

Sociedad Venezolana de gastroenterología, Sección de Educación
Febrero 3, 2023

Cáncer Gástrico y *Helicobacter pylori*: ¿Cuál es el impacto práctico de esta relación?



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Universidad Nacional de Colombia
Hospital Universitario Nacional de Colombia

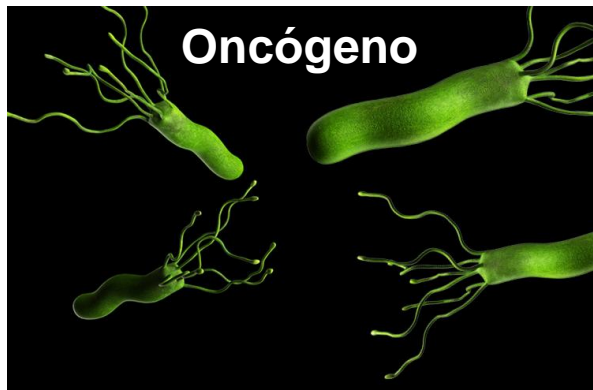


Cáncer Gástrico

**5^o cáncer más común
3^a causa muerte por cáncer
Llegan avanzados**



Globocan. Available from: <https://gco.iarc.fr/>. 2018



H.pylori
OMS IARC1994/2009
Carcinógeno tipo I

60% mundo
Tiene *H.pylori*

1.220.000 casos
2017
800.000 muertes

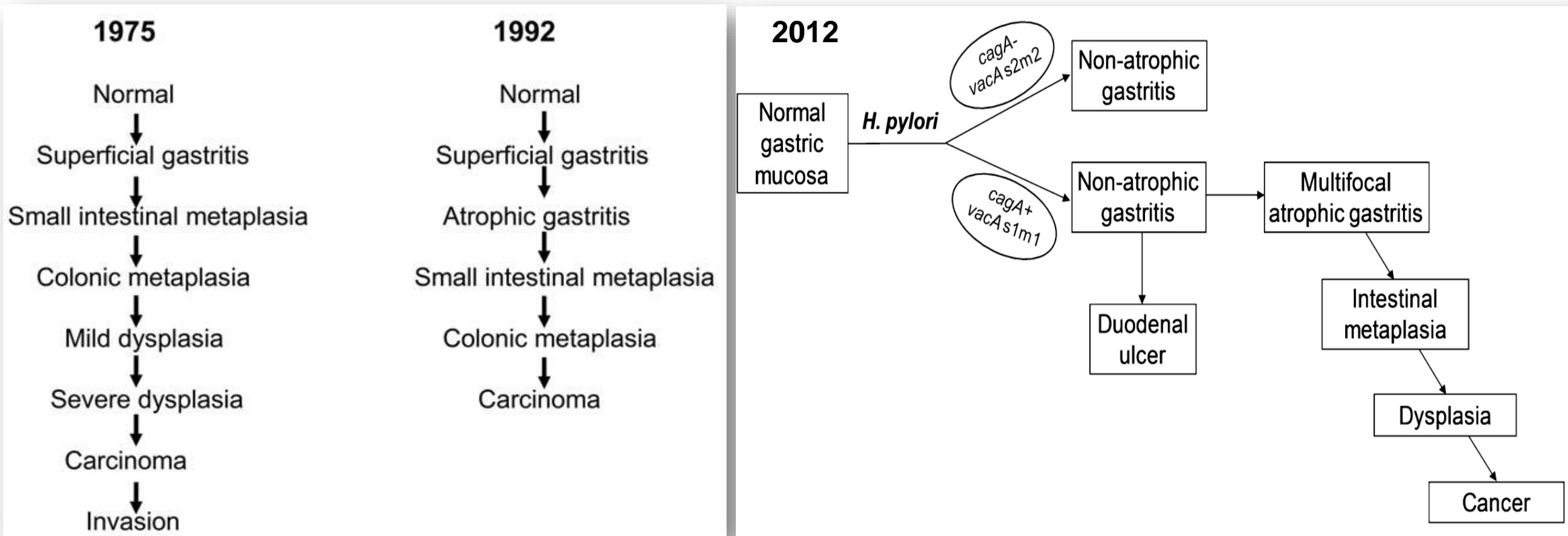
1-3%

Riesgo atribuible
Global 85-90%
Japón Korea 90-95%

Graham DY, Gastroenterology 2015;148:719-31
Tsuda M, Helicobacter 2017;e12415

Lancet Gastroenterol Hepatol 2020;5:42-54
Global Burden Disease. JAMA Oncol 2017;3:524-41

Cascadas de Correa 1975-2012

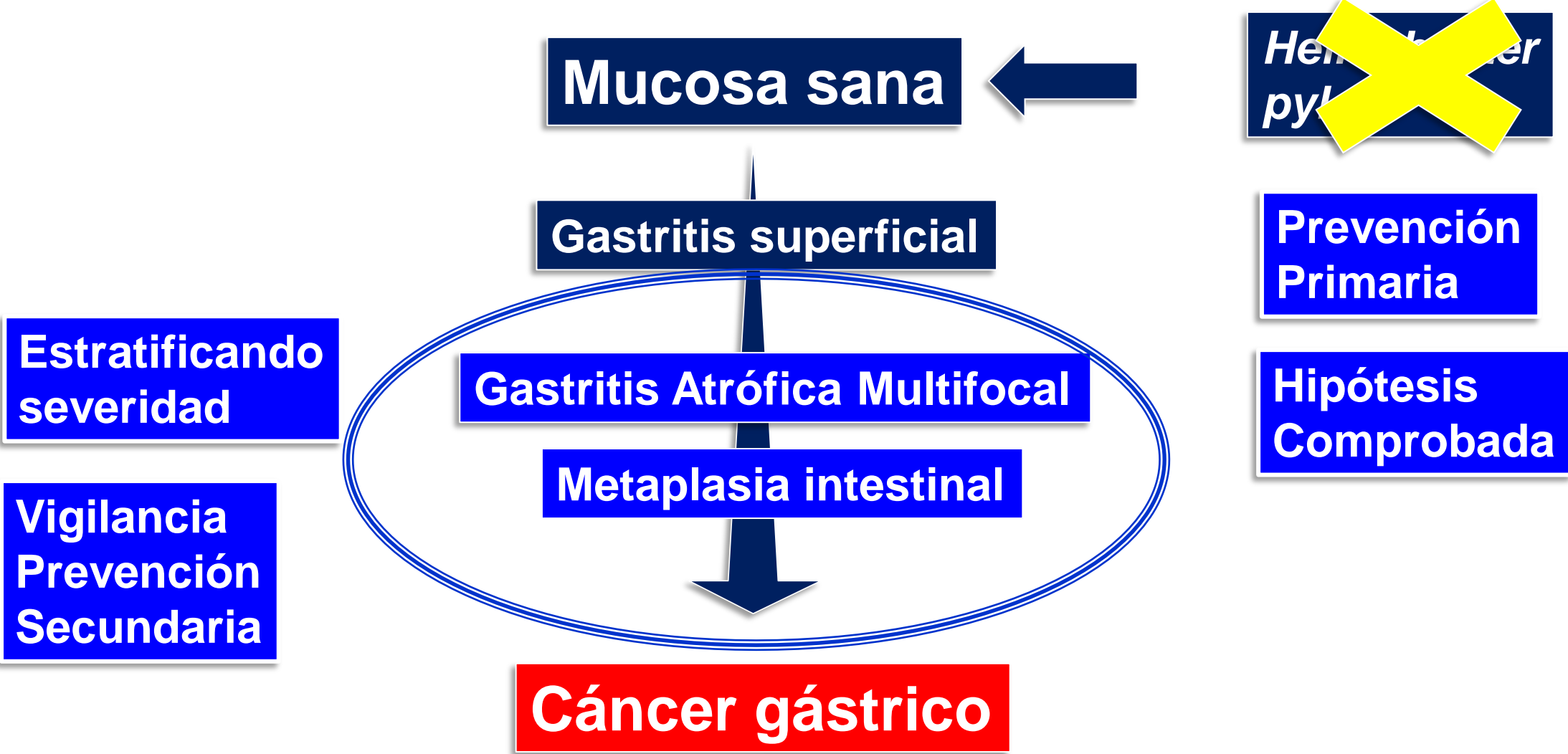


Correa P,
Lancet 1975; 2:58–60.

Correa P.
Cancer Res 1992; 52:6735–6740.

Correa P, J Dig Dis 2012;13: 2–9

Cáncer Gástrico modelo Pelayo Correa



Erradicación *H.pylori*
Prevención primaria



 ***cáncer gástrico***

Evidencias 2023

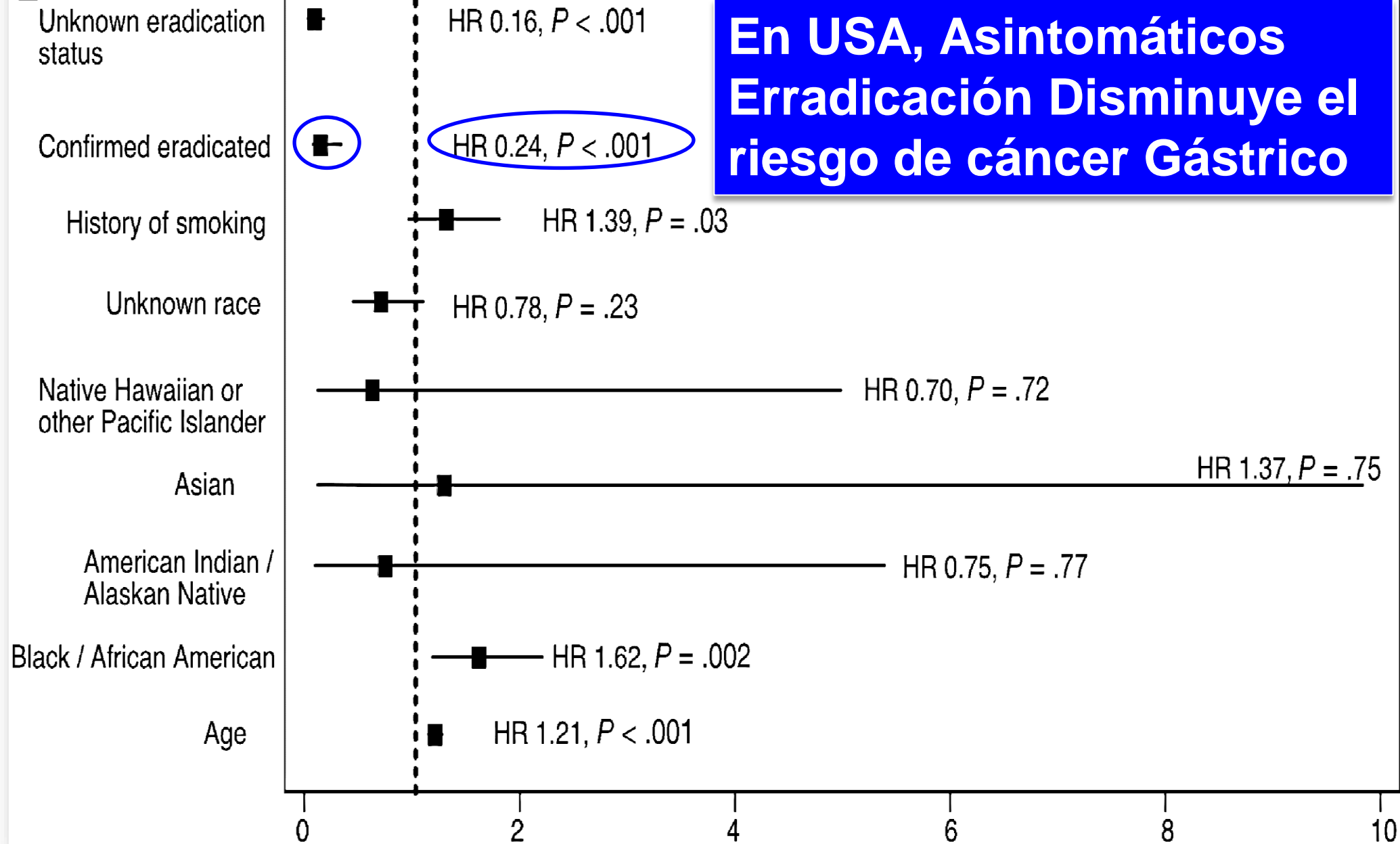
CC Cohorte ECC MA

Risk Factors and Incidence of Gastric Cancer After Detection of *Helicobacter pylori* Infection: A Large Cohort Study



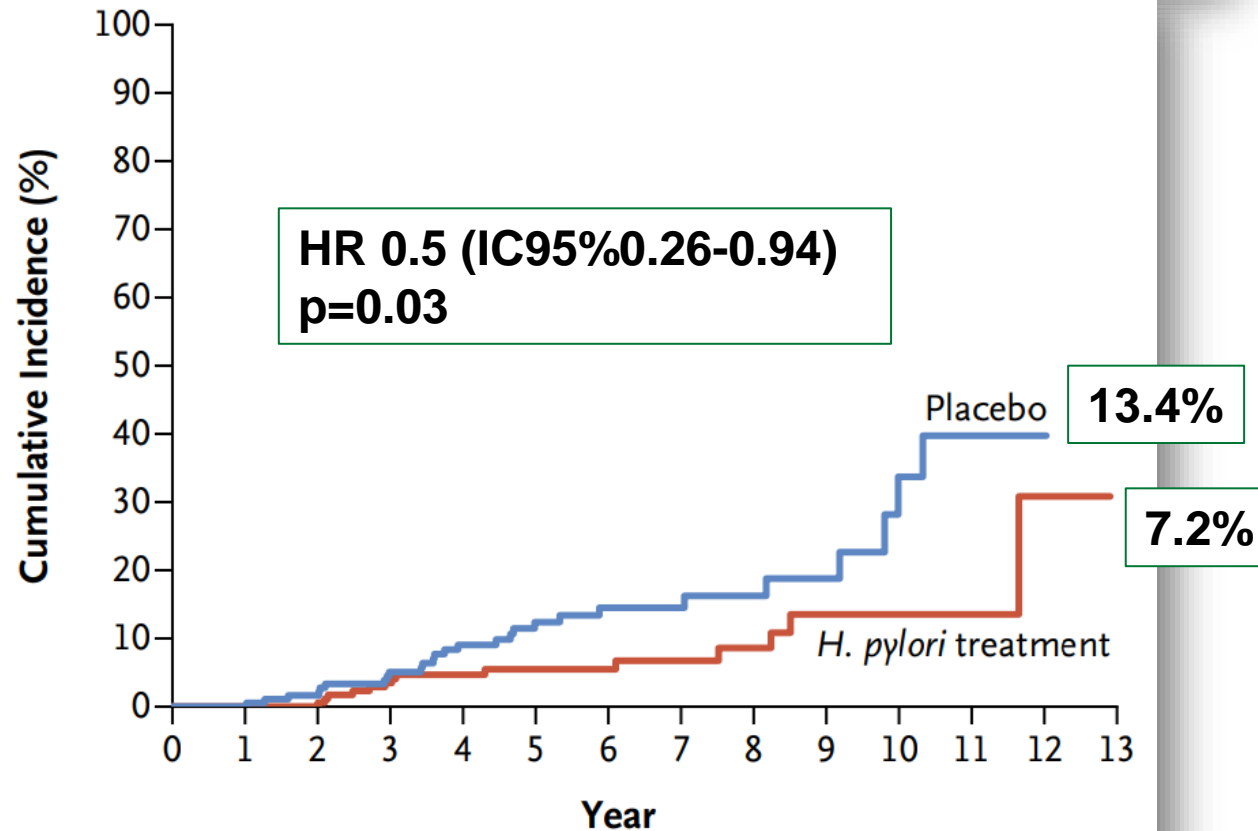
Shria Kumar,¹ David C. Metz,¹ Susan Ellenberg,² David E. Kaplan,^{1,3} and David S. Goldberg^{2,4}

Cohorte retrospectiva, Hospital Veteranos > 370.000

B

Helicobacter pylori Therapy for the Prevention of Metachronous Gastric Cancer

Il Ju Choi, M.D., Ph.D., Myeong-Cherl Kook, M.D., Ph.D., Young-Il Kim, M.D., Soo-Jeong Cho, M.D., Ph.D., Jong Yeul Lee, M.D., Chan Gyo Kim, M.D., Ph.D., Boram Park, M.S., and Byung-Ho Nam, Ph.D.



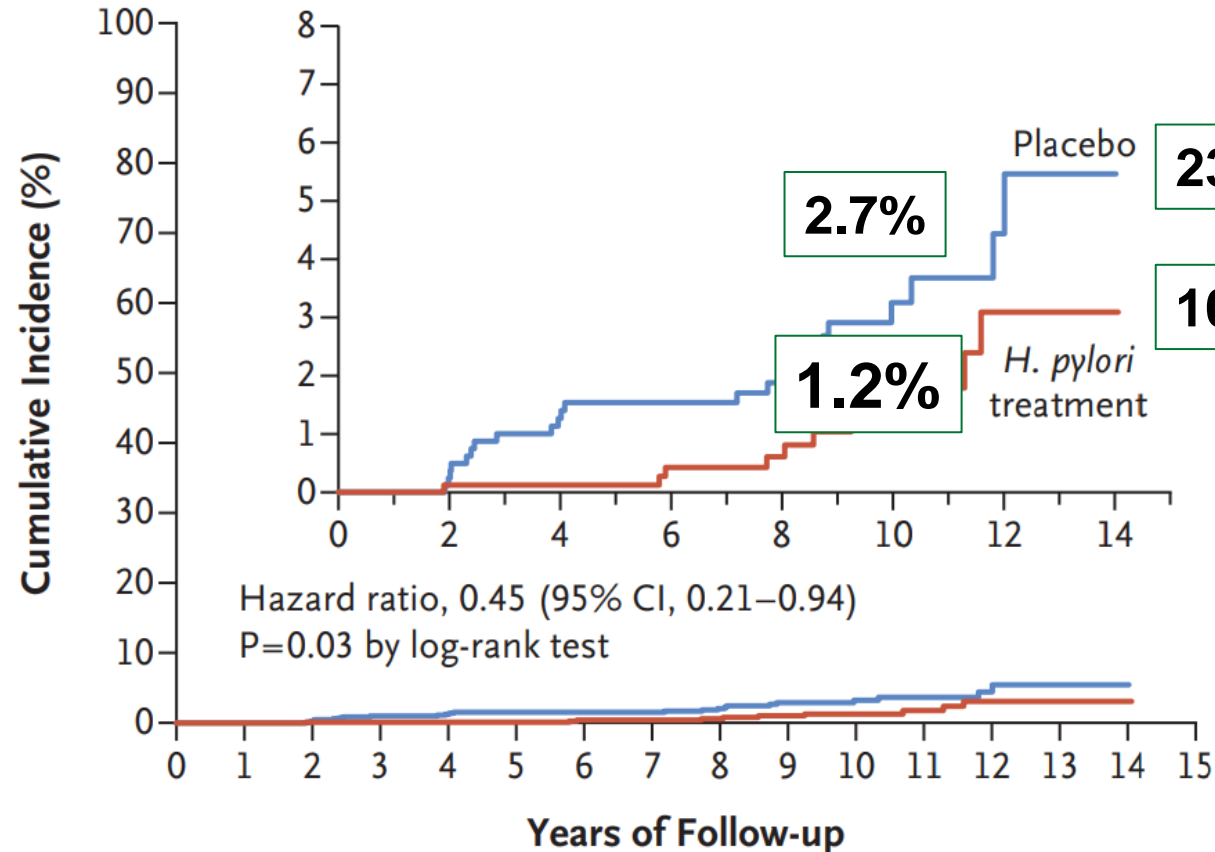
No. at Risk

Placebo	202	188	175	158	125	95	67	51	34	25	12	6	1	0
<i>H. pylori</i> treatment	194	187	175	162	128	96	79	62	44	26	11	9	2	0

Family History of Gastric Cancer and *Helicobacter pylori* Treatment

Il Ju Choi, M.D., Ph.D., Chan Gyoo Kim, M.D., Ph.D., Jong Yeul Lee, M.D., Young-Il Kim, M.D., Myeong-Cherl Kook, M.D., Ph.D., Boram Park, Ph.D., and Jungnam Joo, Ph.D.


HR 0.45 (IC95% 0.21-0.94)
P=0.03



No. at Risk

Placebo	844	842	804	769	731	701	640	600	515	423	271	194	94	33	1	0
<i>H. pylori</i> treatment	832	832	793	766	727	697	634	593	496	419	275	180	89	31	1	0

Helicobacter pylori eradication therapy to prevent gastric cancer: systematic review and meta-analysis

Alexander Charles Ford ,^{1,2} Yuhong Yuan,³ Paul Moayyedi³

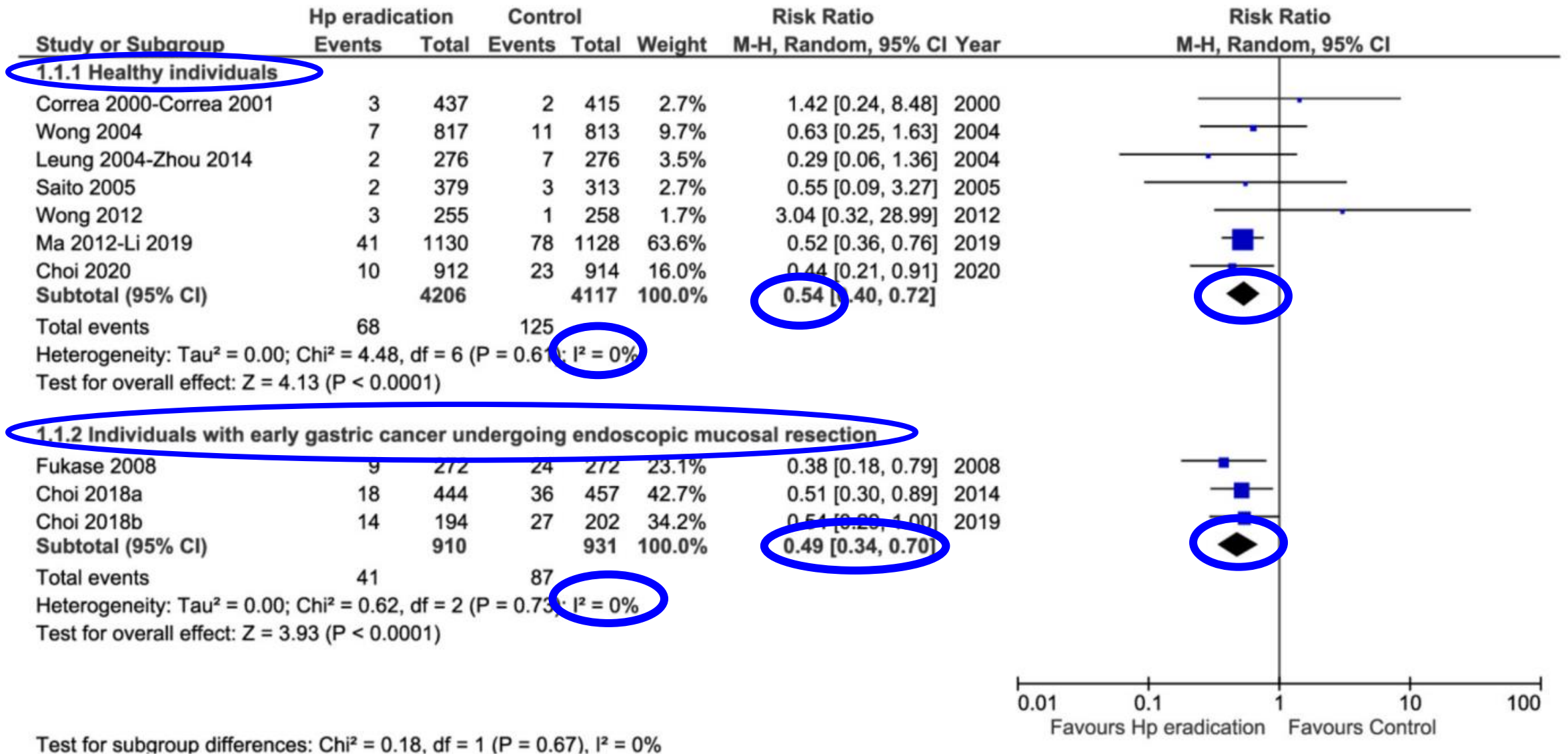
10 ensayos clínicos

8323 individuos sanos

1841 pacientes Ca gástrico


Ford AC, Gut 2020;69:2113–21.

Cáncer gástrico erradicación



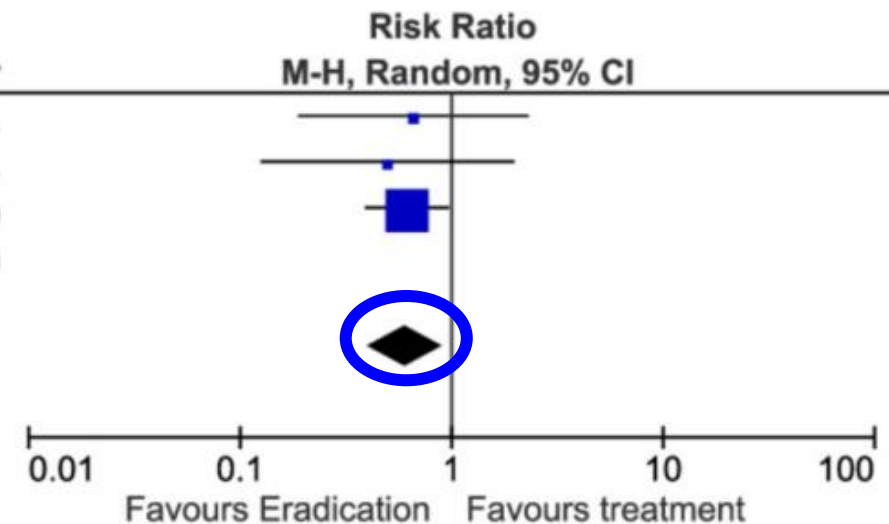
Ford AC, Gut 2020;69:2113–21.

Helicobacter pylori eradication therapy to prevent gastric cancer: systematic review and meta-analysis

Alexander Charles Ford ,^{1,2} Yuhong Yuan,³ Paul Moayyedi³

Mortalidad por Cáncer Gástrico

Study or Subgroup	Hp eradication		Control		Weight	Risk Ratio	
	Events	Total	Events	Total		M-H, Random, 95% CI	Year
Leung 2004-Zhou 2014	4	295	6	292	10.6%	0.66 [0.19, 2.31]	2004
Wong 2004	3	817	6	813	8.7%	0.50 [0.12, 1.98]	2004
Ma 2012-Li 2019	29	1130	47	1128	80.6%	0.62 [0.39, 0.97]	2019
Choi 2020	0	912	0	914		Not estimable	2020
Total (95% CI)		3154		3147	100.0%	0.61 [0.40, 0.92]	
Total events	36		59				
Heterogeneity: Tau ² = 0.00; Chi ² = 0.10, df = 2 (P = 0.95); I ² = 0%							
Test for overall effect: Z = 2.38 (P = 0.02)							



Mass eradication of *Helicobacter pylori* to reduce gastric cancer incidence and mortality: a long-term cohort study on Matsu Islands

Tsung-Hsien Chiang,^{1,2,3} Wei-Jung Chang,⁴ Sam Li-Sheng Chen,⁵
Amy Ming-Fang Yen ⁵, Jean Ching-Yuan Fann,⁶ Sherry Yueh-Hsia Chiu ^{7,8},
Yi-Ru Chen,⁹ Shu-Ling Chuang,^{4,10} Chun-Fu Shieh,¹¹ Cheng-Ying Liu,¹²
Han-Mo Chiu ^{1,4}, Hung Chiang,¹³ Chia-Tung Shun,^{14,15} Ming-Wei Lin,¹⁶
Ming-Shiang Wu ¹, Jaw-Town Lin ^{1,17}, Chang-Chuan Chan,^{18,19}
David Y Graham ²⁰, Hsiu-Hsi Chen ^{4,19}, Yi-Chia Lee ^{1,4,10,19}

Erradicación en masa
Población alto riesgo
≥ 30 años
2004-2018

Prevención primaria

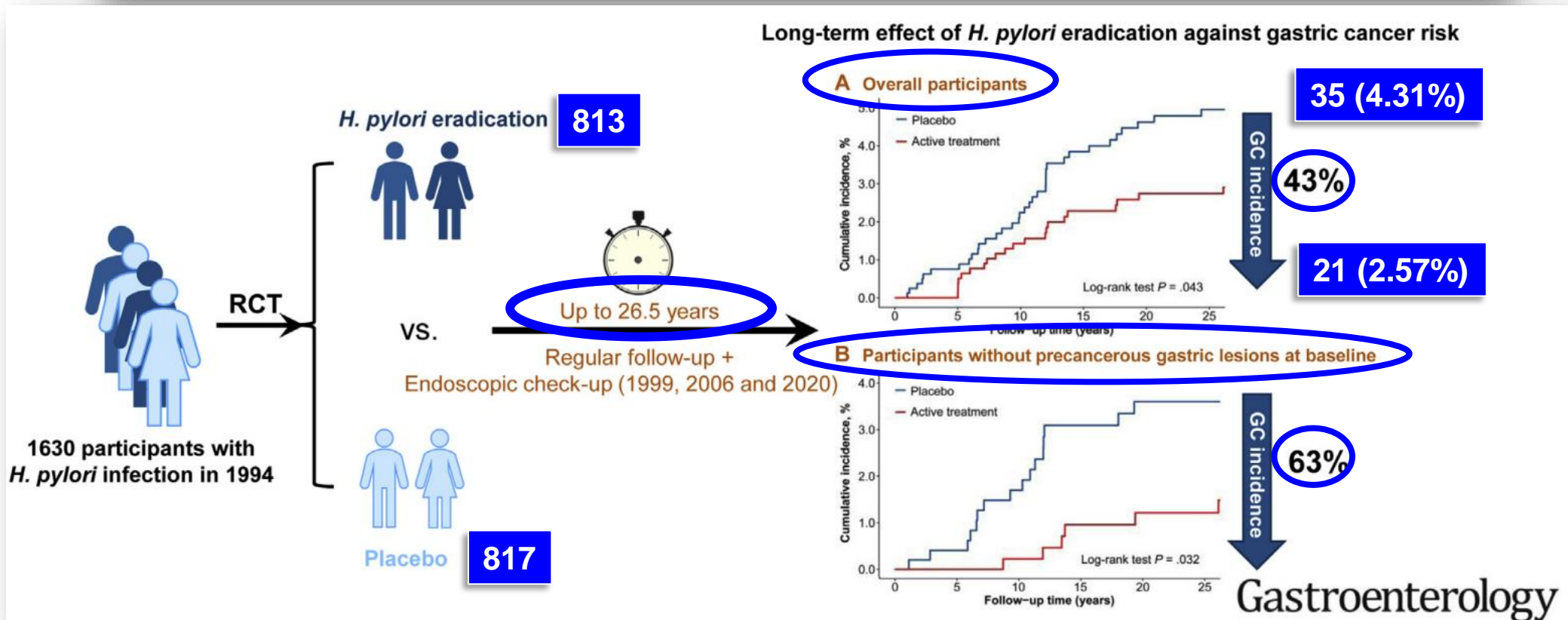
Incidencia	<< 50%
Mortalidad	<< 25%
<u>Cáncer esófago</u>	<u>No cambió</u>
<u>Cancer de colon</u>	<u>NO cambió</u>

China


Effect of *Helicobacter pylori* Eradication on Gastric Cancer Prevention: Updated Report From a Randomized Controlled Trial With 26.5 Years of Follow-up



Lingjun Yan,^{1,2,*} Ying Chen,^{3,4,*} Fa Chen,^{1,2} Tao Tao,^{1,2} Zhijian Hu,^{1,2} Junzhuo Wang,^{1,2} Jianwang You,⁴ Benjamin C. Y. Wong,⁵ Jianshun Chen,^{3,4} and Weimin Ye^{1,2,6}

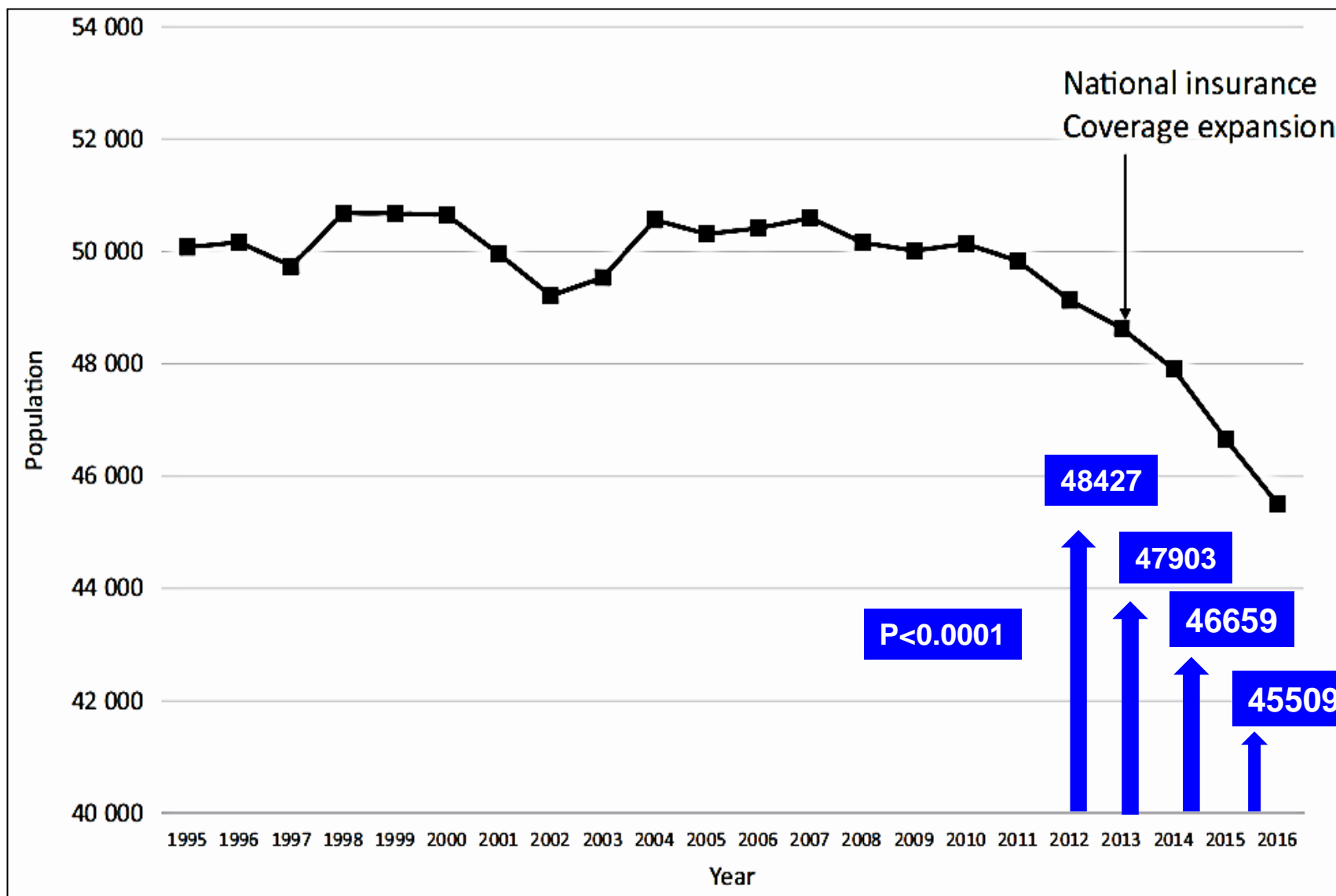


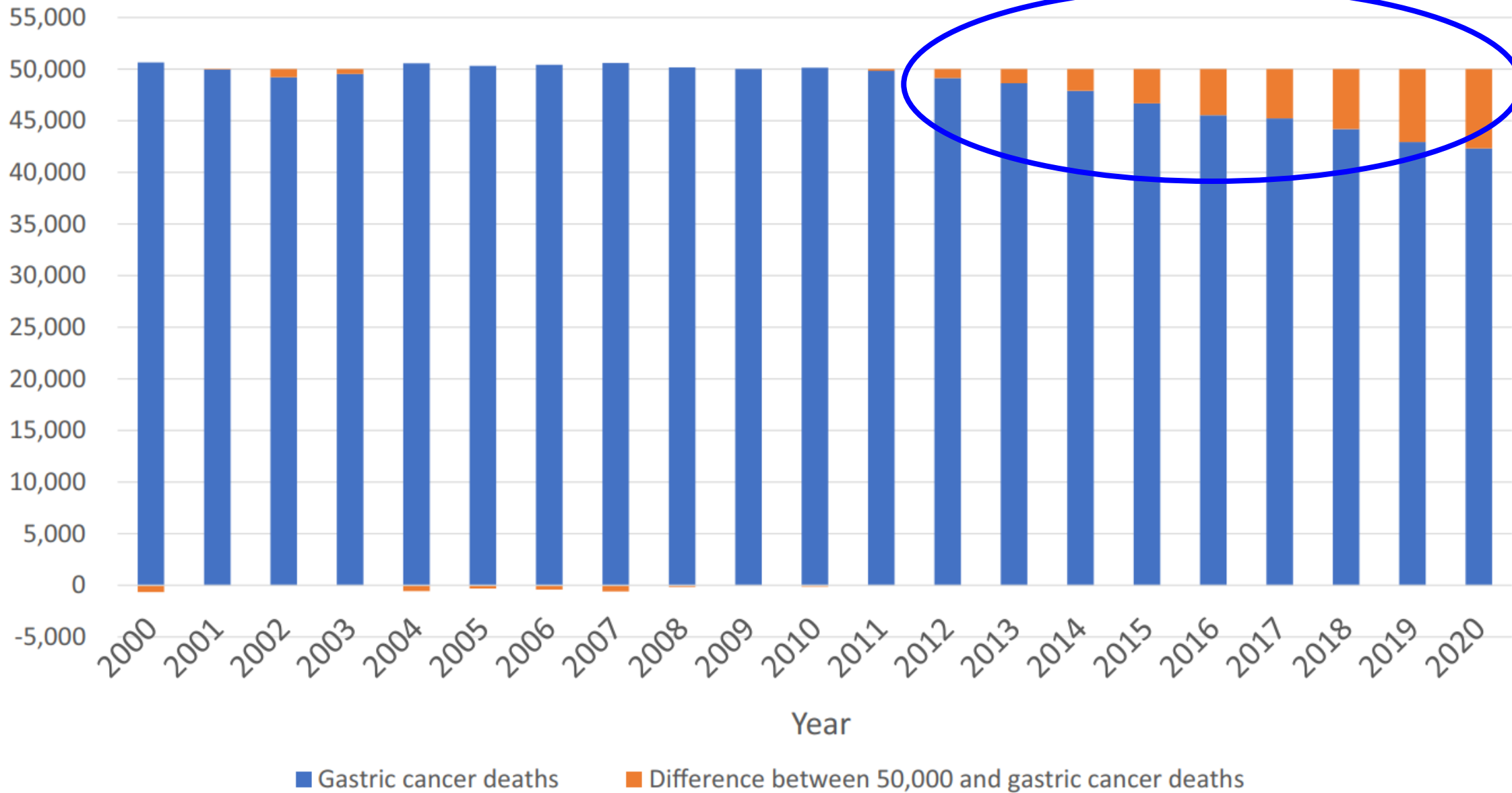
Effect on *Helicobacter pylori* eradication therapy against gastric cancer in Japan

Momoko Tsuda¹ | Masahiro Asaka²  | Mototsugu Kato³ | Rumiko Matsushima¹ | Kenji Fujimori⁴ | Kozo Akino² | Shogo Kikuchi⁵ | Yingsong Lin⁵ | Naoya Sakamoto¹

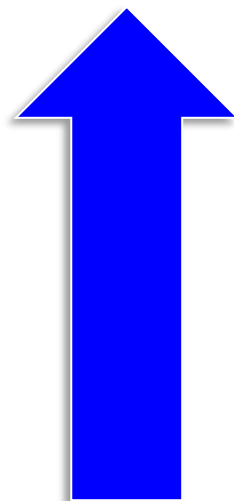
**Durante décadas: prevención secundaria (Rx)
50.000 muertes/año, últimos 40 años (ningún cambio)**

Erradicación de *Helicobacter* y cáncer en Japón





Kowada A, Helicobacter. 2021 Jul 18:e12837.



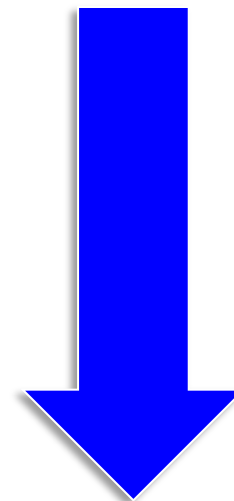
Refrigerar

**Prevención
Primaria
Cáncer Gástrico**

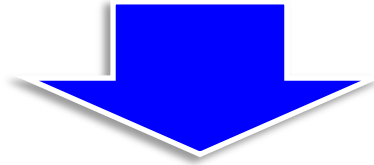
**Erradicar
*H.pylori***



Licor

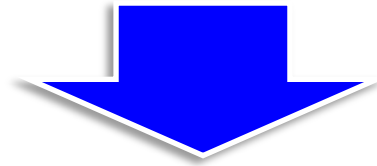


Prevención secundaria



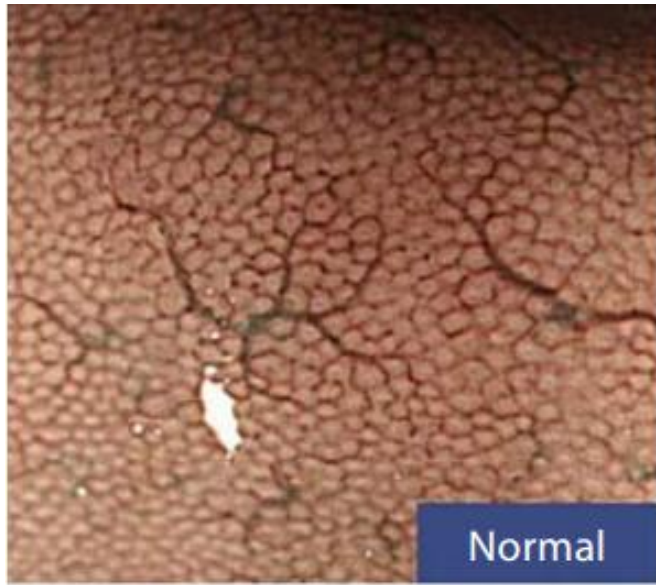
***Vigilar* Gastritis crónica avanzada**
Tamización endoscópica
Serología

Prevención secundaria

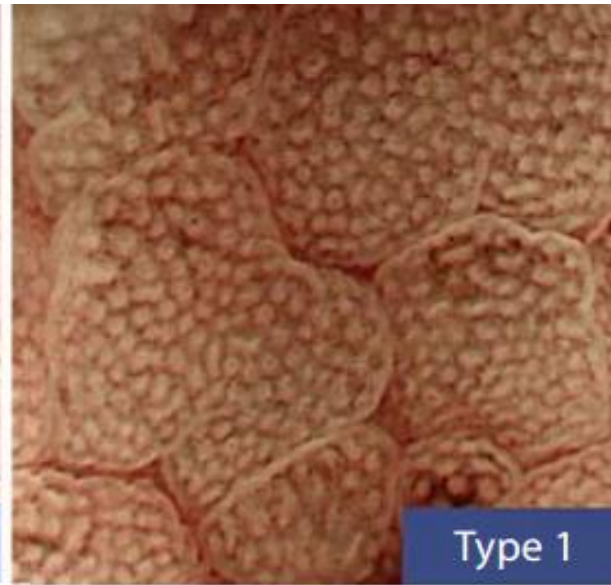


***Vigilar* Gastritis crónica avanzada**

Endoscopios avanzados



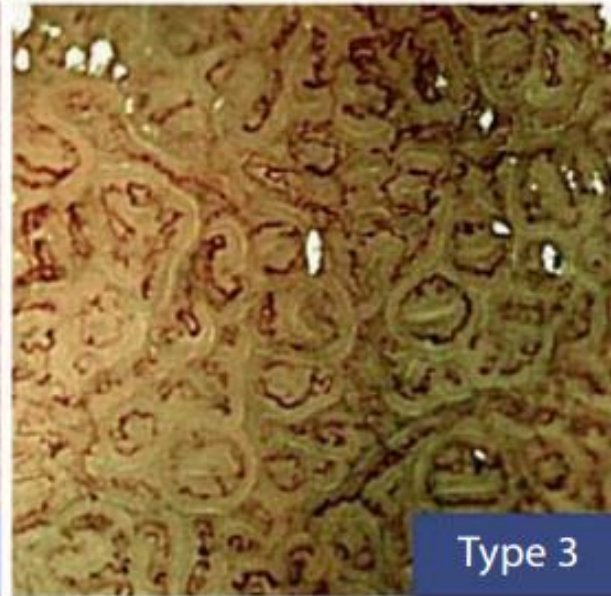
Normal



Type 1



Type 2





Type 3

“Gastritis Crónica moderada”

“Gastritis Crónica leve”

“Gastritis Crónica severa con Atrofia y metaplasia intestinal”

Endoscopic grading of gastric intestinal metaplasia on risk assessment for early gastric neoplasia: can we replace histology assessment also in the West?

Pedro Marcos ,^{1,2} Gisela Brito-Gonçalves,³ Diogo Libânio,^{1,4} Inês Pita,¹ Rui Castro,¹ Inês Sá ,¹ Mário Dinis-Ribeiro,^{1,4} Pedro Pimentel-Nunes^{1,4,5}

OLGIM, OLGA











EKGIM: Graduación endoscópica Metaplasia intestinal

Antro C>, C<, Cuerpo C>, C<, Incisura: estaciones de Sídney

Cada sitio 0-2 puntos

0=no MI, 1: MI(focal) <30%, 2: MI Extensa ≥ 30%

Management of *Helicobacter pylori* infection: the Maastricht VI/Florence consensus report

Peter Malfertheiner ,^{1,2} Francis Megraud ,³ Theodore Rokkas ,^{4,5}
Javier P Gisbert ,^{6,7} Jyh-Ming Liou ,⁸ Christian Schulz ,^{1,9}
Antonio Gasbarrini,¹⁰ Richard H Hunt,^{11,12} Marcis Leja ,^{13,14} Colm O'Morain,¹⁵
Massimo Rugge ,^{16,17} Sebastian Suerbaum,^{9,18} Herbert Tilg ,¹⁹
Kentaro Sugano ,²⁰ Emad M El-Omar ,^{21,22} On behalf of the European
Helicobacter and Microbiota Study group

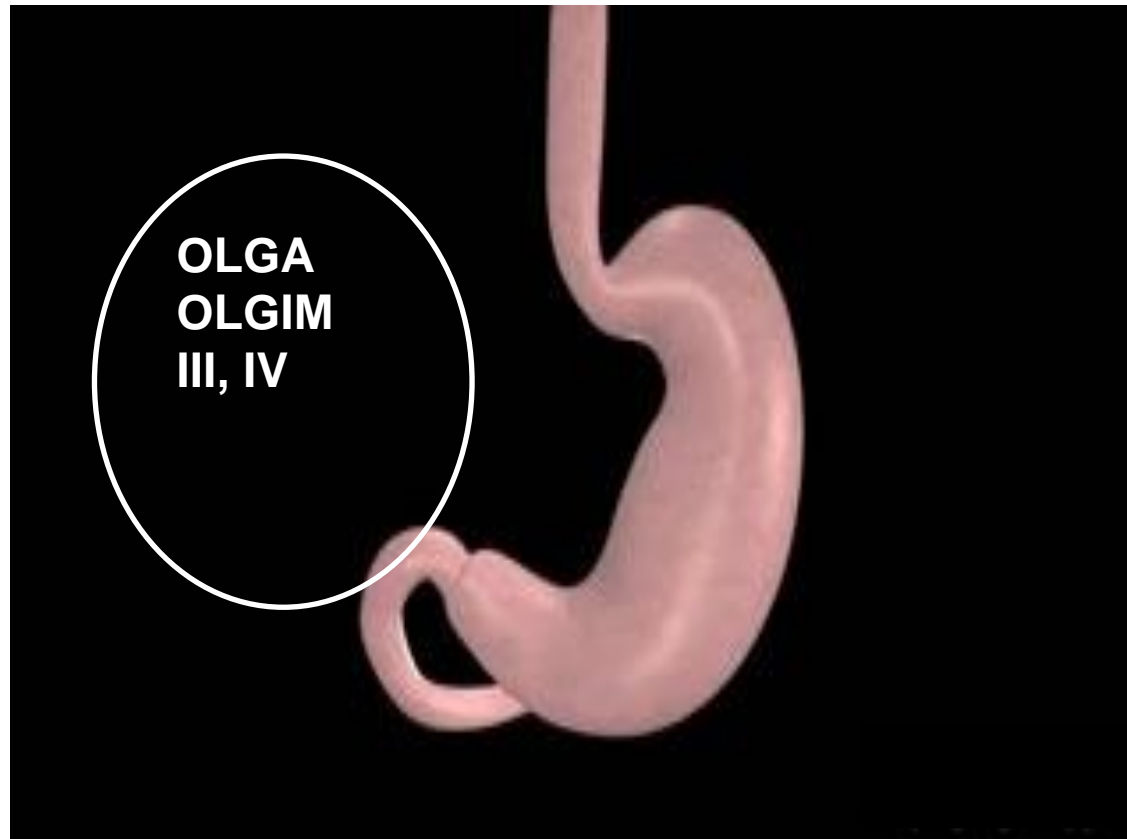
***Statement 3:* When endoscopy is indicated it should: (1) apply the best available technologies; (2) include biopsy sampling. Biopsy samples, as obtained in accordance with validated protocols, should result in both aetiological diagnosis and gastritis staging. Any focal lesions should be additionally sampled.**

Agreement 100%

Grade A2

Estratificación de la atrofia o MI Biopsias

Identificar el “Estómago premaligno”



Sugano K, Gut 2015;64:1353-67

Take S, J Gastroenterol 2020;55:281-8

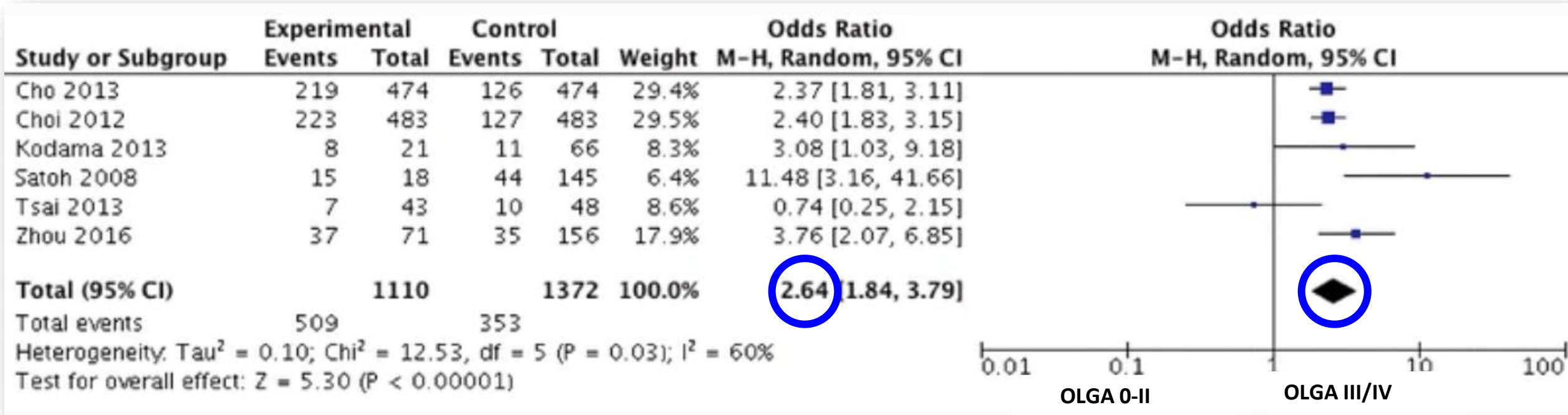
Malfertheiner P, Maastricht VI. Gut 2022 Online agosto 15

The significance of OLGA and OLGIM staging systems in the risk assessment of gastric cancer: a systematic review and meta-analysis



Hu Yue^{1,2} · Liu Shan¹ · Lv Bin^{1,2}

OLGA III/IV Casos y controles

Cáncer gástrico

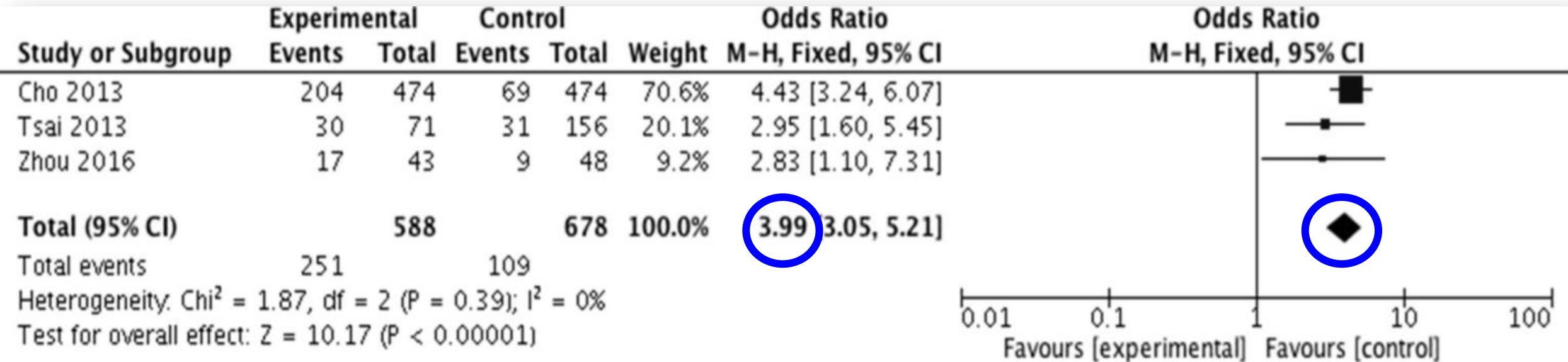


The significance of OLGA and OLGIM staging systems in the risk assessment of gastric cancer: a systematic review and meta-analysis

Hu Yue^{1,2}  · Liu Shan¹ · Lv Bin^{1,2} 

OLGIM III/IV, Casos y controles

Cáncer gástrico



Yue H, et al. Gastric Cancer 2018;21: 579–87



Authors
Pedro Pimentel-Nunes¹,
Gianluca Esposito⁷, Mon
Jean-Marc Dumonceau¹⁶
Ernst J. Kuipers¹⁶, Mario

OLGA OLGIM

Study
Guideline
65-88

Annibale⁷,
Hoofft¹⁵,

British Society of Gastroenterology guidelines on the diagnosis and management of patients at risk of gastric adenocarcinoma

Matthew Banks,^{1,2} David Graham,^{1,3} Marnix Jansen,⁴ Takuji Gotoda,⁵ Sergio Coda,⁶ Massimiliano di Pietro,^{7,8} Noriya Uedo,⁹ Pradeep Bhandari,¹⁰ D Mark Pritchard,¹¹ Ernst J Kuipers,¹² Manuel Rodriguez-Justo,⁴ Marco R Novelli,⁴ Krish Rangunath,¹³ Neil Shepherd,¹⁴ Mario Dinis-Ribeiro¹⁵

Banks M, et al. Gut 2019;68:1545-75

Guidelines

Chronic atrophic gastritis: Natural history, diagnosis and therapeutic management. A position paper by the Italian Society of Hospital Gastroenterologists and Digestive Endoscopists [AIGO], the Italian Society of Digestive Endoscopy [SIED], the Italian Society of Gastroenterology [SIGE], and the Italian Society of Internal Medicine [SIMI]

Edith Lahner^{a,*}, Rocco Maurizio Zagari^b, Angelo Zullo^c, Antonio Di Sabatino^d, Alberto Meggio^e, Paola Cesaro^f, Marco Vincenzo Lenti^d, Bruno Annibale^a, Gino Roberto Corazza^d

Lahner E, et al. Dig Liver Dis 2019;51:1621-32

Kyoto global consensus report on *Helicobacter pylori* gastritis

Sugano K, et al. Gut 2015;64:1353-1367

Kentaro Sugano,¹ Jan Tack,² Ernst J Kuipers,³ David Y Graham,⁴ Emad M El-Omar,⁵ Soichiro Miura,⁶ Ken Haruma,⁷ Masahiro Asaka,⁸ Naomi Uemura,⁹ Peter Malfertheiner,¹⁰ on behalf of faculty members of Kyoto Global Consensus

Management of *Helicobacter pylori* infection: the Maastricht VI/Florence consensus report

Peter Malfertheiner^{1,2}, Francis Megraud³, Theodore Rokkas^{4,5}, Javier P Gisbert^{6,7}, Jyh-Ming Liou⁸, Christian Schulz^{1,9}, Antonio Gasbarrini,¹⁰ Richard H Hunt,^{11,12} Marcis Leja^{13,14}, Colm O'Morain,¹⁵ Massimo Rugge^{16,17}, Sebastian Suerbaum,^{9,18} Herbert Tilg¹⁹, Kentaro Sugano²⁰, Emad M El-Omar^{21,22} On behalf of the European Helicobacter and Microbiota Study group

Malfertheiner P, Gut 2022 Online agosto 15

British Society of Gastroenterology guidelines on the diagnosis and management of patients at risk of gastric adenocarcinoma

Matthew Banks,^{1,2} David Graham,^{1,3} Marnix Jansen,⁴ Takuji Gotoda,⁵ Sergio Coda,⁶ Massimiliano di Pietro,^{7,8} Noriya Uedo,⁹ Pradeep Bhandari,¹⁰ D Mark Pritchard,¹¹ Ernst J Kuipers,¹² Manuel Rodriguez-Justo,⁴ Marco R Novelli,⁴ Krish Ragunath,¹³ Neil Shepherd,¹⁴ Mario Dinis-Ribeiro¹⁵

13. *We recommend endoscopic surveillance every 3 years should be offered to patients diagnosed with extensive GA or GIM, defined as that affecting the antrum and body (evidence level: low quality; grade of recommendation: strong; level of agreement: 100%).*



Management of epithelial precancerous conditions and lesions in the stomach (MAPS II): European Society of Gastrointestinal Endoscopy (ESGE), European *Helicobacter* and Microbiota Study Group (EHMSG), European Society of Pathology (ESP), and Sociedade Portuguesa de Endoscopia Digestiva (SPED) guideline update 2019














Authors

Pedro Pimentel-Nunes^{1,2,3}, Diogo Libânio^{1,2}, Ricardo Marcos-Pinto^{2,4}, Miguel Areia^{2,5}, Marcis Leja⁶, Gianluca Esposito⁷, Monica Garrido⁴, Ilze Kikuste⁶, Francis Megraud⁸, Tamara Matysiak-Budnik⁹, Bruno Annibale⁷, Jean-Marc Dumonceau¹⁰, Rita Barros^{11,12}, Jean-François Fléjou¹³, Fátima Carneiro^{11,12,14}, Jeanin E. van Hooft¹⁵, Ernst J. Kuipers¹⁶, Mario Dinis-Ribeiro^{1,2}

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 (low quality evidence, strong recommendation)

Management of *Helicobacter pylori* infection: the Maastricht VI/Florence consensus report

Peter Malfertheiner ,^{1,2} Francis Megraud ,³ Theodore Rokkas ,^{4,5}
Javier P Gisbert ,^{6,7} Jyh-Ming Liou ,⁸ Christian Schulz ,^{1,9}
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Kentaro Sugano ,²⁰ Emad M El-Omar ,^{21,22} On behalf of the European
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Statement 20: Follow-up at regular intervals, and by use of endoscopic biopsy protocols, is mandatory in patients with severe atrophic gastritis (OLGA III/IV or OLGIM III/IV).

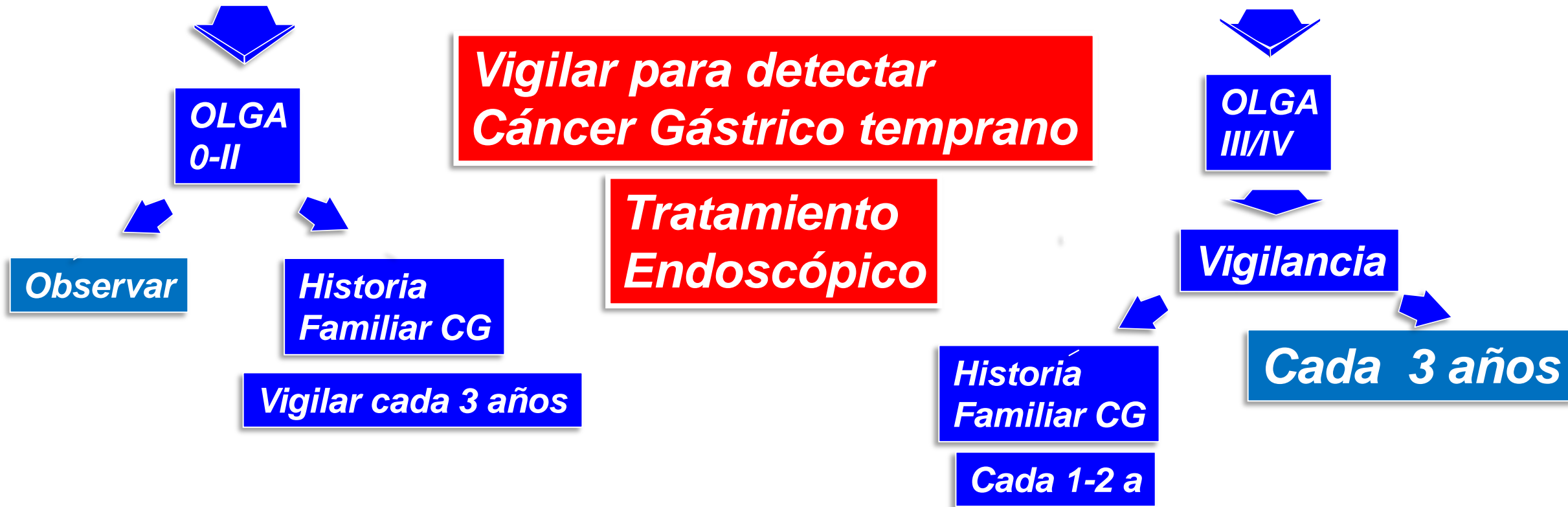
Agreement 97%

Grade B1

Malfertheiner P, Gut 2022 Online agosto 15

Vigilancia de Gastritis Crónica

5 Biopsias: cuerpo (2), Antro (2), Incisura (1)

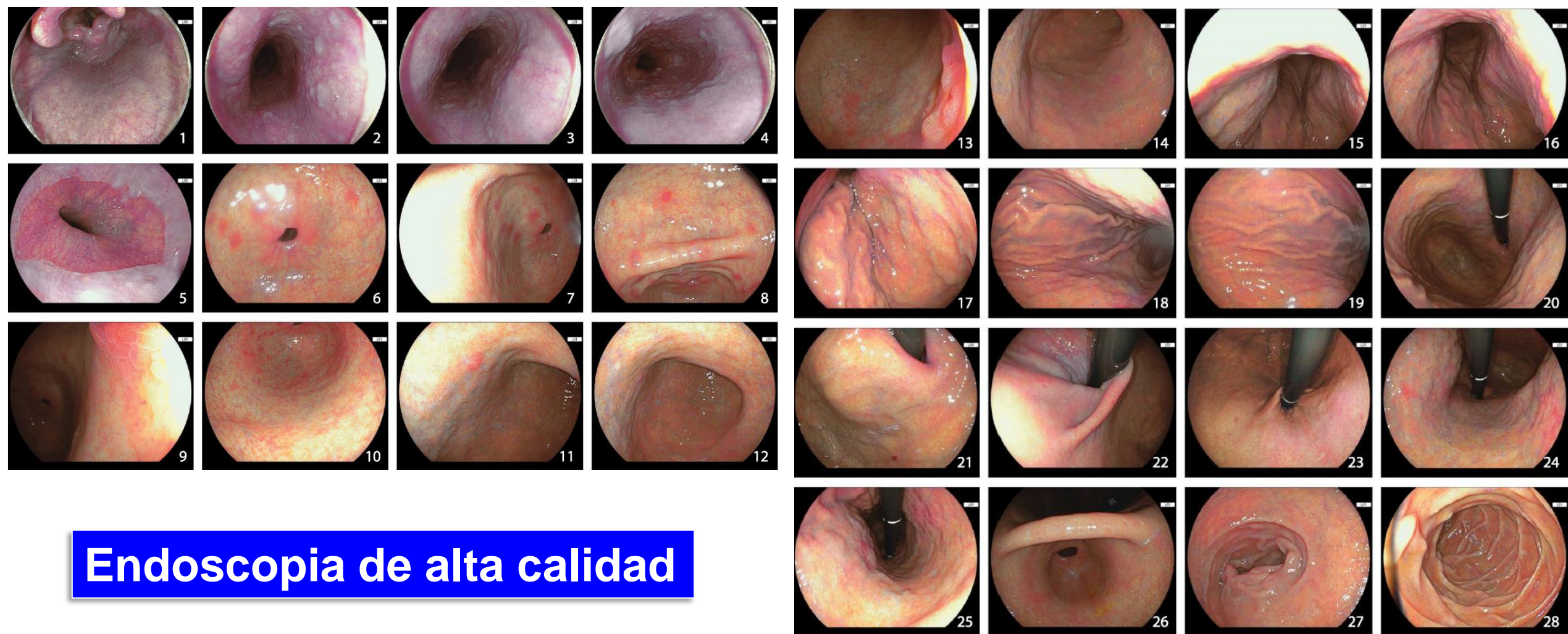


Sugano K, Kyoto Consensus. Gut 2015; 64:1353-67
Zagari RM, Dig Liver Dis 2015;903-12
Rollán A, Rev Med Chile 2014;142:1181-92
Yue H, Gastric Cancer 2018;21:579-87
Shah SC Gastroenterology 2021;161:1325-32
Pimentel-Nunes P, Endoscopy 2019;51:365-88

Mujer 52 años, OLGA IV 2 años de seguimiento

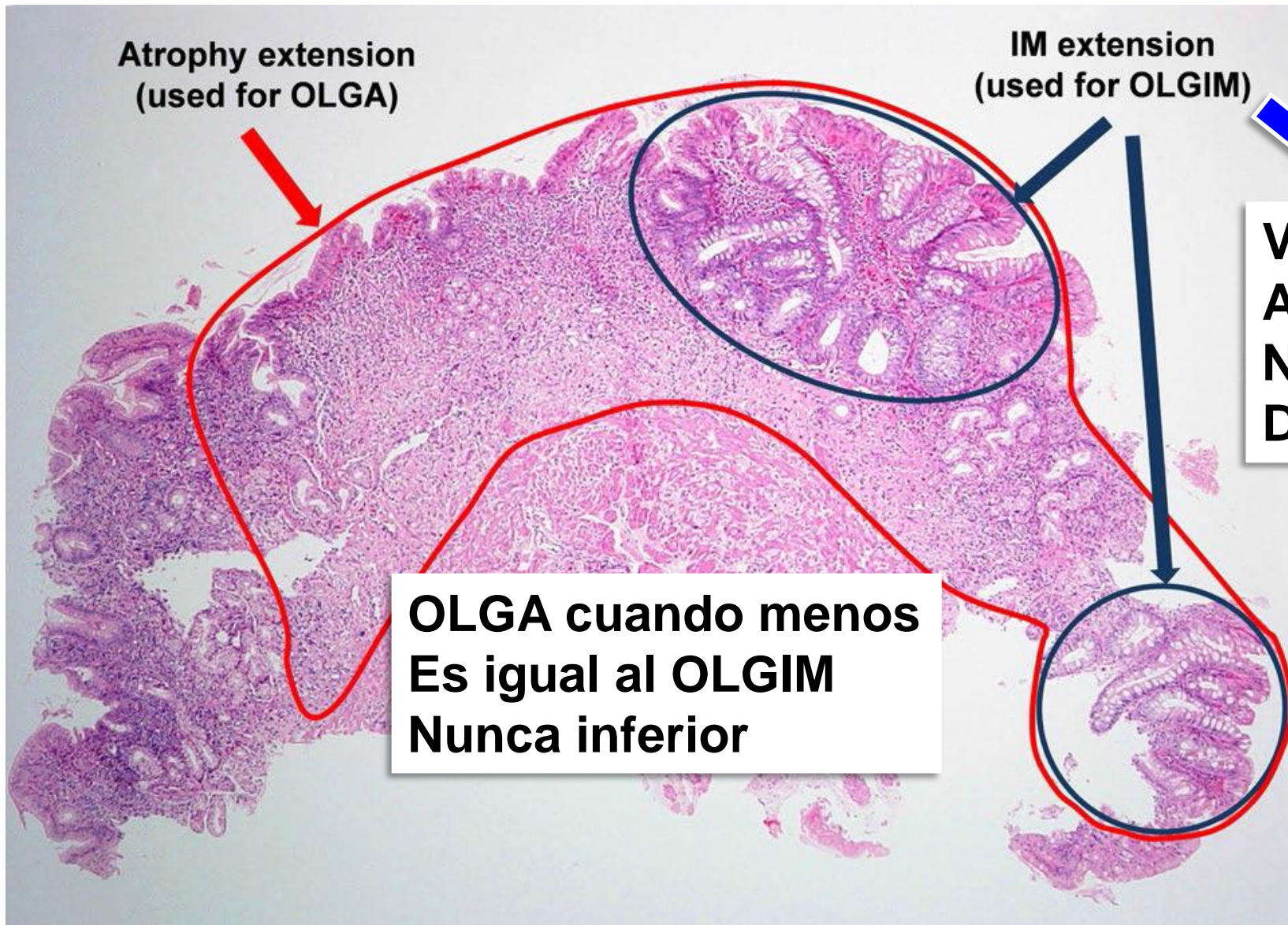


Endoscopia sistemática codificada alfa numérica 28 estaciones



Endoscopia de alta calidad

**OLGA identifica todos
Los tipos de atrofia**



Atrophy extension
(used for OLGA)












IM extension
(used for OLGIM)

Variante de
Atrofia
No entidad
Diferente

OLGA cuando menos
Es igual al OLGIM
Nunca inferior

Matysiak-Budnik T, Dig Dis Sci 2020, abril 20
Rugge M, Gastrointest Endosc. 2011;73:411-2.

Management of *Helicobacter pylori* infection: the Maastricht VI/Florence consensus report

Peter Malfertheiner ,^{1,2} Francis Megraud ,³ Theodore Rokkas ,^{4,5}
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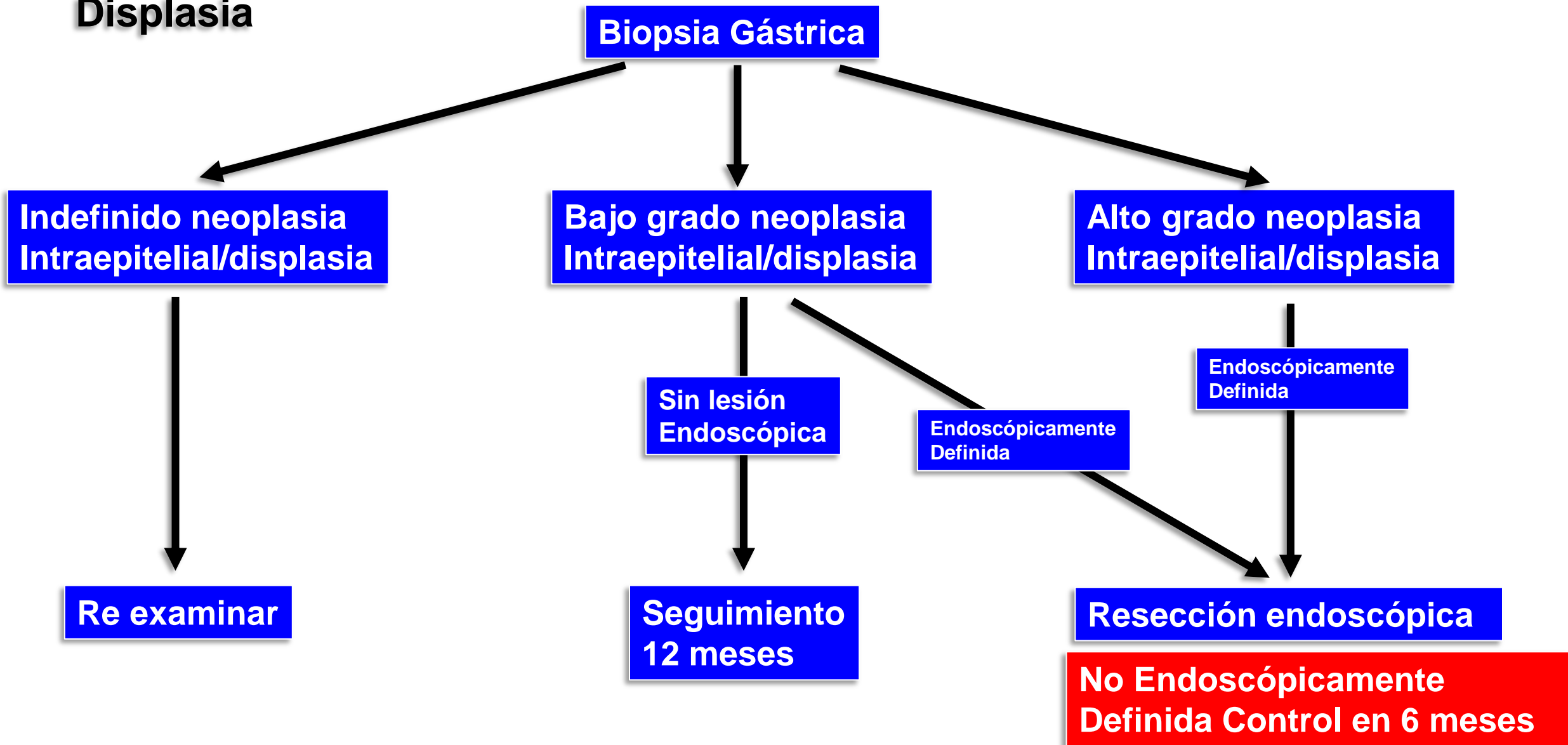
Statement 13: The histological assessment of atrophy should result in a conclusive gastritis staging (OLGA/OLGIM), which consistently ranks the patient-specific cancer risk. Histological staging makes IM subtyping clinically redundant.

Agreement 97%

Grade A1

OLGA identifica todos los tipos de atrofia

Displasia



Estómago premaligno

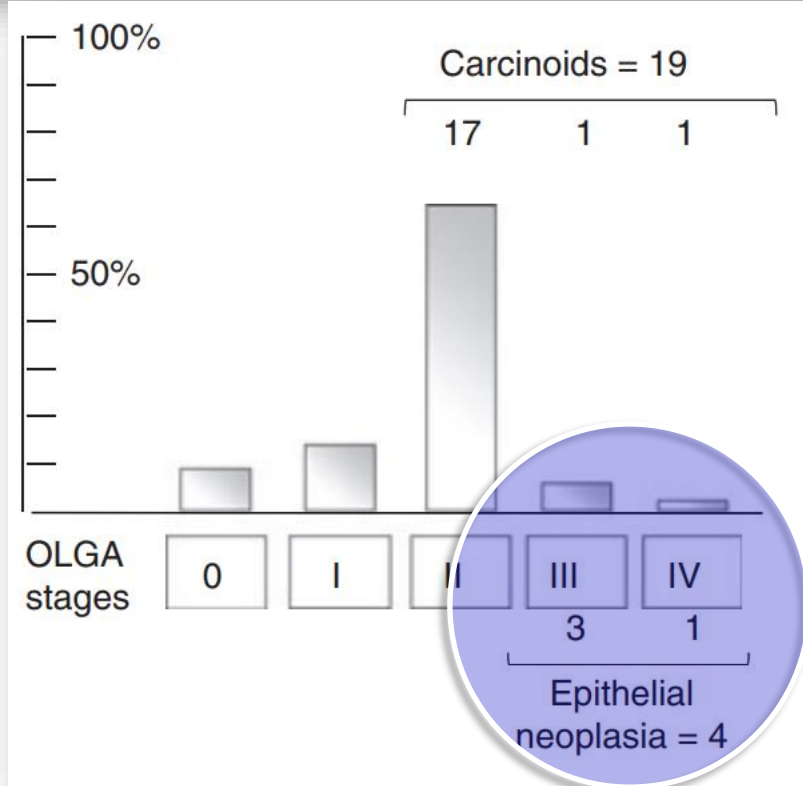
**Gastritis
autoinmune**



Vigilar c/3- 5años

Autoimmune gastritis: histology phenotype and OLGA staging

M. Rugge^{*,†,1}, M. Fassan^{*,‡,1}, M. Pizzi[‡], V. Zorzetto[‡], G. Maddalo[‡], S. Realdon[†], M. DeBernard[§], C. Betterle^{*}, R. Cappellesso^{*}, G. Pennelli^{*}, M. de Boni[¶] & F. Farinati[‡]



Management of upper gastrointestinal symptoms in patients with autoimmune gastritis

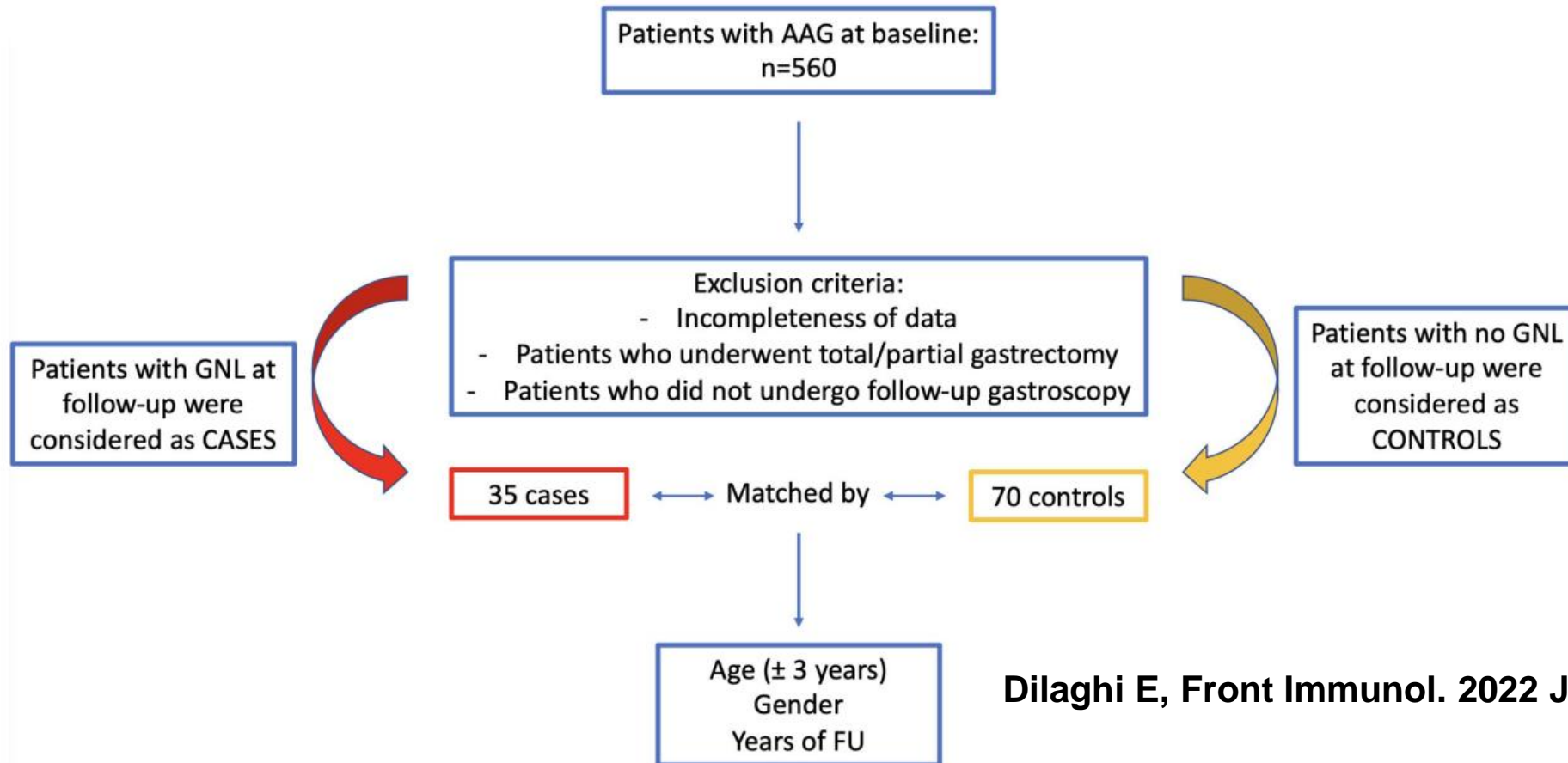
Juan D. Gomez Cifuentes^a, Jordan Sparkman^b and David Y. Graham^c

Tumores Neuroendocrinos Tipo I (Hipergastrinemia)

Gómez JD, Curr Opin Gastroenterol 2022;38:600-6

The Impact of Proton Pump Inhibitors on the Development of Gastric Neoplastic Lesions in Patients With Autoimmune Atrophic Gastritis

Emanuele Dilaghi[†], Mario Bellisario[†], Gianluca Esposito, Marilia Carabotti, Bruno Annibale[†] and Edith Lahner^{*†}



	Cases n=35	Controls n=70	p-value
Females	20 (57.1)	42 (60.0)	NS (matched)
Median age, years, median (range)	67.6 (44–84)	67.7 (42–86)	NS (matched)
Age >50 years	32 (91.4)	65 (92.9)	NS (matched)
Prior use of PPIs	19 (54.3)	13 (18.6)	<0.001
Body mass index ≥25	17 (48.6)	26 (37.1)	0.297
Smoking habit	4 (11.4)	34 (48.6)	<0.001
First-degree family history for gastric cancer	3 (8.6)	7 (10.0)	1.000
Dyspepsia	17 (48.6)	28 (40.0)	0.412
Use of antiplatelet or anticoagulant drugs	14 (40.0)	11 (15.7)	0.008
Iron deficiency anemia	4 (11.4)	13 (18.6)	0.412
Pernicious anemia	13 (37.1)	28 (40.0)	0.834
Severe corpus atrophy	13 (37.1)	27 (38.6)	1.000
Presence of corpus intestinal metaplasia	26 (74.3)	58 (82.9)	0.312

Management of upper gastrointestinal symptoms in patients with autoimmune gastritis

Juan D. Gomez Cifuentes^a, Jordan Sparkman^b and David Y. Graham^c

KEY POINTS

- The most common symptoms in autoimmune gastritis (AIG) are dyspepsia and typical gastroesophageal reflux (GERD) symptoms.
- Typical GERD symptoms are caused by weakly acid and alkaline reflux, the exact mechanism behind dyspepsia is unknown.
- Acid suppressant medications should be discontinued as their physiologic targets are absent in AIG patients.
- Therapy for AIG patients should be approached based on the predominant symptoms of GERD and dyspepsia.

Otras estrategias de prevención secundaria

Tamización Endoscópica

Endoscopic Screening in Asian Countries Is Associated With Reduced Gastric Cancer Mortality: A Meta-analysis and Systematic Review

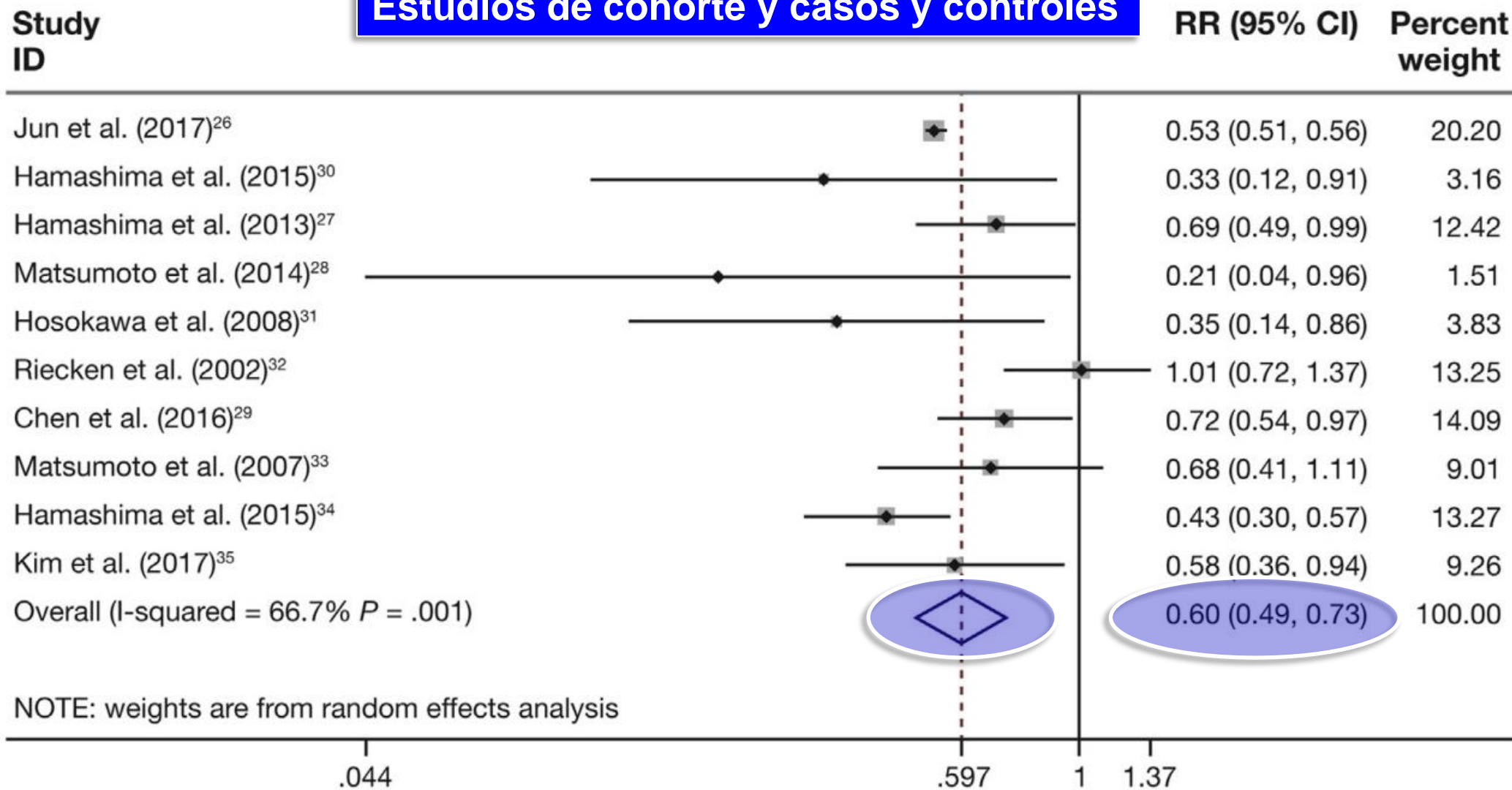
Xing Zhang,^{1,2,*} Meng Li,^{1,2,*} Shuntai Chen,^{1,2,*} Jiaqi Hu,^{1,2,*} Qiujun Guo,^{1,*} Rui Liu,¹ Honggang Zheng,¹ Zhichao Jin,¹ Yuan Yuan,^{1,2} Yupeng Xi,^{1,2} and Baojin Hua¹

Zhang X,et al. Gastroenterology 2018;155:347–354

Endoscopia Tamización

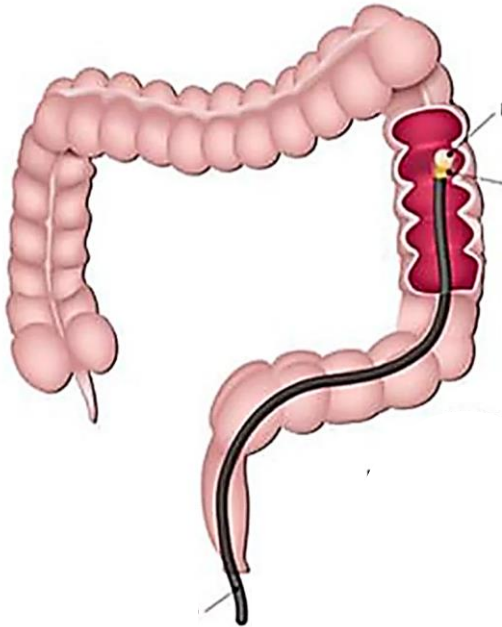
Mortalidad por cáncer gástrico

Estudios de cohorte y casos y controles



Statement 18: Screening modalities for gastric cancer prevention (noninvasive or endoscopic) combined with colorectal cancer screening is an opportunity

Agreement 81%



A los 50 años

10% *H.pylori* +

Atrofia, MI avanzada



19% Europa

Grade C2



Role of gastrointestinal endoscopy in the screening of digestive tract cancers in Europe: European Society of Gastrointestinal Endoscopy (ESGE) Position Statement

ESGE

Authors

Adrian Săftoiu^{1,2}, Cesare Hassan³, Miguel Areia^{4,5}, Manoop S. Bhutani⁶, Raf Bisschops⁷, Erwan Bories⁸, Irina M. Cazacu^{1,6}, Evelien Dekker⁹, Pierre H. Deprez¹⁰, Stephen P. Pereira¹¹, Carlo Senore¹², Riccardo Capocaccia¹³, Giulio Antonelli³, Jeanin van Hooft⁹, Helmut Messmann¹⁴, Peter D. Siersema¹⁵, Mario Dinis-Ribeiro^{5,16}, Thierry Ponchon¹⁷

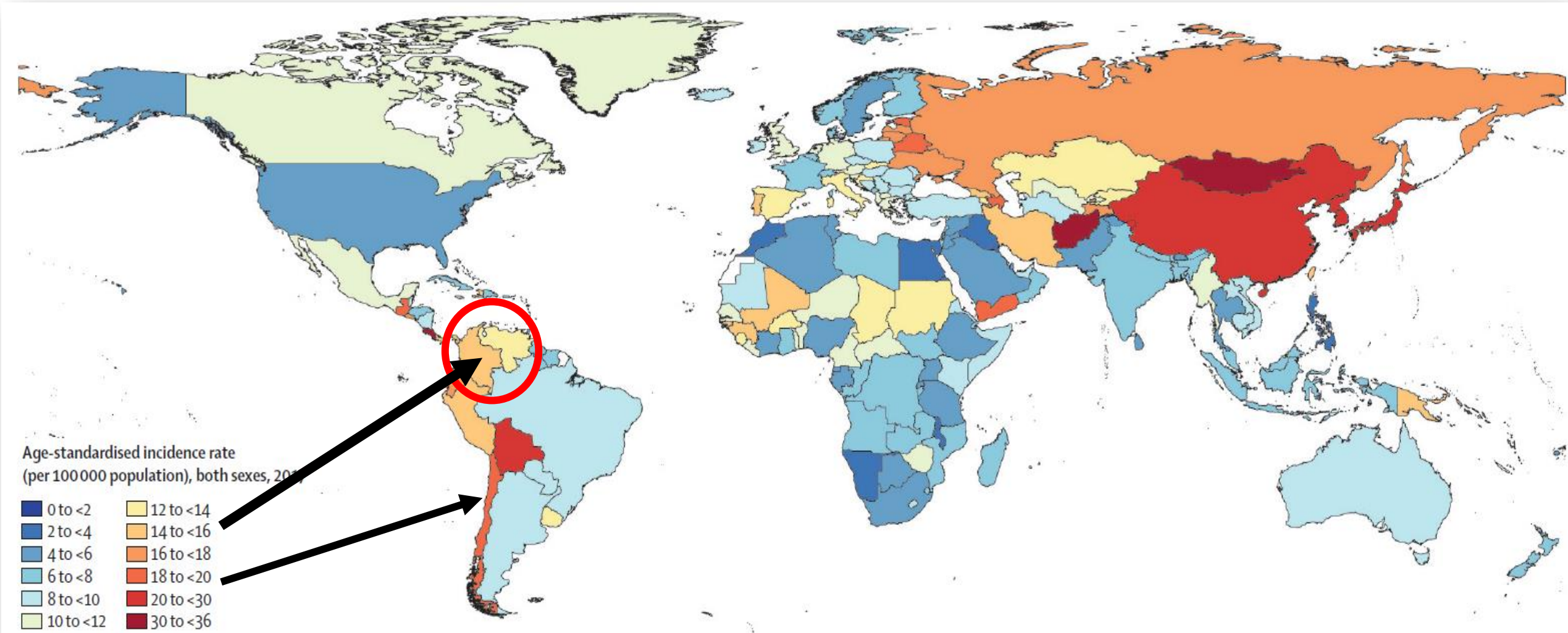
STATEMENT

In high-risk populations, endoscopic screening **for gastric cancer** should be considered for individuals aged **more than 40 years**. Its use in countries/regions with intermediate risk may be considered on the basis of local settings and availability of endoscopic resources.

Alto riesgo $\geq 20/10^5$
Cada dos años

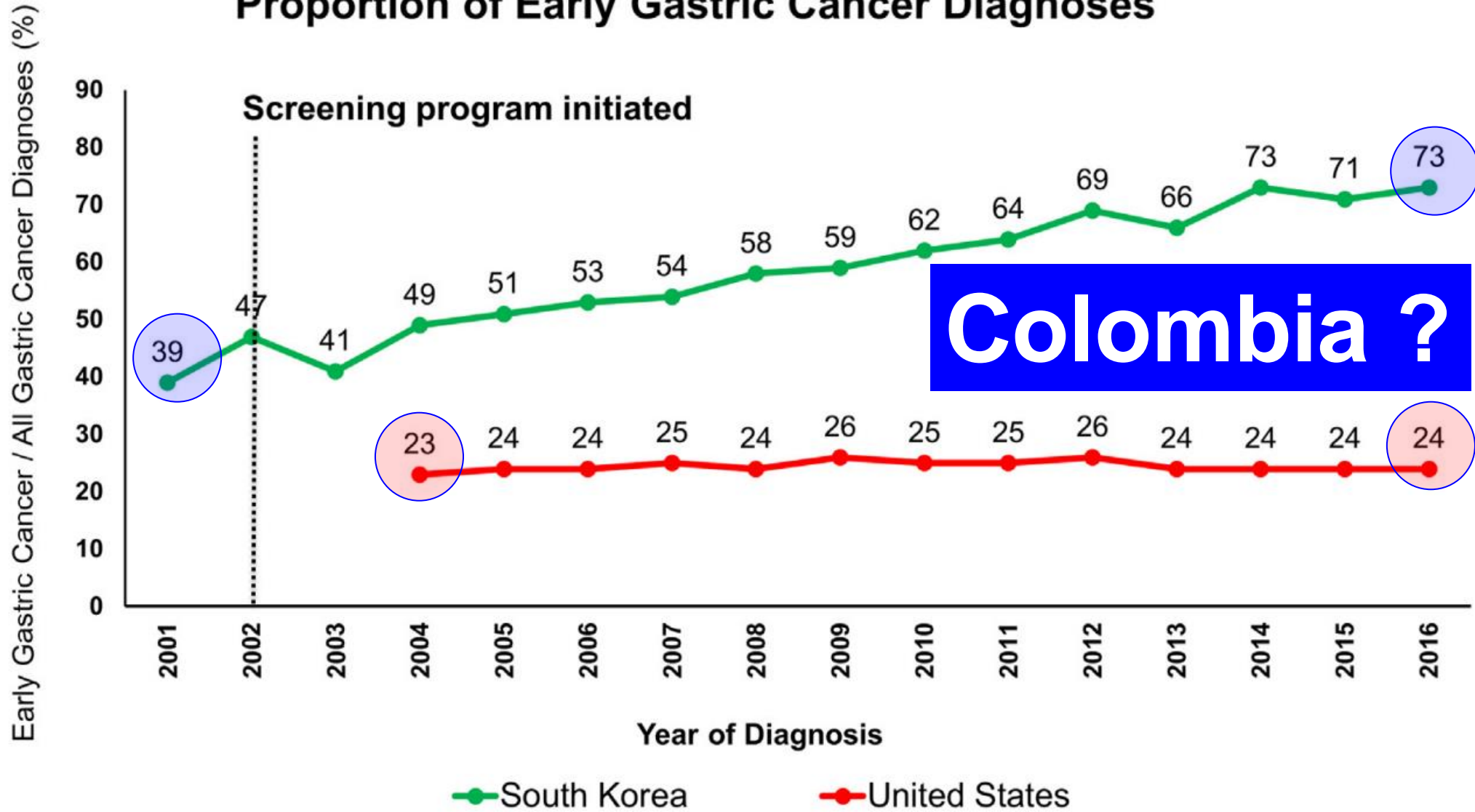
Intermedio 10-20/10⁵
Cada 5 años

Bajo riesgo $< 10/10^5$
No se recomienda



***GBD 2017 Stomach Cancer Collaborators*
Lancet Gastroenterol Hepatol 2020; 5: 42–54***


Proportion of Early Gastric Cancer Diagnoses



Gastritis atrófica por serología

WILEY AP&T Alimentary Pharmacology & Therapeutics

Systematic review with meta-analysis: diagnostic performance of the combination of pepsinogen, gastrin-17 and anti-*Helicobacter pylori* antibodies serum assays for the diagnosis of atrophic gastritis

R. M. Zagari¹ | S. Rabitti¹ | D. C. Greenwood² | L. H. Eusebi¹  | A. Vestito³ | F. Bazzoli¹

PG I mucosa oxíntica del cuerpo
PG II: antro duodeno,
G17:mucosa del antro
Anti *H.pylori* +

PGI/PGII <3
PG I < 3mcr/L
Atrofia corporal

Anti *H.pylori* +
G17 disminuida
Atrofia antral

Sensibilidad

74.7% (IC95% 62-84.3)

Especificidad

95.6% (IC 95% 92.6-97.4)

VPN

91%

Mensajes para la casa

Prevención Cáncer Gástrico LATAM?

Prevención primaria
Erradicar *H.pylori* a
Todos los infectados

Prevención secundaria
Vigilando Atrofia/MI avanzadas
OLGA/OLGIM
Endoscopios avanzados

Tamización endoscópica?
Estudiarlo en cada país

Muchas gracias!