

***H.pylori* y otras causas de cáncer gástrico**

William Otero R MD FAGA FACP
Profesor Titular de Medicina,
Universidad Nacional de Colombia
Hospital Universitario Nacional de Colombia



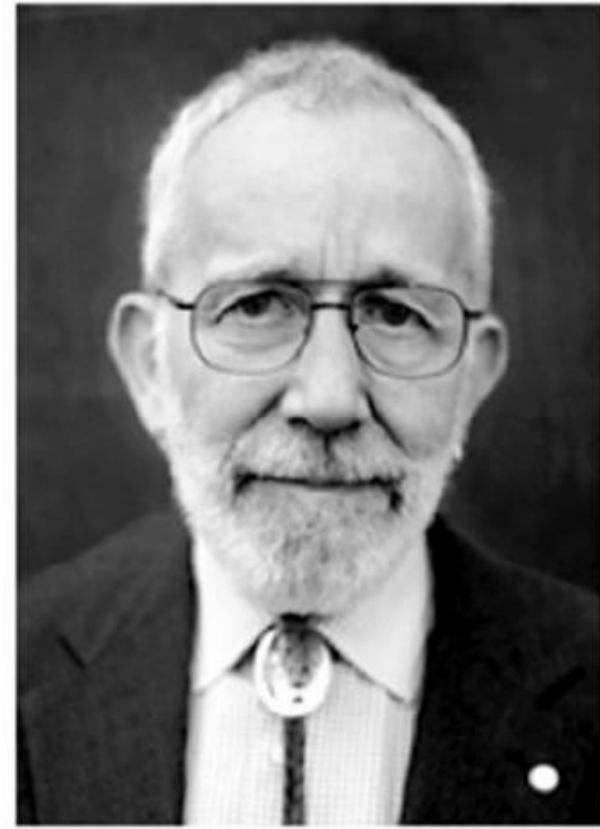
Cáncer Gástrico



Rudolph Virchow



Pelayo Correa



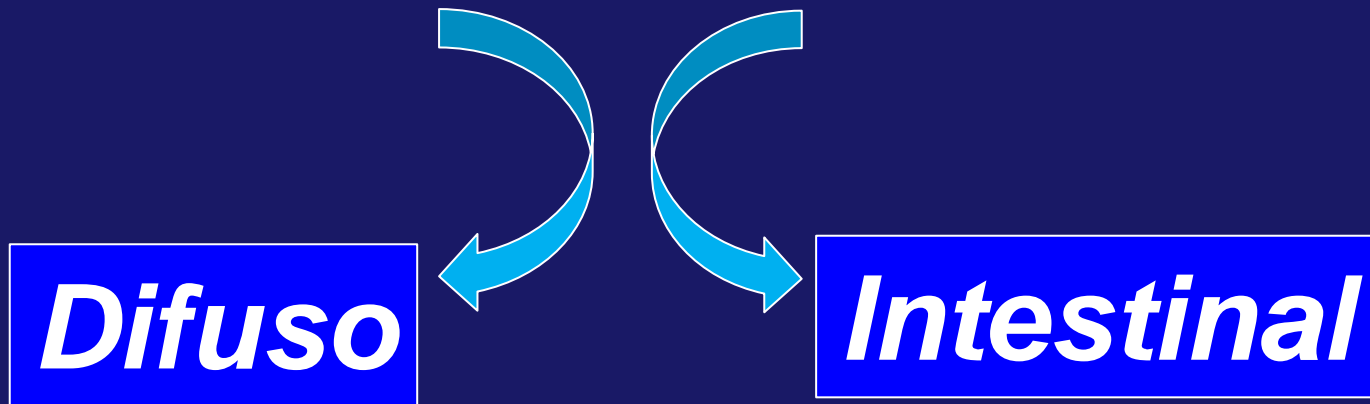
Robin Warren

Cáncer gástrico



Cancer gàstrico

90% adenocarcinomas

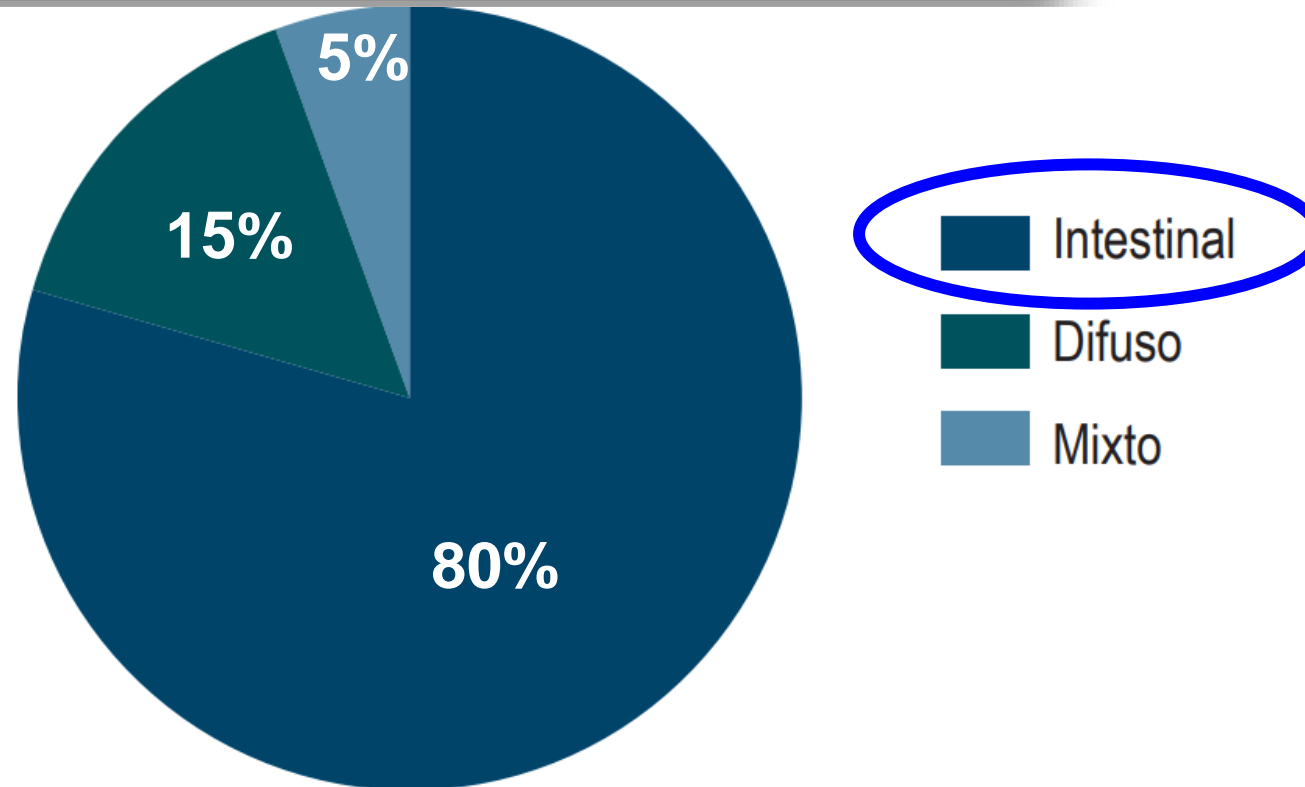


Lauren P, Acta Pathol, Microbiol Scand 1965;64:31-49

Características sociodemográficas e histopatológicas en pacientes con cáncer gástrico en una población con alto riesgo en Colombia

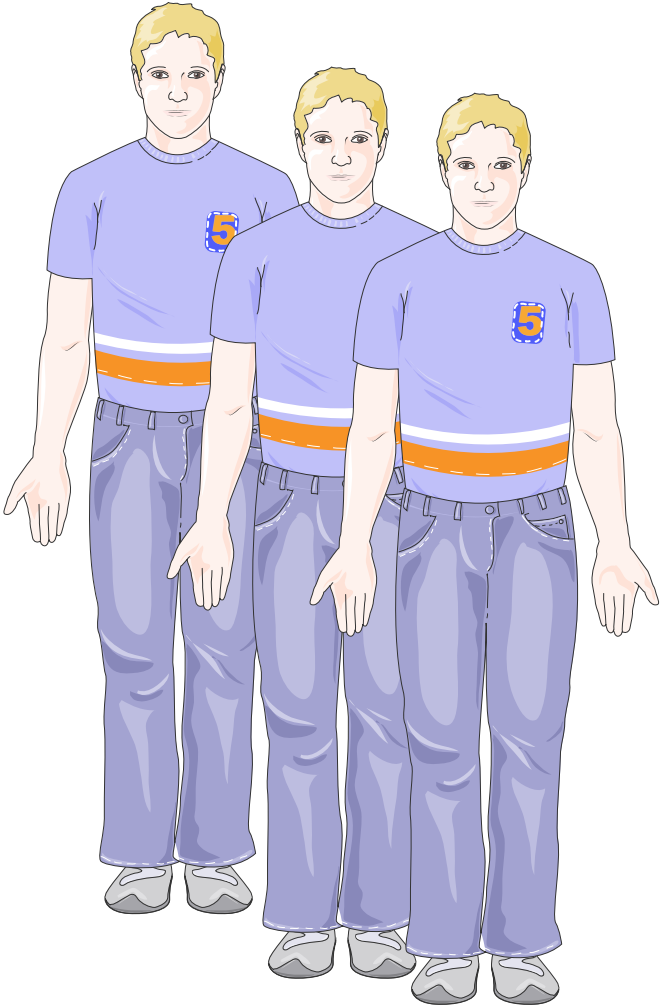
Sociodemographic and histopathological characteristics of patients with gastric cancer in a high-risk population in Colombia

José Darío Portillo-Miño,^{1*}  Laura María Araújo-Prado,²  Jorge Mauricio Melo,³  Yeison Harvey Carlosama-Rosero.⁴ 



Cáncer gástrico

2-3



1



Adenocarcinoma gástrico



Tumores Epiteliales Heterogéneos



Clínica, Biológica, Genética, Histología



Causas Medio-Ambientales, Genéticas

Cáncer gástrico

Esporádicos
80-90%

Familiares
7-10%

Genéticos
1-3%

CG familiar intestinal

**Adenocarcinoma con
Pólipos Proximales**

**CG difuso hereditario
E Cadherina (CDH1)**

Riesgo CG 80 años 70%
Gastrectomía profiláctica

Cáncer gástrico

Diagnóstico endoscópico

Cancer of the Esophagus and Esophagogastric Junction: An Eighth Edition Staging Primer

Thomas W. Rice, MD,^{a,*} Hemant Ishwaran, PhD,^b Mark K. Ferguson, MD,^c
Eugene H. Blackstone, MD,^a Peter Goldstraw, MD^d

^aCleveland Clinic, Cleveland, Ohio

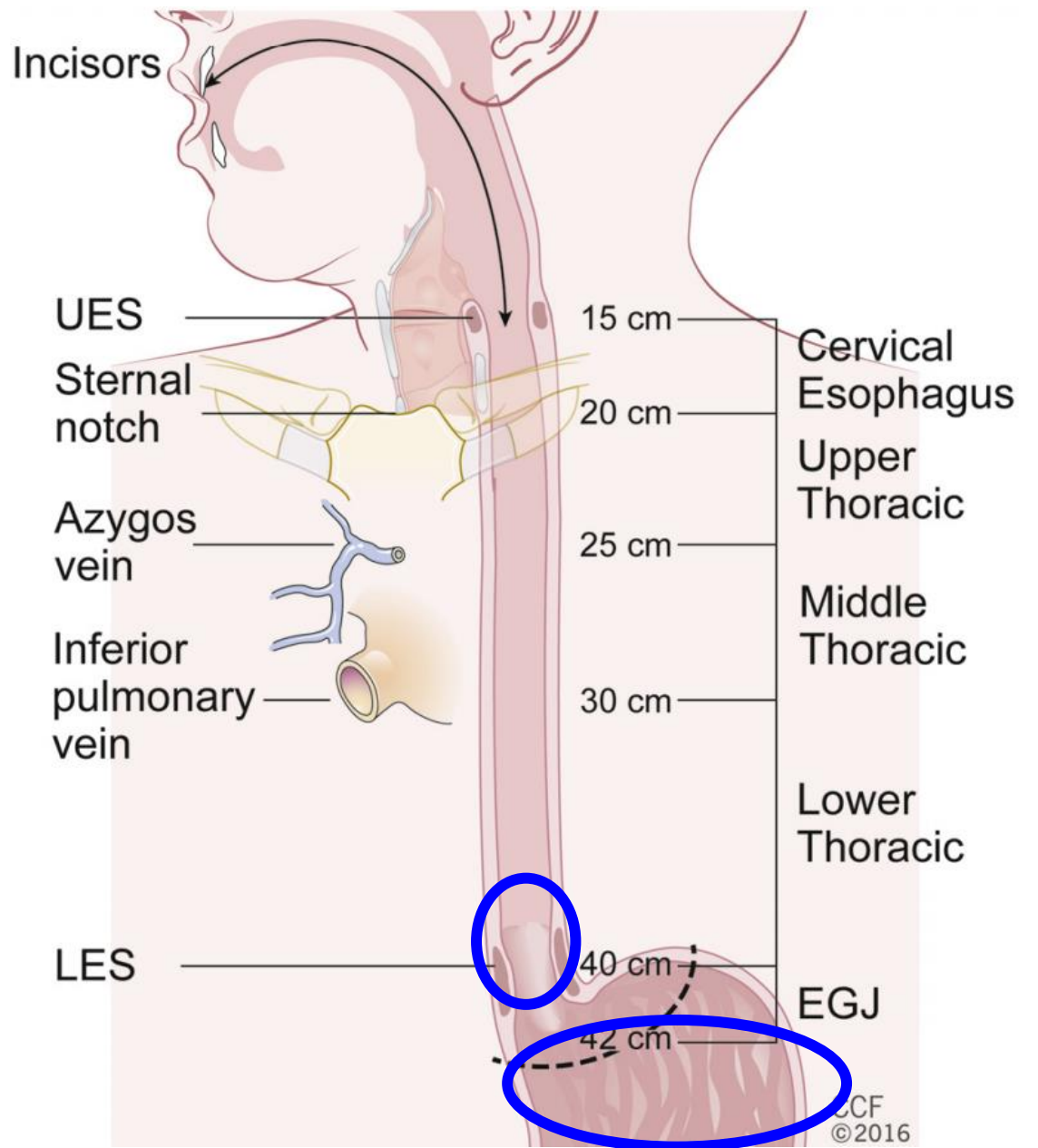
^bUniversity of Miami, Miami, Florida

^cThe University of Chicago, Chicago, Illinois

^dNational Heart and Lung Institute, Imperial College, London, United Kingdom

**Esófago:
Epicentro 2 cm más proximales
al estómago, Afectan
unión esófago- gástrica**

**Estómago:
Epicentro 2-5 cm proximales
del estómago, no cruzan
unión esófago- gástrica**



Cáncer Gástrico endoscopia

Temprano

Mucosa, submucosa

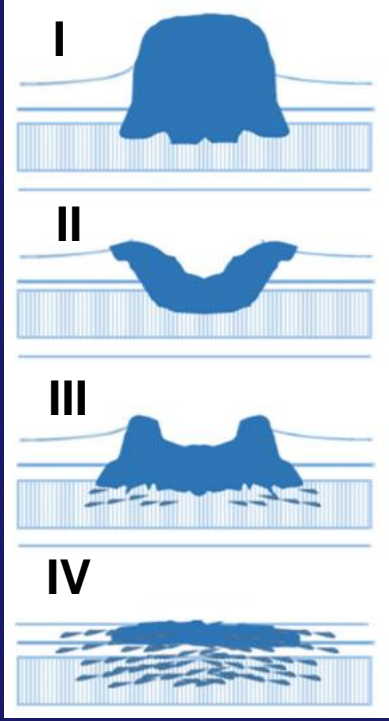
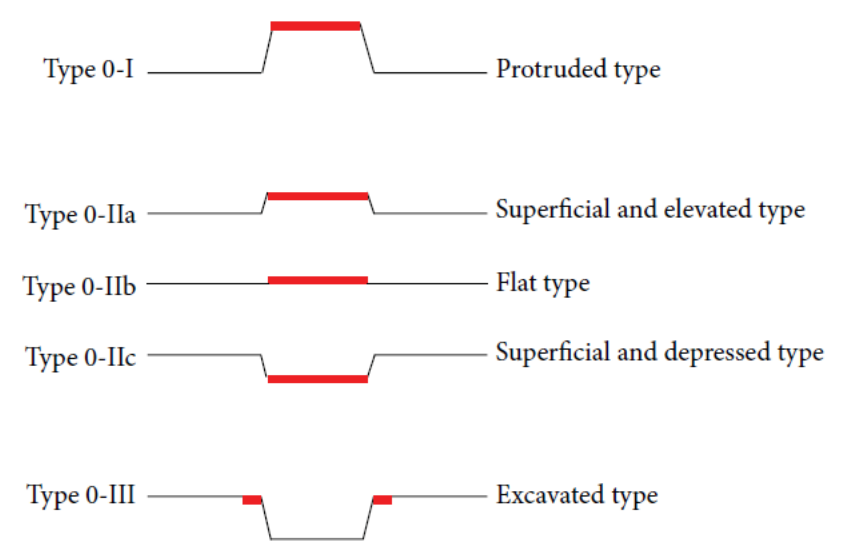
Con o sin ganglios

Sobrevida 5 años 100%

37 meses

Avanzado

Sobrevida 5 años 5-10%

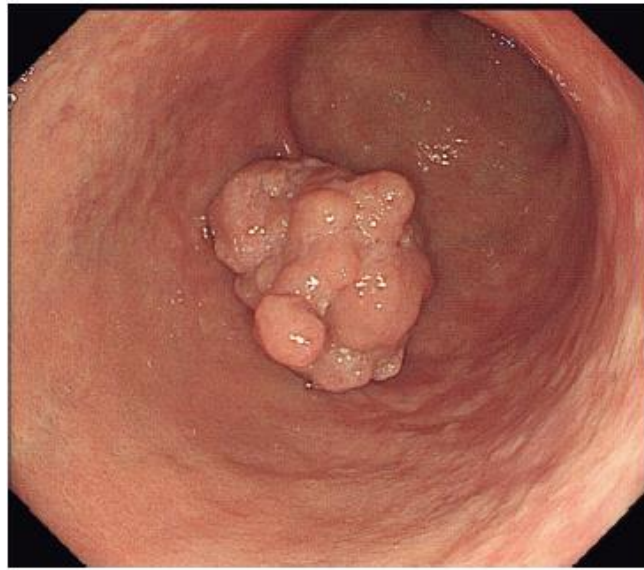


Elevado
Masa

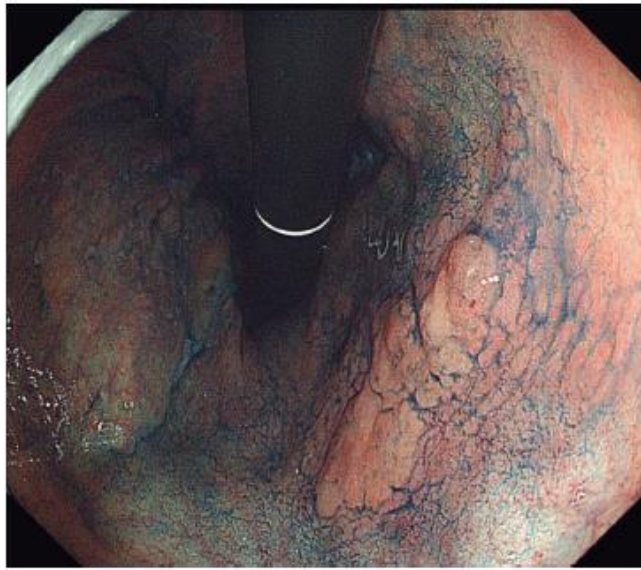
Ulcerado

Infiltrante,
Ulcerado

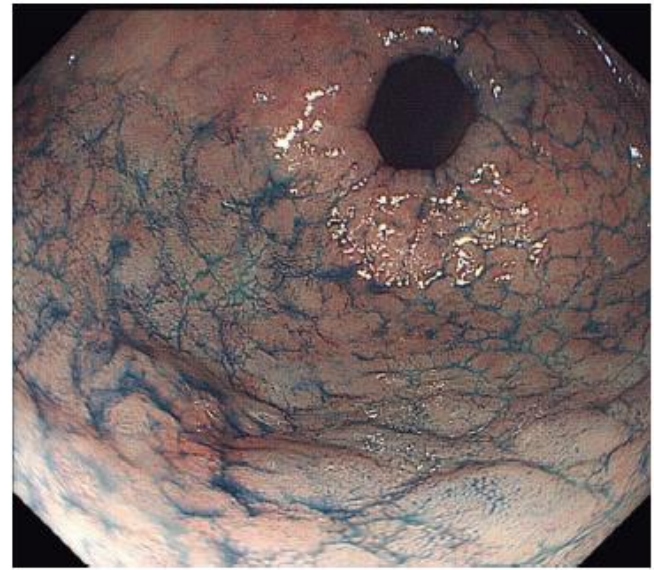
Linitis
Plástica



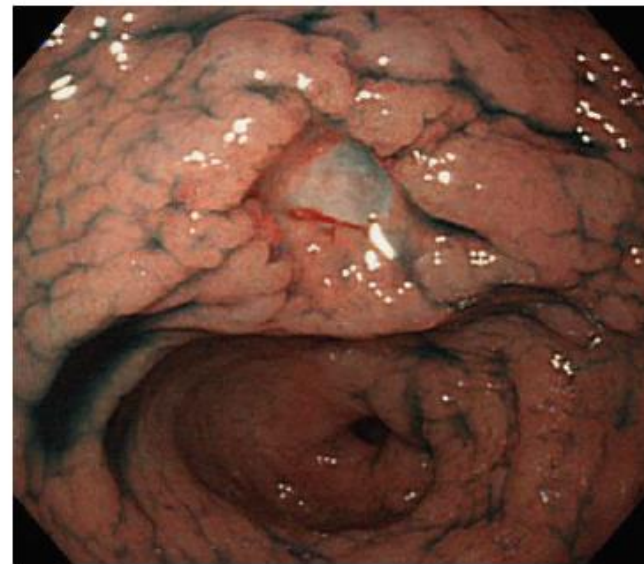
(a)



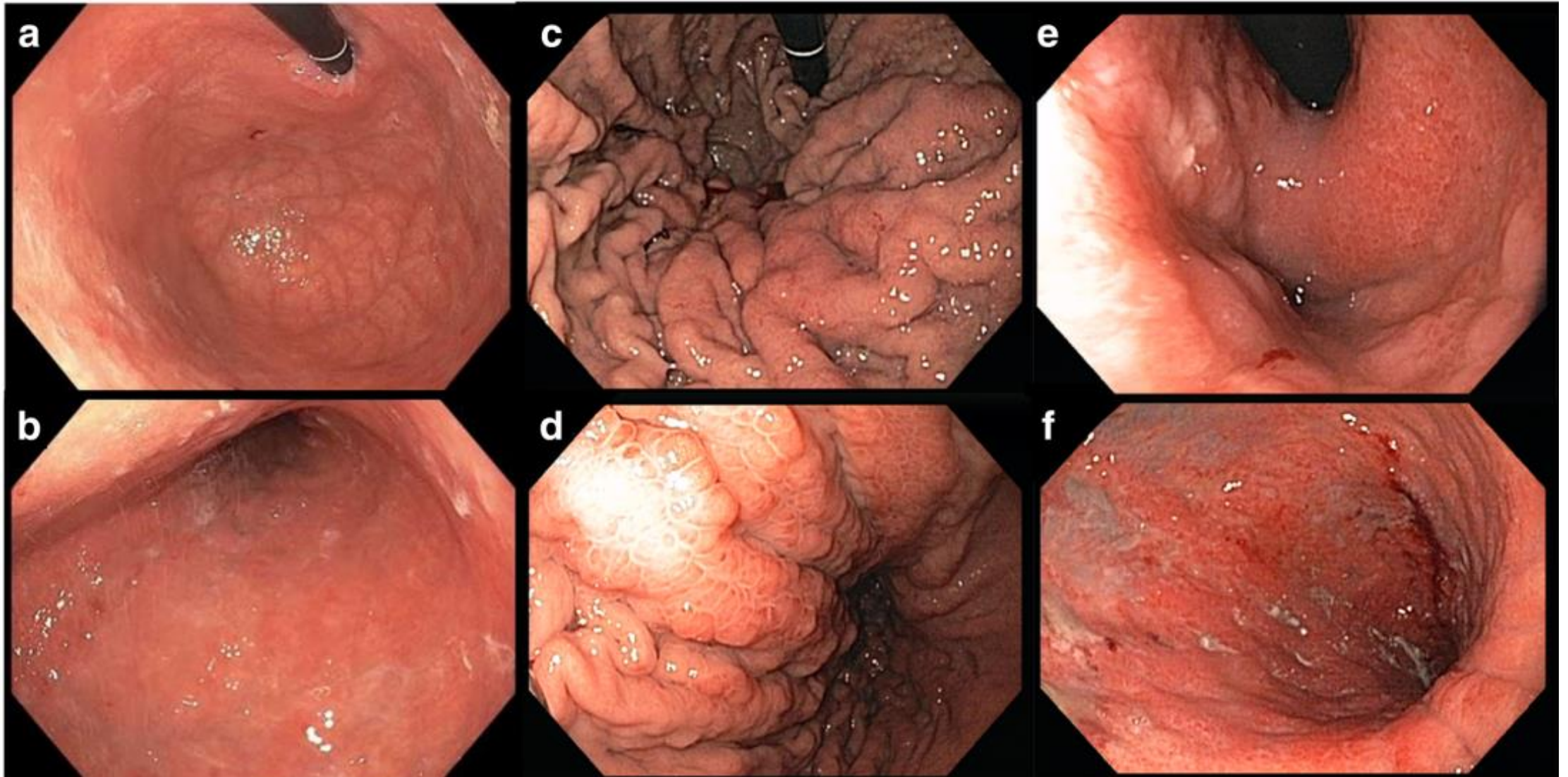
(b)

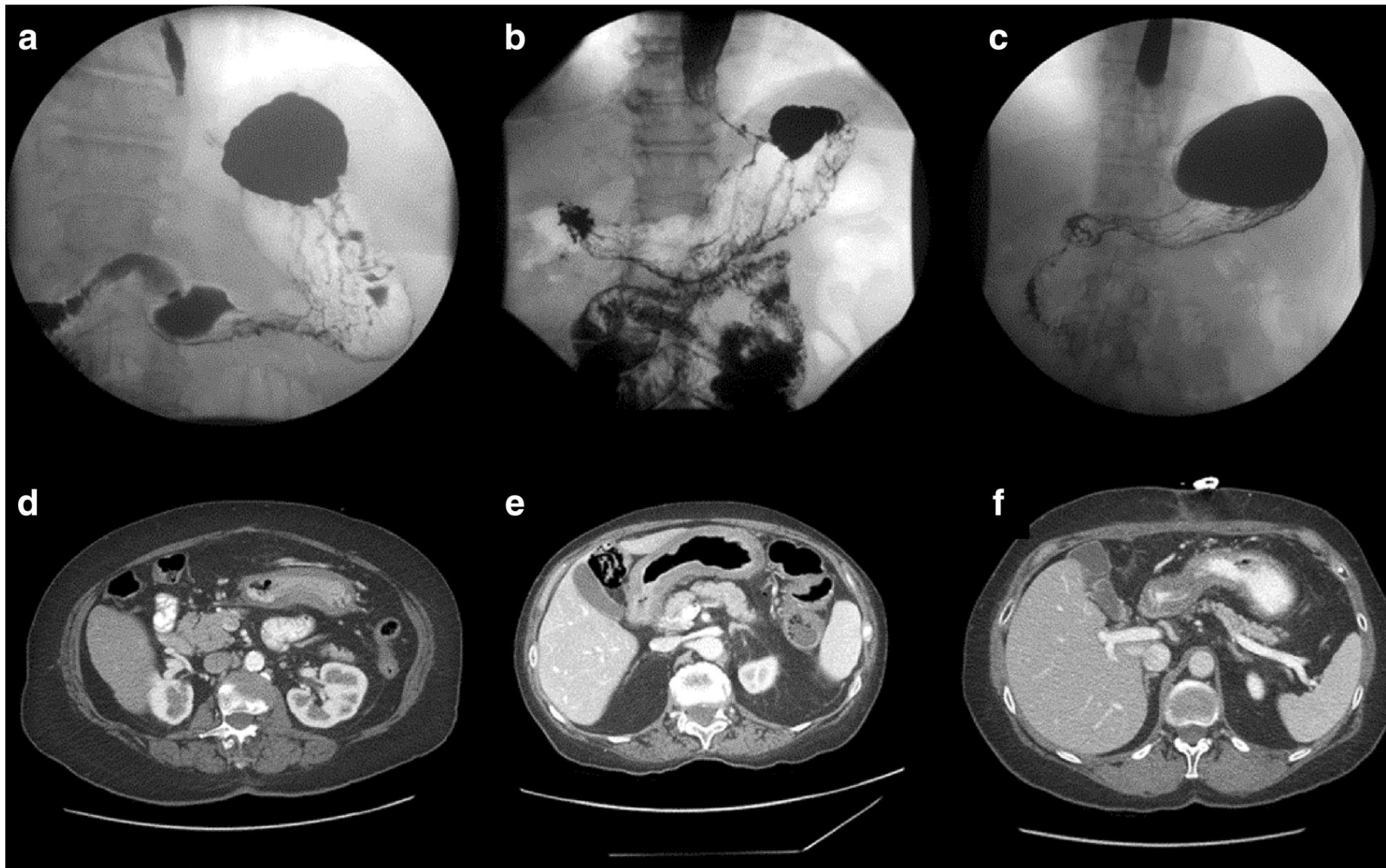


(c)



Linitis plástica





Ecoendoscopia, Tomografía emisora de positrones

Diagnóstico definitivo

**“Estándar
de oro”**



**Úlceras gástricas
5% Malignas ≈ Benignas**

**1 Biopsia 70% S
5 Biopsias 98% S**

Càncer gàstrico



Histologia

+

Inmunoquímica

**Expresión (HER2)
Receptor 2, Factor de
Crecimiento humano**

**Error de replicación
RER**


**Drogas Anti HER2
Inmunoterapia RER+
Inestabilidad Microsatelite**



Check for updates

Targeted Therapies in Advanced Gastric Cancer

Timil H. Patel, MD

Michael Cecchini, MD* 

Immunotherapy

In the past several years, the ICIs have revolutionized the treatment for many cancers. One such checkpoint is programmed death 1 (PD1), which is an inhibitory receptor expressed mainly on activated T cells [67]. In tumor cells, inhibition of PD-1 prevents PD-1 from binding to its ligands, PD-L1 and PD-L2, thus restoring anti-tumor immunity [68]. Studies have shown overexpression of PD-L1 in gastric cancer, making the inhibition of PD-1 an exciting target in this disease group [5].

Nivolumab and ipilimumab

Nivolumab is a fully human IgG4 monoclonal antibody inhibitor of PD-1. In 2017, the phase 3 ATTRACTION-2 trial evaluated the efficacy of third-line nivolumab versus placebo in Asian patients with advanced gastric or GEJ cancer regardless of PD-L1 expression [69]. Patients were randomly assigned 2:1 to receive nivolumab or placebo, and the results revealed improved mOS with nivolumab of 5.26 months vs 4.14 months with placebo (HR 0.63; 95% CI 0.51–0.78; $P < 0.001$). Furthermore, the nivolumab 12-month OS was 26.2% vs 10.9% with placebo. These results led to the approval of nivolumab in Japan regardless of PD-L1 status. Nivolumab is not currently approved for gastric cancer in the USA.

Anti HER2

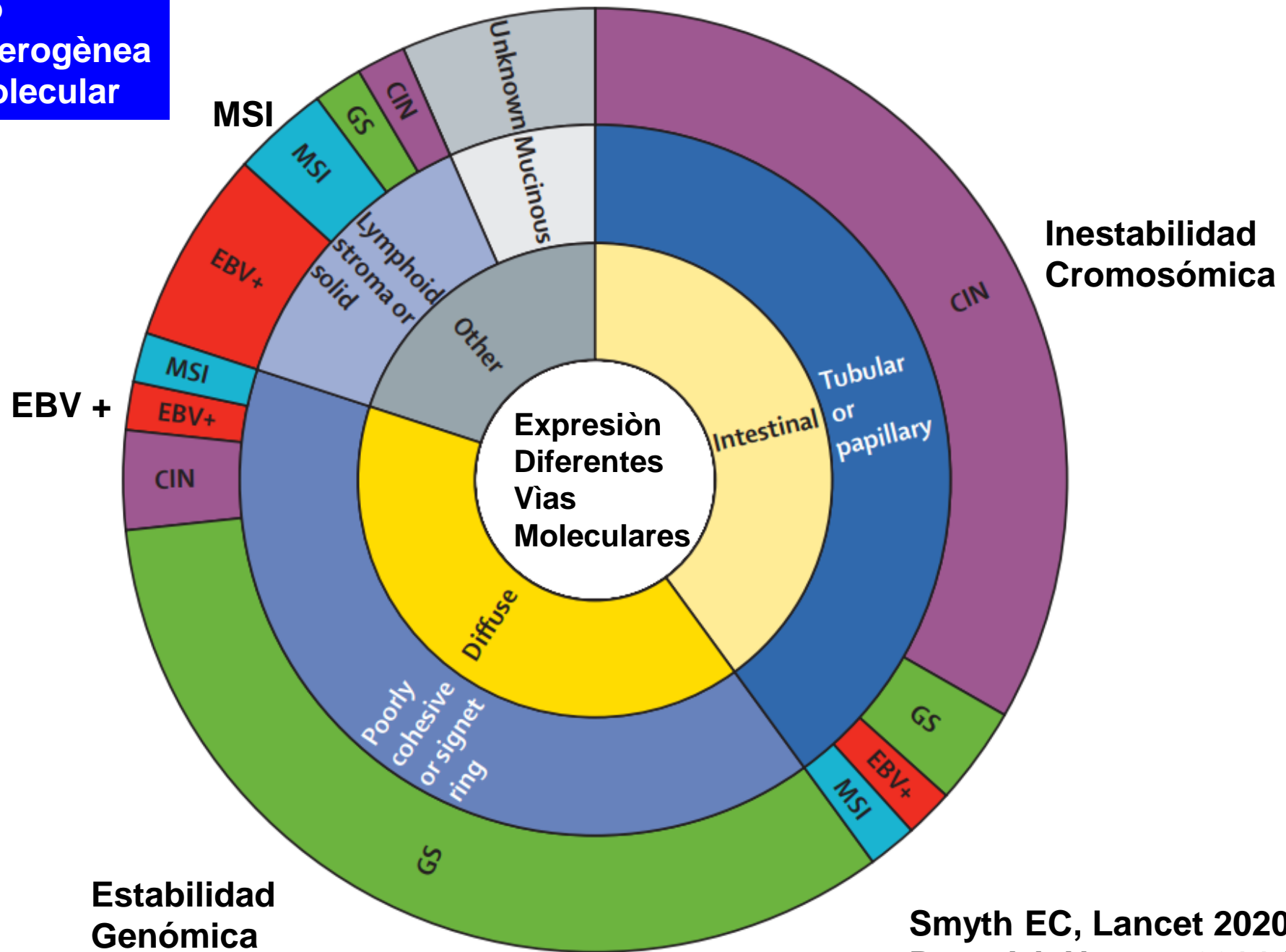
Anti EGFR

Anti VEGF

Anti MTOR

Inhibidores
PARP

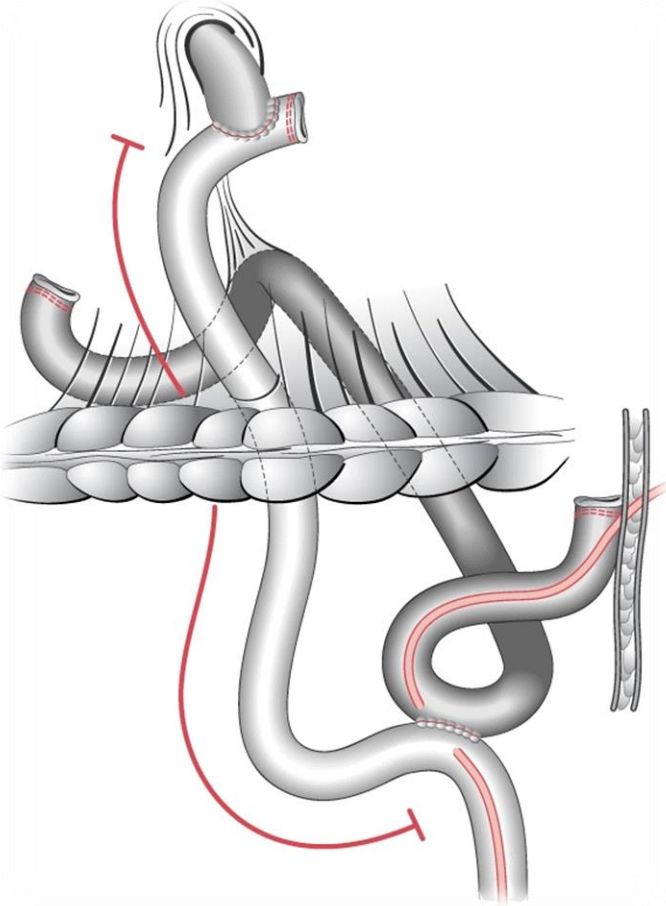
Cancer Gàstrico
Enfermedad heterogènea
Clasificaciòn Molecular



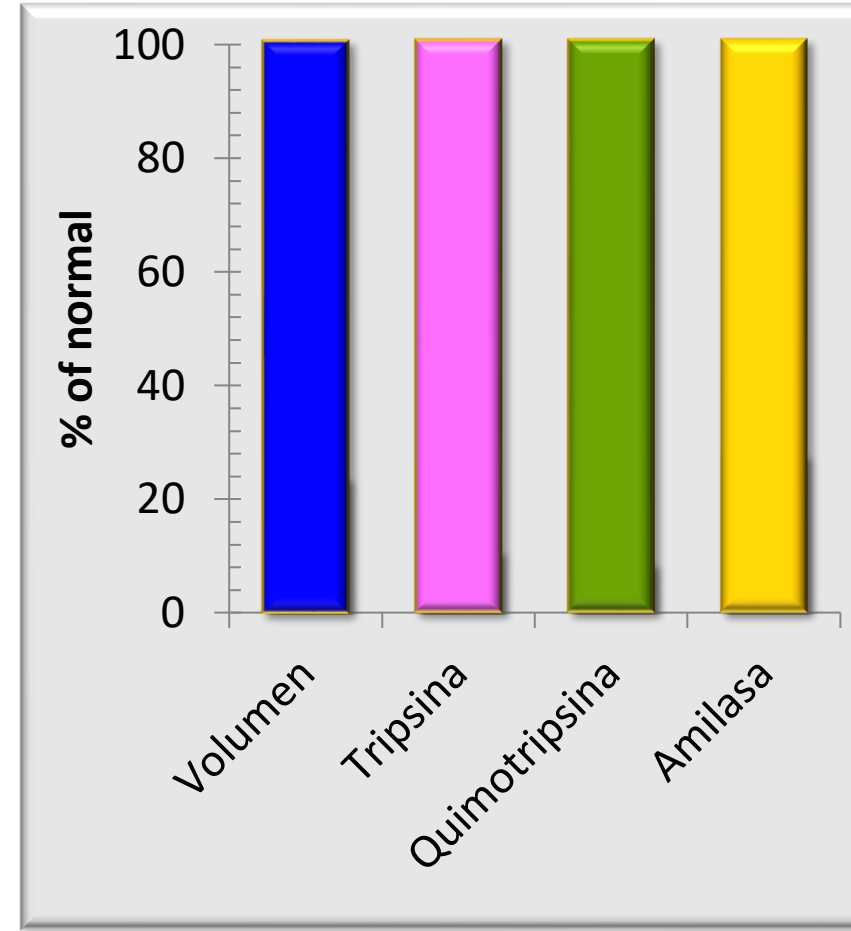
Smyth EC, Lancet 2020;396:635–48
 Bass AJ, Nature 2014;513:202-9

Insuficiencia pancreática
Exocrina pos cirugía
Cáncer gástrico

Secreción pancreática pos gastrectomía



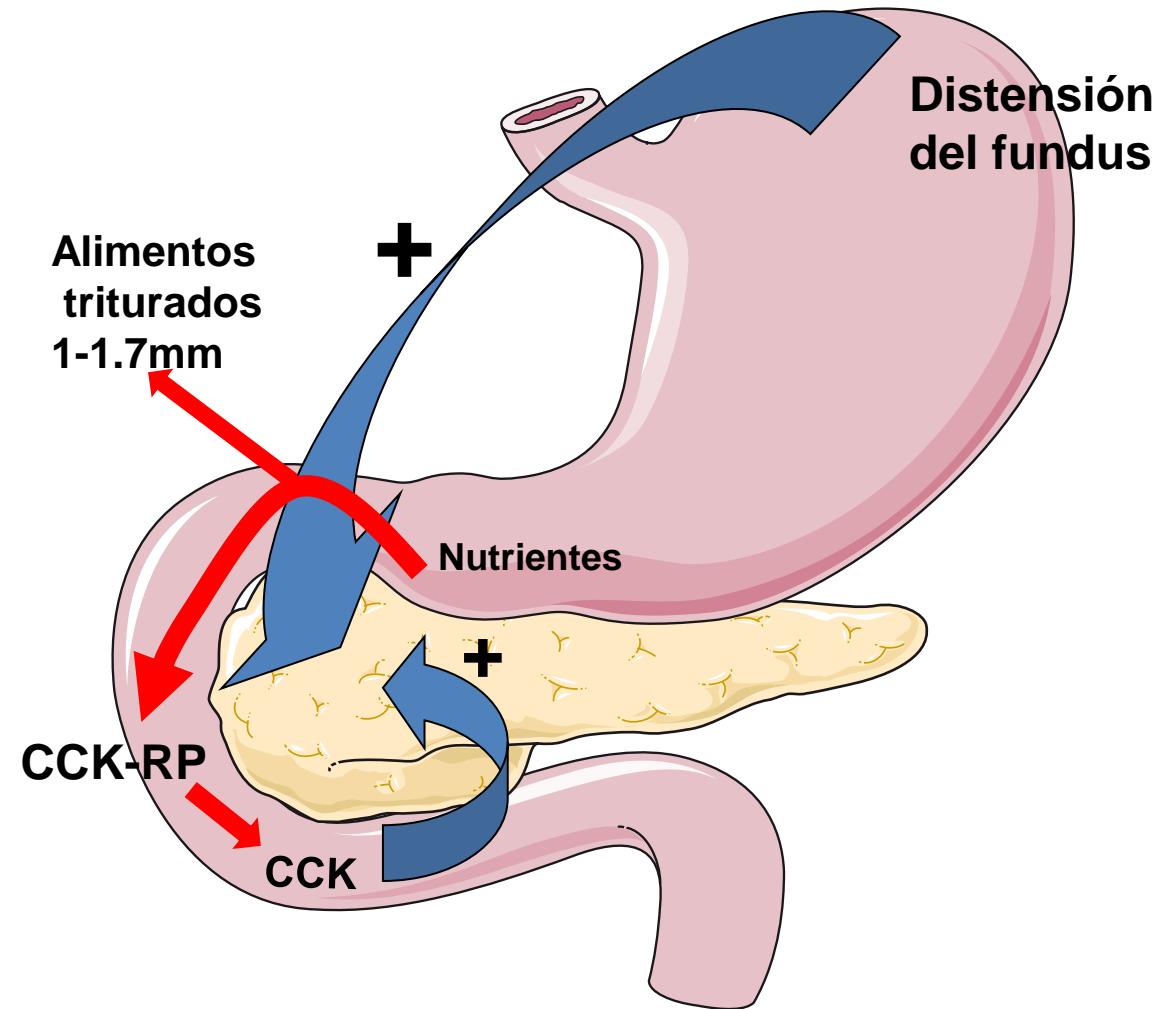
IPE 6 meses: Parcial 80%, Total 100%



Cortesía Dr Domínguez-Muñoz

Friess et al, Am J Gastroenterol 1996
Keller J, Gut 2005;54 (Suppl.6):vi1-vi28,

Fisiología pancreática



IPE Manifestaciones clínicas



ORIGINAL ARTICLE

Pancreatic enzyme supplementation after gastrectomy for gastric cancer: a randomized controlled trial

**Marco Catarci^{1,3} · Manuele Berlanda¹ · Giovanni Battista Grassi¹ ·
Francesco Masedu² · Stefano Guadagni²**

Càncer gàstrico



Histologia

+

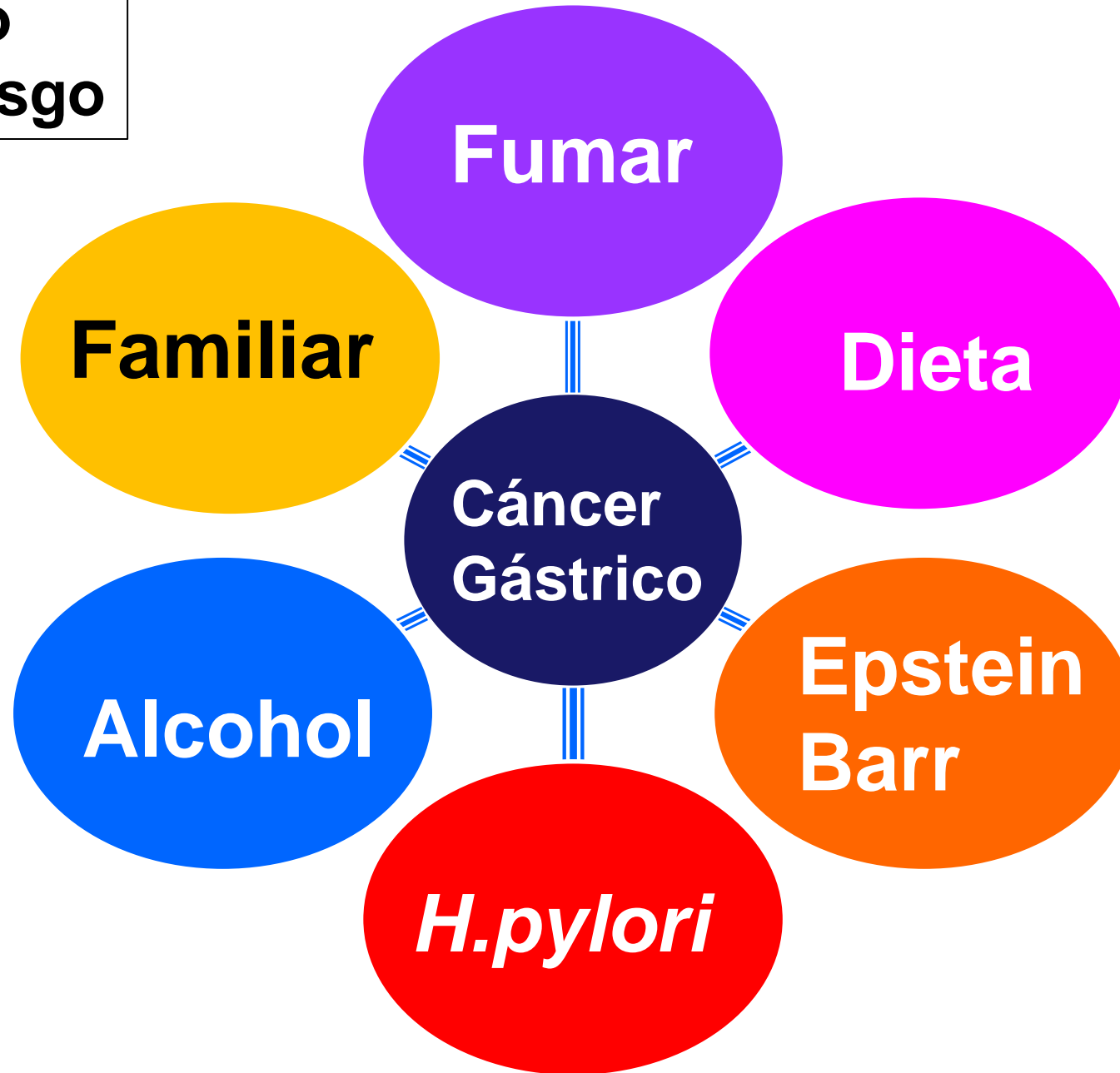
Inmunoquímica

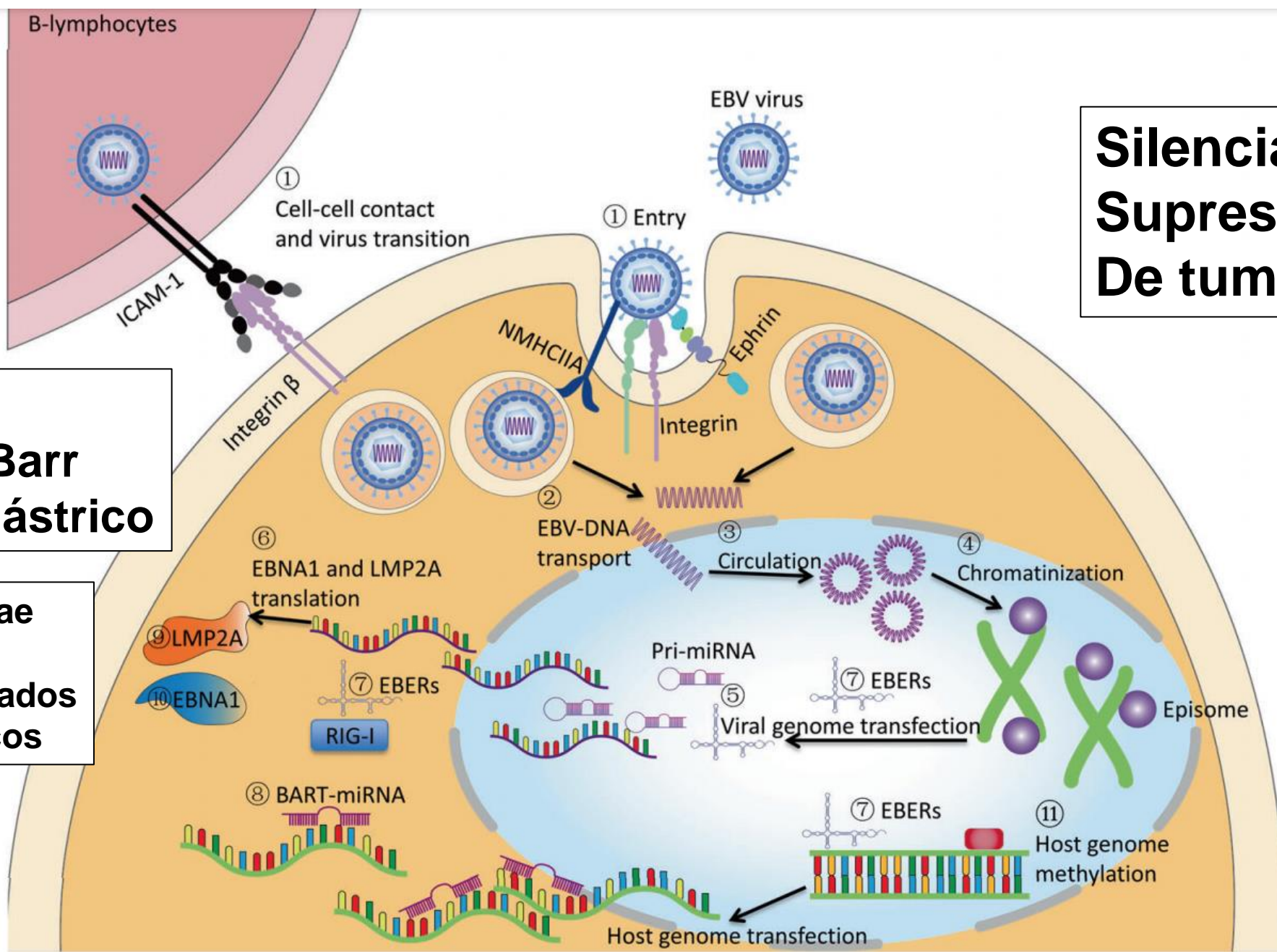
**Expresión (HER2)
Receptor 2, Factor de
Crecimiento humano**

**Error de replicación
RER**

**Drogas Anti HER2
Inmunoterapia RER+
Inestabilidad Microsatelite**

Cáncer Gástrico
Factores de Riesgo





**Silencia genes
Supresores
De tumores**

**Virus
Epstein Barr
Cáncer gástrico**

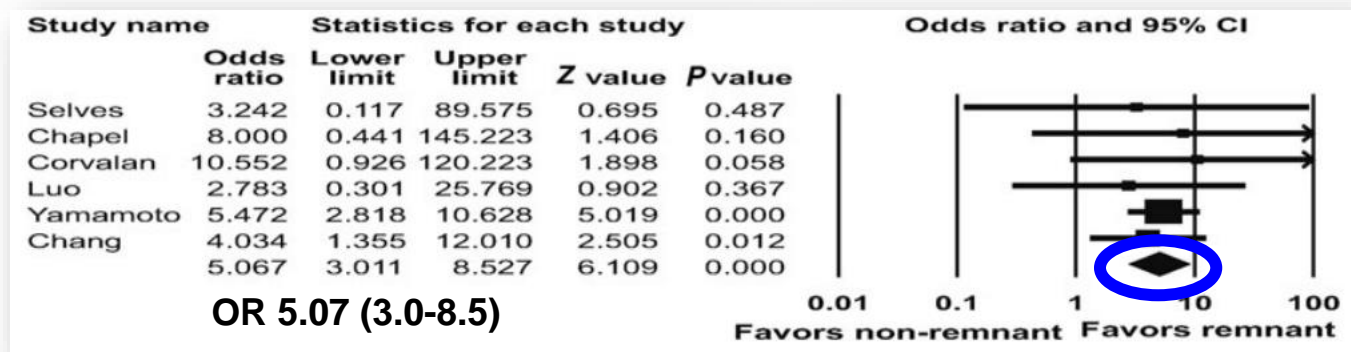
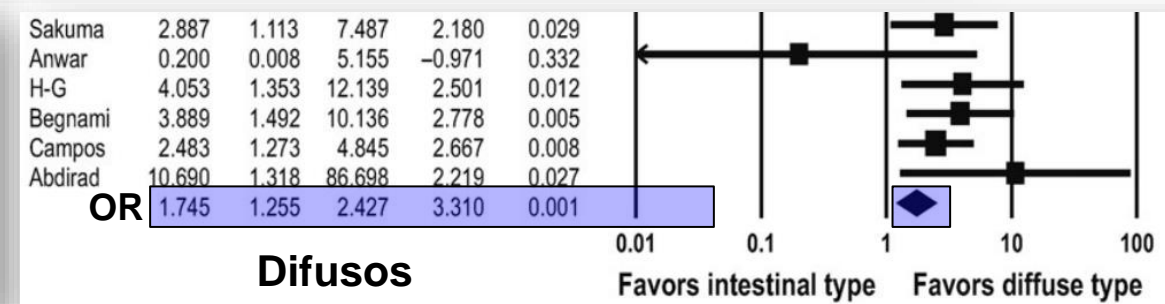
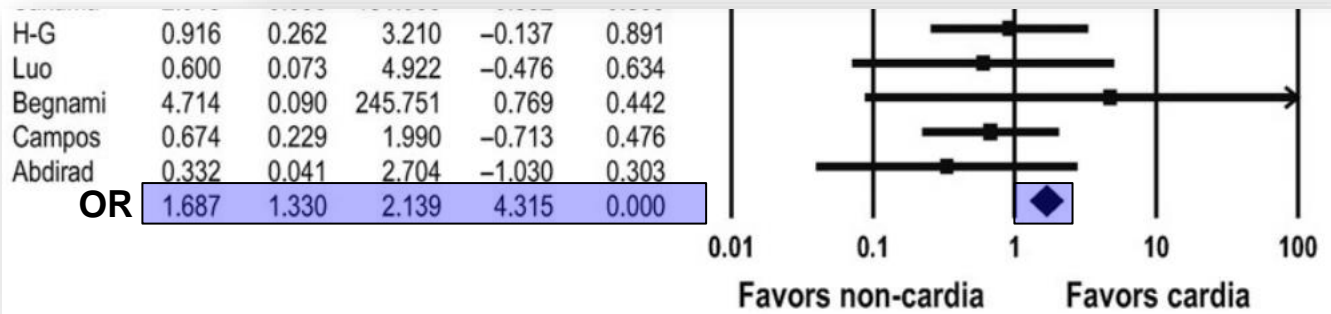
**Herpesviridae
DNA
>90% infectados
Asintomáticos**

REVIEW

Clinicopathological and molecular characteristics of Epstein-Barr virus-associated gastric carcinoma: A meta-analysis

Ju-Han Lee, Seo-Hee Kim, Sun-Hee Han, Jung-Suk An, Eung-Seok Lee and Young-Sik Kim

Department of Pathology, Bioinformatics Interest Group, Korea University Ansan Hospital, Ansan, Korea



Difusos
Estroma linfoide
Linfo-epitelioma "like"

Dieta

Dieta y reducción riesgo CG

IARC

**Alto consumo
de frutas**



“Probablemente”

**Alto consumo
de vegetales**

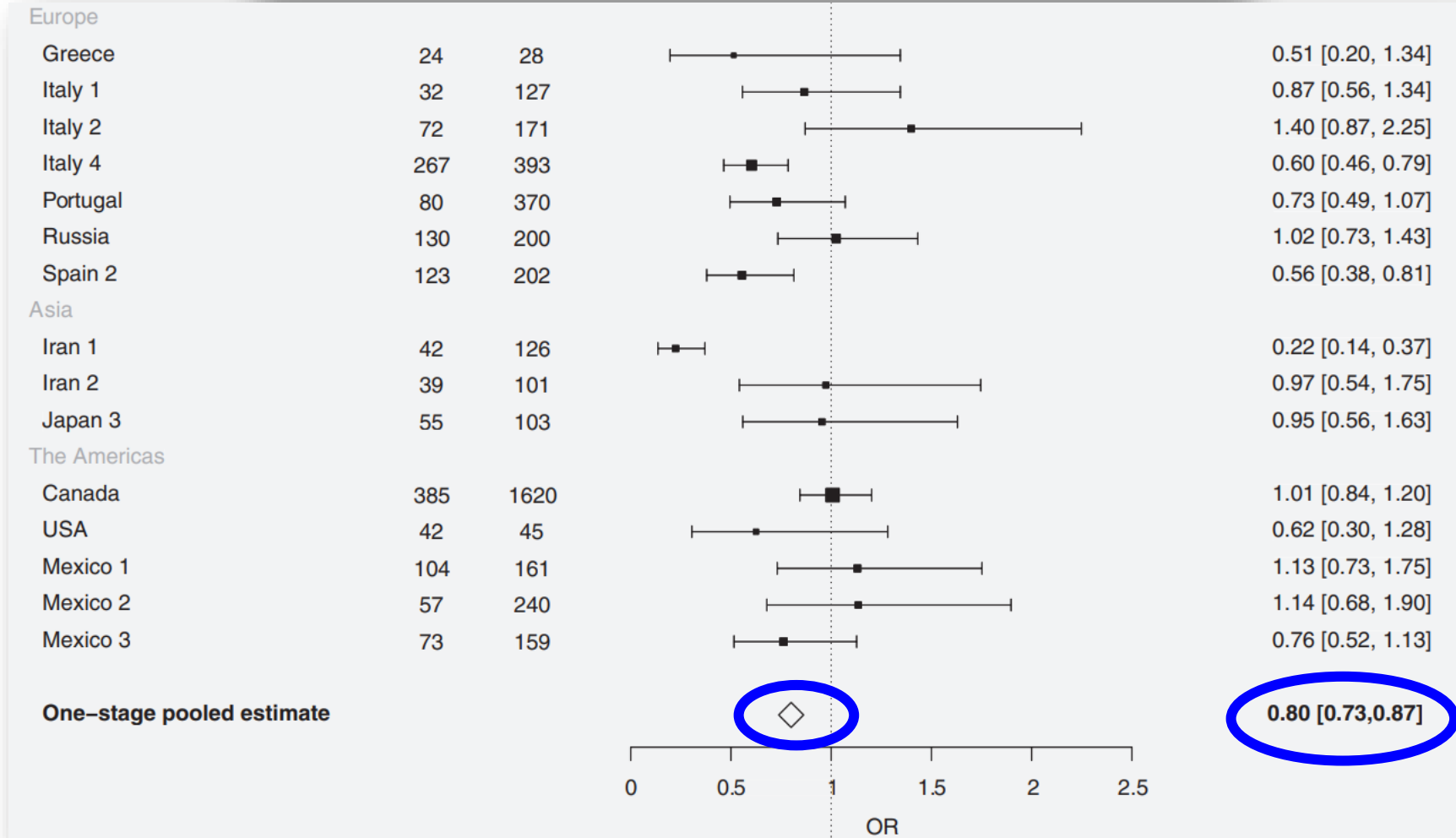


“Posiblemente”

Citrus fruit intake and gastric cancer: The stomach cancer pooling (StoP) project consortium

Paola Bertuccio ¹, Gianfranco Alicandro ¹, Matteo Rota ¹, Claudio Pelucchi ¹, Rossella Bonzi ¹, Carlotta Galeone ¹, Francesca Bravi ¹, Kenneth C. Johnson ², Jinfu Hu ³, Domenico Palli ⁴, Monica Ferraroni ¹, Lizbeth López-Carrillo ⁵, Nuno Lunet ^{6,7}, Ana Ferro ⁷, Reza Malekzadeh ⁸, David Zaridze ⁹, Dmitry Maximovitch ⁹, Jesus Vioque ^{10,11}, Eva M. Navarrete-Munoz ^{10,11}, Mohammadreza Pakseresh ^{8,12,13}, Raúl U. Hernández-Ramírez ^{5,14}, Malaquias López-Cervantes ¹⁵, Mary Ward ¹⁶, Farhad Pourfarzi ^{8,17}, Shoichiro Tsugane ¹⁸, Akihisa Hidaka ¹⁸, Zuo-Feng Zhang ¹⁹, Robert C. Kurtz ²⁰, Pagona Lagiou ^{21,22}, Areti Lagiou ²³, Paolo Boffetta ²⁴, Stefania Boccia ^{25,26}, Eva Negri ²⁷ and Carlo La Vecchia ¹

Frutas





ELSEVIER

Contents lists available at ScienceDirect

Food Research International

journal homepage: www.elsevier.com/locate/foodres

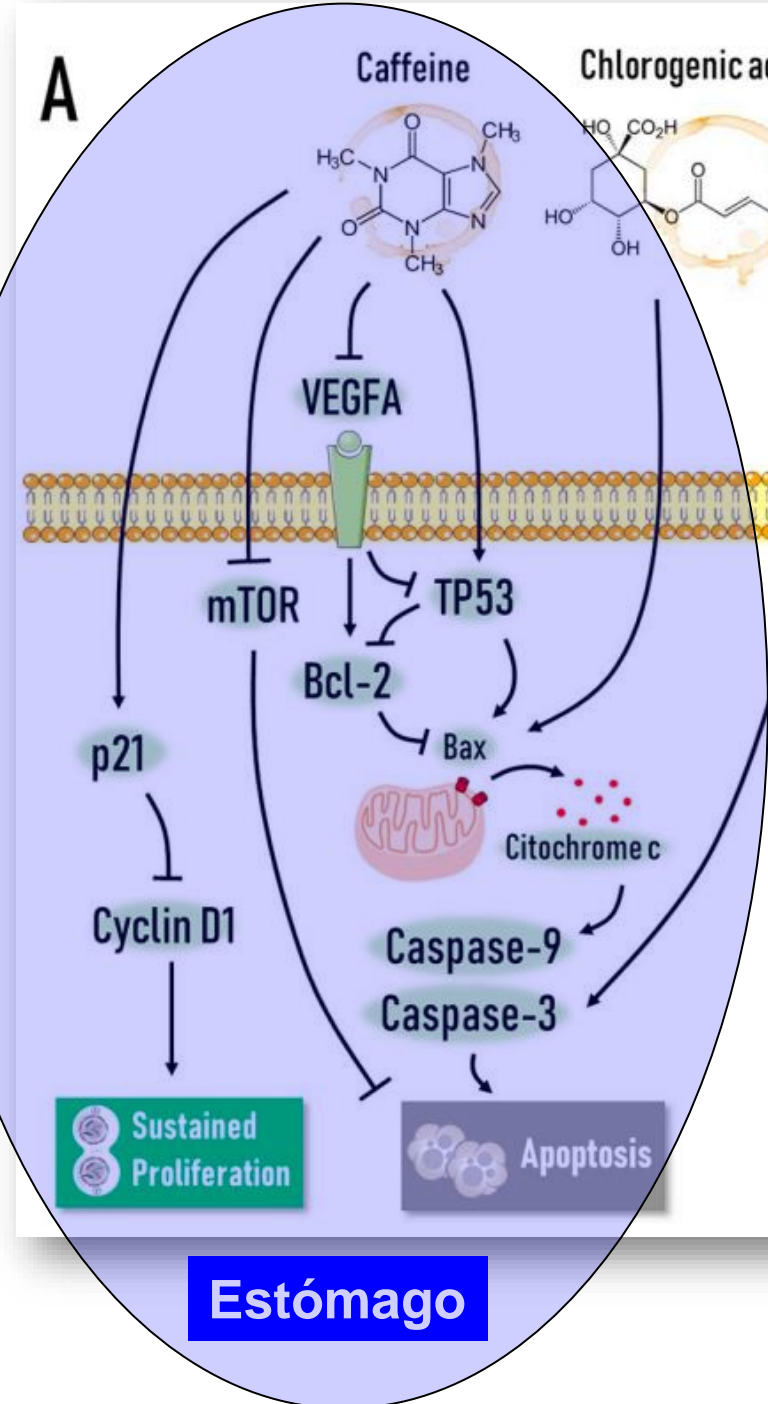
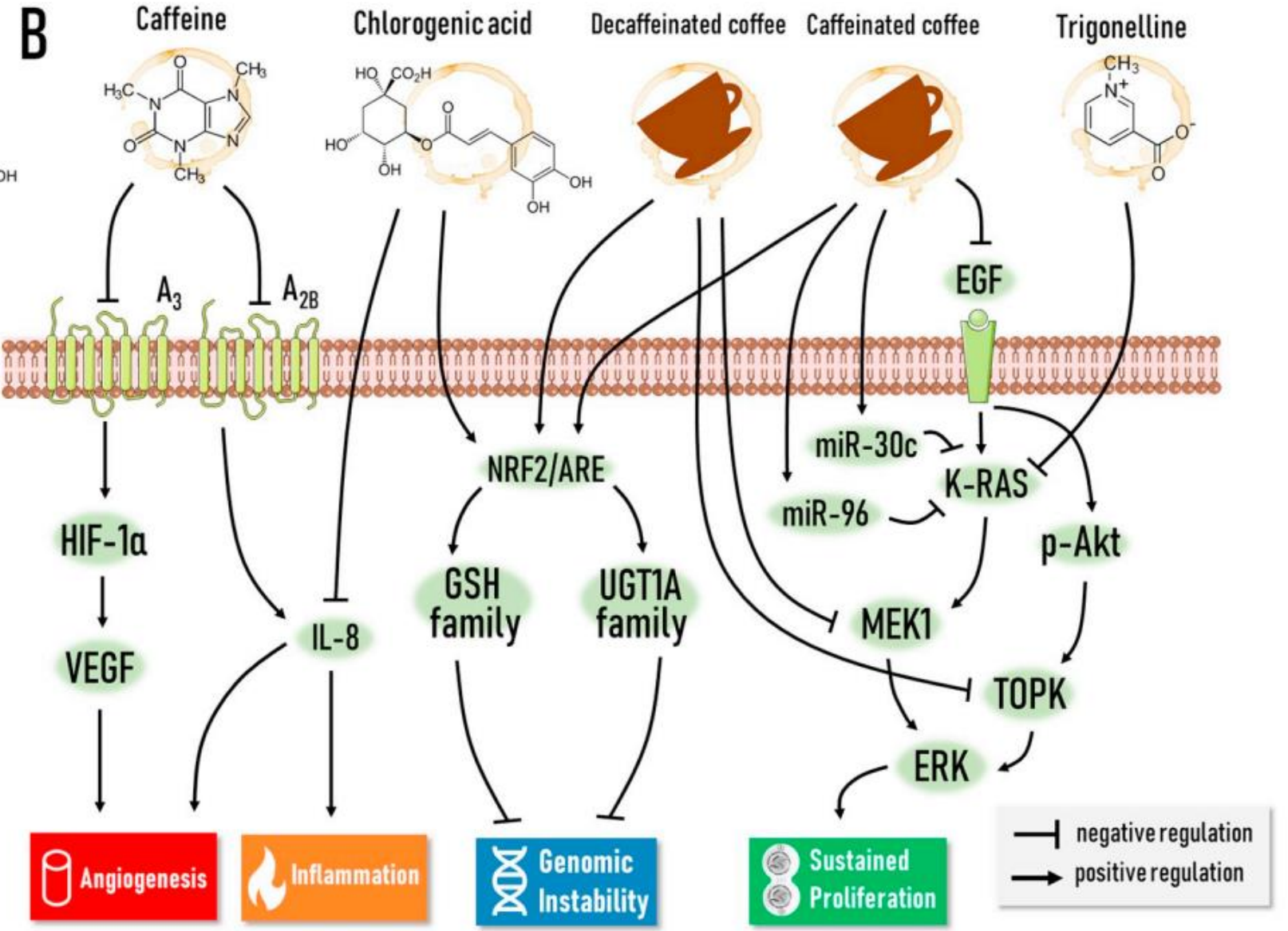


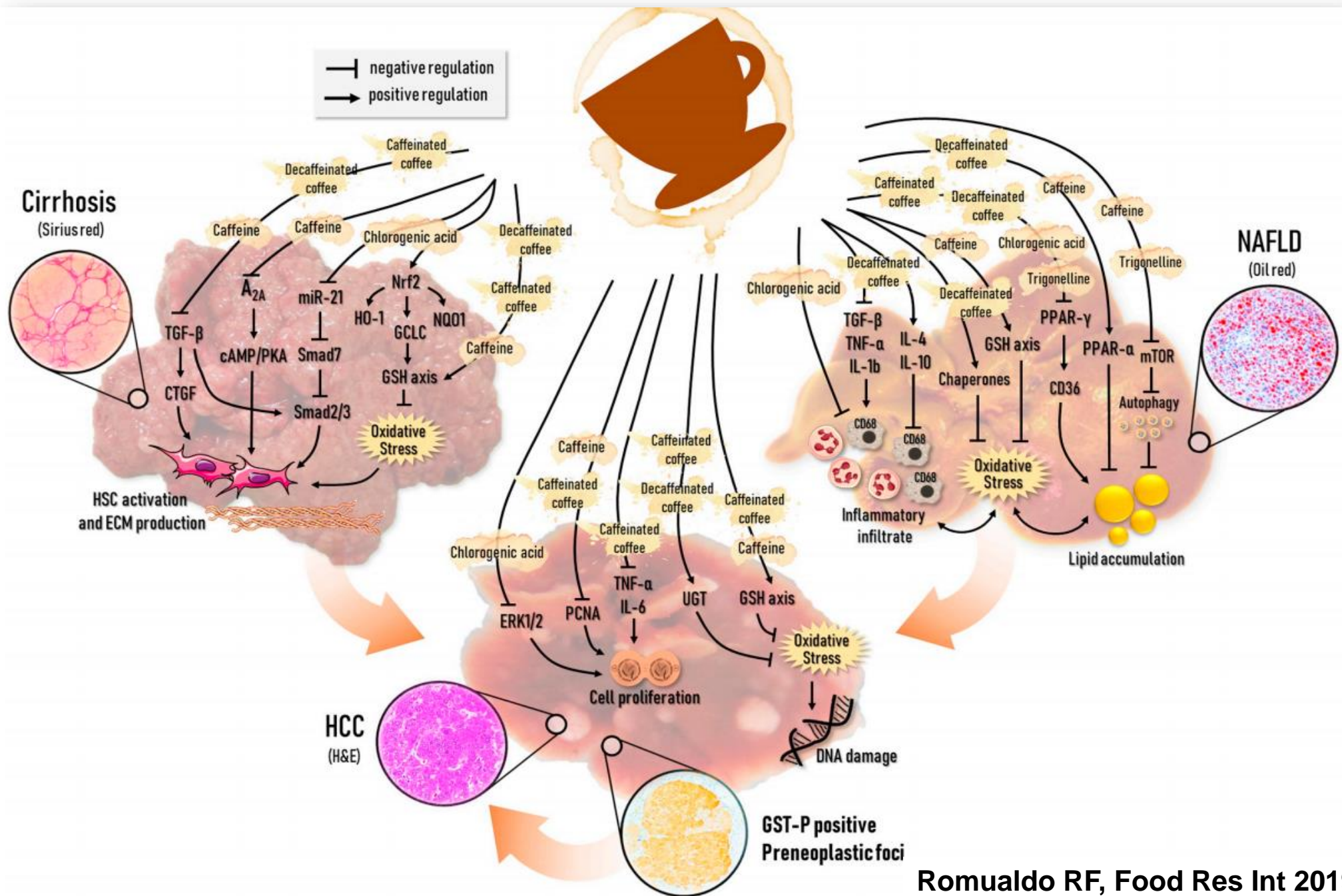
Review

Drinking for protection? Epidemiological and experimental evidence on the beneficial effects of coffee or major coffee compounds against gastrointestinal and liver carcinogenesis

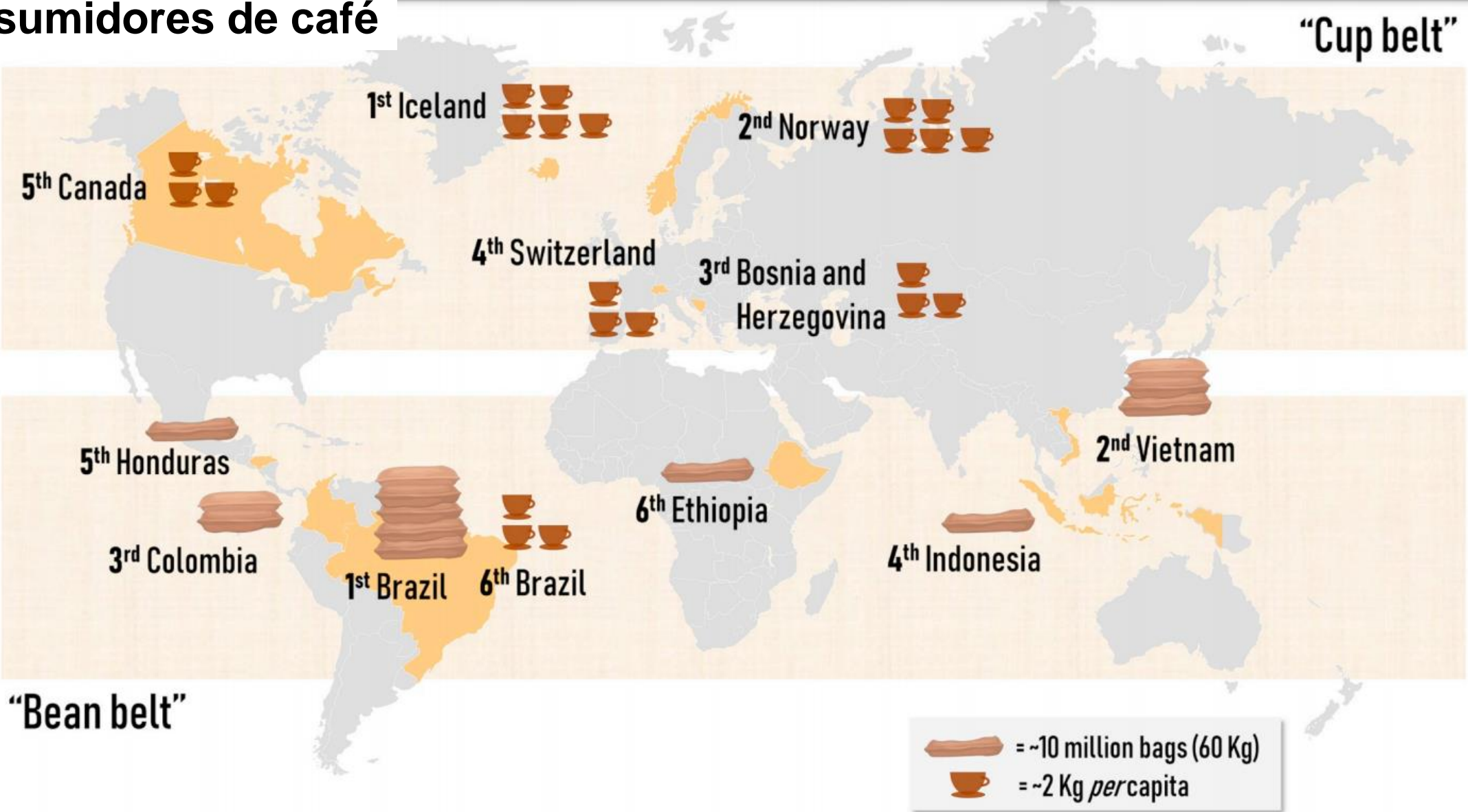


Guilherme Ribeiro Romualdo^a, Ariane Bartolomeu Rocha^a, Mathieu Vinken^b, Bruno Cogliati^c, Fernando Salvador Moreno^d, María Angel García Chaves^e, Luis Fernando Barbisan^{f,*}

A**B**



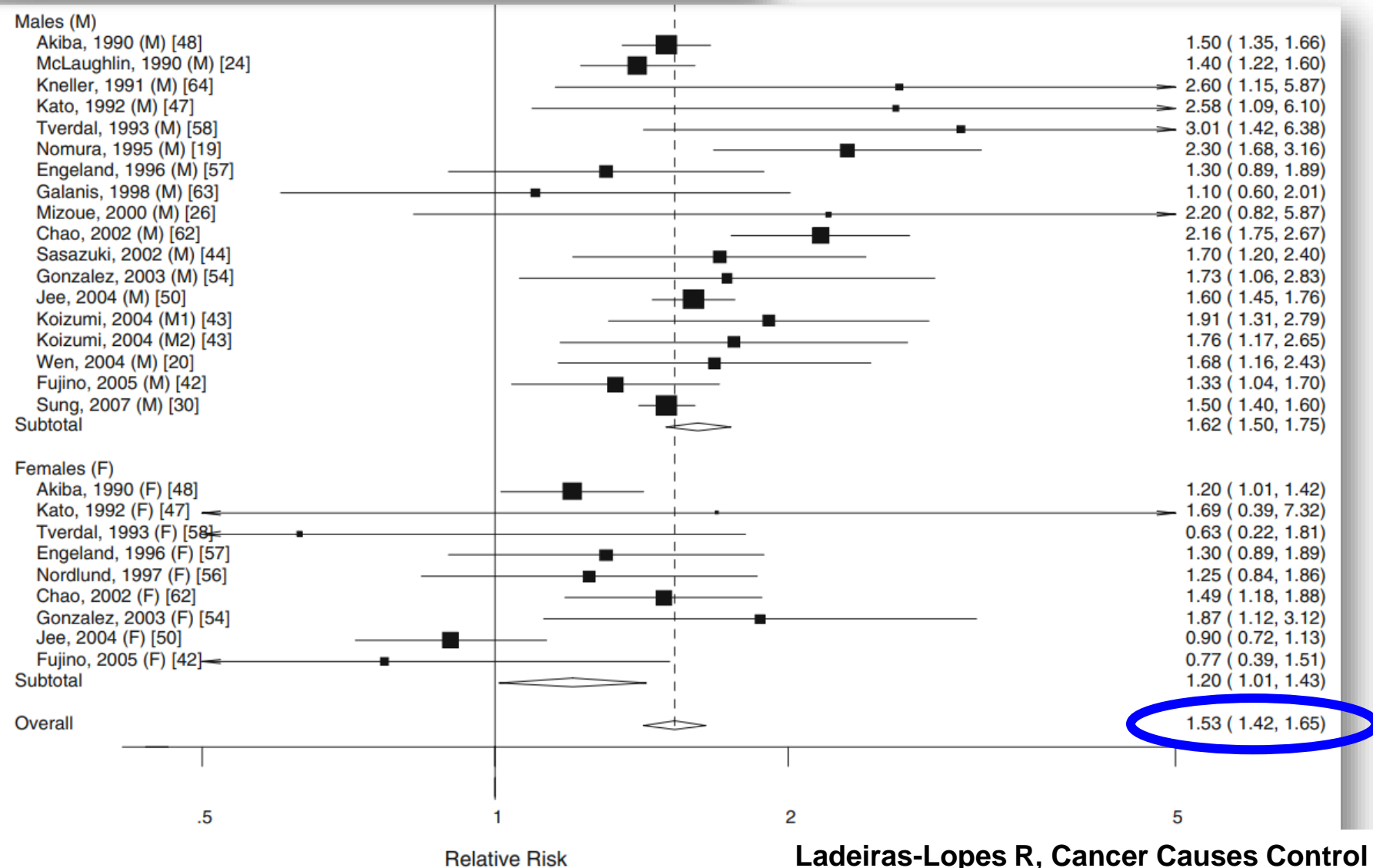
6 consumidores de café



Smoking and gastric cancer: systematic review and meta-analysis of cohort studies

Ricardo Ladeiras-Lopes · Alexandre Kirchhofer Pereira · Amanda Nogueira ·
Tiago Pinheiro-Torres · Isabel Pinto · Ricardo Santos-Pereira ·
Nuno Lunet

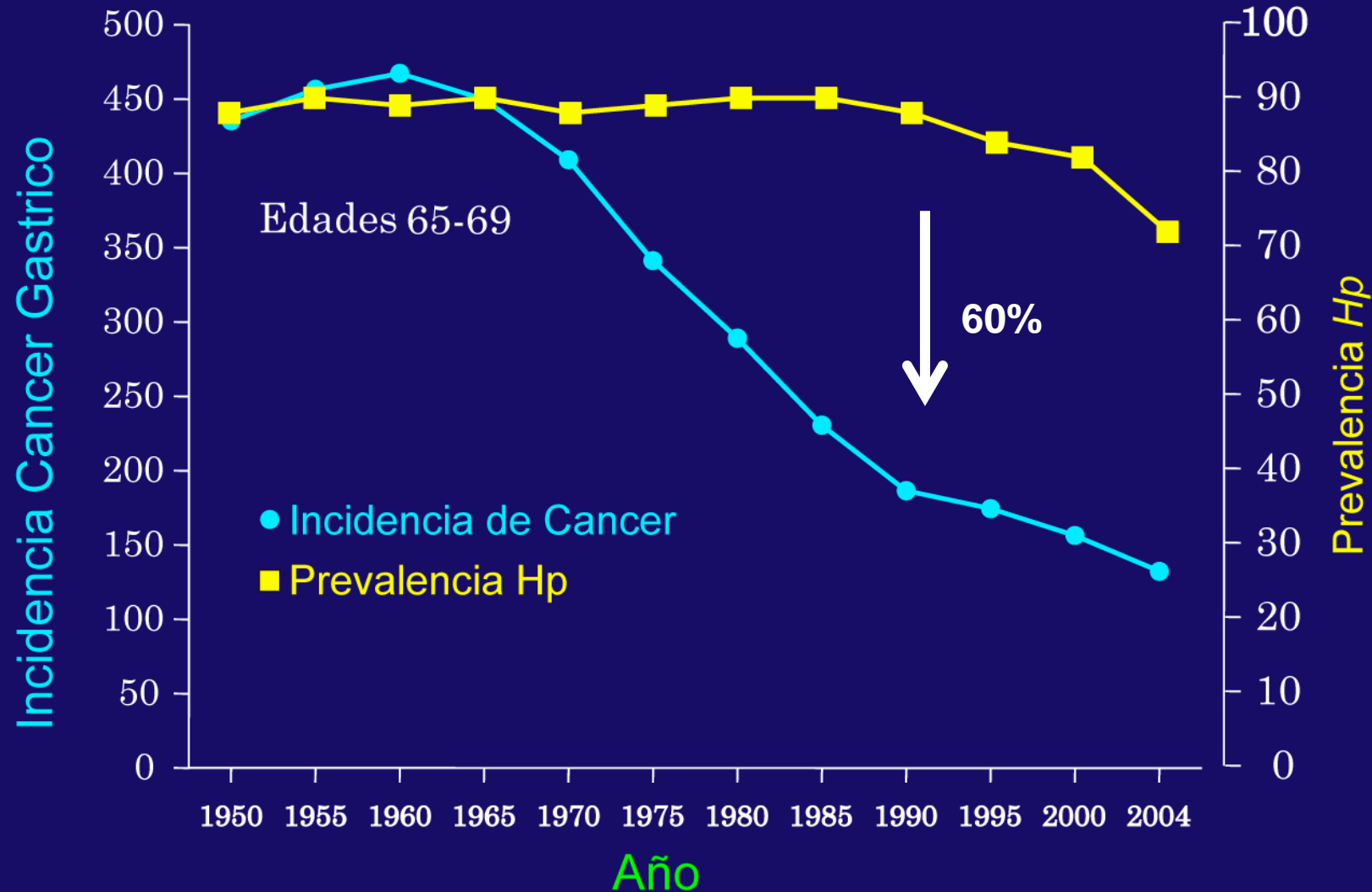
Fumar



Sal

**“Tremendo veneno
Para el estómago”**

H. pylori-Cáncer Gástrico en Japón



Concentración de sal y expresión Cag A y UreB por *Helicobacter pylori*

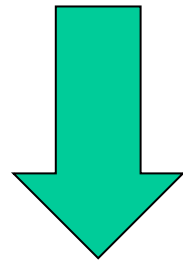
Grupo	Cag A (%)	Ure B
NaCl 3%	3.21	72.73
NaCl 15%	3.99*	74.81
NaCl 30%	10.09*	70.20

* $p < 0.05$

Low sodium diet for gastric cancer prevention in the United States: Results of a Markov model

Judith Kim¹  | Aaron Oh² | Han Truong² | Monika Laszkowska³ |
M. Constanza Camargo⁴ | Julian Abrams¹ | Chin Hur^{1,2} 

Riesgo de CG



24.8% Hombres 27 casos 10^5
21.2% Mujeres 14 casos 10^5

Risk factors for gastric cancer in Latin America: a meta-analysis

Patricia Bonequi · Fernando Meneses-González ·
Pelayo Correa · Charles S. Rabkin ·
M. Constanza Camargo

Factor de riesgo	OR(IC95%)
IL 1RN*2	1.51 (1.15-1.99)
Tabaquismo	1.47 (1.19-1.81)
Alcohol	1.61 (1.26-2.05)
Carne procesada	1.64 (1.08-2.48)
Sal	2.24 (1.53-3.29)

***Helicobacter pylori* riesgo atribuible 85-90%**

1-3% infectados



Causa necesaria, pero insuficiente

Graham DY, Gastroenterology 2015;148:719-31

**Dejarlo y
No tratarlo**



Dejarlo y No tratarlo

**Lento proceso
Décadas**

**Atrofia
Metaplasia**

Cáncer Gástrico

Hipótesis



*Erradicar H.pylori reduce
El riesgo de cáncer gástrico*

Ha sido comprobada!



Cochrane
Library

Cochrane Database of Systematic Reviews

6 ECC
ASIA
1 Colombia

***Helicobacter pylori* eradication for the prevention of gastric neoplasia (Review)**

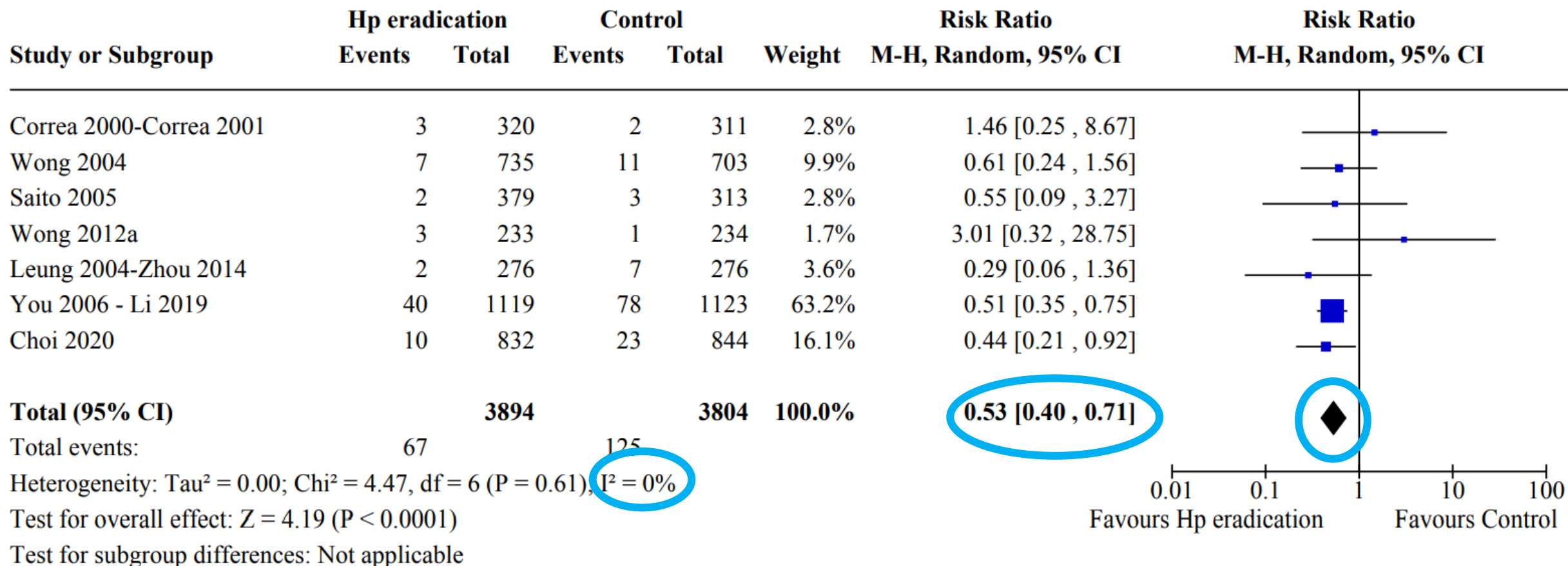
Ford AC, Yuan Y, Forman D, Hunt R, Moayyedi P.

Helicobacter pylori eradication for the prevention of gastric neoplasia.

Cochrane Database of Systematic Reviews 2020, Issue 7. Art. No.: CD005583.

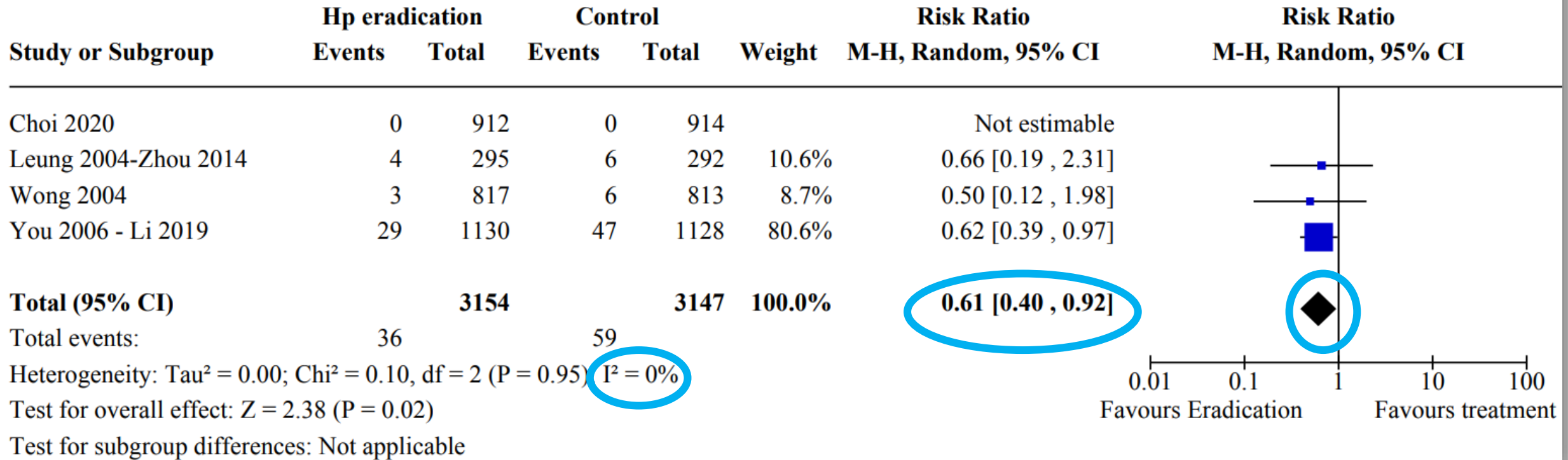
Analysis 1.2. Comparison 1: *H. pylori* eradication vs control - main analyses, Outcome 2: Incidence of gastric cancer - complete case analysis

Incidencia



Ford AC, Yuan Y, Forman D, Hunt R, Moayyedi P.
Helicobacter pylori eradication for the prevention of gastric neoplasia.
 Cochrane Database of Systematic Reviews 2020, Issue 7. Art. No.: CD005583.

Analysis 1.3. Comparison 1: *H. pylori* eradication vs control - main analyses, Outcome 3: Death from gastric cancer - modified ITT analysis



Ford AC, Yuan Y, Forman D, Hunt R, Moayyedi P.
Helicobacter pylori eradication for the prevention of gastric neoplasia.
 Cochrane Database of Systematic Reviews 2020, Issue 7. Art. No.: CD005583.

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}

Prevención primaria

Incidencia << 50%

Mortalidad << 25%

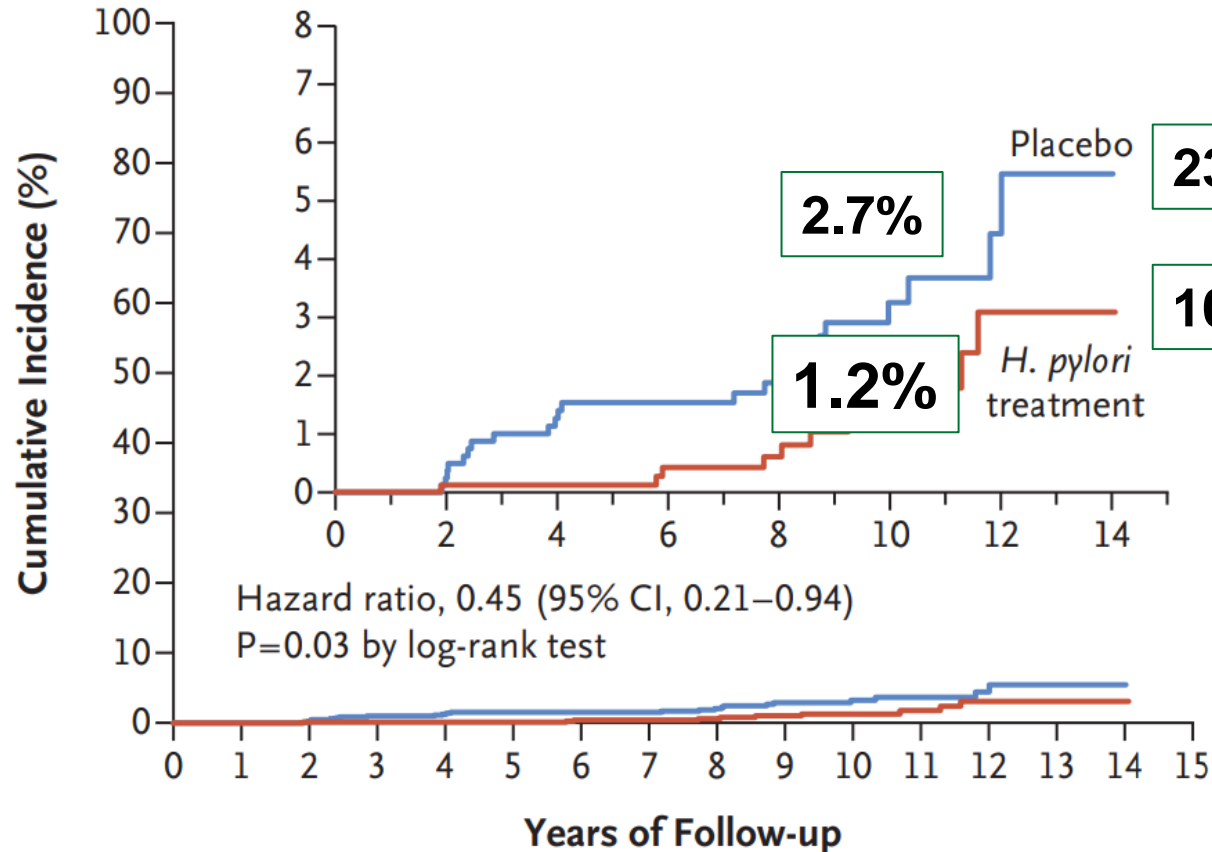
Cáncer esófago *No cambió*

Cáncer de colon *NO cambió*

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

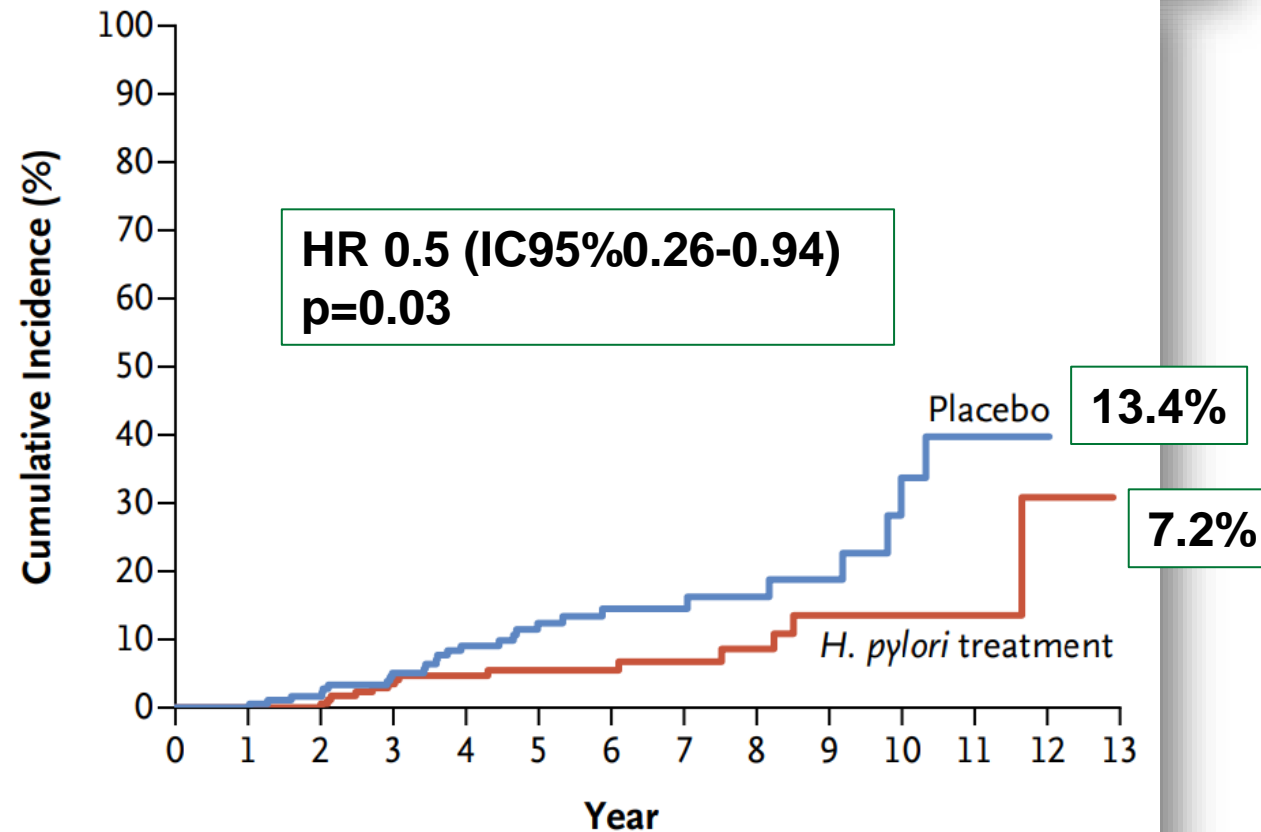


No. at Risk

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 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

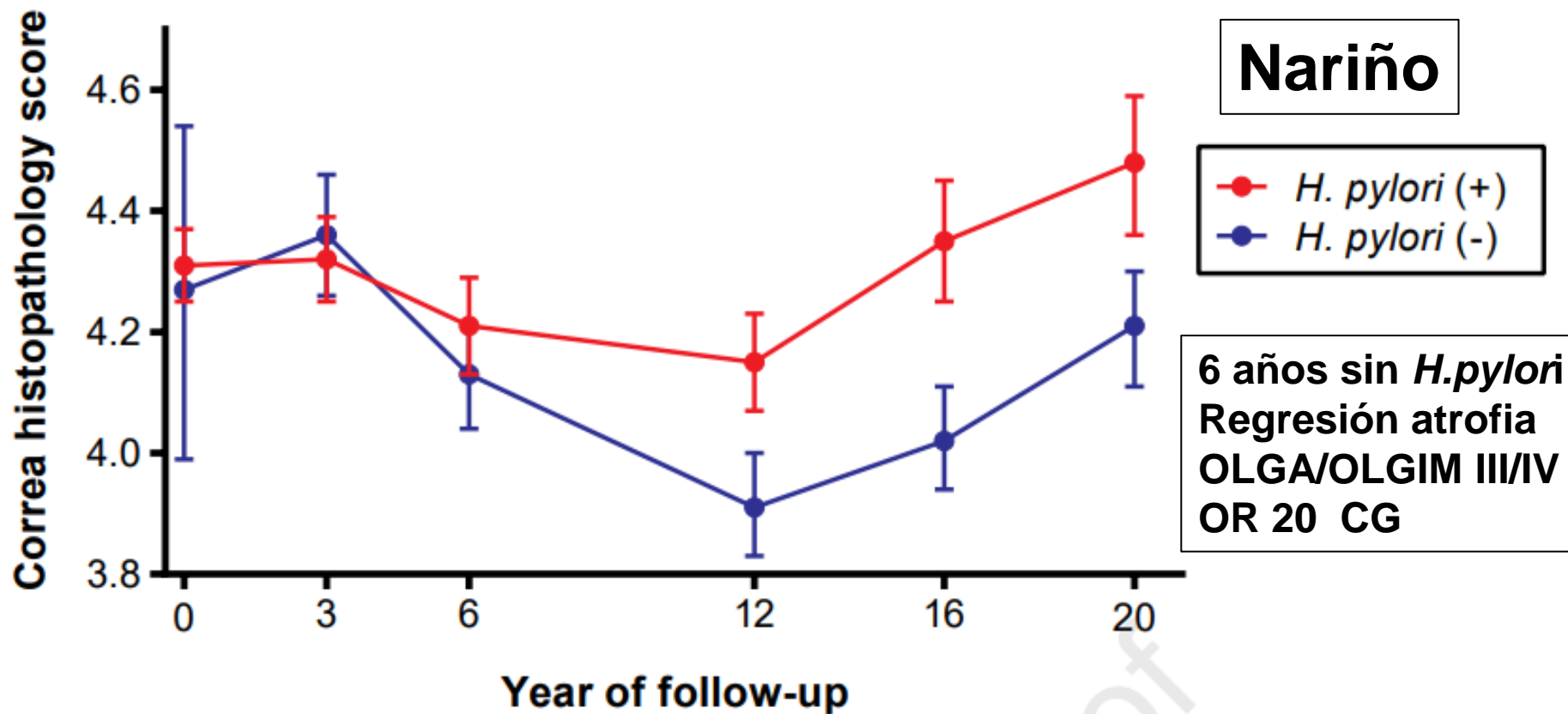
The Colombian Chemoprevention Trial: 20-Year Follow-Up of a Cohort of Patients With Gastric Precancerous Lesions



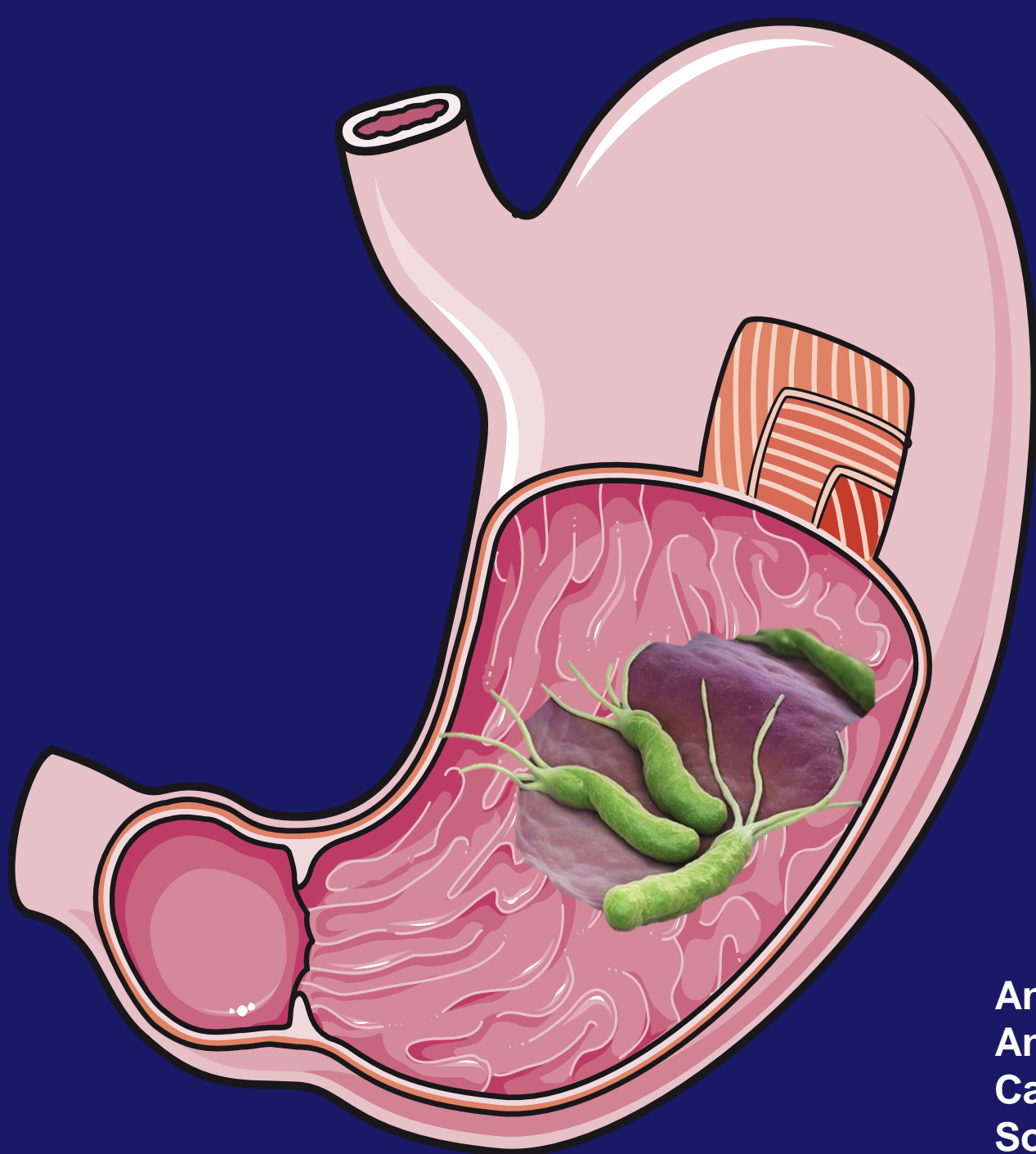
M. Blanca Piazuelo,^{1,2} Luis E. Bravo,³ Robertino M. Mera,¹ M. Constanza Camargo,⁴ Juan C. Bravo,³ Alberto G. Delgado,¹ M. Kay Washington,⁵ Alicia Rosero,⁶ Luz S. Garcia,³ Jose L. Realpe,⁷ Sandra P. Cifuentes,⁷ Douglas R. Morgan,^{1,8} Richard M. Peek Jr,^{1,2,5} Pelayo Correa,¹ and Keith T. Wilson^{1,2,5,9}

**Estudio más largo en
población Hispana**





Year of follow-up	0	3	6	12	16	20
<i>H. pylori</i> (+) score mean (95% CI)	4.31 (4.25-4.37)	4.32 (4.25-4.39)	4.21 (4.13-4.29)	4.15 (4.07-4.23)	4.35 (4.25-4.45)	4.48 (4.36-4.59)
<i>H. pylori</i> (-) score mean (95% CI)	4.27 (3.99-4.54)	4.36 (4.26-4.46)	4.13 (4.04-4.21)	3.91 (3.83-4.0)	4.02 (3.94-4.11)	4.21 (4.11-4.3)
P value	.76	.48	.12	< .0001	< .0001	.0001



**Nuevo patrón de
Cáncer gástrico**

**Mujeres jóvenes, cuerpo
("CYF")**

Anderson WF, JNCI J Natl Cancer Inst 2018;110: djx262

Anderson WF, JAMA 2010;303:1723-8

Camargo MC, Gut 2011;60:1644-9

Song H, Clin Gastroenterol Hepatol 2015;13:1592-600

OXFORD

JNCI J Natl Cancer Inst (2018) 110(6): djx262

doi: 10.1093/jnci/djx262

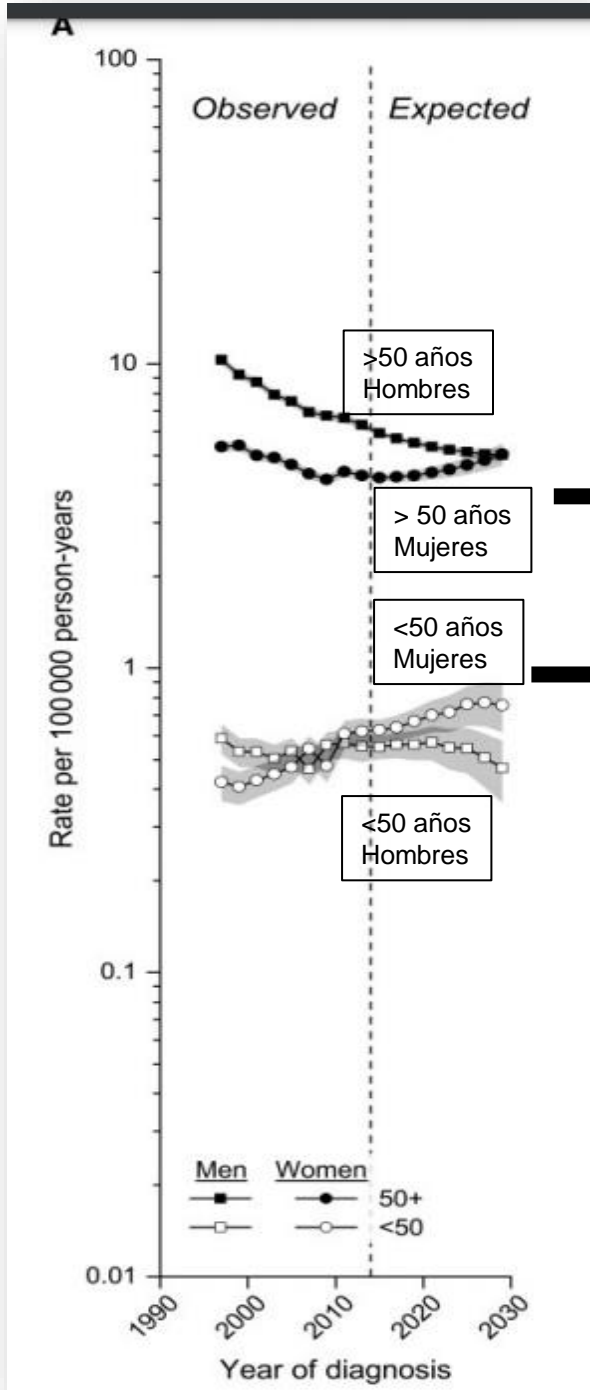
First published online January 19, 2018

Article

ARTICLE

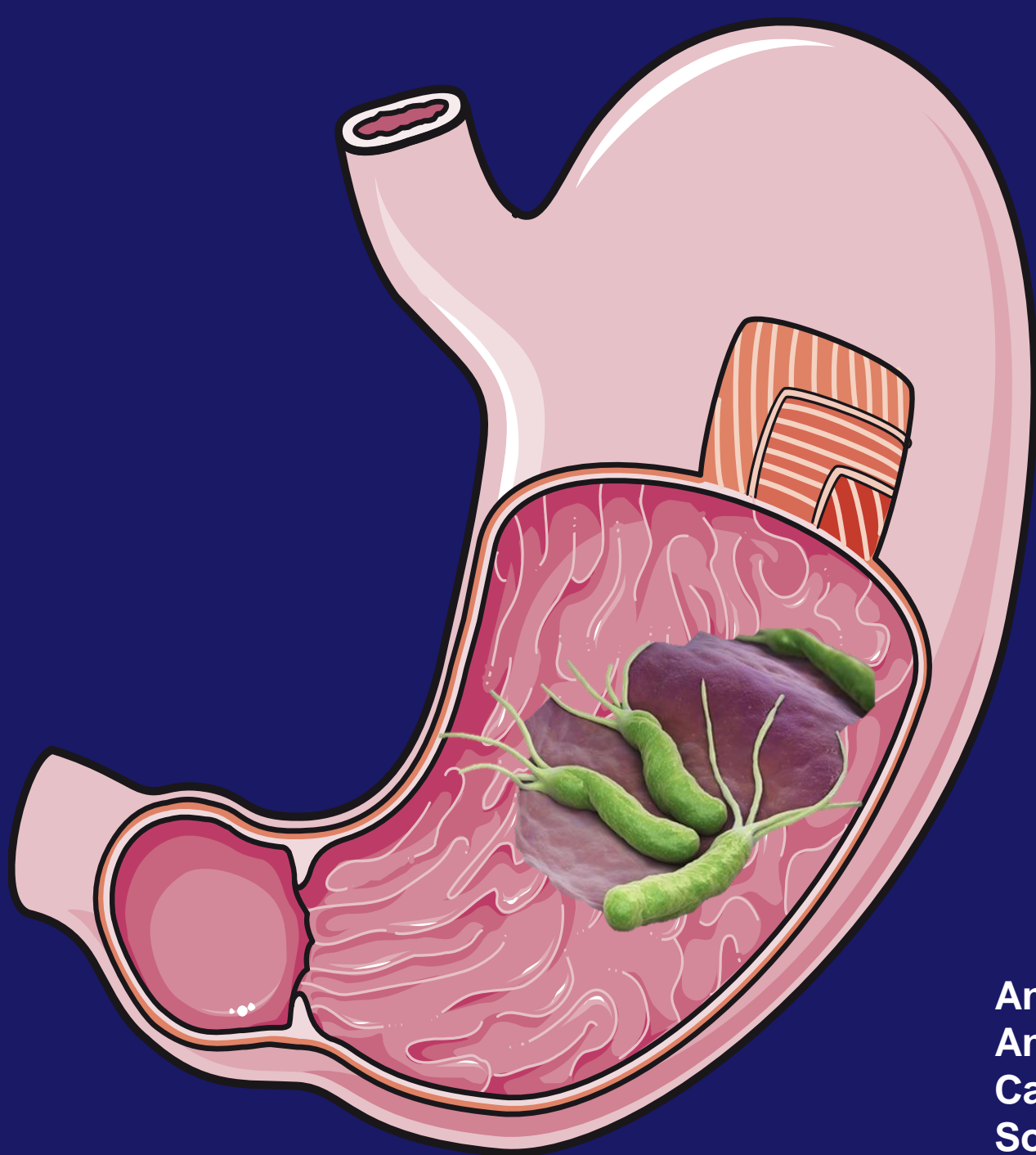
The Changing Face of Noncardia Gastric Cancer Incidence Among US Non-Hispanic Whites

William F. Anderson, Charles S. Rabkin, Natalie Turner,
Joseph F. Fraumeni Jr., Philip S. Rosenberg, M. Constanza Camargo



**>50 años Disminuyó
2.6% Anualmente**

**< 50 años Aumentó
1.3% Anualmente**



Autoinmunidad ? Microbiota ?

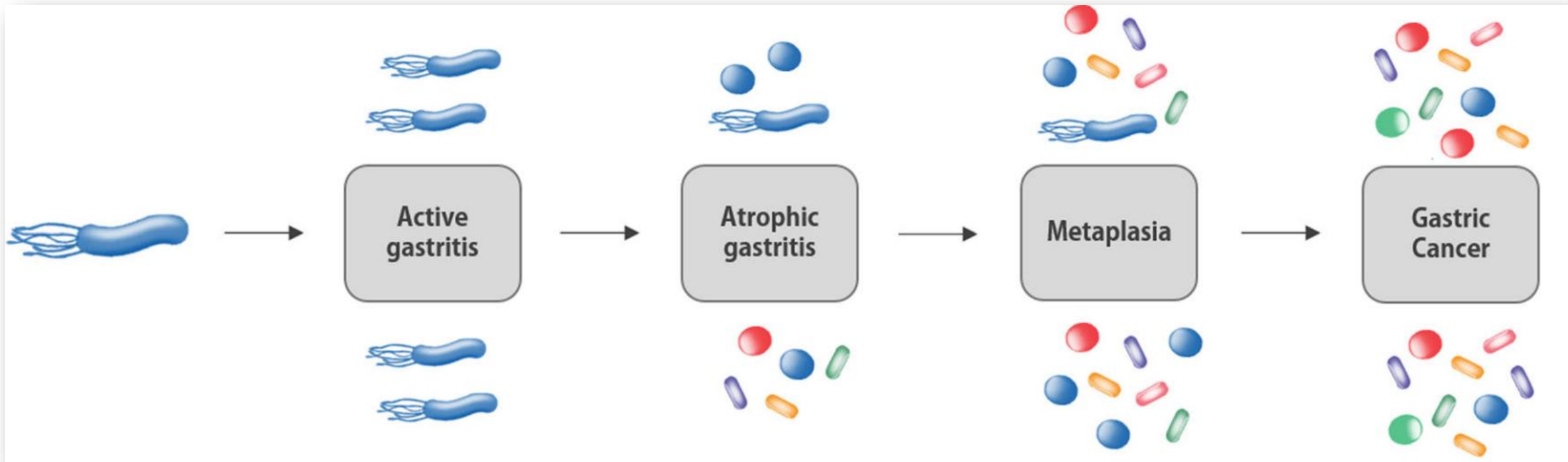
Anderson WF, JNCI J Natl Cancer Inst 2018;110: djx262

Anderson WF, JAMA 2010;303:1723-8

Camargo MC, Gut 2011;60:1644-9

Song H, Clin Gastroenterol Hepatol 2015;13:1592-600

Suicidio de *H.pylori* y microbiota oncogénica



Pimentel de Assumpção P, Eur J Clin Microbiol Infect Dis 2019;38:1591-7.

Increase in the Prevalence of Atrophic Gastritis Among Adults Age 35 to 44 Years Old in Northern Sweden Between 1990 and 2009



Huan Song,^{*} Maria Held,[‡] Sven Sandin,^{*} Hilpi Rautelin,^{§,||} Mats Eliasson,[¶] Stefan Söderberg,[#] Göran Hallmans,^{**} Lars Engstrand,^{‡‡} Olof Nyrén,^{*} and Weimin Ye^{*}

Clin Gastroenterol Hepatol 2015;13:1592–1600



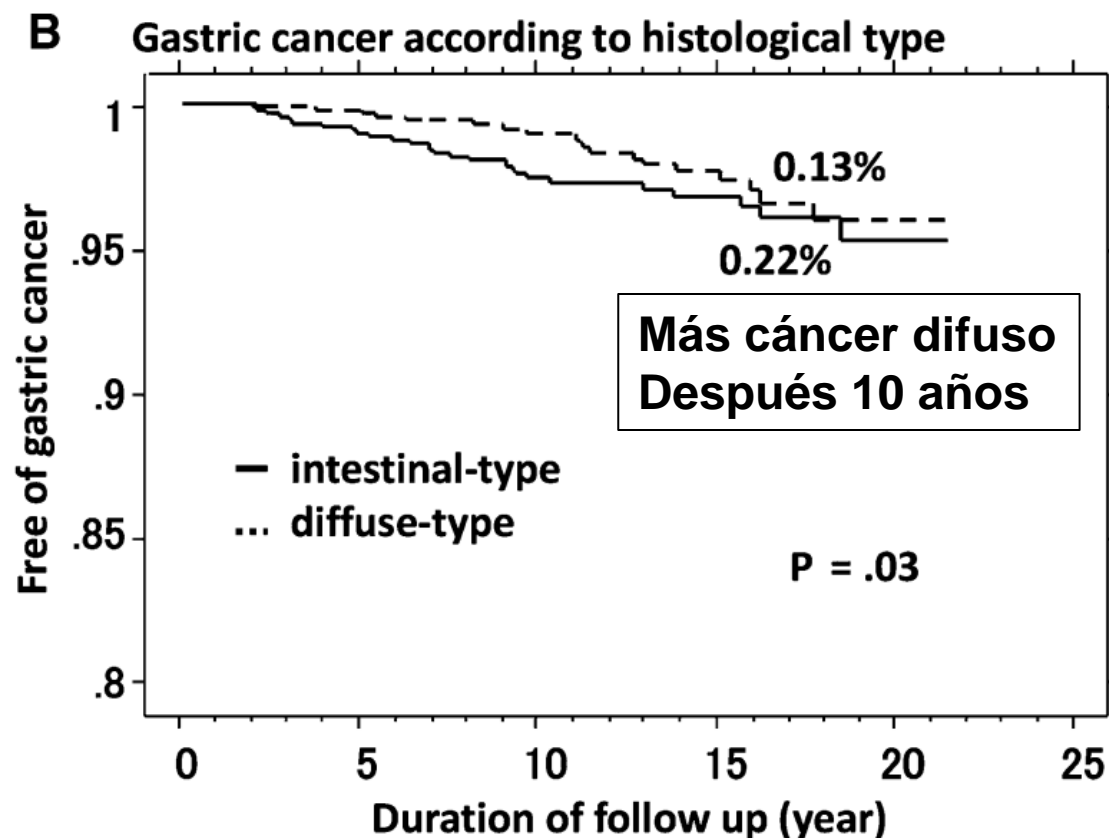
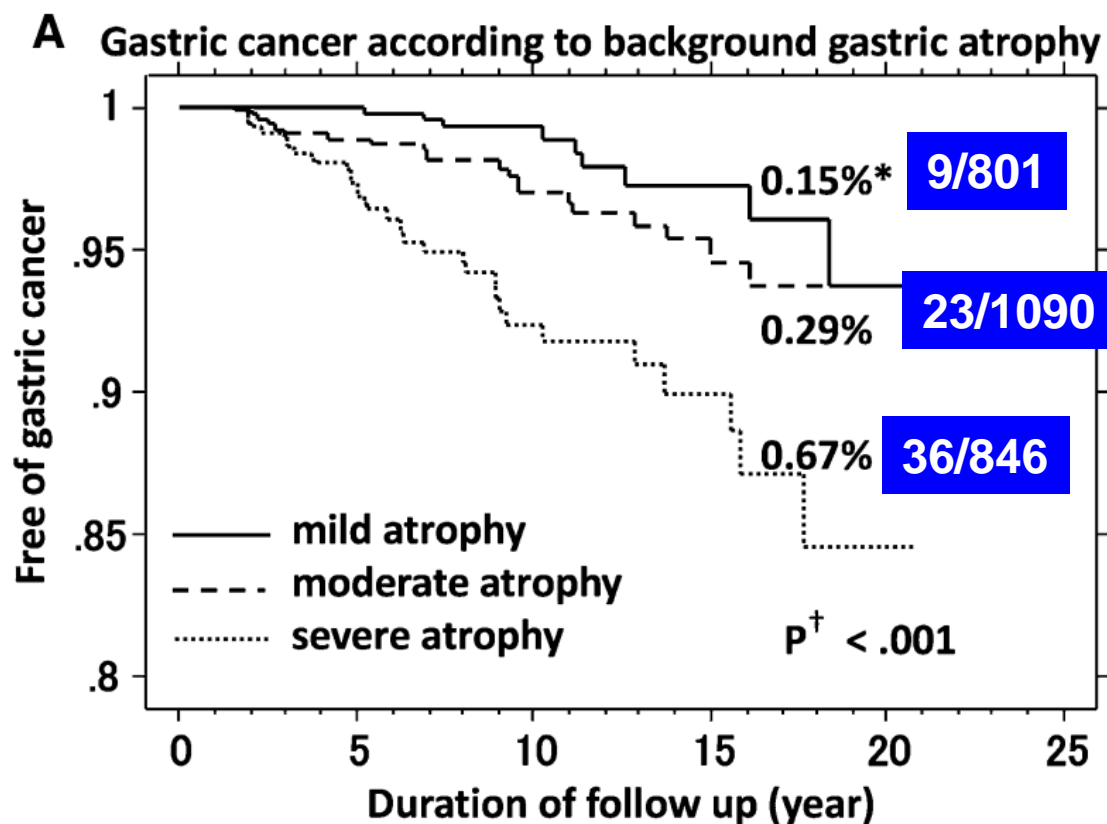
ORIGINAL ARTICLE—ALIMENTARY TRACT

Risk of gastric cancer in the second decade of follow-up after *Helicobacter pylori* eradication

Susumu Take^{1,3} · Motowo Mizuno² · Kuniharu Ishiki³ · Chiaki Kusumoto³ · Takayuki Imada³ · Fumihiko Hamada⁴ · Tomowo Yoshida³ · Kenji Yokota⁵ · Toshiharu Mitsuhashi⁶ · Hiroyuki Okada⁷

21.4 años

Libre de cáncer
Después erradicar *H.pylori*



Riesgo de CG en la segunda década de seguimiento

	Mild ^a <i>n</i> = 801				Moderate <i>n</i> = 1090				Severe <i>n</i> = 846			
	Observed ^b	Expected ^c	SIR	95% CI	Observed	Expected	SIR	95% CI	Observed	Expected	SIR	95% CI
Total cancer	6	1.23	4.89	2.19–10.8	6	5.40	1.11	0.50–2.47	6	7.29	0.82	0.37–1.83
Intestinal ^d	2	1.71	1.17	0.29–4.68	1	6.26	0.16	0.02–1.13	4	5.25	0.76	0.29–2.03
Diffuse	4	0	∞	n/a	5	0.46	10.9	4.53–26.1	2	2.12	0.94	0.24–3.77

**Vigilancia endoscópica
Más allá de 10 años
por erradicación**

CG endoscopia prevención secundaria

Temprano

Mucosa, submucosa

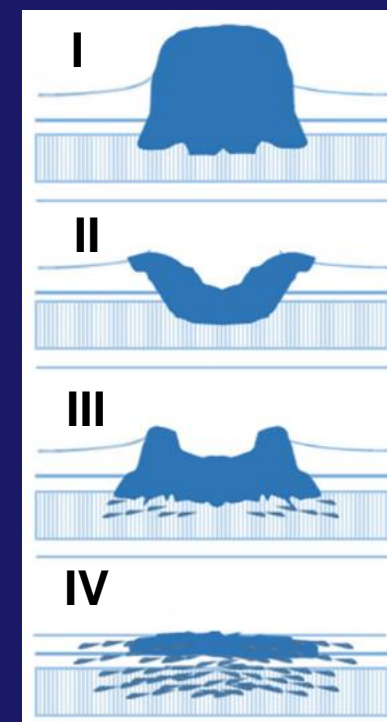
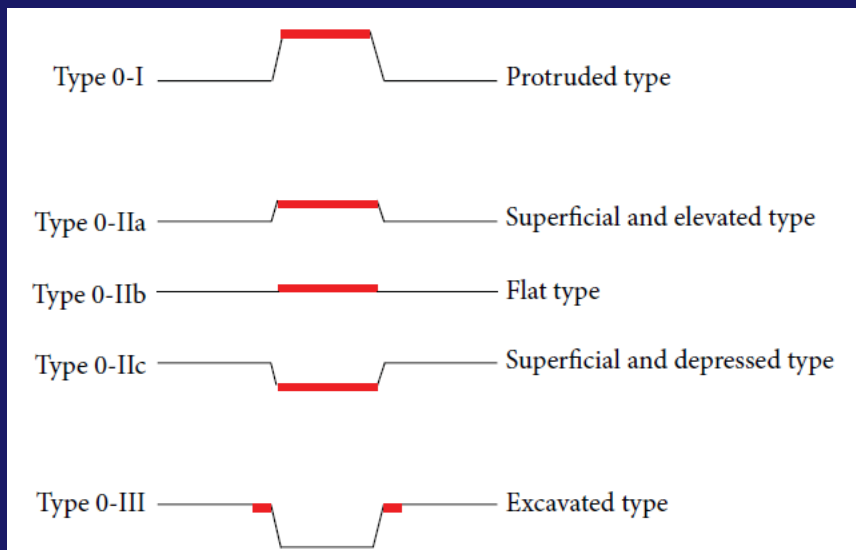
Con o sin ganglios

Sobrevida 5 años 100%

37 meses

Avanzado

Sobrevida 5 años 5-10%

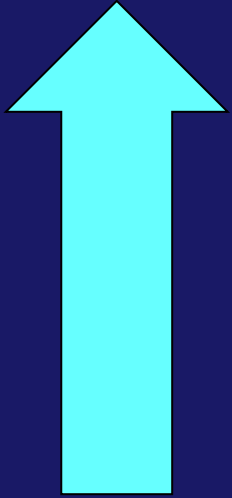


Elevado
Masa

Ulcerado

Infiltrante,
Ulcerado

Linitis
Plástica



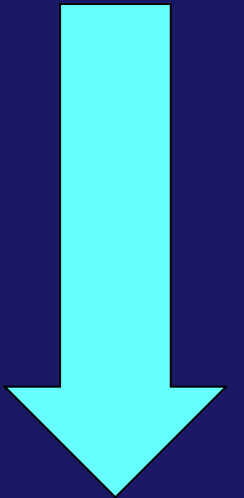
Refrigerar

**Prevención
Primaria
Cáncer Gástrico**

**Erradicar
*H.pylori***



Licor



Mensajes para la casa

Mayoría CG intestinal esporádico

H.pylori explica 85-90% CG intestinal

Nuevo CG poco H.pylori y altos ingresos

Microbiota y autoinmunidad

Prevención primaria dieta, no alcohol, tabaco

Erradicar H.pylori disminuye el CG

Después de erradicar vigilar endoscópicamente

“Cuando creíamos que teníamos todas las respuestas, cambiaron las preguntas”

Mario Benedetti

**Escritor, poeta, dramaturgo y
periodista uruguayo, 1920-2009**

Muchas gracias !