Machen wir zu viel oder zu wenig?
Gastroskopie (Barrett-, Gastritis-, SMT-Kontrollen)

Linz, 30. Jänner 2020

Michael Gschwantler

Machen wir zu viel oder zu wenig?

- Barrett-Ösophagus
- Gastritis
- Submukosale Tumore des oberen GI-Traktes

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Surveillance of Barrett´s esophagus (BE)

- Endoscopic surveillance of Barrett´s esophagus is recommended.
- Biopsies should be taken from any visible lesion, in addition 4-quadrant biopsies every 2cm.
- Surveillance intervals in patients without dysplasia:

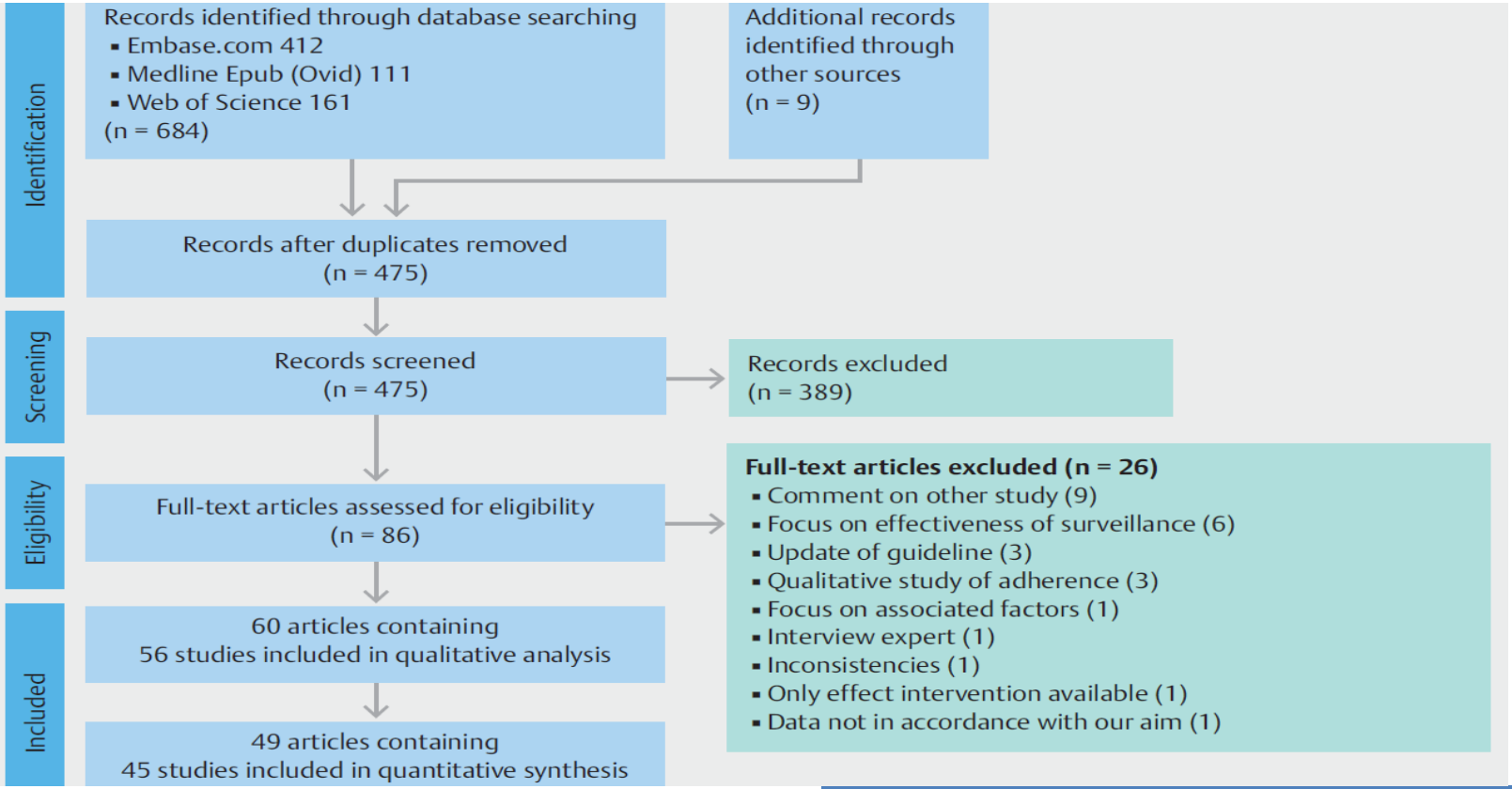
<1cm:	no endoscopic surveillance
1-3cm:	5 years
3-10cm:	3 years
≥10cm:	send to expert center

- The diagnosis of any degree of dysplasia (including „indefinite for dysplasia“) requires confirmation by an expert GI pathologist.
- Surveillance intervals in patients with dysplasia (without visible lesions):

LGD:	6 months (if no dysplasia: next control in 1 year)
HGD:	control at expert center (if negativ: control in 3 months)

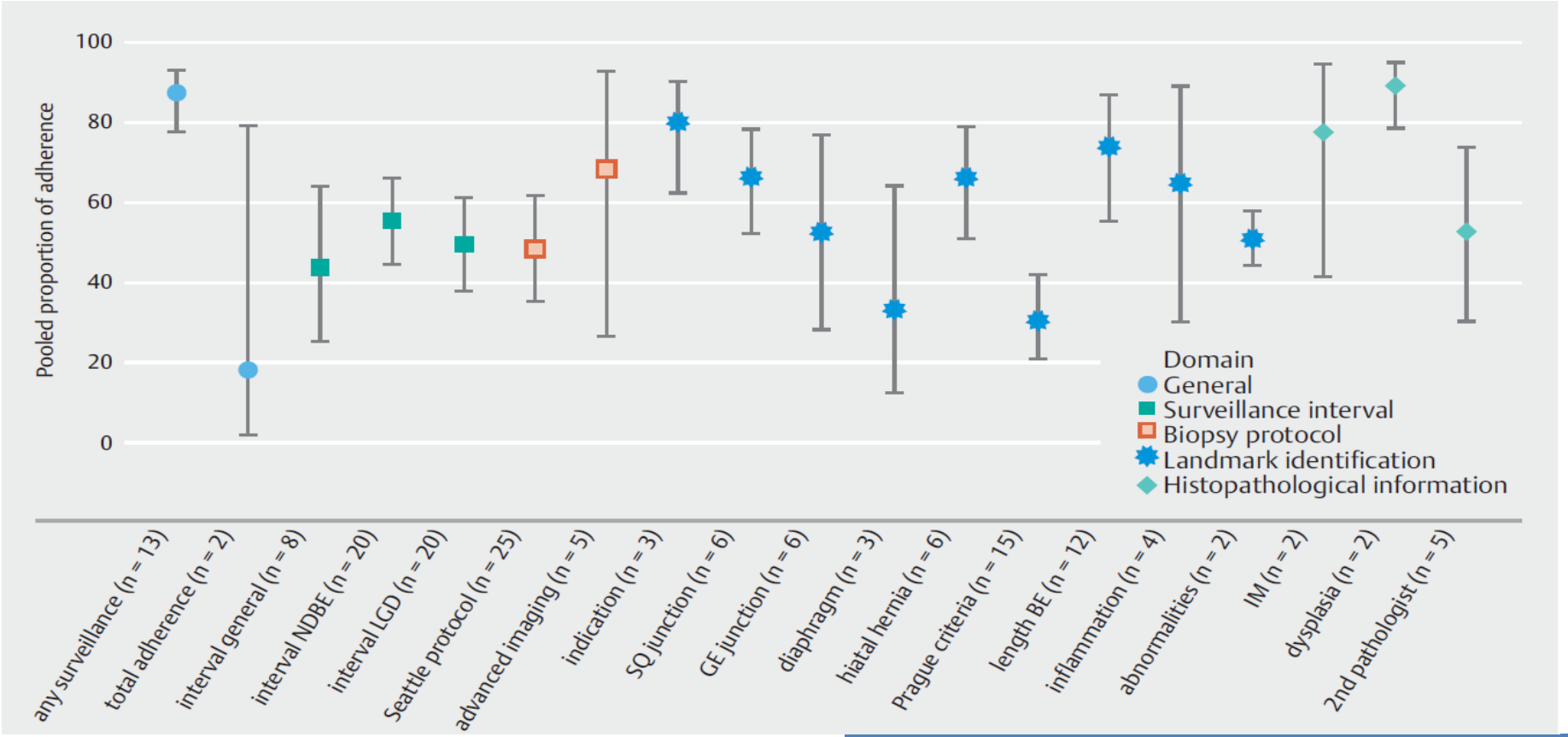
Weusten B et al. Endoscopy 2017; 49: 191-198

Adherence to recommendations of Barrett´s esophagus surveillance guidelines: a systematic review and meta-analysis



Roumans CAM et al. Endoscopy 2020; 52: 17-28

Summary of pooled proportions and 95% CI of adherence to guideline recommendations



Roumans CAM et al. Endoscopy 2020; 52: 17-28

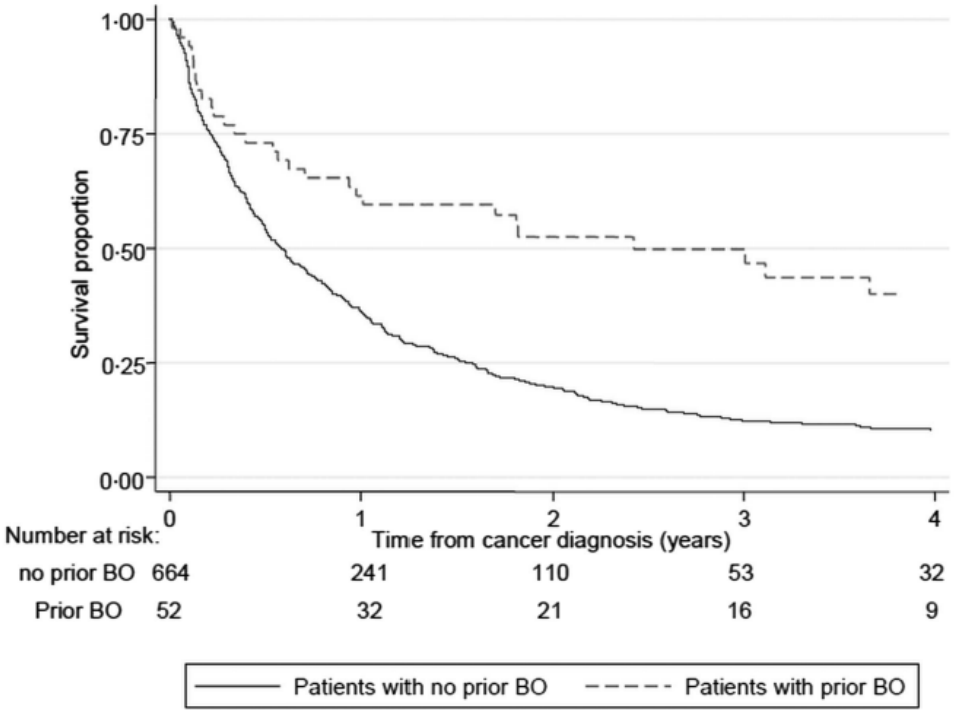
Factors associated with better adherence

- **Shorter BE** (Seattle protocol)
- **Salaried employment instead of productivity-based employment** (surveillance intervals)
- **University hospitals** (Seattle protocol and Prague classification)
- **Dedicated surveillance programs** (surveillance intervals, Seattle protocol, Prague classification)
- Younger age of endoscopist (surveillance interval and Seattle protocol)
- Physicians compared with surgeons (Prague criteria)

Roumans CAM et al. Endoscopy 2020; 52: 17-28

Does surveillance of patients with Barrett´s esophagus make sense?

- **Design:** retrospective population-based study
- **Patients:** all patients (n=716) with esophageal adenocarcinoma in Northern Ireland between 2003 and 2008; 52 patients (7.3%) had a prior diagnosis of Barrett´s esophagus (BE)
- **Primary endpoint:** Clinical outcome in patients with a prior diagnosis of BE versus patients without a diagnosis of BE



Bhat SK et al. Gut 2015; 64: 20-25

Machen wir zu viel oder zu wenig?

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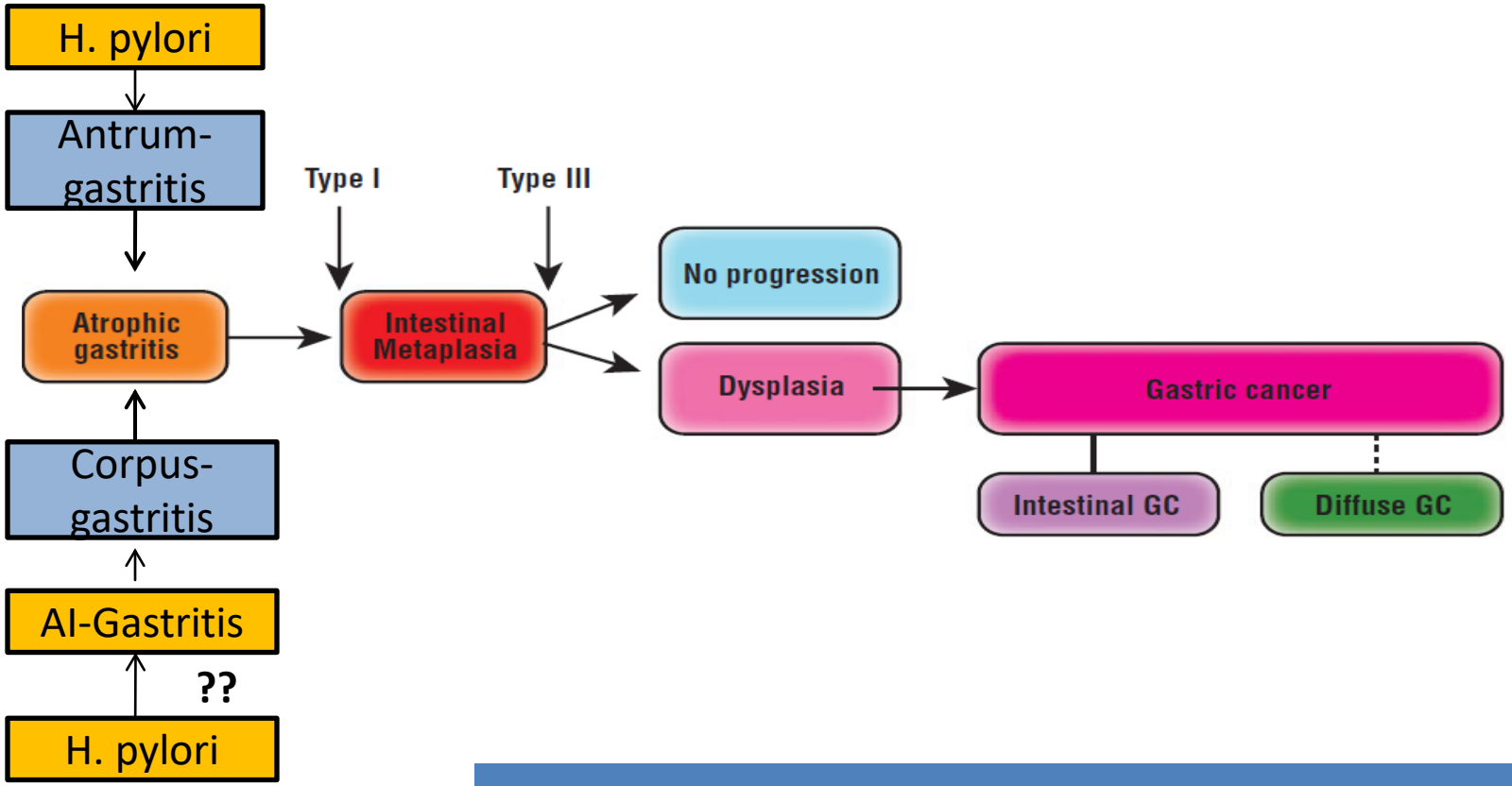
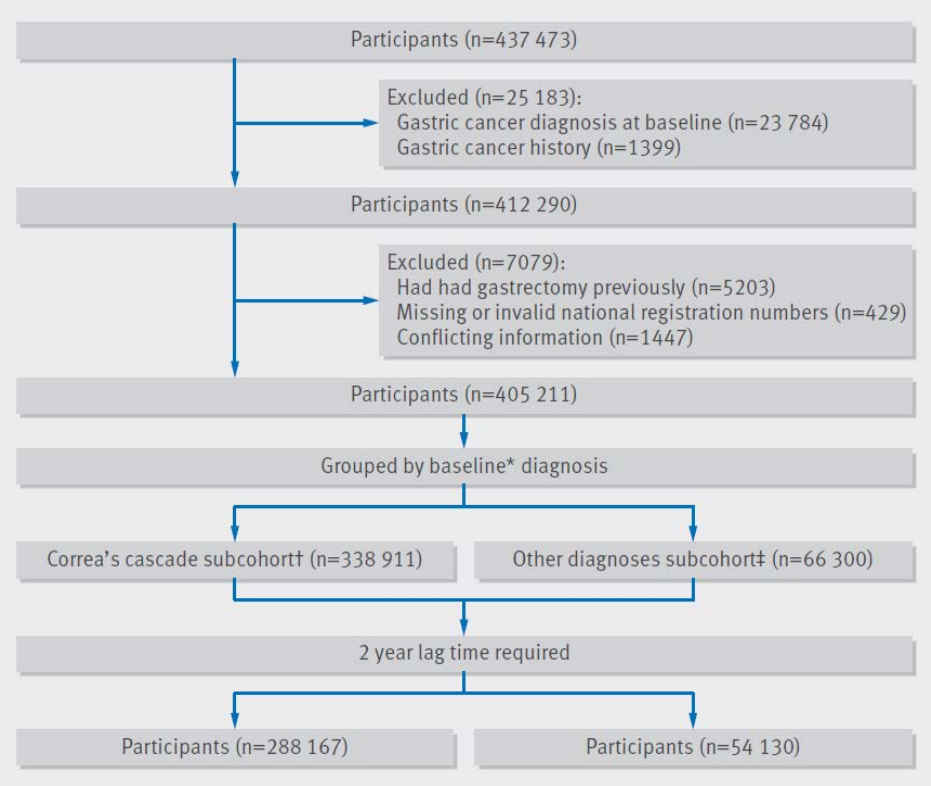
Premalignant stages of gastric cancer („Correa Cascade“)

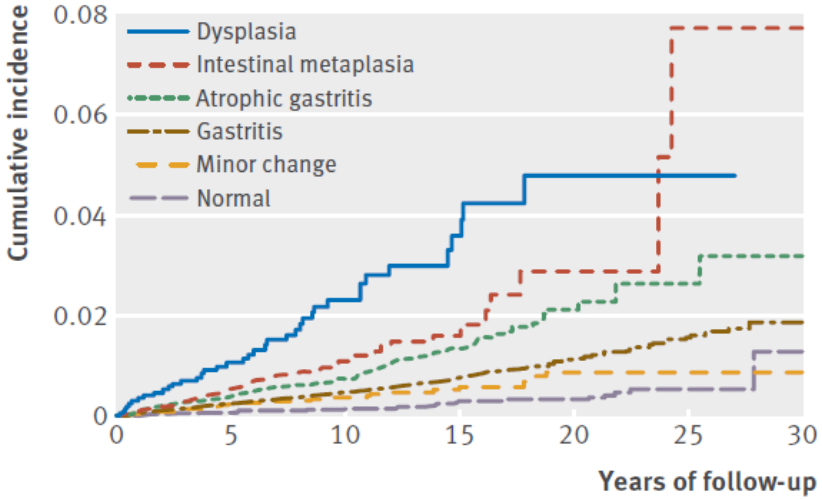


nach Busuttil RA et al. J Gastroenterol Hepatol 2009; 24: 193-201

Incidence of gastric cancer among patients with precancerous lesions

Population based cohort study from Sweden including patients who had gastric biopsy samples taken for non-malignant indications between 1979 and 2011



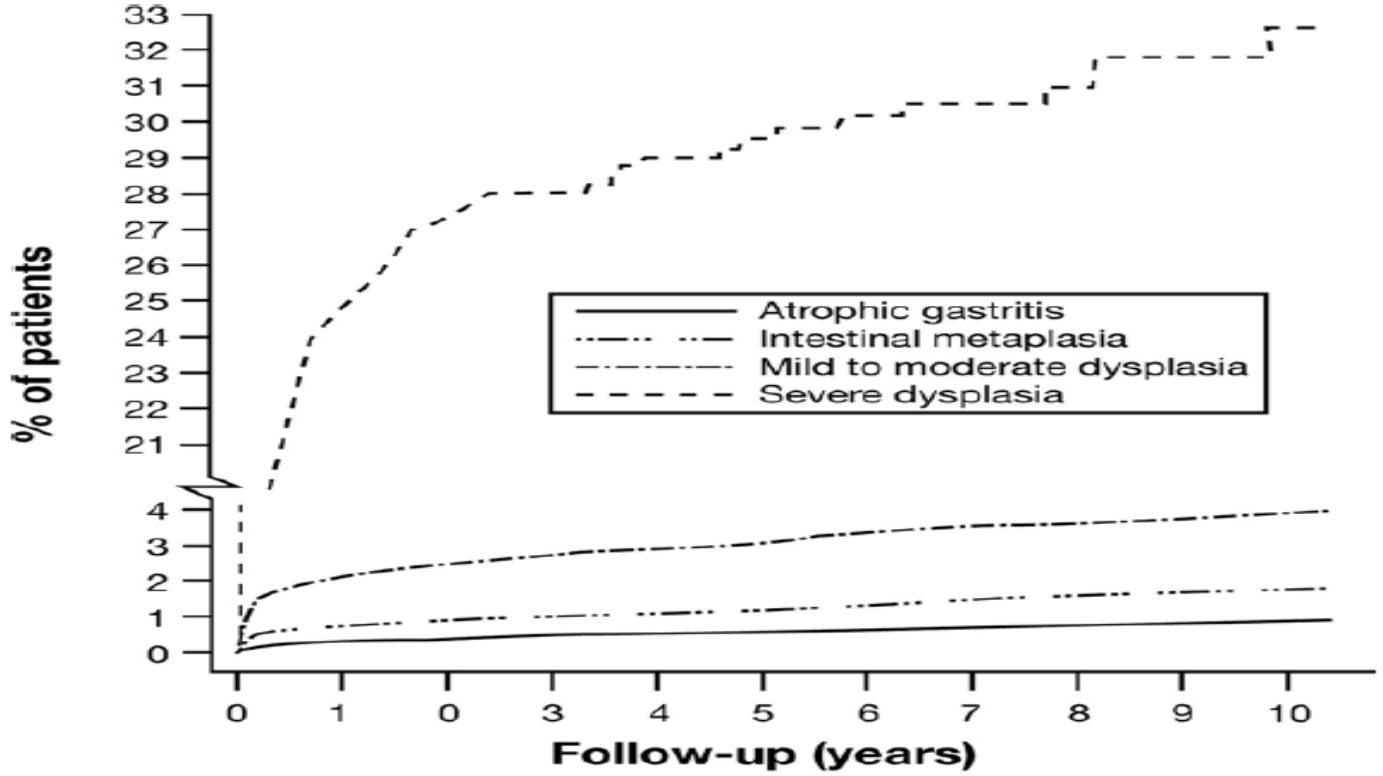


Gastric cancer within 20 years:

- normal mucosa: 1:256
- Atrophic gastritis: 1:50
- Intestinal metaplasia: 1:39
- Dysplasia: 1:19

Song H et al. BMJ 2015; 351: h3867

Progression rate of premalignant gastric lesions to gastric cancer in 92,250 patients with premalignant gastric lesions



De Vries AC et al. Gastroenterology 2008; 134: 945-952

Grading of chronic gastritis according to OLGA

(Operative Link on Gastritis Assessment)

		CORPUS			
		No Atrophy (score 0)	Mild Atrophy (score 1)	Moderate Atrophy (score 2)	Severe Atrophy (score 3)
ANTRUM	No Atrophy (score 0) (including *incisura angularis*)	STAGE 0	STAGE I	STAGE II	STAGE III
	Mild Atrophy (score 1) (including *incisura angularis*)	STAGE I	STAGE II	STAGE II	STAGE III
	Moderate Atrophy (score 2) (including *incisura angularis*)	STAGE II	STAGE II	STAGE III	STAGE IV
	Severe Atrophy (score 3) (including *incisura angularis*)	STAGE III	STAGE III	STAGE IV	STAGE IV

Rugge M et al. Human Pathology 2005; 36: 228-233-587

Grading of chronic gastritis according to OLGIM

(Operative Link on Gastric Intestinal Metaplasia Assessment)

		Corpus			
	IM score	**Not fat: no IM (score 0)**	**Mild IM (score 1)**	**Moderate IM (score 2)**	**Severe IM (score 3)**
Antrum (including incisura angularis)	No IM (score 0)	Stage 0	Stage I	Stage II	Stage II
	Mild IM (score 1)	Stage I	Stage I	Stage II	Stage III
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IM, Intestinal metaplasia; *OLGIM*, operative link on gastric intestinal metaplasia assessment.

Capelle LG et al. Gastrointest Endosc 2010; 71: 1150-1158

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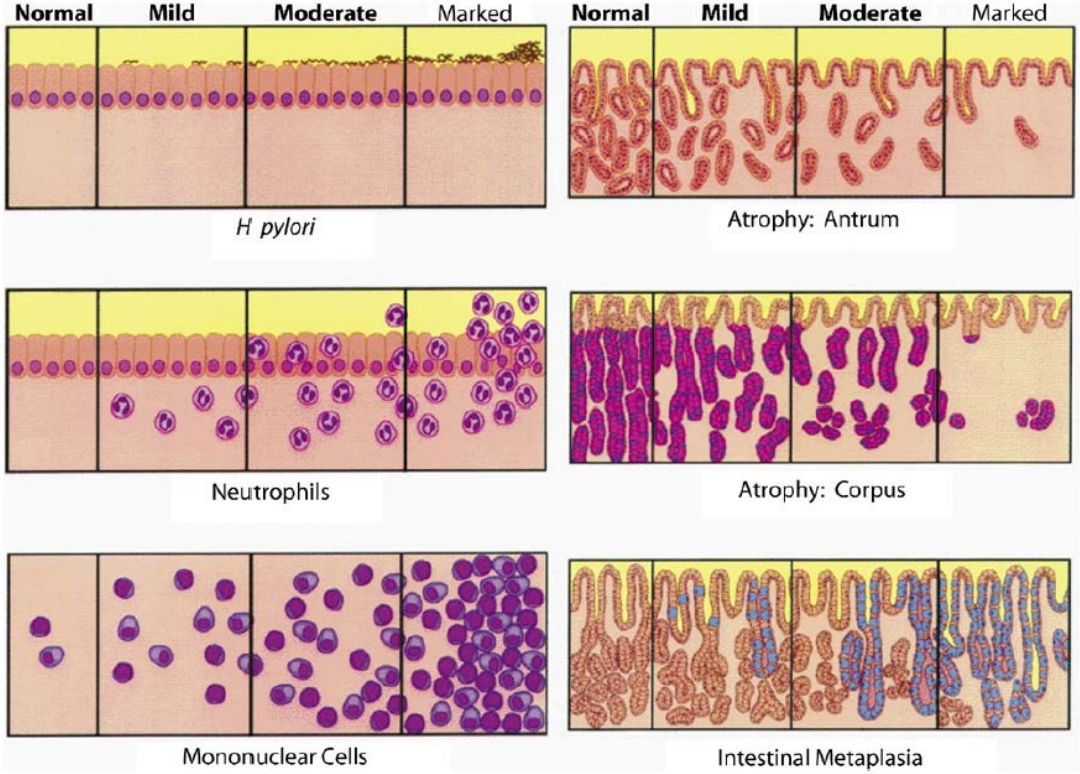


Interobserver agreement (kappa values) for different stages of the OLGA and OLGIM staging systems

Stage(s)	OLGA	OLGIM
0-IV	0.38	0.58
0	0.56	0.88
I	0.19	0.48
II	0.29	0.31
III	0.36	0.48
IV	0.48	0.59
III-IV	0.48	0.61

OLGA, operative link on gastritis assessment; *OLGIM*, operative link on gastric intestinal metaplasia assessment.

Capelle LG et al. Gastrointest Endosc 2010; 71: 1150-1158

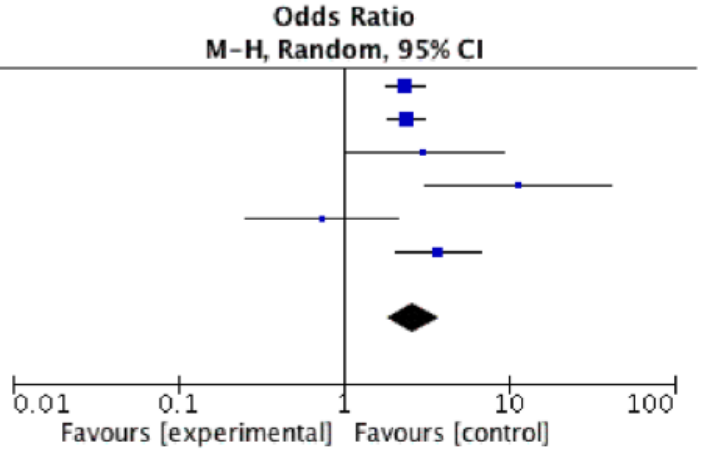
The significance of OLGA staging system in the risk assessment of gastric cancer

Forest plot of odds ratio (OR) for gastric cancer (GC) of high stage of OLGA versus low stage in case-control studies:

Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Odds Ratio M-H, Random, 95% CI
Cho 2013	219	474	126	474	29.4%	2.37 [1.81, 3.11]
Choi 2012	223	483	127	483	29.5%	2.40 [1.83, 3.15]
Kodama 2013	8	21	11	66	8.3%	3.08 [1.03, 9.18]
Satoh 2008	15	18	44	145	6.4%	11.48 [3.16, 41.66]
Tsai 2013	7	43	10	48	8.6%	0.74 [0.25, 2.15]
Zhou 2016	37	71	35	156	17.9%	3.76 [2.07, 6.85]
Total (95% CI)		**1110**		**1372**	**100.0%**	**2.64 [1.84, 3.79]**
Total events	509		353			

Heterogeneity: $Tau^2 = 0.10$; $Chi^2 = 12.53$, df = 5 (P = 0.03); $I^2 = 60\%$

Test for overall effect: Z = 5.30 (P < 0.00001)



The cumulative GC risk among patients with OLGA stage III/IV was **2.64** (95% CI 1.84-3.79; I^2=60%; n=6)

Yue H et al. Gastric Cancer 2018; 21: 579-587

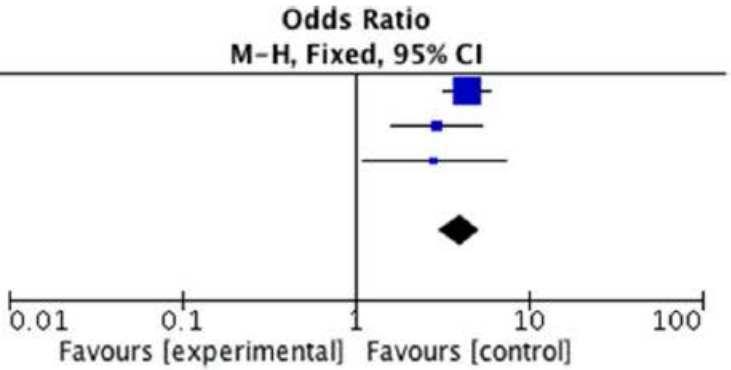
The significance of OLGIM staging system in the risk assessment of gastric cancer

Forest plot of odds ratio (OR) for gastric cancer (GC) of high stage of OLGIM versus low stage in case-control studies:

Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Cho 2013	204	474	69	474	70.6%	4.43 [3.24, 6.07]
Tsai 2013	30	71	31	156	20.1%	2.95 [1.60, 5.45]
Zhou 2016	17	43	9	48	9.2%	2.83 [1.10, 7.31]
Total (95% CI)		**588**		**678**	**100.0%**	**3.99 [3.05, 5.21]**
Total events	251		109			

Heterogeneity: $Chi^2 = 1.87$, $df = 2$ ($P = 0.39$); $I^2 = 0\%$

Test for overall effect: $Z = 10.17$ ($P < 0.00001$)

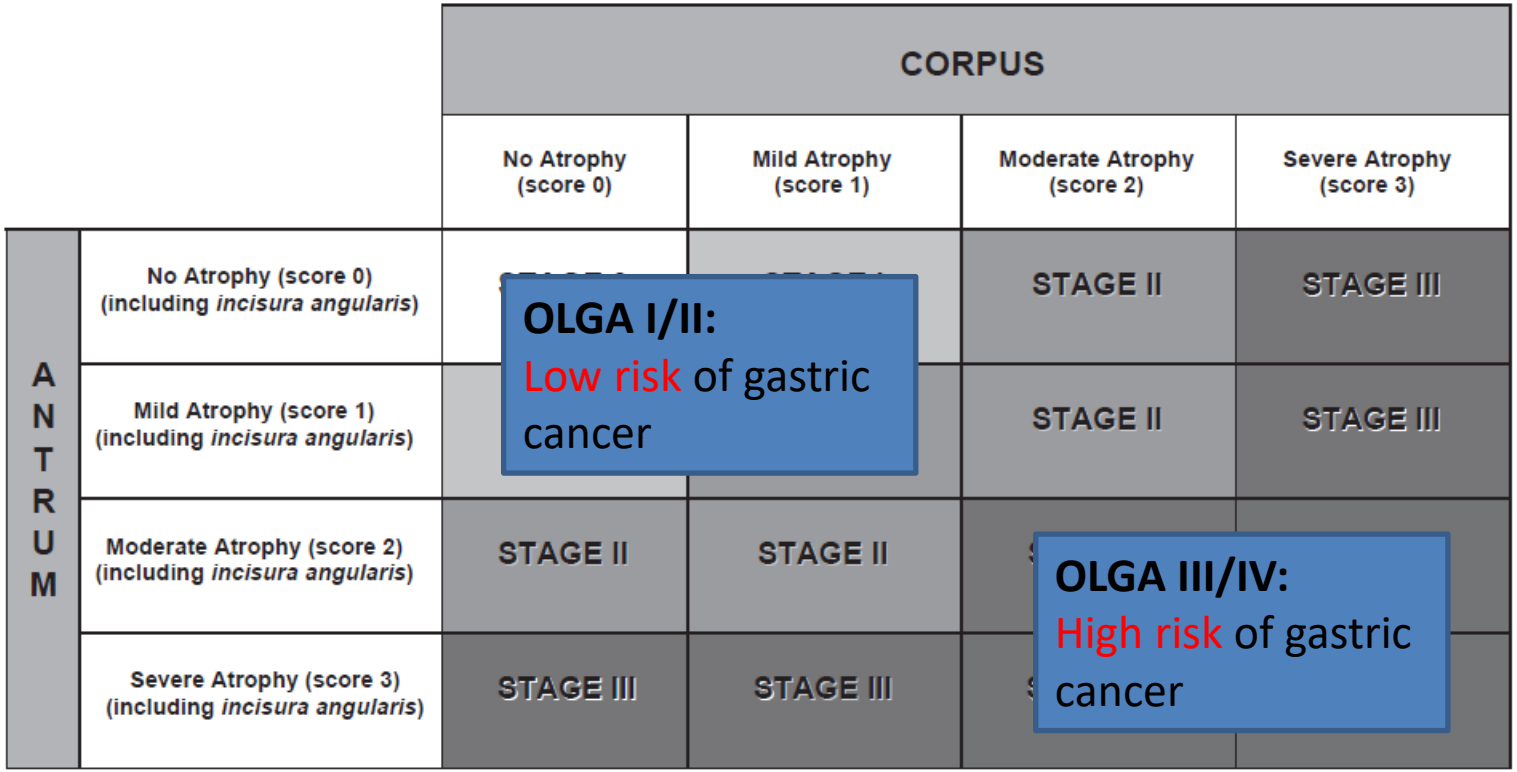


The cumulative GC risk among patients with OLGIM stage III/IV was **3.99** (95% CI 3.05-5.21; I^2=0%; n=3)

Yue H et al. Gastric Cancer 2018; 21: 579-587

Grading of chronic gastritis according to OLGA

(Operative Link on Gastritis Assessment)



ANTRUM	CORPUS: No Atrophy (score 0)	CORPUS: Mild Atrophy (score 1)	CORPUS: Moderate Atrophy (score 2)	CORPUS: Severe Atrophy (score 3)
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OLGA I/II:
Low risk of gastric cancer

OLGA III/IV:
High risk of gastric cancer

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		Corpus			
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	Mild IM (score 1)	S		St	
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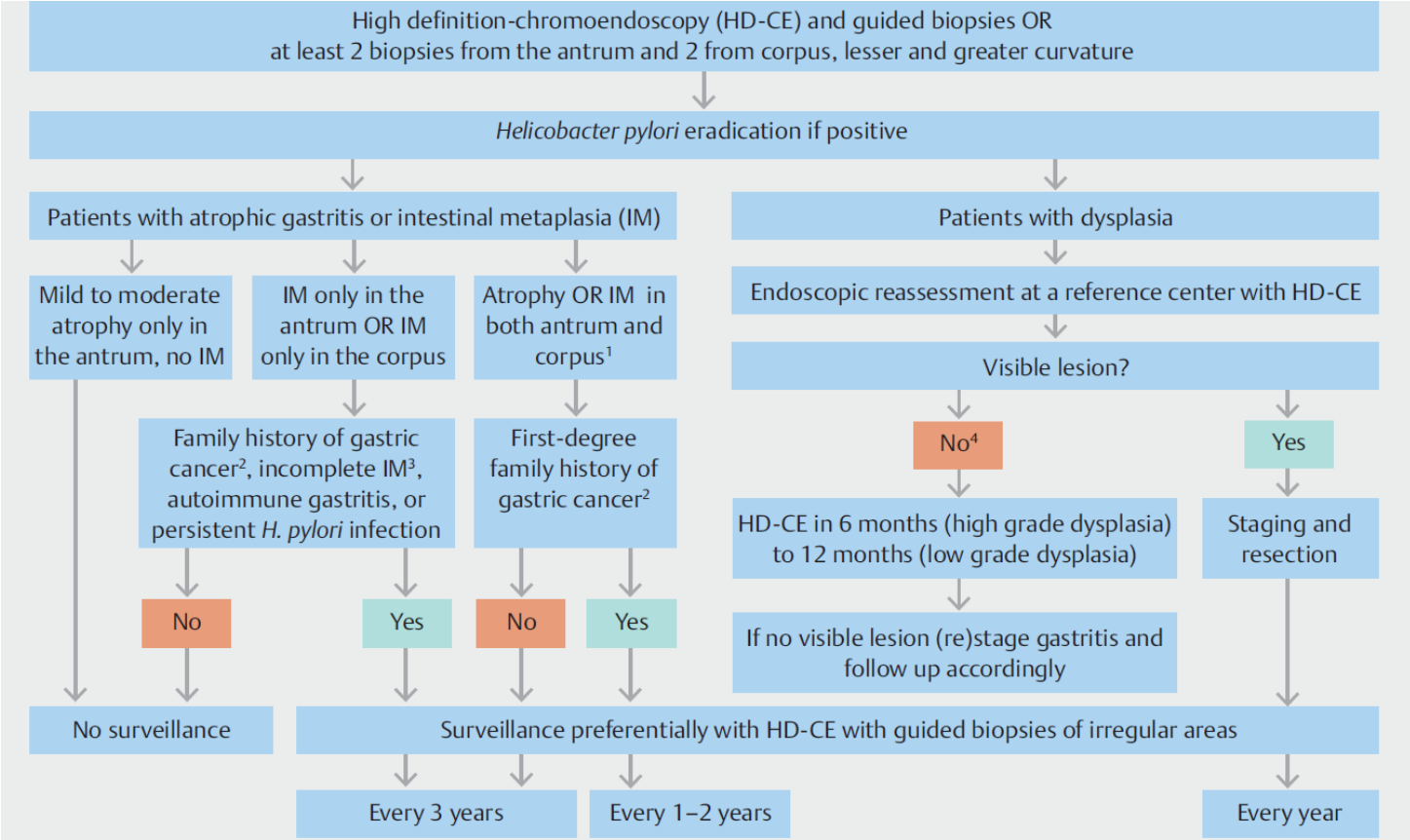
Capelle LG et al. Gastrointest Endosc 2010; 71: 1150-1158

Management of precancerous conditions in the stomach (MAPS II)



1) OLGA III/IV bzw. OLGIM III/IV

2) Recommendations do not apply to hereditary diffuse gastric cancer

3) Additional studies are required before subtyping of IM can routinely be recommended

4) Slides should be sent to an expert gastrointestinal pathologist

ESGE, EHMSG, ESP, SPED

Pimentel-Nunes P et al. Endoscopy 2019; 51: 365-388

H.p.-Eradikation 2019 bei hoher Clarithromycinresistenz

Amoxicillin 2 x 1000 mg

plus

Clarithromycin 2 x 500 mg

plus

Metronidazol 2 x 500 mg

plus

PPI 2 x 1

Therapiedauer: 14 Tage

Pylera® Kapseln

4 x 3 Kapseln täglich

(1 Kapsel = 140mg Bismuth subcitrat,

125mg Metronidazol,

125mg Tetracyclin)

plus

PPI 2 x 1

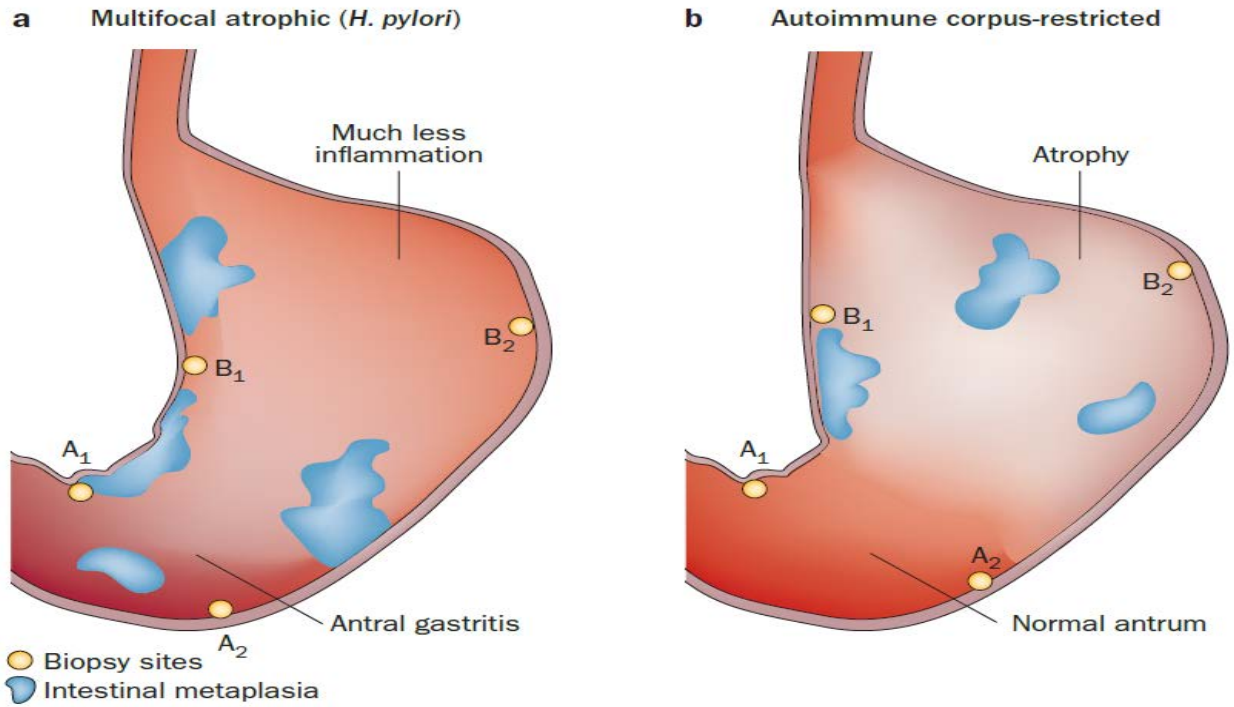
Therapiedauer: 10 Tage

Additional recommendations

- HD-endoscopy with chromoendoscopy (CE) is better than HD-white-light-endoscopy alone (alternative: virtual CE).
- Patients with a diagnosis of „indefinite for dysplasia/neoplasia“ should be promptly referred to an expert endoscopy center.
- H.p. 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; → H.p. eradication recommended.
- In patients with established IM, H.p. eradication does not appear to significantly reduce the risk of gastric cancer, but reduces inflammation and atrophy; → H.p. eradication should be considered.
- H.p. eradication reduces risk of recurrence after endoscopic resection of gastric neoplasia; → H.p. eradication recommended.

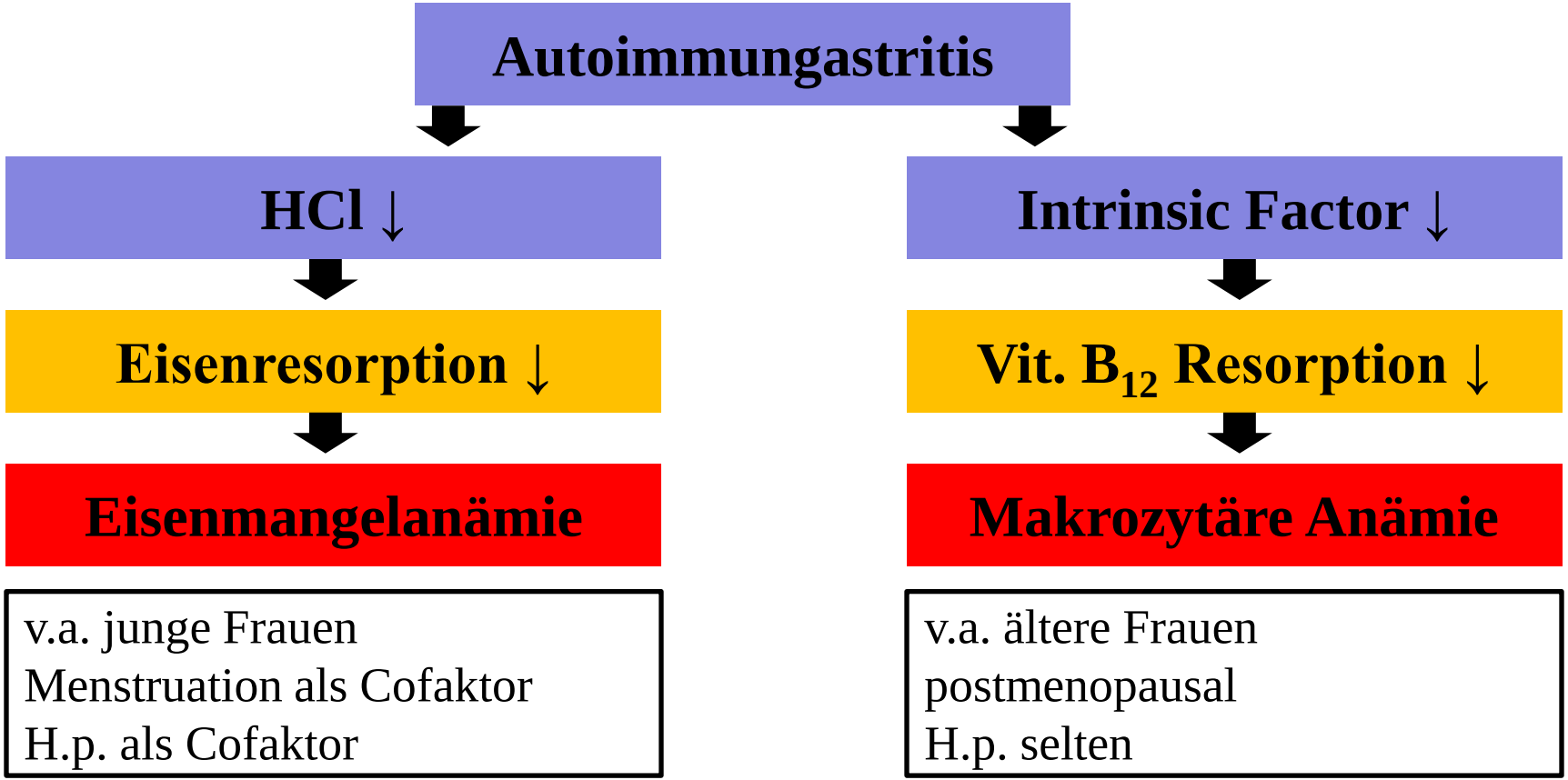
Pimentel-Nunes P et al. Endoscopy 2019; 51: 365-388

Atrophy in H.p.-gastritis versus autoimmune gastritis



Neumann WL et al. Nat Rev Gastroenterol Hepatol 2013; 10: 529-541

Autoimmungastritis und Anämie



Prävalenz der Autoimmungastritis bei Patienten mit Eisenmangelanämie

Study	Number	Prevalence of autoimmune gastritis in iron deficiency		
		Patients	Test	Prevalence (%)
Dickey et al. [3]	41	Iron deficiency anemia	Histology and pos PCA/IFA	15
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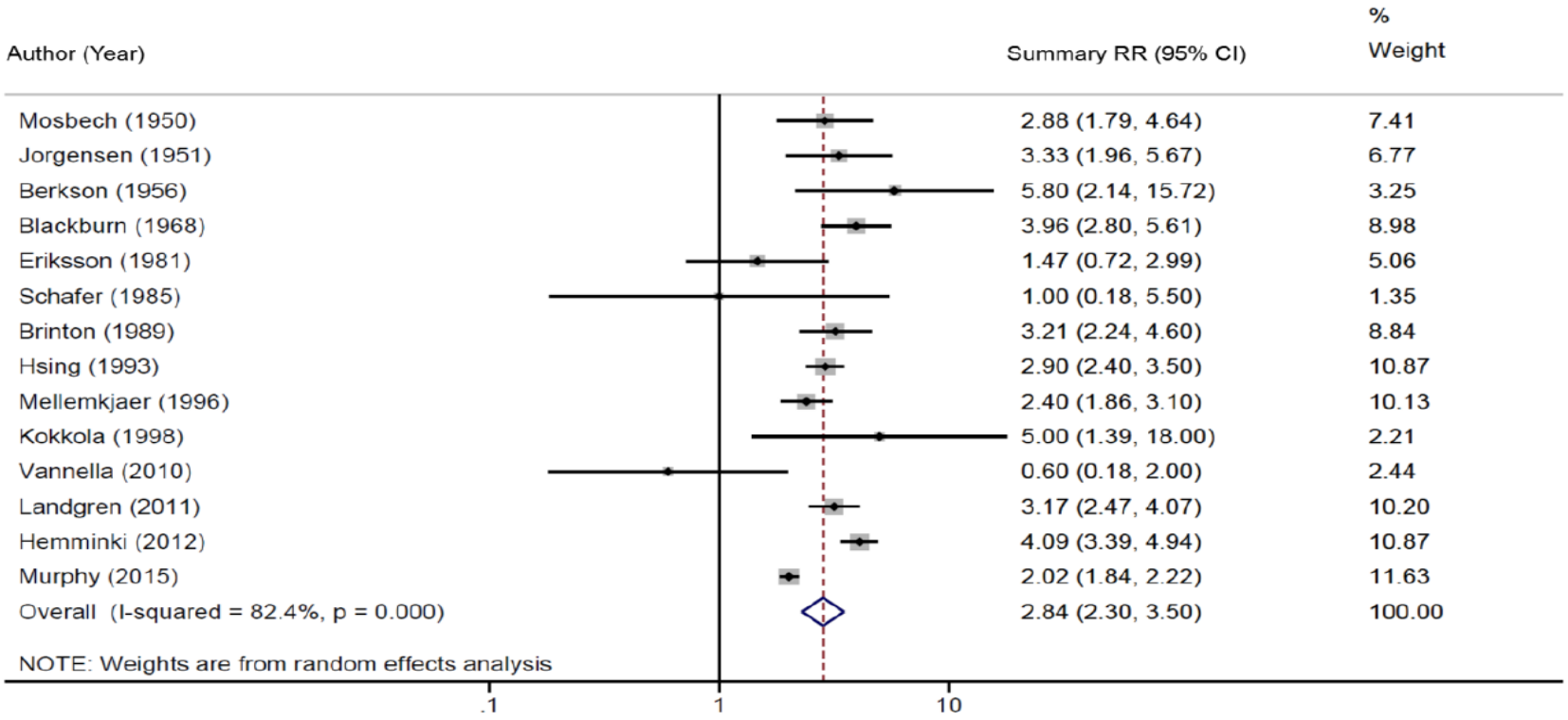
Kaye et al. [26]	156 44	Iron deficiency anemia	Histology (body atrophy) Pos PCA	26 27
Kulnigg-Dabsch et al. [27]	409	Iron deficiency	Pos PCA	19

PCA parietal cell antibodies, IFA intrinsic factor antibodies, *pos* positive

Kulnigg-Dabsch S et al. Wien Med Wochenschr 2016; 166: 424-430

Realtive risk (RR) and 95% confidence interval (CI) for gastric cancer among individuals with pernicious anemia



Song M et al. Cancer Res Treat 2019: in press

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- H.p. eradication reduces risk of recurrence after endoscopic resection of gastric neoplasia; → H.p. eradication recommended.
- **Patients with autoimmune gastritis may benefit from endoscopic follow-up every 3-5 years.**

Pimentel-Nunes P et al. Endoscopy 2019; 51: 365-388

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Subepithelial lesions of the upper GI tract

- **GI stromal tumors:** most common mesenchymal neoplasm of the GI-trakt, 95% CD117-pos, relevant malignant potential

TABLE 3. Gastric GI stromal tumors: proposed guidelines for assessing the malignant potential[28]

Tumor size	Mitotic rate	Predicted biologic behavior
≤2 cm	≤5 mitoses/50 HPF	Metastasis rate or tumor-related mortality: 0 metastasis
	>5 mitoses/50 HPF	rate or tumor-related mortality: <4%
>2 cm ≤5 cm	>5 mitoses/50 HPF	Metastasis rate or tumor-related mortality: 16%
>2 cm ≤10 cm	≤5 mitoses/50 HPF	Metastasis rate or tumor-related mortality: <4%
>5 cm ≤10 cm	>5 mitoses/50 HPF	Metastasis rate or tumor-related mortality: 55%
>10 cm	≤5 mitoses/50 HPF	Metastasis rate or tumor-related mortality: 12%
>10 cm	>5 mitoses/50 HPF	Metastasis rate or tumor-related mortality: 86%

HPF, High-power field.

Faulx AL et al. Gastrointest Endosc 2017; 85: 1117-1132

Subepithelial lesions of the upper GI tract

- **GI stromal tumors:** most common mesenchymal neoplasm of the GI-trakt, 95% CD117-pos, relevant malignant potential
- **Leiomyoma:** CD117-neg, pos for desmin and α-smooth muscle actin, very low malignant potential
- **Lipoma:** „pillow sign“, negible malignant potential
- **GI neuroendocrine neoplasms:** malignant potential depending on etiology
- **Pancreatic rests:** often found along the greater curve of the stomach
- **Granular cell tumor:** arise from Schwann cells, staining pos for S-100, very low malignant potential
- **Duplication cyst**
- **Metastasis**
- **Glomus tumor**

Faulx AL et al. Gastrointest Endosc 2017; 85: 1117-1132

NEN des Magens – Klassifikation nach Rindi

Typ 1: 70-80%

- Assoziiert mit atropher Gastritis, oft mit perniziöser Anämie (65%), selten mit Helicobacter pylori
- Oft multipel, meist < 1cm, meist im Fundus und Corpus
- Meist Polypen mit kleinem zentralen Ulkus
- Meist hoch differenziert
- Pos. für CgA (Chromogranin A) und VMAT 2 (vesikulärer Monoamintransporter), keine Hormonproduktion
- Begleitend ECL-Zell Hyperplasie in Fundus und Corpus sowie G-Zell-Hyperplasie in Antrum und Pylorusbereich

Typ 2: 5%

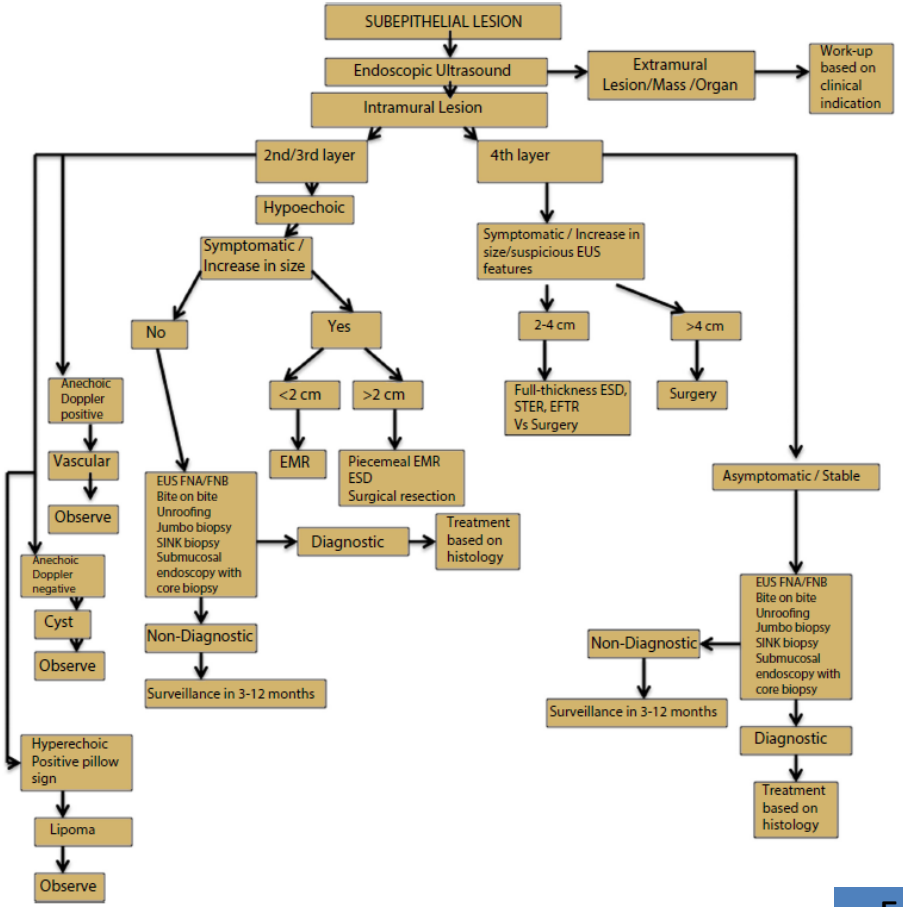
- Assoziiert mit Gastrinom (Zollinger-Ellison) oder MEN Typ 1
- Oft assoziiert mit Mutationen im Genlokus MEN1 (Tumor Suppressor Gen auf Chromosom 11q13)
- Meist hoch differenziert
- Hypertrophe Schleimhaut in Corpus und Fundus mit ECL-Hyperplasie

Typ 3: 20%

- Sporadisch, meist solitär, meist > 2 cm
- Am aggressivsten, meist G2, häufig Lebermetastasen (50-100%)

Rindi G et al. Gastroenterology 1993; 104: 994-1006

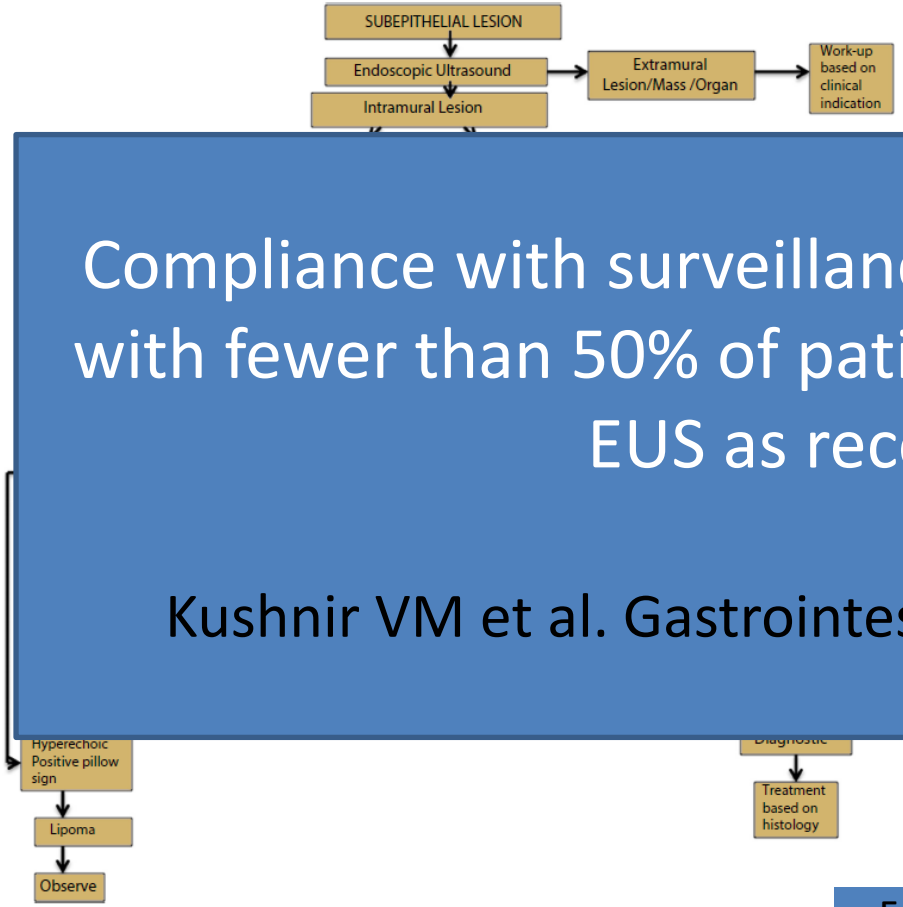
Management of subepithelial lesions of the GI tract



- Surveillance EUS for gastric GI stromal tumors <2cm (without high-risk features) in 6-12 month intervals
- Surgery for gastric GI stromal tumors >2cm and those with high-risk features
- Leiomyomas and lipomas do not require endoscopic surveillance or therapy unless symptomatic
- Firm, round subepithelial lesions with central umbilication along the greater curve of the antrum of the stomach be considered diagnostic for a pancreatic rest

Faulx AL et al. Gastrointest Endosc 2017; 85: 1117-1132

Management of subepithelial lesions of the GI tract



- Surveillance EUS for gastric GI stromal tumors <2cm (without high-risk features) in 6-12 month

Compliance with surveillance recommendations is poor, with fewer than 50% of patients undergoing surveillance EUS as recommended.

Kushnir VM et al. Gastrointest Endosc 2015; 81: 1378-1384

for a pancreatic rest

Faulx AL et al. Gastrointest Endosc 2017; 85: 1117-1132

Take Home Messages

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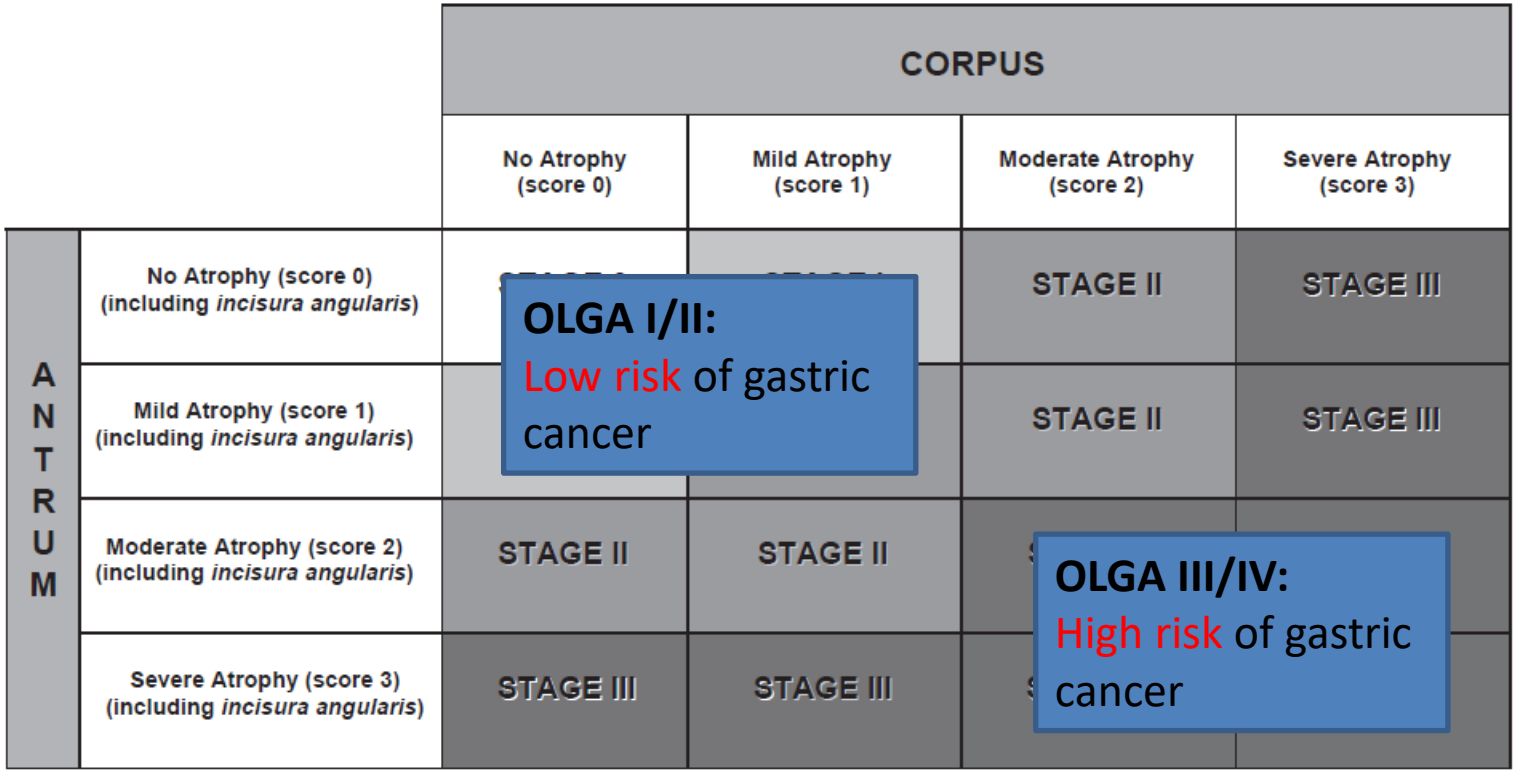

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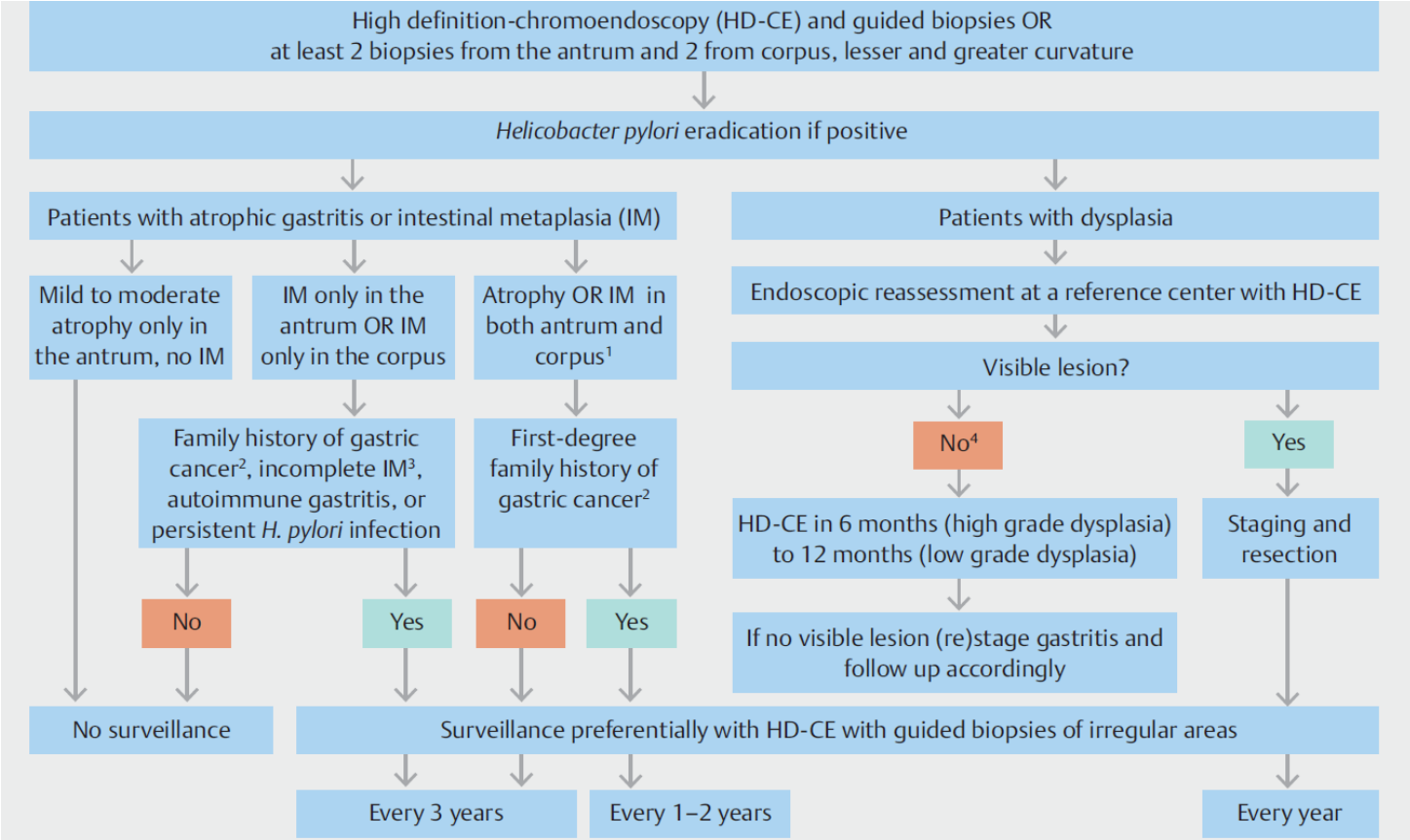
Kaye et al. [26]	156 44	Iron deficiency anemia	Histology (body atrophy) Pos PCA	26 27
Kulnigg-Dabsch et al. [27]	409	Iron deficiency	Pos PCA	19

PCA parietal cell antibodies, IFA intrinsic factor antibodies, *pos* positive

Kulnigg-Dabsch S et al. Wien Med Wochenschr 2016; 166: 424-430

Management of precancerous conditions in the stomach (MAPS II)



1) OLGA III/IV bzw. OLGIM III/IV

2) Recommendations do not apply to hereditary diffuse gastric cancer

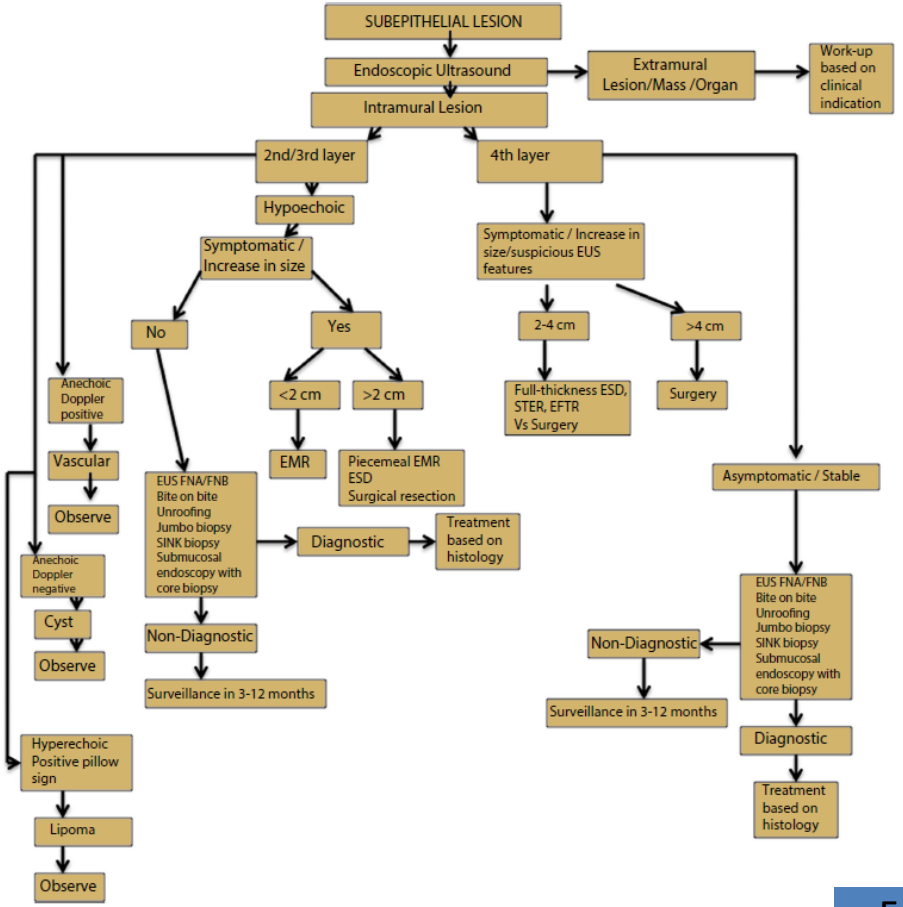
3) Additional studies are required before subtyping of IM can routinely be recommended

4) Slides should be sent to an expert gastrointestinal pathologist

ESGE, EHMSG, ESP, SPED

Pimentel-Nunes P et al. Endoscopy 2019; 51: 365-388

Management of subepithelial lesions of the GI tract



- Surveillance EUS for gastric GI stromal tumors <2cm (without high-risk features) in 6-12 month intervals
- Surgery for gastric GI stromal tumors >2cm and those with high-risk features
- Leiomyomas and lipomas do not require endoscopic surveillance or therapy unless symptomatic
- Firm, round subepithelial lesions with central umbilication along the greater curve of the antrum of the stomach be considered diagnostic for a pancreatic rest

Faulx AL et al. Gastrointest Endosc 2017; 85: 1117-1132