OR "screenings"[All Fields] OR "screened"[All Fields] OR "screens"[All Fields]))) AND ((y_5[Filter]) AND (meta-analysis[Filter] OR randomizedcontrolledtrial[Filter] OR systematicreview[Filter]))
Table of evidence	

Study ID	Study design Score	Risk of Bias (alinea(s)) *	Quality Score **(0 to -2)** **	Consistency Score **(-1 to 1)** #	Directness Score **(0 to -2)** @	Publication bias † **(0: No, 1: Yes)**	Reported ICER	Effect size Score **(0 to 2)** §	Evidence Level ¶	Type of study according to SIGN	Recommendation SIGN													
									High	Mod	Low	Very Low	1++	1+	1-	2++	2+	2-	3	4	A	B	C	D
29579788 Yusefi, A. (2018)	2	Systematic review to identify the most important risk factors of gastric cancer. 52 risk factors for gastric cancer were identified.	0	1	0	n/a	n/a	n/a		x				x							x			
35017181 Gu, J. (2022)	2	Systematic review of the available evidence about the construction and verification of gastric cancer predictive models.	0	1	0	n/a	n/a	n/a		x				x							x			
38717039 LI, Y. (2024)	2	Systematic review to explore the clinicopathological features and risk factors associated with young-onset (<50 years) gastric carcinoma	-1	1	-1	n/a	n/a	n/a		x					x							x		
35944925 Malfertheiner, P (2022)	2	Sixth edition of the Maastricht/Florence 2021 Consensus Report, key aspects related to the clinical role of H. pylori infection were re-evaluated and updated.	0	1	-1	n/a	n/a	n/a		x										x				x

Sentence	**ESGE/EHMSG/ESP recommend opportunistic risk stratification of precancerous conditions in all endoscopies, because endoscopic surveillance every 3 years in patients with high-risk premalignant conditions is cost-effective irrespective of country.**																								
GRADE	**Strength of recommendation: Strong**							**Quality of evidence: Moderate**																	
PICO	Is endoscopic screening/ surveillance of premalignant gastric lesions/gastric cancer cost-effective in low/ intermediate risk areas? P: Patients with high-risk premalignant gastric conditions under surveillance I: Cost-effectiveness of endoscopic surveillance C: No surveillance and different time intervals of surveillance O: Cost-effectiveness of surveillance in patients with high-risk premalignant conditions																								
Query(ies) and databases searched	Search: ((cost-effectiveness) AND (early detection gastric cancer)) AND (gastric cancer screening) Filters: Meta-Analysis, Randomized Controlled Trial, Systematic Review. (("cost effectiveness analysis"[MeSH Terms] OR ("cost effectiveness"[All Fields] AND "analysis"[All Fields]) OR "cost effectiveness analysis"[All Fields] OR ("cost"[All Fields] AND "effectiveness"[All Fields]) OR "cost effectiveness"[All Fields]) AND (("early diagnosis"[MeSH Terms] OR ("early"[All Fields] AND "diagnosis"[All Fields]) OR "early diagnosis"[All Fields] OR ("early"[All Fields] AND "detection"[All Fields]) OR "early detection"[All Fields]) AND ("stomach neoplasms"[MeSH Terms] OR ("stomach"[All Fields] AND "neoplasms"[All Fields]) OR "stomach neoplasms"[All Fields] OR ("gastric"[All Fields] AND "cancer"[All Fields]) OR "gastric cancer"[All Fields])) AND (("stomach neoplasms"[MeSH Terms] OR ("stomach"[All Fields] AND "neoplasms"[All Fields]) OR "stomach neoplasms"[All Fields] OR ("gastric"[All Fields] AND "cancer"[All Fields]) OR "gastric cancer"[All Fields]) AND ("diagnosis"[MeSH Subheading] OR "diagnosis"[All Fields] OR "screening"[All Fields] OR "mass screening"[MeSH Terms] OR ("mass"[All Fields] AND "screening"[All Fields]) OR "mass screening"[All Fields] OR "early detection of cancer"[MeSH Terms] OR ("early"[All Fields] AND "detection"[All Fields] AND "cancer"[All Fields]) OR "early detection of cancer"[All Fields] OR "screen"[All Fields] OR "screenings"[All Fields] OR "screened"[All Fields] OR "screens"[All Fields]))) AND Search: ((cost-effectiveness) AND (early detection gastric cancer)) AND (gastric cancer screening) Filters: in the last 10 years (("cost effectiveness analysis"[MeSH Terms] OR ("cost effectiveness"[All Fields] AND "analysis"[All Fields]) OR "cost effectiveness analysis"[All Fields] OR ("cost"[All Fields] AND "effectiveness"[All Fields]) OR "cost effectiveness"[All Fields]) AND (("early diagnosis"[MeSH Terms] OR ("early"[All Fields] AND "diagnosis"[All Fields]) OR "early diagnosis"[All Fields] OR ("early"[All Fields] AND "detection"[All Fields]) OR "early detection"[All Fields]) AND ("stomach neoplasms"[MeSH Terms] OR ("stomach"[All Fields] AND "neoplasms"[All Fields]) OR "stomach neoplasms"[All Fields] OR ("gastric"[All Fields] AND "cancer"[All Fields]) OR "gastric cancer"[All Fields])) AND (("stomach neoplasms"[MeSH Terms] OR ("stomach"[All Fields] AND "neoplasms"[All Fields]) OR "stomach neoplasms"[All Fields] OR ("gastric"[All Fields] AND "cancer"[All Fields]) OR "gastric cancer"[All Fields]) AND ("diagnosis"[MeSH Subheading] OR "diagnosis"[All Fields] OR "screening"[All Fields] OR "mass screening"[MeSH Terms] OR ("mass"[All Fields] AND "screening"[All Fields]) OR "mass screening"[All Fields] OR "early detection of cancer"[MeSH Terms] OR ("early"[All Fields] AND "detection"[All Fields] AND "cancer"[All Fields]) OR "early detection of cancer"[All Fields] OR "screen"[All Fields] OR "screenings"[All Fields] OR "screened"[All Fields] OR "screens"[All Fields]))) AND (y_10[Filter])																								
Table of evidence																									

Study ID (PMID)	Study design Score	Risk of bias (alinea(s))*	Quality Score **(0 to -2)** **	Consistency Score **(-1 to 1)** #	Directness Score **(0 to -2)** @	Publication bias † **(0: No,1: Yes)**	Reported ICER	Effect size Score **(0 to 2)** §	Evidence Level¶				Type of study according to SIGN								Recommendation SIGN			
									High	Mod	Low	Very Low	1++	1+	1-	2++	2+	2-	3	4	A	B	C	D
38051169 Becker, E.C. (2023)		Markov state transition model to provide new evidence-based data that can be used to support the implementation of biennial surveillance guidelines in individuals with nondysplastic noncardia GIM and detect early malignant lesions, thereby decreasing morbidity and mortality.	0	0	0	n/a	Study showed that it is significantly cost-effective to perform biennial endoscopy surveillance in patients who have been incidentally found to have noncardia mixed GIM, with a cost savings of $5783.84 per person, and in those with iGIM, with a cost savings of $8093.08 per person.	n/a		x					x							x			
37302442	2	Semi-Markov microsimulation model of	0	0	0	n/a	Compared with no	n/a	x					x							x			

Thiruvengadam N.R. (2024)		patients with incidentally detected GIM, to compare the effectiveness of EGD surveillance with no surveillance at 10-year, 5-year, 3-year, 2-year, and 1-year intervals.					surveillance, all modeled surveillance intervals yielded greater life expectancy (87-190 undiscounted life-years gained per 1000); 5-year surveillance provided the greatest number of life-years gained per EGD performed and was the cost-effective strategy ($40,706/QALY). In individuals with risk factors of family history of GA or anatomically extensive, incomplete-type GIM intensified 3-year surveillance was cost-effective (incremental cost-effectiveness ratio $28,156/QALY and $87,020/QALY, respectively).															
32728390 Canakis, A. (2020)	2	Systematic review, decision model analyses of upper endoscopy for gastric cancer screening and preneoplasia surveillance.	0	1	0	n/a	n/a	n.a	x					x							x			

PICO	P: Individuals of countries with intermediate-high gastric cancer incidence submitted to EGD I: Routine mucosal biopsy sampling C: No biopsies / other diagnostic modalities O: Identification/staging of precancerous conditions (*H. pylori* infection diagnosis)
Query(ies) and databases searched	Search (PubMed): **prevalence AND gastric precancerous** Filters: **from 2020/1/1 - 3000/12/12** (("epidemiology"[MeSH Subheading] OR "epidemiology"[All Fields] OR "prevalence"[All Fields] OR "prevalence"[MeSH Terms] OR "prevalance"[All Fields] OR "prevalences"[All Fields] OR "prevalence s"[All Fields] OR "prevalent"[All Fields] OR "prevalently"[All Fields] OR "prevalents"[All Fields]) AND (("gastrics"[All Fields] OR "stomach"[MeSH Terms] OR "stomach"[All Fields] OR "gastric"[All Fields]) AND "precancerous"[All Fields])) AND (2020/1/1:3000/12/12[pdat]) Search (PubMed): **gastric cancer AND biopsy strategy** ("stomach neoplasms"[MeSH Terms] OR ("stomach"[All Fields] AND "neoplasms"[All Fields]) OR "stomach neoplasms"[All Fields] OR ("gastric"[All Fields] AND "cancer"[All Fields]) OR "gastric cancer"[All Fields]) AND (("biopsie"[All Fields] OR "biopsy"[MeSH Terms] OR "biopsy"[All Fields] OR "biopsied"[All Fields] OR "biopsies"[All Fields] OR "biopsy s"[All Fields] OR "biopsying"[All Fields] OR "biopsys"[All Fields] OR "pathology"[MeSH Subheading] OR "pathology"[All Fields]) AND ("strategie"[All Fields] OR "strategies"[All Fields] OR "strategy"[All Fields] OR "strategy s"[All Fields]))
Table of evidence	***Are there any cohorts?***

Study ID	Study design Score **(2)**	Risk of bias (alinea(s)) *	Quality Score **(0 to -3) ****	Consistency Score **(-1 to 1) #**	Directness Score **(0 to -2) @**	Publication bias **(0: No,1:Yes)**	Reported OR/RR/HR	Effect size Score **(0 to 2)** §	Evidence Level¶				Type of study according to SIGN								Recommendation SIGN			
									High	Mod	Low	Very Low	1++	1+	1-	2++	2+	2-	3	4	A	B	C	D
Buxbaum J (2017)	1	-	0	1	0	NA	Reported OR	1			X						X						X	
Esposito G (2019)	1	1) Only academic centers	-1	1	-1	NA	Reported P<0.01 for comparison scores	1			X						X						X	

* 1) Selection; 2) Comparability; 3) Outcome
** -1 per problem Selection: -1: selected group of users or no description; Comparability -1: no comparison between the cohorts; Outcome -1: No description, no follow up
# Evidence of dose response across or within studies (or inconsistency across studies is explained by a dose response); also up to one point added if adjustment for confounders would have increased the effect size (1); All / most studies show similar results (0); Lack of agreement between studies (e.g. statistical heterogeneity between RCTs, conflicting results) (-1)
@ -1 per problem in generalizability to the target population
†: only for meta-analysis
§ 0 if Not all effect sizes more than 2 or less than 0.5 and significant; or if OR/RR/HR not significant; 1 if Effect size more than 2 or less than 0.5 for all studies/meta-analyses included in comparison and significant; 2 if Effect size more than 5 or less tha.2 for all studies/meta-analyses included in comparison and significant
¶: High: Further research is very unlikely to change our confidence in the estimate of effect; Moderate: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate; Low: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate; Very low: Any estimate of effect is very uncertain

Table of evidence		***Are there only case-controls/cross-sectional?***																						
Study ID	Study design Score **(2)**	Risk of bias (alinea(s)) *	Quality Score **(0 to -3) ****	Consistency Score **(-1 to 1) #**	Directness Score **(0 to -2) @**	Publication bias † **(0: No,1: Yes)**	Reported OR/RR/HR	Effect size Score **(0 to 2)** §	Evidence Level¶				Type of study according to SIGN								Recommendation SIGN			
									High	Mod	Low	Very Low	1++	1+	1-	2++	2+	2-	3	4	A	B	C	D
Weck MN (2006)	2 (Systematic review)	2 (Meta-analysis)	2) No control group	-1	1	0	Not evaluated	NR		X						X						X		
Marques-Silva L (2014)	2 (Meta-analysis)	2 (Meta-analysis)	2) No control group	-1	1	0	OR	0		X					X							X		
Yin Y (2022)	2 (Meta-analysis)	2 (Meta-analysis)	2) No control group	-1	1	0	OR	0		X					X							X		
Li Y (2023)	2 (Meta-analysis)	2 (Meta-analysis)	2) No control group	-1	1	0	OR	0		X					X							X		
Faknak N (2022)	1	1) Only IM patients	-1	1	0	NA	Not reported. P<0.01 for validity scores	0			X					X							X	

* 1) Selection; 2) Comparability; 3) Exposure

** -1 per problem: Selection: -1: selected group of users or no description; Comparability -1: no comparison between the cohorts; Outcome -1: No description, no follow up

Evidence of dose response across or within studies (or inconsistency across studies is explained by a dose response); also up to one point added if adjustment for confounders would have increased the effect size (1); All / most studies show similar results (0); Lack of agreement between studies (e.g. statistical heterogeneity between RCTs, conflicting results) (-1)

@ -1 per problem in generalizability to the target population

†: only for meta-analysis

§ 0 if Not all effect sizes more than 2 or less than 0.5 and significant; or if OR/RR/HR not significant; 1 if Effect size more than 2 or less than 0.5 for all studies/meta-analyses included in comparison and significant; 2 if Effect size more than 5 or less tha.2 for all studies/meta-analyses included in comparison and significant

¶: High: Further research is very unlikely to change our confidence in the estimate of effect; Moderate: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate; Low: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate; Very low: Any estimate of effect is very uncertain

Sentence	**ESGE/EHMSG/ESP suggest *H. pylori* non-invasive screening and eradication between the age of 20 and 30 for first-degree relatives of patients with GC.**	
GRADE	**Strength of recommendation: Conditonal**	**Quality of evidence: Moderate**
Sentence	**ESGE/EHMSG/ESP suggest endoscopic screening for GC in first-degree relatives of patients with GC at the age of 45 years or 10 years before the age of diagnosis of the affected relative.**	
GRADE	**Strength of recommendation: Conditonal**	**Quality of evidence: Moderate**
PICO	P: Patients with a first-degree family history of gastric cancer I: Gastric precancerous lesion and gastric cancer C: Patients without a first-degree family history of gastric cancer O: Risk of gastric cancer and precancerous conditions	
Query(ies) and databases searched	Search: Pubmed (((gastric cancer) OR (gastric adenocarcinoma)) OR (gastric tumor)) AND (family history) + (((gastric cancer) OR (gastric adenocarcinoma)) OR (gastric tumor)) AND (first degree relatives) + ("stomach neoplasms"[MeSH Terms] OR ("stomach"[All Fields] AND "neoplasms"[All Fields]) OR "stomach neoplasms"[All Fields] OR ("gastric"[All Fields] AND "cancer"[All Fields]) OR "gastric cancer"[All Fields]) AND (first-degree[All Fields] AND ("family"[MeSH Terms] OR "family"[All Fields] OR "relatives"[All Fields])) AND (increased[All Fields] AND ("risk"[MeSH Terms] OR "risk"[All Fields])) + Crosse references	
Table of evidence		

Study	**Type**	**Endpoint**	**Bias/concerns**	**Patients**	**Principal findings**	**Evidence Level¶**				**Type of study according to SIGN**								**Recommendation SIGN**			
						High	Mod	Low	Very Low	1++	1+	1-	2++	2+	2-	3	4	A	B	C	D
Ligato I 2024	Systematic review and meta-analysis	GC Incidence	High Heterogeneity	NA	OR = 2.92; 95% CI 2.402-3.552; p < 0.001; I2 = 81.85%; p < 0.001		x							x						x	
Yaghoobi M 2017	Systematic review and meta-analysis	GC Incidence	High Heterogeneity	80690	Pooled RR 2.35 (95%CI: 1.96-2.81), (P < 0.00001, I^2 = 90%), exclusively analysed the history of gastric cancer in first-degree relatives, the relative risk was 2.71 (95%CI: 2.08-3.53; P < 0.00001)		x							x						x	
Gui He 2021	Systematic review and meta-analysis	GC Incidence	High Heterogeneity	NA	RR of GC was 2.08 (95% CI=1.86-2.34 Individuals with sibling history of GC than those with parental history of GC (RR=3.18, 95% CI=2.12-4.79 vs. RR=1.66, 95% CI=1.46-1.89, P=0.021). For individuals with 2 or more first-degree relatives (FDRs) with GC, the RR was 2.81(95% CI=1.89-3.99). Subjects with both family history and Helicobacter pylori (H. pylori)		x							x						x	

					infection confer a higher risk of GC (RR = 4.03, 95%CI=2.46-6.59).																		
Vitelli-Storelli F, 2021	Consortium of epidemiological studies	GC Incidence	High Heterogeneity	5946	OR for GC was 1.84 (95% CI: 1.64–2.04; I2 = 6.1%, P heterogeneity = 0.383) in subjects with vs. those without first-degree relatives with GC.		x							x							x		

Sentence	**ESGE/EHMSG/ESP suggest that GC screening or surveillance of precancerous conditions in asymptomatic individuals over 80 should be discontinued or not started.**	
GRADE	**Strength of recommendation: Strong**	**Quality of evidence: Moderate**
PICO	P: Elderly patients with gastric precancerous conditions I: endoscopic screening C: no screening O: important outcomes: cancer incidence, survival, quality of life	
Query(ies) and databases searched	(elderly patients with gastric preneoplastic conditions OR elderly patients with intestinal metaplasia OR elderly patients with atrophic gastritis OR elderly patients with gastric atrophy OR old patients with intestinal metaplasia OR old patients with atrophic gastritis OR old patients with gastric atrophy) AND (endoscopy OR screening OR surveillance) AND (survival OR complications OR gastric cancer OR quality of life)	

Sentence	**ESGE/EHMSG/ESP recommend endoscopic screening for precancerous condition in individuals with low pepsinogen I serum levels or/and a low pepsinogen I/II ratio, particularly if H. pylori serology is negative.**	
GRADE	**Strength of recommendation: Strong**	**Quality of evidence: Moderate**
PICO	P: Patients with low pepsinogen I or/and low pepsinogen I/II ratio with or without gastrin-17 level and Helicobacter pylori antibodies I: Gastroscopy for screening for gastric precancerous conditions C: Endoscopy based on clinical indications O: Risk stratification of gastric precancerous conditions	
Query(ies) and databases searched	Search PubMed: ((atrophic gastritis[Title/Abstract]) OR (gastric atrophy[Title/Abstract])) AND (diagnosis[Title/Abstract]) AND ((pepsinogens[Title/Abstract]) OR (pepsinogen[Title/Abstract])) AND (gastritis[Title/Abstract]) ((gastro panel[Title/Abstract]) AND (atrophic gastritis[Title/Abstract])) OR (gastric atrophy[Title/Abstract])	
Table of evidence	***Are there only case-controls/cross-sectional?***	

Study ID	Study design Score **(2)**	Risk of bias (alinea(s)) *	Quality Score **(0 to -3)** **	Consistency Score **(-1 to 1)** #	Directness Score **(0 to -2)** @	Publication bias † **(0: No,1:Yes)**	Reported OR/RR/HR	Effect size Score **(0 to 2)** §	Evidence Level¶				Type of study according to SIGN								Recommendation SIGN			
									High	Mod	Low	Very Low	1++	1+	1-	2++	2+	2-	3	4	A	B	C	D
Lin X, Saudi J Gastroenterol 2023	1	1) patients referred to EGD, no all completed serum testing 2) no info regarding biopsy sampling manner	-2	0	0		Not reported	NR		x								x					X	
Sivandzadeh G, Middle East J Dig Dis 2023	1	2) no info about CAG an controls numbers	-2	-1	0		Not reported	NR		x								x					X	
Chapelle N, Diagnostics	1		0	0	0		Not reported	NR	x							x							X	

2022																						
Huang RJ, Clinical Gastroenterology and Hepatology 2022	1	1	-1	0	0		Not reported	NR		x							x					X	
Nguyen CL, Ann Med Surg (Lond) 2022	1	1	-1	0	-1		Not reported	NR		x							x					X	
Miftahussurur J M, Res Med Sci 2022	1		0	0	0		Not reported	NR		x							x					X	
Ogutmen Koc D, Postgrad Med J 2022	1	1) Not defined selection to control 2) no information regarding premalignant lesion diagnosis, some IM not treated as AG (not defined if it was treated as premalignant lesion)	-2	0	-1		Not reported	NR		x								x				X	
Cai HL, World J Clin Cases 2021	1		0	0	0		Not reported	NR		x							x					X	
Chapelle N, Helicobacter 2020	1	2) not clearly defined if IM is defined as AG and included in the analysis	0	0	0		Not reported	NR		x							x					X	
Whary MT, Cancer Epidemiol 2020	1	2) not clear variables in regression	-2	0	0		Not clear outcomes	n/a		x								x				X	
Miftahussurur M, PLoS ONE 2020	1		0	0	0		Not reported	NR		x							x					X	
Zeng W, BMC Medical Genetics 2020	1	1) not defined how controls were selected 2) no information regarding diagnosis of AG	-2	0	-1		Not reported	NR		x								x				X	
Mattar R, Arq Gastroenterol 2020	1	2) no data for any kind of AG or its severity according to OLGA	-1	0	-1		Not reported	NR										x				X	
Wang X, JBUON 2020	1	1) not defined how controls were selected 2) no combined PGI and PGR results, no severity of AG analysis	-2	0	-2		Not reported	NR										x				X	
Bang CS, J Clin Med 2019	2 (meta-analysis)		0	1	0	Not evaluated <10 studies	Not reported	NR	x					x							X		
Mezmale L, Asian Pac J Cancer Prev 2019	1	2 results for corpus AG only	-1	0	-1		Not reported	NR		x								x				X	
Dondov G, PLoS ONE 2022	1	1 mached with age and sex with some with some differences in family history o GC 2) no info about hispathological exam	-1	0	-1		Not reported	NR		x								x				X	
Chiang TH, J Gastroenterol Hepatol. 2021	1	1 PG positive patient all invited for EGD and negative based on clinical indications	-1	0	-1		Not reported	NR		x							x					X	
Syrjanen K, Anticancer Res, 2022	3	1 only AG in corpus	-1	0	-1	1	Not reported	NR	x						x						X		

* 1) Selection; 2) Comparability; 3) Exposure
** -1 per problem: Selection: -1: selected group of users or no description; Comparability -1: no comparison between the cohorts; Outcome -1: No description, no follow up
# Evidence of dose response across or within studies (or inconsistency across studies is explained by a dose response); also up to one point added if adjustment for confounders would have increased the effect size (1); All / most studies show similar results (0); Lack of agreement between studies (e.g. statistical heterogeneity between RCTs, conflicting results) (-1)

@ -1 per problem in generalizability to the target population
†: only for meta-analysis
§ 0 if Not all effect sizes more than 2 or less than 0.5 and significant; or if OR/RR/HR not significant; 1 if Effect size more than 2 or less than 0.5 for all studies/meta-analyses included in comparison and significant; 2 if Effect size more than 5 or less tha.2 for all studies/meta-analyses included in comparison and significant
¶: High: Further research is very unlikely to change our confidence in the estimate of effect; Moderate: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate; Low: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate; Very low: Any estimate of effect is very uncertain

Sentence	**ESGE/EHMSG/ESP recommend a high-quality endoscopy including virtual chromoendoscopy (VCE), for screening, diagnosis and surveillance of gastric precancerous conditions and lesions.**	
GRADE	**Strength of recommendation: Strong**	**Quality of evidence: Moderate**
PICO	**Patients:** Patients screened for or under surveillance of gastric precancerous conditions (chronic atrophic gastritis and/or intestinal metaplasia and/or dysplasia). **Intervention:** Preparation with defoaming or/and mucolytic agents. **Comparator:** No preparation with defoaming or/and mucolytic agents. **Outcome:** Gastric precancerous conditions; neoplastic lesions; mucosal visibility. **Patients:** Patients screened for or under surveillance of gastric precancerous conditions (chronic atrophic gastritis and/or intestinal metaplasia and/or dysplasia). **Intervention:** Appropriate examination of gastric mucosa determined as time spend for examination, sedation and photodocumentation.	
Query(ies) and databases searched	("time"[Title/Abstract] OR "duration"[Title/Abstract] OR"photodocumentation"[Title/Abstract] OR "simethicone"[Title/Abstract] OR "pronase"[Title/Abstract] OR "dimethicone"[Title/Abstract] OR "n-acetylcysteine"[Title/Abstract] OR "preparation"[Title/Abstract] OR "premedication"[Title/Abstract] OR "sedation"[Title/Abstract]) AND ("gastric atrophy"[Title/Abstract] OR "atrophic gastritis"[Title/Abstract] OR "gastric precancerous conditions"[Title/Abstract] OR " gastric neoplasm"[Title/Abstract] OR ("gastric cancer"[Title/Abstract] AND detection[Title/Abstract]))	
Table of evidence	***Are there any RCT?***	

Study ID	Study design Score **(4)**	Risk of bias (alinea(s)) *	Quality Score **(0 to -2)** **	Consistency Score **(-1 to 1)** #	Directness Score **(0 to -2)** @	Publication bias † **(0: No,1: Yes)**	Reported OR/RR/HR	Effect size Score **(0 to 2)** §	Evidence Level¶				Recommendation SIGN								Recommendation SIGN			
									High	Mod	Low	Very Low	1++	1+	1-	2++	2+	2-	3	4	A	B	C	D
Zhang LY, Dig Endosc 2018	4	5 single center, 1 not defined how AG and IM were diagnosed 1 not defined inf patients were blinded	-2	0	-2		Atrophic gastritis (4.8% vs. 18.5%, p =0.014) and intestinal metaplasia (12.9% vs. 28.3%, p =0.024); low-grade intraepithelial neoplasia (1.6% vs. 8.7%, p=0.085). No HGD in the group				x				x							x		
Liu X, Surg Endosc. 2018	4	5 no statistical part for comined UGI neoplasm 5 no analysis of visibility and lesions detection	-2	0	-2		NS for detection of cancer and dysplasia				x				x							x		
Zhang LY, Digestive Endoscopy. 2018	4	1 pateint's not blinded 5 single center	-2	0	-2		Higher detection of AG (0.014) and IM (0.024) NS for LGD (0.085)				x				x							x		

** Low risk of bias would indicate "no serious limitations" = 0; Presence of serious limitations then downgrade the quality of evidence for this outcome by 1 level = -1; Presence of very serious limitations then downgrade the quality of evidence for this outcome by 2 level = -2
# Evidence of dose response across or within studies (or inconsistency across studies is explained by a dose response); also up to one point added if adjustment for confounders would have increased the effect size (1); All / most studies show similar results (0); Lack of agreement between studies (e.g. statistical heterogeneity between RCTs, conflicting results) (-1)
@ -1 per problem in generalizability to the target population
†: only for meta-analysis
§ 0 if Not all effect sizes more than 2 or less than 0.5 and significant; or if OR/RR/HR not significant; 1 if Effect size more than 2 or less than 0.5 for all studies/meta-analyses included in comparison and significant; 2 if Effect size more than 5 or less tha.2 for all studies/meta-analyses included in comparison and significant
¶: High: Further research is very unlikely to change our confidence in the estimate of effect; Moderate: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate; Low: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate; Very low: Any estimate of effect is very uncertain

Table of evidence	***Are there any cohorts?***

Study ID	Study	Risk of bias	Quality	Consistency	Directness	Publication	Reported OR/RR/HR	Effect size	Evidence Level¶	Type of study according to SIGN	Recommendation SIGN

	design Score **(2)**	(alinea(s))*	Score **(0 to -3)****	Score **(-1 to 1) #**	Score **(0 to -2) @**	bias **(0:No,1:Yes)**		Score **(0 to 2)** §															
									High	Mod	Low	Very Low	1++	1+	1-	2++	2+	2-	3	4	A	B	C	D
Gao Y, Clin Transl Gastroenterol 2023	2	2 no case-based analysis (EGD with achieved threshold)	-1	0	-1		Focal lesions OR1.25 (1.03–1.52) p=0.022; High risk lesions OR, 1.65; 95% CI, 1.04–2.64; P=0.035; Neoplasm NS	0		x							x							x	
Kim TJ, Clin Gastroenterol Hepatol . 2023	2	1 Retrospective	-1	0	-1		<3min obsercation time – ACG vs EGC OR 2.27 (95% CI, 1.20-4.30)				x							x						x	
Kim HY, Gastroenterol Rep (Oxf) 2023	2	1 retrospective 2 con clear how ROC was peroformed	-2	0	-2		AUC 0.738 (95% CI, 0.677–0.799; P < 0.001), Se62% Sp 74%; Observation time for missed adenoma OR 0.990 0.986–0.993 <0.001				x								x						x
Park JM, GIE 2021	2	1 single center 2 not defined if time during baseline period was measured for all the procedures	-2		-2		UGI neoplasms OR 1.51; 95% CI, 1.21 –1.9)	0		x								x						x	

* 1) Selection; 2) Comparability; 3) Outcome
** -1 per problemSelection: -1: selected group of users or no description; Comparability -1: no comparison between the cohorts; Outcome -1: No description, no follow up
# Evidence of dose response across or within studies (or inconsistency across studies is explained by a dose response); also up to one point added if adjustment for confounders would have increased the effect size (1); All / most studies show similar results (0); Lack of agreement between studies (e.g. statistical heterogeneity between RCTs, conflicting results) (-1)
@ -1 per problem in generalizability to the target population
†: only for meta-analysis
§ 0 if Not all effect sizes more than 2 or less than 0.5 and significant; or if OR/RR/HR not significant; 1 if Effect size more than 2 or less than 0.5 for all studies/meta-analyses included in comparison and significant; 2 if Effect size more than 5 or less tha.2 for all studies/meta-analyses included in comparison and significant
¶: High: Further research is very unlikely to change our confidence in the estimate of effect; Moderate: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate; Low: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate; Very low: Any estimate of effect is very uncertain

Table of evidence — ***Are there only case-controls/cross-sectional?***

Study ID	Study design Score **(2)**	Risk of bias (alinea(s)) *	Quality Score **(0 to -3) ****	Consistency Score **(-1 to 1) #**	Directness Score **(0 to -2) @**	Publication bias † **(0: No,1: Yes)**	Reported OR/RR/HR	Effect size Score **(0 to 2)** §	Evidence Level¶				Type of study according to SIGN								Recommendation SIGN			
									High	Mod	Low	Very Low	1++	1+	1-	2++	2+	2-	3	4	A	B	C	D
Kawamura T, Dig Endosc 2017	1	1 restrospective 2 analysis per endoscopists	-1	0	-1		5-7 min 1.90 (95%CI, 1.06-3.40) >7 min 1.89 (95% CI, 0.98-3.64)	0			x						x						x	
Park JM, Gastroenterology 2017	1	1 retrospective 2 time assessment during only first year 2 analysis per endoscopists	-2	0	-2		1.52; 95% CI, 1.17-1.97 p=0.0018	0			x						x						x	
The JL, Clin Gastroenterol Hepatol 2015	1	1 restrospective 1 not precise time measurment	-2	0	-2		2.50 (95% CI 1.52 – 4.12); 3.42 95% CI 1.25-10.38 for gastric dysplasia/cancer; OR14.26 per 7 min EGD duration p 0.005	0			x						x						x	
Yoshimizu S, EIO2018	1	1 retrospective 2 only analysis per operator	-2	0	-1		NS for EGD time, min. 1 year of intensive training - OR 1.65 (1.02 – 2.68) 0.041 for UGI neoplasm; 1.83 (1.01 – 3.30) 0.045 for gastric neoplasm	0			x						x						x	
Romańczyk M, Eur J Gastroenterol Hepatol 2022	1	1 no fast vs slow operator's analysis	-1	0	-1		0 vs 1.8% for UGI neoplasm (p=0.004), 0 vs 1.1% for gastric cancer (p=0.02)				x						x						x	
Lee H, Yonsei Med J 2015	1	1 restrospective 2 endoscopists given propofol	-2	0	-2		Early GC OR 1.145 (95%CI 0.995–1.317) p=0.058; advanced GC OR 0.896 (95%CI 0.768–1.044) p=0.160				x							x						x	
Wu H, Scand J Gastroenterol 2022	1	1 retrospecive	-1	0	-1		Overall small UGI neoplasms OR1.40 (1.16–1.68) <.001. 10mm neoplasm UGI (2.80%				x						x						x	

							vs. 2.02%; p < .001); ≤10 mm neoplasm in antrum (1.60% vs. 1.09%; p = .002); ≤10 mm neoplasm in angulus (0.66% vs. 0.45%; p = .044)																	
Sang YK, JAMA Netw Open2022	1	1 retrospective	-1	0	-1		For cimetropium bromide OR, 1.54; 95% CI, 1.11-2.13; P = .009; for observation time OR1.49 (1.09-2.04 p=0.01	0			x						x							x	
Iwagami H, JGH Open 2022	1	1 retrospecive 2 no regression for gastric neoplasm	-2	0	-2		NS				x							x						x	
Di L, BMC Gastroenterol 2017	1	1 retrospective 1 not clear selection for " intensive gastriscopies of high risk patients" 3 non standardizedtrningin	-3	0	-2		0.05% vs 0.15% p <0;001				x							x						x	
Zhang Q, Medicine (Baltimore) 2015	1	1 retrospective 3 no defined how endoscopists were selected	-2	0	-2						x							x						x	
Wang Q, J Dig Dis 2021	1	2 not clear primary outcome (gastric lesions)	-1	0	-1						x							x						x	
Ishibashi F, Clin Endosc 2020	1	1 retrospective 2 no threshold analysis 2 not clear if the observation time was calculated per endoscopists or oer case	-3	0	-2						x							x						x	
Manfredi G, Eur J Gastroenterol Hepatol . 2023	1	1 retrospective	-1	0	-1						x							x						x	
Li Y, Saudi Journal of Gastroenterology 2019	2(meta-analysis)					0	Simethicone MD = −3.62, (−4.65, −2.60), P < 0.00001, I2 = 67%); simethicone+NAC; MD = −3.29 (−4.38, −2.21), P < 0.00001, I2 = 60%; pathologies detection simethicone+NAC (RR = 1.31, 95%CI: 1.12–1.53, P = 0.0006		x					x									x		
Burke E, Surgery Research and Practice 2021	2(meta-analysis)					1	MD −2.69 [−3.50, −1.88], I2 = 93%			x					x									x		
Sajid MS, Transl Gastroenterol Hepatol 2018	2(meta-analysis)					0	SMD, −2.83; 95% CI, −4.38, −1.27; I2=97%		x					x										x		
Romańczyk M, J Gastroenterol Hepatol 2022	1	1 retrospective 1 photographs assessment 2 analysis per semgment	-3	0							x							x						x	
Romańczyk M, GIE 2024	1	2 no analysis for AG/Im nor powred for dysplasia	-1	0	-1						x							x						x	

** -1 per problem: Selection: -1: selected group of users or no description; Comparability -1: no comparison between the cohorts; Outcome -1: No description, no follow up
# Evidence of dose response across or within studies (or inconsistency across studies is explained by a dose response); also up to one point added if adjustment for confounders would have increased the effect size (1); All / most studies show similar results (0); Lack of agreement between studies (e.g. statistical heterogeneity between RCTs, conflicting results) (-1)
@ -1 per problem in generalizability to the target population
ϯ: only for meta-analysis
§ 0 if Not all effect sizes more than 2 or less than 0.5 and significant; or if OR/RR/HR not significant; 1 if Effect size more than 2 or less than 0.5 for all studies/meta-analyses included in comparison and significant; 2 if Effect size more than 5 or less tha.2 for all studies/meta-analyses included in comparison and significant
¶: High: Further research is very unlikely to change our confidence in the estimate of effect; Moderate: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate; Low: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate; Very low: Any estimate of effect is very uncertain.

PICO	P: Patients submitted to endoscopy I: Virtual chromoendoscopy (NBI, BLI, FICE, i-scan, OE, TXI) C: High-definition white-light endoscopy O: Accuracy, sensitivity and specificity for atrophy / IM / neoplasia

Query(ies) and databases searched	"narrow-band imaging"[Title/Abstract] OR "narrow-band imaging"[Title/Abstract] OR "NBI"[Title/Abstract] OR "blue laser imaging"[Title/Abstract] OR "blue light imaging"[Title/Abstract] OR "linked color imaging"[Title/Abstract] OR "LCI"[Title/Abstract] OR "FICE"[Title/Abstract] OR "optical enhancement"[Title/Abstract] OR "texture and color enhancement"[Title/Abstract] OR "TXI"[Title/Abstract] OR "virtual chromoendoscopy"[Title/Abstract] OR "high-definition"[Title/Abstract] OR "white-light"[Title/Abstract] AND "gastric atrophy"[Title/Abstract] OR "atrophic gastritis"[Title/Abstract] OR "intestinal metaplasia"[Title/Abstract] OR "precancerous conditions"[Title/Abstract] OR "premalignant conditions"[Title/Abstract] OR "early gastric cancer"[Title/Abstract] OR "dysplasia"[Title/Abstract] OR "neoplasia"[Title/Abstract] AND "stomach"[Title/Abstract] OR "gastric"[Title/Abstract] NOT Duodenal

Table of evidence — ***Are there any RCT?***

Study ID	Study design Score **(4)**	Risk of bias (alinea(s)) *	Quality Score **(0 to -2)** **	Consistency Score **(-1 to 1)** #	Directness Score **(0 to -2)** @	Publication bias † **(0: No,1: Yes)**	Reported OR/RR/HR	Effect size Score **(0 to 2)** §	Evidence Level¶				Type of study according to SIGN								Recommendation SIGN			
									High	Mod	Low	Very Low	1++	1+	1-	2++	2+	2-	3	4	A	B	C	D
Min M, Annals of Medicine, 2022	3	1)	0	1	0	NA	NR P<0.001	0		X				X								x		
Wu CCH, J Gastroenterol Hepatol., 2021	3	1)	0	1	0	NA	NR P<0.01	0		X				X								x		
Gao J, Dig Dis Sci, 2021	3	1)	0	1	0	NA	OR 1.93	0		X				X								x		

* 1) blinding of measurements (test and outcome); 2) allocation; 3) verification (all individuals were submitted to both tests); 4) complete follow-up; 5) other – please identify

** Low risk of bias would indicate "no serious limitations" = 0; Presence of serious limitations then downgrade the quality of evidence for this outcome by 1 level = -1; Presence of very serious limitations then downgrade the quality of evidence for this outcome by 2 level = -2

Evidence of dose response across or within studies (or inconsistency across studies is explained by a dose response); also, up to one point added if adjustment for confounders would have increased the effect size (1); All / most studies show similar results (0); Lack of agreement between studies (e.g. statistical heterogeneity between RCTs, conflicting results) (-1)

@ -1 per problem in generalizability to the target population

†: only for meta-analysis

§ 0 if Not all effect sizes more than 2 or less than 0.5 and significant; or if OR/RR/HR not significant; 1 if Effect size more than 2 or less than 0.5 for all studies/meta-analyses included in comparison and significant; 2 if Effect size more than 5 or less tha.2 for all studies/meta-analyses included in comparison and significant

¶: High: Further research is very unlikely to change our confidence in the estimate of effect; Moderate: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate; Low: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate; Very low: Any estimate of effect is very uncertain

Table of evidence — ***Are there only case-controls/cross-sectional?***

Study ID	Study design Score **(2)**	Risk of bias (alinea(s)) *	Quality Score **(0 to -3)** **	Consistency Score **(-1 to 1)** #	Directness Score **(0 to -2)** @	Publication bias † **(0: No,1: Yes)**	Reported OR/RR/HR	Effect size Score **(0 to 2)** §	Evidence Level¶				Type of study according to SIGN								Recommendation SIGN			
									High	Mod	Low	Very Low	1++	1+	1-	2++	2+	2-	3	4	A	B	C	D
TXI																								
Futakushi T, BMC Gastroenterology, 2024	1	1) Only neoplastic lesions	-1	1	0	NA	Not reported. P<0.01 for visibility score between WLI and TXI	0				X					X						x	
NBI/BLI																								
Rokkas T, Ann Gastroenterol, 2023	2 (Meta-analysis)	2) No control group	-1	1	0	0	Not reported, no comparator	0	X						X							x		
Desai M, J Gastroenterol Hepatol, 2021	2 (Meta-analysis)	-	0	1	0	0	1.79	0	X						X							x		

Le H, Medicine (Baltimore), 2021	2 (meta-analysis)	-	0	1	0	0	OR ME vs WLI 2.97 (1.68~5.25) OR ME-NBI vs WLI 2.56 (2.13~3.13) OR ME-BLI vs WLI 3.13 (1.85~5.71)	1	X					X								x		
Rodriguez-Carrasco M, Endoscopy, 2020	2 (meta-analysis)	1) No control group	0	1	0	0	NR	1	X					X								x		
LCI																								
Lu JH, Exp Ther Med, 2023	1	1)	-1	1	0	NA	NR	0				X						X					x	
Higashino M, J Gastroenterol Hepatol, 2023	1	1)	-1	1	0	NA	NR	0				X						X					x	
Shu X, Ann Transl Med, 2021	2 (Meta-analysis)	2) No control group	-1	1	0	Not evaluated	NR	0			X							X					x	
i-scan OE																								
Song YH, World J Clin Cases, 2021	1	1)	-1	1	0	NA	NR	0				X						X					x	

* 1) Selection; 2) Comparability; 3) Exposure

** -1 per problem: Selection: -1: selected group of users or no description; Comparability -1: no comparison between the cohorts; Outcome -1: No description, no follow up

Evidence of dose response across or within studies (or inconsistency across studies is explained by a dose response); also up to one point added if adjustment for confounders would have increased the effect size (1); All / most studies show similar results (0); Lack of agreement between studies (e.g. statistical heterogeneity between RCTs, conflicting results) (-1)

@ -1 per problem in generalizability to the target population

†: only for meta-analysis

§ 0 if Not all effect sizes more than 2 or less than 0.5 and significant; or if OR/RR/HR not significant; 1 if Effect size more than 2 or less than 0.5 for all studies/meta-analyses included in comparison and significant; 2 if Effect size more than 5 or less tha.2 for all studies/meta-analyses included in comparison and significant

Sentence	**ESGE/EHMSG/ESP recommend that VCE should be used to guide biopsies in case of suspected neoplastic lesions.**	
GRADE	**Strength of recommendation: Conditional**	**Quality of evidence: Moderate**
Sentence	**ESGE/EHMSG/ESP recommend guided biopsies with VCE for diagnosis and staging of gastric precancerous conditions, and random biopsies in the absence of endoscopic suspected precancerous conditions.**	
GRADE	**Strength of recommendation: Strong**	**Quality of evidence: Moderate**

PICO	P: Patients submitted to endoscopy I: Virtual chromoendoscopy guided biopsies (NBI, BLI, FICE, i-scan, OE, TXI) C1: High-definition white-light endoscopy guided biopsies C2: Random biopsies O: Accuracy, sensitivity and specificity for atrophy / IM
Query(ies) and databases searched	"sydney houston"[Title/Abstract] OR "Sydney system"[Title/Abstract] OR "Sydney protocol"[Title/Abstract] OR "sydney houston"[Title/Abstract] OR "random biopsies"[Title/Abstract] OR "mapping"[Title/Abstract] OR "targeted"[Title/Abstract] AND "virtual chromoendoscopy"[Title/Abstract] OR "narrow-band imaging"[Title/Abstract] OR "narrow-band imaging"[Title/Abstract] OR "NBI"[Title/Abstract] OR "blue laser imaging"[Title/Abstract] OR "blue light imaging"[Title/Abstract] OR "BLI"[Title/Abstract] OR "optical enhancement"[Title/Abstract] OR "chromoendoscopy"[Title/Abstract] AND

	"intestinal metaplasia"[Title/Abstract] OR "atrophic gastritis"[Title/Abstract] OR "gastric atrophy"[Title/Abstract] OR "gastric precancerous conditions"[Title/Abstract] ➔ 58 results, 18 since 2018

Evidence table – targeted vs. random biopsies

	Study design	Population	Intervention	Comparator	Outcome	Results, 95% CI	
Fatnak N, Endosc Int Open, 2022	Cross-sectional	Patients with known GIM submitted to upper GI endoscopy	NBI targeted biopsies	NBI targeted + Sydney protocol	Extensive GIM	Sensitivity 88% vs 100% Specificity 90% vs 90% PPV 88% vs 90% NPV 90% vs 100% Accuracy 88% vs 95%, p<0.01 LR+ 9 vs 10 LR- 0.13 vs 0	Accuracy higher with NBI + mapping 5% false negatives for extensive GIM with NBI targeted alone
Ji R, Dig Liv Dis, 2020	RCT	154 patients with atrophic gastrites or GIM submitted to upper GI endoscopy	OE targeted biopsies	Acetic acid targeted biopsies	GIM identification on targeted biopsies and random biopsies	Per-patient yield OE 60.5% Random biopsy 35% OE + random biopsy 79% P<0.0001 Acetic acid 67% Random biopsy 31% AA + random biopsy 84%	
Esposito G, Endoscopy, 2020	Cross-sectional	250 patients submitted to upper GI endoscopy	NBI targeted biopsies (EGGIM)	NBI targeted + random biopsies in the absence of endoscopically suspected GIM	GIM	114 patients with GIM 3 patients detected only on biopsies Sensitivity for GIM 97% Sensitivity for extensive GIM 100%	
Chen H, Las Med Sci, 2020	Cross-sectional	100 patients submitted to upper GI endoscopy	ME-BLI	WLE	GIM	Sensitivity 89% vs 35% Specificity 97% vs 39% PPV 94% vs 25% NPV 94% vs 57% Accuracy 94% vs 43%	4 patients in 36 were identified only on random biopsies (not on WLE nor BLI) Sensitivity targeted 32/36 = 88%

Diagnostic/Prognostic related key question

Are there any RCT? *If yes please complete (add each study per line in the table)*

Study ID	Study design Score **(4)**	Risk of bias (alinea(s))*	Quality Score **(0 to -2)****	Consistency Score **(-1 to 1)** #	Directness Score **(0 to -2)** @	Publication bias † (**0:No,1:Yes**)	Reported OR/RR/HR	Effect size Score **(0 to 2)** §	Evidence Level¶				Type of study according to SIGN								Recommendation SIGN			
									High	Mod	Low	Very Low	1++	1+	1-	2++	2+	2-	3	4	A	B	C	D
Ji R, Dig Liv Dis, 2020	3	1)	-1	1	-1	NA	NR	0		X					X							x		

* 1) blinding of measurements (test and outcome); 2) allocation; 3) verification (all individuals were submitted to both tests); 4) complete follow-up; 5) other – please identify

** Low risk of bias would indicate “no serious limitations” = 0; Presence of serious limitations then downgrade the quality of evidence for this outcome by 1 level = -1; Presence of very serious limitations then downgrade the quality of evidence for this outcome by 2 level = -2

Evidence of dose response across or within studies (or inconsistency across studies is explained by a dose response); also up to one point added if adjustment for confounders would have increased the effect size (1); All / most studies show similar results (0); Lack of agreement between studies (e.g. statistical heterogeneity between RCTs, conflicting results) (-1)

@ -1 per problem in generalizability to the target population

†: only for meta-analysis

§ 0 if Not all effect sizes more than 2 or less than 0.5 and significant; or if OR/RR/HR not significant; 1 if Effect size more than 2 or less than 0.5 for all studies/meta-analyses included in comparison and significant; 2 if Effect size more than 5 or less tha.2 for all studies/meta-analyses included in comparison and significant

¶: High: Further research is very unlikely to change our confidence in the estimate of effect; Moderate: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate; Low: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate; Very low: Any estimate of effect is very uncertain

Are there only case-controls/cross-sectional? *If yes please complete (add each study per line in the table)*

Study ID	Study design Score **(2)**	Risk of bias (alinea(s))*	Quality Score **(0 to -3)****	Consistency Score **(-1 to 1) #**	Directness Score **(0 to -2) @**	Publication bias † **(0:No,1:Yes)**	Reported OR/RR/HR	Effect size Score **(0 to 2)** §	Evidence Level¶				Type of study according to SIGN								Recommendation SIGN			
									High	Mod	Low	Very Low	1++	1+	1-	2++	2+	2-	3	4	A	B	C	D
Fatnak N, Endosc Int Open, 2022	2-	1) Only patients with known GIM	-1	1	-1	NA	NR	0			X							X					x	
Esposito G, Endoscopy, 2020	2	-	0	1	0	NA	NR	0		X							X						x	
Chen H, 2020	2	-	0	1	0	NA	NR	0		X							X						x	

* 1) Selection; 2) Comparability; 3) Exposure

** -1 per problem: Selection: -1: selected group of users or no description; Comparability -1: no comparison between the cohorts; Outcome -1: No description, no follow up

Evidence of dose response across or within studies (or inconsistency across studies is explained by a dose response); also up to one point added if adjustment for confounders would have increased the effect size (1); All / most studies show similar results (0); Lack of agreement between studies (e.g. statistical heterogeneity between RCTs, conflicting results) (-1)

@ -1 per problem in generalizability to the target population

†: only for meta-analysis

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¶: High: Further research is very unlikely to change our confidence in the estimate of effect; Moderate: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate; Low: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate; Very low: Any estimate of effect is very uncertain

Sentence	**ESGE/EHMSG/ESP recommend that when there is suspicion of a neoplastic lesion, the lesion should be** **- properly described (size, morphology according to Paris classification, location, vascular and mucosal patterns)** **- photo documented** **- and 2 targeted biopsies should be taken.**	
GRADE	**Strength of recommendation: Conditional**	**Quality of evidence: Moderate**
PICO 1	Population – Patients with premalignant or malignant gastric lesion Intervention – biopsy sampling of LGD/HGD/carcinoma during upper endoscopy Comparison – description of the lesion	

PICO 2	Outcome – necessity and number of biopsy samples of gastric neoplastic lesion, fibrosis; ESD outcomes (en-bloc, bleeding, perforation) in relation to pre-resection biopsies Population – Patients with premalignant or malignant gastric lesion Intervention – evaluation of endoscopic resectability of the lesion during upper endoscopy Comparison – predictors of submucosal invasion and risk factors (also for non-curative resection) Outcome – endoscopic or surgical resection
Query(ies) and databases searched	Search for: [Title/Abstract]; database: PubMed ("early gastric cancer" OR "gastric cancer" OR dysplasia OR neoplasia) AND (biops* OR “biopsy sampl*” OR “endoscopic evaluation” OR “endoscopic prediction” OR “endoscopically resectable” OR “lesion description” OR morphology) AND (“endoscopic resection” OR “endoscopic mucosal resection” OR EMR OR “endoscopic submucosal dissection” OR ESD) AND (outcome* OR “adverse event*” OR bleeding OR perforation* OR fibrosis) ("early gastric cancer" OR "gastric cancer" OR dysplasia OR neoplasia) AND (“submucosal invasion“ OR “endoscopic evaluation” OR “endoscopic prediction” OR “endoscopically resectable” OR “non-curative resection” OR “non curative resection” OR “deep submucosal invasion”) AND (“endoscopic resection” OR “endoscopic mucosal resection” OR EMR OR “endoscopic submucosal dissection” OR ESD OR “surgical resection” OR surgery)
Table of evidence	**(PICO 1) *Are there any cohorts or case-controls/cross-sectional?***

Study ID	Study design Score **(2)**	Risk of bias (linea(s)) *	Quality Score **(0 to -3) ****	Consistency Score **(-1 to 1) #**	Directness Score **(0 to -2) @**	Publication bias **(0: No,1: Yes)**	Reported OR/RR/HR	Effect size Score **(0 to 2) §**	Evidence Level¶				Type of study according to SIGN								Recommendation SIGN			
									High	Mod	Low	Very Low	1++	1+	1-	2++	2+	2-	3	4	A	B	C	D
Vos 2023	2, Prospective Multicentric observational study	1	0	1	0	0	OR, 3.07	1		X	X					X						X		
Milhomem, 2021	1, Observational retrospective	1	-1	0	-1	0	OR, 0.41	0			X							X					X	
Duan, 2022	2, Observational retrospective	1	-2	0	-1	1	OR, 2.76	1				X						X					X	
Pyo, 2019	1, Observational study	1	-1	0	-1	0	OR, 1.64	0			X						X						X	
De Marco, 2020	2, Meta-analysis	-	-1	1	-2	0	OR, 0.10	0		X	X						X						X	
Lee, 2020	1, Observational retrospective	-	-1	1	-1	NA	OR, 9.74	2			X						X	X					X	
Han, 2023	1, Observational retrospective	1	-1	0	-1	NA	OR, 11,61	2			X							X					X	
Ma, 2021	1, Observational retrospective	1	-1	0	-1	0	OR, 4.9	1			X						X						X	
Tang, 2023	1, Observational retrospective	-	-2	0	-1	NA	OR, 29.7	2			X	X						X					X	
Embaye, 2021	1, Observational retrospective	1	-2	-1	-1	0	OR, 15.5	2				X						X					X	
Kanesaka, 2018	2, Prospective Multicentric observational	1	-1	0	-1	0	NA	0									X						X	

	study																						
Kim, 2020	1, Observational retrospective	-	-1	-1	-1	0	NA	0									X					X	
Jeon, 2018	1, Observational retrospective	1	-1	-1	-1	0	NA	0									X					X	

* 1) Selection; 2) Comparability; 3) Outcome
** -1 per problemSelection: -1: selected group of users or no description; Comparability -1: no comparison between the cohorts; Outcome -1: No description, no follow up
# Evidence of dose response across or within studies (or inconsistency across studies is explained by a dose response); also up to one point added if adjustment for confounders would have increased the effect size (1); All / most studies show similar results (0); Lack of agreement between studies (e.g. statistical heterogeneity between RCTs, conflicting results) (-1)
@ -1 per problem in generalizability to the target population
†: only for meta-analysis
§ 0 if Not all effect sizes more than 2 or less than 0.5 and significant; or if OR/RR/HR not significant; 1 if Effect size more than 2 or less than 0.5 for all studies/meta-analyses included in comparison and significant; 2 if Effect size more than 5 or less tha.2 for all studies/meta-analyses included in comparison and significant
¶: High: Further research is very unlikely to change our confidence in the estimate of effect; Moderate: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate; Low: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate; Very low: Any estimate of effect is very uncertain

Table of evidence **(PICO 2) *Are there any cohorts or case-controls/cross-sectional?***

Study ID	Study design Score **(2)**	Risk of bias (alinea(s)) *	Quality Score **(0 to -3) ** **	Consistency Score **(-1 to 1) #**	Directness Score **(0 to -2)** @	Publication bias (**0: No,1: Yes**)	Reported OR/RR/HR	Effect size Score **(0 to 2)** §	Evidence Level¶				Type of study according to SIGN								Recommendation SIGN			
									High	Mod	Low	Very Low	1++	1+	1-	2++	2+	2-	3	4	A	B	C	D
Figueiroa, 2019	2, meta-analysis	1	0	1	0	0	OR, 5.01	2		X				X								X		
De Marco, 2020	2, meta-analysis	1	0	0	0	0	OR, 3.94	1		X					X							X		
Lee, 2020	2, Observational retrospective	1	-1	0	0	0	OR, 3.81	1		X	X					X							X	
Kim, 2021	1, Observational retrospective	1	-1	0	0	0	OR, 3.6	1		X	X					X							X	
Han, 2023	1, Observational retrospective	1	-1	0	-1	NA	OR, 5.13	2			X						X						X	
Ma, 2021	1, Observational retrospective	1	-1	0	-1	0	OR, 3.9	1			X						X						X	
Tang, 2023	1, Observational retrospective	-	-2	0	-1	0	OR, 16.3	2			X						X						X	
Libânio, 2017	1, Observational retrospective	1	-1	0	-1	0	OR, 2.4	1			X						X						X	
Embaye, 2021	1, Observational retrospective	1	-1	0	-1	0	OR, 5,45	2			X						X						X	
Tsuji, 2023	1, Multicentric prospective study	1	-1	0	-2	0	OR, 4.9	1			X						X						X	
Toyoshima, 2021	1, Observational retrospective	-	-2	-1	-1	0	OR, 3.39	1			X							X					X	
Nagahama, 2017	1, Observational retrospective	2	-1	0	-1	0	NA	0			X						X	X					X	
Hatta, 2020	2, meta-analysis	1	0	-1	-1	0	OR, 1.77	0		X	X						X						X	
Vos, 2023	1, Prospective Multicentric observational study	-	-1	-1	-1	0	OR, 1.03	0			X							X					X	
Pyo, 2019	1,	1	-1	-1	-1	0	OR, 2.28	1			X							X					X	

	Observational study																							
Lin, 2019	1, Observational study	1	-1	0	-1	0	OR, 1.5	0			X							X					X	

* 1) Selection; 2) Comparability; 3) Outcome
** -1 per problemSelection: -1: selected group of users or no description; Comparability -1: no comparison between the cohorts; Outcome -1: No description, no follow up
# Evidence of dose response across or within studies (or inconsistency across studies is explained by a dose response); also up to one point added if adjustment for confounders would have increased the effect size (1); All / most studies show similar results (0); Lack of agreement between studies (e.g. statistical heterogeneity between RCTs, conflicting results) (-1)
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¶: High: Further research is very unlikely to change our confidence in the estimate of effect; Moderate: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate; Low: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate; Very low: Any estimate of effect is very uncertain

Sentence	**ESGE/EHMSG/ESP do not recommend routine performance of endoscopic ultrasonography (EUS), computed tomography (CT), magnetic resonance imaging (MRI), or positron emission tomography (PET)-CT prior to endoscopic resection unless there are signs suspicious of deep submucosal invasion or the lesion is not considered suitable for endoscopic resection.**	
GRADE	**Strength of recommendation: Strong**	**Quality of evidence: Moderate**
PICO	Population – Patients with premalignant or malignant gastric lesion Intervention – endoscopic prediction Comparison – cross-sectional imaging (magnetic resonance imaging or computed tomography or PET/CT or EUS) Outcome – accuracy / sensitivity / specificity / PPN, NPV, likelihood ratios	
Query(ies) and databases searched	Search for: [Title/Abstract]; database: PubMed ("early gastric cancer" OR "gastric cancer" OR dysplasia OR neoplasia) AND (“cross-sectional imaging” OR “cross sectional imaging” OR “magnetic resonance” OR “magnetic resonance imaging” OR “computed tomography” OR “endoscopic ultrasound” OR “endoscopic ultrasonography” OR “positron emission tomography–computed tomography” OR “positron emission tomography computed tomography” OR “pet/ct” OR “pet-ct” OR ct OR mr OR mri OR EUS) AND (“endoscopic resection” OR “endoscopically resectable” OR “endoscopic mucosal resection” OR EMR OR “endoscopic submucosal dissection” OR ESD) AND (“submucosal invasion“ OR accuracy OR “endoscopic evaluation” OR “endoscopic prediction” OR “deep submucosal invasion” OR staging OR overstaging OR understaging)	
Table of evidence	***Are there any cohorts or case-controls/cross-sectional?***	

Study ID	Study design Score **(2)**	Risk of bias (alinea(s)) *	Quality Score **(0 to -3) ****	Consistency Score **(-1 to 1) #**	Directness Score **(0 to -2) @**	Publication bias (**0: No,1: Yes**)	Reported OR/RR/HR	Effect size Score **(0 to 2) §**	Evidence Level¶				Type of study according to SIGN								Recommendation SIGN			
									High	Mod	Low	Very Low	1++	1+	1-	2++	2+	2-	3	4	A	B	C	D
Shi, 2019	2, meta-analysis	1	0	0	0	0	NA	0		X					X							X		
Fairweather, 2015	2, Retrospective observational study	2	-1	-1	0	NA	NA	0			X					X							X	
Wang, 2021	1, Retrospective observational study	1	-1	0	0	NA	NA	0			X						X						X	
Chung, 2019	2, Retrospective observational study	1	-1	0	0	0	NA	0			X					X							X	
Kuroki, 2021	1, Retrospective observational study	1	-1	0	0	0	OR	1			X					X							X	
Lee, 2016	2, Retrospective observational	1	-1	-1	-1	0	NA	0			X						X						X	

	study																						
Li, 2021	1, Retrospective observational study	1	-1	-1	0	0	OR	1			X					X							X	
Kim, 2022	2, Retrospective observational study	1	-1	0	0	0	OR	1			X					X							X	
Tsuji, 2023	1, Multicentric prospective study	2	-1	0	-1	0	Accuracy, p<0.001	1			X						X						X	
Hamada, 2021	1, Observational study	2	-3	-1	-2	NA	NA	0				X						X					X	
Zhao, 2023	1, Observational study	2	-2	-1	-2	NA	NA	0				X						X					X	
Gambitta, 2023	1, Observational study	2	-3	-1	-2	NA	NA	0				X						X					X	
Chen, 2022	1, Observational study	2	-3	-1	-2	NA	NA	0				X						X					X	

* 1) Selection; 2) Comparability; 3) Outcome
** -1 per problemSelection: -1: selected group of users or no description; Comparability -1: no comparison between the cohorts; Outcome -1: No description, no follow up
# Evidence of dose response across or within studies (or inconsistency across studies is explained by a dose response); also up to one point added if adjustment for confounders would have increased the effect size (1); All / most studies show similar results (0); Lack of agreement between studies (e.g. statistical heterogeneity between RCTs, conflicting results) (-1)
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§ 0 if Not all effect sizes more than 2 or less than 0.5 and significant; or if OR/RR/HR not significant; 1 if Effect size more than 2 or less than 0.5 for all studies/meta-analyses included in comparison and significant; 2 if Effect size more than 5 or less tha.2 for all studies/meta-analyses included in comparison and significant
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Sentence	**ESGE/EHMSG/ESP suggest the use of validated endoscopic classifications of atrophy (e.g. Kimura–Takemoto) or GIM (e.g. EGGIM) to endoscopically stage precancerous conditions and stratify risk for GC.**	
GRADE	**Strength of recommendation: Conditional**	**Quality of evidence: Low**
PICO	Patients: Patients submitted to endoscopy Intervention: Endoscopic extensive atrophy / IM (Kimura-Takemoto) Comparator: No endoscopic extensive atrophy/IM Outcome: OLGA III/IV or extensive histological atrophy / IM / cancer	
Query(ies) and databases searched	Search: **endoscopic grading of gastric intestinal metaplasia**; Database: PubMed ("endoscope s"[All Fields] OR "endoscoped"[All Fields] OR "endoscopes"[MeSH Terms] OR "endoscopes"[All Fields] OR "endoscope"[All Fields] OR "endoscopical"[All Fields] OR "endoscopically"[All Fields] OR "endoscopy"[MeSH Terms] OR "endoscopy"[All Fields] OR "endoscopic"[All Fields]) AND ("grade"[All Fields] OR "graded"[All Fields] OR "grades"[All Fields] OR "grading"[All Fields] OR "gradings"[All Fields]) AND ("gastrics"[All Fields] OR "stomach"[MeSH Terms] OR "stomach"[All Fields] OR "gastric"[All Fields]) AND ("intestinalization"[All Fields] OR "intestinalized"[All Fields] OR "intestinally"[All Fields] OR "intestinals"[All Fields] OR "intestine s"[All Fields] OR "intestines"[MeSH Terms] OR "intestines"[All Fields] OR "intestinal"[All Fields] OR "intestine"[All Fields]) AND ("metaplasia"[MeSH Terms] OR "metaplasia"[All Fields] OR "metaplasias"[All Fields]) Search: **endoscopic grading of gastric atrophy**; Database: PubMed ("endoscope s"[All Fields] OR "endoscoped"[All Fields] OR "endoscopes"[MeSH Terms] OR "endoscopes"[All Fields] OR "endoscope"[All Fields] OR "endoscopical"[All Fields] OR "endoscopically"[All Fields] OR "endoscopy"[MeSH Terms] OR "endoscopy"[All Fields] OR "endoscopic"[All Fields]) AND ("grade"[All Fields] OR "graded"[All Fields] OR "grades"[All Fields] OR "grading"[All Fields] OR "gradings"[All Fields]) AND ("gastritis, atrophic"[MeSH Terms] OR ("gastritis"[All Fields] AND "atrophic"[All Fields]) OR "atrophic gastritis"[All Fields] OR ("gastric"[All Fields] AND "atrophy"[All Fields]) OR "gastric atrophy"[All Fields]); Database: PubMed	

Table of evidence		*Are there any cohorts?*																						
Study ID	Study design Score (2)	Risk of bias (alinea(s))*	Quality Score (0 to -3)**	Consistency Score (-1 to 1) #	Directness Score (0 to -2) @	Publication bias (0:No,1:Yes)	Reported OR/RR/HR	Effect size Score (0 to 2) §	Evidence Level¶				Type of study according to SIGN								Recommendation SIGN			
									High	Mod	Low	Very Low	1++	1+	1-	2++	2+	2-	3	4	A	B	C	D
Endoscopic grading of gastric intestinal metaplasia (IM)																								
Pimentel-Nunes P (2016)	Prospective cohort study	1	-1 Only academic centers	0	-1	NA	OR	Reported OR		X						X						X		
Castro R (2019)	Prospective cohort study	1	-1 Only academic centers	0	-1	NA	OR	Reported OR		X						X						X		
Esposito G (2019)	Prospective cohort study	1	-1 Only academic centers	0	-1	NA	OR	Reported OR		X						X						X		
Zhang G (2020)	Prospective cohort study	1	-1	0	-1	NA	NA	Reported P<0.01 for comparison scores		X						X						X		
Kawamura M (2022)	Prospective cohort study	-	0	-1	-1	-1	OR	Reported P<0.01 for comparison scores		X						X						X		
Endoscopic grading of gastric atrophy																								
Hosokawa (2001)	Retrospective cohort	2	-2	0	-1	NA	NR	1				X					X						X	
Uemura N (2001)	Retrospective cohort	2	-2	0	-1	NA	NR	1				X					X						X	
Take S (2010)	Prospective cohort study	-	0	0	-1	NA	NA	1				X					X						X	
Kodama M (2013)	Prospective cohort study	1	-1 Only academic center	-1	-1	NA	Reported OR	1				X					X						X	
Masuyama H (2015)	Retrospective cohort	1	-1 Only academic center	-1	-1	NA	NR	1				X					X						X	
Sakitani K (2015)	Retrospective cohort	-	0	0	-1	NA	NR	1				X					X						X	
Mori G (2015)	Retrospective cohort	1	-1 Only academic center	0	-1	NA	Reported HR	1				X					X						X	
Sekikawa A (2016)	Retrospective cohort	0	0	-1	-1	NA	Reported OR	1				X					X						X	
Shichijo S (2016)	Retrospective cohort	1	-1 Only academic center	-1	-1	NA	Reported HR	1				X					X						X	
Shichijo S (2017)	Retrospective cohort	1	-1 Only academic center	-1	-1	NA	Reported OR	1				X					X						X	
Song JH (2017)	Retrospective cohort	1	-1 Only academic centers	-1	-1	NA	Reported HR	1				X					X						X	
Sugimoto M (2017)	Retrospective cohort	1	-1 Only academic centers	0	-1	NA	Reported OR	1				X					X						X	
Toyoshima O (2017)	Retrospective cohort	0	0	-1	-1	NA	Reported OR	1				X					X						X	
Nam H (2018)	Retrospective cohort	1	-1 Only academic centers	-1	-1	NA	NR	1				X					X						X	

Kaji K (2018)	Retrospective cohort	1	-1 Only academic centers	-1	-1	NA	Reported OR	1				X					X						X	
Na HK (2022)	Prospective cohort study	1	-1 Only academic centers	-1	-1	NA	Reported OR	1				X					X						X	

* 1) Selection; 2) Comparability; 3) Outcome
** -1 per problem Selection: -1: selected group of users or no description; Comparability -1: no comparison between the cohorts; Outcome -1: No description, no follow up
# Evidence of dose response across or within studies (or inconsistency across studies is explained by a dose response); also up to one point added if adjustment for confounders would have increased the effect size (1); All / most studies show similar results (0); Lack of agreement between studies (e.g. statistical heterogeneity between RCTs, conflicting results) (-1)
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¶: High: Further research is very unlikely to change our confidence in the estimate of effect; Moderate: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate; Low: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate; Very low: Any estimate of effect is very uncertain

Table of evidence ***Are there only case-controls/cross-sectional?***

Study ID	Study design Score **(2)**	Risk of bias (alinea(s)) *	Quality Score **(0 to -3) ****	Consistency Score **(-1 to 1) #**	Directness Score **(0 to -2) @**	Publication bias † **(0: No,1: Yes)**	Reported OR/RR/HR	Effect size Score **(0 to 2) §**	Evidence Level¶				Type of study according to SIGN								Recommendation SIGN			
									High	Mod	Low	Very Low	1++	1+	1-	2++	2+	2-	3	4	A	B	C	
Endoscopic grading of gastric intestinal metaplasia (IM)																								
Marcos P (2020)	Case-control study	1	-1 Only academic center	0	-1	NA	OR	0		X						X						X		
Zheng J (2020)	Case-control study	1	1 Only academic center	0	-1	NA	OR	0		X					X							X		
Kawamura M (2022)	Case-control study	1	2) No control group	0	-1	NA	OR	0			X						X						X	
Fang S (2022)	Meta-analysis	0	-1	-1	0	0	OR	0		X					X							X		
Wei N (2022)	Meta-analysis	0	-1	-1	0	0	OR	0		X					X							X		
Endoscopic grading of gastric atrophy																								
Kono S (2015)	Cross sectional study	1	2) No control group	0	-1	NA	OR	0			X						X						X	
Chen M (2023)	Case-control	0	-1	-1	0	0	OR	0		X					X							X		
Xiao S (2022)	Meta-analysis	0	-1	-1	0	0	OR	0		X					X							X		

Sentence	**ESGE/EHMSG/ESP recommends biopsy of 2 fragments from the antrum/incisura and 2 from the corpus, guided by VCE clearly labeled in two separate vials. Additional biopsy from the incisura is optional.**	
GRADE	**Strength of recommendation: Strong**	**Quality of evidence: Moderate**
PICO	P: Patients with gastric precancerous conditions (chronic atrophic gastritis and/or intestinal metaplasia); I: Biopsies of two topographic sites (from both the antrum/incisura and the corpus, guided by virtual chromoendoscopy); C: Addition of incisura biopsy to standard biopsy protocol	

	O: Additional yield in adequate staging of gastric precancerous conditions
Query(ies) and databases searched	Search: PubMed ("gastrics"[All Fields] OR "stomach"[MeSH Terms] OR "stomach"[All Fields] OR "gastric"[All Fields]) AND "incisura"[All Fields] AND ("biopsie"[All Fields] OR "biopsy"[MeSH Terms] OR "biopsy"[All Fields] OR "biopsied"[All Fields] OR "biopsies"[All Fields] OR "biopsy s"[All Fields] OR "biopsying"[All Fields] OR "biopsys"[All Fields] OR "pathology"[MeSH Subheading] OR "pathology"[All Fields])

Table of evidence — ***Are there any cohorts?***

Study ID	Study design Score **(2)**	Risk of bias (alinea(s)) *	Quality Score **(0 to -3)** **	Consistency Score **(-1 to 1)** #	Directness Score **(0 to -2)** @	Publication bias **(0: No,1: Yes)**	Reported OR/RR/HR	Effect size Score **(0 to 2)** §	Evidence Level¶				Type of study according to SIGN								Recommendation SIGN			
									High	Mod	Low	Very Low	1++	1+	1-	2++	2+	2-	3	4	A	B	C	D
Eriksson N. K. (2005)	Prospective cohort study	1	-1	0	-1	NA	NR	1			X						X						X	
Lash J. G. (2013)	Prospective cohort study	1	-1 Only academic centers	-1	-1	NA	Reported OR	1			X						X						X	
Isajevs S (2014)	Prospective cohort study	-	0	0	-1	NA	NA	1			X						X						X	
Varbanova M (2015)	Prospective cohort study	1	-1 Only academic center	-1	-1	NA	NR	1			X						X						X	
Kim Y-I (2017)	Prospective cohort study	1	-1 Only academic center	-1	-1	NA	NR	1			X						X						X	
Castro R (2019)	Prospective cohort study	1	-1 Only academic centers	-1	-1	-1	NR	1			X						X						X	
Zhang M (2019)	Prospective cohort study	1	-1	0	-1	NA	NR	1			X						X						X	
Ferrari F (2023)	Prospective cohort study	1	-1 Only academic centers	-1	-1	NA	NR	1			X						X						X	
Khomeriki S (2023)	Prospective cohort study	1	-1 Only academic centers	-1	-1	NA	NR	1			X						X						X	

* 1) Selection; 2) Comparability; 3) Outcome
** -1 per problem Selection: -1: selected group of users or no description; Comparability -1: no comparison between the cohorts; Outcome -1: No description, no follow up
# Evidence of dose response across or within studies (or inconsistency across studies is explained by a dose response); also up to one point added if adjustment for confounders would have increased the effect size (1); All / most studies show similar results (0); Lack of agreement between studies (e.g. statistical heterogeneity between RCTs, conflicting results) (-1)
@ -1 per problem in generalizability to the target population
†: only for meta-analysis
§ 0 if Not all effect sizes more than 2 or less than 0.5 and significant; or if OR/RR/HR not significant; 1 if Effect size more than 2 or less than 0.5 for all studies/meta-analyses included in comparison and significant; 2 if Effect size more than 5 or less tha.2 for all studies/meta-analyses included in comparison and significant
¶: High: Further research is very unlikely to change our confidence in the estimate of effect; Moderate: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate; Low: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate; Very low: Any estimate of effect is very uncertain

Table of evidence — ***Are there only case-controls/cross-sectional?***

Study ID	Study design Score **(2)**	Risk of bias (alinea(s)) *	Quality Score **(0 to -3)** **	Consistency Score **(-1 to 1)** #	Directness Score **(0 to -2)** @	Publication bias † **(0: No,1: Yes)**	Reported OR/RR/HR	Effect size Score **(0 to 2)** §	Evidence Level¶				Type of study according to SIGN								Recommendation SIGN			
									High	Mod	Low	Very Low	1++	1+	1-	2++	2+	2-	3	4	A	B	C	D
Marcos-Pinto R. (2012)	Case-control study	1	-1 Only CAG/IM patients	-1	1	NA	NR	Not reported. P<0.01			X						X						X	

* 1) Selection; 2) Comparability; 3) Exposure

** -1 per problem: Selection: -1: selected group of users or no description; Comparability -1: no comparison between the cohorts; Outcome -1: No description, no follow up
# Evidence of dose response across or within studies (or inconsistency across studies is explained by a dose response); also up to one point added if adjustment for confounders would have increased the effect size (1); All / most studies show similar results (0); Lack of agreement between studies (e.g. statistical heterogeneity between RCTs, conflicting results) (-1)
@ -1 per problem in generalizability to the target population
†: only for meta-analysis
§ 0 if Not all effect sizes more than 2 or less than 0.5 and significant; or if OR/RR/HR not significant; 1 if Effect size more than 2 or less than 0.5 for all studies/meta-analyses included in comparison and significant; 2 if Effect size more than 5 or less tha.2 for all studies/meta-analyses included in comparison and significant
¶: High: Further research is very unlikely to change our confidence in the estimate of effect; Moderate: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate; Low: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate; Very low: Any estimate of effect is very uncertain

Sentence	**ESGE/EHMSG/ESP suggest that systems for histopathological staging of atrophy or preferably IM (e.g. OLGA, OLGIM) can be used and integrated with endoscopic information in the management of patients.**	
GRADE	**Strength of recommendation: Conditional**	**Quality of evidence: Moderate**
PICO	P: Patients with gastric precancerous conditions (chronic atrophic gastritis and/or intestinal metaplasia) I: Histopathological staging (e. g. OLGA and OLGIM assessment) systems of precancerous conditions implementation C: Addition of incisura biopsy to standard biopsy protocol O: Risk stratification for early gastric neoplasia	
Query(ies) and databases searched	Search (PubMed): **operative link on gastritis assessment AND gastric cancer** "operation s"[All Fields] OR "operational"[All Fields] OR "operative"[All Fields] OR "operatively"[All Fields] OR "operatives"[All Fields] OR "operator"[All Fields] OR "operator s"[All Fields] OR "operators"[All Fields] OR "surgery"[MeSH Subheading] OR "surgery"[All Fields] OR "operations"[All Fields] OR "surgical procedures, operative"[MeSH Terms] OR ("surgical"[All Fields] AND "procedures"[All Fields] AND "operative"[All Fields]) OR "operative surgical procedures"[All Fields] OR "operation"[All Fields]) AND "link"[All Fields] AND ("gastritis"[MeSH Terms] OR "gastritis"[All Fields] OR "gastritides"[All Fields]) AND ("assess"[All Fields] OR "assessed"[All Fields] OR "assessement"[All Fields] OR "assesses"[All Fields] OR "assessing"[All Fields] OR "assessment"[All Fields] OR "assessment s"[All Fields] OR "assessments"[All Fields]) AND ("stomach neoplasms"[MeSH Terms] OR ("stomach"[All Fields] AND "neoplasms"[All Fields]) OR "stomach neoplasms"[All Fields] OR ("gastric"[All Fields] AND "cancer"[All Fields]) OR "gastric cancer"[All Fields]) Search (PubMed): **operative link on gastric intestinal metaplasia AND gastric cancer** ("operability"[All Fields] OR "operable"[All Fields] OR "operate"[All Fields] OR "operated"[All Fields] OR "operates"[All Fields] OR "operating"[All Fields] OR "operation s"[All Fields] OR "operational"[All Fields] OR "operative"[All Fields] OR "operatively"[All Fields] OR "operatives"[All Fields] OR "operator"[All Fields] OR "operator s"[All Fields] OR "operators"[All Fields] OR "surgery"[MeSH Subheading] OR "surgery"[All Fields] OR "operations"[All Fields] OR "surgical procedures, operative"[MeSH Terms] OR ("surgical"[All Fields] AND "procedures"[All Fields] AND "operative"[All Fields]) OR "operative surgical procedures"[All Fields] OR "operation"[All Fields]) AND "link"[All Fields] AND ("gastrics"[All Fields] OR "stomach"[MeSH Terms] OR "stomach"[All Fields] OR "gastric"[All Fields]) AND ("intestinalization"[All Fields] OR "intestinalized"[All Fields] OR "intestinally"[All Fields] OR "intestinals"[All Fields] OR "intestine s"[All Fields] OR "intestines"[MeSH Terms] OR "intestines"[All Fields] OR "intestinal"[All Fields] OR "intestine"[All Fields]) AND ("metaplasia"[MeSH Terms] OR "metaplasia"[All Fields] OR "metaplasias"[All Fields]) AND ("stomach neoplasms"[MeSH Terms] OR ("stomach"[All Fields] AND "neoplasms"[All Fields]) OR "stomach neoplasms"[All Fields] OR ("gastric"[All Fields] AND "cancer"[All Fields]) OR "gastric cancer"[All Fields])	
Table of evidence	***Are there any cohorts?***	

Study ID	Study design Score **(2)**	Risk of bias (alinea(s)) *	Quality Score **(0 to -3) ** **	Consistency Score **(-1 to 1) #**	Directness Score **(0 to -2) @**	Publication bias **(0: No,1:Yes)**	Reported OR/RR/HR	Effect size Score **(0 to 2) §**	Evidence Level¶				Type of study according to SIGN								Recommendation SIGN			
									High	Mod	Low	Very Low	1++	1+	1-	2++	2+	2-	3	4	A	B	C	D
Rugge M (2007)	Cohort study	1	-1 region	0	-1	NA	NR	1			X						X						X	
Capelle L (2010)	Cohort study	1	-1 Only academic centers	0	-1	NA	NR	Reported OR			X						X						X	
Rugge M (2010)	Cohort study	1	-1 Only academic centers	0	-1	NA	OR	Reported OR			X						X						X	
Cho S (2013)	Retrospective study	1	-1 Only academic	0	-1	NA	NA	Reported P<0.01 for			X						X						X	

			centers					comparison scores																	
Rugge M (2018)	Cohort study	-	0	-1	-1	NA	OR	Reported P<0.01 for comparison scores			X					X							X	
den Hollander (2019)	Cohort study	1	-1 Only academic centers	0	-1	NA	OR	Reported OR			X					X							X	
Rugge M (2019)	Cohort study	1	-1 Only academic centers	0	-1	NA	OR	Reported OR			X					X							X	
Chapelle N (2020)	Cohort study	1	-1 Only academic centers	0	-1	NA	OR	Reported OR			X					X							X	
Lee J (2022)	Cohort study	1	-1 Only academic centers	0	-1	NA	NA	Reported P<0.01 for comparison scores			X					X							X	
Sun L (2022)	Retrospective study	-	0	-1	-1	NA	OR	NR			X						X						X	
Na Y (2023)	Retrospective study	-	0	-1	-1	NA	OR	Reported HR			X					X							X	

* 1) Selection; 2) Comparability; 3) Outcome
** -1 per problem Selection: -1: selected group of users or no description; Comparability -1: no comparison between the cohorts; Outcome -1: No description, no follow up
# Evidence of dose response across or within studies (or inconsistency across studies is explained by a dose response); also up to one point added if adjustment for confounders would have increased the effect size (1); All / most studies show similar results (0); Lack of agreement between studies (e.g. statistical heterogeneity between RCTs, conflicting results) (-1)
@ -1 per problem in generalizability to the target population
†: only for meta-analysis
§ 0 if Not all effect sizes more than 2 or less than 0.5 and significant; or if OR/RR/HR not significant; 1 if Effect size more than 2 or less than 0.5 for all studies/meta-analyses included in comparison and significant; 2 if Effect size more than 5 or less tha.2 for all studies/meta-analyses included in comparison and significant
¶: High: Further research is very unlikely to change our confidence in the estimate of effect; Moderate: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate; Low: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate; Very low: Any estimate of effect is very uncertain

Table of evidence ***Are there only case-controls/cross-sectional?***

Study ID	Study design Score **(2)**	Risk of bias (alinea(s)) *	Quality Score **(0 to -3) **	Consistency Score **(-1 to 1) #**	Directness Score **(0 to -2) @**	Publication bias † **(0: No,1: Yes)**	Reported OR/RR/HR	Effect size Score **(0 to 2)** §	Evidence Level¶				Type of study according to SIGN								Recommendation SIGN			
									High	Mod	Low	Very Low	1++	1+	1-	2++	2+	2-	3	4	A	B	C	D
Satoh K (2008)	Case–control study	1	-1 Only academic center	0	-1	NA	NR	1			X						X						X	
Quach D (2010)	Cross-sectional study	1	-1 Only academic center	-1	-1	NA	NR	1				X					X						X	
Kodama M (2013)	Case–control study	1	-1 Only academic center	-1	-1	NA	Reported HR	1				X					X						X	
Tsai Y (2013)	Case–control study	1	-1 Only academic center	-1	-1	NA	Reported OR	1				X					X						X	
Zhou Y (2016)	Case–control study	1	-1 Only academic centers	-1	-1	NA	Reported HR	1				X					X						X	
Yun C (2018)	Case–control study	1	-1 Only academic centers	0	-1	NA	Reported OR	1				X					X						X	
Huang Y (2023)	Case–control study	0	0	-1	-1	NA	Reported OR	1				X					X						X	
Yue H (2018)	Meta-analysis	0	0	-1	-1	0	0	OR		X				X								X		
Wang J (2022)††	Meta-analysis	0	0	-1	-1	0	0			X				X								X		

								OR																	

* 1) Selection; 2) Comparability; 3) Exposure
** -1 per problem: Selection: -1: selected group of users or no description; Comparability -1: no comparison between the cohorts; Outcome -1: No description, no follow up
# Evidence of dose response across or within studies (or inconsistency across studies is explained by a dose response); also up to one point added if adjustment for confounders would have increased the effect size (1); All / most studies show similar results (0); Lack of agreement between studies (e.g. statistical heterogeneity between RCTs, conflicting results) (-1)
@ -1 per problem in generalizability to the target population
†: only for meta-analysis
§ 0 if Not all effect sizes more than 2 or less than 0.5 and significant; or if OR/RR/HR not significant; 1 if Effect size more than 2 or less than 0.5 for all studies/meta-analyses included in comparison and significant; 2 if Effect size more than 5 or less tha.2 for all studies/meta-analyses included in comparison and significant
¶: High: Further research is very unlikely to change our confidence in the estimate of effect; Moderate: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate; Low: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate; Very low: Any estimate of effect is very uncertain

Sentence	**ESGE/EHMSG/ESP suggest that patients with dysplasia (or indefinite for dysplasia) but no lesions seen on gastroscopy, are referred to a high quality endoscopy (namely, high definition white-light endoscopy with virtual chromoendoscopy [VCE]), staging of precancerous conditions and *H. pylori* if not previously performed. If no endoscopic lesions are again not seen, a follow-up high quality endoscopy is then needed in 6 months for high grade dysplasia, or 12 months for low grade dysplasia/indefinite for dysplasia.**																							
GRADE	**Strength of recommendation: Conditional**																					**Quality of evidence: Moderate**			
PICO	P: Patients submitted to endoscopy I: Virtual chromoendoscopy guided biopsies (NBI, BLI), dye-based chromoendoscopy guided biopsies C: High-definition white-light endoscopy guided biopsies O: Accuracy, sensitivity, and specificity for dysplasia/cancer																							
Query(ies) and databases searched	Search (PubMed): "gastroscopy"[Title/Abstract] OR "upper endoscopy"[Title/Abstract] AND "virtual chromoendoscopy"[Title/Abstract] OR "narrow-band imaging"[Title/Abstract] OR "NBI"[Title/Abstract] OR "blue laser imaging"[Title/Abstract] OR "blue light imaging"[Title/Abstract] OR "BLI"[Title/Abstract] OR "optical enhancement"[Title/Abstract] OR "chromoendoscopy"[Title/Abstract] OR "inspection time"[Title/Abstract] OR "evaluation time"[Title/Abstract] OR "high definition endoscopy"[Title/Abstract] OR "high quality endoscopy"[Title/Abstract] AND "gastric cancer"[Title/Abstract] OR "gastric precancerous conditions"[Title/Abstract] OR "gastric dysplasia"[Title/Abstract] Filters: Clinical Trial, Meta-Analysis, Randomized Controlled Trial																							
Table of evidence	***Are there any RCT?***																							

Study ID	Study design Score **(4)**	Risk of bias (alinea(s)) *	Quality Score **(0 to -2)** **	Consistency Score **(-1 to 1)** #	Directness Score **(0 to -2)** @	Publication bias † (**0: No,1: Yes**)	Reported OR/RR/HR	Effect size Score **(0 to 2)** §	Evidence Level¶				Type of study according to SIGN								Recommendation SIGN			
									High	Mod	Low	Very Low	1++	1+	1-	2++	2+	2-	3	4	A	B	C	D
Nakano T. Dig Dis. 2021		single center bias, selection bias in biopsy confirmation (only outside the lesion), exclusion bias (exclusion of moderately or poorly differentiated adenocarcinomas), Japan population	-1	NA	0	NA	NR	0		x					x								X	
Yoshida N, Gut. 2021		selection bias (EGC detection rate lower than expected and higher than in the general population), observer bias (impossible to blind the endoscopist to technology used), power issue (small number od EGS detected), high risk population, Japan population	-1	NA	0	NA	NR	0		x					x								X	
Dohi O. Gastrointest Endosc. 2019		observer bias, selection bias, Japan population	-1	NA	0	NA	NR	0		x					x								X	
Nagahama T.		scope limitation bias (study	-1	NA	0	NA	NR	0		x					x								x	

Endoscopy. 2018		designed to target only the proximal margins of lesions), selection bias (only lesions 10mm or larger), Japan population																					

* 1) blinding of measurements (test and outcome); 2) allocation; 3) verification (all individuals were submitted to both tests); 4) complete follow-up; 5) other – please identify
** Low risk of bias would indicate "no serious limitations" = 0; Presence of serious limitations then downgrade the quality of evidence for this outcome by 1 level = -1; Presence of very serious limitations then downgrade the quality of evidence for this outcome by 2 level = -2
# Evidence of dose response across or within studies (or inconsistency across studies is explained by a dose response); also up to one point added if adjustment for confounders would have increased the effect size (1); All / most studies show similar results (0); Lack of agreement between studies (e.g. statistical heterogeneity between RCTs, conflicting results) (-1)
@ -1 per problem in generalizability to the target population
†: only for meta-analysis
§ 0 if Not all effect sizes more than 2 or less than 0.5 and significant; or if OR/RR/HR not significant; 1 if Effect size more than 2 or less than 0.5 for all studies/meta-analyses included in comparison and significant; 2 if Effect size more than 5 or less tha.2 for all studies/meta-analyses included in comparison and significant
¶: High: Further research is very unlikely to change our confidence in the estimate of effect; Moderate: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate; Low: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate; Very low: Any estimate of effect is very uncertain

Table of evidence — ***Are there only case-controls/cross-sectional?***

Study ID	Study design Score **(2)**	Risk of bias (alinea(s)) *	Quality Score **(0 to -3)** **	Consistency Score **(-1 to 1)** #	Directness Score **(0 to -2)** @	Publication bias † **(0: No,1: Yes)**	Reported OR/RR/HR	Effect size Score **(0 to 2)** §	Evidence Level¶				Type of study according to SIGN								Recommendation SIGN			
									High	Mod	Low	Very Low	1++	1+	1-	2++	2+	2-	3	4	A	B	C	D
Yamamoto Y. JAMA Netw Open. 2022		only high risk patients, Japan population	-1	0	-1	NA	NR	0			x							x						x

* 1) Selection; 2) Comparability; 3) Exposure
** -1 per problem: Selection: -1: selected group of users or no description; Comparability -1: no comparison between the cohorts; Outcome -1: No description, no follow up
# Evidence of dose response across or within studies (or inconsistency across studies is explained by a dose response); also up to one point added if adjustment for confounders would have increased the effect size (1); All / most studies show similar results (0); Lack of agreement between studies (e.g. statistical heterogeneity between RCTs, conflicting results) (-1)
@ -1 per problem in generalizability to the target population
†: only for meta-analysis
§ 0 if Not all effect sizes more than 2 or less than 0.5 and significant; or if OR/RR/HR not significant; 1 if Effect size more than 2 or less than 0.5 for all studies/meta-analyses included in comparison and significant; 2 if Effect size more than 5 or less tha.2 for all studies/meta-analyses included in comparison and significant
¶: High: Further research is very unlikely to change our confidence in the estimate of effect; Moderate: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate; Low: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate; Very low: Any estimate of effect is very uncertain

Sentence	**ESGE/EHMSG/ESP suggest that patients with indefinite for dysplasia (confirmed by an expert pathologist) and an endoscopic lesion identified are referred to a high-quality endoscopy and, according to endoscopic findings, guided biopsies or resection considered.**	
GRADE	**Strength of recommendation: Conditional**	**Quality of evidence: Low**
PICO	P: Patients with gastric lesions diagnosed as indefinite for dysplasia or atypia or indefinite for neoplasia I: Endoscopic resection C: Repeated biopsy O: Accuracy, sensitivity, and specificity for dysplasia/cancer	
Query(ies) and databases searched	Search PubMed: ("indefinite dysplasia"[Title/Abstract] OR "indefinite for dysplasia"[Title/Abstract] OR "indefinite pathology"[Title/Abstract]) AND "stomach"[Title/Abstract] OR "gastric"[Title/Abstract]) OR ("indefinite neoplasia"[Title/Abstract] OR "indefinite for neoplasia"[Title/Abstract] OR "indefinite for neoplasm"[Title/Abstract]) AND ("stomach"[Title/Abstract] OR "gastric"[Title/Abstract]) OR ("epithelial atypia"[Title/Abstract]) AND ("stomach"[Title/Abstract] OR "gastric"[Title/Abstract]) OR ("intraepithelial neoplasia"[Title/Abstract] AND "indefinite"[Title/Abstract]) AND ("stomach"[Title/Abstract] OR "gastric"[Title/Abstract]) OR (("gastric biopsy"[Title/Abstract] OR "stomach biopsy"[Title/Abstract]) AND "indefinite pathology"[Title/Abstract]) AND ("stomach"[Title/Abstract] OR "gastric"[Title/Abstract]) Filters: Clinical Trial, Meta-Analysis, Randomized Controlled Trial	

Table of evidence — ***Are there any cohorts?***

Study ID	Study design Score **(2)**	Risk of bias (alinea(s)) *	Quality Score **(0 to -3)** **	Consistency Score **(-1 to 1)** #	Directness Score **(0 to -2)** @	Publication bias **(0: No,1: Yes)**	Reported OR/RR/HR	Effect size Score **(0 to 2)** §	Evidence Level¶				Type of study according to SIGN								Recommendation SIGN			
									High	Mod	Low	Very Low	1++	1+	1-	2++	2+	2-	3	4	A	B	C	D

Cho YS Korean J Intern Med. 2021		1), 3)	-1	0	0	NA	NR	NA			x						x						x	
Yim K Gastroenterol Res Pract. 2020		1), 3)	-1	0	0	NA	NR	NA			x						x						x	
Kwon MJ World J Gastroenterol. 2019		1), 3)	-1	0	0	NA	NR	NA									x						x	
Goo JJ Surg Endosc. 2015		1), 3)	-1	0	0	NA	NR	NA			x						x						x	
Yu CH Dig Dis Sci. 2014		1), 3)	-1	0	0	NA	NR	NA			x						x						x	

* 1) Selection; 2) Comparability; 3) Outcome
** -1 per problemSelection: -1: selected group of users or no description; Comparability -1: no comparison between the cohorts; Outcome -1: No description, no follow up
# Evidence of dose response across or within studies (or inconsistency across studies is explained by a dose response); also up to one point added if adjustment for confounders would have increased the effect size (1); All / most studies show similar results (0); Lack of agreement between studies (e.g. statistical heterogeneity between RCTs, conflicting results) (-1)
@ -1 per problem in generalizability to the target population
↑: only for meta-analysis
§ 0 if Not all effect sizes more than 2 or less than 0.5 and significant; or if OR/RR/HR not significant; 1 if Effect size more than 2 or less than 0.5 for all studies/meta-analyses included in comparison and significant; 2 if Effect size more than 5 or less tha.2 for all studies/meta-analyses included in comparison and significant
¶: High: Further research is very unlikely to change our confidence in the estimate of effect; Moderate: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate; Low: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate; Very low: Any estimate of effect is very uncertain

Sentence	**ESGE/EHMSG/ESP recommend that patients with an endoscopically visible lesion harboring dysplasia (low-grade or high-grade) or carcinoma should undergo staging and treatment.**																						
GRADE	**Strength of recommendation: Strong**							**Quality of evidence: Moderate**															
PICO	Population – Patients with premalignant or malignant gastric lesion Intervention – biopsy sampling of LGD/HGD/carcinoma during upper endoscopy Comparison – endoscopic resection specimen evaluation Outcome – histological accuracy																						
Query(ies) and databases searched	Search for: [Title/Abstract]; database: PubMed ("early gastric cancer" OR "gastric cancer" OR dysplasia OR neoplasia) AND (biops* OR “biopsy sampl*” OR “endoscopic evaluation” OR “endoscopic prediction” OR “low-grade dysplasia” OR “high-grade dysplasia”) AND (“endoscopic resection” OR “endoscopically resectable” OR “endoscopic mucosal resection” OR EMR OR “endoscopic submucosal dissection” OR ESD) AND (“submucosal invasion“ OR accuracy OR “histological upgrade”)																						
Table of evidence	***Are there any cohorts or case-controls/cross-sectional?***																						
Study ID	Study design Score **(2)**	Risk of bias (alinea(s)) *	Quality Score **(0 to -3) ** **	Consistency Score **(-1 to 1) #**	Directness Score **(0 to -2) @**	Publication bias **(0: No,1: Yes)**	Reported OR/RR/HR	Effect size Score **(0 to 2) §**	Evidence Level¶				Type of study according to SIGN								Recommendation SIGN			
									High	Mod	Low	Very Low	1++	1+	1-	2++	2+	2-	3	4	A	B	C	D
Zhao, 2015	2, meta-analysis	1	-1	0	0	0	Upgraded diagnosis rate	p<0.001		X					X							X		
Lim, 2014	1, Retrospective observational	1	-1	0	-1	NA	NA	0			X						X						X	
Yang, 2018	1, Retrospective observational study	1	-2	-1	-1	NA	NA	0			X							X					X	
Pimentel-Nunes, 2014	2, Retrospective observational	3	-1	-1	-2	NA	NA	0				X						X					X	

	study																					
Jeon, 2021	2, Multicentric retrospective observational study	1	-1	0	0	0	NA	0			X						X					X	
Shin, 2023	2, Retrospective observational study	1	-1	0	-1	NA	NA	0			X						X					X	
Ngamruengphong, 2021	1, Retrospective observational study	1	-1	0	-1	0	NA	0				X						X				X	
Libânio, 2017	2, Observational study	1	-1	0	-1	NA	OR, P = 0.038	1			X					X						X	

* 1) Selection; 2) Comparability; 3) Outcome
** -1 per problemSelection: -1: selected group of users or no description; Comparability -1: no comparison between the cohorts; Outcome -1: No description, no follow up
# Evidence of dose response across or within studies (or inconsistency across studies is explained by a dose response); also up to one point added if adjustment for confounders would have increased the effect size (1); All / most studies show similar results (0); Lack of agreement between studies (e.g. statistical heterogeneity between RCTs, conflicting results) (-1)
@ -1 per problem in generalizability to the target population
†: only for meta-analysis
§ 0 if Not all effect sizes more than 2 or less than 0.5 and significant; or if OR/RR/HR not significant; 1 if Effect size more than 2 or less than 0.5 for all studies/meta-analyses included in comparison and significant; 2 if Effect size more than 5 or less tha.2 for all studies/meta-analyses included in comparison and significant
¶: High: Further research is very unlikely to change our confidence in the estimate of effect; Moderate: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate; Low: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate; Very low: Any estimate of effect is very uncertain

Sentence	**ESGE/EHMSG/ESP suggest that age and comorbidities should be taken into account to select patients for endoscopic treatment of an early gastric lesion.**	
GRADE	**Strength of recommendation: Conditional**	**Quality of evidence: Low**
PICO	P : Gastric ESD/EMR I : (1) Elderly (aged ≥75/80/85); (2) Comorbidities (ASA III/IV, cirrhosis, kidney failure, cardipathy, pulmonary disease); (3) Antithrombotics C : Non elderly / No severe comorbidities / No antitrhombitics O : Survival / Mortality complications (bleeding, perforation)	
Query(ies) and databases searched	Gastric ESD for EGC improves survival in patients eldery/Very elderly? Gastric ESD for EGC improves survival in patients with severe comorbidities? Gastric ESD for EGC has worse outcomes in elderly vs nonelderly/severe comorbidities vs no severe comorbidities, antithrombotcis vs no antithrombotics patients? Search (PubMed): **endoscopic resection AND age** ((((("gastrics"[All Fields] OR "stomach"[MeSH Terms] OR "stomach"[All Fields] OR "gastric"[All Fields]) AND ("empir musicol rev"[Journal] OR "emr"[All Fields])) OR (("gastrics"[All Fields] OR "stomach"[MeSH Terms] OR "stomach"[All Fields] OR "gastric"[All Fields]) AND ("earth syst dyn"[Journal] OR "esd"[All Fields])) OR (("gastrics"[All Fields] OR "stomach"[MeSH Terms] OR "stomach"[All Fields] OR "gastric"[All Fields]) AND ("endoscope s"[All Fields] OR "endoscoped"[All Fields] OR "endoscopes"[MeSH Terms] OR "endoscopes"[All Fields] OR "endoscope"[All Fields] OR "endoscopical"[All Fields] OR "endoscopically"[All Fields] OR "endoscopy"[MeSH Terms] OR "endoscopy"[All Fields] OR "endoscopic"[All Fields]) AND ("resect"[All Fields] OR "resectability"[All Fields] OR "resectable"[All Fields] OR "resectates"[All Fields] OR "resected"[All Fields] OR "resecting"[All Fields] OR "resection"[All Fields] OR "resectional"[All Fields] OR "resectioned"[All Fields] OR "resectioning"[All Fields] OR "resections"[All Fields] OR "resective"[All Fields] OR "resects"[All Fields]))) AND (("aged"[MeSH Terms] OR "aged"[All Fields] OR "elderly"[All Fields] OR "elderlies"[All Fields] OR "elderly s"[All Fields] OR "elderlys"[All Fields]) AND ("patient s"[All Fields] OR "patients"[MeSH Terms] OR "patients"[All Fields] OR "patient"[All Fields] OR "patients s"[All Fields])) AND ("non"[All Fields] AND ("aged"[MeSH Terms] OR "aged"[All Fields] OR "elderly"[All Fields] OR "elderlies"[All Fields] OR "elderly s"[All Fields] OR "elderlys"[All Fields])) AND ("mortality"[MeSH Subheading] OR "mortality"[All Fields] OR "survival"[All Fields] OR "survival"[MeSH Terms] OR "survivability"[All Fields] OR "survivable"[All Fields] OR "survivals"[All Fields] OR "survive"[All Fields] OR "survived"[All Fields] OR "survives"[All Fields] OR "surviving"[All Fields] OR ("epidemiology"[MeSH Subheading] OR "epidemiology"[All Fields] OR "morbidity"[All Fields] OR "morbidity"[MeSH Terms] OR "morbid"[All Fields] OR "morbidities"[All Fields] OR "morbids"[All Fields]) OR ("mortality"[MeSH Terms] OR "mortality"[All Fields] OR "mortalities"[All Fields] OR "mortality"[MeSH Subheading]) OR ("perforant"[All Fields] OR "perforants"[All Fields] OR "perforate"[All Fields] OR "perforated"[All Fields] OR "perforates"[All Fields]	

	OR "perforating"[All Fields] OR "perforation"[All Fields] OR "perforations"[All Fields] OR "perforative"[All Fields] OR "perforator"[All Fields] OR "perforator s"[All Fields] OR "perforators"[All Fields]) OR ("bleedings"[All Fields] OR "hemorrhage"[MeSH Terms] OR "hemorrhage"[All Fields] OR "bleed"[All Fields] OR "bleeding"[All Fields] OR "bleeds"[All Fields]) OR ("surgery"[MeSH Subheading] OR "surgery"[All Fields] OR "surgical procedures, operative"[MeSH Terms] OR ("surgical"[All Fields] AND "procedures"[All Fields] AND "operative"[All Fields]) OR "operative surgical procedures"[All Fields] OR "general surgery"[MeSH Terms] OR ("general"[All Fields] AND "surgery"[All Fields]) OR "general surgery"[All Fields] OR "surgery s"[All Fields] OR "surgerys"[All Fields] OR "surgeries"[All Fields]))) Search (PubMed): **endoscopic resection AND comorbidities** ((("gastrics"[All Fields] OR "stomach"[MeSH Terms] OR "stomach"[All Fields] OR "gastric"[All Fields]) AND ("earth syst dyn"[Journal] OR "esd"[All Fields])) OR (("gastrics"[All Fields] OR "stomach"[MeSH Terms] OR "stomach"[All Fields] OR "gastric"[All Fields]) AND ("empir musicol rev"[Journal] OR "emr"[All Fields]))) AND ("comorbid"[All Fields] OR "comorbidity"[MeSH Terms] OR "comorbidity"[All Fields] OR "comorbidities"[All Fields] OR "comorbids"[All Fields] OR (("anal sci adv"[Journal] OR "asa"[All Fields]) AND "III"[All Fields]) OR (("anal sci adv"[Journal] OR "asa"[All Fields]) AND ("ieee intell veh symp"[Journal] OR "iv"[All Fields])) OR ("kidney diseases"[MeSH Terms] OR ("kidney"[All Fields] AND "diseases"[All Fields]) OR "kidney diseases"[All Fields] OR ("renal"[All Fields] AND "disease"[All Fields]) OR "renal disease"[All Fields]) OR 28[UID] OR ("heart diseases"[MeSH Terms] OR ("heart"[All Fields] AND "diseases"[All Fields]) OR "heart diseases"[All Fields] OR "cardiopathies"[All Fields] OR "cardiopathy"[All Fields]) OR ("lung diseases"[MeSH Terms] OR ("lung"[All Fields] AND "diseases"[All Fields]) OR "lung diseases"[All Fields] OR ("pulmonary"[All Fields] AND "disease"[All Fields]) OR "pulmonary disease"[All Fields])) AND ("mortality"[MeSH Subheading] OR "mortality"[All Fields] OR "survival"[All Fields] OR "survival"[MeSH Terms] OR "survivability"[All Fields] OR "survivable"[All Fields] OR "survivals"[All Fields] OR "survive"[All Fields] OR "survived"[All Fields] OR "survives"[All Fields] OR "surviving"[All Fields] OR ("epidemiology"[MeSH Subheading] OR "epidemiology"[All Fields] OR "morbidity"[All Fields] OR "morbidity"[MeSH Terms] OR "morbid"[All Fields] OR "morbidities"[All Fields] OR "morbids"[All Fields]) OR ("mortality"[MeSH Terms] OR "mortality"[All Fields] OR "mortalities"[All Fields] OR "mortality"[MeSH Subheading]) OR ("perforant"[All Fields] OR "perforants"[All Fields] OR "perforate"[All Fields] OR "perforated"[All Fields] OR "perforates"[All Fields] OR "perforating"[All Fields] OR "perforation"[All Fields] OR "perforations"[All Fields] OR "perforative"[All Fields] OR 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"anticoagulation"[All Fields] OR "anticoagulations"[All Fields] OR "anticoagulative"[All Fields])) AND ("mortality"[MeSH Subheading] OR "mortality"[All Fields] OR "survival"[All Fields] OR "survival"[MeSH Terms] OR "survivability"[All Fields] OR "survivable"[All Fields] OR "survivals"[All Fields] OR "survive"[All Fields] OR "survived"[All Fields] OR "survives"[All Fields] OR "surviving"[All Fields] OR ("epidemiology"[MeSH Subheading] OR "epidemiology"[All Fields] OR "morbidity"[All Fields] OR "morbidity"[MeSH Terms] OR "morbid"[All Fields] OR "morbidities"[All Fields] OR "morbids"[All Fields]) OR ("mortality"[MeSH Terms] OR "mortality"[All Fields] OR "mortalities"[All Fields] OR "mortality"[MeSH Subheading]) OR ("perforant"[All Fields] OR "perforants"[All Fields] OR "perforate"[All Fields] OR "perforated"[All Fields] OR "perforates"[All Fields] OR "perforating"[All Fields] OR "perforation"[All Fields] OR "perforations"[All Fields] OR "perforative"[All Fields] OR "perforator"[All Fields] OR "perforator s"[All Fields] OR "perforators"[All Fields]) OR ("bleedings"[All Fields] OR "hemorrhage"[MeSH Terms] OR "hemorrhage"[All Fields] OR "bleed"[All Fields] OR "bleeding"[All Fields] OR "bleeds"[All Fields])) **Table of evidence**	***Are there any cohorts?***

Study ID	Study design Score **(2)**	Risk of bias (alinea(s)) *	Quality Score **(0 to -3)** **	Consistency Score **(-1 to 1)** #	Directness Score **(0 to -2)** @	Publication bias † (**0: No,1: Yes**)	Reported OR/RR/HR	Effect size Score **(0 to 2)** §	Evidence Level¶				Type of study according to SIGN								Recommendation SIGN			
									High	Mod	Low	Very Lo	1++	1+	1-	2++	2+	2-	3	4	A	B	C	D

												w										
Zhao, 2022 (Front Onc)	2 (SR)	SR/MA: 10/17 included studies scored 6 points NOS, the others 7-8 points. Clear inclusion/Exclusion criteria & outcomes definitions. All included studies compares elderly patients undergoing ESD with non-elderly patients, all retrospective, none propensity score matching) Low-unclear/moderate risk	-1 (no long FU)	0	-1	0 (No)	En bloc resection(OR): 0.92, 95% CI: 0.68, 1.26, I2 = 8%, p=0.62. Perforation (>80vs<80) OR: 1.50 95% CI: 1.00, 2.24 I2 = 3% p=0.05 (total events=70/5823 vs 201/23217)) Bleeding OR: 1.07 95% CI: 0.87, 1.32 I2 = 19% p=0.52 (total events=300/7982 vs 805/25589)	0		+ mod							2 +						x	
Waki, 2022 (GIE)	2	Retrospective single cohort without comparison (EGC ESD in >=75yo, n=400) 1)Selection: low-risk (***/****) 2)Comparison: additional factors (*/**) 3)Outcome (***/***): low-moderate (surgery decided after discussion) NOS=7 (Low-Risk)	-1	0	0	n/a	Poor OS: age ≥77 (HR, 2.35; 95% CI, 1.16-4.74) ECOG-PS 2-4 (HR, 8.84; 95% CI, 3.07-25.4) PNI <49.1 (HR, 2.49; 95% CI, 1.53-4.06), eCura C-2 (HR, 1.79; 95% CI, 1.11-2.88)	0			+ low						2 +						x	
Kang, 2023 (Surg End)	2	Retrospective single cohort comparing ESD (n=59) vs surgery (n=235) for cT1N0M0 in >=75yo beyond ESD	0	0	0	n/a	Factor associated with OS ≥ 78 years; hazard ratio 1.90; 95%	0			+ low						2 +						x	

		indication 1)Selection(***/***): low- risk 2)Comparability(*/**): moderate-high (ESD or surgery decided after MDT discussion) 3)Outcome: (**/***)(smaller lesions and higher % differentiated EGC in ESD group). Median observation perdioi 91 months. moderate-risk NOS=6 (Unclear-Risk)					confidence interval 1.35–2.68; p < 0.001)																
Inokuchi 2021 (WJGE)	2	Retrospective single center cohort >=80yo EGC (n=124 patients, 175 lesions) NOS: 1)Selection(***/***): moderate-risk(might be selection bias because of single center oncologic hospital, 30% circulatory diseases in this cohort) 2)Comparability (*/**): subgroups for OS (noncurative vs curative ESD; high Charlson Comorbidity Index vs Low CCI) 3) Outcome(***/***)s: FU median 2005 days. NOS=7 (low-risk)	-1	0	0	n/a	Bleeding (Events=6) - Size >41mm (RR 6.3, p=0.03) -Ulcer+ (RR 13.9, p=0.003) Perforation (events=2) - Upper third (RR=63, p=0.033) OS Charlson Comorbidity Index>=2 vs CCI<=1 differente p<0.001; HR stimated from extracted data* (not specified) = 1.6 (Cox LASSO coefficient for CCI > 1 is 0.477)	2			+low								3				x	
Yoshikawa, 2022	2	Retrospective, ,single center	0	0	0	n/a	Poor OS prognosis:	0			low						2+						x	

(Cancers)		Comparing EGC ESD in patients aged ≥85 years (n=44 patients,49 lesions) vs <85yo (n= 786 patients, 687 lesions) 1)Selection(***/***): excluded bedridden patients. 2)Comparison: **/(** 3) Outcomes: ***/***median FU 1151 days NOS: 8 (low risk)					Geriatric Nutritional Risk Index (HR, 0.89; 95% confidence interval, 0.83–0.95; p < 0.001). 3y & 5y OS ≥85 years 85.7% and 61.9%, significantly worse than younger groups (p = 0.003 and p < 0.001). After propensity score matching, no diferences. Curative resection no differences AEs no differences																
Yamada, 2022 (digestion)	2	Retrospective, multicenter, n=297 cT1N0 EGC in aged ≥85, comparing outcomes after ESD (n=238)vs non invasive conservative treatment (n=59) (PSM 46-46). 1)Selection: (***/****) 2) Comparability: (*/**) 3) Outcomes median FU 44 (ESD) and 24 (consevative) months (**/***).																					x	

		NOS=6 (unclear)																				
Watanabe, 2017 (EIO)	2	Retrospective, single center, comparing gastric ESD in very elderly (≥ 85 years; 48 lesions in 43 patients), elderly (65 – 84 years; 652 lesions in 511 patients), and non-elderly (≤ 64 years; 177 lesions in 161 patients). 1)Selection(***/***):, ESD was not performed for very elderly patients with PSs of 2 or greater or those with severe comorbidities. 2)Comparability (**/**) 3) Outcome (**/***): median follow-up 48 months. NOS: 7 (low risk)	0	0	0	n/a	No reported OR/RR/HR OS lower in the very elderly group (1-, 5-, and 10y OS 92.7 %, 66.8 %, and 34.4 % vs elderly patients: 97.2 %, 86.2 %, and 61.9%; and non-elderly patients: 98.6 %, 90.2 %, and 74.7 %, respectively). very elderly patients with cardiovascular disease was significantly lower than that of the very elderly patients without cardiovascular disease (P <0.001, 1-, 5-, and 10-year OS were 63.5%, 0%, and 0%, vs 100%, 77.7%, and 39.9%)	0			low						2 +						x	
Natsagdorj, 2021 (JGC)	2	Retrospective, single center, EGC ESD in patients with comorbidities (n=558) vs previously healthy (n=411) 1)Selection ****/**** 2)Comparability:*/**	0	0	0	n/A	OS & comorbidities (multivariate logistic regresion) Chronic liver disease OR 2.49 (1.30–4.79),p=0.006	1		moderate							2 +						x	

		3) Outcome **/*** NOS: 7 (low risk)					Coronary heart disease OR 2.61 (1.35–5.05), p 0.005 Other cáncer OR 4.18 (2.31–7.58), p= 0.0001																
Misawa, 2020 (Geria Geront Int)	2	Retrospective single center, comparison of gastric ESD in >=80yo with frailty (nn=41) vs >=80yo without frailty (n=101) 1)Selection ***/**** 2)Comparability */** based on Clinical Frailty Scale (CFS) 1 (very fit) to 9 (terminally ill), CFS ≥4 were frail. 3) Outcome: medical history or phone call , median FU 48 months **/*** NOS=6 (unclear risk)	0	0	0	n/a	Multivariate analysis factor associated with poor OS: Frailty (CFS ≥4): HR 2.47, 95% confidence interval 1.02–5.98; P = 0.046)	1			low						2 +						x	
Kishida, 2021 (DEN)	2	Retrospective, single center ESD (n=114) vs Surgery (n=303) in >=75yo with relative ER indication 1)Selection(****/****) 2)Comparability (**/**) 3) Outcome (*/***): median follow-up 34 months for ESD,	0	0	0	n/a	OS-associated factors in males Age ≥79 : HR 2.21, P=.001; PNI <45, HR 2.06, P=.031) OS-associated factors in females Age ≥82, HR 4.06, P=.004	1			low						2 +						x	

		61 months for surgery NOS: 7 (low risk)					No OS difference between ESD vs surgery															
Hatta, 2023 (J Gastro)	2	Retrospective multicenter, noncurative gastric ESD ≥ 85yo with no additional treatment (n=127) vs Surgery (n=16) 1)Selection(****/****) 2)Comparability (*/**) 3) Outcome (***/***): median follow-up 51 months NOS: 8 (low risk)	0	0	0	n/a	OS did not differ FUvsSurgery Risk factors for poor OS (multivariate) in patients with no additional treatment -High-risk eCura (hazard ratio [HR], 2.91), -Charlson comorbidity index (CCI) 3 (HR, 2.78) -Male (HR, 2.04).	1			low						2+						x	
Ogata, 2022 (DEN)	2	Retrospective single center analysis od predictors of early and late mortality after ER or Surgery for EGC Selection ***/**** Comparability */** Outcome **/*** Median FU 79 months NOS=6 (unclear)	0	0	0	n/a	Predictors of mortality HR early, -HR late Age ≥85 years HR 2.88 and 4.54 Eastern Cooperative Oncology Group Performance Status ≥2 HR 3.00 and 4.19 Charlson comorbidity index ≥2 HR 2.76 and 1.99, ASA ≥3 HR 2.35 and 1.79	0			low						2+						x	

							C- reactive protein/albumin ratio ≥0.028 (HR 2.30 and 1.58, respectively) Predictors early mortality only Male (HR 2.26) intermediate-risk eCura (HR 2.12) high-risk eCura(HR 1.85) of LNM in eCura system sarcopenia evaluated by the psoas muscle mass index (HR 1.70)																	
Ito, 2023 (DEN)	2	Retrospective analysis of gastric ESD in >=75yo with development (n=103) and validation (n=295) of predictive scor for prognosis Selection ***/**** Comparability */** Outcome *** NOS 7	0	0	0	n/a	Survival Factors (multivariat) Charlson comorbidity index (CCI) ≥3 (HR 3.017; 1.377-6.609, p=0.006) High psoas muscle index (PMI) (HR 2.206, 1-048-4.643, p=0.037) SoAge ≥80 years (HR 1.978, 1.087-3.601, p=0.02)	0			low						2+						x	

							Scoring system High CCI (1), low PMI (1), and age ≥80 years (1) Low>=1 point (5yOS 91.5%) High >=2 (5yOS 57.8%)															
Kim, 2021 (Cancers)	2	Retrospective single center, gastric ESD ≥ 80yo (n=280) with comorbidities 1)Selection(****/****) 2)Comparability (*/**) 3) Outcome (***/***): median follow-up 70 months NOS: 8 (low risk)	0	0	0		OS related factors: -Prognostic nutritional index (hazard ratio [HR], 0.93; 95% confidence interval [CI]: 0.90–0.98; p = 0.002) - Charlson comorbidity index (HR 1.19; 95% CI: 1.03–1.37; p = 0.018)	0			low						2+						x	
Toya 2021 (BMC Gas)	2	Retrospective single center, gastric ESD ≥ 85yo (n=70, n=98 lesions) 1)Selection(***/***) 2)Comparability () 3) Outcome (***/***): median follow-up 6 years NOS: 6 (unclear risk)	-1	0	0	n/a	OS related: - Low Prognostic Nutritional Index PNI (< 42.5) (hazard ratio, 3.40; 95% CI, 1.47–7.86; P=0.004	0			low						2+						x	
Nagami 2022 (DEN)	2	Retrospective multicenter n=11,452 EGC ESD, comparison of 1353 matched pairs (PSM and IPTW) with vs without antithrombotic For bleeding Seletion ****/****	0	0	0	N/a	OR for bleeding Antithrombotic agents, [OR] 4.15, 95% CI 2.88–5.99; P < 0.001). Heparin bridging	1			low						2+						x	

		Comparability */** Outcome ***/***					therapy had high OR (8.80), and the continuation (OR 3.46) and cessation (OR 2.95) of antithrombotic agent use had similar risk.															
Miura 2023 (GIE)	2	Retrospective multicenter comparing gastric ESD bleeding in antiplatelets (Aspirin=665; Thienopyridine=227, Cilostazol n=158) vs no antitrhombotics users 1)Selection(****/****) 2)Comparability (*/**) 3) Outcome (**/***): median follow-up 6 years NOS: 7(low risk)	0	0	0	n/a	PPB: Aspirin continuation group PPB risk OR 2.79 (95& CI 1.77-4.37), no significant if interruption (OR, 1.53; 95% CI, .90-2.60). Thienopyridine continuation (OR, 5.13; 95% CI, 1.62-16.22) and interruption (OR, 4.44; 95% CI, 2.57-7.54) groups had a significant risk of the bleeding. Replacement group (aspirin or cilostazol) did not (OR, 1.85; 95% CI, .72-4.78). Cilostazol not (OR 0.52)	0			low						2+						x	
Hatta, 2021 (GUT)	2	Retrospective multicenter (derivation cohort n=8291, validation cohort n=2029) to develop & validate	0	0	0	n/a	OR (multivariate logistic regression of predictive factors for PPB)	0		moderate							2+						x	

		PPB prediction model (BEST-J score) 1)Selection(****/****) 2)Comparability (*/**) 3) Outcome (**/***): median follow-up 6 years NOS: 7(low risk					- CKD with haeemodialysis OR 4.33(95% CI 2.71 to 6.91) -Aspirin OR 2.24(95% CI 1.55 to 3.24) -P2Y12RA OR 3.13 (95% CI 1.91 to 5.12) -Cilostazol OR 2.04 (95% CI 1.09 to 3.80) -Warfarin OR 8.74 (95% CI 4.92 to 15.54) -DOAC OR 8.16 (95% CI 4.74 to 14.04) -Interruption of AT agents OR 0.67 (95% CI 0.46 to 0.97)																
Tanoue, 2019 (gastric Cancer)	2	Retrospective single center. Outcomes after gatric ESD in ASA 1-2 (n=375) vs ASA 3 (n=113) 1)Selection: only “curative” gastric ESD without surgery and other cancers (***/****) 2) Comparability: ASA 1-2 vs 3 and score matching(**/**) 3) Outcome Mortality Risk minimum 3 years FU (**/***) NOS 7 (low-risk)	0	0	0	n/a	Mortality risk ASA 3 compared to ASA 1-2 Cox analysis HR 2.56 (95% CI 1.18–5.52; p = 0.02) IPTWmethod HR 3.14 (95% CI 1.91–5.14; p < 0.01) No differences in adverse events	1			low						2 +						x	
Yo IK 2020	2	Retrospectivee	-1	0	0	n/a	OR for bleeding	1			low						2						x	

(CE)		multicenter. PPB after gastric ESD,in end-stage Renal Disease on dialysis (n=47) vs control (n=470) 1)Selection: (***/****) 2) Comparability: control with matching 1:10 (**/**) 3) Outcome Bleeding in electronic medical FU not specified (*/***) NOS 6 (unclear)					ESRD dyalysis vs control OR 6.1; 95% confidence interval, 2.7–13.6; p<0.0001									+							
Okimoto 2019 (Can J Gas Hep)	2	Retrospective single center, Comparing long term outcomes after EGC ESD in patients aged ≥80 years (n=108, 128 lesions) vs <80yo (n=425, 504 lesions) 1)Selection: (***/****) 2) Comparability: (**/**) 3) Outcomes for elderly and nonelderly grupos:mean FU 26 & 36 months , rate of FU >3 years 28.7% and 41.9% (*/***) NOS 6 (unclear)	-1 (relative short FU)	0	0	n/a	Risl Faactor for death in elderly >80yo: Renal Dysfunction GFR <30 ml/min/1.73 m2 HR 5.32; 95% CI 1.39–20.5; P 0.015 Shorter survival time in >80yo (75.8 ± 5.9 vs 122.8 ± 2.6 month, p<0.05 log-rank test).	1			low						2 +						x	
Choi, 2018 (GIE)	2	Retrospective single center, Comparing efficacy/safety of EGC ESD in patients cirrhosis (n=158) vs	0	0	-1 (low number of descompensated cirrhosis)	N/a	Cirrhotic vs noncirrhotic, OS: HR 3.52 (95% CI, 1.35-9.23, p=0.01)	1			low						2 +						x	

		noncirrotic (n=158) 1)Selection: (***/****) 2) Comparability: (**/**) 3) Outcomes median FU 50.8 months (cirrhosis) and 59.8months (noncirrhotics) (**/***) NOS 7 (low risk)					Cirrhotic with HCC vs cirrhotics without HCC, poor survival HR 3.86; 95% CI, 1.5-9.9, p=0.05 Mortality after ESD HCC: HR 4.22 (95% CI 1.59 to 11.15, p=0.04)																

** -1 per problem Selection: -1: selected group of users or no description; Comparability -1: no comparison between the cohorts; Outcome -1: No description, no follow up
# Evidence of dose response across or within studies (or inconsistency across studies is explained by a dose response); also up to one point added if adjustment for confounders would have increased the effect size (1); All / most studies show similar results (0); Lack of agreement between studies (e.g. statistical heterogeneity between RCTs, conflicting results) (-1)
@ -1 per problem in generalizability to the target population
†: only for meta-analysis
§ 0 if Not all effect sizes more than 2 or less than 0.5 and significant; or if OR/RR/HR not significant; 1 if Effect size more than 2 or less than 0.5 for all studies/meta-analyses included in comparison and significant; 2 if Effect size more than 5 or less tha.2 for all studies/meta-analyses included in comparison and significant
¶: High: Further research is very unlikely to change our confidence in the estimate of effect; Moderate: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate; Low: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate; Very low: Any estimate of effect is very uncertain

Sentence	**ESGE/EHMSG/ESP recommend endoscopic submucosal dissection (ESD) as the treatment of choice for most superficial gastric lesions**	
GRADE	**Strength of recommendation: Strong**	**Quality of evidence: Moderate**
PICO	P: Early gastric lesions I: ESD C: Surgery/EMR O: Efficacy	
Query(ies) and databases searched	What is the treatment of choice for superficial gastric lesions? Search (PubMed): ESD versus surgery/EMR ((("early"[All Fields] AND ("stomach neoplasms"[MeSH Terms] OR ("stomach"[All Fields] AND "neoplasms"[All Fields]) OR "stomach neoplasms"[All Fields] OR ("gastric"[All Fields] AND "cancer"[All Fields]) OR "gastric cancer"[All Fields])) OR ("early"[All Fields] AND ("gastrics"[All Fields] OR "stomach"[MeSH Terms] OR "stomach"[All Fields] OR "gastric"[All Fields]) AND ("lesion"[All Fields] OR "lesion s"[All Fields] OR "lesional"[All Fields] OR "lesions"[All Fields]))) AND ("endoscopic mucosal resection"[MeSH Terms] OR ("endoscopic"[All Fields] AND "mucosal"[All Fields] AND "resection"[All Fields]) OR "endoscopic mucosal resection"[All Fields] OR ("endoscopic"[All Fields] AND "submucosal"[All Fields] AND "dissection"[All Fields]) OR "endoscopic submucosal dissection"[All Fields] OR ("earth syst dyn"[Journal] OR "esd"[All Fields])) AND ("gastrectomy"[MeSH Terms] OR "gastrectomy"[All Fields] OR "gastrectomies"[All Fields] OR ("endoscopic mucosal resection"[MeSH Terms] OR ("endoscopic"[All Fields] AND "mucosal"[All Fields] AND "resection"[All Fields]) OR "endoscopic mucosal resection"[All Fields]) OR ("empir musicol rev"[Journal] OR "emr"[All Fields])) AND ("efficacies"[All Fields] OR "efficacious"[All Fields] OR "efficaciously"[All Fields] OR "efficaciousness"[All Fields] OR "efficacy"[All Fields] OR (("enzymology"[MeSH Subheading] OR "enzymology"[All Fields] OR "en"[All Fields]) AND "bloc"[All Fields] AND ("resect"[All Fields] OR "resectability"[All Fields] OR "resectable"[All Fields] OR "resectates"[All Fields] OR "resected"[All Fields] OR "resecting"[All Fields] OR "resection"[All Fields] OR "resectional"[All Fields] OR "resectioned"[All Fields] OR "resectioning"[All Fields] OR "resections"[All Fields] OR "resective"[All Fields] OR "resects"[All Fields])) OR (("complete"[All Fields] OR "completed"[All Fields] OR "completely"[All Fields] OR "completeness"[All Fields] OR "completer"[All Fields] OR "completers"[All Fields] OR "completes"[All Fields] OR "completing"[All Fields] OR "completion"[All Fields] OR "completions"[All Fields]) AND ("resect"[All Fields] OR "resectability"[All Fields] OR "resectable"[All Fields] OR "resectates"[All Fields] OR "resected"[All Fields] OR "resecting"[All Fields] OR "resection"[All Fields] OR "resectional"[All Fields] OR "resectioned"[All Fields] OR "resectioning"[All Fields] OR "resections"[All Fields] OR "resective"[All Fields] OR "resects"[All Fields])) OR ("recurrance"[All Fields] OR "recurrence"[MeSH Terms] OR "recurrence"[All Fields] OR "recurrences"[All Fields] OR "recurrencies"[All Fields] OR "recurrency"[All Fields] OR "recurrent"[All Fields] OR "recurrently"[All Fields] OR "recurrents"[All Fields]))	
Table of evidence	No new evidence	

Sentence	**ESGE/EHMSG/ESP recommend ESD for differentiated gastric lesions clinically staged as dysplastic (low and high-grade) or as intramucosal carcinoma (of any size if not ulcerated and ≤ 30mm if ulcerated), with EMR being an alternative for Paris 0-IIa lesions with size ≤ 10mm with low likelihood of malignancy.**	
GRADE	**Strength of recommendation: Strong**	**Quality of evidence: Moderate**
PICO	P: Dysplastic gastric lesions/Gastric intramucosal carcinoma/ulcerated gastric intramucosal carcinoma I: ESD C: Surgery/EMR O: Efficacy/safety	
Query(ies) and databases searched	What are the clinical indications for gastric ESD? What are the available evidences on the efficacy/safety of ESD for each of these indications? Search (PubMed): **ESD for intramucosal lesions. Filter: From 2021** (((("early"[All Fields] AND ("stomach neoplasms"[MeSH Terms] OR ("stomach"[All Fields] AND "neoplasms"[All Fields]) OR "stomach neoplasms"[All Fields] OR ("gastric"[All Fields] AND "cancer"[All Fields]) OR "gastric cancer"[All Fields])) OR ("early"[All Fields] AND ("gastrics"[All Fields] OR "stomach"[MeSH Terms] OR "stomach"[All Fields] OR "gastric"[All Fields]) AND	

	("lesion"[All Fields] OR "lesion s"[All Fields] OR "lesional"[All Fields] OR "lesions"[All Fields])) AND ("endoscopic mucosal resection"[MeSH Terms] OR ("endoscopic"[All Fields] AND "mucosal"[All Fields] AND "resection"[All Fields]) OR "endoscopic mucosal resection"[All Fields] OR ("endoscopic"[All Fields] AND "submucosal"[All Fields] AND "dissection"[All Fields]) OR "endoscopic submucosal dissection"[All Fields] OR ("earth syst dyn"[Journal] OR "esd"[All Fields])) AND ("gastrectomy"[MeSH Terms] OR "gastrectomy"[All Fields] OR "gastrectomies"[All Fields] OR ("endoscopic mucosal resection"[MeSH Terms] OR ("endoscopic"[All Fields] AND "mucosal"[All Fields] AND "resection"[All Fields]) OR "endoscopic mucosal resection"[All Fields]) OR ("empir musicol rev"[Journal] OR "emr"[All Fields])) AND ("efficacies"[All Fields] OR "efficacious"[All Fields] OR "efficaciously"[All Fields] OR "efficaciousness"[All Fields] OR "efficacy"[All Fields] OR (("enzymology"[MeSH Subheading] OR "enzymology"[All Fields] OR "en"[All Fields]) AND "bloc"[All Fields] AND ("resect"[All Fields] OR "resectability"[All Fields] OR "resectable"[All Fields] OR "resectates"[All Fields] OR "resected"[All Fields] OR "resecting"[All Fields] OR "resection"[All Fields] OR "resectional"[All Fields] OR "resectioned"[All Fields] OR "resectioning"[All Fields] OR "resections"[All Fields] OR "resective"[All Fields] OR "resects"[All Fields])) OR (("complete"[All Fields] OR "completed"[All Fields] OR "completely"[All Fields] OR "completeness"[All Fields] OR "completer"[All Fields] OR "completers"[All Fields] OR "completes"[All Fields] OR "completing"[All Fields] OR "completion"[All Fields] OR "completions"[All Fields]) AND ("resect"[All Fields] OR "resectability"[All Fields] OR "resectable"[All Fields] OR "resectates"[All Fields] OR "resected"[All Fields] OR "resecting"[All Fields] OR "resection"[All Fields] OR "resectional"[All Fields] OR "resectioned"[All Fields] OR "resectioning"[All Fields] OR "resections"[All Fields] OR "resective"[All Fields] OR "resects"[All Fields])) OR ("recurrance"[All Fields] OR "recurrence"[MeSH Terms] OR "recurrence"[All Fields] OR "recurrences"[All Fields] OR "recurrencies"[All Fields] OR "recurrency"[All Fields] OR "recurrent"[All Fields] OR "recurrently"[All Fields] OR "recurrents"[All Fields]) OR ("safety"[MeSH Terms] OR "safety"[All Fields] OR "safeties"[All Fields] OR ("complicances"[All Fields] OR "complicate"[All Fields] OR "complicated"[All Fields] OR "complicates"[All Fields] OR "complicating"[All Fields] OR "complication"[All Fields] OR "complication s"[All Fields] OR "complications"[MeSH Subheading] OR "complications"[All Fields]) OR ("mortality"[MeSH Terms] OR "mortality"[All Fields] OR "mortalities"[All Fields] OR "mortality"[MeSH Subheading]) OR ("bleedings"[All Fields] OR "hemorrhage"[MeSH Terms] OR "hemorrhage"[All Fields] OR "bleed"[All Fields] OR "bleeding"[All Fields] OR "bleeds"[All Fields]) OR ("perforant"[All Fields] OR "perforants"[All Fields] OR "perforate"[All Fields] OR "perforated"[All Fields] OR "perforates"[All Fields] OR "perforating"[All Fields] OR "perforation"[All Fields] OR "perforations"[All Fields] OR "perforative"[All Fields] OR "perforator"[All Fields] OR "perforator s"[All Fields] OR "perforators"[All Fields])))))
Table of evidence	No new evidence

Sentence	**ESGE/EHMSG/ESP suggest that a decision about ESD can be considered for malignant lesions clinically staged as with minimal submucosal invasion if differentiated and <30mm; or for lesions clinically staged as intramucosal, when undifferentiated and <20mm; and in both cases with no ulcerative findings.**	
GRADE	**Strength of recommendation: Conditional**	**Quality of evidence: Low**
PICO	(P) Gastric Submucosal carcinoma/undifferentiated (I) ESD (C) Surgery/EMR (O) Efficacy/safety	
Query(ies) and databases searched	What are the clinical indications for gastric ESD? What are the available evidence on the efficacy/safety of ESD for each of these indications? Search (PubMed): **ESD for carcinoma with submucosal invasion. Filter: From 2021** ((("early"[All Fields] AND ("stomach neoplasms"[MeSH Terms] OR ("stomach"[All Fields] AND "neoplasms"[All Fields]) OR "stomach neoplasms"[All Fields] OR ("gastric"[All Fields] AND "cancer"[All Fields]) OR "gastric cancer"[All Fields])) OR ("early"[All Fields] AND ("gastrics"[All Fields] OR "stomach"[MeSH Terms] OR "stomach"[All Fields] OR "gastric"[All Fields]) AND ("lesion"[All Fields] OR "lesion s"[All Fields] OR "lesional"[All Fields] OR "lesions"[All Fields]))) AND (("submucosal"[All Fields] OR "submucosally"[All Fields]) AND ("invasibility"[All Fields] OR "invasible"[All Fields] OR "invasion"[All Fields] OR "invasions"[All Fields] OR "invasive"[All Fields] OR "invasively"[All Fields] OR "invasiveness"[All Fields] OR "invasives"[All Fields] OR "invasivity"[All Fields])) AND ("endoscopic mucosal resection"[MeSH Terms] OR ("endoscopic"[All Fields] AND "mucosal"[All Fields] AND "resection"[All Fields]) OR "endoscopic mucosal resection"[All Fields] OR ("endoscopic"[All Fields] AND "submucosal"[All Fields] AND "dissection"[All Fields]) OR "endoscopic submucosal dissection"[All Fields] OR ("earth syst dyn"[Journal] OR "esd"[All Fields])) AND ("gastrectomy"[MeSH Terms] OR "gastrectomy"[All Fields] OR "gastrectomies"[All Fields] OR ("endoscopic mucosal resection"[MeSH Terms] OR ("endoscopic"[All Fields] AND "mucosal"[All Fields] AND "resection"[All Fields]) OR "endoscopic mucosal resection"[All Fields]) OR ("empir musicol rev"[Journal] OR "emr"[All Fields]))	

	AND ("efficacies"[All Fields] OR "efficacious"[All Fields] OR "efficaciously"[All Fields] OR "efficaciousness"[All Fields] OR "efficacy"[All Fields] OR (("enzymology"[MeSH Subheading] OR "enzymology"[All Fields] OR "en"[All Fields]) AND "bloc"[All Fields] AND ("resect"[All Fields] OR "resectability"[All Fields] OR "resectable"[All Fields] OR "resectates"[All Fields] OR "resected"[All Fields] OR "resecting"[All Fields] OR "resection"[All Fields] OR "resectional"[All Fields] OR "resectioned"[All Fields] OR "resectioning"[All Fields] OR "resections"[All Fields] OR "resective"[All Fields] OR "resects"[All Fields])) OR (("complete"[All Fields] OR "completed"[All Fields] OR "completely"[All Fields] OR "completeness"[All Fields] OR "completer"[All Fields] OR "completers"[All Fields] OR "completes"[All Fields] OR "completing"[All Fields] OR "completion"[All Fields] OR "completions"[All Fields]) AND ("resect"[All Fields] OR "resectability"[All Fields] OR "resectable"[All Fields] OR "resectates"[All Fields] OR "resected"[All Fields] OR "resecting"[All Fields] OR "resection"[All Fields] OR "resectional"[All Fields] OR "resectioned"[All Fields] OR "resectioning"[All Fields] OR "resections"[All Fields] OR "resective"[All Fields] OR "resects"[All Fields])) OR ("recurrance"[All Fields] OR "recurrence"[MeSH Terms] OR "recurrence"[All Fields] OR "recurrences"[All Fields] OR "recurrencies"[All Fields] OR "recurrency"[All Fields] OR "recurrent"[All Fields] OR "recurrently"[All Fields] OR "recurrents"[All Fields]) OR ("safety"[MeSH Terms] OR "safety"[All Fields] OR "safeties"[All Fields] OR ("complicances"[All Fields] OR "complicate"[All Fields] OR "complicated"[All Fields] OR "complicates"[All Fields] OR "complicating"[All Fields] OR "complication"[All Fields] OR "complication s"[All Fields] OR "complications"[MeSH Subheading] OR "complications"[All Fields]) OR ("mortality"[MeSH Terms] OR "mortality"[All Fields] OR "mortalities"[All Fields] OR "mortality"[MeSH Subheading]) OR ("bleedings"[All Fields] OR "hemorrhage"[MeSH Terms] OR "hemorrhage"[All Fields] OR "bleed"[All Fields] OR "bleeding"[All Fields] OR "bleeds"[All Fields]) OR ("perforant"[All Fields] OR "perforants"[All Fields] OR "perforate"[All Fields] OR "perforated"[All Fields] OR "perforates"[All Fields] OR "perforating"[All Fields] OR "perforation"[All Fields] OR "perforations"[All Fields] OR "perforative"[All Fields] OR "perforator"[All Fields] OR "perforator s"[All Fields] OR "perforators"[All Fields]))) Search (PubMed): **ESD for poorly differentiated/poorly cohesive /undifferentiated carcinoma. Filter: From 2021** (("early"[All Fields] AND ("stomach neoplasms"[MeSH Terms] OR ("stomach"[All Fields] AND "neoplasms"[All Fields]) OR "stomach neoplasms"[All Fields] OR ("gastric"[All Fields] AND "cancer"[All Fields]) OR "gastric cancer"[All Fields])) OR ("early"[All Fields] AND ("gastrics"[All Fields] OR "stomach"[MeSH Terms] OR "stomach"[All Fields] OR "gastric"[All Fields]) AND ("lesion"[All Fields] OR "lesion s"[All Fields] OR "lesional"[All Fields] OR "lesions"[All Fields]))) AND ("undifferentiate"[All Fields] OR "undifferentiated"[All Fields] OR "undifferentiating"[All Fields] OR "undifferentiation"[All Fields] OR ("poorly"[All Fields] AND ("cohesion"[All Fields] OR "cohesions"[All Fields] OR "cohesive"[All Fields] OR "cohesively"[All Fields] OR "cohesiveness"[All Fields] OR "cohesivity"[All Fields])) OR ("poorly"[All Fields] AND ("cell differentiation"[MeSH Terms] OR ("cell"[All Fields] AND "differentiation"[All Fields]) OR "cell differentiation"[All Fields] OR "differentiated"[All Fields] OR "differentiation"[All Fields] OR "differential"[All Fields] OR "differentials"[All Fields] OR "differentiate"[All Fields] OR "differentiates"[All Fields] OR "differentiating"[All Fields] OR "differentiational"[All Fields] OR "differentiations"[All Fields] OR "differentiative"[All Fields])) OR ("signet"[All Fields] AND "ring"[All Fields] AND ("cells"[MeSH Terms] OR "cells"[All Fields] OR "cell"[All Fields]))) AND ("endoscopic mucosal resection"[MeSH Terms] OR ("endoscopic"[All Fields] AND "mucosal"[All Fields] AND "resection"[All Fields]) OR "endoscopic mucosal resection"[All Fields] OR ("endoscopic"[All Fields] AND "submucosal"[All Fields] AND "dissection"[All Fields]) OR "endoscopic submucosal dissection"[All Fields] OR ("earth syst dyn"[Journal] OR "esd"[All Fields])) AND ("gastrectomy"[MeSH Terms] OR "gastrectomy"[All Fields] OR "gastrectomies"[All Fields] OR ("endoscopic mucosal resection"[MeSH Terms] OR ("endoscopic"[All Fields] AND "mucosal"[All Fields] AND "resection"[All Fields]) OR "endoscopic mucosal resection"[All Fields]) OR ("empir musicol rev"[Journal] OR "emr"[All Fields])) AND ("efficacies"[All Fields] OR "efficacious"[All Fields] OR "efficaciously"[All Fields] OR "efficaciousness"[All Fields] OR "efficacy"[All Fields] OR (("enzymology"[MeSH Subheading] OR "enzymology"[All Fields] OR "en"[All Fields]) AND "bloc"[All Fields] AND ("resect"[All Fields] OR "resectability"[All Fields] OR "resectable"[All Fields] OR "resectates"[All Fields] OR "resected"[All Fields] OR "resecting"[All Fields] OR "resection"[All Fields] OR "resectional"[All Fields] OR "resectioned"[All Fields] OR "resectioning"[All Fields] OR "resections"[All Fields] OR "resective"[All Fields] OR "resects"[All Fields])) OR (("complete"[All Fields] OR "completed"[All Fields] OR "completely"[All Fields] OR "completeness"[All Fields] OR "completer"[All Fields] OR "completers"[All Fields] OR "completes"[All Fields] OR "completing"[All Fields] OR "completion"[All Fields] OR "completions"[All Fields]) AND ("resect"[All Fields] OR "resectability"[All Fields] OR "resectable"[All Fields] OR "resectates"[All Fields] OR "resected"[All Fields] OR "resecting"[All Fields] OR "resection"[All Fields] OR "resectional"[All Fields] OR "resectioned"[All Fields] OR "resectioning"[All Fields] OR "resections"[All Fields] OR "resective"[All Fields] OR "resects"[All Fields])) OR ("recurrance"[All Fields] OR "recurrence"[MeSH Terms] OR "recurrence"[All Fields] OR "recurrences"[All Fields] OR "recurrencies"[All Fields] OR "recurrency"[All Fields] OR "recurrent"[All Fields] OR "recurrently"[All Fields] OR "recurrents"[All Fields]) OR ("safety"[MeSH Terms] OR "safety"[All Fields] OR "safeties"[All Fields] OR ("complicances"[All Fields] OR "complicate"[All Fields] OR "complicated"[All Fields] OR "complicates"[All Fields] OR "complicating"[All Fields] OR "complication"[All Fields] OR "complication s"[All Fields] OR "complications"[MeSH Subheading] OR "complications"[All Fields]) OR ("mortality"[MeSH Terms] OR "mortality"[All Fields] OR "mortalities"[All Fields] OR "mortality"[MeSH Subheading]) OR ("bleedings"[All Fields] OR "hemorrhage"[MeSH Terms] OR "hemorrhage"[All Fields] OR "bleed"[All Fields] OR "bleeding"[All Fields] OR "bleeds"[All Fields]) OR ("perforant"[All Fields] OR "perforants"[All Fields] OR "perforate"[All Fields] OR "perforated"[All Fields] OR "perforates"[All Fields] OR "perforating"[All Fields] OR "perforation"[All Fields] OR "perforations"[All Fields] OR "perforative"[All Fields] OR "perforator"[All Fields] OR "perforator s"[All Fields] OR "perforators"[All Fields]))

Table of evidence		***Are there any cohorts?***																						
Study ID	Study design Score **(2)**	Risk of bias (alinea(s)) *	Quality Score **(0 to -3) ****	Consistency Score **(-1 to 1) #**	Directness Score **(0 to -2) @**	Publication bias † (**0: No,1: Yes**)	Reported OR/RR/HR	Effect size Score **(0 to 2)** §	Evidence Level¶				Type of study according to SIGN								Recommendation SIGN			
									High	Mod	Low	Very Low	1++	1+	1-	2++	2+	2-	3	4	A	B	C	D
Xu 2022 (BMJ)	2	SR/MA 9 retrospective studies comparing ESD vs Surgery for expanded indications: (1) >20mm cT1a Diff UL-; (2) ≤30mm cT1a Diff UL+; (3) ≤30mm cT1b<500µm (SM1); and (4) ≤20mm cT1a UL- NOS >7 for all studies, low risk	0	0	0	0 (no publication bias for metachronous lesions)	Favours Surgery vs ESD: MetachronousOR=0.12, 95% CI=0.05 to 0.25, p<0.00001 Synchronous: OR=0.11, 95% CI=0.02 to 0.46, p=0.003 Favours ESD vs Surgery Fewer AEs: OR=0.49, 95% CI=0.34 to 0.72. p=0.002 5-year OS in 1727 patients no significant difference (HR=1.22, 95% CI=0.66 to 2.25, p=0.53 5-year DFS favours Surgery : ESD vs surgery, HR=3.29, 95% CI=1.60 to 6.76, p=0.001 Comment: ESD fewer Aes with similar OS but higher metachronous/synchronus lesión and lower DFS in expanded indication	1		Mod						2++					x		
Sun 2023 (J Surg Res)	2	Retrospective single center n=730 EGC gastrectomy Selection ***/**** Comparability (*/**): Diff n=311 (pap or tub1, tub2) or Undiff n=217 (por1,por2, sig, muc) vs mixed n=202 (both Diff/Undiff) Outcome (***/***): LNM confirmed histologically after D1,D1+ or D2 dissection. Median FU 65 months (7-127) NOS: 7 (Low-risk)	0	0	0	n/a	<u>LNM+ in pT1a+pT1b</u> **Mixed Type** OR 2.522 (95% CI 1.512-4.207) p<0.001 vs diff **Undiff** OR 2.659 (95% CI 1.581-4.471) p<0.001 vs diff <u>LNM+ in pT1a:</u> **Mixed Type** OR 3.835 (95% CI 0.857-16.70) p=0.079 vs diff <u>LNM+ in pT1b:</u> **Mixed Type** (LNM **36.2%)** OR 2.256 (95% CI 1.298 - 3.922) p=0.004 vs diff **Undiff** (LNM 36.7%) OR 2.560 (95% CI 1443 -4.543) p=0.001 vs diff Similar OS and DSS	1		Mod							2+						x	
Benites-Goñi 2023 (REED)	2	SR/MA, 7 retrospective cohort studies (3 with PSM), 5 studies NOS 7 and 2 studies low-risk Selection: retrospective Comparability: 3 studies with PSM. Outcome: most studies did nnot differentiate Signet cell from poorly diff.	0	0	0	Unknown (no funnel plots or Eggers` s test because <10 studies)	ESD vs Surgery Higher recurrence (any): aRR, 7.89; 95 % CI, 1.52-40.95 and aHR, 3.73; 95 % CI, 1.17-11.90.	0			Low						2+						x	

		Unclear risk					Similar adjusted all cause mortality: aRR, 2.28; 95 % CI, 0.95-5.47 and aHR, 1.97; 95 % CI, 0.85- 4.53 Risk of distant metastasis was similar (RR, 3.01; 95 % CI, 0.23-39.59; I^2 = 0 %), similar risk of complications.																
Meng, 2023 (J Gast Surg)	2	SR/MA 10 studies, retrospective ROB-INS-I score 2-3 (moderate-serious risk of bias) Several studies did not differentiate recurrence vs metachronous de novo cancers	-1 (selection)	0	-1	0 (no)	Treatment of metachronous lesions (including recurrences) ESD vs EMR OR 5.88, 95% confdence intervals, CI, 1.79–19.35 ESD vs Surgery no different (OR 0.57, 95% CI 0.04–8.24)				Low						2+						x	
Liu 2023 (WJ Surg Onc)	2	SR/MA, 8 retrospective studies comparing ESD vs surgery for EGC in elderly. ROBINS-I lo to moderate risk Selection: elderly definitnion variable (≥60, 75, 77 or 80) Comparability: ESD n=1017 vs Surg n=1317 Unclear risk	-1 (selection)	0	0	0	ESD vs survery ESD group had a worse OS (HR=2.81, 95% CI=2.20 to 3.58, I 2=12.28%, P=0.00<0.05) ESD Operation time (MD= -3.38, 95% CI= -5.19 to -1.57, I 2=98.31%, P=0.00<0.05), length of hospital stay (MD= -3.01, 95% CI= -4.81 to -1.20, I 2=98.83%, P=0.00<0.05) and hospitalization expenses (MD= -2.67, 95% CI= -3.59 to -1.75, I 2=93.21%, P=0.00<0.05)					Very low						2+						x	
Kishida, 2021 (DEN) *(also in Table statement 40.)	2	Retrospective, single center ESD (n=114) vs Surgery (n=303) in >=75yo with relative ER indication 1)Selection(****/****) 2)Comparability (**/**) 3) Outcome (*/***): median follow-up 34 months for ESD, 61 months for surgery NOS: 7 (low risk)	0	0	0	n/a	OS-associated factors in males Age ≥79 : HR 2.21, P=.001; PNI <45, HR 2.06, P=.031) OS-associated factors in females Age ≥82, HR 4.06, P=.004 No OS difference between ESD vs surgery	1			Low						2+						x	

* 1) Selection; 2) Comparability; 3) Outcome
** -1 per problem Selection: -1: selected group of users or no description; Comparability -1: no comparison between the cohorts; Outcome -1: No description, no follow up
# Evidence of dose response across or within studies (or inconsistency across studies is explained by a dose response); also up to one point added if adjustment for confounders would have increased the effect size (1); All / most studies show similar results (0); Lack of agreement between studies (e.g. statistical heterogeneity between RCTs, conflicting results) (-1)
@ -1 per problem in generalizability to the target population
†: only for meta-analysis
§ 0 if Not all effect sizes more than 2 or less than 0.5 and significant; or if OR/RR/HR not significant; 1 if Effect size more than 2 or less than 0.5 for all studies/meta-analyses included in comparison and significant; 2 if Effect size more than 5 or less tha.2 for all studies/meta-analyses included in comparison and significant
¶: High: Further research is very unlikely to change our confidence in the estimate of effect; Moderate: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate; Low: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate; Very low: Any estimate of effect is very uncertain

Sentence	**28.** ESGE/EHMSG/ESP recommends patient management based on the following histological risk after endoscopic resection: - *Curative/very low-risk resection (LNM risk < 0.5 %–1 %)* En bloc R0 resection; dysplastic/pT1a, differentiated lesion, no lymphovascular invasion, independent of size if no ulceration and ≤ 30 mm if ulcerated. No further staging procedure or treatment is recommended.

	- *Curative/low-risk resection (LNM risk <3%)* En bloc R0 resection; lesion with no lymphovascular invasion, and: – pT1b, submucosal invasion ≤500 µm, differentiated, size ≤30 mm; or – pT1a, undifferentiated, size ≤20 mm and no ulceration. Staging should be completed, and further treatment is generally not necessary after a multidisciplinary discussion. - *Local-risk resection (very low-risk of LNM but increased risk of persistence/recurrence)* – Piecemeal resection or tumor-positive horizontal margin of a lesion otherwise meeting curative/very low-risk criteria; or – Provided there is no submucosally invasive tumor at the resection margin in the case of piecemeal resection or tumor-positive horizontal margin, for otherwise low-risk pT1b lesion (submucosal Invasion ≤500 µm, well-differentiated, size ≤30 mm, and VM0) Endoscopic surveillance/re-treatment is recommended rather than other additional treatment. *High-risk resection* (noncurative): Any lesion with any of the following: - a) a positive vertical margin (if carcinoma) or lymphovascular invasion or deep submucosal invasion (>500 µm from the muscularis mucosae); - b) poorly differentiated lesions if ulceration or size >20 mm; - c) in pT1b differentiated lesions with submucosal invasion <500 µm with size >30 mm; - or d) in intramucosal ulcerative lesion with size >30 mm. - Complete staging and strong consideration for additional treatments (surgery) in multidisciplinary discussion.	
GRADE	**Strength of recommendation: Strong**	**Quality of evidence: Moderate**
PICO	P : patients treated by ESD I : free margin/mucosal tumor/differentiated/lyv+ C : Vs positive margin/submucosal/undifferentiated/lyv- O : recurrence; need for surgery	
Query(ies) and databases searched	What is the post-ESD management according to technical and histological outcomes? Search (PubMed**): positive vertical margin. Filter: From 2021** ((((("gastrics"[All Fields] OR "stomach"[MeSH Terms] OR "stomach"[All Fields] OR "gastric"[All Fields]) AND ("earth syst dyn"[Journal] OR "esd"[All Fields])) OR (("gastrics"[All Fields] OR "stomach"[MeSH Terms] OR "stomach"[All Fields] OR "gastric"[All Fields]) AND ("endoscope s"[All Fields] OR "endoscoped"[All Fields] OR "endoscopes"[MeSH Terms] OR "endoscopes"[All Fields] OR "endoscope"[All Fields] OR "endoscopical"[All Fields] OR "endoscopically"[All Fields] OR "endoscopy"[MeSH Terms] OR "endoscopy"[All Fields] OR "endoscopic"[All Fields]) AND ("resect"[All Fields] OR "resectability"[All Fields] OR "resectable"[All Fields] OR "resectates"[All Fields] OR "resected"[All Fields] OR "resecting"[All Fields] OR "resection"[All Fields] OR "resectional"[All Fields] OR "resectioned"[All Fields] OR "resectioning"[All Fields] OR "resections"[All Fields] OR "resective"[All Fields] OR "resects"[All Fields]))) AND ("free"[All Fields] AND ("margin"[All Fields] OR "margin s"[All Fields] OR "marginal"[All Fields] OR "marginals"[All Fields] OR "margined"[All Fields] OR "margins"[All Fields])) AND ((("positive"[All Fields] OR "positively"[All Fields] OR "positiveness"[All Fields] OR "positives"[All Fields] OR "positivities"[All Fields] OR "positivity"[All Fields]) AND ("margin"[All	

	Fields] OR "margin s"[All Fields] OR "marginal"[All Fields] OR "marginals"[All Fields] OR "margined"[All Fields] OR "margins"[All Fields])) OR (("tangential"[All Fields] OR "tangentially"[All Fields] OR "tangentials"[All Fields]) AND ("margin"[All Fields] OR "margin s"[All Fields] OR "marginal"[All Fields] OR "marginals"[All Fields] OR "margined"[All Fields] OR "margins"[All Fields]))) AND ("mortality"[MeSH Subheading] OR "mortality"[All Fields] OR "survival"[All Fields] OR "survival"[MeSH Terms] OR "survivability"[All Fields] OR "survivable"[All Fields] OR "survivals"[All Fields] OR "survive"[All Fields] OR "survived"[All Fields] OR "survives"[All Fields] OR "surviving"[All Fields] OR "mortaliy"[All Fields] OR ("surgery"[MeSH Subheading] OR "surgery"[All Fields] OR "surgical procedures, operative"[MeSH Terms] OR ("surgical"[All Fields] AND "procedures"[All Fields] AND "operative"[All Fields]) OR "operative surgical procedures"[All Fields] OR "general surgery"[MeSH Terms] OR ("general"[All Fields] AND "surgery"[All Fields]) OR "general surgery"[All Fields] OR "surgery s"[All Fields] OR "surgerys"[All Fields] OR "surgeries"[All Fields]) OR ("metastasi"[All Fields] OR "neoplasm metastasis"[MeSH Terms] OR ("neoplasm"[All Fields] AND "metastasis"[All Fields]) OR "neoplasm metastasis"[All Fields] OR "metastasis"[All Fields]) OR "LNM"[All Fields])) Search (PubMed): **submucosal invasion. Filter: From 2021** ((((("gastrics"[All Fields] OR "stomach"[MeSH Terms] OR "stomach"[All Fields] OR "gastric"[All Fields]) AND ("earth syst dyn"[Journal] OR "esd"[All Fields])) OR (("gastrics"[All Fields] OR "stomach"[MeSH Terms] OR "stomach"[All Fields] OR "gastric"[All Fields]) AND ("endoscope s"[All Fields] OR "endoscoped"[All Fields] OR "endoscopes"[MeSH Terms] OR "endoscopes"[All Fields] OR "endoscope"[All Fields] OR "endoscopical"[All Fields] OR "endoscopically"[All Fields] OR "endoscopy"[MeSH Terms] OR "endoscopy"[All Fields] OR "endoscopic"[All Fields]) AND ("resect"[All Fields] OR "resectability"[All Fields] OR "resectable"[All Fields] OR "resectates"[All Fields] OR "resected"[All Fields] OR "resecting"[All Fields] OR "resection"[All Fields] OR "resectional"[All Fields] OR "resectioned"[All Fields] OR "resectioning"[All Fields] OR "resections"[All Fields] OR "resective"[All Fields] OR "resects"[All Fields]))) AND ("mucosalization"[All Fields] OR "mucosalized"[All Fields] OR "mucosally"[All Fields] OR "mucose"[All Fields] OR "mucoses"[All Fields] OR "mucositis"[MeSH Terms] OR "mucositis"[All Fields] OR "mucositides"[All Fields] OR "mucous membrane"[MeSH Terms] OR ("mucous"[All Fields] AND "membrane"[All Fields]) OR "mucous membrane"[All Fields] OR "mucosal"[All Fields] OR "intramucosal"[All Fields]) AND ("submucosal"[All Fields] OR "submucosally"[All Fields] OR "sm1"[All Fields] OR "sm2"[All Fields]) AND ("mortality"[MeSH Subheading] OR "mortality"[All Fields] OR "survival"[All Fields] OR "survival"[MeSH Terms] OR "survivability"[All Fields] OR "survivable"[All Fields] OR "survivals"[All Fields] OR "survive"[All Fields] OR "survived"[All Fields] OR "survives"[All Fields] OR "surviving"[All Fields] OR "mortaliy"[All Fields] OR ("surgery"[MeSH Subheading] OR "surgery"[All Fields] OR "surgical procedures, operative"[MeSH Terms] OR ("surgical"[All Fields] AND "procedures"[All Fields] AND "operative"[All Fields]) OR "operative surgical procedures"[All Fields] OR "general surgery"[MeSH Terms] OR ("general"[All Fields] AND "surgery"[All Fields]) OR "general surgery"[All Fields] OR "surgery s"[All Fields] OR "surgerys"[All Fields] OR "surgeries"[All Fields]) OR ("metastasi"[All Fields] OR "neoplasm metastasis"[MeSH Terms] OR ("neoplasm"[All Fields] AND "metastasis"[All Fields]) OR "neoplasm metastasis"[All Fields] OR "metastasis"[All Fields]) OR "LNM"[All Fields])) Search (PubMed): **poorly differentiated/cohesive carcinoma. Filter: From 2021** ("gastrics"[All Fields] OR "stomach"[MeSH Terms] OR "stomach"[All Fields] OR "gastric"[All Fields]) AND ("earth syst dyn"[Journal] OR "esd"[All Fields]) AND ("undifferentiate"[All Fields] OR "undifferentiated"[All Fields] OR "undifferentiating"[All Fields] OR "undifferentiation"[All Fields] OR ("poorly"[All Fields] AND ("cohesion"[All Fields] OR "cohesions"[All Fields] OR "cohesive"[All Fields] OR "cohesively"[All Fields] OR "cohesiveness"[All Fields] OR "cohesivity"[All Fields])) OR ("poorly"[All Fields] AND ("cell differentiation"[MeSH Terms] OR ("cell"[All Fields] AND "differentiation"[All Fields]) OR "cell differentiation"[All Fields] OR "differentiated"[All Fields] OR "differentiation"[All Fields] OR "differential"[All Fields] OR "differentials"[All Fields] OR "differentiate"[All Fields] OR "differentiates"[All Fields] OR "differentiating"[All Fields] OR "differentiational"[All Fields] OR "differentiations"[All Fields] OR "differentiative"[All Fields])) OR ("signet"[All Fields] AND "ring"[All Fields] AND ("cells"[MeSH Terms] OR "cells"[All Fields] OR "cell"[All Fields]))) AND ("cell differentiation"[MeSH Terms] OR ("cell"[All Fields] AND "differentiation"[All Fields]) OR "cell differentiation"[All Fields] OR "differentiated"[All Fields] OR "differentiation"[All Fields] OR "differential"[All Fields] OR "differentials"[All Fields] OR "differentiate"[All Fields] OR "differentiates"[All Fields] OR "differentiating"[All Fields] OR "differentiational"[All Fields] OR "differentiations"[All Fields] OR "differentiative"[All Fields]) AND ("mortality"[MeSH Subheading] OR "mortality"[All Fields] OR "survival"[All Fields] OR "survival"[MeSH Terms] OR "survivability"[All Fields] OR "survivable"[All Fields] OR "survivals"[All Fields] OR "survive"[All Fields] OR "survived"[All Fields] OR "survives"[All Fields] OR "surviving"[All Fields] OR "mortaliy"[All Fields] OR ("surgery"[MeSH Subheading] OR "surgery"[All Fields] OR "surgical procedures, operative"[MeSH Terms] OR ("surgical"[All Fields] AND "procedures"[All Fields] AND "operative"[All Fields]) OR "operative surgical procedures"[All Fields] OR "general surgery"[MeSH Terms] OR ("general"[All Fields] AND "surgery"[All Fields]) OR "general surgery"[All Fields] OR "surgery s"[All Fields] OR "surgerys"[All Fields] OR "surgeries"[All Fields]) OR ("metastasi"[All Fields] OR "neoplasm metastasis"[MeSH Terms] OR ("neoplasm"[All Fields] AND "metastasis"[All Fields]) OR "neoplasm metastasis"[All Fields] OR "metastasis"[All Fields]) OR "LNM"[All Fields]) Search (PubMed): **lymphovascular invasion. Filter: From 2021** ((((("gastrics"[All Fields] OR "stomach"[MeSH Terms] OR "stomach"[All Fields] OR "gastric"[All Fields]) AND ("earth syst dyn"[Journal] OR "esd"[All Fields])) OR (("gastrics"[All Fields] OR

	"stomach"[MeSH Terms] OR "stomach"[All Fields] OR "gastric"[All Fields]) AND ("endoscope s"[All Fields] OR "endoscoped"[All Fields] OR "endoscopes"[MeSH Terms] OR "endoscopes"[All Fields] OR "endoscope"[All Fields] OR "endoscopical"[All Fields] OR "endoscopically"[All Fields] OR "endoscopy"[MeSH Terms] OR "endoscopy"[All Fields] OR "endoscopic"[All Fields]) AND ("resect"[All Fields] OR "resectability"[All Fields] OR "resectable"[All Fields] OR "resectates"[All Fields] OR "resected"[All Fields] OR "resecting"[All Fields] OR "resection"[All Fields] OR "resectional"[All Fields] OR "resectioned"[All Fields] OR "resectioning"[All Fields] OR "resections"[All Fields] OR "resective"[All Fields] OR "resects"[All Fields])) AND "lymphovascular"[All Fields] AND ("mortality"[MeSH Subheading] OR "mortality"[All Fields] OR "survival"[All Fields] OR "survival"[MeSH Terms] OR "survivability"[All Fields] OR "survivable"[All Fields] OR "survivals"[All Fields] OR "survive"[All Fields] OR "survived"[All Fields] OR "survives"[All Fields] OR "surviving"[All Fields] OR "mortaliy"[All Fields] OR ("surgery"[MeSH Subheading] OR "surgery"[All Fields] OR "surgical procedures, operative"[MeSH Terms] OR ("surgical"[All Fields] AND "procedures"[All Fields] AND "operative"[All Fields]) OR "operative surgical procedures"[All Fields] OR "general surgery"[MeSH Terms] OR ("general"[All Fields] AND "surgery"[All Fields]) OR "general surgery"[All Fields] OR "surgery s"[All Fields] OR "surgerys"[All Fields] OR "surgeries"[All Fields]) OR ("metastasi"[All Fields] OR "neoplasm metastasis"[MeSH Terms] OR ("neoplasm"[All Fields] AND "metastasis"[All Fields]) OR "neoplasm metastasis"[All Fields] OR "metastasis"[All Fields]) OR "LNM"[All Fields])
Table of evidence	***Are there any cohorts?***

Study ID	Study design Score **(2)**	Risk of bias (alinea(s)) *	Quality Score **(0 to -3) ****	Consistency Score **(-1 to 1) #**	Directness Score **(0 to -2) @**	Publication bias † **(0: No,1: Yes)**	Reported OR/RR/HR	Effect size Score **(0 to 2)** §	Evidence Level¶				Type of study according to SIGN								Recommendation SIGN			
									High	Mod	Low	Very Low	1++	1+	1-	2++	2+	2-	3	4	A	B	C	D
Suzuki, 2023 (Clin Gas Hep)	2	Multicenter prosoective cohort, long term outcomes after EGC ER n=9054 (10021 lesions) Selection: ****/**** Included pT1aUL-≤20 mm(A1):n=4545 pT1aUL>20 mm or UL+-≤30 mm(A2) n=2084; Undiff pT1aUL-≤20 mm (A3): n=226; pT1b(sm1)≤30 mm (B): n=387; HM+/orVM+/-Ly+/-V+/-(C): n=1812 Comparability: (*/**) compare to expected 5y OS after surgery Outcome: ***/***, >90% 5-y follow-up. NOS: 8 (low-risk)	-1	0	0	n/1	5-year OS was 89.0% (95% CI, 88.3%–89.6%) HR similar beteween curability A1,2,3 and B on multivariate adjusted HRs	0		Mod							2++						x	
Shin, 2022 (Gut Liver)	2	Retrospective, multicenter. Outcomes after ESD for Papillary EGC (n=97) Selection: ***/**** Comparability: No control group Outcomes: **/*** mean follow-uuo 50.3 months. 13 noncurative resections, 8 underwent surgery. 3 local recurrences, 0 death. NOS 5 (unclear)	-1	0	0	n/a	LNM risk in papillary type EGC: Submucosa vs mucosa: OR 3.735 (95% CI 1.026-12.177) p=0.047; Lv+ OR 7.636 (1.730-22.857) p=0.004. On multivariate	1			Low						2+						x	

Sentence	**ESGE/EHMSG/ESP suggest a surveillance high-quality endoscopy at 3–6 months and then annually after a very low- or low-risk ESD resection or after a local-risk ESD resection without recurrence. Routine use of EUS, MRI, CT, or PET in the follow-up after very low-risk resections is not suggested but it could be considered in higher-risk lesions.**	
GRADE	**Strength of recommendation: Conditional**	**Quality of evidence: Low**
PICO	P : patients treated by ESD with a low-risk/high risk/local risk resection I : endoscopic surveillance C : Vs no surveillance /extended surveillance O: recurrence; metachronous lesions; survival	

Query(ies) and databases searched	What is the post-ESD surveillance according to technical and histological outcomes? Search (PubMed): **low-risk resection surveillance. Filter: From 2021** ((("low-risk"[All Fields] AND ("gastrics"[All Fields] OR "stomach"[MeSH Terms] OR "stomach"[All Fields] OR "gastric"[All Fields]) AND ("earth syst dyn"[Journal] OR "esd"[All Fields])) OR (("curative"[All Fields] OR "curatively"[All Fields] OR "curativity"[All Fields]) AND ("gastrics"[All Fields] OR "stomach"[MeSH Terms] OR "stomach"[All Fields] OR "gastric"[All Fields]) AND ("earth syst dyn"[Journal] OR "esd"[All Fields]))) AND (("annual"[All Fields] OR "annuality"[All Fields] OR "annualized"[All Fields] OR "annually"[All Fields] OR "annuals"[All Fields]) AND ("epidemiology"[MeSH Subheading] OR "epidemiology"[All Fields] OR "surveillance"[All Fields] OR "epidemiology"[MeSH Terms] OR "surveilance"[All Fields] OR "surveillances"[All Fields] OR "surveilled"[All Fields] OR "surveillence"[All Fields])) AND ("other"[All Fields] OR ("biannual"[All Fields] OR "biannually"[All Fields])) AND ("recurrance"[All Fields] OR "recurrence"[MeSH Terms] OR "recurrence"[All Fields] OR "recurrences"[All Fields] OR "recurrencies"[All Fields] OR "recurrency"[All Fields] OR "recurrent"[All Fields] OR "recurrently"[All Fields] OR "recurrents"[All Fields] OR ("metachronic"[All Fields] OR "metachronous"[All Fields] OR "metachronously"[All Fields]) OR ("mortality"[MeSH Subheading] OR "mortality"[All Fields] OR "survival"[All Fields] OR "survival"[MeSH Terms] OR "survivability"[All Fields] OR "survivable"[All Fields] OR "survivals"[All Fields] OR "survive"[All Fields] OR "survived"[All Fields] OR "survives"[All Fields] OR "surviving"[All Fields]))) Search (PubMed): **high-risk resection surveillance. Filter: From 2021** "high"[All Fields] AND ("risk"[MeSH Terms] OR "risk"[All Fields]) AND ("gastrics"[All Fields] OR "stomach"[MeSH Terms] OR "stomach"[All Fields] OR "gastric"[All Fields]) AND ("earth syst dyn"[Journal] OR "esd"[All Fields]) AND ("epidemiology"[MeSH Subheading] OR "epidemiology"[All Fields] OR "surveillance"[All Fields] OR "epidemiology"[MeSH Terms] OR "surveilance"[All Fields] OR "surveillances"[All Fields] OR "surveilled"[All Fields] OR "surveillence"[All Fields] OR ("non-invasive"[All Fields] AND ("manage"[All Fields] OR "managed"[All Fields] OR "management s"[All Fields] OR "managements"[All Fields] OR "manager"[All Fields] OR "manager s"[All Fields] OR "managers"[All Fields] OR "manages"[All Fields] OR "managing"[All Fields] OR "managment"[All Fields] OR "organization and administration"[MeSH Terms] OR ("organization"[All Fields] AND "administration"[All Fields]) OR "organization and administration"[All Fields] OR "management"[All Fields] OR "disease management"[MeSH Terms] OR ("disease"[All Fields] AND "management"[All Fields]) OR "disease management"[All Fields]))) AND ("surgery"[MeSH Subheading] OR "surgery"[All Fields] OR "surgical procedures, operative"[MeSH Terms] OR ("surgical"[All Fields] AND "procedures"[All Fields] AND "operative"[All Fields]) OR "operative surgical procedures"[All Fields] OR "general surgery"[MeSH Terms] OR ("general"[All Fields] AND "surgery"[All Fields]) OR "general surgery"[All Fields] OR "surgery s"[All Fields] OR "surgerys"[All Fields] OR "surgeries"[All Fields] OR ("chemoradiotherapy"[MeSH Terms] OR "chemoradiotherapy"[All Fields] OR "chemoradiotherapies"[All Fields]) OR ("chemotherapy s"[All Fields] OR "drug therapy"[MeSH Terms] OR ("drug"[All Fields] AND "therapy"[All Fields]) OR "drug therapy"[All Fields] OR "chemotherapies"[All Fields] OR "drug therapy"[MeSH Subheading] OR "chemotherapy"[All Fields]) OR ("radiotherapy"[MeSH Terms] OR "radiotherapy"[All Fields] OR "radiotherapies"[All Fields] OR "radiotherapy"[MeSH Subheading] OR "radiotherapy s"[All Fields])) AND ("recurrance"[All Fields] OR "recurrence"[MeSH Terms] OR "recurrence"[All Fields] OR "recurrences"[All Fields] OR "recurrencies"[All Fields] OR "recurrency"[All Fields] OR "recurrent"[All Fields] OR "recurrently"[All Fields] OR "recurrents"[All Fields] OR ("metachronic"[All Fields] OR "metachronous"[All Fields] OR "metachronously"[All Fields]) OR ("mortality"[MeSH Subheading] OR "mortality"[All Fields] OR "survival"[All Fields] OR "survival"[MeSH Terms] OR "survivability"[All Fields] OR "survivable"[All Fields] OR "survivals"[All Fields] OR "survive"[All Fields] OR "survived"[All Fields] OR "survives"[All Fields] OR "surviving"[All Fields]) OR ("persist"[All Fields] OR "persistance"[All Fields] OR "persistant"[All Fields] OR "persisted"[All Fields] OR "persistence"[All Fields] OR "persistences"[All Fields] OR "persistencies"[All Fields] OR "persistency"[All Fields] OR "persistent"[All Fields] OR "persistently"[All Fields] OR "persistents"[All Fields] OR "persister"[All Fields] OR "persisters"[All Fields] OR "persisting"[All Fields] OR "persists"[All Fields] OR "LNM"[All Fields] OR ("metastasi"[All Fields] OR "neoplasm metastasis"[MeSH Terms] OR ("neoplasm"[All Fields] AND "metastasis"[All Fields]) OR "neoplasm metastasis"[All Fields] OR "metastasis"[All Fields]))) Search (PubMed): **local-risk resection management. Filter: From 2021** (("focal"[All Fields] OR "focalities"[All Fields] OR "focality"[All Fields] OR "focalization"[All Fields] OR "focalized"[All Fields] OR "focally"[All Fields] OR "focals"[All Fields] OR "local"[All Fields] OR "localisation"[All Fields] OR "localisations"[All Fields] OR "localise"[All Fields] OR "localised"[All Fields] OR "localises"[All Fields] OR "localising"[All Fields] OR "localization"[All Fields] OR "localizations"[All Fields] OR "localize"[All Fields] OR "localized"[All Fields] OR "localizer"[All Fields] OR "localizers"[All Fields] OR "localizes"[All Fields] OR "localizing"[All Fields] OR "locally"[All Fields] OR "locals"[All Fields]) AND ("risk"[MeSH Terms] OR "risk"[All Fields]) AND ("gastrics"[All Fields] OR "stomach"[MeSH Terms] OR "stomach"[All Fields] OR "gastric"[All Fields]) AND ("earth syst dyn"[Journal] OR "esd"[All Fields]) AND (("endoscope s"[All Fields] OR "endoscoped"[All Fields] OR "endoscopes"[MeSH Terms] OR "endoscopes"[All Fields] OR "endoscope"[All Fields] OR "endoscopical"[All Fields] OR "endoscopically"[All Fields] OR "endoscopy"[MeSH Terms] OR "endoscopy"[All Fields] OR "endoscopic"[All Fields]) AND ("epidemiology"[MeSH Subheading] OR "epidemiology"[All Fields] OR "surveillance"[All Fields] OR "epidemiology"[MeSH Terms] OR "surveilance"[All Fields] OR "surveillances"[All Fields] OR "surveilled"[All Fields] OR "surveillence"[All Fields])) AND ("epidemiology"[MeSH Subheading] OR "epidemiology"[All Fields] OR "surveillance"[All

	Fields] OR "epidemiology"[MeSH Terms] OR "surveilance"[All Fields] OR "surveillances"[All Fields] OR "surveilled"[All Fields] OR "surveillence"[All Fields] OR ("tomography, x ray computed"[MeSH Terms] OR ("tomography"[All Fields] AND "x ray"[All Fields] AND "computed"[All Fields]) OR "x-ray computed tomography"[All Fields] OR ("ct"[All Fields] AND "scan"[All Fields]) OR "ct scan"[All Fields]) OR ("endosonography"[MeSH Terms] OR "endosonography"[All Fields] OR ("endoscopic"[All Fields] AND "ultrasound"[All Fields]) OR "endoscopic ultrasound"[All Fields])) AND ("recurrance"[All Fields] OR "recurrence"[MeSH Terms] OR "recurrence"[All Fields] OR "recurrences"[All Fields] OR "recurrencies"[All Fields] OR "recurrency"[All Fields] OR "recurrent"[All Fields] OR "recurrently"[All Fields] OR "recurrents"[All Fields] OR ("metachronic"[All Fields] OR "metachronous"[All Fields] OR "metachronously"[All Fields]) OR ("mortality"[MeSH Subheading] OR "mortality"[All Fields] OR "survival"[All Fields] OR "survival"[MeSH Terms] OR "survivability"[All Fields] OR "survivable"[All Fields] OR "survivals"[All Fields] OR "survive"[All Fields] OR "survived"[All Fields] OR "survives"[All Fields] OR "surviving"[All Fields]))) Search (PubMed): **EUS, CT , MRI and PET scan. Filter: From 2021** ("gastrics"[All Fields] OR "stomach"[MeSH Terms] OR "stomach"[All Fields] OR "gastric"[All Fields]) AND ("earth syst dyn"[Journal] OR "esd"[All Fields]) AND ("magnetic resonance imaging"[MeSH Terms] OR ("magnetic"[All Fields] AND "resonance"[All Fields] AND "imaging"[All Fields]) OR "magnetic resonance imaging"[All Fields] OR "mri"[All Fields] OR ("tomography, x ray computed"[MeSH Terms] OR ("tomography"[All Fields] AND "x ray"[All Fields] AND "computed"[All Fields]) OR "x-ray computed tomography"[All Fields] OR ("ct"[All Fields] AND "scan"[All Fields]) OR "ct scan"[All Fields]) OR ("endosonography"[MeSH Terms] OR "endosonography"[All Fields] OR ("endoscopic"[All Fields] AND "ultrasound"[All Fields]) OR "endoscopic ultrasound"[All Fields]) OR ("positron emission tomography"[MeSH Terms] OR ("positron emission"[All Fields] AND "tomography"[All Fields]) OR "positron emission tomography"[All Fields] OR ("pet"[All Fields] AND "scan"[All Fields]) OR "pet scan"[All Fields])) AND ("conservancies"[All Fields] OR "conservancy"[All Fields] OR "conservancy s"[All Fields] OR "conservation"[All Fields] OR "conservational"[All Fields] OR "conservations"[All Fields] OR "conservative"[All Fields] OR "conservatively"[All Fields] OR "conservatives"[All Fields] OR "conserve"[All Fields] OR "conserved"[All Fields] OR "conserves"[All Fields] OR "conserving"[All Fields] OR ("epidemiology"[MeSH Subheading] OR "epidemiology"[All Fields] OR "surveillance"[All Fields] OR "epidemiology"[MeSH Terms] OR "surveilance"[All Fields] OR "surveillances"[All Fields] OR "surveilled"[All Fields] OR "surveillence"[All Fields])) AND ("mortality"[MeSH Subheading] OR "mortality"[All Fields] OR "survival"[All Fields] OR "survival"[MeSH Terms] OR "survivability"[All Fields] OR "survivable"[All Fields] OR "survivals"[All Fields] OR "survive"[All Fields] OR "survived"[All Fields] OR "survives"[All Fields] OR "surviving"[All Fields] OR ("recurrance"[All Fields] OR "recurrence"[MeSH Terms] OR "recurrence"[All Fields] OR "recurrences"[All Fields] OR "recurrencies"[All Fields] OR "recurrency"[All Fields] OR "recurrent"[All Fields] OR "recurrently"[All Fields] OR "recurrents"[All Fields]) OR ("lymphatic metastasis"[MeSH Terms] OR ("lymphatic"[All Fields] AND "metastasis"[All Fields]) OR "lymphatic metastasis"[All Fields] OR ("lymph"[All Fields] AND "node"[All Fields] AND "metastasis"[All Fields]) OR "lymph node metastasis"[All Fields]) OR ("metachronic"[All Fields] OR "metachronous"[All Fields] OR "metachronously"[All Fields])))
Table of evidence	***Are there any cohorts?***

Study ID	Study design Score **(2)**	Risk of bias (alinea(s))*	Quality Score **(0 to -3)****	Consistency Score **(-1 to 1) #**	Directness Score **(0 to -2) @**	Publication bias † **(0:No,1:Yes)**	Reported OR/RR/HR	Effect size Score **(0 to 2)** §	Evidence Level¶				Type of study according to SIGN								Recommendation SIGN			
									High	Mod	Low	Very Low	1++	1+	1-	2++	2+	2-	3	4	A	B	C	D
Ortigao 2022 (Endoscopy)	2 (SR/MA)	SR/MA 49 studies (41 retrospective, 5 prospective, 3 RCTs) evaluating risk factors for metachronous gastric lesions (MGL) after ESD or gastrectomy Median NOS 8 (IQR 7-9) 1 RCT low.ris, 2 unclear.	0	-1	-1	0 (no)	Risk Factors: Older age (mean difference 1.08 years, 95 %CI 0.21 to 1.96), male sex (odds ratio [OR] 1.43, 95 %CI 1.22 to 1.66), family history of gastric cancer (OR 1.88, 95 %CI 1.03 to 3.41), synchronous lesions (OR 1.72, 95 %CI 1.30 to 2.28), severe gastric mucosal atrophy (OR 2.77, 95 %CI 1.22 to 6.29), intestinal metaplasia in corpus (OR 3.15, 95 %CI 1.67 to 5.96), persistent Helicobacter pylori infection (OR 2.08, 95 %CI 1.60 to 2.72), and lower pepsinogen I/II ratio (mean difference -0.54, 95 %CI -0.86 to -0.22) were significantly associated	0		Mod					2++									x	

							with MGL after ER.															
Rei 2023 (Endoscopy)	2	Reetrospective single center, Score Validation of FAMISH score in gastric ESD >3y FU (n=263) FAMISH (9 points): family history of gastric cancer (1), older age(1), male sex(1), corpus intestinal metaplasia(3), synchronous gastric lesions(1), and persistent Helicobacter pylori infection (2). Selection ***/**** Comparaibilty(*/**) Outcome ***/*** NOS: 7 (low risk)	-1	0	0	n/a	MGL at 3 y FU-predictor: Synchronous lesions OR 3 years 3.53, 95 %CI 1.01–12.4), p=0.048 FAMISH diagnostic accuracy for MGL at 3 years' follow-up: AUC, 0.704 (95 %CI 0.603-0.806). If cutoff < 2, maximal sensitivity and negative predictive value 15 % of patients could be assigned to a low-risk group, in which the progression to MGL was significantly lower than for the high-risk group (P = 0.04).				LOw					2+							x	
Niu 2024 (Eur J Gas Hep)	2	Multicenter retrospective of EGC after ESD n=618 Validation of FAMISH score Selection: ***/**** Comparator: */** Outcomee: ***/*** Follow-up minimum 3 years NOS 7 (low risk)	0	0	0	n/a	HR compared to low-risk FAMISH group Intermediate risk for MGL: HRs of 2.859 (95% CI, 1.537–5.317) High risk: 7.892 (95% CI, 4.116–15.479) being observed (P < 0.001; Multivariate Risk Factors GML: Male sex (P = 0.021), Corpus IM (P = 0.002),Synchronous lesions (P = 0.027), and persistent H. pylori infection (P = 0.002)																x	
Meng, 2023 (J Gast Surg *also In table statement 43	2	SR/MA 10 studies, retrospective ROB-INS-I score 2-3 (moderate-serious risk of bias) Several studies did not differentiate recurrence vs metachronous de novo cancers	-1	0	-1	0	Treatment of metachronous lesions (including recurrences) ESD vs EMR OR 5.88, 95% confdence intervals, CI, 1.79–19.35 ESD vs Surgery no different (OR 0.57, 95% CI 0.04–8.24)				low						2+						x	
Noh, 2021 (Sci Rep)	2	Retrospective single center, identification of risk factors for recurrence after ESD for gastric adenoma (n=698) Selection ***/**** Comparability () Outcome ***/*** NOS 6 (unclear risk)	0	0	0	n/a	Risk Factors for recurrence after ER gastric adenoma male (hazard ratio [HR], 2.60, P= 0.030), protruded scar (HR, 3.18, P< 0.001), and age ≥ 59 years (HR, 1.05, P< 0.001).	0			low						2+						x	

Sentence	**ESGE/EHMSG/ESP recommend that after a high-risk resection the need for additional treatment is decided in a multidisciplinary team discussion taking into account LNM risk, age, comorbidities and life-expectancy.**	
GRADE	**Strength of recommendation: Strong**	**Quality of evidence: Moderate**

PICO	P : low-risk/medium risk/high risk noncurative gastric ESD I : conservative management C : surgery O : Survival
Query(ies) and databases searched	What Is the best management after noncurative gastric ESD, surgery or only follow-up? Search (PubMed): **surveillance vs surgery after noncurative gastric ESD.** ("gastrics"[All Fields] OR "stomach"[MeSH Terms] OR "stomach"[All Fields] OR "gastric"[All Fields]) AND ("earth syst dyn"[Journal] OR "esd"[All Fields]) AND (("high"[All Fields] AND ("risk"[MeSH Terms] OR "risk"[All Fields])) OR ("non"[All Fields] AND ("curative"[All Fields] OR "curatively"[All Fields] OR "curativity"[All Fields]))) AND ("conservancies"[All Fields] OR "conservancy"[All Fields] OR "conservancy s"[All Fields] OR "conservation"[All Fields] OR "conservational"[All Fields] OR "conservations"[All Fields] OR "conservative"[All Fields] OR "conservatively"[All Fields] OR "conservatives"[All Fields] OR "conserve"[All Fields] OR "conserved"[All Fields] OR "conserves"[All Fields] OR "conserving"[All Fields] OR ("epidemiology"[MeSH Subheading] OR "epidemiology"[All Fields] OR "surveillance"[All Fields] OR "epidemiology"[MeSH Terms] OR "surveilance"[All Fields] OR "surveillances"[All Fields] OR "surveilled"[All Fields] OR "surveillence"[All Fields])) AND ("gastrectomy"[MeSH Terms] OR "gastrectomy"[All Fields] OR "gastrectomies"[All Fields]) AND ("mortality"[MeSH Subheading] OR "mortality"[All Fields] OR "survival"[All Fields] OR "survival"[MeSH Terms] OR "survivability"[All Fields] OR "survivable"[All Fields] OR "survivals"[All Fields] OR "survive"[All Fields] OR "survived"[All Fields] OR "survives"[All Fields] OR "surviving"[All Fields] OR "mortaliy"[All Fields] OR ("surgery"[MeSH Subheading] OR "surgery"[All Fields] OR "surgical procedures, operative"[MeSH Terms] OR ("surgical"[All Fields] AND "procedures"[All Fields] AND "operative"[All Fields]) OR "operative surgical procedures"[All Fields] OR "general surgery"[MeSH Terms] OR ("general"[All Fields] AND "surgery"[All Fields]) OR "general surgery"[All Fields] OR "surgery s"[All Fields] OR "surgerys"[All Fields] OR "surgeries"[All Fields]) OR ("metastasi"[All Fields] OR "neoplasm metastasis"[MeSH Terms] OR ("neoplasm"[All Fields] AND "metastasis"[All Fields]) OR "neoplasm metastasis"[All Fields] OR "metastasis"[All Fields]) OR "LNM"[All Fields]) Search (PubMed): **outcomes after noncurative gastric ESD, Filter: From 2021.** (("gastrics"[All Fields] OR "stomach"[MeSH Terms] OR "stomach"[All Fields] OR "gastric"[All Fields]) AND ("earth syst dyn"[Journal] OR "esd"[All Fields]) AND (("high"[All Fields] AND ("risk"[MeSH Terms] OR "risk"[All Fields])) OR ("non"[All Fields] AND ("curative"[All Fields] OR "curatively"[All Fields] OR "curativity"[All Fields]))) AND ("mortality"[MeSH Subheading] OR "mortality"[All Fields] OR "survival"[All Fields] OR "survival"[MeSH Terms] OR "survivability"[All Fields] OR "survivable"[All Fields] OR "survivals"[All Fields] OR "survive"[All Fields] OR "survived"[All Fields] OR "survives"[All Fields] OR "surviving"[All Fields] OR "mortaliy"[All Fields] OR ("surgery"[MeSH Subheading] OR "surgery"[All Fields] OR "surgical procedures, operative"[MeSH Terms] OR ("surgical"[All Fields] AND "procedures"[All Fields] AND "operative"[All Fields]) OR "operative surgical procedures"[All Fields] OR "general surgery"[MeSH Terms] OR ("general"[All Fields] AND "surgery"[All Fields]) OR "general surgery"[All Fields] OR "surgery s"[All Fields] OR "surgerys"[All Fields] OR "surgeries"[All Fields]) OR ("metastasi"[All Fields] OR "neoplasm metastasis"[MeSH Terms] OR ("neoplasm"[All Fields] AND "metastasis"[All Fields]) OR "neoplasm metastasis"[All Fields] OR "metastasis"[All Fields]) OR "LNM"[All Fields]))
Table of evidence	***Are there any cohorts?***

Study ID	Study design Score **(2)**	Risk of bias (alinea(s))*	Quality Score **(0 to -3) ****	Consistency Score **(-1 to 1) #**	Directness Score **(0 to -2) @**	Publication bias † **(0: No,1: Yes)**	Reported OR/RR/HR	Effect size Score **(0 to 2)** §	Evidence Level¶				Type of study according to SIGN							Recommendation SIGN			
									High	Mod	Low	Very Low	1++	1+	1-	2++	2+	2-	3	4	A	B	C	D
Kishida, 2021 (DEN) *(also in Table statement 40, 42-43)	2	Retrospective, single center ESD (n=114) vs Surgery (n=303) in >=75yo with relative ER indication 1)Selection(****/****) 2)Comparability (**/**) 3) Outcome (*/***): median follow-up 34 months for ESD, 61 months for surgery NOS: 7 (low risk)	0	0	0	n/a	OS-associated factors in males Age ≥79 : HR 2.21, P=.001; PNI <45, HR 2.06, P=.031) OS-associated factors in females Age ≥82, HR 4.06, P=.004 No OS difference between ESD vs surgery	1			Low							2+						x	
Han, 2023 (Surg End)	2	Retrospective, Comparison Non-curative (NC=142)) vs Curative	0	+1	0	n/a	Pre-ESD risk factors for noncurative:	0			low							2+						x	

		(C=682) ESD to develop Nomogram for prediction NC. Selection ***/**** Comparability */** Outcome **/*** NOS: 6 (unclear)					redness OR 2.52; 95% CI 1.54–4.12, whitish mucosal change OR 2.17; 95% CI 1.17–4.03, fold convergence OR 5.13; 95% CI 3.11–8.47, lesion size over 20 mm OR 3.04; 95% CI 1.98–4.69, and elevated lesion OR 1.85; 95% CI 1.10–3.14; pathology of moderately differentiated adenocarcinoma OR 2.29; 95% CI 1.42–3.71, poorly diferentiated adenocarcinoma OR 11.61; 95% CI 5.70–8.32, or signet ring cell carcinoma OR 3.60; 95% CI 1.55–8.32; and abnormal CT fndings, including LN enlargement OR 2.18; 95% CI 1.21–3.96, or the combination of fold thickening and LN enlargement OR 4.62; 95% CI 1.33-16.1.																	
Zhao 2023 (Am J Cancer Res)	2	Retrospective observational, to develop predictive model of LNM from gastrectomies (n=3158), evaluating also an ESD cohort as external validation (n=323) Selection ***/**** Comparaibilty */** Outcome ***/*** NOS 7 (low)	o	0	-1 (1 variable in the prediction model is year when diagnosed)	n/a	Multivariate: Femal OR=1.35, 95% CI: 1.08-1.69, P=0.008, year when diagnosed (OR=0.81, 95% CI: 0.55-1.18, P=0.265; OR=0.56, 95% CI: 0.40-0.78, P=0.001; OR=0.45, 95% CI: 0.31-0.64, P<0.001), tumor size 20-40 mmOR=1.51, 95% CI: 1.19- 1.92, P=0.001; >40 mm OR=1.97, 95% CI: 1.51-2.56, P<0.001), tumor grade poorly-moderately OR=0.72, 95% CI: 0.54-0.94, P=0.016; moderately OR= 0.48, 95% CI: 0.35-0.66, P<0.001; well moderately OR=0.17, 95% CI: 0.09-0.31, P<0.001; well OR= 0.28, 95% CI: 0.16-0.47, P<0.001), vascular invasion (OR=4.36, 95% CI: 3.35-5.67, P<0.001), and pT1bvs1a (OR= 1.97, 95% CI: 1.57-2.48, P< 0.001)	0			low						2-					x	
Li, 2023 (Frontieres Surg)	2	Retrospective clinicopathological evaluation of n=626 EGC Surgery to develop a nomogram to predict LNM according to % of undifferentiated component. 0% of undifferentiated component (PUC)=Pure Differentiated (PD) 100% PUC=Pure Undifferentiated (PUD) M1:0% < PUC ≤ 20%, M2:20%<PUC ≤ 40%, M3:40%<PUC ≤ 60%, M4:60%<PUC ≤ 80%, M5:80% <PUC < 100% Selection ***/**** Comp */** Outcome **/***	0	0	o	n/a	Multivariate OR for LNM >20 mm OR 3.157 (95% CI 1.581,6.303) p 0.012 SM2 OR 2.869 (95% CI 1.262,6.523) p <0.001 LVI+ OR 12.648 (95% CI 6.246,25.611) p<0.001 M4 OR 12.205 (95% CI 4.791,31.088) AUC of 0.899 (P < 0.05)	1			low						2+					x	

		NOS 6 (unclear)																				
Zhang 2023 (Front Onc)	2	Retrospective analysis of n=952 EGC gastrectomies to develop nomogram for LNM Selection ***/**** Comparability */** Outcome **/*** NOS 6 (unclear)	0	0	0	n/a	Multivariate OR (95% CI) p Female 0.508 (0.334-0.774) 0.002 CEA <5 4.5 (2.486-8.251) <0.01 CA19.9<39 4.529 (1.360-12.056) 0.012 Poorly Diff 4.209 (1.360-13.028) 0.013 SM invasión 3.613 (2.053-6.355) <0.001	1			low						2+						x	
Lee, 2023 (Can Res Treat)	2	Retrospective analysis 2556 gastrectomies to develop prediction model (Gradient Boosting Machine, a machine learning method) and external validation on n=548 ESD Selection ***/**** Compaarability */** Outcomee **/*** LNM according to CT+ in ESD cohort NOS 7 (low)	0	0	0	n/a	OR multivariate (95% CI),p 45-59 years, 0.57 (0.36-0.91), 0.019 age 60-74 years,0.051 (0.32-0.82)0,005,(compared to <44yo) SM2 2.6 (1.78-3.80),<0.01 Undifferentiated 1.94 (1.37-2.73),<0.001 LVI+ 8.43 (5.86-12.15),<0.001 >20 mm. 1.84(1.34-2.54), <0.001	0			low						2+						x	
Morais 2023 (Gut)	2	Retrospective multicenter analysis of noncurative ESD (n=323) to validate and modification of eCura in western, (W-eCura) Selection ***/**** N=225 (72%) were high risk resection (HRR) and 89 (28%) local risk. Copmparability **/** Outcome ***/*** 314 (97%) proper follow-up (median 16 months). 69% of HRR (n=156) underwent surgery(25% parietal lesion and 15% LNM) NOS=8 (low)	0	0	0	n/a	Risk for LNM (operated patients) (OR)(95%CI), univariate venous invasio n: 8.306, (3.172-21.747), extension of SM invasión:3.007, (1.500-6.027) , SM invasion ≥1 mm: 10.476, (1.293-84.904) Risk for parietal residual lesion (OR, 95% CI) multivariate VM +: 5.323, (1.968-14.398) Ly+: 3.407, (1.203-9.651) Risk for residual (parietal &/or LNM) (OR, 95% CI) multivariate Piecemeal resection: 5.286, (1.329-21.025), Extension of SM invasión: 1.970, (1.158-3.351) Ly+:5.070, (1.781-14.427)	0			low						2+						x	
Liu, 2021 (JGO)	2	Retrospective analysis of risk factors for LNM in n=812 EGC gastrectomies according to: -pure moderately differerntiated (PMD), mixed predominantly moderately differentiated (MMD),	0	0	0	n/A	Risk factors for LNM in Mixed Type Tumor size [odds ratio (OR) =1.419, P=0.008],	0			low						2+						x	

		mixed predominantly poorly differentiated (MPD) and pure poorly differentiated (PPD) Selection ***/**** Comp */** Outcome ***/*** NOS=7 (low)					MPD (OR =3.278, P=0.002), Sm invasion ≥500 µm (OR =5.059, P=0.002) LVI+ (OR =5.836, P<0.001)																	
Sun, 2023 (BMC)	2	Retrospective analysis of risk factors of LNM in n=133 gastrectomies after noncurative EGC ESD Selection ***/***** Comp (*/**) Outcome ***/*** NOS=7 (low)	0	0	0	n/a	Multivariate lymphatic invasion (OR=8.797, 95% CI: 1.051–73.64, P=0.045)	1			Low						2+						x	
Zhang, 2023 (BMC Gas)	2	Retrospective analysis of risk factors for LNM in n=346 gastrectomies for undifferentiated EGC Selectionn ***/**** Comparability */** Outcome *** NOS=7	0	0	0	n/a	Multivariate Preoperative risk factors for LNM >20 mm OR2.49, 95% CI 1.20–5.15) SM infiltration (OR=4.77, 95% CI: 2.14– 10.66) (P<0.05); Postoperative risk factors size >2 OR=3.35, 95% CI: 1.02–5.40) LVI + OR=13.21, 95% CI: 5.18–36.70	1			low						2+						x	
Yang, 2022 (Plos one)	2	SR/MA, 24 retrospective studies, NOS >5 (6-9)	0	0	0	unclear	Risk factors for LNM (multivariate) Size (>20 mm vs. <20 mm: OR = 2.05, 95% CI: 1.06–3.94, z = 2.14, p = 0.032; I^2 = 83.2%, p = 0.003, random-effect) Depth of invasion (SM vs. M: OR = 3.00, 95% CI: 2.16–4.16, z = 6.58, p = 0.000; I 2 = 22.9%, p = 0.273, fixedeffect) Pure undifferentiated (PU vs. PD: OR = 1.89, 95% CI: 1.49–2.40, z = 5.21, p = 0.000; I^2 = 28.4%, p = 0.232, fixed-effect) Mixed type (mixed vs. PD: OR = 2.96, 95% CI: 2.24–3.92, z = 7.58, p = 0.000; I 2 = 0%, p = 0.836, fixed-effect) Lyv (present vs. absent: OR = 7.68, 95% CI: 6.17–9.56, z = 18.27, p = 0.000; I 2 = 0%, p = 0.512, fixed-effect) Ulceration (present vs. absent: OR = 1.82, 95% CI: 1.42–2.32, z = 4.78, p = 0.000; I 2 = 47.5%, p = 0.168, fixed-effect)	0			low				1-						x		
Lee, 2022	2	Retrospective comparisons of n=343	0	0	0	n/a	Similar OS in surgery vs	0				Very					2+						x	

(Surg End)		noncurative EGC ESD divided into Surgery (n=191) vs Observation (n=152) and classified according to eCura. Selection ***/**** Comparability */** Outcome **/***, at least 1 year FU NOS 6 (unclerar)					observational group in low-intermediate risk according to eCura Higher OS in high-risk surgery vs obs: 95.2% vs. 71.4%, p<0.001)					Low												
Bhandari, 2023 (Endoscopy)	2	Multicenter Retrospective analysis of n=415 ESD Selection ***/**** Comp () Outcome **/*** Median FU 52months. NOS=5	0	0	0	n/a	Multivariate OR associated with noncurative resection Size,mm OR 1.41 (1-1.97), p 0.05 Ulceration+ OR 17.6 (2.31-134), p 0.006 Relative (vs absolute) indication OR 316 (58.6-1699), p<0.001 R1vsR0 OR 250 (37.9-1648), p<0.001	0				Very low					2+						x	
Shimada, 2022 (Surg End)	2	Retrospective comparison (PSM) between gastrectomy after noncurative ESD vs only surgery (n=75 each group) Selection ***/**** Comparability */** Outcome ***/*** Median follow-up 60 months	0	0	0	n/a	no signifcant diferences in postoperative morbidity or mortality. Similar overall survival or disease-specifc survival	0				Very low					2+						x	
Duan, 2022 (can J Gas Hep)	2	Retrospective comparison of n=30 gastrectomies after noncurative EGC ESD vs n=59 upfront surgery for EGC Selection ***/**** Comparability */** Outcome ***/*** NOS=7 (lowr)	0	0	0	n/a	RF for residual cancer Diffuse type (OR 2.28, 95% CI: 1.81–2.45, P 0.014), Submucosal invasión (OR 1.87, 95% CI: 1.32–2.14, P 0.023) Positive HER-2 (OR 2.41, 95% CI: 2.03–2.71, P 0.008) RF for LNM Undifferentiated (OR 2.76, 95% CI: 1.87–3.21, P 0.021) Vascular invasion (OR 2.53, 95% CI: 2.21–2.98, P 0.013) Positive vertical margin (OR 1.81, 95% CI: 1.65–2.13, P 0.027)	0				Very low					2+						x	

* 1) Selection; 2) Comparability; 3) Outcome
** -1 per problemSelection: -1: selected group of users or no description; Comparability -1: no comparison between the cohorts; Outcome -1: No description, no follow up
# Evidence of dose response across or within studies (or inconsistency across studies is explained by a dose response); also up to one point added if adjustment for confounders would have increased the effect size (1); All / most studies show similar results (0); Lack of agreement between studies (e.g. statistical heterogeneity between RCTs, conflicting results) (-1)
@ -1 per problem in generalizability to the target population
†: only for meta-analysis
§ 0 if Not all effect sizes more than 2 or less than 0.5 and significant; or if OR/RR/HR not significant; 1 if Effect size more than 2 or less than 0.5 for all studies/meta-analyses included in comparison and significant; 2 if Effect size more than 5 or less tha.2 for all studies/meta-analyses included in comparison and significant
¶: High: Further research is very unlikely to change our confidence in the estimate of effect; Moderate: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate; Low: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate; Very low: Any estimate of effect is very uncertain

Sentence	**ESGE/EHMSG/ESP recommend that patients with extensive endoscopic changes (C3+ or EGGIM 5+) or advanced histological stages of atrophic gastritis (severe CAG or GIM and/or significant changes in both antrum and corpus, OLGA/OLGIM III/IV) should be followed up with high-quality endoscopy every 3 years.**

GRADE	**Strength of recommendation: Strong**	**Quality of evidence: Moderate**
PICO	P: Patients with severe atrophic changes or IM in both antrum and corpus, OLGA/OLGIM III/IV I: Incidence of gastric neoplasm and risk factors for gastric neoplasm C: Absence or different stages of chronic gastritis O: Incidence of gastric neoplasm, effect size measure (HR/OR/RR)	
Query(ies) and databases searched	((((gastric[Title/Abstract] OR stomach[Title/Abstract] OR gastritis[Title/Abstract]) AND (cancer*[Title/Abstract] OR tumor*[Title/Abstract] OR neoplas*[Title/Abstract] OR carcinoma*[Title/Abstract] OR adenocarcinoma*[Title/Abstract] OR dysplas*[Title/Abstract] OR adenoma*[Title/Abstract] OR lesion*[Title/Abstract] OR malignan*[Title/Abstract])) OR (stomach neoplasms[Mesh])) AND ((intestinal[Title/Abstract] AND metaplasia[Title/Abstract]) OR atroph*[Title/Abstract] OR (precancerous[Title/Abstract] AND condition*[Title/Abstract]) OR (premalignant[Title/Abstract] AND condition*[Title/Abstract]) OR OLGA[Title/Abstract] OR OLGIM[Title/Abstract] OR EGGIM[Title/Abstract])) AND ((randomized controlled trial[Publication Type]) OR (randomized[Title/Abstract] AND controlled[Title/Abstract] AND trial[Title/Abstract]) OR (cohort studies[Mesh]) OR cohort[Title/Abstract] OR (follow up studies[Mesh]) OR (case-control studies[Mesh]) OR case-control[Title/Abstract] OR (cross-sectional studies[Mesh]) OR cross-sectional[Title/Abstract] OR (meta-analysis[Publication Type]) OR meta-analysis[Title/Abstract])	
Table of evidence	***Are there any cohorts?***	

Study ID	Study design Score **(2)**	Risk of bias (alinea(s)) *	Quality Score **(0 to -3)** **	Consistency Score **(-1 to 1)** #	Directness Score **(0 to -2)** @	Publication bias **(0: No,1: Yes)**	Reported OR/RR/HR	Effect size Score **(0 to 2)** §	Evidence Level¶				Type of study according to SIGN								Recommendation SIGN			
									High	Mod	Low	Very Low	1++	1+	1-	2++	2+	2-	3	4	A	B	C	D
Rugge2018	2	Retrospective cohort 7436 consecutive patients who underwent EGD between 2007 and 2011 at the Gastroenterology Unit of the University of Padua Hospital, a regional hospital located in Northeastern Italy 1) 2) Stages of OLGA / GNL 3) Quantify the GC risk associated with each different gastritis OLGA stage	-1	0	-1	-	In a long-term retrospective cohort in Italy, the baseline distribution of patients by OLGA was: Stage 0=80.8%; Stage I=12.6%; Stage II=4.3%; Stage III=2.0%; Stage IV=0.3%. by OLGA stage at the enrollment, the rate of incident neoplasia was: Stage 0=1 case; rate/103 person-years=0.03; 95%CI: 0.004–0.19; Stage I=2 cases; rate/103 person-years=0.34; 95%CI: 0.09–1.36; Stage II=3 cases; rate/103 person-years=1.48; 95%CI: 0.48–4.58; Stage III=17 cases; rate/103 person-years=19.1; 95%CI: 11.9–30.7; Stage IV=5 cases; rate/103 person-years=41.2; 95%CI: 17.2–99.3. the multivariate analysis including all the considered variables, reported the HR for developing neoplastic lesions at follow-up by OLGA stage: OLGA I: HR 12.7 (95CI 1.14–140.7); OLGA II: HR 54.9 (95CI 5.63–534.6); OLGA III: 712.4 92.5–5484.5; OLGA	2		mod						2+						x	

							IV: 1,450.7 (95CI 166.7–12,626.0).															
Zhang2018	2	Retrospective cohort in China 1) Enrolled 332 AG patients who underwent initial gastroscopy from 2002 to 2005 2) GNL vs no GNL Incidence of GNL and risk factors	-1	0	-1	-	A retrospective cohort of patients with gastric atrophy and/or IM in China (median FUP of 9.17 years) found that the annual incidence rates per person-year of total gastric neoplastic lesions, gastric HGIN, early GC and advanced GC were 0.53% (95%CI: 0.27–0.78%), 0.07% (95%CI: 0.01–0.21%), 0.20% (95%CI: 0.04–0.36%) and 0.27% (95%CI: 0.09–0.45%), respectively. In a retrospective cohort of patients in China with AG and/or IM, a multivariate Cox showed that extensive AG and/or IM (concomitant gastric antral and corporal atrophy or IM) (HR 2.898, 95CI 1.64-5.12), and H. pylori infection (HR 3.946, 95CI 1.27-12.27), were risk factors for progression for GC and/or HGIN. The multivariate Cox analysis also indicated that a 2- to 3-year surveillance interval may benefit early detection of GC in patients with extensive AG and/or IM (HR 0.015, 95 CI 0.001–0.34).	1		mod						2+						x	
Rugge2019	2	Prospective cohort in Italy 1) 1755 patients with dyspepsia who underwent an initial (T-0) EGD between 2011 and 2013 at the Gastroenterology Department of the Rovereto Hospital, a county hospital located in a subalpine region of Northeastern 2) Italy with a regional GC incidence (standardised on world population) of 8.6/100000/year 3) – 4) Risk of developing GNL	-1	0	-1	-	The risk of developing neoplastic lesions significantly varied with the baseline stage of gastritis, being null in patients with stages 0, I and II (95%CI 0 to 0.4), 36.5 per 1000 person-years in patients enrolled with stage III (95%CI 13.7 to 97.4) and 63.1 per 1000 person-years in those enrolled with stage IV (95%CI 20.3 to 195.6).	2		mod						2+						x	
Dhingra2020	2	Retrospective cohort in USA 1)Retrospective chart review of patients 18 years and older who had undergone an EGD with biopsies from 01/01/1993 to 12/31/2013 and were diagnosed with non-dysplastic GIM of the	-1	0	-1	-	In a single-center retrospective cohort study in USA with patients with non-dysplastic IM (mean FUP 4.6 years), the annual incidence rate of low-grade dysplasia was 2.1 (95% CI 1.3–3.5)	2			low						2-						x	

		antrum, body, or both.– n: 358 3)Incidence rate of GNL in patients with IM					cases per 1000 person-years, 0.5 (95% 0.2–1.3) per 1000 person-years for high-grade dysplasia, and 0.8 (95% CI 0.3–1.6) cases per 1000 person-years for gastric adenocarcinoma (ie, among patients with GIM, there was a 0.05–0.2% annual incidence rate of progression to dysplastic lesions and a 0.08% annual incidence rate of progression to GAC; the incidence rate of GAC was more than tenfold higher as compared with the control population, since the historical control group had an annual adenocarcinoma incidence rate of 0.07 per 1000 person-years). The time from index endoscopy to diagnosis increased with greater severity of gastric lesions (median of 2.5 years for LGD, 4.8 years for HGD, and 5.0 years for GAC). In a single center retrospective cohort in USA following patients with non-dysplastic GIM (mean FUP 4.6 years), extensive intestinal metaplasia (antrum and body) was an independent risk factor for progression (HR 4.06, 95% CI 1.45–11.34).																			
Lee2022	2	Prospective cohort in Singapore 1) The study participants comprised 2980 patients undergoing screening gastroscopy with standardised gastric mucosal sampling, from January 2004 and December 2010, with scheduled surveillance endoscopies at year 3 and 5. 2) Participants were also matched against the National Registry of Diseases Office for missed diagnoses of early gastric neoplasia (EGN) 3) To investigate the incidence of gastric cancer (GC) attributed to gastric intestinal metaplasia (IM), and validate the Operative Link on Gastric Intestinal Metaplasia (OLGIM) for targeted endoscopic surveillance in regions with low-intermediate incidence of GC	0	0	0	-	In a multicentre prospective cohort study in Singapore, the age-adjusted EGN incidence rates for patients with and without IM were 133.9 and 12.5 per 100 000 person-years. IM was a significant risk factor for EGN (adjusted-HR 5.36; 95% CI 1.51 to 19.0; p<0.01). Participants with OLGIM stages III–IV were at greatest risk (adjusted-HR 20.7; 95% CI 5.04 to 85.6; p<0.01). More than half of the EGNs (n=4/7) attributed to baseline OLGIM III–IV developed within 2 years (range: 12.7–44.8 months). Participants with OLGIM II were also at significant risk of EGN (adjusted-HR	2	high							2++						x		

							7.34; 95% CI 1.60 to 33.7; p=0.02) - patients with OLGIM II are now identified to be at intermediate risk of EGN. This group accounts for one-quarter of the subsequent EGN cases in our study. Patients with OLGIM II would benefit from endoscopic surveillance. A significant smoking history (≥20 pack years) increases the risk of EGN among patients with intermediate-risk and high-risk IM (ie, OLGIM II–IV). Authors suggest a risk-stratified approach and recommend that high-risk patients (OLGIM III–IV) have endoscopic surveillance in 2 years, intermediate-risk patients (OLGIM II) in 5 years, while majority of the patients who are low risk OLGIM (OLGIM 0–I) may not require routine surveillance endoscopy. Multivariate cox regression analysis showed that older age (adjusted-HR 1.08; 95%CI 1.02 to 1.16; p=0.02), positive serum pepsinogen index (adjusted-HR 4.23; 95%CI 1.34 to 13.37; p=0.01) and the presence of either atrophic gastritis (adjusted-HR 2.69; 95%CI 1.03 to 7.06; p=0.04) or gastric IM (adjusted-HR 5.36; 95%CI 1.51 to 19.0; p<0.01) were significant risk factors for EGN. The adjusted HR for subsequent early gastric neoplastic (EGN) for each stage of OLGIM were: OLGIM I – HR 1.95 (0.39 to 9.74); OLGIM II - 7.34 (1.60 to 33.7); OLGIM III-IV - 20.77 (5.04 to 85.6). There was an increasing trend of EGN risk with higher OLGIM stages, whereby the age-adjusted EGN rates with OLGIM I, II and III–IV were 21.5, 108.8, 543.8 per 100000 person-years, respectively. the incomplete subtype carries an eightfold increased risk of																				

							developing EGN (n=546; OR 8.4; 95%CI 1.9 to 37.8; p=0.005) compared with complete subtype of IM among participants with mucin staining.																	
Yue2018	2	RS/MA 1-2) articles published before March 2017 on the association between OLGA/OLGIM stages and risk of gastric cancer 3) assess the efficacy of the OLGA and OLGIM staging systems in evaluating gastric cancer risk	0	0	0	0	Using a random-effect model, the meta-analysis of case-control studies odds ratios (OR) demonstrated that GC risk was significantly higher among patients with OLGA stage III/IV (OR 2.64; 95% CI 1.84–3.79; P < 0.00001), but with significant heterogeneity (P = 0.03, I2 = 60%) Using a fixed-effect model, the meta-analysis of case-control studies OR manifested that GC risk was significantly higher among subjects with gastric lesions of OLGIM stages III/IV (OR 3.99; 95% CI 3.05–5.21: P < 0.00001), but no significant heterogeneity was observed (P = 0.39; I2 = 0%) In cohort studies, Stages III/IV stage of OLGA and risk of developing GC (RR 27.70; 95% CI 3.75–204.87; P < 0.001; Fig. 4), without any significant difference in heterogeneity (P = 0.56, I2 = 0%) This meta-analysis revealed that stage III/IV of the OLGA or OLGIM system was indeed associated with increased risk of gastric cancer. In	1	high				1+					A			x			
Sui2020	2	SR/MA 1-2) cohort or nested case-control study, association between the risk for gastric cancer and atrophy investigated, and estimated hazard ratio (HR) or risk ratio (RR) 3)To calculate the association between gastric atrophy and gastric cancer	-1	0	-1	0	The pooled results indicated that gastric atrophy was positively associated with the risk for non-cardia gastric cancer (pooled RR =3.12, 95% CI: 2.17–4.49)	2		mod						1+						x		

* 1) Selection; 2) Comparability; 3) Outcome
** -1 per problemSelection: -1: selected group of users or no description; Comparability -1: no comparison between the cohorts; Outcome -1: No description, no follow up
# Evidence of dose response across or within studies (or inconsistency across studies is explained by a dose response); also up to one point added if adjustment for confounders would have increased the effect size (1); All / most studies show similar results (0); Lack of agreement between studies (e.g. statistical heterogeneity between RCTs, conflicting results) (-1)

@ -1 per problem in generalizability to the target population
†: only for meta-analysis
§ 0 if Not all effect sizes more than 2 or less than 0.5 and significant; or if OR/RR/HR not significant; 1 if Effect size more than 2 or less than 0.5 for all studies/meta-analyses included in comparison and significant; 2 if Effect size more than 5 or less tha.2 for all studies/meta-analyses included in comparison and significant
¶: High: Further research is very unlikely to change our confidence in the estimate of effect; Moderate: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate; Low: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate; Very low: Any estimate of effect is very uncertain

Table of evidence — ***Are there only case-controls/cross-sectional?***

Study ID	Study design Score (2)	Risk of bias (alinea(s)) *	Quality Score (0 to -3) **	Consistency Score (-1 to 1) #	Directness Score (0 to -2) @	Publication bias † (0: No,1: Yes)	Reported OR/RR/HR	Effect size Score (0 to 2) §	Evidence Level¶				Type of study according to SIGN								Recommendation SIGN			
									High	Mod	Low	Very Low	1++	1+	1-	2++	2+	2-	3	4	A	B	C	D
Marcos2020	2	Case-control study in Portugal 1-2) including 187 patients with egn treated endoscopically and 187 agematched and sex-matched control subject 3) individuals were classified according to eggiM, Olga and OlgiM systems. egn risk according to gastritis stages and other clinical parameters was further evaluated	0	0	-1	-	ore patients with egn had eggiM of ≥5 than control subjects (68.6% vs 13.3%, p<0.001). Olga and OlgiM stages iii/iV were more prevalent in patients with egn than in control subjects (68% vs 11%, p<0.001,and 61% vs 3%, p<0.001, respectively). The three systems were the only parameters significantly related to the risk of egn in multivariate analysis: for eggiM 1–4 (adjusted Or (aOr) 12.9, 95% ci 1.4 to 118.6) and eggiM 5–10 (aOr 21.2, 95% ci 5.0 to 90.2); for Olga i/ii (aOr 5.0, 95% ci 0.56 to 44.5) and Olga iii/iV (aOr 11.1, 95% ci 3.7 to 33.1); for OlgiM i/ii (aOr 11.5, 95% ci 4.1 to 32.3) and OlgiM iii/iV (aOr 16.0, 95% ci 7.6 to 33.4).	2		mod							2+						x	
Chen2023	2	Case-control study in China 1-2) including 68 patients with EGC treated with endoscopic submucosal dissection and 68 ageand sex-matched control subjects 3)Assess KTc, OLGA, OLGIM risk stratification	0	0	0	-	O-type Kimura–Takemoto classification (adjusted odds ratio [AOR] 3.282, 95% confidence interval [CI] 1.106–9.744, P = 0.032) and OLGIM stage III/IV (AOR 17.939, 95% CI 1.874–171.722, P = 0.012) were significantly related to a higher risk of EGC. OLGIM I/II was not: AOR 5.080 (0.722–35.736) 0.102 OLGA I/II (AOR 0.522 (0.074–3.696) 0.515) and OLGA III/IV (AOR 3.372 0.477–23.854 0.223	2		mod							2+						x	

							Current/ex-smoker » AOR 3.121 (1.045–9.318) p=0.041 Family history of gastric cancer (1st or 2nd degree): AOR 8.079 (2.634–24.781) <0.001																
Huang2023	2	Case-control in China (no acess to full-text) 1-2) single-centre, case–control study included 196 patients with EGC and 196 age-matched and sex-matched health screening control subjects 3) to validate OLGA and OLGIM staging systems for early GC (EGC) in Chinese population	-	-	-	-	OLGA and OLGIM stages II/III/IV were more prevalent in patients with EGC than in the control subjects. Multivariable analysis revealed family history of GC, previous Helicobacter pylori (H. pylori) infection, OLGA stages II and III-IV, OLGIM stages II and III-IV as independent risk factors for EGC (ORs, 4.04, 1.87, 2.52, 6.79, 4.11 and 10.78, respectively). Area under the receiver operating characteristic curve on EGC risk estimation was improved for OLGIM compared with OLGA (0.78 vs 0.71, p<0.001). Surveillance of intermediate-risk patients (OLGA/OLGIM II) should be emphasised in our region. The OLGIM may be preferred over the OLGA for EGC risk estimation.	2															x	

* 1) Selection; 2) Comparability; 3) Exposure
** -1 per problem: Selection: -1: selected group of users or no description; Comparability -1: no comparison between the cohorts; Outcome -1: No description, no follow up
# Evidence of dose response across or within studies (or inconsistency across studies is explained by a dose response); also up to one point added if adjustment for confounders would have increased the effect size (1); All / most studies show similar results (0); Lack of agreement between studies (e.g. statistical heterogeneity between RCTs, conflicting results) (-1)
@ -1 per problem in generalizability to the target population
†: only for meta-analysis
§ 0 if Not all effect sizes more than 2 or less than 0.5 and significant; or if OR/RR/HR not significant; 1 if Effect size more than 2 or less than 0.5 for all studies/meta-analyses included in comparison and significant; 2 if Effect size more tha 5 or less tha.2 for all studies/meta-analyses included in comparison and significant
¶: High: Further research is very unlikely to change our confidence in the estimate of effect; Moderate: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate; Low: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate; Very low: Any estimate of effect is very uncertain

Sentence	**ESGE/EHMSG/ESP recommend opportunistic risk stratification of precancerous conditions in all endoscopies, because endoscopic surveillance every 3 years in patients with high-risk premalignant conditions is cost-effective irrespectively of country.**																								
GRADE	**Strength of recommendation: Strong**							**Quality of evidence: Moderate**																	
PICO	Is endoscopic screening/ surveillance of premalignant gastric lesions/gastric cancer cost-effective in low/ intermediate risk areas?																								
Query(ies) and databases searched	Search: ((gastric cancer) AND (cost effectiveness)) AND (surveillance) Database: Pubmed Filters: Meta-Analysis, Randomized Controlled Trial, Systematic Review ("stomach neoplasms"[MeSH Terms] OR ("stomach"[All Fields] AND "neoplasms"[All Fields]) OR "stomach neoplasms"[All Fields] OR ("gastric"[All Fields] AND "cancer"[All Fields]) OR "gastric cancer"[All Fields]) AND ("cost effectiveness analysis"[MeSH Terms] OR ("cost effectiveness"[All Fields] AND "analysis"[All Fields]) OR "cost effectiveness analysis"[All Fields] OR ("cost"[All Fields] AND "effectiveness"[All Fields]) OR "cost effectiveness"[All Fields]) AND ("epidemiology"[MeSH Subheading] OR "epidemiology"[All Fields] OR "surveillance"[All Fields] OR "epidemiology"[MeSH Terms] OR "surveillance"[All Fields] OR "surveillances"[All Fields] OR "surveilled"[All Fields] OR "surveillence"[All Fields]) AND Search: ((gastric cancer) AND (cost effectiveness)) AND (surveillance) Database: Pubmed Filter: in the last 10 years																								
Table of evidence																									
Study ID (PMID)	Study design Score	Risk of bias (alinea)☰	Quality Score (0 to -2) **	Consistency Score (-1 to 1) #	Directness Score (0 to -2) @	Publication bias † (0: No,1: Yes)	Reported ICER	Effect size Score (0 to 2) §	Evidence Level¶				Type of study according to SIGN								Recommendation SIGN			
									High	Mod	Low	Very Low	1++	1+	1-	2++	2+	2-	3	4	A	B	C	D
38051169 Becker, E.C. (2023)		Markov state transition model to provide new evidence-based data that can be used to support the implementation of biennial surveillance guidelines in individuals with nondysplastic noncardia GIM and detect early malignant lesions, thereby decreasing morbidity and mortality.	0	0	0	n/a	Study showed that it is significantly cost-effective to perform biennial endoscopy surveillance in patients who have been incidentally found to have noncardia mixed GIM, with a cost savings of $5783.84 per person, and in those with IGIM, with a cost savings of $8093.08 per person.	n/a		x					x						x			
37302442 Thiruvengadam N.R. (2024)	2	Semi-Markov microsimulation model of patients with incidentally detected GIM, to compare the effectiveness of EGD surveillance with no surveillance at 10-year, 5-year, 3-year, 2-year, and 1-year intervals.	0	0	0	n/a	Compared with no surveillance, all modeled surveillance intervals yielded greater life expectancy (87-190 undiscounted life-years gained per 1000); 5-year surveillance provided the greatest number of life-years gained per EGD performed and was the cost-effective strategy ($40,706/QALY). In individuals with risk factors of family history of GA or anatomically extensive, incomplete-type GIM intensified 3-year surveillance was cost-effective (incremental cost-effectiveness ratio $28,156/QALY and $87,020/QALY, respectively).	n/a	x					x							x			
32728390 Canakis, A. (2020)	2	Systematic review, decision model analyses of upper endoscopy for gastric cancer screening and preneoplasia surveillance.	0	1	0	n/a	n/a	=	x					x							x			

Sentence	**ESGE/EHMSG/ESP suggest that endoscopic features of extensive changes (C3+ or EGGIM 5+) or histological advanced stages of atrophic gastritis (severe atrophic changes or IM in both antrum and corpus, OLGA/OLGIM III/IV) and with a first degree relative may benefit from intensive follow-up (e.g. every 1 – 2 years after diagnosis).**	
GRADE	**Strength of recommendation: Conditional**	**Quality of evidence: Low**
PICO	P: Patients with advanced stages of atrophy/IM in the stomach and family history of gastric cancer I: Incidence of gastric neoplasm and risk factors for gastric neoplasm C: Absence or different stages of chronic gastritis; absence of family history of gastric cancer O: Incidence/prevalence of gastric neoplasm, effect size measure (HR/OR/RR)	
Query(ies) and	((((gastric[Title/Abstract] OR stomach[Title/Abstract] OR gastritis[Title/Abstract]) AND (cancer*[Title/Abstract] OR tumor*[Title/Abstract] OR neoplas*[Title/Abstract] OR	

databases searched	carcinoma*[Title/Abstract] OR adenocarcinoma*[Title/Abstract] OR dysplas*[Title/Abstract] OR adenoma*[Title/Abstract] OR lesion*[Title/Abstract] OR malignan*[Title/Abstract])) OR (stomach neoplasms[Mesh])) AND ((intestinal[Title/Abstract] AND metaplasia[Title/Abstract]) OR atroph*[Title/Abstract] OR (precancerous[Title/Abstract] AND condition*[Title/Abstract]) OR (premalignant[Title/Abstract] AND condition*[Title/Abstract]) OR OLGA[Title/Abstract] OR OLGIM[Title/Abstract] OR EGGIM[Title/Abstract])) AND ((randomized controlled trial[Publication Type]) OR (randomized[Title/Abstract] AND controlled[Title/Abstract] AND trial[Title/Abstract]) OR (cohort studies[Mesh]) OR cohort[Title/Abstract] OR (follow up studies[Mesh]) OR (case-control studies[Mesh]) OR case-control[Title/Abstract] OR (cross-sectional studies[Mesh]) OR cross-sectional[Title/Abstract] OR (meta-analysis[Publication Type]) OR meta-analysis[Title/Abstract])
Table of evidence	***Are there only case-controls/cross-sectional?***

Study ID	Study design Score **(2)**	Risk of bias (alinea(s)) *	Quality Score **(0 to -3) ****	Consistency Score **(-1 to 1) #**	Directness Score **(0 to -2) @**	Publication bias † **(0: No,1: Yes)**	Reported OR/RR/HR	Effect size Score **(0 to 2) §**	Evidence Level¶				Type of study according to SIGN								Recommendation SIGN			
									High	Mod	Low	Very Low	1++	1+	1-	2++	2+	2-	3	4	A	B	C	D
Dong2022	2	Prospective pilot screening study 1-2) Prospective pilot screening program of patients with a confirmed first-degree relative with gastric cancer in USA 3)descriptive analysis/prevalence	1	0	-1	-	27 of the 61 patients (44%) had GIM and 4 of the 61 patients (6.6%) had low-grade dysplasia. Among those with GIM (n = 27), 21 (78%) were defined as extensive GIM.	-			low									3					x
Chen2023	2	Case-control study in China 1-2) including 68 patients with EGC treated with endoscopic submucosal dissection and 68 ageand sex-matched control subjects 3)Assess KTc, OLGA, OLGIM risk stratification	0	0	0	-	O-type Kimura–Takemoto classification (adjusted odds ratio [AOR] 3.282, 95% confidence interval [CI] 1.106–9.744, P = 0.032) and OLGIM stage III/IV (AOR 17.939, 95% CI 1.874–171.722, P = 0.012) were significantly related to a higher risk of EGC. OLGIM I/II was not: AOR 5.080 (0.722–35.736) 0.102 OLGA I/II (AOR 0.522 (0.074–3.696) 0.515) and OLGA III/IV (AOR 3.372 0.477–23.854 0.223 Current/ex-smoker » AOR 3.121 (1.045–9.318) p=0.041 Family history of gastric cancer (1st or 2nd degree): AOR 8.079 (2.634–24.781) <0.001	2		mod							2+						x	
Huang2023	2	Case-control in China (no acess to full-text) 1-2) single-centre, case–control study included 196 patients with EGC and 196 age-matched and sex-matched health screening control subjects 3) to validate OLGA and OLGIM staging systems for early GC (EGC) in Chinese population	-	-	-	-	OLGA and OLGIM stages II/III/IV were more prevalent in patients with EGC than in the control subjects. Multivariable analysis revealed family history of GC, previous Helicobacter pylori (H. pylori) infection, OLGA stages II and III-IV, OLGIM stages II and III-IV as independent risk factors for EGC (ORs, 4.04, 1.87,	2																x	

							2.52, 6.79, 4.11 and 10.78, respectively). Area under the receiver operating characteristic curve on EGC risk estimation was improved for OLGIM compared with OLGA (0.78 vs 0.71, p<0.001). Surveillance of intermediate-risk patients (OLGA/OLGIM II) should be emphasised in our region. The OLGIM may be preferred over the OLGA for EGC risk estimation.																	
Sotelo2023	2	Cross-sectional study in Chile 1-2) cross-sectional study including One hundred and ten FDR, aged between 50 and 65 years, 54.5 female, obtained through convenience sampling, 3) Prevalence of Gastric Preneoplastic Lesions in First-Degree Relatives of Patients with Gastric Cancer	0	0	0	-	the prevalence of pre-neoplastic lesion, AG, IM, and DYS were 86.4%, 82.7%, 54.5%, and 12.7% respectively. OLGA 0, I/II, and III/IV were verified in 17.3%, 64.5%, and 18.2%, respectively. OLGIM 0, I/II, and III/IV were verified in 41.0%, 42.7%, and 16.3%, respectively.	-			mo d				3							x	
Kowada202	2	Endoscopy Is Cost-Effective for Gastric Cancer Screening After Successful Helicobacter pylori Eradication 1-2) cost-effectiveness of annual endoscopy versus biennial endoscopy versus no screening for gastric cancer screening in patients after successful Helicobacter pylori eradication 3) decision trees with Markov models for a hypothetical cohort of patients aged 50 years after successful Helicobacter pylori eradication over a lifetime horizon from a healthcare payer perspective. Main outcomes were costs, quality-adjusted life-years (QALYs), life expectancy life-years (LYs) with discounting at a fixed annual rate of 3%, and incremental cost-effectiveness ratios (ICERs)	0	0	0	-	A cost-effectiveness analysis in Japan concluded that endoscopy was cost-effective compared to no screening in patients after successful H. pylori eradication with gastric mucosal atrophy. Biennial endoscopy for patients with mild-to-moderate gastric mucosal atrophy and annual endoscopy for patients with severe gastric mucosal atrophy were the most cost-effective	-	high							2+						x		

* 1) Selection; 2) Comparability; 3) Exposure
** -1 per problem: Selection: -1: selected group of users or no description; Comparability -1: no comparison between the cohorts; Outcome -1: No description, no follow up
# Evidence of dose response across or within studies (or inconsistency across studies is explained by a dose response); also up to one point added if adjustment for confounders would have increased the effect size (1); All / most studies show similar results (0); Lack of agreement between studies (e.g. statistical heterogeneity between RCTs, conflicting results) (-1)
@ -1 per problem in generalizability to the target population
ϯ: only for meta-analysis
§ 0 if Not all effect sizes more than 2 or less than 0.5 and significant; or if OR/RR/HR not significant; 1 if Effect size more than 2 or less than 0.5 for all studies/meta-analyses included in comparison and significant; 2 if Effect size more than 5 or less tha.2 for all studies/meta-analyses included in comparison and significant
¶: High: Further research is very unlikely to change our confidence in the estimate of effect; Moderate: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate; Low: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate; Very low: Any estimate of effect is very uncertain

Sentence	ESGE/EHMSG/ESP recommend no surveillance endoscopy to patients with mild to moderate CAG or GIM restricted to the antrum, in the absence of endoscopic signs of

	extensive lesions or other risk factors (family history, incomplete intestinal metaplasia or persistent *H. pylori* infection) surveillance. This group constitute most individuals found in clinical practice.
GRADE	**Strength of recommendation: Strong** / **Quality of evidence: Moderate**
PICO	P: Patients with mild to moderate atrophy restricted to the antrum I: Characteristics of chronic atrophic gastritis C: Patients without antral atrophy O: The risk of developing gastric cancer
Query(ies) and databases searched	Search PubMed: ("Gastritis, Atrophic"[Mesh] OR "chronic atrophic gastritis"[All Fields]) AND (severity[All Fields] OR type[All Fields] OR grade[All Fields] OR extension[All Fields] OR pathology[All Fields] OR "pathology"[MeSH Terms]) AND ("gastric cancer"[All Fields] OR "Stomach Neoplasms"[Mesh]) AND ("risk"[MeSH Terms] OR "risk"[All Fields]) Filtered for Clinical Trial, Meta-Analysis, Randomized Controlled Trial
Table of evidence	***Are there any cohorts?***

Study ID	Study design Score **(2)**	Risk of bias (alinea(s)) *	Quality Score **(0 to -3) ****	Consistency Score **(-1 to 1) #**	Directness Score **(0 to -2) @**	Publication bias **(0: No,1:Yes)**	Reported OR/RR/HR	Effect size Score **(0 to 2) §**	Evidence Level¶				Type of study according to SIGN								Recommendation SIGN			
									High	Mod	Low	Very Low	1++	1+	1-	2++	2+	2-	3	4	A	B	C	D
Shichijo2015	2	Retrospective cohort study in Japan. 1)From June 1998 to December 2000, using biopsy specimens, one from the antrum and one from the corpus, from 1450 patients, among whom 729 revisited for follow-up endoscopy. 2)Patients were classified into three groups according to the distribution of IM at initial endoscopy. IM group A had no IM, IM group B had IM in the antrum only, and IM group C had IM in the corpus. 3)Development of gastric cancer	-2	0	-1	-	A retrospective cohort study in Japan (mean FUP of 6.7 years) reported cumulative incidences of gastric cancer in those had no IM, in those had IM in the antrum only, and in IM in those had IM in the corpus only or in both the antrum and the corpus, were 0.4%, 1.5%, and 1.3% at 1 year; 0.8%, 3.3%, and 2.7% at 5 years; and 1.8%, 4.6%, and 9.4% at 10 years, respectively A retrospective cohort study in Japan reported that presence of IM was an independent risk factor by multivariate analysis compared with no IM: HR 3.6 (95% CI 1.1–12.1) in those had IM in antrum only and HR 3.8 (95% CI 1.01–14.1) in those had IM in the corpus only or in both the antrum and the corpus.	1		mod							2-							x	
Song2015	2	Retrospective cohort in Sweden 1)Population of Sweden using data from its national disease registers. Participants 405 172 patients who had gastric biopsy samples taken for non-malignant indications between 1979 and 2011 2)Normal group	-2	0	-1	-	A large retrospective cohort in Sweden reported an crude incidence rate of non-cardia gastric cancer of 90.0 per 100,000 person years in patients with atrophic gastritis (SIR 3.0, 95% CI 2.5-3.7) and 111.6	2		mod							2-						x	

		3)Incidence of GC					per 100,000 person years in patients with intestinal metaplasia (SIR 3.7, 95% CI 2.9-4.6). This study predict that about 1 in 256 people with normal mucosa, 1 in 85 with gastritis, 1 in 50 with atrophic gastritis, 1 in 39 with intestinal metaplasia, and 1 in 19 with dysplasia will develop gastric cancer (cardia or non-cardia) within 20 years after gastroscopy. In a large retrospective cohort Sweden study, HR and 95% CI for gastric cancer among patients with different lesions in the stomach compared with normal group were: 5.0 (3.8 to 6.7) for atrophic gastritis and 6.5 (4.8 to 8.9) for intestinal metaplasia.																	
Lee2016	2	Retrospective Cohort in Taiwan 1)Hospital-based study that included all patients with gastric IM between 1992 and 2010, and the development of gastric adenocarcinoma was evaluated until July 2011. Patients developing gastric cancer r180 days after the index diagnosis of IM were excluded. 2-3)– Incidence and HR	-2	1	-2	-	in IM patients without concurrent dysplasia, the cumulative incidence of gastric cancer increased steadily and slowly during the follow-up period, and the 5-, 10-, and 15-year cumulative incidences were 0.7% (95% CI, 0.4-0.9), 1.8% (95% CI, 1.3-2.3), and 2.4% (95% CI, 1.5-3.2), respectively. Overall, the incidence rate of gastric cancer development after an initial diagnosis of gastric IM without concurrent dysplasia was 1.5 cases per 1000 person-years (95% CI 1.2-1.9), and the SIR was 2.0 (95% CI 1.5-2.6) as compared with that in the general population.	-				Low					2-						x	
Li2016	2	Retrospective Cohort in California (USA) Patients identified between 1997 and 2006 from KPNC pathology database	-1	0	-1	-	In a large retrospective cohort study in USA (median FUP 7.1 years), the incidence rate of gastric adenocarcinoma was 0.72/1,000 person-years in patients with intestinal metaplasia, with a relative risk of 2.56 (95% confidence interval (CI) 1.49–4.10) compared with the Kaiser Permanente member population Authors estimated that the median time for	-			mod												x	

							gastric intestinal metaplasia to progress to adenocarcinoma was 6.1 years, and for low-grade dysplasia, 2.6 years																
Reddy2016	2	Retrospective Cohort in USA 1)Patients diagnosed with GIM from 2000 through 2011, collected from the Kaiser Permanente Southern California region. GIM was identified by a keyword search of pathology reports; gastric cancer cases were identified by cross-reference with an internal cancer registry. 2)The incidence of gastric cancer in patients with GIM (n=923; median age at diagnosis, 68 years) was compared with that of an age- and sexmatched reference population (controls). 3)Incidence of gastric cancer among patients with GIM and risk factors for gastric cancer.	-1	0	-1	-	the overall age- and gender-adjusted incidence rate of gastric cancer in patient with GIM was 172 per 100,000 person-years (95% CI, 0.74–3.39). The incidence of gastric cancer during this same time period in the reference population was 9.67 per 100,000 person-years. Using Poisson regression analysis, the overall age- and gender-adjusted Standardized Incidence Ratio (SIR) for gastric cancer was 4.2 extensive intestinal metaplasia (IM was present in at least two gastric locations or moderate or marked IM was noted in at least two biopsy specimens) was associated with increased risk of progression to gastric cancer compared to focal IM (OR 9.4, 95% CI 1.8-50.4). family history was a significant risk factor for gastric cancer (HR 3.8; 95% CI, 1.5–9.7) in patients with IM; the incidence rate for gastric cancer in those with a positive family history was 8.12 (95% CI, 0.1.67–23.73). Patients with both a family history of gastric cancer as well as intestinal metaplasia were 84 times more likely to develop gastric cancer compared to the reference population	2			mod							2-						x	
Nieminen2020	2	Retrospective Cohort in Finland In the Helsinki Gastritis Study, 22346 elderly male smokers from southwestern Finland were screened for serum pepsinogen I (PGI). Between the years 1989 and 1993, men with low PGI values (PGI < 25 µg/L), were invited to undergo an oesophagogastroduodenoscopy. In this retrospective cohort study, 1147 men that underwent gastroscopy were					The cancer risk associated positively with high TAIM (vs low) [Hazard ratio (HR) 2.70, 95%CI: 1.09–6.69, P = 0.03]. The risk increased through OLGIM stages compared to OLGIM 0: OLGIM I: HR 1.82 0.37-8.83 OLGIM II: HR 3.55 0.77-16.36																x	

		followed for gastric cancer for a median of 13.7 years, and a maximum of 27.3 years.					OLGIM III: HR 5.91 1.14-30.73 OLGIM IV: HR 5.72 1.03-31.77 The cancer risk did not associated to OLGA: OLGA I: HR 2.66 0.28-25.72 OLGA II: HR 2.84 0.38-21.38 OLGA III: HR 1.85 0.11-29.87 OLGA IV: HR 5.77 0.67-49.77 The OLGA staging and number of men gastroscopied and incident gastric cancer cases in each subgroup are shown in Table 3. The incidence rates of gastric cancer were 0.62, 1.60, 1.75, 1.11, and 3.40 per 1000 patient-years in stages 0–IV, respectively, (P for trend 0.10, Table 4). The majority of gastric cancers (n = 22, 79%) were diagnosed in low-risk OLGA stages (0–II), and only six cancers (21%) in high-risk (III–IV) stages. At the end of follow-up the cumulative cancer event rate was 4.4% in OLGA stages 0–II, and 6.4% in stages III–IV The OLGIM staging and number of men gastroscopied and incident gastric cancer cases in each subgroup are shown in Table 5. The gastric cancer incidence rate increased by OLGIM stages being 0.62, 1.21, 2.24, 3.37, and 3.22 per 1000 patient-years in stages 0–IV, respectively, (P for trend 0.004, Table 4). Similar to OLGA stages, the majority of cancers appeared in low-risk OLGIM groups (0–II, n = 19, 68%), and the minority in high-risk groups (III–IV, n = 9, 32%). In the end of the follow-up in OLGIM stages 0–II, the cumulative gastric cancer																		

							event rate was 3.5%, and in stages III–IV, 10.8%																
Chapelle2020	2	Retrospective cohort in France 1)All the patients diagnosed with GPL (atrophic gastritis, intestinal metaplasia [IM], and dysplasia) between 2000 and 2015 and fulfilling criteria for evolution assessment (at least 2 endoscopies, minimal follow-up of 6 months, and at least 2 biopsies obtained from the antrum and corpus) were included 2)Baseline vs End of FUP 3)Progression, regression, RR	-2	0	-1	-	Progression of the lesions was significantly higher in patients with incomplete type of IM (relative risk of progression for incomplete IM: 11.5; 95% confidence interval 2.5–53.1). This study shows that the patients with antrum-limited IM, especially of incomplete type, are at the highest risk of developing gastric cancer.	2			low						2-						x	
Piazuelo2021	2	Prospective cohort of an H. pylori eradication trial in a Hispanic population (Colombia) 1)800 adults with precancerous lesions were randomized to anti-H. pylori treatment or placebo. Gastric biopsies at baseline, 3, 6, 12, 16, and 20 years were assessed by our Correa histopathology score. 2)Baseline vs End FUP 3)Estimate progression by baseline diagnosis, and GC risk by intestinal metaplasia (IM) subtype and anatomic location	-1	0	-1	-	A total of 222 individuals with MAG without IM at baseline accumulated 3440 years of follow-up (mean, 15.5 years; median, 16.6 years). Among them, 117 individuals progressed to IM, 16 to ID, and 3 to LGD/HGD. Incidence rates were 4.70/100 PY (95% CI, 3.84–5.54) for IM, 0.47/100 PY (95% CI, 0.24–0.70) for ID, and 0.09/100 PY (95% CI, 0–0.18) for LGD/HGD. None of the individuals with MAG developed GC. A total of 502 individuals with IM at baseline accumulated a total of 7133 years of follow-up (mean, 14.2 years; median, 16.1 years). Among them, 166 individuals progressed to ID, 66 to LGD/HGD, and 8 to GC. Incidence rates were 2.43/100 PY (95% CI, 2.05–2.79) for ID, 0.98/100 PY (95% CI, 0.74–1.21) for LGD/HGD, and 0.11/100 PY (95% CI, 0.03–0.19) for GC. The rate of progression to GC among individuals with complete IM at baseline was 0.028/100 PY (95% CI, 0.026–0.082) and for incomplete IM was 0.37/100 PY (95% CI, 0.15–0.59). Multivariable analyses	2		mod							2-						x	

							showed that individuals with incomplete-type IM were 13.4 times more likely to progress to GC than those with the complete- type (OR 13.4, 95% CI, 1.8–103.8).																
Laszkowska2022	2	Retrospective cohort in USA 1) individuals age ≥ 18 years with GIM diagnosed on upper endoscopy between 1/1/1990 and 8/1/2019 at Columbia University Irving Medical Center. Only samples from the first available endoscopy with biopsy specimens available from both the distal stomach (antrum/pre-pylorus/pylorus) and proximal stomach (body/fundus) were included to allow for accurate diagnosis of extensive and limited GIM (n = 1256) 2) limited vs extensive GIM; Baseline histology vs End FUP histology 3) prevalence and progression rates of extensive GIM in a US cohort	-2	-1	-2	-	The annual incidence of GC for GIM overall was 0.09% (included auotimunne gastristis). There was no difference in progression to GC between extensive or limited GIM (IRR 0, 95% CI 0–2.6), or to advanced lesions overall (IRR 0.37, 95% CI 0.04–1.62).	0			low						2-						x	
Lee2022	2	Prospective cohort in Singapore 1) The study participants comprised 2980 patients undergoing screening gastroscopy with standardised gastric mucosal sampling, from January 2004 and December 2010, with scheduled surveillance endoscopies at year 3 and 5. 2) Participants were also matched against the National Registry of Diseases Office for missed diagnoses of early gastric neoplasia (EGN) 3) To investigate the incidence of gastric cancer (GC) attributed to gastric intestinal metaplasia (IM), and validate the Operative Link on Gastric Intestinal Metaplasia (OLGIM) for targeted endoscopic surveillance in regions with low-intermediate incidence of GC	0	0	0	-	In a multicentre prospective cohort study in Singapore, the age-adjusted EGN incidence rates for patients with and without IM were 133.9 and 12.5 per 100 000 person-years. IM was a significant risk factor for EGN (adjusted-HR 5.36; 95% CI 1.51 to 19.0; p<0.01). Participants with OLGIM stages III–IV were at greatest risk (adjusted-HR 20.7; 95% CI 5.04 to 85.6; p<0.01). More than half of the EGNs (n=4/7) attributed to baseline OLGIM III–IV developed within 2 years (range: 12.7–44.8 months). Participants with OLGIM II were also at significant risk of EGN (adjusted-HR 7.34; 95% CI 1.60 to 33.7; p=0.02) - patients with OLGIM II are now identified to be at intermediate risk of EGN. This group accounts for one-quarter of the subsequent EGN cases in our study. Patients with OLGIM II would benefit from endoscopic surveillance. A significant smoking history (≥20 pack	2	high							2++						x		

							years) increases the risk of EGN among patients with intermediate-risk and high-risk IM (ie, OLGIM II–IV). Authors suggest a risk-stratified approach and recommend that high-risk patients (OLGIM III–IV) have endoscopic surveillance in 2 years, intermediate-risk patients (OLGIM II) in 5 years, while majority of the patients who are low risk OLGIM (OLGIM 0–I) may not require routine surveillance endoscopy. Multivariate cox regression analysis showed that older age (adjusted-HR 1.08; 95%CI 1.02 to 1.16; p=0.02), positive serum pepsinogen index (adjusted-HR 4.23; 95%CI 1.34 to 13.37; p=0.01) and the presence of either atrophic gastritis (adjusted-HR 2.69; 95%CI 1.03 to 7.06; p=0.04) or gastric IM (adjusted-HR 5.36; 95%CI 1.51 to 19.0; p<0.01) were significant risk factors for EGN. The adjusted HR for subsequent early gastric neoplastic (EGN) for each stage of OLGIM were: OLGIM I – HR 1.95 (0.39 to 9.74); OLGIM II - 7.34 (1.60 to 33.7); OLGIM III-IV - 20.77 (5.04 to 85.6). There was an increasing trend of EGN risk with higher OLGIM stages, whereby the age-adjusted EGN rates with OLGIM I, II and III–IV were 21.5, 108.8, 543.8 per 100000 person-years, respectively. the incomplete subtype carries an eightfold increased risk of developing EGN (n=546; OR 8.4; 95%CI 1.9 to 37.8; p=0.005) compared with complete subtype of IM among participants with mucin staining.																			
Akbari2019	2	SR/MA 1-2) Original studies reporting the incidence rate of gastric cancer in patients with gastric atrophy or intestinal metaplasia 3) incidence rate of GC and progress rate,	0	0	0	1	The pooled GC incidence rate in patients with GA was 1.24 (95% CI, 0.80, 1.76; I2: 83.6%) cases per 1,000 person-years. The rates of later		mod						1-					x				

		regress and persistence proportion in both GA and IM patients were assessed					diagnosis of IM and gastric dysplasia in patients with GA were estimated as 41.42 (95% CI, 3.11, 64.45; I2: 95.6%) and 6.23 (95% CI, 2.34, 11.46; I2: 83.0%) cases per 1,000 person-years, respectively In IM studies, the pooled incidence rate of GC was 3.38 (95% CI, 2.13, 4.85; I2: 93.4%) cases per 1,000 person-years. The progressed rate to dysplasia in IM patient was estimated to be 12.51 (95% CI, 5.45, 22.03; I2: 95.1%) cases per 1,000 person-years. When stratified by type of GA and IM lesions, the highest incidence rate of GC was observed in severe GA (4.82 per 1,000 person-years) and IM incomplete patients (6.60 cases per 1,000 person-years) compared to other strata. Overall, the incidence of GC in patients with IM and GA are low but there is heterogeneity in data with the highest rate in Asian, males with those with incomplete IM.																
Wang2022	2	SR/MA 1-2) The Risk of Diffuse-type Gastric Cancer Following Diagnosis with Gastric Precancerous Lesions 3) odds ratio (OR) of the association, Subgroup analysis was performed on studies reporting histologic severity (using operative link systems) to assess if histologic severity of AG/IM was associated with higher risk.	0	0	0	0	Both AG (pooled OR=1.9, 95% CI 1.5 to 2.4, p<0.001) and IM (pooled OR=2.3, 95% CI 1.9 to 2.9, p<0.001) demonstrated an association with DTGC Compared to low OLGA score (defined as scores of 1 or 2), high OLGA score (defined as scores of 3 or 4) was associated with an increased risk of DTGC (OR=1.7, 95% CI 1.2 to 2.3, p=<0.01) Compared to low OLGIM score (defined as scores of 1 or 2), high OLGIM score (defined as scores of 3 or 4) was associated with an increased risk of DTGC (OR=1.9, 95% CI 1.3 to 2.7, p=<0.01).	0		mod					1+							x		

* 1) Selection; 2) Comparability; 3) Outcome
** -1 per problemSelection: -1: selected group of users or no description; Comparability -1: no comparison between the cohorts; Outcome -1: No description, no follow up
# Evidence of dose response across or within studies (or inconsistency across studies is explained by a dose response); also up to one point added if adjustment for confounders would have increased the effect size (1); All / most studies show similar results (0); Lack of agreement between studies (e.g. statistical heterogeneity between RCTs, conflicting results) (-1)
@ -1 per problem in generalizability to the target population
†: only for meta-analysis
§ 0 if Not all effect sizes more than 2 or less than 0.5 and significant; or if OR/RR/HR not significant; 1 if Effect size more than 2 or less than 0.5 for all studies/meta-analyses included in comparison and significant; 2 if Effect size more than 5 or less tha.2 for all studies/meta-analyses included in comparison and significant
¶: High: Further research is very unlikely to change our confidence in the estimate of effect; Moderate: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate; Low: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate; Very low: Any estimate of effect is very uncertain

Table of evidence — ***Are there only case-controls/cross-sectional?***

Study ID	Study design Score **(2)**	Risk of bias (alinea(s)) *	Quality Score **(0 to -3)** **	Consistency Score **(-1 to 1)** #	Directness Score **(0 to -2)** @	Publication bias † **(0: No,1: Yes)**	Reported OR/RR/HR	Effect size Score **(0 to 2)** §	Evidence Level¶				Type of study according to SIGN								Recommendation SIGN			
									High	Mod	Low	Very Low	1++	1+	1-	2++	2+	2-	3	4	A	B	C	D
Cho2013	2	Case-control study in Korea 1-2)474 GC patients and age- and sexmatched health screening control persons in a cancer centre hospital 3) GC risk according to the OLGA and OLGIM stages	0	0	-1	-	More GC patients had OLGA stages III–IV (46.2%) than controls (26.6%, P < 0.001), particularly among patients with intestinal-type GCs (62.2%) compared with diffuse-type GCs (30.9%). OLGA stages III and IV were significantly associated with increased risk of GC [odds ratios (ORs), 2.09; P = 0.008 and 2.04; P = 0.014 respectively] in multivariate analysis. The association was more significant for intestinal-type (ORs, 4.76; P = 0.001 and 4.19; P = 0.002 respectively), but not diffuse-type GC. OLGIM stages from I to IV were significantly associated with increased risk of both intestinal-type (ORs, 3.64, 5.15, 7.89 and 13.20 respectively) and diffuse-type GC (ORs, 1.84, 2.59, 5.08 and 6.32 respectively) with a significantly increasing trend. Family history of first-degree relatives was an independent risk factor for GC: AOR 7.84 (3.59–17.12)	2		mod							2+						x	
Choi2018	2	Case-Control study in USA 1-2) with cases of biopsy-proven gastric cancer matched (by age and gender) to controls without gastric cancer who had undergone EGD	-1	0	-1	-	2 significant predictors of gastric cancer; the presence of gastric intestinal metaplasia (odds ratio	2			low							2-					x	

		3) Conditional logistic regression was used to identify independent risk factors for gastric cancer.					(OR), 9.3; 95% CI, 4.5-18.9; P<0.001) and East Asian ethnicity (OR, 15.9; 95% CI, 5.8-43.6; P<0.001)																	
Marcos2020	2	Case-control study in Portugal 1-2) including 187 patients with egn treated endoscopically and 187 agematched and sex-matched control subject 3) individuals were classified according to eggiM, Olga and OlgiM systems. egn risk according to gastritis stages and other clinical parameters was further evaluated	0	0	-1	-	ore patients with egn had eggiM of ≥5 than control subjects (68.6% vs 13.3%, p<0.001). Olga and OlgiM stages iii/iV were more prevalent in patients with egn than in control subjects (68% vs 11%, p<0.001,and 61% vs 3%, p<0.001, respectively). The three systems were the only parameters significantly related to the risk of egn in multivariate analysis: for eggiM 1–4 (adjusted Or (aOr) 12.9, 95% ci 1.4 to 118.6) and eggiM 5–10 (aOr 21.2, 95% ci 5.0 to 90.2); for Olga i/ii (aOr 5.0, 95% ci 0.56 to 44.5) and Olga iii/iV (aOr 11.1, 95% ci 3.7 to 33.1); for OlgiM i/ii (aOr 11.5, 95% ci 4.1 to 32.3) and OlgiM iii/iV (aOr 16.0, 95% ci 7.6 to 33.4).	2		mod							2+						x	
Huang2023	2	Case-control in China (no acess to full-text) 1-2) single-centre, case–control study included 196 patients with EGC and 196 age-matched and sex-matched health screening control subjects 3) to validate OLGA and OLGIM staging systems for early GC (EGC) in Chinese population	-	-	-	-	OLGA and OLGIM stages II/III/IV were more prevalent in patients with EGC than in the control subjects. Multivariable analysis revealed family history of GC, previous Helicobacter pylori (H. pylori) infection, OLGA stages II and III-IV, OLGIM stages II and III-IV as independent risk factors for EGC (ORs, 4.04, 1.87, 2.52, 6.79, 4.11 and 10.78, respectively). Area under the receiver operating characteristic curve on EGC risk estimation was improved for OLGIM compared with OLGA (0.78 vs 0.71, p<0.001). Surveillance of intermediate-risk patients (OLGA/OLGIM II) should be emphasised in our region. The OLGIM may be preferred over the OLGA for EGC risk estimation.	2																x	

* 1) Selection; 2) Comparability; 3) Exposure

** -1 per problem: Selection: -1: selected group of users or no description; Comparability -1: no comparison between the cohorts; Outcome -1: No description, no follow up
# Evidence of dose response across or within studies (or inconsistency across studies is explained by a dose response); also up to one point added if adjustment for confounders would have increased the effect size (1); All / most studies show similar results (0); Lack of agreement between studies (e.g. statistical heterogeneity between RCTs, conflicting results) (-1)
@ -1 per problem in generalizability to the target population
↟: only for meta-analysis
§ 0 if Not all effect sizes more than 2 or less than 0.5 and significant; or if OR/RR/HR not significant; 1 if Effect size more than 2 or less than 0.5 for all studies/meta-analyses included in comparison and significant; 2 if Effect size more than 5 or less tha.2 for all studies/meta-analyses included in comparison and significant
¶: High: Further research is very unlikely to change our confidence in the estimate of effect; Moderate: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate; Low: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate; Very low: Any estimate of effect is very uncertain

PICO	P: Patients with intestinal metaplasia I: Incidence of gastric neoplasm and risk factors for gastric neoplasm in patients with mild to moderate intestinal metaplasia at a single location (OLGIM I-II and OLGA 0-II) C: Absence or different stages of intestinal metaplasia O: Incidence of gastric neoplasm in patients with intestinal metaplasia, effect size measure (HR/OR/RR)
Query(ies) and databases searched	Search: PubMed ((((gastric[Title/Abstract] OR stomach[Title/Abstract] OR gastritis[Title/Abstract]) AND (cancer*[Title/Abstract] OR tumor*[Title/Abstract] OR neoplas*[Title/Abstract] OR carcinoma*[Title/Abstract] OR adenocarcinoma*[Title/Abstract] OR dysplas*[Title/Abstract] OR adenoma*[Title/Abstract] OR lesion*[Title/Abstract] OR malignan*[Title/Abstract])) OR (stomach neoplasms[Mesh])) AND ((intestinal[Title/Abstract] AND metaplasia[Title/Abstract]) OR atroph*[Title/Abstract] OR (precancerous[Title/Abstract] AND condition*[Title/Abstract]) OR (premalignant[Title/Abstract] AND condition*[Title/Abstract]) OR OLGA[Title/Abstract] OR OLGIM[Title/Abstract] OR EGGIM[Title/Abstract])) AND ((randomized controlled trial[Publication Type]) OR (randomized[Title/Abstract] AND controlled[Title/Abstract] AND trial[Title/Abstract]) OR (cohort studies[Mesh]) OR cohort[Title/Abstract] OR (follow up studies[Mesh]) OR (case-control studies[Mesh]) OR case-control[Title/Abstract] OR (cross-sectional studies[Mesh]) OR cross-sectional[Title/Abstract] OR (meta-analysis[Publication Type]) OR meta-analysis[Title/Abstract])
Table of evidence	***Are there any cohorts?***

Study ID	Study design Score **(2)**	Risk of bias (alinea(s)) *	Quality Score **(0 to -3) ** **	Consistency Score **(-1 to 1) #**	Directness Score **(0 to -2)** @	Publication bias **(0: No,1: Yes)**	Reported OR/RR/HR	Effect size Score **(0 to 2)** §	Evidence Level¶				Type of study according to SIGN								Recommendation SIGN			
									High	Mod	Low	Very Low	1++	1+	1-	2++	2+	2-	3	4	A	B	C	D
Shichijo2015	2	Retrospective cohort study in Japan. 1)From June 1998 to December 2000, using biopsy specimens, one from the antrum and one from the corpus, from 1450 patients, among whom 729 revisited for follow-up endoscopy. 2)Patients were classified into three groups according to the distribution of IM at initial endoscopy. IM group A had no IM, IM group B had IM in the antrum only, and IM group C had IM in the corpus. 3)Development of gastric cancer	-2	0	-1	-	A retrospective cohort study in Japan (mean FUP of 6.7 years) reported cumulative incidences of gastric cancer in those had no IM, in those had IM in the antrum only, and in IM in those had IM in the corpus only or in both the antrum and the corpus, were 0.4%, 1.5%, and 1.3% at 1 year; 0.8%, 3.3%, and 2.7% at 5 years; and 1.8%, 4.6%, and 9.4% at 10 years, respectively A retrospective cohort study in Japan reported that presence of IM was an independent risk factor by multivariate analysis compared with no IM: HR 3.6 (95% CI 1.1–12.1) in those had IM in antrum only and HR 3.8 (95% CI 1.01–14.1) in those had IM in the corpus only or in both the antrum and the corpus.	1		mod								2-						x	
Song2015	2	Retrospective cohort in Sweden	-2	0	-1	-	A large retrospective	2		mo							2-						x	

		1)Population of Sweden using data from its national disease registers. Participants 405 172 patients who had gastric biopsy samples taken for non-malignant indications between 1979 and 2011 2)Normal group 3)Incidence of GC					cohort in Sweden reported an crude incidence rate of non-cardia gastric cancer of 90.0 per 100,000 person years in patients with atrophic gastritis (SIR 3.0, 95% CI 2.5-3.7) and 111.6 per 100,000 person years in patients with intestinal metaplasia (SIR 3.7, 95% CI 2.9-4.6). This study predict that about 1 in 256 people with normal mucosa, 1 in 85 with gastritis, 1 in 50 with atrophic gastritis, 1 in 39 with intestinal metaplasia, and 1 in 19 with dysplasia will develop gastric cancer (cardia or non-cardia) within 20 years after gastroscopy. In a large retrospective cohort Sweden study, HR and 95% CI for gastric cancer among patients with different lesions in the stomach compared with normal group were: 5.0 (3.8 to 6.7) for atrophic gastritis and 6.5 (4.8 to 8.9) for intestinal metaplasia.			d															
Lee2016	2	Retrospective Cohort in Taiwan 1)Hospital-based study that included all patients with gastric IM between 1992 and 2010, and the development of gastric adenocarcinoma was evaluated until July 2011. Patients developing gastric cancer r180 days after the index diagnosis of IM were excluded. 2-3)– Incidence and HR	-2	1	-2	-	in IM patients without concurrent dysplasia, the cumulative incidence of gastric cancer increased steadily and slowly during the follow-up period, and the 5-, 10-, and 15-year cumulative incidences were 0.7% (95% CI, 0.4-0.9), 1.8% (95% CI, 1.3-2.3), and 2.4% (95% CI, 1.5-3.2), respectively. Overall, the incidence rate of gastric cancer development after an initial diagnosis of gastric IM without concurrent dysplasia was 1.5 cases per 1000 person-years (95% CI 1.2-1.9), and the SIR was 2.0 (95% CI 1.5-2.6) as compared with that in the general population.	-				Low					2-						x	
Li2016	2	Retrospective Cohort in California (USA) Patients identified between 1997 and 2006 from KPNC pathology database	-1	0	-1	-	In a large retrospective cohort study in USA (median FUP 7.1 years), the incidence rate of gastric adenocarcinoma was 0.72/1,000 person-years in patients with intestinal metaplasia, with a relative risk of 2.56	-			mod												x	

							(95% confidence interval (CI) 1.49–4.10) compared with the Kaiser Permanente member population Authors estimated that the median time for gastric intestinal metaplasia to progress to adenocarcinoma was 6.1 years, and for low-grade dysplasia, 2.6 years																
Reddy2016	2	Retrospective Cohort in USA 1)Patients diagnosed with GIM from 2000 through 2011, collected from the Kaiser Permanente Southern California region. GIM was identified by a keyword search of pathology reports; gastric cancer cases were identified by cross-reference with an internal cancer registry. 2)The incidence of gastric cancer in patients with GIM (n=923; median age at diagnosis, 68 years) was compared with that of an age- and sexmatched reference population (controls). 3)Incidence of gastric cancer among patients with GIM and risk factors for gastric cancer.	-1	0	-1	-	the overall age- and gender-adjusted incidence rate of gastric cancer in patient with GIM was 172 per 100,000 person-years (95% CI, 0.74–3.39). The incidence of gastric cancer during this same time period in the reference population was 9.67 per 100,000 person-years. Using Poisson regression analysis, the overall age- and gender-adjusted Standardized Incidence Ratio (SIR) for gastric cancer was 4.2 extensive intestinal metaplasia (IM was present in at least two gastric locations or moderate or marked IM was noted in at least two biopsy specimens) was associated with increased risk of progression to gastric cancer compared to focal IM (OR 9.4, 95% CI 1.8-50.4). family history was a significant risk factor for gastric cancer (HR 3.8; 95% CI, 1.5–9.7) in patients with IM; the incidence rate for gastric cancer in those with a positive family history was 8.12 (95% CI, 0.1.67–23.73). Patients with both a family history of gastric cancer as well as intestinal metaplasia were 84 times more likely to develop gastric cancer compared to the reference population	2			mo d						2-						x	
Nieminen2020	2	Retrospective Cohort in Finland In the Helsinki Gastritis Study, 22346 elderly male smokers from southwestern Finland were screened for serum pepsinogen I (PGI). Between the					The cancer risk associated positively with high TAIM (vs low) [Hazard ratio (HR) 2.70, 95%CI: 1.09–6.69, P = 0.03].																	

		years 1989 and 1993, men with low PGI values (PGI < 25 µg/L), were invited to undergo an oesophagogastroduodenoscopy. In this retrospective cohort study, 1147 men that underwent gastroscopy were followed for gastric cancer for a median of 13.7 years, and a maximum of 27.3 years.					The risk increased through OLGIM stages compared to OLGIM 0: OLGIM I: HR 1.82 0.37-8.83 OLGIM II: HR 3.55 0.77-16.36 OLGIM III: HR 5.91 1.14-30.73 OLGIM IV: HR 5.72 1.03-31.77 The cancer risk did not associated to OLGA: OLGA I: HR 2.66 0.28-25.72 OLGA II: HR 2.84 0.38-21.38 OLGA III: HR 1.85 0.11-29.87 OLGA IV: HR 5.77 0.67-49.77 The OLGA staging and number of men gastroscopied and incident gastric cancer cases in each subgroup are shown in Table 3. The incidence rates of gastric cancer were 0.62, 1.60, 1.75, 1.11, and 3.40 per 1000 patient-years in stages 0–IV, respectively, (P for trend 0.10, Table 4). The majority of gastric cancers (n = 22, 79%) were diagnosed in low-risk OLGA stages (0–II), and only six cancers (21%) in high-risk (III–IV) stages. At the end of follow-up the cumulative cancer event rate was 4.4% in OLGA stages 0–II, and 6.4% in stages III–IV The OLGIM staging and number of men gastroscopied and incident gastric cancer cases in each subgroup are shown in Table 5. The gastric cancer incidence rate increased by OLGIM stages being 0.62, 1.21, 2.24, 3.37, and 3.22 per 1000 patient-years in stages 0–IV, respectively, (P for trend 0.004, Table 4). Similar to OLGA stages, the majority of cancers appeared in low-risk																		

							OLGIM groups (0–II, n = 19, 68%), and the minority in high-risk groups (III–IV, n = 9, 32%). In the end of the follow-up in OLGIM stages 0–II, the cumulative gastric cancer event rate was 3.5%, and in stages III–IV, 10.8%															
Chapelle2020	2	Retrospective cohort in France 1)All the patients diagnosed with GPL (atrophic gastritis, intestinal metaplasia [IM], and dysplasia) between 2000 and 2015 and fulfilling criteria for evolution assessment (at least 2 endoscopies, minimal follow-up of 6 months, and at least 2 biopsies obtained from the antrum and corpus) were included 2)Baseline vs End of FUP 3)Progression, regression, RR	-2	0	-1	-	Progression of the lesions was significantly higher in patients with incomplete type of IM (relative risk of progression for incomplete IM: 11.5; 95% confidence interval 2.5–53.1). This study shows that the patients with antrum-limited IM, especially of incomplete type, are at the highest risk of developing gastric cancer.	2			low						2-						x	
Piazuelo2021	2	Prospective cohort of an H. pylori eradication trial in a Hispanic population (Colombia) 1)800 adults with precancerous lesions were randomized to anti-H. pylori treatment or placebo. Gastric biopsies at baseline, 3, 6, 12, 16, and 20 years were assessed by our Correa histopathology score. 2)Baseline vs End FUP 3)Estimate progression by baseline diagnosis, and GC risk by intestinal metaplasia (IM) subtype and anatomic location	-1	0	-1	-	A total of 222 individuals with MAG without IM at baseline accumulated 3440 years of follow-up (mean, 15.5 years; median, 16.6 years). Among them, 117 individuals progressed to IM, 16 to ID, and 3 to LGD/HGD. Incidence rates were 4.70/100 PY (95% CI, 3.84–5.54) for IM, 0.47/100 PY (95% CI, 0.24–0.70) for ID, and 0.09/100 PY (95% CI, 0–0.18) for LGD/HGD. None of the individuals with MAG developed GC. A total of 502 individuals with IM at baseline accumulated a total of 7133 years of follow-up (mean, 14.2 years; median, 16.1 years). Among them, 166 individuals progressed to ID, 66 to LGD/HGD, and 8 to GC. Incidence rates were 2.43/100 PY (95% CI, 2.05–2.79) for ID, 0.98/100 PY (95% CI, 0.74–1.21) for LGD/HGD, and 0.11/100 PY (95% CI, 0.03–0.19) for GC. The rate of progression to GC among individuals with	2		mod						2-						x	

							complete IM at baseline was 0.028/ 100 PY (95% CI, 0.026–0.082) and for incomplete IM was 0.37/100 PY (95% CI, 0.15–0.59). Multivariable analyses showed that individuals with incomplete-type IM were 13.4 times more likely to progress to GC than those with the complete- type (OR 13.4, 95% CI, 1.8–103.8).																
Laszkowska2022	2	Retrospective cohort in USA 1) individuals age ≥ 18 years with GIM diagnosed on upper endoscopy between 1/1/1990 and 8/1/2019 at Columbia University Irving Medical Center. Only samples from the first available endoscopy with biopsy specimens available from both the distal stomach (antrum/pre-pylorus/pylorus) and proximal stomach (body/fundus) were included to allow for accurate diagnosis of extensive and limited GIM (n = 1256) 2) limited vs extensive GIM; Baseline histology vs End FUP histology 3) prevalence and progression rates of extensive GIM in a US cohort	-2	-1	-2	-	The annual incidence of GC for GIM overall was 0.09% (included auotimunne gastristis). There was no difference in progression to GC between extensive or limited GIM (IRR 0, 95% CI 0–2.6), or to advanced lesions overall (IRR 0.37, 95% CI 0.04–1.62).	0			low						2-						x	
Lee2022	2	Prospective cohort in Singapore 1) The study participants comprised 2980 patients undergoing screening gastroscopy with standardised gastric mucosal sampling, from January 2004 and December 2010, with scheduled surveillance endoscopies at year 3 and 5. 2) Participants were also matched against the National Registry of Diseases Office for missed diagnoses of early gastric neoplasia (EGN) 3) To investigate the incidence of gastric cancer (GC) attributed to gastric intestinal metaplasia (IM), and validate the Operative Link on Gastric Intestinal Metaplasia (OLGIM) for targeted endoscopic surveillance in regions with low-intermediate incidence of GC	0	0	0	-	In a multicentre prospective cohort study in Singapore, the age-adjusted EGN incidence rates for patients with and without IM were 133.9 and 12.5 per 100 000 person-years. IM was a significant risk factor for EGN (adjusted-HR 5.36; 95% CI 1.51 to 19.0; p<0.01). Participants with OLGIM stages III–IV were at greatest risk (adjusted-HR 20.7; 95% CI 5.04 to 85.6; p<0.01). More than half of the EGNs (n=4/7) attributed to baseline OLGIM III–IV developed within 2 years (range: 12.7–44.8 months). Participants with OLGIM II were also at significant risk of EGN (adjusted-HR 7.34; 95% CI 1.60 to 33.7; p=0.02) - patients with OLGIM II are now identified to be at intermediate risk of EGN.	2	high							2++						x		

							This group accounts for one-quarter of the subsequent EGN cases in our study. Patients with OLGIM II would benefit from endoscopic surveillance. A significant smoking history (≥20 pack years) increases the risk of EGN among patients with intermediate-risk and high-risk IM (ie, OLGIM II–IV). Authors suggest a risk-stratified approach and recommend that high-risk patients (OLGIM III–IV) have endoscopic surveillance in 2 years, intermediate-risk patients (OLGIM II) in 5 years, while majority of the patients who are low risk OLGIM (OLGIM 0–I) may not require routine surveillance endoscopy. Multivariate cox regression analysis showed that older age (adjusted-HR 1.08; 95%CI 1.02 to 1.16; p=0.02), positive serum pepsinogen index (adjusted-HR 4.23; 95%CI 1.34 to 13.37; p=0.01) and the presence of either atrophic gastritis (adjusted-HR 2.69; 95%CI 1.03 to 7.06; p=0.04) or gastric IM (adjusted-HR 5.36; 95%CI 1.51 to 19.0; p<0.01) were significant risk factors for EGN. The adjusted HR for subsequent early gastric neoplastic (EGN) for each stage of OLGIM were: OLGIM I – HR 1.95 (0.39 to 9.74); OLGIM II - 7.34 (1.60 to 33.7); OLGIM III-IV - 20.77 (5.04 to 85.6). There was an increasing trend of EGN risk with higher OLGIM stages, whereby the age-adjusted EGN rates with OLGIM I, II and III–IV were 21.5, 108.8, 543.8 per 100000 person-years, respectively. the incomplete subtype carries an eightfold increased risk of developing EGN (n=546; OR 8.4; 95%CI 1.9 to 37.8; p=0.005) compared with complete subtype of IM among participants																		

							with mucin staining.															
Akbari2019	2	SR/MA 1-2) Original studies reporting the incidence rate of gastric cancer in patients with gastric atrophy or intestinal metaplasia 3) incidence rate of GC and progress rate, regress and persistence proportion in both GA and IM patients were assessed	0	0	0	1	The pooled GC incidence rate in patients with GA was 1.24 (95% CI, 0.80, 1.76; I2: 83.6%) cases per 1,000 person-years. The rates of later diagnosis of IM and gastric dysplasia in patients with GA were estimated as 41.42 (95% CI, 3.11, 64.45; I2: 95.6%) and 6.23 (95% CI, 2.34, 11.46; I2: 83.0%) cases per 1,000 person-years, respectively In IM studies, the pooled incidence rate of GC was 3.38 (95% CI, 2.13, 4.85; I2: 93.4%) cases per 1,000 person-years. The progressed rate to dysplasia in IM patient was estimated to be 12.51 (95% CI, 5.45, 22.03; I2: 95.1%) cases per 1,000 person-years. When stratified by type of GA and IM lesions, the highest incidence rate of GC was observed in severe GA (4.82 per 1,000 person-years) and IM incomplete patients (6.60 cases per 1,000 person-years) compared to other strata. Overall, the incidence of GC in patients with IM and GA are low but there is heterogeneity in data with the highest rate in Asian, males with those with incomplete IM.		mod						1-							x		
Wang2022	2	SR/MA 1-2) The Risk of Diffuse-type Gastric Cancer Following Diagnosis with Gastric Precancerous Lesions 3) odds ratio (OR) of the association, Subgroup analysis was performed on studies reporting histologic severity (using operative link systems) to assess if histologic severity of AG/IM was associated with higher risk.	0	0	0	0	Both AG (pooled OR=1.9, 95% CI 1.5 to 2.4, p<0.001) and IM (pooled OR=2.3, 95% CI 1.9 to 2.9, p<0.001) demonstrated an association with DTGC Compared to low OLGA score (defined as scores of 1 or 2), high OLGA score (defined as scores of 3 or 4) was associated with an increased risk of DTGC (OR=1.7, 95% CI 1.2 to 2.3, p=<0.01) Compared to low OLGIM	0		mo d					1+							x		

							score (defined as scores of 1 or 2), high OLGIM score (defined as scores of 3 or 4) was associated with an increased risk of DTGC (OR=1.9, 95% CI 1.3 to 2.7, p=<0.01).																

* 1) Selection; 2) Comparability; 3) Outcome
** -1 per problemSelection: -1: selected group of users or no description; Comparability -1: no comparison between the cohorts; Outcome -1: No description, no follow up
# Evidence of dose response across or within studies (or inconsistency across studies is explained by a dose response); also up to one point added if adjustment for confounders would have increased the effect size (1); All / most studies show similar results (0); Lack of agreement between studies (e.g. statistical heterogeneity between RCTs, conflicting results) (-1)
@ -1 per problem in generalizability to the target population
†: only for meta-analysis
§ 0 if Not all effect sizes more than 2 or less than 0.5 and significant; or if OR/RR/HR not significant; 1 if Effect size more than 2 or less than 0.5 for all studies/meta-analyses included in comparison and significant; 2 if Effect size more than 5 or less tha.2 for all studies/meta-analyses included in comparison and significant
¶: High: Further research is very unlikely to change our confidence in the estimate of effect; Moderate: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate; Low: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate; Very low: Any estimate of effect is very uncertain

Table of evidence — ***Are there only case-controls/cross-sectional?***

Study ID	Study design Score **(2)**	Risk of bias (alinea(s)) *	Quality Score **(0 to -3) ****	Consistency Score **(-1 to 1) #**	Directness Score **(0 to -2)** @	Publication bias † **(0: No,1: Yes**)	Reported OR/RR/HR	Effect size Score **(0 to 2)** §	Evidence Level¶				Type of study according to SIGN								Recommendation SIGN			
									High	Mod	Low	Very Low	1++	1+	1-	2++	2+	2-	3	4	A	B	C	D
Cho2013	2	Case-control study in Korea 1-2)474 GC patients and age- and sexmatched health screening control persons in a cancer centre hospital 3) GC risk according to the OLGA and OLGIM stages	0	0	-1	-	More GC patients had OLGA stages III–IV (46.2%) than controls (26.6%, P < 0.001), particularly among patients with intestinal-type GCs (62.2%) compared with diffuse-type GCs (30.9%). OLGA stages III and IV were significantly associated with increased risk of GC [odds ratios (ORs), 2.09; P = 0.008 and 2.04; P = 0.014 respectively] in multivariate analysis. The association was more significant for intestinal-type (ORs, 4.76; P = 0.001 and 4.19; P = 0.002 respectively), but not diffuse-type GC. OLGIM stages from I to IV were significantly associated with increased risk of both intestinal-type (ORs, 3.64, 5.15, 7.89 and 13.20 respectively) and diffuse-type GC (ORs, 1.84, 2.59, 5.08 and 6.32 respectively) with a significantly increasing trend. Family history of first-degree relatives was an independent risk factor for GC: AOR 7.84 (3.59–	2		mod						2+						x	

							17.12)															
Choi2018	2	Case-Control study in USA 1-2) with cases of biopsy-proven gastric cancer matched (by age and gender) to controls without gastric cancer who had undergone EGD 3) Conditional logistic regression was used to identify independent risk factors for gastric cancer.	-1	0	-1	-	2 significant predictors of gastric cancer; the presence of gastric intestinal metaplasia (odds ratio (OR), 9.3; 95% CI, 4.5-18.9; P<0.001) and East Asian ethnicity (OR, 15.9; 95% CI, 5.8-43.6; P<0.001)	2			low							2-					x	
Marcos2020	2	Case-control study in Portugal 1-2) including 187 patients with egn treated endoscopically and 187 agematched and sex-matched control subject 3) individuals were classified according to eggiM, Olga and OlgiM systems. egn risk according to gastritis stages and other clinical parameters was further evaluated	0	0	-1	-	ore patients with egn had eggiM of ≥5 than control subjects (68.6% vs 13.3%, p<0.001). Olga and OlgiM stages iii/iV were more prevalent in patients with egn than in control subjects (68% vs 11%, p<0.001,and 61% vs 3%, p<0.001, respectively). The three systems were the only parameters significantly related to the risk of egn in multivariate analysis: for eggiM 1–4 (adjusted Or (aOr) 12.9, 95% ci 1.4 to 118.6) and eggiM 5–10 (aOr 21.2, 95% ci 5.0 to 90.2); for Olga i/ii (aOr 5.0, 95% ci 0.56 to 44.5) and Olga iii/iV (aOr 11.1, 95% ci 3.7 to 33.1); for OlgiM i/ii (aOr 11.5, 95% ci 4.1 to 32.3) and OlgiM iii/iV (aOr 16.0, 95% ci 7.6 to 33.4).	2		mod							2+						x	
Huang2023	2	Case-control in China (no acess to full-text) 1-2) single-centre, case–control study included 196 patients with EGC and 196 age-matched and sex-matched health screening control subjects 3) to validate OLGA and OLGIM staging systems for early GC (EGC) in Chinese population	-	-	-	-	OLGA and OLGIM stages II/III/IV were more prevalent in patients with EGC than in the control subjects. Multivariable analysis revealed family history of GC, previous Helicobacter pylori (H. pylori) infection, OLGA stages II and III-IV, OLGIM stages II and III-IV as independent risk factors for EGC (ORs, 4.04, 1.87, 2.52, 6.79, 4.11 and 10.78, respectively). Area under the receiver operating characteristic curve on EGC risk estimation was improved for OLGIM compared with OLGA (0.78 vs 0.71, p<0.001). Surveillance of intermediate-risk patients (OLGA/OLGIM II) should	2																x	

							be emphasised in our region. The OLGIM may be preferred over the OLGA for EGC risk estimation.																

* 1) Selection; 2) Comparability; 3) Exposure
** -1 per problem: Selection: -1: selected group of users or no description; Comparability -1: no comparison between the cohorts; Outcome -1: No description, no follow up
# Evidence of dose response across or within studies (or inconsistency across studies is explained by a dose response); also up to one point added if adjustment for confounders would have increased the effect size (1); All / most studies show similar results (0); Lack of agreement between studies (e.g. statistical heterogeneity between RCTs, conflicting results) (-1)
@ -1 per problem in generalizability to the target population
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§ 0 if Not all effect sizes more than 2 or less than 0.5 and significant; or if OR/RR/HR not significant; 1 if Effect size more than 2 or less than 0.5 for all studies/meta-analyses included in comparison and significant; 2 if Effect size more than 5 or less tha.2 for all studies/meta-analyses included in comparison and significant
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Sentence	**ESGE/EHMSG/ESP suggest that in patients with GIM at a single location but with a family history of GC, or with incomplete IM, or with persistent *H. pylori* gastritis, high-quality endoscopic surveillance every 3 years may be considered.**																						
GRADE	**Strength of recommendation: Conditional**								**Quality of evidence: Low**														
PICO	P: Patients with intestinal metaplasia I: Incidence of gastric neoplasm and risk factors for gastric neoplasm in patients with mild to moderate intestinal metaplasia at a single location (OLGIM I-II and OLGA 0-II) C: Absence or different stages of intestinal metaplasia O: Incidence of gastric neoplasm in patients with intestinal metaplasia, effect size measure (HR/OR/RR)																						
Query(ies) and databases searched	Search: PubMed ((((gastric[Title/Abstract] OR stomach[Title/Abstract] OR gastritis[Title/Abstract]) AND (cancer*[Title/Abstract] OR tumor*[Title/Abstract] OR neoplas*[Title/Abstract] OR carcinoma*[Title/Abstract] OR adenocarcinoma*[Title/Abstract] OR dysplas*[Title/Abstract] OR adenoma*[Title/Abstract] OR lesion*[Title/Abstract] OR malignan*[Title/Abstract])) OR (stomach neoplasms[Mesh])) AND ((intestinal[Title/Abstract] AND metaplasia[Title/Abstract]) OR atroph*[Title/Abstract] OR (precancerous[Title/Abstract] AND condition*[Title/Abstract]) OR (premalignant[Title/Abstract] AND condition*[Title/Abstract]) OR OLGA[Title/Abstract] OR OLGIM[Title/Abstract] OR EGGIM[Title/Abstract])) AND ((randomized controlled trial[Publication Type]) OR (randomized[Title/Abstract] AND controlled[Title/Abstract] AND trial[Title/Abstract]) OR (cohort studies[Mesh]) OR cohort[Title/Abstract] OR (follow up studies[Mesh]) OR (case-control studies[Mesh]) OR case-control[Title/Abstract] OR (cross-sectional studies[Mesh]) OR cross-sectional[Title/Abstract] OR (meta-analysis[Publication Type]) OR meta-analysis[Title/Abstract])																						
Table of evidence	***Are there any cohorts?***																						

Study ID	Study design Score **(2)**	Risk of bias (alinea(s)) *	Quality Score **(0 to -3)** **	Consistency Score **(-1 to 1)** #	Directness Score **(0 to -2)** @	Publication bias **(0: No,1: Yes)**	Reported OR/RR/HR	Effect size Score **(0 to 2)** §	Evidence Level¶				Type of study according to SIGN								Recommendation SIGN			
									High	Mod	Low	Very Low	1++	1+	1-	2++	2+	2-	3	4	A	B	C	D
Chapelle2020	2	Retrospective cohort in France 1)All the patients diagnosed with GPL (atrophic gastritis, intestinal metaplasia [IM], and dysplasia) between 2000 and 2015 and fulfilling criteria for evolution assessment (at least 2 endoscopies minimal follow-up of 6 months, and at least 2 biopsies obtained from the antrum and corpus) were included 2)Baseline vs End of FUP 3)Progression, regression, RR	-2	0	-1	-	Progression of the lesions was significantly higher in patients with incomplete type of IM (relative risk of progression for incomplete IM: 11.5; 95% confidence interval 2.5–53.1). This study shows that the patients with antrum-limited IM, especially of incomplete type, are at the highest risk of developing gastric cancer.	2			low							2-						x	
Du2021	2	SR/MA 1-2) published	0	0	0	1	Compared with complete IM, the pooled	2	high					1+							x			

		cohort studies of patients with complete IM (type I) or incomplete IM (type II or type III) from inception to May 15, 2021 3) pooled risk ratios (RRs) and 95% confidence intervals (CIs) comparing the GC risk with IM subtypes					relative risk of GC risk of patients with incomplete IM was 5.16 (95% CI, 3.28–8.12), and the GC risk of type III IM was the highest, with a pooled relative risk of 2.88 (95% CI, 1.37–6.04) compared with that of type II. Compared with complete IM, the pooled relative risk of dysplasia risk in patients with incomplete IM was 3.72 (95% CI, 1.42–9.72), and the dysplasia risk of type III IM was 11.73 (95% CI, 2.08–66.08) compared with that of type I. Patients with incomplete IM, especially type III, were at a higher risk of GC and dysplasia than those with complete IM.																
Wei2021	2	SR/MA aimed to pool relative risk (RR) of cancer/dysplasia of IIM compared with CIM in GIM patients 1-2) studies concerning cancer/dysplasia in GIM patients 3) studies concerning cancer/dysplasia in GIM patients	0	0	0	1	Compared with CIM, pooled RR of cancer/dysplasia in IIM patients was 4.48 (95% CI 2.50–8.03), and the RR was 4.96 (95% CI 2.72–9.04) for cancer, and 4.82 (95% CI 1.45–16.0) for dysplasia. The pooled RR for cancer/dysplasia in type III IM was 6.27 (95% CI 1.89–20.77) compared with type II+I IM, while it was 5.55 (95% CI 2.07–14.92) compared with type II IM. Pooled RR between type II IM and type I IM was 1.62 (95% CI 1.16–2.27). Subgroup analyses showed that IIM was associated with a higher risk of gastric cancer/dysplasia in Western population (pooled RR=4.65 95% CI 2.30–9.42), but not in East Asian population (pooled RR=4.01 95% CI 0.82–19.61) IIM was related to a higher risk of cancer/dysplasia compared with CIM. Risk of developing cancer/dysplasia from type I, II, and III intestinal metaplasia increased gradually.	2	high					1+							x			

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between RCTs, conflicting results) (-1)
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Table of evidence — ***Are there only case-controls/cross-sectional?***

Study ID	Study design Score **(2)**	Risk of bias (alinea(s)) *	Quality Score **(0 to -3)** **	Consistency Score **(-1 to 1)** #	Directness Score **(0 to -2)** @	Publication bias † **(0: No,1:Yes)**	Reported OR/RR/HR	Effect size Score **(0 to 2)** §	Evidence Level¶				Type of study according to SIGN								Recommendation SIGN			
									High	Mod	Low	Very Low	1++	1+	1-	2++	2+	2-	3	4	A	B	C	D
Chen2023	2	Case-control study in China 1-2) including 68 patients with EGC treated with endoscopic submucosal dissection and 68 ageand sex-matched control subjects 3)Assess KTc, OLGA, OLGIM risk stratification	0	0	0	-	O-type Kimura–Takemoto classification (adjusted odds ratio [AOR] 3.282, 95% confidence interval [CI] 1.106–9.744, P = 0.032) and OLGIM stage III/IV (AOR 17.939, 95% CI 1.874–171.722, P = 0.012) were significantly related to a higher risk of EGC. OLGIM I/II was not: AOR 5.080 (0.722–35.736) 0.102 OLGA I/II (AOR 0.522 (0.074–3.696) 0.515) and OLGA III/IV (AOR 3.372 0.477–23.854 0.223 Current/ex-smoker » AOR 3.121 (1.045–9.318) p=0.041 Family history of gastric cancer (1st or 2nd degree): AOR 8.079 (2.634–24.781) <0.001	2		mod							2+					x		
Huang2023	2	Case-control in China (no acess to full-text) 1-2) single-centre, case–control study included 196 patients with EGC and 196 age-matched and sex-matched health screening control subjects 3) to validate OLGA and OLGIM staging systems for early GC (EGC) in Chinese population	-	-	-	-	OLGA and OLGIM stages II/III/IV were more prevalent in patients with EGC than in the control subjects. Multivariable analysis revealed family history of GC, previous Helicobacter pylori (H. pylori) infection, OLGA stages II and III-IV, OLGIM stages II and III-IV as independent risk factors for EGC (ORs, 4.04, 1.87, 2.52, 6.79, 4.11 and 10.78, respectively). Area under the receiver operating characteristic curve on EGC risk estimation was improved for OLGIM compared with OLGA (0.78 vs 0.71, p<0.001).	2													x		

							Surveillance of intermediate-risk patients (OLGA/OLGIM II) should be emphasised in our region. The OLGIM may be preferred over the OLGA for EGC risk estimation.																

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Sentence	**ESGE/EHMSG/ESP recommend against any tailored surveillance strategy based on genetic status, birthplace or ethnicity in patients with gastric precancerous conditions.**																						
GRADE	**Strength of recommendation: Conditional**							**Quality of evidence: Low**															
PICO	Patients: Patients with gastric precancerous lesion Intervention: tailored surveillance strategies according to risk factors Comparison: Patients with gastric precancerous lesions in other populations (ethnic groups…) Outcome: Worsening gastric precancerous lesion/ gastric cancer.																						
Query(ies) and databases searched	((("stomach"[MeSH Terms] OR "stomach"[All Fields] OR "gastric"[All Fields]) AND ("precancerous lesions"[All Fields] OR "Precancerous Conditions"[Mesh])) OR ("chronic atrophic gastritis"[All Fields] OR "Gastritis, Atrophic"[Mesh]) OR "intestinal metaplasia"[All Fields] OR dysplasia[All Fields]) AND (follow-up[All Fields] OR "Follow-Up Studies"[Mesh] OR "surveillance"[All Fields] OR "Population Surveillance"[Mesh] OR "endoscopic surveillance"[All Fields] OR ("Endoscopy, Gastrointestinal"[Mesh] AND "Population Surveillance"[Mesh])) AND "Stomach Neoplasms/diagnosis"[Mesh] + Cross referencing																						
Table of evidence	***Are there any RCT?***																						

Study ID	Study design Score **(4)**	Risk of bias (alinea(s)) *	Quality Score **(0 to -2)** **	Consistency Score **(-1 to 1)** #	Directness Score **(0 to -2)** @	Publication bias † (**0: No,1: Yes**)	Reported OR/RR/HR	Effect size Score **(0 to 2)** §	Evidence Level¶				Type of study according to SIGN								Recommendation SIGN			
									High	Mod	Low	Very Low	1++	1+	1-	2++	2+	2-	3	4	A	B	C	D
Bianca-piazuelo	1+	4)Lost to FU >50%	0		-1	NA	OR	/	x					x								x		
Mera	1+	4)Lost to FU >50%	0		-1	NA	OR	/	x					x								x		

* 1) blinding of measurements (test and outcome); 2) allocation; 3) verification (all individuals were submitted to both tests); 4) complete follow-up; 5) other – please identify
** Low risk of bias would indicate "no serious limitations" = 0; Presence of serious limitations then downgrade the quality of evidence for this outcome by 1 level = -1; Presence of very serious limitations then downgrade the quality of evidence for this outcome by 2 level = -2
# Evidence of dose response across or within studies (or inconsistency across studies is explained by a dose response); also up to one point added if adjustment for confounders would have increased the effect size (1); All / most studies show similar results (0); Lack of agreement between studies (e.g. statistical heterogeneity between RCTs, conflicting results) (-1)
@ -1 per problem in generalizability to the target population
†: only for meta-analysis
§ 0 if Not all effect sizes more than 2 or less than 0.5 and significant; or if OR/RR/HR not significant; 1 if Effect size more than 2 or less than 0.5 for all studies/meta-analyses included in comparison and significant; 2 if Effect size more than 5 or less tha.2 for all studies/meta-analyses included in comparison and significant
¶: High: Further research is very unlikely to change our confidence in the estimate of effect; Moderate: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate; Low: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate; Very low: Any estimate of effect is very uncertain

Table of evidence	***Are there any cohorts?***

Study ID	Study design Score **(2)**	Risk of bias (alinea(s)) *	Quality Score **(0 to -3)** **	Consistency Score **(-1 to 1)** #	Directness Score **(0 to -2)** @	Publication bias (**0: No,1: Yes**)	Reported OR/RR/HR	Effect size Score **(0 to 2)** §	Evidence Level¶	Type of study according to SIGN	Recommendation SIGN

									High	Mod	Low	Very Low	1++	1+	1-	2++	2+	2-	3	4	A	B	C	D
Akbari	2++		0	0	-1	0	/	/		*						x							x	
den Hollander	2+	2)	0	NA	-1		/			x							x						x	
Dhinga	2-	1)3)	-1	NA	-1		HR	1			x							x					x	
Gonzalez	2-	1)	-1	NA	-1		HR	2			x							x					x	
Huang	2-	1)	-1	NA	-1						x							x					x	
Shao	2++		0	0	0	1	OR	1		x						x							x	
Prakash	2-	1)	-1	NA	0	NA	/	/			x							x					x	
Nieuwenburg	2+	2)	-1	NA	0	NA	OR	0			x						x						x	

* 1) Selection; 2) Comparability; 3) Outcome
** -1 per problem Selection: -1: selected group of users or no description; Comparability -1: no comparison between the cohorts; Outcome -1: No description, no follow up
# Evidence of dose response across or within studies (or inconsistency across studies is explained by a dose response); also up to one point added if adjustment for confounders would have increased the effect size (1); All / most studies show similar results (0); Lack of agreement between studies (e.g. statistical heterogeneity between RCTs, conflicting results) (-1)
@ -1 per problem in generalizability to the target population
†: only for meta-analysis
§ 0 if Not all effect sizes more than 2 or less than 0.5 and significant; or if OR/RR/HR not significant; 1 if Effect size more than 2 or less than 0.5 for all studies/meta-analyses included in comparison and significant; 2 if Effect size more than 5 or less tha.2 for all studies/meta-analyses included in comparison and significant
¶: High: Further research is very unlikely to change our confidence in the estimate of effect; Moderate: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate; Low: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate; Very low: Any estimate of effect is very uncertain

Table of evidence — ***Are there only case-controls/cross-sectional?***

Study ID	Study design Score **(2)**	Risk of bias (alinea(s)) *	Quality Score **(0 to -3) ** **	Consistency Score **(-1 to 1) #**	Directness Score **(0 to -2)** @	Publication bias † **(0: No,1: Yes)**	Reported OR/RR/HR	Effect size Score **(0 to 2)** §	Evidence Level¶				Type of study according to SIGN								Recommendation SIGN			
									High	Mod	Low	Very Low	1++	1+	1-	2++	2+	2-	3	4	A	B	C	D
Choi	2-	2)	-1	NA	-1	N/A						x											x	
Gawron	2++		0	0	0	NR						x											x	
Reddy	2-	1)2)	-1	NA	-1	N/A	HR	1			x							x					x	
Usui	2+	1)	-1	NA	-1	NA	RER				x												x	

* 1) Selection; 2) Comparability; 3) Exposure
** -1 per problem: Selection: -1: selected group of users or no description; Comparability -1: no comparison between the cohorts; Outcome -1: No description, no follow up
# Evidence of dose response across or within studies (or inconsistency across studies is explained by a dose response); also up to one point added if adjustment for confounders would have increased the effect size (1); All / most studies show similar results (0); Lack of agreement between studies (e.g. statistical heterogeneity between RCTs, conflicting results) (-1)
@ -1 per problem in generalizability to the target population
†: only for meta-analysis
§ 0 if Not all effect sizes more than 2 or less than 0.5 and significant; or if OR/RR/HR not significant; 1 if Effect size more than 2 or less than 0.5 for all studies/meta-analyses included in comparison and significant; 2 if Effect size more than 5 or less tha.2 for all studies/meta-analyses included in comparison and significant
¶: High: Further research is very unlikely to change our confidence in the estimate of effect; Moderate: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate; Low: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate; Very low: Any estimate of effect is very uncertain

Sentence	**ESGE/EHMSG/ESP suggest that random biopsies are not required during surveillance of cases with advanced OLGA/OLGIM stages at baseline endoscopy once no superficial lesions are observed.**	
GRADE	**Strength of recommendation: Conditional**	**Quality of evidence: Low**
PICO	P: Patients with gastric precancerous conditions and different risks I: endoscopic biopsies C: endoscopy without biopsies O: important outcomes: cancer incidence, survival, quality of life	
Query(ies) and databases searched	Search PubMed: (gastric precancerous conditions OR gastric intestinal metaplasia OR atrophic gastritis OR gastric atrophy) AND (endoscopic biopsies) AND (surveillance)	

Sentence	**ESGE/EHMSG/ESP recommend *H. pylori* eradication in individuals with nonatrophic chronic gastritis and atrophic gastritis to reduce the risk of GC.**	
GRADE	**Strength of recommendation: Strong**	**Quality of evidence: High**
PICO	P: Patients with established preneoplastic lesions (atrophic gastritis and intestinal metaplasia) I: H. pylori eradication C: Placebo – no H.Pylori treatment O: (1) Risk of gastric cancer (2) Incidence of gastric cancer (3) Improvement/regression of atrophic gastritis; (4) Improvement/regression of intestinal metaplasia	
Query(ies) and databases searched	(("helicobacter pylori"[All Fields] OR "HP"[All Fields] OR "H.pylori"[All Fields] OR "helicobacter pylori eradication"[All Fields]) AND (“eradication” [All Fields] OR “treatment” [All Fields] OR “therapy” [All Fields]) AND ("gastric"[All Fields] OR ("gastritis"[All Fields] OR "atrophy"[All Fields] OR “atrophic gastritis”[All Fields] OR "intestinal metaplasia"[All Fields] OR "precancerous lesions” [All Fields]) AND (“gastric cancer risk"[All Fields] OR “gastric cancer incidence"[All Fields] OR "cancer"[All Fields] OR "cancer risk"[All Fields]))	

Table of evidence — ***Are there any RCT?***

Study ID	Study design Score **(4)**	Risk of bias (alinea(s)) *	Quality Score **(0 to -2)** **	Consistency Score **(-1 to 1)** #	Directness Score **(0 to -2)** @	Publication bias † **(0: No,1: Yes)**	Reported OR/RR/HR	Effect size Score **(0 to 2)** §	Evidence Level¶				Type of study according to SIGN								Recommendation SIGN			
									High	Mod	Low	Very Low	1++	1+	1-	2++	2+	2-	3	4	A	B	C	D
Yan L. 2022	4	0 Low risk	0	0	0	-	GC risk after HP eradication, individuals without baseline premalignant lesions HR 0.37; 95% CI 0.15-0.95	1		x				x									x		
Choi IJ, 2018	4	0 Low risk	0	0	0	-	Metachronous GC after Hp treatment. HR ratio in the treatment group, 0.50; 95% confidence interval, 0.26 to 0.94; P=0.03.	0		x				x									x		
Piazuelo MB, 2020	4	0 Low risk	0	0	0	-	Reduced progression in Correa score (OR 0.59, 95%CI 0.35-0.93)	0		x				x									x		

* 1) blinding of measurements (test and outcome); 2) allocation; 3) verification (all individuals were submitted to both tests); 4) complete follow-up; 5) other – please identify
** Low risk of bias would indicate “no serious limitations” = 0; Presence of serious limitations then downgrade the quality of evidence for this outcome by 1 level = -1; Presence of very serious limitations then downgrade the quality of evidence for this outcome by 2 level = -2
# Evidence of dose response across or within studies (or inconsistency across studies is explained by a dose response); also up to one point added if adjustment for confounders would have increased the effect size (1); All / most studies show similar results (0); Lack of agreement between studies (e.g. statistical heterogeneity between RCTs, conflicting results) (-1)
@ -1 per problem in generalizability to the target population
†: only for meta-analysis
§ 0 if Not all effect sizes more than 2 or less than 0.5 and significant; or if OR/RR/HR not significant; 1 if Effect size more than 2 or less than 0.5 for all studies/meta-analyses included in comparison and significant; 2 if Effect size more than 5 or less tha.2 for all studies/meta-analyses included in comparison and significant
¶: High: Further research is very unlikely to change our confidence in the estimate of effect; Moderate: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate; Low: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate; Very low: Any estimate of effect is very uncertain

Table of evidence — ***Are there any cohorts?***

Study ID	Study design Score **(2)**	Risk of bias (alinea(s))*	Quality Score **(0 to -3)** **	Consistency Score **(-1 to 1)** #	Directness Score **(0 to -2)** @	Publication bias † (**0: No,1: Yes**)	Reported OR/RR/HR	Effect size Score **(0 to 2)** §	Evidence Level¶				Type of study according to SIGN								Recommendation SIGN			
									High	Mod	Low	Very Low	1++	1+	1-	2++	2+	2-	3	4	A	B	C	D
Li D, 2023	3	Low risk. Comparability	-1	0	0	-	HR for GC in HP+/untreated and HP+/treated individuals:6.07 (4.20-8.76) and 2.68 (1.86-3.86)	0		x								x						x	
Suna N, 2020	3	-1. Comparability	-2	-1	-1	-	No	-			x							x						x	

* 1) Selection; 2) Comparability; 3) Outcome
** -1 per problem Selection: -1: selected group of users or no description; Comparability -1: no comparison between the cohorts; Outcome -1: No description, no follow up
# Evidence of dose response across or within studies (or inconsistency across studies is explained by a dose response); also up to one point added if adjustment for confounders would have increased the effect size (1); All / most studies show similar results (0); Lack of agreement between studies (e.g. statistical heterogeneity between RCTs, conflicting results) (-1)
@ -1 per problem in generalizability to the target population

†: only for meta-analysis
§ 0 if Not all effect sizes more than 2 or less than 0.5 and significant; or if OR/RR/HR not significant; 1 if Effect size more than 2 or less than 0.5 for all studies/meta-analyses included in comparison and significant; 2 if Effect size more than 5 or less tha.2 for all studies/meta-analyses included in comparison and significant
¶: High: Further research is very unlikely to change our confidence in the estimate of effect; Moderate: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate; Low: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate; Very low: Any estimate of effect is very uncertain

Sentence	**ESGE /EHMSG/ESP recommend that *H. pylori* eradication should be considered in patients with established GIM.**	
GRADE	**Strength of recommendation: Conditional**	**Quality of evidence: Moderate**
PICO	P: Patients with established preneoplastic lesions (atrophic gastritis and intestinal metaplasia) I: H. pylori eradication C: Placebo – no H.Pylori treatment O: (1) Risk of gastric cancer (2) Incidence of gastric cancer (3) Improvement/regression of atrophic gastritis; (4) Improvement/regression of intestinal metaplasia	
Query(ies) and databases searched	(("helicobacter pylori"[All Fields] OR "HP"[All Fields] OR "H.pylori"[All Fields] OR "helicobacter pylori eradication"[All Fields]) AND (“eradication” [All Fields] OR “treatment” [All Fields] OR “therapy” [All Fields]) AND ("gastric"[All Fields] OR ("gastritis"[All Fields] OR "atrophy"[All Fields] OR “atrophic gastritis”[All Fields] OR "intestinal metaplasia"[All Fields] OR "precancerous lesions” [All Fields]) AND (“gastric cancer risk"[All Fields] OR “gastric cancer incidence"[All Fields] OR "cancer"[All Fields] OR "cancer risk"[All Fields]))	
Table of evidence	***Are there any RCT?***	

Study ID	Study design Score **(4)**	Risk of bias (alinea(s)) *	Quality Score **(0 to -2)** **	Consistency Score **(-1 to 1)** #	Directness Score **(0 to -2)** @	Publication bias † **(0: No,1: Yes)**	Reported OR/RR/HR	Effect size Score **(0 to 2)** §	Evidence Level¶				Type of study according to SIGN								Recommendation SIGN			
									High	Mod	Low	Very Low	1++	1+	1-	2++	2+	2-	3	4	A	B	C	D
Khan et al (2020)	4	1) Performance Bias (7 low-risk; 2 high risk) Detection Bias (6 low risk; 3 unclear) 2) Allocation bias (5 low-risk; 4 unclear) 3) ? 4) Low risk in 4; Unclear risk in 5	0	0	0	?	(OR 0.61; 95% CI; 0.42-1.07) Incidence of gastric cancer with precancerous lesions (OR 2.61; 95% CI; 1.41-4.81) Improvement/regression of atrophic gastritis (OR 2.61; 95% CI; 1.66-4.11) Improvement/regression of IM (OR, 0.54; 95% CI; 0.38-0.76) Mean duration follow-up ≥ 5 years	0		x				x									x		
Ford et al (2022)	4	Not mention	0	1	0	?	(OR 0.54; 95% CI; 0.41-0.72) Effect of HP eradication on gastric cancer occurrence	0	x					x									x		
Zhu et al (2023)	4	1) Performance Bias (Low risk in 9; Unclear in 2; high risk in 1); Detection Bias (Low risk in 7; Unclear in 5) 2)Low risk in 7; Unclear in 4 3) ? 4) Attrition Bias (High risk of bias in 2; unclear in 6; low risk in 4	-1	0	0	Not acessed	(RR 1.32; 95% CI; 1.17-1.50) Effect of HP eradication on preneoplastic lesions regression (RR 1.84; 95%CI; 1.30-2.61) Effect of HP eradication on IM (RR 1.41; 95% CI; 1.30-2.61) Effect of HP eradication on Atrophic gastritis	0		x				x									x		

* 1) blinding of measurements (test and outcome); 2) allocation; 3) verification (all individuals were submitted to both tests); 4) complete follow-up; 5) other – please identify
** Low risk of bias would indicate “no serious limitations” = 0; Presence of serious limitations then downgrade the quality of evidence for this outcome by 1 level = -1; Presence of very serious limitations then downgrade the quality of evidence for this outcome by 2 level = -2
# Evidence of dose response across or within studies (or inconsistency across studies is explained by a dose response); also up to one point added if adjustment for confounders would have increased the effect size (1); All / most studies show similar results (0); Lack of agreement between studies (e.g. statistical heterogeneity between RCTs, conflicting results) (-1)
@ -1 per problem in generalizability to the target population
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§ 0 if Not all effect sizes more than 2 or less than 0.5 and significant; or if OR/RR/HR not significant; 1 if Effect size more than 2 or less than 0.5 for all studies/meta-analyses included in comparison and significant; 2 if Effect size more than 5 or less tha.2 for all studies/meta-analyses included in comparison and significant
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Table of evidence		*Are there any cohorts?* (Diagnostic/Prognostic related key question)																							
Study ID	Study design Score (2)	Risk of bias (alinea(s))*	Quality Score (0 to -3) **	Consistency Score (-1 to 1) #	Directness Score (0 to -2) @	Publication bias (0: No,1:Yes)	Reported OR/RR/HR	Effect size Score (0 to 2) §	Evidence Level¶				Type of study according to SIGN								Recommendation SIGN			
									High	Mod	Low	Very Low	1++	1+	1-	2++	2+	2-	3	4	A	B	C	D
Kodama et al (2021)	2	1) Low risk 2) Unclear Unclear	3	0	-1	?	?	-								x						x		

* 1) Selection; 2) Comparability; 3) Outcome
** -1 per problemSelection: -1: selected group of users or no description; Comparability -1: no comparison between the cohorts; Outcome -1: No description, no follow up
# Evidence of dose response across or within studies (or inconsistency across studies is explained by a dose response); also up to one point added if adjustment for confounders would have increased the effect size (1); All / most studies show similar results (0); Lack of agreement between studies (e.g. statistical heterogeneity between RCTs, conflicting results) (-1)
@ -1 per problem in generalizability to the target population
†: only for meta-analysis

Sentence	**ESGE/EHMSG/ESP recommend *H. pylori* eradication for patients with gastric neoplasia after endoscopic or surgical therapy**								
PICO	P: Patients with established gastric cancer applicable for endoscopic resection I: H. pylori eradication C: Placebo – no H.pylori treatment O: (1) Risk of metachronous gastric cancer (2) Improvement/regression of atrophic gastritis;								
Query(ies) and databases searched	(("helicobacter pylori"[All Fields] OR "HP"[All Fields] OR "H.pylori"[All Fields] OR "helicobacter pylori eradication"[All Fields]) AND (“eradication” [All Fields] OR “treatment” [All Fields] OR “therapy” [All Fields]) AND ("gastric"[All Fields] OR ("gastritic cancer"[All Fields] OR "early gastric cancer"[All Fields] [AND (“gastric cancer risk"[All Fields] OR “ metachronous gastric cancer "[All Fields] OR "recurrence"[All Fields] OR "cancer risk"[All Fields]))								
GRADE	**Strength of recommendation: Strong**						**Quality of evidence: Moderate**		
Author (year)	**Methods**	**Population**		**Intervention**			**Outcomes**			**Remarks**
	Design	**Randomization/ blinding**	**N**	**Age**	**Inclusion criteria**	**Protocol (details) of Intervention**	**Protocol (details) of Comparison**	**Outcome measures (+ definitions)**	**Principal findings**	**Remarks**
Bae SE (2014)	Retropective cohort study	NA	2089	63	Adults who underwent endoscopic resection of gastric low-grade neoplasia, high-grade neoplasia, or differentiated	Incidence of metachronous recurrence	Dividing into three groups: those without active H. pylori infection (Hp negative group), those who successfully underwent H. pylori eradication (eradicated group),	Incidence of metachronous recurrence overall and in the three groups	The incidence of metachronous gastric cancer was 10.9 cases per 1,000 person-years in the Hp negative group, 14.7 cases per 1,000 person-years in the eradicated group, and 29.7 cases per 1,000 person-years in the noneradicated group. Hazard ratios in the noneradicated group compared with the Hp negative and eradicated groups were 2.5 (P<0.01) and 1.9 (P=0.02), respectively.	

					invasive neoplasia		and those who failed or did not undergo H. pylori eradication (noneradicated group).			
Choi Ij (2018)	Prospective, single center, double-blind, placebo-controlled, randomized trial	Yes	470	59.7	Patients who had undergone endoscopic resection of early gastric cancer or high-grade adenoma	Comparison of H. pylori eradication therapy with antibiotics or placebo	Comparison of H. pylori eradication therapy with antibiotics or placebo	Incidence of metachronous gastric cancer detected on endoscopy performed at the 1-year follow-up or later and improvement from baseline in the grade of glandular atrophy in the gastric corpus lesser curvature at the 3-year follow-up	Metachronous gastric cancer: 7.2% H. Pylori vs.13.4 % placebo, (HR in the treatment group, 0.50; 95% CI, 0.26 to 0.94; P=0.03) Improvement from baseline in the atrophy grade at the gastric corpus lesser curvature: 48.4% H. Pylori vs.15 % placebo	
Choi Jm (2018)	Prospective, single center, open-label, prospective, randomized controlled	Yes	877	59.7	Patients treated with endoscopic resection (ER) for gastric dysplasia or early gastric cancer	Comparison of H. pylori eradication therapy with antibiotics or no treatment	Comparison of H. pylori eradication therapy with antibiotics or no treatment	Incidence of metachronous gastric cancer detected on endoscopy performed at the 1-year follow-up	Metachronous gastric cancer: 4.1% H. pylori vs.8.2 % in placebo group, (HR control vs. treatment: 2.02 (95% CI, 1.14-3.56; P = 0.02) Improvement of astrophy compared to baseline in 48% of eradicated patients	
Han Sj (2018)	Retropective cohort study	NA	565	62,9	Patients who had undergone endoscopic resection of early gastric cancer	Incidence of metachronous recurrence and changes in precancerous lesions according to H. pylori	Dividing into two groups: those who successfully underwent H. pylori eradication (eradicated group), and those who failed or did not undergo H. pylori	Incidence of metachronous recurrence overall and in the two groups	The grade of atrophy on corpus was significantly lower in the H. pylori-eradicated group than in the persistent group during follow-up (p=0.029). In patients <70 years of age, the cumulative incidence rate of metachronous cancer was significantly lower in the H. pylori-eradicated group than in the persistent group (p=0.018). Age was an independent risk factor for	

						eradication and final infection status	eradication (noneradicated group).		metachronous cancer development.	
Choe Y (2023)	Meta-analysis	NA	9 cohort studies 2755	NA	Patients with metachronous gastric cancer after endoscopic resection for gastric cancer.	Occurrence of metachronous gastric cancer, presence of intestinal metaplasia (IM), severe atrophic gastritis (AG), and H. pylori infection	Dividing into three groups: intestinal metaplasia (IM), severe atrophic gastritis (AG), and H. pylori infection	Occurrence of metachronous gastric cancer, presence of intestinal metaplasia (IM), severe atrophic gastritis (AG), and H. pylori infection	Severe AG or presence of IM had higher incidence of MGC than those without (RR 2.00, 95% CI 1.35-2.98, I2 = 52% for severe atrophy on antrum; RR 7.08, 95% CI 3.63-13.80, I2 = 0% for antral IM). Risk difference of MGC 7.1% in those with severe AG and 9.2% in those with IM. The difference in incidence rate per 1,000 person-years was 17.5 person-years for those with severe AG and 24.7 person-years for those with IM. H. pylori eradication did not significantly affect the occurrence of MGC (RR 1.18, 95% CI 0.88-1.59, I2 = 10%).	High heterogeneity

Are there any cohorts? *If yes please complete (add each study per line in the table)*

Study ID	Study design Score **(2)**	Risk of bias (alinea(s))*	Quality Score **(0 to -3)****	Consistency Score **(-1 to 1) #**	Directness Score **(0 to -2)** @	Publication bias (**0:No,1:Yes**)	Reported OR/RR/HR	Effect size Score **(0 to 2)** §	Evidence Level¶				Type of study according to SIGN								Recommendation SIGN			
									High	Mod	Low	Very Low	1++	1+	1-	2++	2+	2-	3	4	A	B	C	D
Bae SE (2014)	Retropective cohort study	1	-1	0	-1	NA	NR	1			X						X						X	
Han Sj (2018)	Retropective cohort study	1	-1	-1	-1	NA	Reported OR	1			X						X						X	
Choe Y (2023)	Meta-analysis	0	-1	-1	0	0	OR	0			X					X							X	

Are there any RCT?

Study ID	Study design	Risk of bias	Quality Score	Consistency Score	Directness Score	Publication bias †	Reported OR/RR/HR	Effect size	Evidence Level¶	Recommendation SIGN	Recommendation SIGN

	Score **(4)**	(alinea(s)) *	**(0 to -2)** **	**(-1 to 1) #**	**(0 to -2)** @	(**0: No,1: Yes**)		Score **(0 to 2)** §															
									High	Mod	Low	Very Low	1++	1+	1-	2++	2+	2-	3	4	A	B	C	D
Choi Ij (2018)	4	Single center,	-2	0	-2	NA	yes see Table			x					x							x		
Choi Jm (2018)	4	Single center, open label	-2	0	-2	NA	yes see Table			x					x							x		

Sentence	**ESGE/EHMSG/ESP recommend against testing for other microbiota than *H. pylori* for preventing or treating gastric precancerous conditions.**	
GRADE	**Strength of recommendation: Strong**	**Quality of evidence: Moderate**
PICO	P: Patients with established gastric precancerous lesions I: Microbiota analysis C: Microbial modulation O: (1) Risk reduction for the development of gastric cancer (2) Improvement/regression of precancerous conditions	
Query(ies) and databases searched	(("helicobacter pylori"[All Fields] OR "HP"[All Fields] OR "H.pylori"[All Fields] AND ("gastric microbiota"[All Fields] OR ("gastritis"[All Fields] OR "atrophy"[All Fields] OR “atrophic gastritis”[All Fields] OR "intestinal metaplasia"[All Fields] OR "precancerous lesions” [All Fields]) AND (“gastric cancer"[All Fields] OR “gastric bacteria"[All Fields] OR "cancer"[All Fields]))	

Sentence	**ESGE/EHMSG/ESP recommend smoking cessation in individuals with precancerous conditions or after ESD for early cancer.**	
GRADE	**Strength of recommendation: Strong**	**Quality of evidence: Low**
PICO	P: Patients after ESD I: Smoking cessation C: Continue smoking O: Incidence of metachronous GC/Incidence of synchronous GC/GC mortality	
Query(ies) and databases searched	Search: PubMed ("Stomach"[Mesh] OR gastric[tw] OR stomach[tw] OR gastroesophageal[tw] OR esophagogastric[tw] OR oesophagogastric*[tw]) AND ("Stomach Neoplasms"[Mesh] OR cancer*[tw] OR adenocarcinoma*[tw] OR neoplasm*[tw] OR tumour*[tw] OR tumour*[tw] OR tumor*[tw]) AND ("ESD"[tw] OR “Endoscopic resection”[tw] OR “Endoscopic submucosal dissection”[tw]) AND (“Smoking”[tw] OR “Tobacco”[tw]) AND (“synchronous”[tw] OR “meta-chronous”[tw] OR “metachronous”[tw] OR “outcome*”[tw])	

Study	**Type**	**Endpoint**	**Bias/concerns**	**Patients**	**Principal findings**	**Evidence Level¶**				**Type of study according to SIGN**								**Recommendation SIGN**			
						High	Mod	Low	Very Low	1++	1+	1-	2++	2+	2-	3	4	A	B	C	D

Hatta 2023	Cohort	Prevalence od synchronus gastric cancer	Possibility of type II error; recall bias	850	Smoking history – risk factor for SC prevalence (OR 1.93; p = 0.048) Current smoking – risk factor for SC prevalence (OR 2.33; p = 0.021)		x						x						x		
Brito-Goncalves 2020	Cohort	Risk factors for multiple lesions	Single center, retrospective design	281	Current/former smoking – independent risk factor for SC prevalence (AOR 3.64, 95% CI 1.07–12.40)			x					x						x		
Ami 2017	Cohort	Incidence of metachronus cancer	Single center, retrospective	539	Current smoking – independent risk factor for metachronus GC after ESD, 1.91 (1.10-3.32), p=0.022			x					x						x		
Abiko 2023	Cohort	Incidence of metachronus cancer	Single centre, retrospective	77	Heavy smoking (HR = 2.36, $P < 0.09$), and cigarette smoking after ER (HR = 2.47, $P < 0.10$) not independently associated with the risk of MC development Cumulative incidence of secondary GC in the cessation and non-cessation groups (heavy smokers prior to ESD): 5-year incidence of MC 19.0% and 45.0%, ($P = 0.03$) (HR [95% CI]: 3.65 [1.01–12.19], $P = 0.04$)			x					x						x		

Sentence	**ESGE/EHMSG/ESP suggest that patients with an appropriate indication for PPI or H2RA should not discontinue the medication.**																				
GRADE	**Strength of recommendation: Conditional**																				**Quality of evidence: Low**
PICO	P: General population I: PPI C: No PPI intake O: Incidence of GC / Incidence of IM/Atr / GC-associated mortality																				
Query(ies) and databases searched	Search: PubMed ("Stomach"[Mesh] OR gastric[tw] OR stomach[tw] OR gastroesophageal[tw] OR esophagogastric[tw] OR oesophagogastric*[tw]) AND ("Stomach Neoplasms"[Mesh] OR cancer*[tw] OR adenocarcinoma*[tw] OR neoplasm*[tw] OR tumour*[tw] OR tumour*[tw] OR tumor*[tw]) AND ("Proton Pump Inhibitors"[Mesh] OR PPI[tw] OR PPIs[tw] OR “Proton pump inhibitor*“[tw]) Filtered for: Guidelines adaptations; Meta-Analysis, Systematic Review, Randomized Controlled Trial																				

Study	**Type**	**Endpoint**	**Bias/concerns**	**Patients**	**Principal findings**	**Evidence Level¶**				**Type of study according to SIGN**								**Recommendation SIGN**			
						High	Mod	Low	Very Low	1++	1+	1-	2++	2+	2-	3	4	A	B	C	D

Ahn 2013	META	Incidence	NOS 5-8	94558	PPI: OR 1.42 (1.29-1.56); H2RA: OR 1.39 (1.19-1.64 (I2 0.0%)		x						x						x	
Gao 2022	META	Incidence	Publication bias likely	4348905	OR 1.94 (1.43-2.64), for non-cardia OR 2.53 (2.03-3.15), not confirmed vs H2RA. Risk decrease over time.		x						x						x	
Guo 2023	Syst Rev / META	Incidence	NOS 6-9 (mean 7.3), no obvious publication bias.	8066349	RR 1.82 (1.46-2.29), non-cardia: RR 2.75 (2.09-3.62), risk increase WITH duration.		x						x						x	
Jiang 2019	Syst Rev	Incidence	Publication bias not fully assessed due to only n=7 studies.	943070	OR 2.50 (1.74-3.85)		x						x						x	
Li 2017	META	Prev atrophy	No obvious publiation bias.	3068	OR 1.55 (1.00-2.41)		x						x						x	
Liu 2023	Syst Rev	Incidence	NOS 6-9	1774583	RR 2.04 (1.33-2.75)		x						x						x	
Lundell 2015	Syst Rev	Atrophy / ECL cell hyperplasia	x	1920	x		x						x						x	
Lv 2023	Syst Rev / META	Incidence atrophy / IM	Publication bias likely	1623	RR 1.90 (0.86-4.16); 4 studies with F/U >12m: RR 2.21 (1.47-3.33); AG 1.50 (0.91-2.47); IM: 1.93 (1.03-3.63)		x						x						x	
Oura 2020	Cohort	Metachroncus recurrence	x	418	HR 1.04 (0.10-1.09.		x						x						x	
Pan 2023	Syst Rev / META	Incidence	Most studies with moderate risk, NOS>6 in 10/15	x	OR 1.67 (1.39-2.00), ns for cardia		x						x						x	
Peng 2023	Syst Rev / META	Incidence	No significant publication bias.	2936935	OR 1.75 (1.28-2.40), CC 1.54 (1.30-1.84), Cohort 2,00 (1.17-3.41); Cardia ns.; No duration effect, but OR higher for <1y than for 1-3 yrs / >3yrs. Higher risk even		x						x						x	

					after eradication.															
Piovani 2022	META	Incidence	6 studies with NOS >=8,	6062231	vs H2RA: RR 1.07 (0.97-1.19; I2 38%), Cardia ns.		x						x						x	
Segna 2021	Syst Rev / META	Incidence	Significant risk of publication bias.	1662881	OR 1.94 (1.47-2.56; I2=82%); Cohort: OR 2.76 (1.56-4.88; I2 =63%); CC: OR 1.59 (1.23-2.05; I2 81%), cardia ns. Duration effect not consistent, ns.		x						x						x	
Song 2014	Syst Rev	Incidence atrophy / IM	4 with high risk, unclear in the remaining 3.	1789	atrophy: OR 1.50 (0.59-3.80); IM: OR 1.46 (0.43-5.03)		x						x						x	
Song 2021	Syst Rev / META	Survival	x	1486	longer PFS (HR 1.38 (1.03-1.85), no asscoiation with OS (0.91; 0.77-1.09)		x						x						x	
TranDuy 2016	Syst Rev / META	Incidence FGP / GC	Significnat publictaion bias for FGP, not assessed for GC.	87324	FGP OR 1.43 (1.24-1.64); GC OR 1.43 (1.23-1.66)		x						x						x	
Zhang 2022	META	Incidence	x	x	GC OR 2.07 (1.30-3.29)		x						x						x	
Zheng 2023	META	Incidence atrophy / IM	x	27283	Maintenance >6m: Atrophy OR 1.01 (0.55-1.85); IM (1.14 (0.49-2.68), GC OR 1.06 (0.79-1.43)		x						x						x	
Poly 2022	Syst Rev	Incidence	Substantial publication bias. NOS 6-9 (avrg 8.07)	x	RR 1.80 (1.46-2.22); Cohort: 1.99 (1.37-2.88);CC 1.69 (1.34-2.13); effect in Asia higher (2.07 vs 1.87 Europe, 1.27 NA)		x						x						x	

PICO	P: General population / Patients with IM/Atr I: PPI C: No PPI intake O: Incidence of GC / Incidence of IM/Atr / GC-associated mortality
Query(ies) and databases searched	Search: PubMed ("Stomach"[Mesh] OR gastric[tw] OR stomach[tw] OR gastroesophageal[tw] OR esophagogastric[tw] OR oesophagogastric*[tw]) AND ("Stomach Neoplasms"[Mesh] OR cancer*[tw] OR adenocarcinoma*[tw] OR neoplasm*[tw] OR tumour*[tw] OR tumour*[tw] OR tumor*[tw]) AND ("Proton Pump Inhibitors"[Mesh] OR PPI[tw] OR PPIs[tw] OR “Proton pump inhibitor*“[tw]) ("Stomach"[Mesh] OR gastric[tw] OR stomach[tw] OR gastroesophageal[tw] OR esophagogastric[tw] OR oesophagogastric*[tw]) AND ("Proton Pump Inhibitors"[Mesh] OR PPI[tw] OR PPIs[tw] OR “Proton pump inhibitor*“[tw]) AND (“preneoplastic condition” [Mesh] OR metaplasia[tw] OR atrophy*[tw] OR preneoplastic*[tw] OR precancerous*[tw] OR premalignant*[tw]) Filtered for: Guidelines adaptations; Meta-Analysis, Systematic Review, Randomized Controlled Trial

PICO	P: Patients after curative intended treatment of GC I: PPI C: No PPI intake O: Recurrence of GC / Incidence of metachronous GC / GC-associated mortality
Query(ies) and databases searched	Search: PubMed ("Stomach"[Mesh] OR gastric[tw] OR stomach[tw] OR gastroesophageal[tw] OR esophagogastric[tw] OR oesophagogastric*[tw]) AND ("Stomach Neoplasms"[Mesh] OR cancer*[tw] OR adenocarcinoma*[tw] OR neoplasm*[tw] OR tumour*[tw] OR tumour*[tw] OR tumor*[tw]) AND ("Proton Pump Inhibitors"[Mesh] OR PPI[tw] OR PPIs[tw] OR "Proton pump inhibitor*"[tw]) AND ("Metachronous neoplasm"[Mesh] OR metachronous[tw] OR recur*[tw]) Filtered for: Guidelines adaptations; Meta-Analysis, Systematic Review, Randomized Controlled Trial

PICO	P: General population / Patients with IM/Atr / Patients after curative intended treatment of GC I: H2RA C: No H2RA intake O: Incidence of GC / Incidence of IM/Atr / GC-associated mortality / Recurrence of GC / Incidence of metachronous GC
Query(ies) and databases searched	Search: PubMed ("Stomach"[Mesh] OR gastric[tw] OR stomach[tw] OR gastroesophageal[tw] OR esophagogastric[tw] OR oesophagogastric*[tw]) AND ("Stomach Neoplasms"[Mesh] OR cancer*[tw] OR adenocarcinoma*[tw] OR neoplasm*[tw] OR tumour*[tw] OR tumour*[tw] OR tumor*[tw]) AND (H2RA*[tw] OR "Histamin blocker"[tw] OR Ranitidine[tw] OR Famotidine[tw]) ("Stomach"[Mesh] OR gastric[tw] OR stomach[tw] OR gastroesophageal[tw] OR esophagogastric[tw] OR oesophagogastric*[tw]) AND (H2RA*[tw] OR "Histamin blocker"[tw] OR Ranitidine[tw] OR Famotidine[tw]) AND ("preneoplastic condition" [Mesh] OR metaplasia[tw] OR atrophy*[tw] OR preneoplastic*[tw] OR precancerous*[tw] OR premalignant*[tw]) ("Stomach"[Mesh] OR gastric[tw] OR stomach[tw] OR gastroesophageal[tw] OR esophagogastric[tw] OR oesophagogastric*[tw]) AND ("Stomach Neoplasms"[Mesh] OR cancer*[tw] OR adenocarcinoma*[tw] OR neoplasm*[tw] OR tumour*[tw] OR tumour*[tw] OR tumor*[tw]) AND ("H2 receptor antagonists"[Mesh] OR H2RA*[tw] OR "Histamin blocker"[tw] OR Ranitidine[tw] OR Famotidine[tw]) AND ("Metachronous neoplasm"[Mesh] OR metachronous[tw] OR recur*[tw]) Filtered for: Guidelines adaptations; Meta-Analysis, Systematic Review, Randomized Controlled Trial

Study	Type	Endpoint	Bias/concerns	Patients	Principal findings	Evidence Level¶				Type of study according to SIGN								Recommendation SIGN			
						High	Mod	Low	Very Low	1++	1+	1-	2++	2+	2-	3	4	A	B	C	D
Ahn 2013	META	Incidence	NOS 5-8	94558	PPI: OR 1.42 (1.29-1.56); H2RA: OR 1.39 (1.19-1.64 (I2 0.0%)		X							X						X	
Gao 2022	META	Incidence	Publication bias likely	4348905	OR 1.94 (1.43-2.64), for non-cardia OR 2.53 (2.03-3.15), not confirmed vs H2RA. Risk decrease over time.		X							X						X	
Jiang 2019	Syst Rev	Incidence	Publication bias not fully assessed due to only n=7 studies.	943070	OR 2.50 (1.74-3.85)		X							X						X	

Piovani 2022	META	Incidence	6 studies with NOS >=8,	6062231	vs H2RA: RR 1.07 (0.97-1.19; I2 38%), Cardia ns.		x							x						x	
Song 2014	Syst Rev	Incidence atrophy / IM	4 with high risk, unclear in the remaining 3.	1789	atrophy: OR 1.50 (0.59-3.80); IM: OR 1.46 (0.43-5.03)		x							x						x	

Sentence	**ESGE/EHMSG/ESP recommend against the use of other specific drugs or supplements (including probiotics) for chemoprevention in any clinical setting outside of clinical studies.**	
GRADE	**Strength of recommendation: Conditional**	**Quality of evidence: Low**
PICO	P: General population / Patients with IM/Atr / Patients after curative intended treatment of GC I: Statins C: No Statins intake O: Incidence of GC / Incidence of IM/Atr / GC-associated mortality / Recurrence of GC / Incidence of metachronous GC	
Query(ies) and databases searched	Search: PubMed ("Stomach"[Mesh] OR gastric[tw] OR stomach[tw] OR gastroesophageal[tw] OR esophagogastric[tw] OR oesophagogastric*[tw]) AND ("Stomach Neoplasms"[Mesh] OR cancer*[tw] OR adenocarcinoma*[tw] OR neoplasm*[tw] OR tumour*[tw] OR tumour*[tw] OR tumor*[tw]) AND ("Hydroxymethylglutaryl-CoA Reductase Inhibitors"[Mesh] OR statin*[tw] OR Hydroxymethylglutaryl-CoA Reductase Inhibitor*[tw] OR HMG-CoA Reductase Inhibitor*[tw]) ("Stomach"[Mesh] OR gastric[tw] OR stomach[tw] OR gastroesophageal[tw] OR esophagogastric[tw] OR oesophagogastric*[tw]) AND (H2RA*[tw] OR “Histamin blocker”[tw] OR Ranitidine[tw] OR Famotidine[tw]) AND ("preneoplastic condition" [Mesh] OR metaplasia[tw] OR atrophy*[tw] OR preneoplastic*[tw] OR precancerous*[tw] OR premalignant*[tw]) AND ("Hydroxymethylglutaryl-CoA Reductase Inhibitors"[Mesh] OR statin*[tw] OR Hydroxymethylglutaryl-CoA Reductase Inhibitor*[tw] OR HMG-CoA Reductase Inhibitor*[tw]) ("Stomach"[Mesh] OR gastric[tw] OR stomach[tw] OR gastroesophageal[tw] OR esophagogastric[tw] OR oesophagogastric*[tw]) AND ("Stomach Neoplasms"[Mesh] OR cancer*[tw] OR adenocarcinoma*[tw] OR neoplasm*[tw] OR tumour*[tw] OR tumour*[tw] OR tumor*[tw]) AND ("Hydroxymethylglutaryl-CoA Reductase Inhibitors"[Mesh] OR statin*[tw] OR Hydroxymethylglutaryl-CoA Reductase Inhibitor*[tw] OR HMG-CoA Reductase Inhibitor*[tw]) AND (“Metachronous neoplasm”[Mesh] OR metachronous[tw] OR recur*[tw]) Filtered for: Guidelines adaptations; Meta-Analysis, Systematic Review, Randomized Controlled Trial	

Study	**Type**	**Endpoint**	**Bias/concerns**	**Patients**	**Principal findings**	**Evidence Level¶**				**Type of study according to SIGN**								**Recommendation SIGN**			
						High	Mod	Low	Very Low	1++	1+	1-	2++	2+	2-	3	4	A	B	C	D
Ma	META	Incidence	lots of data not available, adjustments not feasible.	94558	RR 0.56 (0.35-0.90)			x							x					X	
Seo	Nat Cohort	Incidence	x	4348905	HR 0.67 (0.49-0.92)			x							x					X	

Singh	META	Incidence	No significant publication bias reported; 6 observ studies NOS >7.	8066349	OR 0.70 (0.51-0.97), adjusted 0.68 90.51-0.91), 6 high quality obs studies: OR 0.83 (0.76-0.90; I2 0%)			x							x					X	
Spence	Cohort	Mortality	Publication bias likely	943070	HR 0.83 (0.74-0.93)			x							x					X	
Su	Syst Rev / META	Incidence	>50% of good quality (NO score>8), risk of bias by observational studies	3068	RR 0.72 (0.64-0.81); Cohort: 0.77 (0.66-0.90); CC 0.61 (0.48-0.77); RCT 0.82 (0.65-1.04)			x							x					X	
Wu	META	Incidence	x	1774583	RR 0.73 (0.58-0.93), exclusion of diabetes only study: RR 0.85 (0.80-0.91); I2 0.0%			x							x					X	
Chen	META	Incidence / Mortality	x	1920	Mort: HR 0.70 (0.52-0.95)			x							x					X	
Yuan	Syst Rev / META	Incidence	low to moderate (NOS 6-8), heterogeneity and publication bias.	1623	HR 0.72 (0.53-0.97)			x							x					X	

PICO	P: General population / Patients with IM/Atr / Patients after curative intended treatment of GC I: COX2 inhibitors C: No COX2 inhibitors intake O: Incidence of GC / Incidence of IM/Atr / GC-associated mortality / Recurrence of GC / Incidence of metachronous GC
Query(ies) and databases searched	Search: PubMed ((("stomach"[Mesh] OR "stomach"[Text Word] OR "gastric"[Text Word] OR "gastroesophageal"[Text Word] OR "esophagogastric*"[Text Word] OR "oesophagogastric*"[Text Word]) AND ("cancer*"[Text Word] OR "adenocarcinoma*"[Text Word] OR "Adenocarcinoma "[Mesh] OR "neoplasm*"[Text Word] OR "neoplasms"[Mesh] OR "tumour*"[Text Word] OR "tumor*"[Text Word] OR "Precancerous conditions" [Mesh] OR (("preneoplastic*"[Text Word] OR "precancerous"[Text Word] OR "premalignant" [Text Word]) AND ("lesion*"[Text Word] OR condition*[Text Word])) OR "dysplasia"[Text Word] OR "gastritis, atrophic"[Mesh] OR ("gastritis"[All Fields] AND "atrophic"[All Fields]) OR "atrophic gastritis"[All Fields] OR "gastritis atrophic"[All Fields] OR "metaplasia"[Mesh] OR metaplasia[Text Word])) AND ("cyclooxygenase 2 inhibitor*"[All Fields] OR "cyclooxygenase-2 inhibitor*"[All Fields] OR "cyclooxygenase 2 inhibitors"[Mesh] OR "cox-2 inhibitor*"[Text Word] OR "cox2 inhibitor*"[Text Word] OR "Cyclooxygenase 2 Inhibitors"[Pharmacological Action] OR "coxibs"[text Word]) AND 2012/01:2024/03[dp]) ((("stomach"[Mesh] OR "stomach"[Text Word] OR "gastric"[Text Word] OR "gastroesophageal"[Text Word] OR "esophagogastric*"[Text Word] OR "oesophagogastric*"[Text Word]) AND ("Precancerous conditions" [Mesh] OR (("preneoplastic*"[Text Word] OR "precancerous"[Text Word] OR "premalignant" [Text Word]) AND (condition*[Text Word] OR lesion*[Text Word])) OR "gastritis, atrophic"[MeSH Terms] OR ("gastritis"[All Fields] AND "atrophic"[All Fields]) OR "atrophic gastritis"[All Fields] OR "gastritis atrophic"[All Fields] OR "metaplasia"[Mesh] OR metaplasia[Text Word])) AND ("cyclooxygenase 2 inhibitor*"[All Fields] OR "cyclooxygenase-2 inhibitor*"[All Fields] OR "cyclooxygenase 2 inhibitors"[Mesh] OR "cox-2 inhibitor*"[Text Word] OR "cox2 inhibitor*"[Text Word] OR "Cyclooxygenase 2 Inhibitors"[Pharmacological Action] OR "coxibs"[text Word]) AND ("regression"[Text Word] OR "progression"[Text Word] OR "disease progression"[Mesh]) AND 2012/01:2024/03[dp]) ((("stomach"[Mesh] OR "stomach"[Text Word] OR "gastric"[Text Word] OR "gastroesophageal"[Text Word] OR "esophagogastric*"[Text Word] OR "oesophagogastric*"[Text Word]) AND ("cancer*"[Text Word] OR "adenocarcinoma*"[Text Word] OR "Adenocarcinoma "[Mesh] OR "neoplasm*"[Text Word] OR "neoplasms"[Mesh] OR "tumour*"[Text Word] OR "tumor*"[Text Word] OR "Precancerous conditions" [Mesh] OR (("preneoplastic*"[Text Word] OR "precancerous"[Text Word] OR "premalignant" [Text Word]) AND ("lesion*"[Text Word] OR condition*[Text Word])) OR "dysplasia"[Text Word])) AND ("endoscopic mucosal resection"[Mesh] OR "Endoscopic Submucosal Dissection"[Text Word] OR "Endoscopic Resection"[Text Word]) AND ((("stomach"[Mesh] OR "stomach"[Text Word] OR "gastric"[Text Word] OR "gastroesophageal"[Text Word] OR "esophagogastric*"[Text Word] OR "oesophagogastric*"[Text Word]) AND ("Neoplasms, Second Primary"[Mesh])) OR metachronous[Text Word] OR recur*[Text Word]) AND ("cyclooxygenase 2 inhibitor*"[All Fields] OR "cyclooxygenase-2 inhibitor*"[All Fields] OR "cyclooxygenase 2 inhibitors"[Mesh] OR "cox-2 inhibitor*"[Text Word] OR "cox2 inhibitor*"[Text Word] OR "Cyclooxygenase 2 Inhibitors"[Pharmacological Action] OR "coxibs"[text Word]) AND 2012/01:2024/03[dp]) Filtered for: Guidelines adaptations; Meta-Analysis, Systematic Review, Randomized Controlled Trial

Study	Type	Endpoint	Bias/concerns	Patients	Principal findings	Evidence Level¶				Type of study according to SIGN								Recommendation SIGN			
						High	Mod	Low	Very Low	1++	1+	1-	2++	2+	2-	3	4	A	B	C	D
MacArthur TA, 2021	COX-2 Inhibitors	Incidence of early onset of gastric cancer (age <= 60 years old)	Matched CC	aOR 0.39 (0.16-0.94)				x							x					x	

Jiang YX, 2022	COX-2 Inhibitors	Regression/Progression of gastric precancerous lesions	Syst Rev / META	OR Dysplasia regression 1.95 (0.92-4.17, p=0.08), I2=80% OR Dysplasia progression 0.99 (0.68-1.43, p=0.94)	NA		x								x					x	
Arai J, 2021	COX-2 Inhibitors (Celecoxib)	Metachronous lesions	Multicenter Retrospective Cohort	AHR 0.85 (0.21-3.43, p=0.814)	NA			x							x					x	

PICO	P: General population (+diabetic population for Metformin) / Patients with IM/Atr / Patients after curative intended treatment of GC I: Metformin C: No metformin intake O: Incidence of GC / Incidence of IM/Atr / GC-associated mortality / Recurrence of GC / Incidence of metachronous GC
Query(ies) and databases searched	Search: PubMed ("Stomach"[Mesh] OR gastric[tw] OR stomach[tw] OR gastroesophageal[tw] OR esophagogastric[tw] OR oesophagogastric*[tw]) AND ("Stomach Neoplasms"[Mesh] OR cancer*[tw] OR adenocarcinoma*[tw] OR neoplasm*[tw] OR tumour*[tw] OR tumour*[tw] OR tumor*[tw]) AND ("Metformin"[Mesh] OR metformin[tw] OR biguanide[tw]) ("Stomach"[Mesh] OR gastric[tw] OR stomach[tw] OR gastroesophageal[tw] OR esophagogastric[tw] OR oesophagogastric*[tw]) AND ("Metformin"[Mesh] OR metformin[tw] OR biguanide[tw]) AND (“preneoplastic condition”[Mesh] OR metaplasia[tw] OR atrophy*[tw] OR preneoplastic*[tw] OR precancerous*[tw] OR premalignant*[tw]) Filtered for: Guidelines adaptations; Meta-Analysis, Systematic Review, Randomized Controlled Trial ("Stomach"[Mesh] OR gastric[tw] OR stomach[tw] OR gastroesophageal[tw] OR esophagogastric[tw] OR oesophagogastric*[tw]) AND ("Stomach Neoplasms"[Mesh] OR cancer*[tw] OR adenocarcinoma*[tw] OR neoplasm*[tw] OR tumour*[tw] OR tumour*[tw] OR tumor*[tw]) AND ("Metformin"[Mesh] OR metformin[tw] OR biguanide[tw]) AND (“Metachronous neoplasm”[Mesh] OR metachronous[tw] OR recur*[tw]) Filtered for: Guidelines adaptations; Meta-Analysis, Systematic Review, Randomized Controlled Trial

Study	**Type**	**Endpoint**	**Bias/concerns**	**Patients**	**Principal findings**	**Evidence Level¶**				**Type of study according to SIGN**								**Recommendation SIGN**			
						High	Mod	Low	Very Low	1++	1+	1-	2++	2+	2-	3	4	A	B	C	D
Franciosi 2013	SR	incidence/prognosis	metformin vs. other antidiabetics	6576/100701	ns & 0.83		x							x						x	
Li 2018	SR	incidence/reccurence/prognosis	metformin vs. other antidiabetics	1804479	ns		x							x						x	

Shuai 2020	SR	incidence/prognosis	metformin vs. other antidiabetics	1239082	ns (p0.051)		x							x						x	
Seo 2022	SR+meta	incidence/prognosis	metformin vs. other antidiabetics	1239082	ns (p0.051)		x							x						x	

PICO	P: General population / Patients with IM/Atr / Patients after curative intended treatment of GC I:Probiotics C: No probiotics intake O: Incidence of GC / Incidence of IM/Atr / GC-associated mortality / Recurrence of GC / Incidence of metachronous GC
Query(ies) and databases searched	Search: PubMed ((("stomach"[Mesh] OR "stomach"[Text Word] OR "gastric"[Text Word] OR "gastroesophageal"[Text Word] OR "esophagogastric*"[Text Word] OR "oesophagogastric*"[Text Word]) AND ("cancer*"[Text Word] OR "adenocarcinoma*"[Text Word] OR "Adenocarcinoma "[Mesh] OR "neoplasm*"[Text Word] OR "neoplasms"[Mesh] OR "tumour*"[Text Word] OR "tumor*"[Text Word] OR "Precancerous conditions" [Mesh] OR (("preneoplastic*"[Text Word] OR "precancerous"[Text Word] OR "premalignant" [Text Word]) AND ("lesion*"[Text Word] OR condition*[Text Word])) OR "dysplasia"[Text Word] OR "gastritis, atrophic"[MeSH Terms] OR ("gastritis"[All Fields] AND "atrophic"[All Fields]) OR "atrophic gastritis"[All Fields] OR "gastritis atrophic"[All Fields] OR "metaplasia"[Mesh] OR metaplasia[Text Word])) AND ("probiotics"[Mesh] OR "Probiotics/therapeutic use"[Mesh] OR probiotic*[Text Word]) AND 2012/01:2024/03[dp]) ((("stomach"[Mesh] OR "stomach"[Text Word] OR "gastric"[Text Word] OR "gastroesophageal"[Text Word] OR "esophagogastric*"[Text Word] OR "oesophagogastric*"[Text Word]) AND ("Precancerous conditions" [Mesh] OR (("preneoplastic*"[Text Word] OR "precancerous"[Text Word] OR "premalignant" [Text Word]) AND condition*[Text Word]) OR "gastritis, atrophic"[MeSH Terms] OR ("gastritis"[All Fields] AND "atrophic"[All Fields]) OR "atrophic gastritis"[All Fields] OR "gastritis atrophic"[All Fields] OR "metaplasia"[Mesh] OR metaplasia[Text Word])) AND ("probiotics"[Mesh] OR "Probiotics/therapeutic use"[Mesh] OR probiotic*[Text Word]) AND ("regression"[Text Word] OR "progression"[Text Word] OR "disease progression"[Mesh]) AND 2012/01:2024/03[dp]) ((("stomach"[Mesh] OR "stomach"[Text Word] OR "gastric"[Text Word] OR "gastroesophageal"[Text Word] OR "esophagogastric*"[Text Word] OR "oesophagogastric*"[Text Word]) AND ("cancer*"[Text Word] OR "adenocarcinoma*"[Text Word] OR "Adenocarcinoma "[Mesh] OR "neoplasm*"[Text Word] OR "neoplasms"[Mesh] OR "tumour*"[Text Word] OR "tumor*"[Text Word] OR "Precancerous conditions" [Mesh] OR (("preneoplastic*"[Text Word] OR "precancerous"[Text Word] OR "premalignant" [Text Word]) AND ("lesion*"[Text Word] OR condition*[Text Word])) OR "dysplasia"[Text Word])) AND ("endoscopic mucosal resection"[Mesh] OR "Endoscopic Submucosal Dissection"[Text Word] OR "Endoscopic Resection"[Text Word]) AND ((("stomach"[Mesh] OR "stomach"[Text Word] OR "gastric"[Text Word] OR "gastroesophageal"[Text Word] OR "esophagogastric*"[Text Word] OR "oesophagogastric*"[Text Word]) AND ("Neoplasms, Second Primary"[Mesh])) OR metachronous[Text Word] OR recur*[Text Word]) AND ("probiotics"[Mesh] OR "Probiotics/therapeutic use"[Mesh] OR probiotic*[Text Word]) AND 2012/01:2024/03[dp]) Filtered for: Guidelines adaptations; Meta-Analysis, Systematic Review, Randomized Controlled Trial

Study	**Type**	**Endpoint**	**Bias/concerns**	**Patients**	**Principal findings**	**Evidence Level**				**Type of study according to SIGN**								**Recommendation SIGN**			
						High	Mod	Low	Very Low	1++	1+	1-	2++	2+	2-	3	4	A	B	C	D
Yangc 2022	SR META	Inflammation	probiotics ?	NA	NA				x							x					x
Penumetcha 2021	SR	H.pylori eradiction	probiotics vs. no probiotics	11					x							x					x

Oh 2016	RCT	H.pylori eradiction	probiotics vs. no probiotics	10	NA				x							x					x

PICO	P: General population / Patients with IM/Atr / Patients after curative intended treatment of GC I: Vitamin compounds C: No vitamin intake O: Incidence of GC / Incidence of IM/Atr / GC-associated mortality / Recurrence of GC / Incidence of metachronous GC
Query(ies) and databases searched	Search: PubMed ("Stomach"[Mesh] OR gastric[tw] OR stomach[tw] OR gastroesophageal[tw] OR esophagogastric[tw] OR oesophagogastric*[tw]) AND ("Stomach Neoplasms"[Mesh] OR cancer*[tw] OR adenocarcinoma*[tw] OR neoplasm*[tw] OR tumour*[tw] OR tumour*[tw] OR tumor*[tw]) AND ("Vitamins"[Mesh] OR vitamins[tw] OR vitamin[tw]) ("Stomach"[Mesh] OR gastric[tw] OR stomach[tw] OR gastroesophageal[tw] OR esophagogastric[tw] OR oesophagogastric*[tw]) AND("Vitamins"[Mesh] OR vitamins[tw] OR vitamin[tw]) AND (“preneoplastic condition”[Mesh] OR metaplasia[tw] OR atrophy*[tw] OR preneoplastic*[tw] OR precancerous*[tw] OR premalignant*[tw]) ("Stomach"[Mesh] OR gastric[tw] OR stomach[tw] OR gastroesophageal[tw] OR esophagogastric[tw] OR oesophagogastric*[tw]) AND ("Stomach Neoplasms"[Mesh] OR cancer*[tw] OR adenocarcinoma*[tw] OR neoplasm*[tw] OR tumour*[tw] OR tumour*[tw] OR tumor*[tw]) AND ("Vitamins"[Mesh] OR vitamins[tw] OR vitamin[tw]) AND (“Metachronous neoplasm”[Mesh] OR metachronous[tw] OR recur*[tw]) Filtered for: Guidelines adaptations; Meta-Analysis, Systematic Review, Randomized Controlled Trial

Study	**Type**	**Endpoint**	**Bias/concerns**	**Patients**	**Principal findings**	**Evidence Level**				**Type of study according to SIGN**								**Recommendation SIGN**			
						High	Mod	Low	Very Low	1++	1+	1-	2++	2+	2-	3	4	A	B	C	D
Wang 2013	Trial	mortality (total)	Vitamins/Nutrition	3318	NA				x							x					x
Wang 2028	Trial	mortality (total)	Vitamins/Nutrition	29584	NA				x							x					x
Dawsey 2014	Trial NIH	incidence	Vitamins/nutrition	490593	NA				x							x					x
Guo 2020	RCT	incidence/mortality	Vitamins Garlic	1677	NA				x							x					x
Li 2019	RCT	incidence/mortality	Vitamins Garlic	1677	NA				x							x					x
Ma 2012	RCT	incidence/mortality	Vitamins Garlic	1677	NA				x							x					x
Su 2023	RCT	incidence/mortality	Garlic	3229 (total)	NA				x							x					x

Hui 2023	Review	incidence	Mix						x						x				x
Kanno 2023	RCT (AMATERASU)	secondary prevention/mortality	VitD	251	NA				x						x				x
Urashima 2019	RCT (AMATERASU)	secondary prevention/mortality	VitD	251	NA				x						x				x
Zhao 2023	SR MA	case control	VitD	1159	NA				x						x				x
Liu 2022	SR MA	case control	VitD	671	NA				x						x				x
Chen 2022	MA	incidence	VitD						x						x				x
Khayatzadeh 2015	SR MA	incidence	VitD	1652	ns 1.09				x						x				x
Kim 2023	MA observational studies	Incidence	Diet						x						x				x
Zhang 2023	Umbrella R	incidence	VitE	3299	0.76				x						x				x
Kong 2014	SR RS	incidence	VitE	1221392	0.78/0.76				x						x				x
Vingeliene 2016	SR	incidence	Citrus fruits		0.95 ns				x						x				x
Vinceti 2018	SR MA	incidence	Selenium		1.01 any/ GC 0.66 ns				x						x				x
Lei 20222	MA	preneoplastic conditions	Folic acid	1252	1.61 (favors control)				x						x				x

Sentence	**ESGE/EHMSG/ESP suggest that low dose daily aspirin can be considered for prevention of GC in selected individuals with high risk for cardiovascular events.**	
GRADE	**Strength of recommendation: Conditional**	**Quality of evidence: Low**
PICO	P: General population / Patients with IM/Atr / Patients after curative intended treatment of GC I: Aspirin C: No aspirin intake O: Incidence of GC / Incidence of IM/Atr / GC-associated mortality / Recurrence of GC / Incidence of metachronous GC	
Query(ies) and	Search: PubMed	

databases searched	((("stomach"[Mesh] OR "stomach"[Text Word] OR "gastric"[Text Word] OR "gastroesophageal"[Text Word] OR "esophagogastric*"[Text Word] OR "oesophagogastric*"[Text Word]) AND ("cancer*"[Text Word] OR "adenocarcinoma*"[Text Word] OR "Adenocarcinoma "[Mesh] OR "neoplasm*"[Text Word] OR "neoplasms"[Mesh] OR "tumour*"[Text Word] OR "tumor*"[Text Word] OR "Precancerous conditions" [Mesh] OR (("preneoplastic*"[Text Word] OR "precancerous"[Text Word] OR "premalignant" [Text Word]) AND ("lesion*"[Text Word] OR condition*[Text Word])) OR "dysplasia"[Text Word] OR "gastritis, atrophic"[MeSH Terms] OR ("gastritis"[All Fields] AND "atrophic"[All Fields]) OR "atrophic gastritis"[All Fields] OR "gastritis atrophic"[All Fields] OR "metaplasia"[Mesh] OR metaplasia[Text Word])) AND ("aspirin"[Mesh] OR "aspirin"[Text Word] OR "acetylsalicylic acid"[Text Word]) AND 2012/01:2024/03[dp]) (((("stomach"[Mesh] OR "stomach"[Text Word] OR "gastric"[Text Word] OR "gastroesophageal"[Text Word] OR "esophagogastric*"[Text Word] OR "oesophagogastric*"[Text Word]) AND ("Precancerous conditions" [Mesh] OR (("preneoplastic*"[Text Word] OR "precancerous"[Text Word] OR "premalignant" [Text Word]) AND condition*[Text Word]) OR "gastritis, atrophic"[MeSH Terms] OR ("gastritis"[All Fields] AND "atrophic"[All Fields]) OR "atrophic gastritis"[All Fields] OR "gastritis atrophic"[All Fields] OR "metaplasia"[Mesh] OR metaplasia[Text Word])) AND ("aspirin"[Mesh] OR "aspirin"[Text Word] OR "acetylsalicylic acid"[Text Word]) AND ("regression"[Text Word] OR "progression"[Text Word] OR "disease progression"[Mesh])) AND 2012/01:2024/03[dp] ((("stomach"[Mesh] OR "stomach"[Text Word] OR "gastric"[Text Word] OR "gastroesophageal"[Text Word] OR "esophagogastric*"[Text Word] OR "oesophagogastric*"[Text Word]) AND ("cancer*"[Text Word] OR "adenocarcinoma*"[Text Word] OR "Adenocarcinoma "[Mesh] OR "neoplasm*"[Text Word] OR "neoplasms"[Mesh] OR "tumour*"[Text Word] OR "tumor*"[Text Word] OR "Precancerous conditions" [Mesh] OR (("preneoplastic*"[Text Word] OR "precancerous"[Text Word] OR "premalignant" [Text Word]) AND ("lesion*"[Text Word] OR condition*[Text Word])) OR "dysplasia"[Text Word])) AND ("endoscopic mucosal resection"[Mesh] OR "Endoscopic Submucosal Dissection"[Text Word] OR "Endoscopic Resection"[Text Word]) AND ((("stomach"[Mesh] OR "stomach"[Text Word] OR "gastric"[Text Word] OR "gastroesophageal"[Text Word] OR "esophagogastric*"[Text Word] OR "oesophagogastric*"[Text Word]) AND ("Neoplasms, Second Primary"[Mesh])) OR metachronous[Text Word] OR recur*[Text Word]) AND ("aspirin"[Mesh] OR "aspirin"[Text Word] OR "acetylsalicylic acid"[Text Word]) AND 2012/01:2024/03[dp]) Filtered for: Guidelines adaptations; Meta-Analysis, Systematic Review, Randomized Controlled Trial

Study	Type	Endpoint	Bias/concerns	Patients	Principal findings	Evidence Level¶				Type of study according to SIGN								Recommendation SIGN			
						High	Mod	Low	Very Low	1++	1+	1-	2++	2+	2-	3	4	A	B	C	D
Wang P, 2024	Aspirin	Incidence (Quality of evidence, validity, and biases of existting systematic reviws and meta-analyses)	Umbrella review	Win TT,2020 OR 0.64 (0.54-0.76) , I2=96%(21 studies, 10 cohort, 11 CC)			x							x						x	
Seo SI, 2022	Aspirin	Incidence of GC	Syst Rev / META (preceded by a nationwide population-based cohort study in Korea)	OR 0.77 (0.70-0.86), I2 = 87% (13 studies, CC); HR 0.73 (0.59-0.90), I2 =61% (5 studies, Cohort) Subgroup differences: P=0.63, I2=0%)	OR 0.73 (0.56-0.95), I2 =84% (8 studies, CC); HR 0.73 (0.62-0.87), I2 =0% (3 studies, Cohort) The effect size of aspirin for the risk of gastric cancer development does not differ between Easter and Western studies (P=0.57, I2=0%)		x							x						x	

Wang L, 2021	Aspirin	Incidence Mortality	META	OR 0.67 (0.52-0.87), I2 = 96% (10 studies, Cohort) OR (>= 5 years) 0.60 (0.38-0.94), I2= 86% (3 studies, Cohort), PEgger=0.0002 OR 1.01 (0.54-1.86, 1 RTC) Cancer-specific mortality: OR 0.69 (0.43-1.10)	NA		x							x					x	
Win TT, 2020	Aspirin	Incidence	Syst Rev / META	OR 0.64 (0.54-0.76), I2=96% (21 studies) OR 0.54 (0.39-0.74) (11 CC studies) vs OR 0.77 (0.58-1.02), I2=97% (10 cohorts), Tests for subgroup differences in study design: p=0.09, I2=64%) OR Female 0.66 (0.45-0.97), I2=0% (3 studies) vs OR Male 0.86 (0.62-1.20), I2=59%, Test for subgroups difference: p=0.31, I2=1.2% OR non-cardia 0.88 (0.79-0.99), I2=68% (5 studies)	OR 0.82 (0.67-1), I2=65% vs OR Asian 3.57 (0.59-21.53), I2=97%		x							x					x	
Bosetti C, 2020	Aspirin	Incidence Mortality	Syst Rev / META	RR 0.64 (0.51-0.82), I2=91% (14 studies) RR Cohort 0.58 (0.44-0.76), I2=84% RR CC 0.63 (0.48-0.83), I2=77% RR Mortality 0.59 (0.46-0.75), PEgger = 0.685 (3 studies, cohorts) RR 5 years 0.81 (0.71-0.92) vs RR 10 years 0.65 (0.50-0.85) (8 studies)	NA		x							x					x	

Niikura R, 2019	Aspirin	Incidence Survival	Syst Rev / META	RR 0.83 (0.74-0.92) RR Death 0.80 (0.68-0.94) RR Daily use 0.65 (0.52-0.83) vs RR Weekly use 0.78 (0.61-1) RR Non-cardia 0.74 (0.58-0.94) vs RR Cardia 0.84 (0.54-1.30)	RR Europe 0.88 (0.69-1.14) vs RR North America 0.82 (0.68-0.99)		x							x					x	
Kim JE, 2021	Aspirin	Metachronous lesions in HP-negative patients	Retrospective Cohort	aHR > 5 years 1.01 (0.54-1.86, p=0.55) (adjusted to age)	NA			x							x					x	
Oura H, 2020	Aspirin	Metachronous lesions	Retrospective Cohort	aHR 0.34 (0.04-2.59)	NA			x							x					x	
Jung S, 2015	Aspirin	Metachronous lesions	Retrospective Cohort	OR 0.50 (0.17-1.67, p=0.22)	NA			x							x					x	
Arai J, 2021	Aspirin	Metachronous lesions	Multicenter Retrospective Cohort	aHR 0.91 (0.49-1.66, p=0.747)	NA			x							x					x	

Sentence	**ESGE/EHMSG/ESP suggest that patients with autoimmune gastritis should have high-quality endoscopic follow-up every 3 years to detect GC and neuroendocrine tumours.**	
GRADE	**Strength of recommendation: Conditonal**	**Quality of evidence: Low**
PICO	P: Patients with autoimmune gastritis I: Gastric precancerous lesion and gastric cancer C: Patients without autoimmune gastritis O: Risk of gastric cancer and follow-up interval	
Query(ies) and databases searched	(((autoimmune gastritis) OR (corpus restricted))) AND ("stomach neoplasms"[MeSH Terms] OR ("stomach"[All Fields] AND "neoplasms"[All Fields]) OR "stomach neoplasms"[All Fields] OR ("gastric"[All Fields] AND "cancer"[All Fields]) OR "gastric cancer"[All Fields])	
Table of evidence		

Study	**Type**	**Endpoint**	**Patients**	**Principal findings**	**Evidence Level¶**				**Type of study according to SIGN**								**Recommendation SIGN**			
					High	Mod	Low	Very Low	1++	1+	1-	2++	2+	2-	3	4	A	B	C	D
Weise 2020	Case control	GC Incidence	572	28 (4.9%) adenocarcinoma			x							x					x	
Hu 2022	Retrospective	GC Incidence	135	3.7% (5/135) single gastric low-grade dysplasia/adenoma, 9% (8/135) single or double gastric high-grade dysplasia or adenocarcinom			x							x					x	
Mahmoud 2019	Retrospective	GC Incidence	150	4.2 cases per 1000 person-years			x							x					x	
Chen 2023	Systematic Review and Case Reports	GC Incidence		0.14% per person-year 11.05 (95% CI: 6.39–19.11) for gastric cancer			x						x						x	

Sentence	**ESGE/EHMSG/ESP suggest that individuals with hereditary syndromes with increased risk of GC, endoscopic surveillance should follow recommendations for specific syndrome or according to the gastric mucosal changes, whatever is shorter.**	
GRADE	**Strength of recommendation: Conditonal**	**Quality of evidence: Very Low**

PICO	P : gastric pre-malignant conditions (atrophy, intestinal metaplasia) I :LS, FAP, PJS, JP, LFS, GAPPS, FIGC patients C: no hereditary gastric cancer syndromes O: pre-malignant lesions/gastric cancer
Query(ies) and databases searched	Search: Pubmed ("stomach neoplasms"[MeSH Terms] OR ("stomach"[All Fields] AND "neoplasms"[All Fields]) OR "stomach neoplasms"[All Fields] OR ("gastric"[All Fields] AND "cancer"[All Fields]) OR "gastric cancer"[All Fields] OR ("gastric"[All Fields] AND "dysplasia"[All Fields]) OR ("intestinal" [All Fields] AND "metaplasia" [All Fields]) OR ("gastric" [All Fields] AND "atrophy" [All Fields])) AND ("hereditary nonpolyposis"[MeSH Terms] OR "lynch syndrome"[All Fields] OR "adenomatous polyposis coli"[MeSH Terms] OR "familial adenomatous polyposis"[All Fields] OR "Peutz-Jeghers Syndrome"[Mesh]) OR "Peutz-Jeghers"[All Fields] OR "Juvenile polyposis syndrome"[Supplementary Concept] OR "Juvenile Polyposis"[All Fields] OR "Li-Fraumeni Syndrome"[Mesh] OR "Li-Fraumeni"[All Fields] OR "GAPPS"[All Fields] OR "Gastric Adenocarcinoma and Proximal Polyposis of the Stomach"[All Fields]) AND (increased[All Fields] AND ("risk"[MeSH Terms] OR "risk"[All Fields])) + Cross referencing
Table of evidence	

Author, year	Type of study; Country	Outcome	No patients, Syndrome	Summary results
Jaihwan Kim, 2020 (PMID 31319185)	Case control USA?	Identify clinical factors associated with gastric cancer in carriers of mutations that cause Lynch syndrome	3828 **Lynch** individuals included	In multivariate analysis, male sex (OR, 2.82; 95% CI, 1.48-5.38), older age (OR, 2.07 per 10 years; 95% CI, 1.64-2.61), mutations in MLH1 (OR, 6.53; 95% CI, 1.50-28.42) or MSH2 (OR, 5.23 compared to mutations in MSH6, PMS2, or EPCAM; 95% CI, 1.21-22.71), and number of first-degree relatives with gastric cancer (OR, 2.52; 95% CI, 1.42-4.45), but not second-degree relatives (OR, 1.12; 95% CI, 0.40-3.18) were independently associated with gastric cancer among carriers of pathogenic mutations.
Shria Kumar, 2020 (PMID 32859614)	Retrospective single center cohort study USA	We identified individuals who underwent upper endoscopy and those with upper GI cancers, and associated demographics, genetic testing results, and endoscopic information.	217 **Lynch** individuals underwent 660 total upper endoscopies	Precancerous upper endoscopy findings included (…) gastric intestinal metaplasia (18, 8.3%), (…) and *Helicobacter pylori* was identified in 6 (2.8%). Upper GI cancers were diagnosed in 11 individuals (3.7%), including gastric in 6. Five (1.7%) of these upper GI cancers were identified on surveillance. Of the upper GI cancers detected on surveillance, 80% (4/5) occurred within 2 years of last upper endoscopy and 80% were stage I. There were no significant differences regarding esophageal or gastric endoscopic findings in those with versus those without upper GI cancers, and overall, *Helicobacter pylori* infection was rare among this Lynch syndrome cohort.
Polymnia Galiatsatos, 2017 (PMID 29086710)	Retrospective single center cohort study Canada	This study aimed to determine the proportion of abnormal gastroscopies among patients screened, including the incidence of gastric cancer and prevalence of precursor lesions.	32 gastroscopies were performed in 21 **Lynch** patients	No gastric cancers were found. The prevalence of precursor lesions, including H. pylori gastritis (2 patients), atrophic gastritis (none), and gastric intestinal metaplasia (2 patients) was 19.05% (95% CI: 5.4-41.9) among the screened patients.
Swetlana Ladigan-Badura, 2021 (PMID 32930401)	Prospective multicenter cohort study Germany	In our study, we evaluated the effectiveness of upper GI endoscopy as an instrument for early gastric cancer (GC) detection in Lynch syndrome (LS) patients	1128 individuals with **Lynch** underwent 5176 upper GI endoscopies	In total, 49 GC in 47 patients and accordingly 2.3% of all registered LS patients were diagnosed with GC. GCs in patients undergoing regular surveillance were diagnosed significantly more often in an early-stage disease (UICC I) than GCs detected through symptoms (83% vs 25%; P = .0231). Thirty-two (68%) patients had a negative family history of GC. The median age at diagnosis was 51 years (range 28-66).

L Renkonen-Sinisalo, 2002 (PMID 12059060)	Multicenter case-control study Finland	Determine whether there are any premalignant lesions to search for in gastric surveillance in HNPCC by comparing gastric histopathology between mutation-positive and mutation-negative family members.	**Lynch** Upper GI endoscopy was performed for 73 mutation-positive and 32 mutation-negative family members.	One case of duodenal cancer was detected in the mutation-positive group, but no gastric neoplastic lesions were seen in either group. There were no differences in the occurrence of polyps, H. pylori, inflammation, activity, atrophy nor intestinal metaplasia tested with binaric, logistic, regression analysis. H. pylori 26 vs 28% Atrophy 10 vs 7% Intestinal Metaplasia 14 vs 19%
Amanda H Ceravolo, 2022 (PMID 34698909)	Retrospective single center cohort study USA	we aim to describe an EGD surveillance program for upper GI precursor lesions and cancer in LS patients	247 **Lynch** individuals	Mean age of 47.1 years (SD 12.6) at first EGD. Mean duration of follow-up was 5.7 years. Average interval between EGDs was 2.3 years. Surveillance EGD detected precursor lesions in 8 (3.2%) patients, two (0.8%) gastric cancers and two (0.8%) duodenal cancers. Two interval cancers were diagnosed: a duodenal adenocarcinoma was detected 2 years, 8 months after prior EGD and a jejunal adenocarcinoma was detected 1 year, 9 months after prior EGD.
Romain Chautard, 2021 (PMID 33916129)	Retrospective multicenter cohort study France	evaluate the prevalence and incidence of gastrointestinal lesions following upper GI endoscopy in Lynch patients.	172 **Lynch** individuals	70 neoplastic gastrointestinal lesions were diagnosed in 45 patients (26%) out of the 172 patients included. The median age at diagnosis of upper gastrointestinal lesions was 54 years. The prevalence of cancer at initial upper GI endoscopy (mean age 44 years) Gastric cancer = 4 Low-grade dysplasia = 2 Atrophy/intestinal metaplasia = 19 Follow-up in 109 patients, mean follow-up of 5 years gastric cancer = 1 high grade dysplasia = 2 low-grade dysplasia = 3 The incidence of gastric metaplasia, atrophic gastritis, gastric dysplasia, duodenal dysplasia, gastric cancer, and duodenal cancer was 26.0, 22.5, 8.7, 8.7, 1.7, and 1.7 per 1000 person-years, respectively. Of the 95 patients with normal findings at the initial UGE, none had cancer. Upper gastrointestinal lesions were more frequent after 40 years of age ($p < 0.001$). *H. pylori* infection was diagnosed in 41 patients (28%). Helicobacter pylori infection was associated with an increased prevalence of gastric, but not duodenal, lesions ($p < 0.001$).
Marya Pulaski, 2024 (PMID	Single center cohort study	we analyze consecutive individuals with LS who underwent upper endoscopic surveillance with biopsies of the gastric antrum and body being	165 **Lynch** patients	6.7% of universally biopsied individuals with LS had GIM and/or HP (5.5% GIM, 3.6% HP). GIM was detected on subsequent surveillance in 2.2% of individuals without prior GIM, which may represent either newly developed GIM or GIM that was missed on a prior

38291131)	USA	performed universally in all individuals.		upper endoscopy due to sampling error.
Raquel Ortigão, 2022 (PMID 35830349)	Retrospective single center cohort study Portugal	We conducted a retrospective cohort study to identify risk factors for gastric precancerous conditions (chronic atrophic gastritis and intestinal metaplasia) and GC in patients with LS and a case-control study to compare the prevalence of these conditions with a control group.	385 **Lynch** patients	During a median follow-up period of 48 months (interquartile range, 24-84 months), precancerous conditions were identified in 110 patients (34%) and the prevalence of advanced stages of atrophic gastritis was 3% for OLGA III/IV and 0.6% OLGIM III/IV. Family history of GC was significantly associated with OLGA III/IV (P = 0.020). Among LS patients, 10 patients (2.6%) were diagnosed with GC (incidence rate of 5/1000 persons-year). Older age and OLGA III/IV were identified as risk factors for GC (P < 0.001). When compared with controls, patients with LS had significantly higher rates of Hp infection (P = 0.035) and lower OLGA and OLGIM stages (P < 0.001 and P = 0.026, respectively).
Valérie Bonadona, 2011 (PMID 21642682)	Retrospective multicenter cohort study France		537 **Lynch** patients	Cumulative gastric cancer risk at 70 years % (95% Confidence Interval) : MLH1 : 6 [0,2-17] MSH2 : 0,2 [0-10 MSH6 0, total : 0,7 [0,08-4,4]. For the authors, the issue of gastric surveillance should be addressed. Limits of this article : no data for PMS2 pathogenic variants and no Hp status.
Pål Møller , 2017 (PMID 28754778)	Prospective multicentre cohort International (Europe)		3119 patients with **Lynch** were followed for a total of 24 475 years	Cumulative incidences at 75 years (risks) for gastric cancers was 7% (95% CI 3.5% to 10.8%) and 8% (95% CI 1.9% to 13.6%) for path_MLH1 and path_MSH2 carriers, respectively. Five-year survival for gastric cancer was at 61%. Potential bias : all patients haven't pathogenic or probably pathogenic variants
Lisette G Capelle, 2010 (PMID 19900449)	Netherlands	evaluate incidence trends and risk of developing gastric cancer among Lynch syndrome mutation carriers in a Western population	2014 **Lynch** patients	Gastric cancer was diagnosed in 32 (1.6%) subjects (male/female: 21/11), 22 (69%) of them had a negative family history of gastric cancer. The standardized incidence ratios of gastric cancer was 3.4 (95% confidence interval, 2.1-5.2) and showed a nonsignificant decline between 1970 and 2003 (P = .30). Absolute risk of developing gastric cancer also showed no significant change over time (P = .51). Lifetime risk of developing gastric cancer was 8.0% in males vs 5.3% in females (P = .02), and 4.8% and 9% for MLH1 and MSH2 carriers, respectively. None of the 378 MSH6 carriers developed gastric cancer (P = .002 vs MLH1 and MSH2 combined lifetime risk).
Mayu Kobashi, 2022 (PMID 36254079) Only abstract	Retrospective single center cohort study Case control Japan	We investigated the phenotypic expression of gastric adenoma (low-grade dysplasia) and gastric cancer (high-grade dysplasia or carcinoma) in patients with FAP and clarified their relationships to endoscopic findings	29 **FAP** patients	11 (38%) had histologically confirmed gastric neoplasms, including 23 lesions of gastric adenoma and 9 lesions of gastric cancer. Follow-up 2005-2020.

GJ Offerhaus, 1992 (PMID 1316858)	Retrospective single center cohort study USA	The incidence rate of upper gastrointestinal cancer in patients with familial adenomatous polyposis in The Johns Hopkins Registry was compared with the rate of the general population through person-year analysis with adjustment for demographics	1391 **FAP** patients, with 18679 person-years of follow-up	2 gastric adenocarcinomas; No significant increased risk was found for gastric or nonduodenal small intestinal cancer.
Kaoru Nakano, 2020 (PMID 31411765)	Retrospective single center cohort study Japan	We aimed to investigate the clinicopathological features of gastric neoplasia (GN) in FAP patients and to clarify their relationship with the endoscopic status of the background mucosa. Patients were divided into two groups according to atrophic gastritis (AG) status.	39 **FAP** patients	Gastric neoplasms were more predominant in the AG-positive group than in the AG-negative group (6/9, 66.7% vs 7/30, 23.3%; P = 0.039). All GN were intramucosal lesions and were curatively resected regardless of AG status. Median follow-up 7.5 years.
Kazuhito Sasaki, 2024 (PMID 38263336)	Retrospective multicenter cohort study Japan	clarify the changes in the incidence risk of developing gastric adenoma or gastric cancer during the lifespan of patients with FAP. The cumulative incidences and hazard rates (HRs) of gastric neoplasms were evaluated.	443 **FAP** patients	The cumulative incidence rates in 50-year-old patients with FAP were 22.8% for gastric adenoma and 7.6% for gastric cancer, respectively. The peak age for the HR of gastric adenoma was 65 years, with the highest HR (0.043). Regarding the incidence of gastric cancer, the HR increased moderately up to the age of 40 years, but the increase accelerated from the age of 50 years (HR = 0.0067).
Tatsuro Yamaguchi, 2016 (PMID 26819281	Retrospective multicenter cohort study Japan	determine the upper gastrointestinal characteristics in Japanese familial adenomatous polyposis patients	303 **FAP** patients	The median tumour risk in 50-year-old familial adenomatous polyposis patients was 55.3, 21.8, 3.8, 39.2 and 7.7% for fundic gland polyp, gastric adenoma, gastric cancer, duodenal adenoma and duodenal cancer, respectively.

Sentence	**ESGE/EHMSG/ESP suggest that patients with common variable immunodeficiency should have a high-quality endoscopy at the time of diagnosis and then should be followed up according to staging of precancerous conditions and/or presence of auto-immune gastritis.**	
GRADE	**Strength of recommendation: Conditional**	**Quality of evidence: Very Low**
PICO	P: Common variable immunodeficiency (CVID)	

	I: Gastric precancerous lesion and gastric cancer C: Patients not receiving immunosuppressive therapies O: No CVID
Query(ies) and databases searched	Search: Pubmed (((((((((cancer of stomach[MeSH Terms]) AND (common variable immunodeficiency[MeSH Terms])) OR (intestinal metaplasia)) AND (common variable immunodeficiencies[MeSH Terms])) OR (common variable immunodeficiencies[MeSH Terms])) AND (atrophic gastritis[MeSH Terms])) OR (common variable immunodeficiencies[MeSH Terms])) AND (precancerous conditions[MeSH Terms])) OR (common variable immunodeficiencies[MeSH Terms])) AND (gastric) (common variable immunodeficiencies[MeSH Terms]) AND (cancer) (common variable immunodeficiencies[MeSH Terms]) AND (gastrointestinal) + Cross referencing

Table of evidence

Study	Type	Endpoint	Bias/concerns	Patients	Principal findings	Evidence Level¶				Type of study according to SIGN								Recommendation SIGN			
						High	Mod	Low	Very Low	1++	1+	1-	2++	2+	2-	3	4	A	B	C	D
Krein P 2021	Retrospective	GC Incidence	NOS 5-8	1101	0,5%, 10/1101			X								X				X	
Milito C 2023	Prospective	GC Incidence	NOS 5-8	512	19.8% and related only to active gastritis, 20% progressed to precancerous lesions,			x								x				x	
Pulvirenti F 2018	Retrospective	GC Incidence	NOS 5-8	455	(Obs = 25; SIR = 6.4; 95%CI = 3.2–12.5).			x								x				x	

§PICO+	P: Patients receiving immunosuppressive therapies I: Gastric precancerous lesion and gastric cancer C: Patients not receiving immunosuppressive therapies O: Risk of gastric cancer
Query(ies) and databases searched	(((((((((cancer of stomach[MeSH Terms]) AND (common variable immunodeficiency[MeSH Terms])) OR (intestinal metaplasia)) AND (common variable immunodeficiencies[MeSH Terms])) OR (common variable immunodeficiencies[MeSH Terms])) AND (atrophic gastritis[MeSH Terms])) OR (common variable immunodeficiencies[MeSH Terms])) AND (precancerous

	conditions[MeSH Terms])) OR (common variable immunodeficiencies[MeSH Terms])) AND (gastric) (common variable immunodeficiencies[MeSH Terms]) AND (cancer) (common variable immunodeficiencies[MeSH Terms]) AND (gastrointestinal) + Cross referencing

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Lee IS 2012	Retrospective	Posttransplant malignancy GC Incidence	Not the primary outcome	2157	Gastric adenocarcinoma occurred 3.44 times more often in men and 8.33 times more often in women than in the same age group of the general population in Korea (176.4/100,000 in men and 67.6/100,000 in women).				X							X					X
Buell JF 2002	Retrospective	Posttransplant malignancy GC Incidence	Not the primary outcome	NA	GC was identified in 34 recipients:				X							X					X

Gruli ch AE 2007	Met aan alysi s	Postt rans plan t mali gnan cy GC Incid ence	Not the primary outcome	N A	stomach cancer (HIV/AIDS 1.90, 1.53-2.36; transplant 2.04, 1.49-2.79).				x								x				x

