Infección por *Helicobacter pylori*

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Profesor Titular de Medicina,
Universidad Nacional de Colombia
Hospital Universitario Nacional de Colombia

Prevalencia mundial *H.pylori* 60%

Países en desarrollo prevalencia > 80%

Infección bacteriana más común en el mundo
Microbio más famoso en los últimos 40 años

Hooi JKY, Gastroenterology 2017;153:420-9

Muertes atribuidas a *H.pylori 2018*

Ulceras Pèpticas *247.000*

Càncer Gàstrico *783.000*

1 de cada 13 Muertes en el mundo

>1.000.000

Bray F, CA Cancer J Clin 2019;68:394-424
Sung H, CA Caner J Clin 2021;71:209-49

Kyoto global consensus report on *Helicobacter pylori* gastritis

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 Conference

CQ6. Is *H. pylori* gastritis an infectious disease irrespective of symptom and complications?

Statement 6

H. pylori gastritis should be defined as an infectious disease, even when patients have no symptoms and irrespective of complications such as peptic ulcers and gastric cancer.

Grade of recommendation: strong

Evidence level: high

Consensus level: 100%

Section 4 Management of gastritis

CQ17. Should all *H. pylori*-positive individuals receive eradication therapy?

Statement 17

H. pylori infected individuals should be offered eradication therapy, unless there are competing considerations.

Grade of recommendation strong

Evidence level: high

Consensus level: 100%

Sugano K, Gut 2015;64:1353-67

Houston Consensus Conference on Testing for *Helicobacter pylori* Infection in the United States

Hashem B. El-Serag,[*,‡] John Y. Kao,[§] Fasiha Kanwal,[*,‡,‖] Mark Gilger,[¶,#] Frank LoVecchio,[**] Steven F. Moss,[‡‡] Sheila Crowe,[§§] Adam Elfant,[‖‖] Thomas Haas,[¶¶] Ronald J. Hapke,[##] and David Y. Graham[*,‡]

Statement 1: We recommend that all patients with active *H pylori* infection be treated (100% agree/strongly agree, Grade 1A).

Clin Gastroenterol Hepatol 2018;16:992–1002

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 Conference

Fifth Chinese National Consensus Report on the management of *Helicobacter pylori* infection

Helicobacter 2018;e12475

Wen Zhong Liu[1] | Yong Xie[2] | Hong Lu[1] | Hong Cheng[3] | Zhi Rong Zeng[4] | Li Ya Zhou[5] | Ye Chen[6] | Jiang Bin Wang[7] | Yi Qi Du[8] | Nong Hua Lu[2] | on behalf of Chinese Society of Gastroenterology, Chinese Study Group on *Helicobacter pylori* and Peptic Ulcer

Screening and eradication of *Helicobacter pylori* for gastric cancer prevention: the Taipei global consensus

Jyh-Ming Liou,[1,2,3] Peter Malfertheiner,[4,5] Yi-Chia Lee,[1,2,6] Bor-Shyang Sheu,[7,8] Kentaro Sugano,[9] Hsiu-Chi Cheng,[7,10] Khay-Guan Yeoh,[11] Ping-I Hsu,[12] Khean-Lee Goh,[13] Varocha Mahachai,[14] Takuji Gotoda,[15] Wei-Lun Chang,[7] Mei-Jyh Chen,[1,2,16] Tsung-Hsien Chiang,[1,2,16] Chieh-Chang Chen,[1,2] Chun-Ying Wu,[17,18] Alex Hwong-Ruey Leow,[13] Jeng-Yih Wu,[8] Deng-Chyang Wu,[8] Tzu-Chan Hong,[1,2,19] Hong Lu,[20] Yoshio Yamaoka,[21,22] Francis Megraud,[23] Francis K L Chan,[24,25] Joseph JY Sung,[24,25] Jaw-Town Lin,[1,26] David Y Graham,[22] Ming-Shiang Wu,[1,2] Emad M El-Omar,[27,28] Asian Pacific Alliance on Helicobacter and Microbiota (APAHAM)

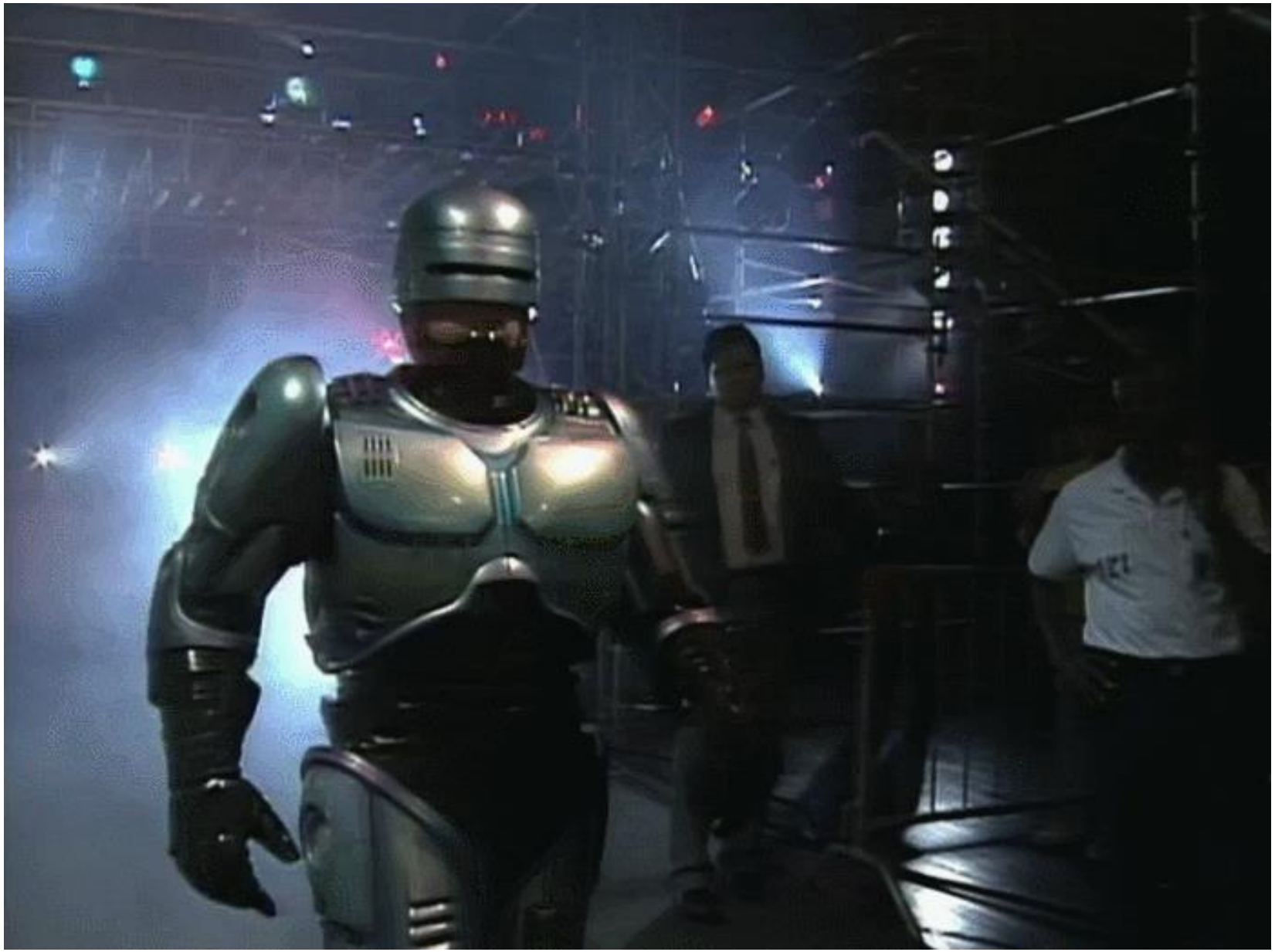
Liou J-M, et al. Gut 2020;69:2093–2112

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

Malfertheiner P, Gut 2022 Online agosto 15

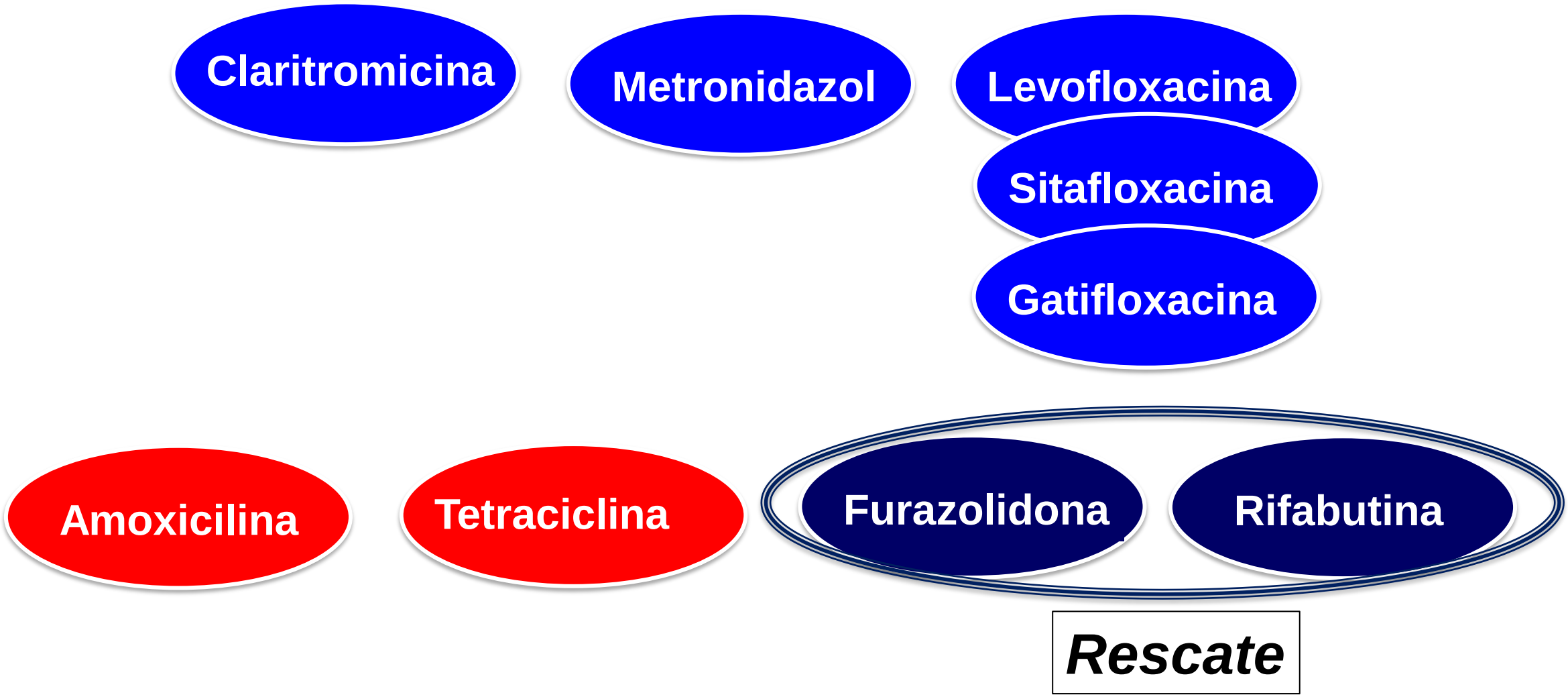
H.pylori, muy difícil de matar



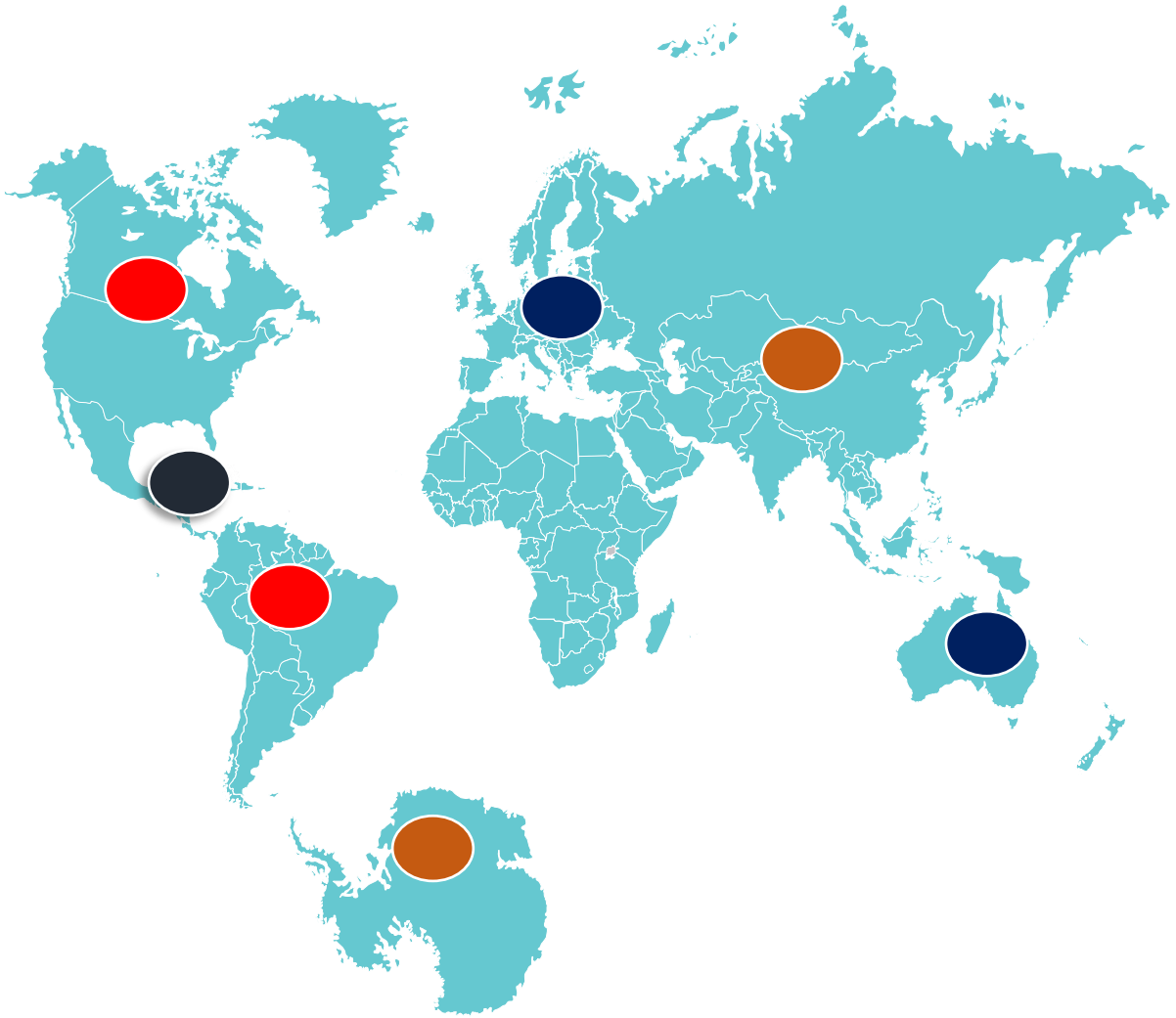
Infancia
Vive en el estòmago

Se ha expuesto a todo tipo de antibòticoss orales

Antibióticos para curar H.pylori



Gisbert JP, Pathogens. 2020;10:15.



Curación *H.pylori*

1982

No hay tratamiento universal

Guías generales

Terapias locales optimizadas
Farmacogenética IBP
Patrón de resistencia

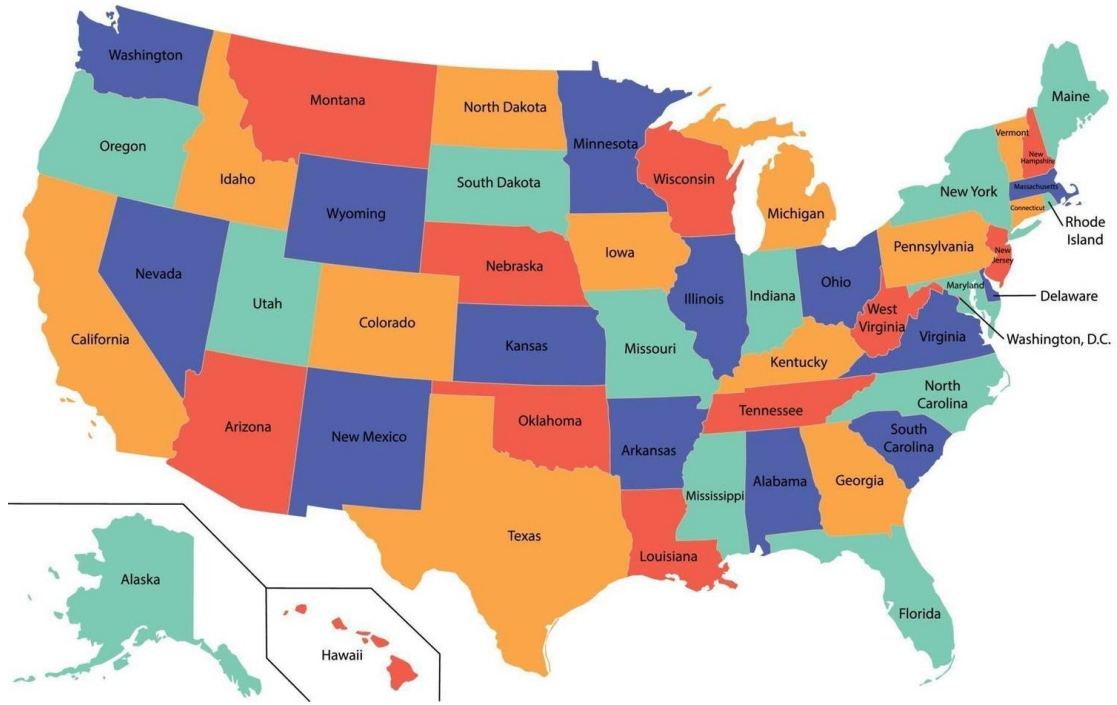
Helicobacter pylori Antibiotic Resistance in the United States Between 2011 and 2021: A Systematic Review and Meta-Analysis

Jonathan J.C. Ho, MD[1], Matthew Navarro, BS[2], Kelsey Sawyer, MS[3], Yousef Elfanagely, MD[1] and Steven F. Moss, MD, AGAF, FACG[4]

7 estados

Metronidazol	**42%**
Levofloxacina	**37%**
Claritromicina	**31%**
Amoxicilina	**2.6%**
Tetraciclina	**0.8%**
Rifabutina	**0.17%**
Dual Claritro/Metr	**11%**

>30%



Jo JJC, Am J Gastroenterol 2022; 117:1221-30

REVIEW

The Problem of *Helicobacter pylori* Resistance to Antibiotics: A Systematic Review in Latin America

M. Constanza Camargo, PhD[1], Apolinaria García, PhD[2], Arnoldo Riquelme, MD[3], William Otero, MD[4,5], Claudia A. Camargo, DMD[6], Tomas Hernandez-García, MD[2], Roberto Candia, MD[3], Michael G. Bruce, MD[7] and Charles S. Rabkin, MD[1]

Camargo MC, Am J Gastroenterol. 2014;109:485-95

Prevalence of *Helicobacter pylori* Antimicrobial Resistance Among Patients Recruited in Endoscopy Units in Santiago, Chile

Patricio González-Hormazábal,[a,*] Alex Arenas,[b,c] Carolina Serrano,[d] Margarita Pizarro,[c] Eduardo Fuentes-López,[e] Jorge Arnold,[c] Zoltan Berger,[f] Maher Musleh,[g] Héctor Valladares,[g] Enrique Lanzarini,[g] Lilian Jara,[a] V. Gonzalo Castro,[a] M. Constanza Camargo,[h] and Arnoldo Riquelme[c,e]

Levo 27 %
Claritro 29%

González-Hormazábal P, Arch Med Res. 2021 ;52:529-534

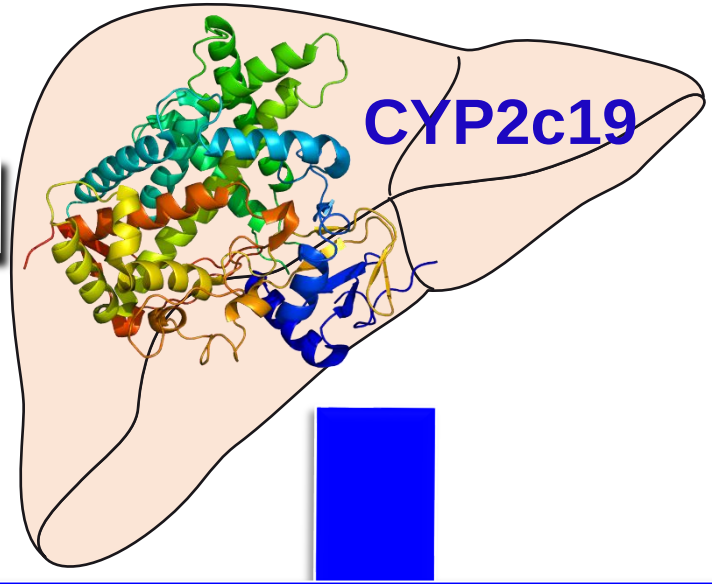
Antibióticos para curar H.pylori

Antibiótico	Resistencia Colombia
Claritromicina	**17.7%**
Levofloxacina	**27%**
Metronidazol	**81%**
Amoxicilina	**< 2%**
Tetraciclina	**< 2%**
Bismuto	**?**
Furazolidona	**?** ★
Rifabutina	**?** ★

Otero W, 2022

Primera Generación
Omeprazol
Lansoprazol
Pantoprazol

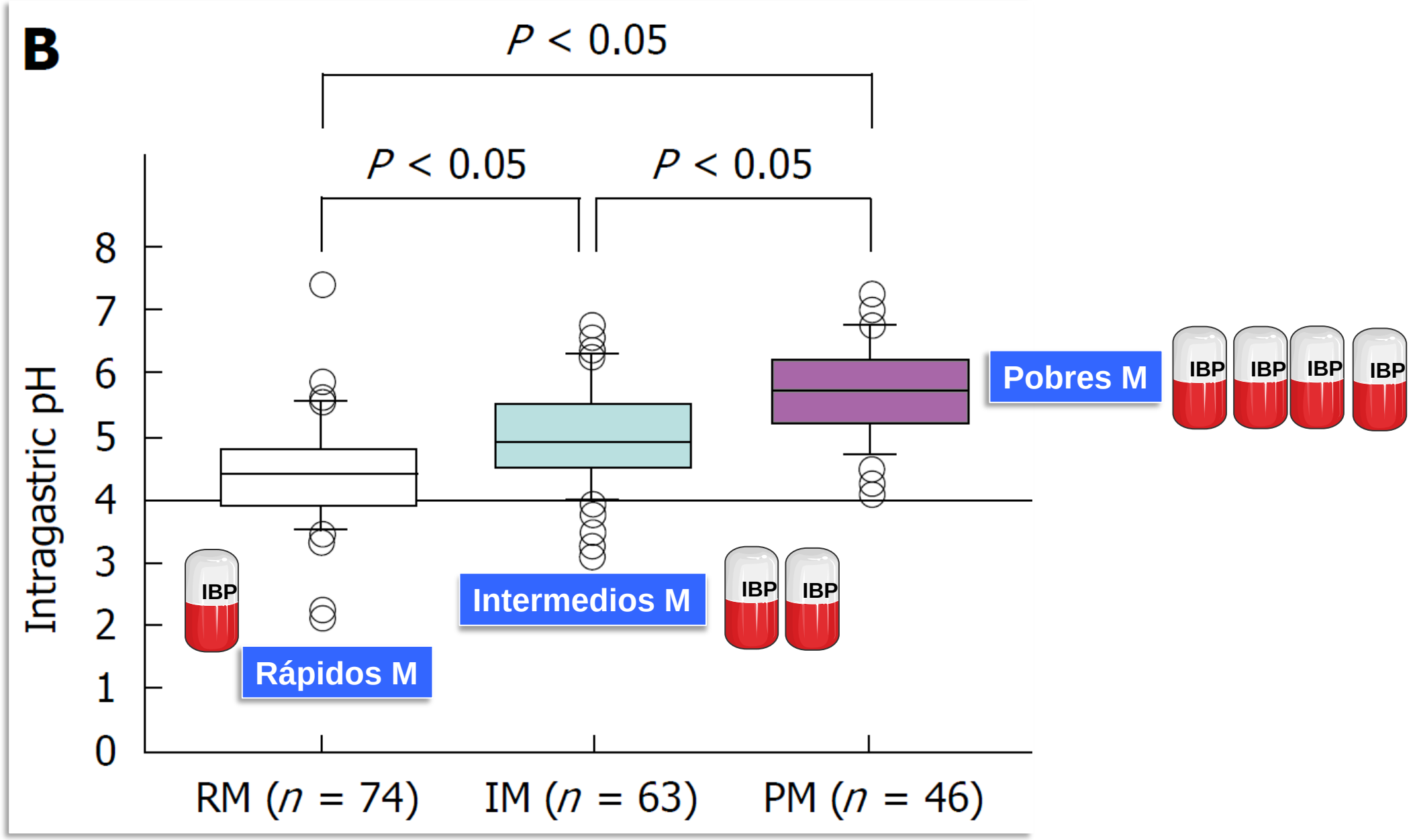
Dependientes



Menos dependientes

Segunda Generación
Esomeprazol
Rabeprazol

El Rouby N, Exp Opin Drug Metab Toxicol 2018;14:447-60
Hagymàsi K, Pharmacogenomics 2011;12:873-88



Sugimoto M, World J Gastroenterol 2014;20: 6400-11

High prevalence of clarithromycin resistance and effect on Helicobacter pylori eradication in a population from Santiago, Chile: cohort study and meta-analysis

A. Arenas[1*], C. Serrano[2], L. Quiñones[3], P. Harris[2], M. Sandoval[2], M. Lavanderos[3], R. Sepúlveda[8], S. Maquilón[1], A. Echeverría[4], C. Ríos[4], E. Fuentes-López[9], L. Rojas[5], A. Jorquera[6], M. Pizarro[1], M. C. Camargo[7] & A. Riquelme[1,9]

Helicobacter pylori (*H. pylori*) eradication using standard triple therapy (STT) with proton pump inhibitors (PPI), amoxicillin and clarithromycin (CLA) has been the standard in Latin America. However, CLA resistance is a rising problem affecting eradication rates. Genetic polymorphisms of *CYP2C19*, a PPI metabolizer may also affect eradication. The primary aims of this study were to evaluate the effect of clarithromycin resistance on *H. pylori* eradication in a population from Santiago, and to establish the pooled clarithromycin resistance in Santiago, Chile. Symptomatic adult patients attending a tertiary hospital in Santiago were recruited for this study. CLA resistance and the polymorphisms of CYP2C19 were determined on DNA extracted from gastric biopsies, using PCR. The STT was indicated for 14 days and eradication was determined by a urea breath test 4–6 weeks after therapy. A meta-analysis of CLA resistance studies among adult residents in Santiago was performed. Seventy-three out of 121 consecutive patients had positive rapid urease test (RUT) and received STT. Sixty-nine patients (95%) completed the study. The *H. pylori* eradication rate was 63% and the prevalence of CLA resistance was 26%. According to the *CYP2C19* polymorphisms, 79.5% of the RUT-positive patients were extensive

Extenso metabolizador 79.5%

Arenas A, et al. Sci Rep. 2019;9:20070.

Cyp2C19

Rápido, Ultrarrápido 80-84%

Esomeprazol Rabeprazol
menos Influido por el CYP
70% vs 90% OME
Rabeprazol se metaboliza diferente

Isaza C, BMC Clin Pharmacol. 2007;7:6.
Arévalo A, Tresplacios A, Otero W, Helicobacter 2019;24:e12574
Arevalo A, Otero W PLoS One. 2021;16:e0245401

Host Genetic Determinants Associated With *Helicobacter pylori* Eradication Treatment Failure: A Systematic Review and Meta-analysis

Shailja C. Shah,[1,2,3,4] Adam Tepler,[5] Cecilia P. Chung,[6,7] Giovanni Suarez,[3] Richard M. Peek Jr,[3] Adriana Hung,[8,9] Christianne Roumie,[8,10] and Neeraj Narula[11]

57 estudios
Pacífico Asiático (Japón 24, Taiwan 6, Korea 5, Tailandia 1)
Europa (Alemania 3, Polonia 3, Italia 1)
Sur américa (Brazil 2)

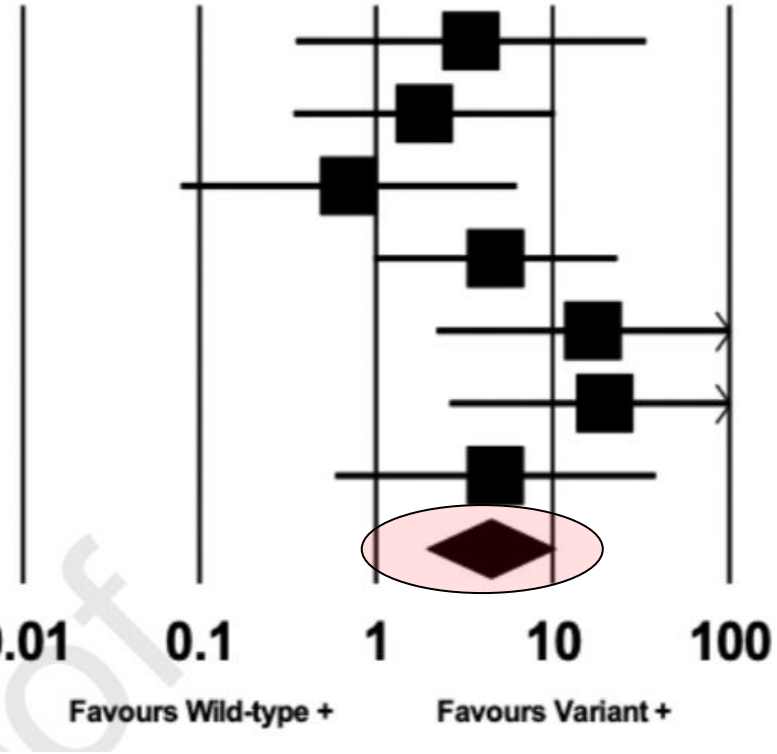
Gastroenterology 2021;161:1443–1459

Hpylori sensible a claritromicina o resistencia < 15% IBP primera generaciòn Lansoprazol, omeprazol pantoprazol Metabolizadores ràpidos

Study name	Odds ratio	Lower limit	Upper limit	Z-Value	p-Value
Isomoto, 2003	3.438	0.352	33.612	1.061	0.289
Kawabata, 2004	1.875	0.342	10.269	0.725	0.469
Miki, 2003	0.700	0.079	6.224	-0.320	0.749
Sheu, 2005	4.742	0.975	23.062	1.929	0.054
Furuta, 2001	16.875	2.202	129.312	2.720	0.007
Furuta, 2004	19.753	2.617	149.103	2.893	0.004
Kang, 2008	4.738	0.589	38.140	1.462	0.144
	4.443	1.944	10.157	3.535	0.000

Statistics for each study

Odds ratio and 95% CI



Riesgo de Falla terapùtica

Shah SC, Gastroenterology 2021;161:1443–1459

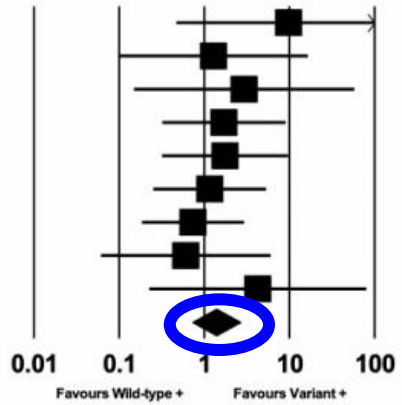
Ràpidos versus Pobres metabolizadors

Esomeprazol 9 estudios

Rabeprazol 18 estudios

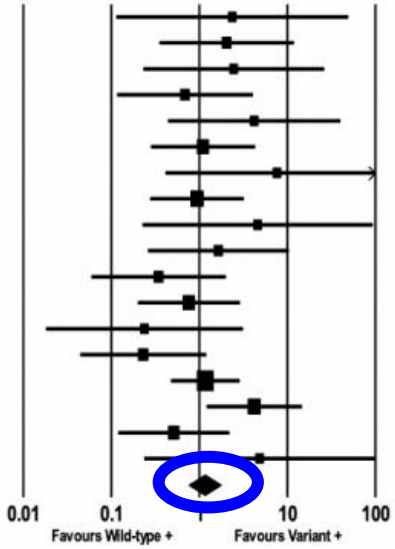
2B.

Study name	Odds ratio	Lower limit	Upper limit	Z-Value	p-Value
Pan, 2010	9.783	0.473	202.374	1.475	0.140
Pan*, 2010	1.286	0.101	16.340	0.194	0.846
Miehlke, 2008	2.941	0.150	57.555	0.711	0.477
Sheu, 2005	1.705	0.323	9.007	0.628	0.530
Wu, 2011	1.750	0.321	9.554	0.646	0.518
Song, 2016	1.159	0.253	5.304	0.191	0.849
Okimoto, 2016	0.735	0.186	2.908	-0.438	0.661
Liou, 2011	0.606	0.061	5.985	-0.429	0.668
Kang, 2008	4.248	0.227	79.518	0.968	0.333
	1.387	0.723	2.662	0.984	0.325



2C.

Study name	Odds ratio	Lower limit	Upper limit	Z-Value	p-Value
Isomoto*, 2003 - 7 days	2.368	0.114	49.041	0.558	0.577
Isomoto*, 2003 - 14 days	2.045	0.354	11.820	0.800	0.424
Yang, 2009	2.462	0.232	26.114	0.748	0.455
Pan, 2010	0.688	0.117	4.056	-0.414	0.679
Inaba, 2002	4.200	0.442	39.943	1.249	0.212
Miyoshi, 2001	1.100	0.283	4.282	0.137	0.891
Lay, 2010	7.638	0.414	140.829	1.367	0.172
Okimoto, 2016	0.942	0.278	3.189	-0.096	0.924
Lin, 2017	4.600	0.227	93.032	0.995	0.320
Dojo, 2001	1.647	0.262	10.359	0.532	0.595
Miki, 2003	0.345	0.060	1.993	-1.190	0.234
Lee, 2003	0.762	0.201	2.884	-0.400	0.689
Phiphatpatthamaamphan, 2016	0.238	0.018	3.121	-1.093	0.274
Kawabata, 2003	0.231	0.045	1.197	-1.746	0.081
Lee, 2010*	1.169	0.478	2.862	0.343	0.732
Kuwayama, 2007	4.211	1.216	14.585	2.268	0.023
Hokari, 2001	0.513	0.120	2.190	-0.902	0.367
Jiang, 2005	4.846	0.237	98.960	1.025	0.305
	1.153	0.761	1.748	0.674	0.501



Shah SC, Gastroenterology 2021;161:1443–1459

Influence of *Cytochrome P450 2C19* Genotype on *Helicobacter pylori* Proton Pump Inhibitor-Amoxicillin-Clarithromycin Eradication Therapy: A Meta-Analysis

OPEN ACCESS

Edited by:

Yuko Morino[1], Mitsushige Sugimoto[2], Naoyoshi Nagata[2], Ryota Niikiura[2], Eri Iwata[2], Mariko Hamada[2], Yusuke Kawai[2], Tatsuhiro Fujimiya[3], Hironori Takeuchi[4], Sakae Unezaki[3] and Takashi Kawai[2]*

25 ensayos clínicos controlados aleatorizados

24 ASIA, 1 Suramérica (Colombia), 5318 pacientes, Tasa resistencia: Amoxi 8.9%, Cla 13%

Morino Y, Front Pharmacol 2021;12:759240

Influence of *Cytochrome P450 2C19* Genotype on *Helicobacter pylori* Proton Pump Inhibitor-Amoxicillin-Clarithromycin Eradication Therapy: A Meta-Analysis

Yuko Morino[1], Mitsushige Sugimoto[2], Naoyoshi Nagata[2], Ryota Niikiura[2], Eri Iwata[2], Mariko Hamada[2], Yusuke Kawai[2], Tatsuhiro Fujimiya[3], Hironori Takeuchi[4], Sakae Unezaki[3] and Takashi Kawai[2]*

Extensos metabolizadores

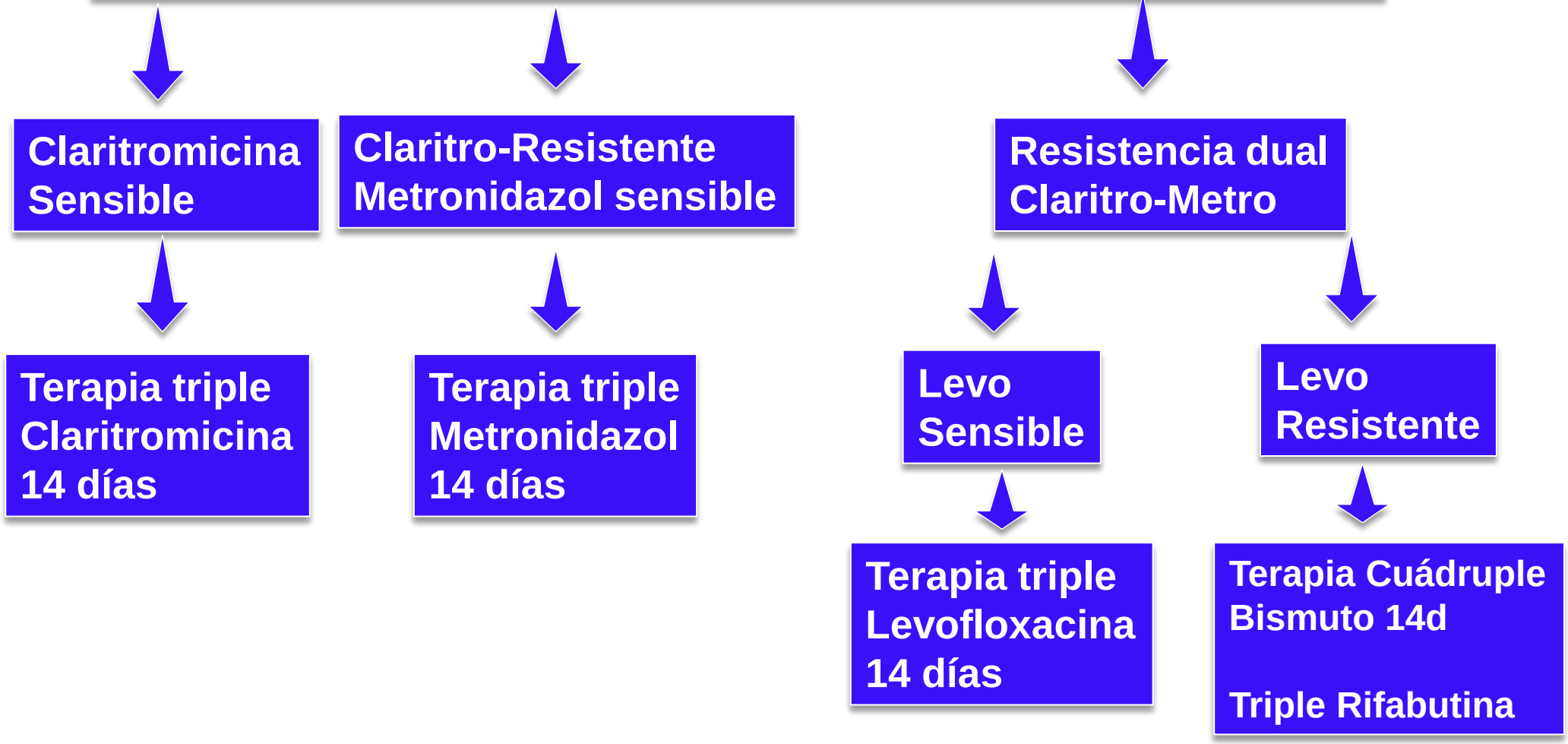
Lansoprazol y omeprazol
Menor tasa erradicación

Esomeprazol y rapeprazol
No son influidos

Morino Y, Front Pharmacol 2021;12:759240

Como toda infección
Pruebas susceptibilidad

Impacto Pruebas de Susceptibilidad



Graham DY, Am J Gastroenterol 2022;117:524-8

Cuádruple Furazolidona?
Dual Amoxicilina +IBP ?

Resistencias

Claritromicina
> 15%

Levofloxacina
>15%

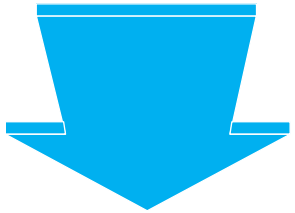
Metronidazol
>60%

No hay disponibilidad
Todos los antibióticos

No hay pruebas
Susceptibilidad

Mundialmente por fuera de USA

No hay disponibilidad Pruebas susceptibilidad

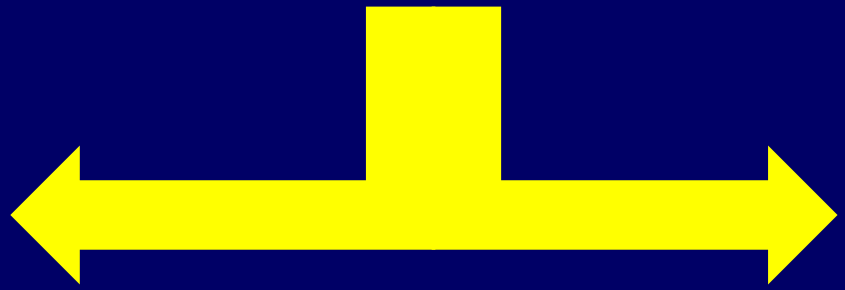


Optimizar Tratamiento empírico

“Nolo” Riquelme

Registro Latinoamericano de *Helicobacter pylori* (Hp-LATAM-Reg)

Colombia y LATAM
Mientras llegan
Resultados Regionales



Terapias Cuádruples

Terapia Dual

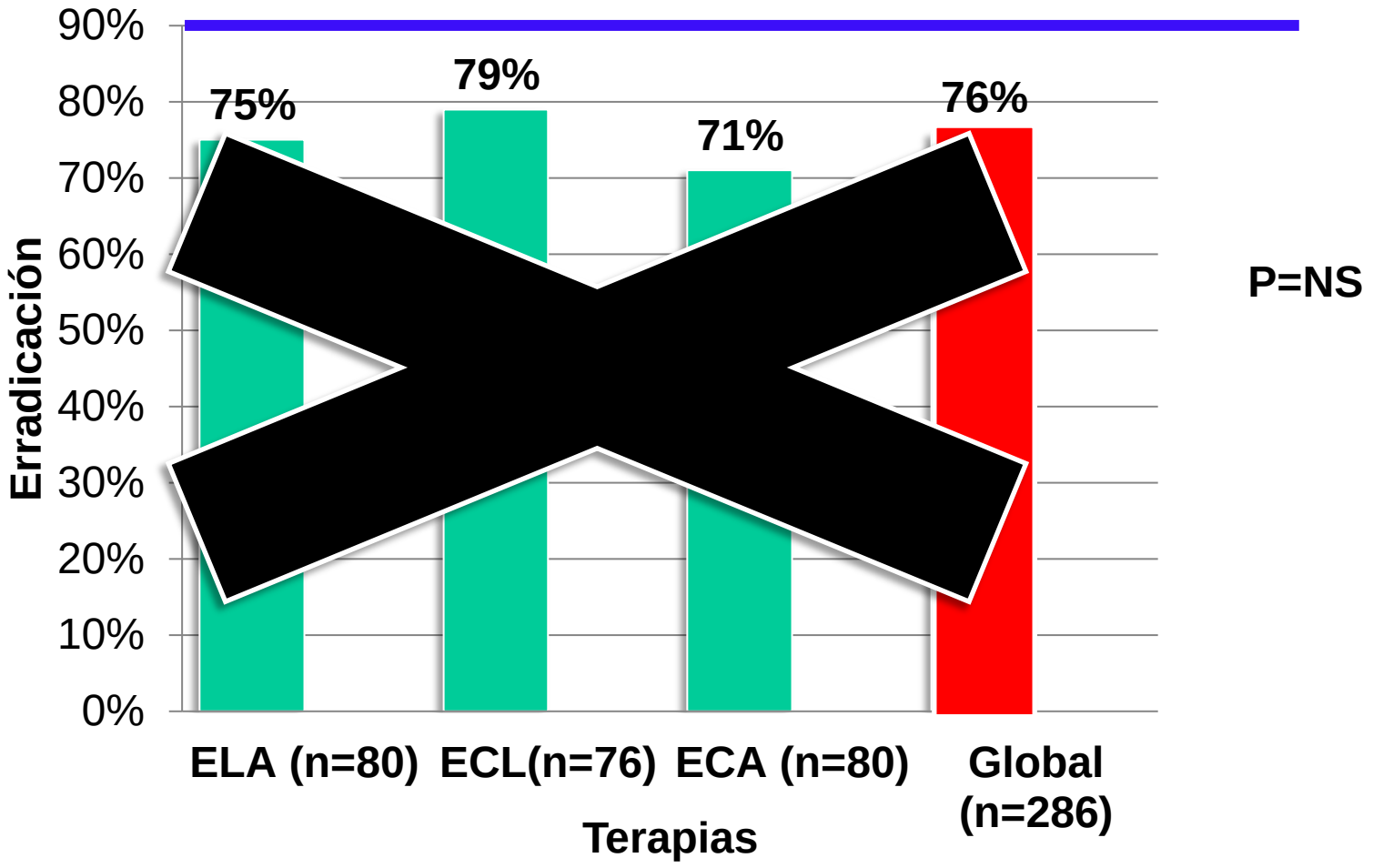
Terapias triples tradicionales con bismuto

No requieren pruebas de susceptibilidad

Cuádruples con Bismuto (Metr/Frz)
Terapia dual

Chey W, Am J Gastroenterol 2017;112:212-25

Eficacia de terapias triples de primera Línea en Colombia
IBP + Amoxicilina +Claritromicina/Levofloxacina



P=NS

Trespalacios A, Otero W, Gastroenterology *DDW 2014:Tu1063.*

Colombia y LATAM

Triples terapias “Antiguas” + Bismuto: 14d

IBP en ayunas y antes de cena +
Amoxi 875 mg 3 v/d o 500mg c/6h +
Claritromicina 500 mg 2v/día O
Levofloxacina 500 mg/ 1/vd

+

SS Bismuto (Bisbacter)
2 tabletas 2v/dìa

Eficacia 88-94%

Ko SW, Helicobacter 2019;24:e12570
Gilbert JP, Moleculas 2020;25:5084
Zhang W, Gut 2015;64:171

Combination of Bismuth and Standard Triple Therapy Eradicates *Helicobacter pylori* Infection in More than 90% of Patients

Adrian G. McNicholl,[*] Dmitry S. Bordin,[‡] Alfredo Lucendo,[§] Galina Fadeenko,[‖] Manuel Castro Fernandez,[¶] Irina Voynovan,[#] Natalia Valerievna Zakharova,[**] Aiman Silkanovna Sarsenbaeva,[‡‡] Luis Bujanda,[§§] Ángeles Perez-Aisa,[‖‖] Liudmila Vologzhanina,[¶¶] Oleg Zaytsev,[##] Tatiana Ilchishina,[***] Cristobal de la Coba,[‡‡‡] Jorge Perez Lasala,[§§§] Sergey Alekseenko,[‖‖‖] Ines Modolell,[¶¶¶] Javier Molina-Infante,[###] Rafael Ruiz-Zorrilla Lopez,[****] Horacio Alonso-Galan,[§§] Nuria Fernandez Moreno,[‖‖] Jen Hinojosa,[‖‖] Inmaculada Santaella,[‖‖] Pilar Varela,[‡‡‡] Pedro Luis Gonzalez-Cordero,[###] Jesus Barrio,[‡‡‡‡] Jose Luis Dominguez-Jimenez,[§§§§] Oscar Nuñez,[‖‖‖‖] Javier Alcedo,[¶¶¶¶] Olga P. Nyssen,[*] Maria Caldas,[*] Maria G. Donday,[*] Oleg Shvetz,[####] Francis Megraud,[*****] Colm O'Morain,[‡‡‡‡‡] and Javier P. Gisbert[*]

1141 pacientes "naive"

Amoxicilina + clariromicina + Bismuto + IBP 14 días

90%

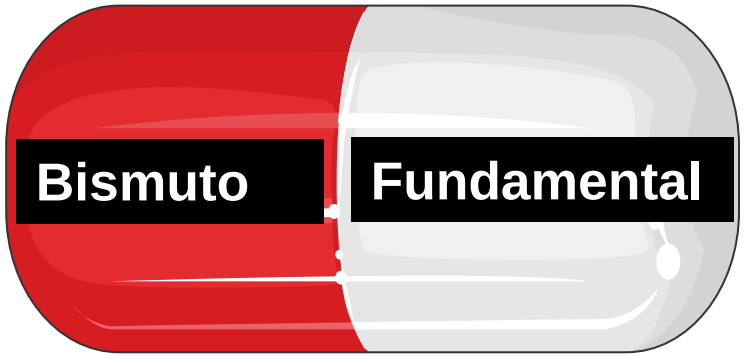
Clin Gastroenterol Hepatol 2020;18:89-98

Adiciòn de Bismuto

10-30%

Dore MP, Gut 2016;65:870-8
Zhang W, Gut 2015;64:1715
Marcus EA, Aliment Pharmacol Ther 2015;42:922-33

7 terapias



Cuádruple Clásica
IBP + Tetracicl + Metronid + *Bi*

Triples tradicionales
IBP + Amox + Clar +*Bi*

Cuádruple FRZ
IBP + FRZ + Tetrac + *Bi*

Triples tradicionales
IBP + Amox + levo+ *Bi*

Cuádruple FRZ
IBP + FRZ+ Amox + *Bi*

Triples tradicionales
IBP + Amox + Metr + *Bi*

Otras Cuádruples
IBP + Amoxi +Tetraci + Bi

Otero W, Rev Col Gastroenterol 2022, sometido a publicación
Cho JH, et al. World J Clin Cas 2022;10:6349-59

Bismuto dos veces al día

Year	Location	Bismuth[a]	Tetracyc	Metro	Meals	PPI**	Days	No.	PP%	ITT%	Ref.
1997	USA	BSS 524 b.i.d.	500 b.i.d.	500 b.i.d.	AM, PM	L 15 b.i.d.	10	46	75	70	56
2002	Italy	BSC 240 b.i.d.	500 b.i.d.	500 b.i.d.	Noon, PM	P 20 b.i.d.	14	118	98	95	52
2003	Italy	BSC 240 b.i.d.	500 b.i.d.	500 b.i.d.	Noon, PM	P 20 b.i.d.	14	71	97	93	53
2004	USA	BSS 524 b.i.d.	500 b.i.d.	500 b.i.d.	AM, PM	R 20 b.i.d.	14	37	92.3	92.3	56
2006	Italy	BSC 240 b.i.d.	500 b.i.d.	500 b.i.d.	AM, PM	E 20 b.i.d.	10	95	95	91	55
2009	China	BSC 220 b.i.d.	750 b.i.d.	400 b.i.d.	AM, PM	P 40 b.i.d.	7	43	82.9	79.1	57
2009	China[a]	BSC 220 b.i.d.	750 b.i.d.	400 b.i.d.	AM, PM	P 40 b.i.d.	10	45	90.9	88.9	57
2010	China[a]	BSC 220 b.i.d.	750 b.i.d.	400 b.i.d.	AM, PM	P 40 b.i.d.	10	85	91.6.	89.9	58
2011	Italy	BSC 240 b.i.d.	500 b.i.d.	500 b.i.d.	Noon, PM	P 20 b.i.d.	14	202	98	92	109
2011	Italy	BSC 240 b.i.d.	500 b.i.d.	500 b.i.d.	Noon, PM	P 20 b.i.d.	10	215	95	92	109
2013	Turkey	BSC 600 b.i.d.	500 b.i.d.	500 b.i.d.	AM, PM	O 20 b.i.d.	14	38	86.8	73.3	110
2005	Iran	BSC 240 b.i.d.	500 b.i.d.	500 b.i.d	AM, PM	O 20 b.i.d.	14	76	-	76.3	111
2006	Iran[a]	BSC 240 b.i.d.	750 b.i.d.	500 b.i.d.	AM, PM	O 20 b.i.d.	3	40	54	50	75
2006	Iran[a]	BSC 240 b.i.d.	750 b.i.d.	500 b.i.d.	AM, PM	O 20 b.i.d.	7	41	45.9	41.4	75
2006	Iran[a]	BSC 240 b.i.d.	750 b.i.d.	500 b.i.d.	AM, PM	O 20 b.i.d.	14	40	40	35	75

Graham DY, Gastroenterol Clin N Am 2015;44: 537–563

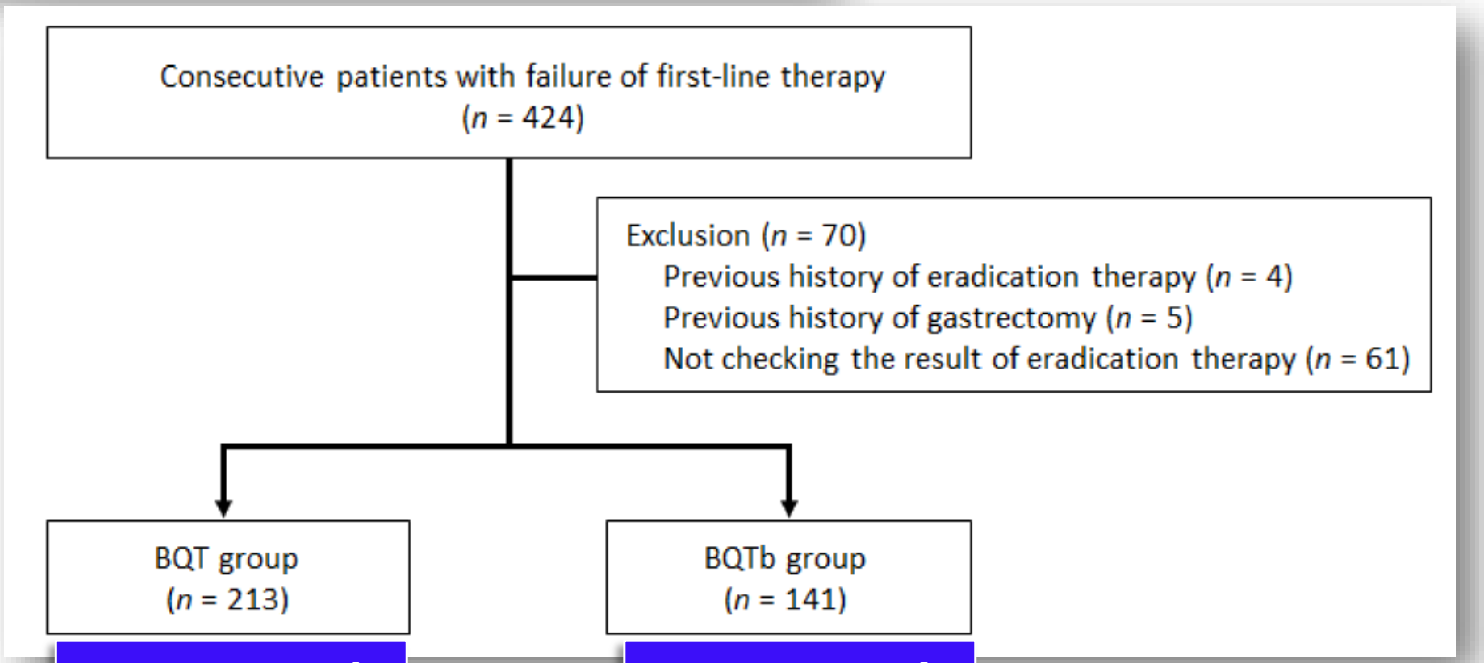
Journal of *Personalized Medicine*

Article

Efficacy of Twice a Day Bismuth Quadruple Therapy for Second-Line Treatment of *Helicobacter pylori* Infection

Jeemyoung Kim, Eun Jeong Gong *, Myeongsook Seo, Hyun Il Seo, Jong Kyu Park, Sang Jin Lee, Koon Hee Han, Woo Jin Jeong, Young Don Kim and Gab Jin Cheon

Kim J, et L. J. Pers Med. 2022;12:56



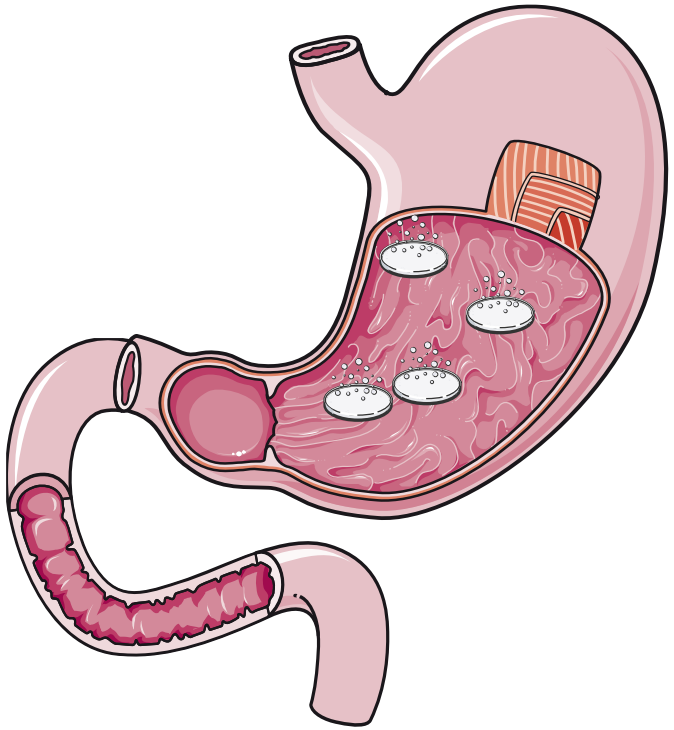
	4 veces al día		2 veces al día
	92.5%	p=0.44	90.1%
>90% cumplimiento	91.2%	p=0.46	96.1%

Dual
14 dìas

Consensos
Rescate

Amoxicilina optimizada
1gr 3v/dia o 500 mg cada 6h?

Dosis altas IBP
Esomeprazol 40 mg 3v/d



Article

Effectiveness and Safety of High-Dose Dual Therapy: Results of the European Registry on the Management of *Helicobacter pylori* Infection (Hp-EuReg)

Luis Fernández-Salazar [1,*], Ana Campillo [2], Luis Rodrigo [3], Ángeles Pérez-Aisa [4], Jesús M. González-Santiago [5], Xavier Segarra Ortega [5], Maja Denkovski [6], Natasa Brglez Jurecic [6], Luis Bujanda [7], Blas José Gómez Rodríguez [8], Juan Ortuño [9], Sotirios Georgopoulos [10], Laimas Jonaitis [11], Ignasi Puig [12,13], Olga P. Nyssen [14], Francis Megraud [15], Colm O'Morain [16] and Javier P. Gisbert [14]

Fernández-Salazar L,et al. J. Clin. Med. 2022, 11, 3544

ORIGINAL PAPER

The efficacy of dual therapy for eradicating *H. pylori* in a Colombian population

JOHANNA BUITRAGO-LAGUADO, CARLOS RUIZ-LINARES, WILLIAM ALBERTO OTERO-REGINO
• BOGOTÁ, D. C. (COLOMBIA)

108 pacientes, Edad 67, 70% mujeres

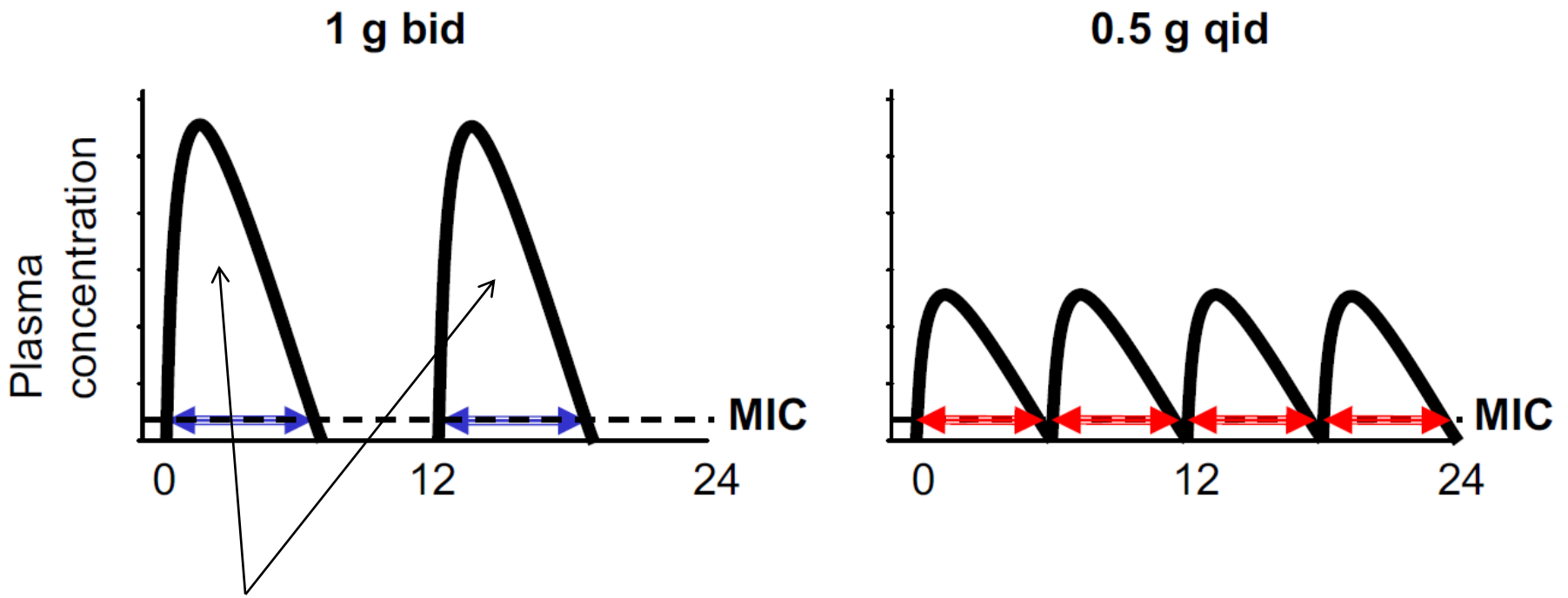
	ITT
Sin terapia previa	86% (95%CI 79.4-92.5%)
2da terapia	85.7% (95%CI 71.8-99.5%)
Efectos adversos leves 31%	Náuseas (26%) Distensión 15%

Buitrago-Laguado J, Acta Med Colomb 2021; 46.

Amoxicilina

2 a 4 veces al día NO es igual

Amoxicilina



Altìsimos niveles Innecesarios

Niveles permanentes Durante 24 horas

Furuta T, Gastroenterol Clin N Am 2010;39:465-80

Tratamiento *H.pylori*

1ª línea

Cuádruple clásica
IBP +Amox+Tetrac+Bi
Triple Claritromicina + Bi
Dual

2ª línea
10-20%

Cuádruple clásica
IBP+Amox+ Tetrac +Bi
Triple *levofloxacina* +Bi
Dual

3ª línea
5-10%

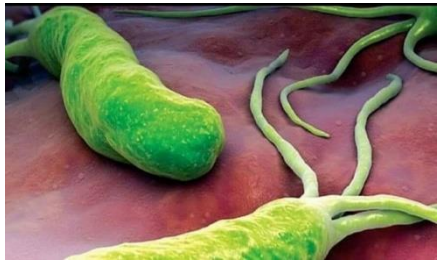
Cuádruple clásica
Triple *levofloxacina* +Bi
Concomitante
Dual

4ª línea

Cuádruples Furazolidona
Cuádruple Rifabutina

Liou JM, Gut Liv 2021 On line March 31c
Otero W, Temas Escogidos Gastroenterlogia, ACG 2022

Solo al paciente o a la familia ?



Houston Consensus Conference on Testing for *Helicobacter pylori* Infection in the United States

Hashem B. El-Serag,[*,‡] John Y. Kao,[§] Fasiha Kanwal,[*,‡,‖] Mark Gilger,[¶,#] Frank LoVecchio,[**] Steven F. Moss,[‡‡] Sheila Crowe,[§§] Adam Elfant,[‖‖] Thomas Haas,[¶¶] Ronald J. Hapke,[##] and David Y. Graham[*,‡]

- *Statement 11:* We recommend that family members residing in the same household of patients with proven active *H pylori* infections undergo *H pylori* testing (experts vs survey: 91% vs 78% agree/strongly agree, Expert Grade 1B) (Supplementary Figure 3).

Consenso ≥ 80%

El-Serag HB,Clin Gastroenterol Hepatol 2018;16:992–1002

ORIGINAL ARTICLE

Helicobacter WILEY

Whole family—based *Helicobacter pylori* eradication is a superior strategy to single-infected patient treatment approach: A systematic review and meta-analysis

Jun-Bo Zhao[1] | Lin Yuan[1] | Xue-Chun Yu[1] | Qiao-Qiao Shao[1] | Jing Ma[1] | Miao Yu[1] | Yue Wu[1] | Ya-Bin Qi[1] | Ruo-Bing Hu[1] | Pei-Ru Wei[1] | Bai-Ling Jia[1] | Lian-Zhong Zhang[2] | Yan-Rui Zhang[1] | Song-Ze Ding[1]

Zhao JB,et al. Helicobacter. 2021;26:e12793.

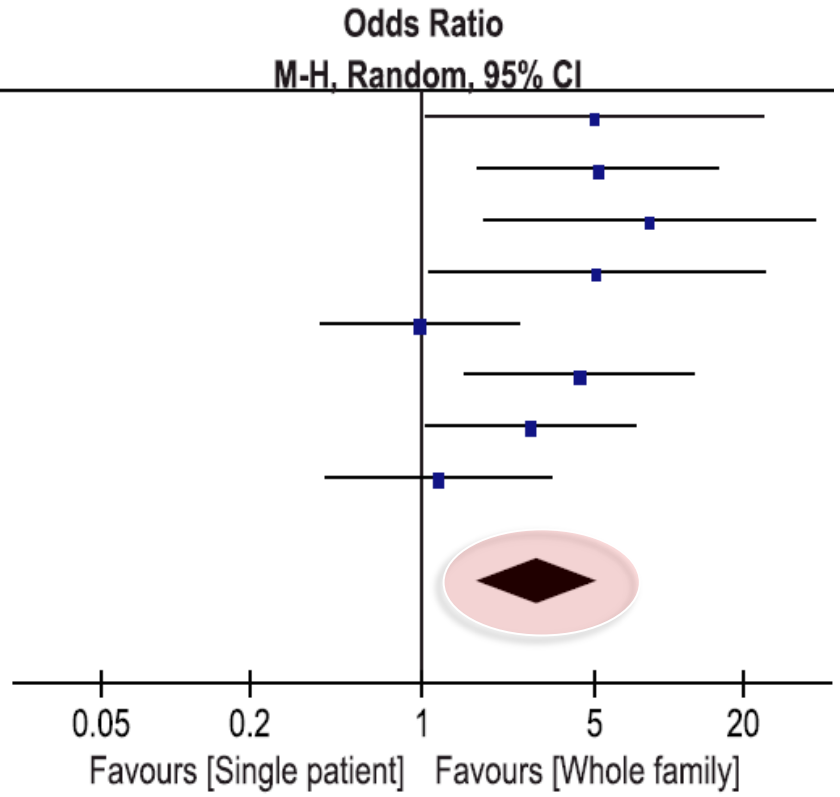
Erradicación

Análisis general

Study or Subgroup	Whole family group Events	Total	Single patient group Events	Total	Weight	Odds Ratio M-H, Random, 95% CI	Year
Chen 2003	40	42	40	50	8.7%	5.00 [1.03, 24.28]	2003
Rong 2012	92	96	80	98	13.4%	5.17 [1.68, 15.93]	2012
Sun 2013	49	51	38	51	9.0%	8.38 [1.78, 39.40]	2013
Cai 2013	69	71	61	70	8.8%	5.09 [1.06, 24.48]	2013
Rakici 2015	92	102	94	104	16.2%	0.98 [0.39, 2.46]	2015
Yang 2017	55	60	43	60	14.0%	4.35 [1.49, 12.73]	2017
Liang 2019	53	60	44	60	15.5%	2.75 [1.04, 7.29]	2019
Chen 2019	105	112	103	111	14.4%	1.17 [0.41, 3.33]	2019
Total (95% CI)		**594**		**604**	**100.0%**	**2.93 [1.68, 5.13]**	
Total events	555		503				

Heterogeneity: Tau² = 0.28; Chi² = 12.52, df = 7 (P = 0.08); I² = 44%

Test for overall effect: Z = 3.78 (P = 0.0002)

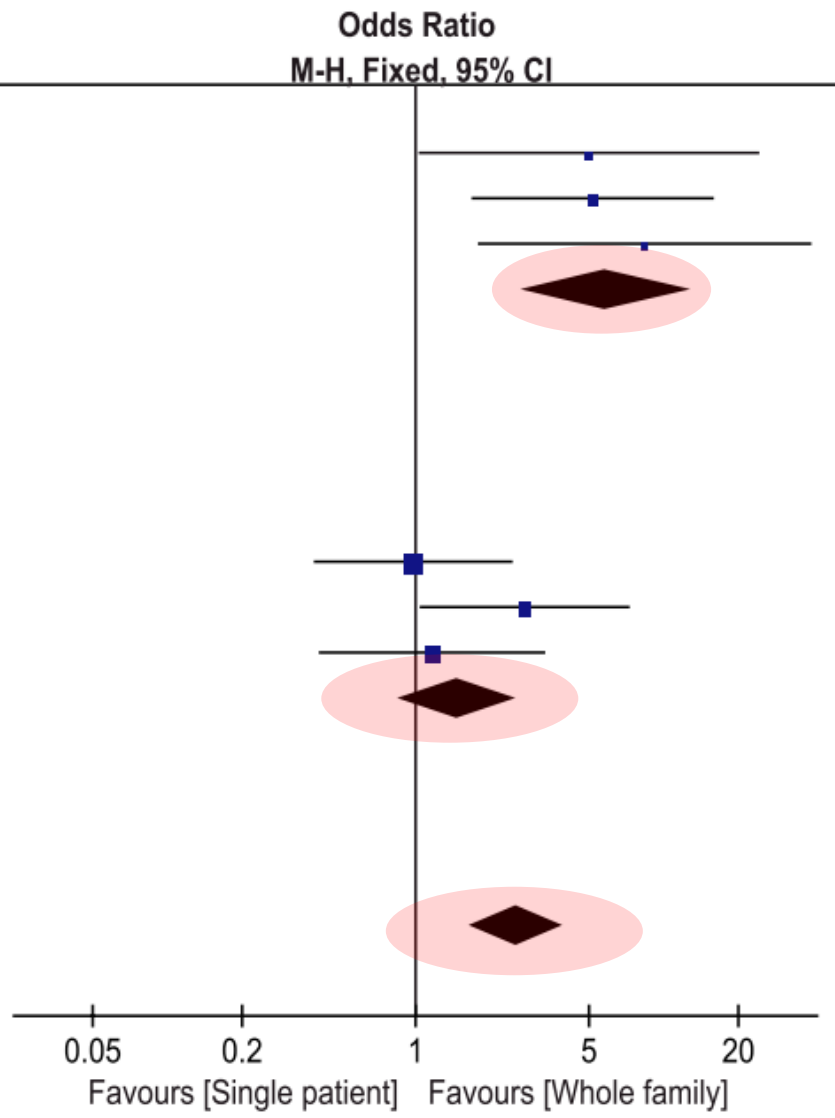


Zhao JB,et al. Helicobacter. 2021;26:e12793.

Erradicación

Análisis subgrupos

Study or Subgroup	Whole family group Events	Total	Single patient group Events	Total	Weight	Odds Ratio M-H, Fixed, 95% CI	Year
2.1.1 Children							
Chen 2003	40	42	40	50	6.4%	5.00 [1.03, 24.28]	2003
Rong 2012	92	96	80	98	12.1%	5.17 [1.68, 15.93]	2012
Sun 2013	49	51	38	51	5.5%	8.38 [1.78, 39.40]	2013
Subtotal (95% CI)		**189**		**199**	**24.0%**	**5.86 [2.67, 12.86]**	
Total events	181		158				
Heterogeneity: Chi² = 0.29, df = 2 (P = 0.86); I² = 0%							
Test for overall effect: Z = 4.41 (P < 0.0001)							
2.1.2 Spouse							
Rakici 2015	92	102	94	104	33.5%	0.98 [0.39, 2.46]	2015
Liang 2019	53	60	44	60	18.8%	2.75 [1.04, 7.29]	2019
Chen 2019	105	112	103	111	23.7%	1.17 [0.41, 3.33]	2019
Subtotal (95% CI)		**274**		**275**	**76.0%**	**1.48 [0.85, 2.57]**	
Total events	250		241				
Heterogeneity: Chi² = 2.53, df = 2 (P = 0.28); I² = 21%							
Test for overall effect: Z = 1.38 (P = 0.17)							
Total (95% CI)		**463**		**474**	**100.0%**	**2.53 [1.64, 3.90]**	
Total events	431		399				
Heterogeneity: Chi² = 10.76, df = 5 (P = 0.06); I² = 54%							
Test for overall effect: Z = 4.18 (P < 0.0001)							
Test for subgroup differences: Chi² = 7.89, df = 1 (P = 0.005), I² = 87.3%							



Zhao JB,et al. Helicobacter. 2021;26:e12793.

Helicobacter pylori

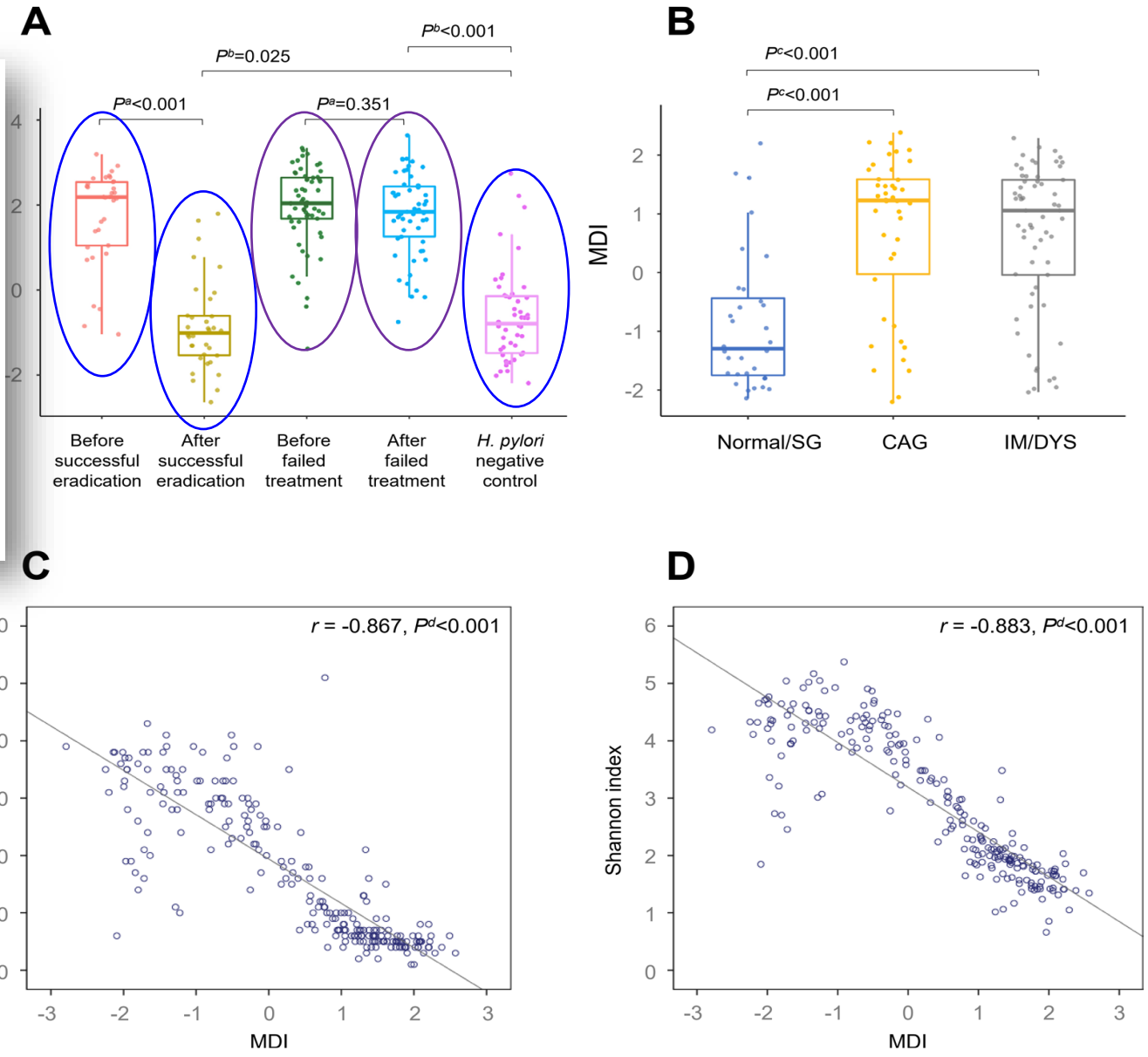
Antibióticos y Microbioma

Cura de *H.pylori* y microbiota

ORIGINAL RESEARCH

Effect of *Helicobacter pylori* on gastrointestinal microbiota: a population-based study in Linqu, a high-risk area of gastric cancer

Yang Guo,[1] Yang Zhang ,[1,2] Markus Gerhard,[2,3,4] Juan-Juan Gao,[1] Raquel Mejias-Luque,[2,3,4] Lian Zhang,[1] Michael Vieth,[2,5] Jun-Ling Ma,[1] Monther Bajbouj,[2,6] Stepan Suchanek,[2,7] Wei-Dong Liu,[8] Kurt Ulm,[2,9] Michael Quante ,[2,6] Zhe-Xuan Li,[1,2] Tong Zhou,[1] Roland Schmid,[2,6] Meinhard Classen,[2,6] Wen-Qing Li,[1,2] Wei-Cheng You,[1,2] Kai-Feng Pan[1,2]



Guo Y, et al. Gut 2020;69:1598–1607

Helicobacter pylori

Probióticos

Aumentan la eficacia De los tratamientos ?

Efectividad y seguridad del uso de probióticos como adyuvantes en la erradicación de *Helicobacter pylori.* Revisión sistemática y metaanálisis

Efficacy and safety of using probiotics as adjuvants in the eradication of *Helicobacter pylori*. Systematic review and meta-analysis

Título corto: Probióticos y *Helicobacter pylori*

Running title: Probiotics and *Helicobacter pylori*

Recibido: 22/07/2021 Aceptado: 06/04/2022

Gilberto Jaramillo-Trujillo[1], William Alberto Otero-Regino[1], Kelly Patricia Estrada-Orozco[2]

1 Universidad Nacional de Colombia - Sede Bogotá - Facultad de Medicina - Departamento de Gastroenterología - Bogotá D.C. - Colombia.

2 Universidad Nacional de Colombia - Sede Bogotá - Facultad de Medicina - Instituto de Investigaciones Clínicas - Bogotá D.C. - Colombia.

Correspondencia: William Alberto Otero-Regino. Departamento de Gastroenterología, Facultad de Medicina, Universidad Nacional de Colombia. Bogotá D.C. Colombia. Correo electrónico: waoteror@gmail.com.

William Alberto Otero-Regino: ORCID https://orcid.org/0000-0002-6825-

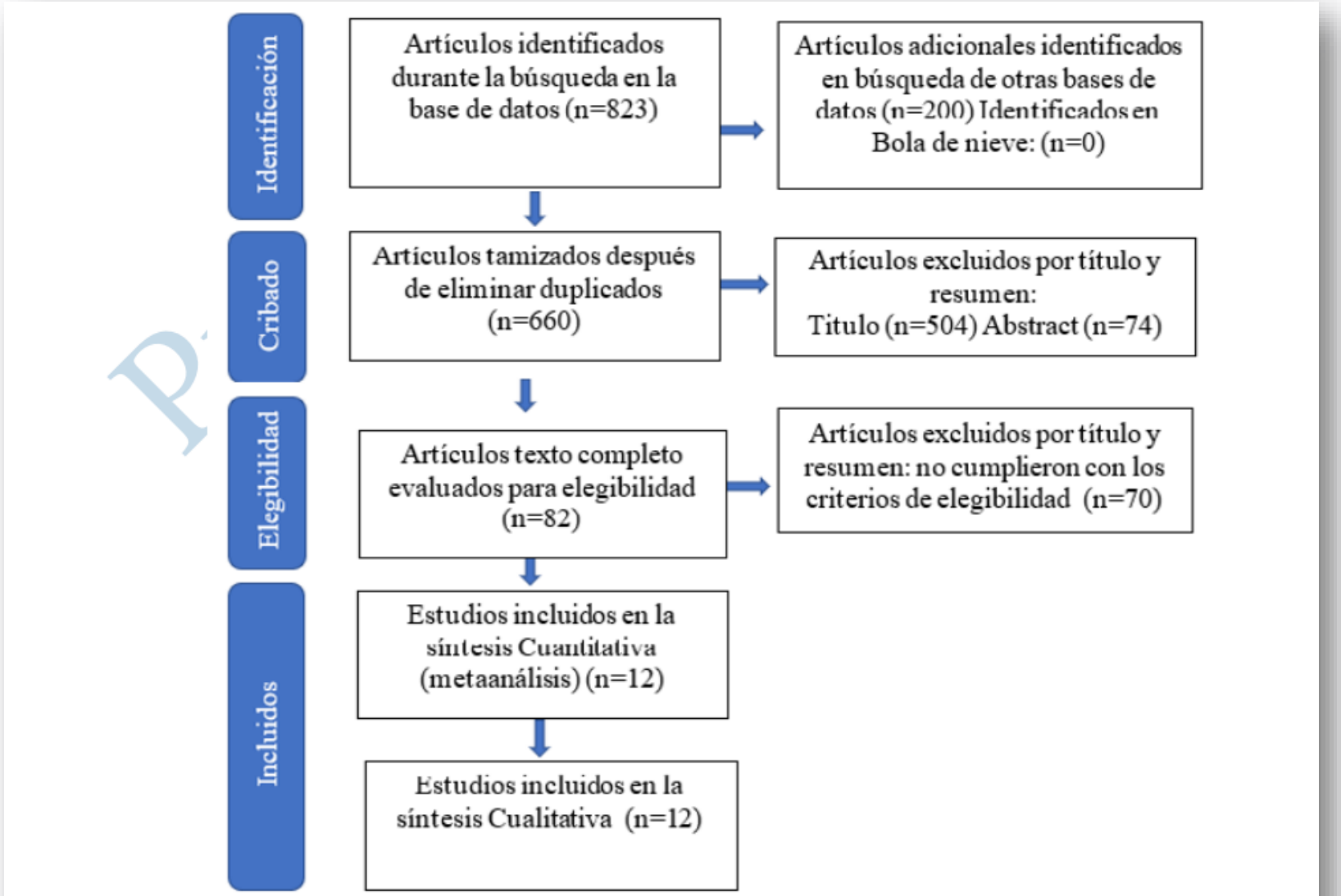


Figura 1. Flujograma de los estudios identificados y seleccionados.

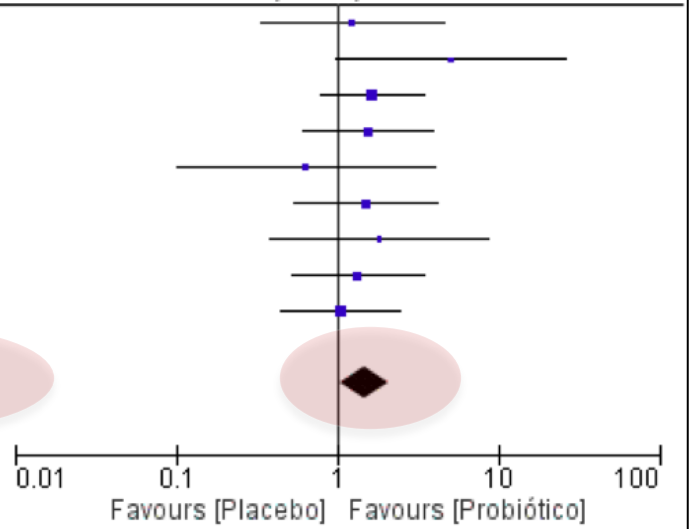
Jaramillo G, Otero W, Estrada K. Rev Fac Med 2022 On line Mayo 1

Curación de *H. pylori* en terapia triple

Study or Subgroup	PROBIOTICO Events	Total	PLACEBO Events	Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Armuzzi, 2001	25	30	24	30	7.6%	1.25 [0.34, 4.64]
Chitapanaru, 2015	28	30	22	30	2.8%	5.09 [0.98, 26.43]
Cindoruk, 2007	44	62	37	62	20.5%	1.65 [0.78, 3.49]
Francavilla, 2014	33	44	29	44	13.8%	1.55 [0.62, 3.91]
McNicholl, 2018	31	34	32	34	5.4%	0.65 [0.10, 4.13]
Mohamed,2014	26	35	23	35	11.3%	1.51 [0.54, 4.22]
Myllyuoma, 2005	21	24	19	24	4.5%	1.84 [0.39, 8.77]
Navarro, 2013	45	55	40	52	14.2%	1.35 [0.53, 3.46]
Nista, 2004	39	54	37	52	19.9%	1.05 [0.45, 2.45]
Total (95% CI)		**368**		**363**	**100.0%**	**1.48 [1.05, 2.09]**
Total events	292		263			

Heterogeneity: Chi² = 3.82, df = 8 (P = 0.87); I² = 0%

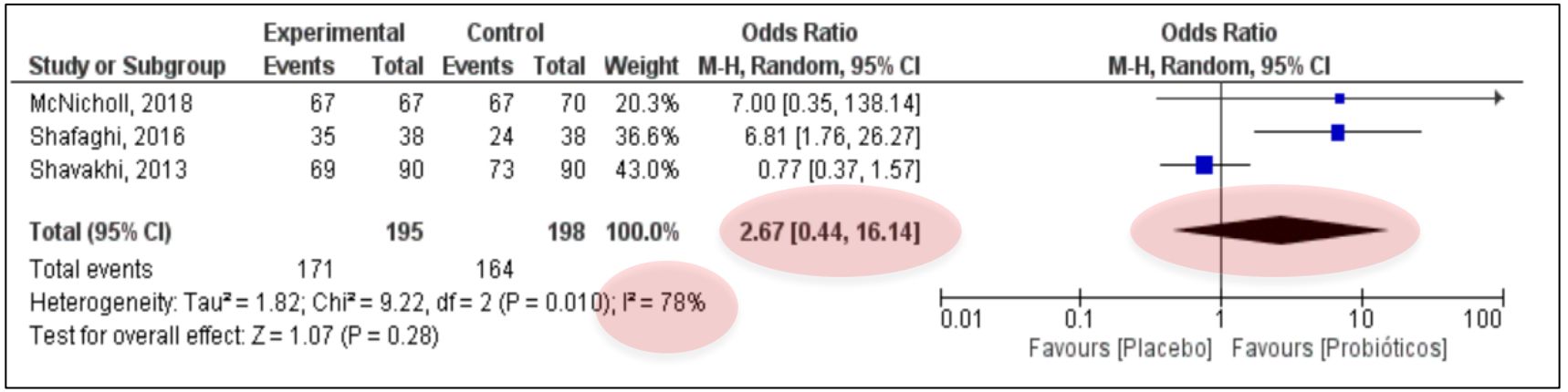
Test for overall effect: Z = 2.21 (P = 0.03)



Aumento de efectividad 8.3%
71.1%. Vs 79.4% NO *logró 90-95%*

Jaramillo G, Otero W, Estrada K. Rev Fac Med 2022 On line Mayo 1

Erradicación de *H. pylori* terapia cuádruple



Study or Subgroup	Experimental Events	Total	Control Events	Total	Weight	Odds Ratio M-H, Random, 95% CI
McNicholl, 2018	67	67	67	70	20.3%	7.00 [0.35, 138.14]
Shafaghi, 2016	35	38	24	38	36.6%	6.81 [1.76, 26.27]
Shavakhi, 2013	69	90	73	90	43.0%	0.77 [0.37, 1.57]
Total (95% CI)		**195**		**198**	**100.0%**	**2.67 [0.44, 16.14]**
Total events	171		164			

Heterogeneity: Tau² = 1.82; Chi² = 9.22, df = 2 (P = 0.010); I² = 78%

Test for overall effect: Z = 1.07 (P = 0.28)

Jaramillo G, Otero W, Estrada K. Rev Fac Med 2022 On line Mayo 1

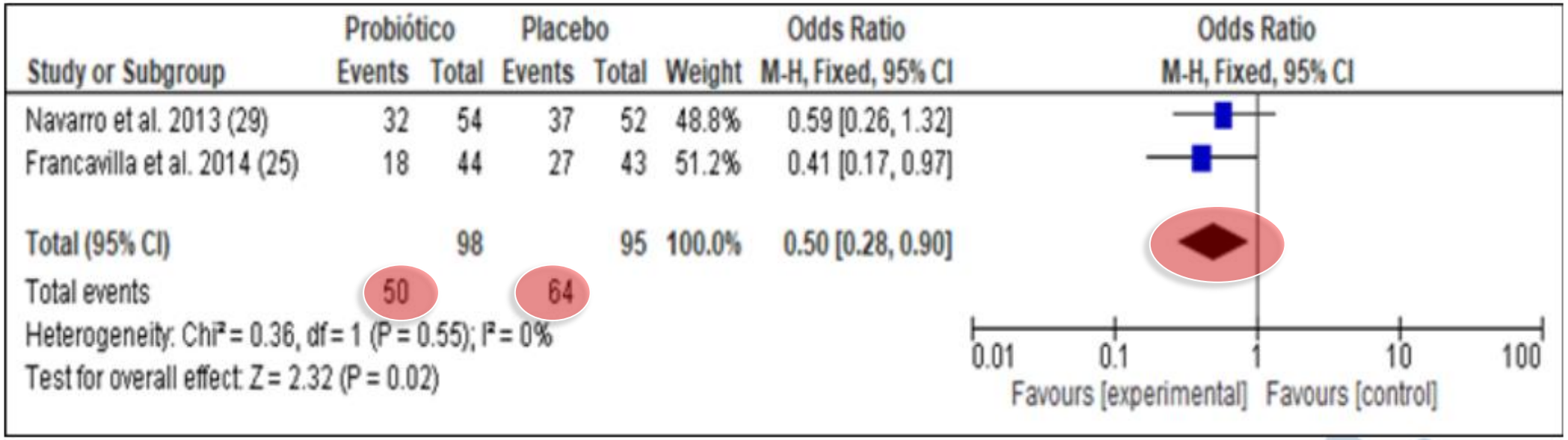


Figura 4. Eventos adversos con terapia triple.

The Toronto Consensus for the Treatment of *Helicobacter pylori* Infection in Adults

2016

Carlo A. Fallone,[1] Naoki Chiba,[2,3] Sander Veldhuyzen van Zanten,[4] Lori Fischbach, Javier P. Gisbert,[6] Richard H. Hunt,[3,7] Nicola L. Jones,[8] Craig Render,[9] Grigorios I. Leontiadis,[3,7] Paul Moayyedi,[3,7] and John K. Marshall[3,7]

Management of *Helicobacter pylori* infection—the Maastricht V/Florence Consensus Report

2017

P Malfertheiner,[1] F Megraud,[2] C A O'Morain,[3] J P Gisbert,[4,5] E J Kuipers,[6] F Bazzoli,[8] A Gasbarrini,[9] J Atherton,[10] D Y Graham,[11] T Rokkas,[15] M Rugge,[16] M Selgrad,[17] on behalf of the Europ

ACG

2021

Javier P. Gisbert[1], Javier Alcedo[2], Javier Amador[3], Luis Bujanda[4], Xavier Calvet[5], Manuel Castro-Fernández[6], Luis Fernández-Salazar[7], Emili Gené[8], Ángel Lanas[9], Alfredo J. Lucendo[10], Javier Molina-Infante[11], Olga P. Nyssen[1], A. Pérez-Aisa[12] e Ignasi Puig[13]

Ninguna guìa los Recomienda por ahora

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 7: Certain probiotics may have a beneficial effect on _H. pylori_ eradication therapy through reduction of antibiotic-related side effects

Agreement 80% **Grade B2**

Consequently, more data are still necessary to assess the direct efficacy of probiotics against *H. pylori*.

Malfertheiner P, Maastricht VI, Gut 2020,Online agosto 8

Gastroenterology 2021;160:1831–1841

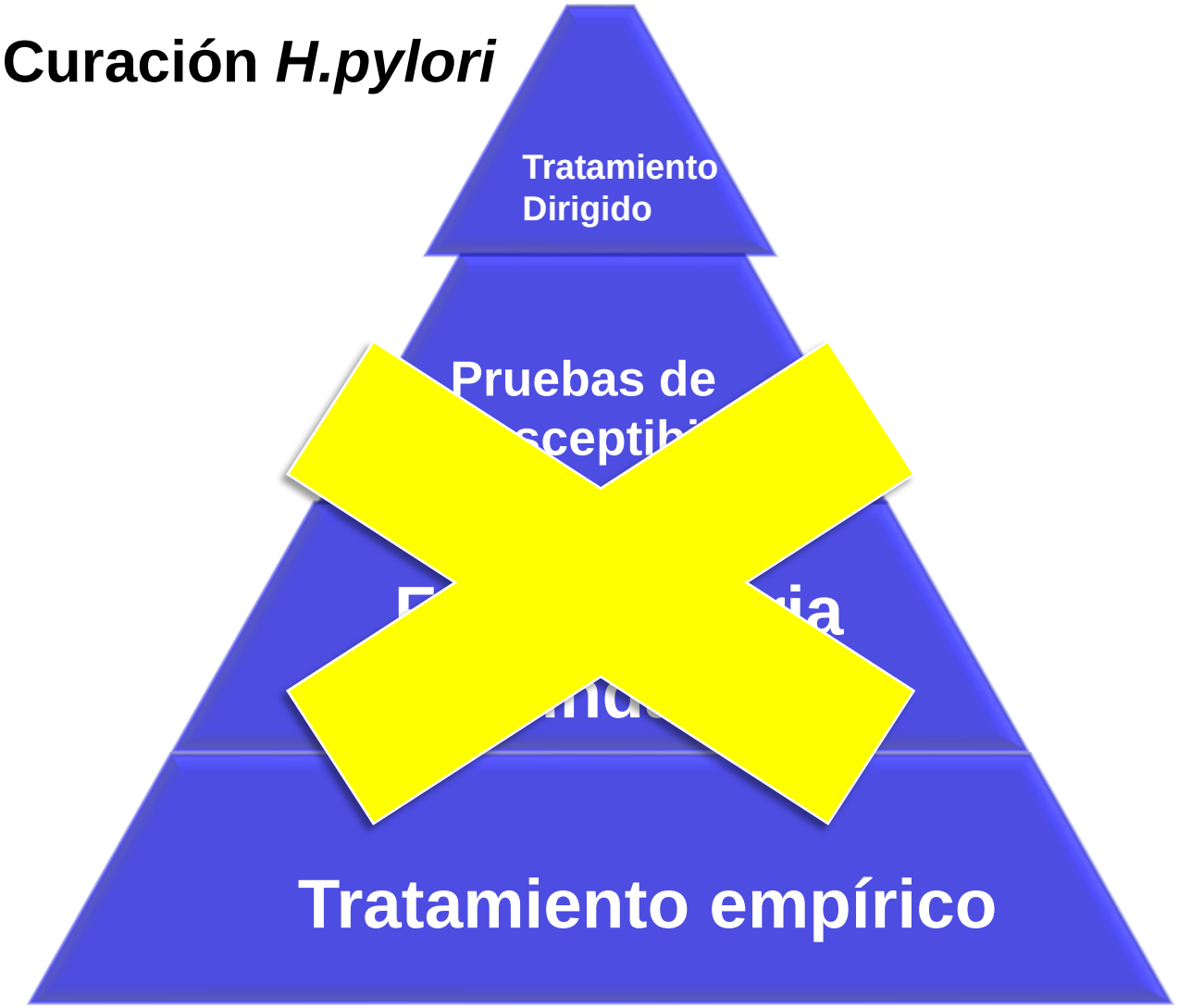
CLINICAL PRACTICE UPDATE

AGA Clinical Practice Update on the Management of Refractory *Helicobacter pylori* Infection: Expert Review

Shailja C. Shah,[1,2,3] Prasad G. Iyer,[4] and Steven F. Moss[5]

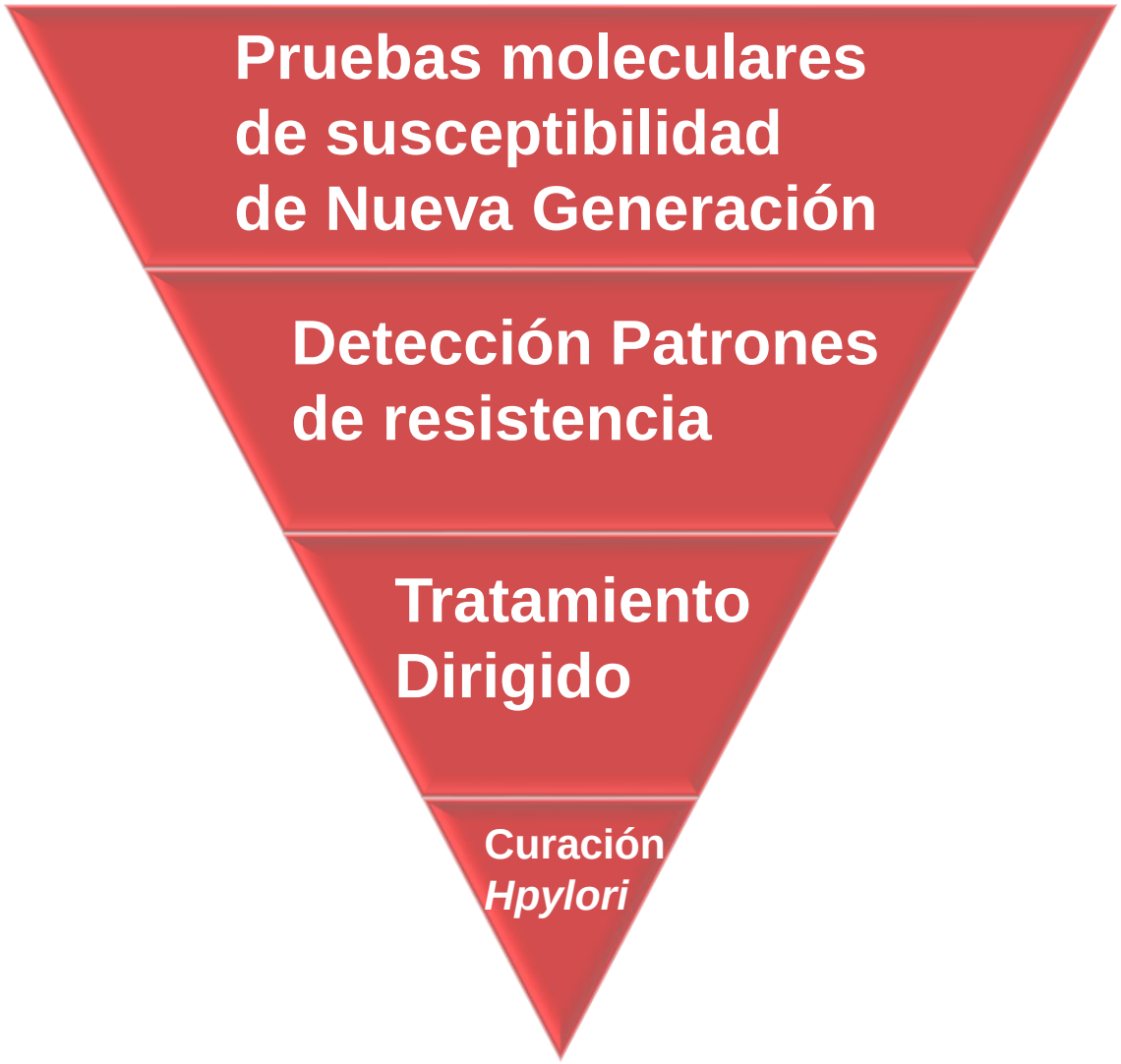
Best Practice Advice 12: Proposed adjunctive therapies, including probiotics, are of unproven benefit as treatment for refractory *H pylori* infection, and thus, their use should be considered experimental.

Curación *H.pylori*



Dogma actual

Nuevo paradigma



Garrido-Teviño LF, et al Rev Gastroenterol Mex 2022, Junio 15

Empirical vs. Susceptibility-Guided Treatment of *Helicobacter pylori* Infection: A Systematic Review and Meta-Analysis

Olga P. Nyssen [1,2,3], *Marta Espada* [1,2,3] *and Javier P. Gisbert* [1,2,3]*

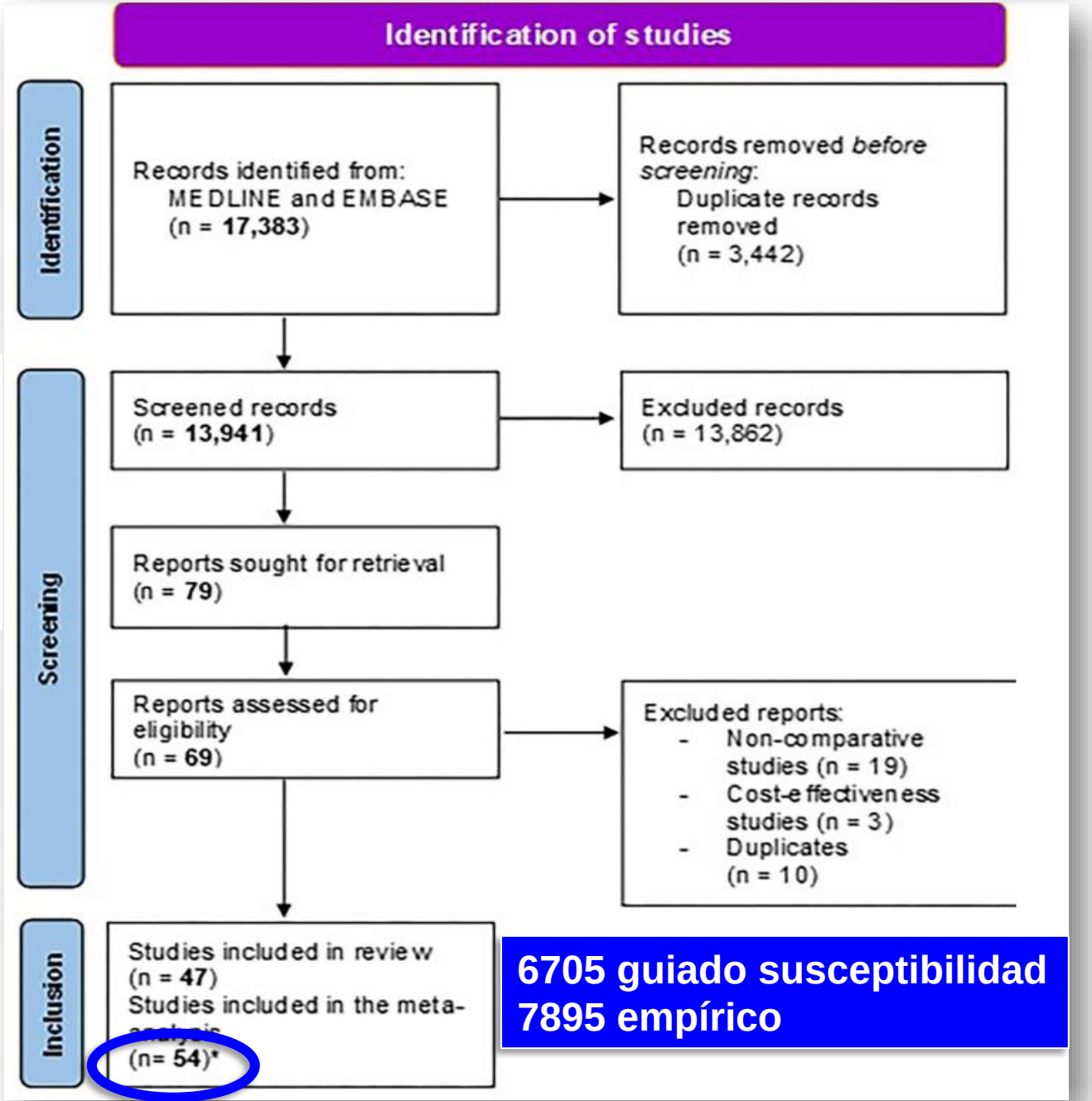
[1] *Gastroenterology Unit, Instituto de Investigación Sanitaria Princesa (IIS-Princesa), Hospital Universitario de La Princesa, Madrid, Spain,* [2] *Universidad Autónoma de Madrid (UAM), Madrid, Spain,* [3] *Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas (CIBEREHD), Madrid, Spain*

Nyssen OP, Front Microbiol 2022;13: Article 913436

Empirical vs. Susceptibility-Guided Treatment of *Helicobacter pylori* Infection: A Systematic Review and Meta-Analysis

*Olga P. Nyssen [1,2,3], Marta Espada [1,2,3] and Javier P. Gisbert [1,2,3]**

[1] *Gastroenterology Unit, Instituto de Investigación Sanitaria Princesa (IIS-Princesa), Hospital Universitario de La Princesa, Madrid, Spain,* [2] *Universidad Autónoma de Madrid (UAM), Madrid, Spain,* [3] *Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas (CIBEREHD), Madrid, Spain*



Nyssen OP, Front Microbiol 2022;13: Article 913436

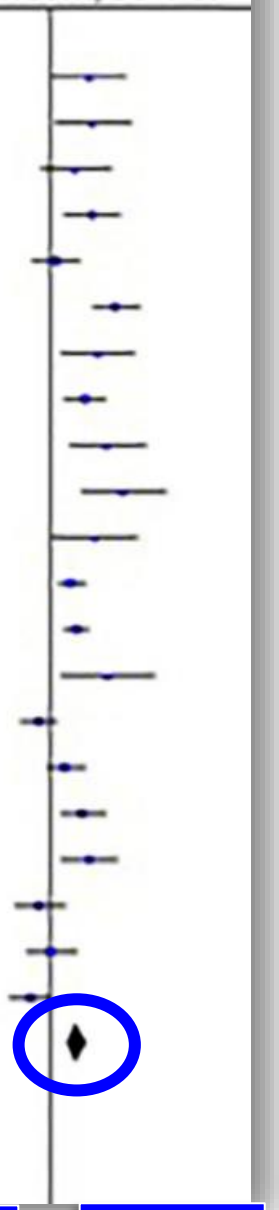
Primera Línea

Study or Subgroup	Susceptibility-guided Events	Total	Empiric regimen Events	Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
1.5.1 First-line							
Toracchio 2000	48	53	42	56	2.6%	1.21 [1.01, 1.44]	2000
Romano 2000	38	40	31	40	2.5%	1.23 [1.02, 1.47]	2000
Neri 2003	88	116	78	116	2.8%	1.13 [0.96, 1.33]	2003
Romano 2003	71	75	58	75	3.2%	1.22 [1.07, 1.40]	2003
Marzio (a) 2006	39	41	36	39	3.5%	1.03 [0.92, 1.16]	2006
Furuta 2007	144	150	105	150	3.5%	1.37 [1.23, 1.53]	2007
Wang 2008	36	40	57	80	2.6%	1.26 [1.06, 1.50]	2008
Zhou 2010	117	125	107	135	3.7%	1.18 [1.07, 1.30]	2010
Park 2014	54	57	41	57	2.6%	1.32 [1.11, 1.57]	2014
Martos 2014	52	55	36	54	2.3%	1.42 [1.16, 1.73]	2014
Dong 2015	41	45	33	45	2.3%	1.24 [1.02, 1.52]	2015
Zhuo 2015	281	313	405	500	4.2%	1.11 [1.05, 1.17]	2015
Zhou 2016	282	318	545	700	4.2%	1.14 [1.08, 1.20]	2016
Kawai 2018	33	35	25	35	2.1%	1.32 [1.05, 1.65]	2018
Ong 2019	164	201	169	196	3.8%	0.95 [0.87, 1.03]	2019
Chen 2019	262	286	82	96	3.8%	1.07 [0.98, 1.17]	2019
Delchier 2019	177	207	152	208	3.7%	1.17 [1.06, 1.29]	2019
Pan 2020	238	310	100	157	3.2%	1.21 [1.06, 1.38]	2020
Bonoso (a) 2021	39	43	43	45	3.4%	0.95 [0.85, 1.06]	2021
Choi 2021	91	110	88	107	3.3%	1.01 [0.89, 1.14]	2021
Cha 2021	118	147	142	161	3.7%	0.91 [0.83, 1.00]	2021
Subtotal (95% CI)		**2767**		**3052**	**67.1%**	**1.14 [1.08, 1.20]**	
Total events	2413		2375				

Heterogeneity: Tau² = 0.01; Chi² = 80.40, df = 20 (P < 0.00001); I² = 75%

Test for overall effect: Z = 5.03 (P < 0.00001)

Risk Ratio M-H, Random, 95% CI



Empírica

Guiada

Nyssen OP,et al. Front Microbiol 2022;13:Art 913436.

Empirical vs. Susceptibility-Guided Treatment of *Helicobacter pylori* Infection: A Systematic Review and Meta-Analysis

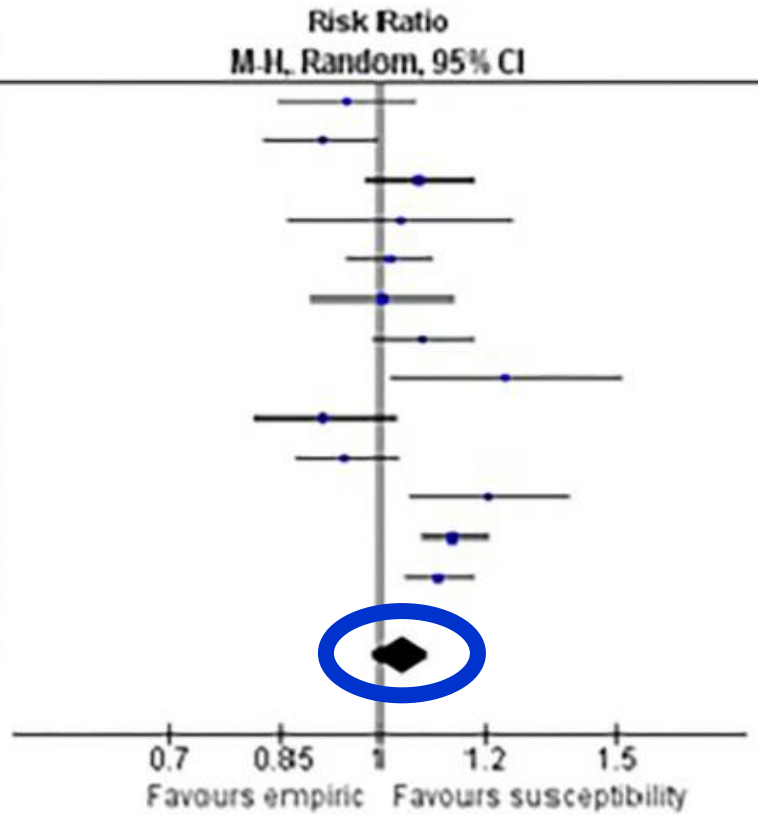
*Olga P. Nyssen [1,2,3], Marta Espada [1,2,3] and Javier P. Gisbert [1,2,3]**

Cuádruple con o sin Bismuto

Study or Subgroup	Susceptibility-guided Events	Total	Empiric regimen Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Bonoso (a) 2021	39	43	43	45	7.3%	0.95 [0.85, 1.06]
Cha 2021	118	147	142	161	8.1%	0.91 [0.83, 1.00]
Chen 2019	262	286	82	96	8.5%	1.07 [0.98, 1.17]
Choe (c) 2021	55	60	15	17	4.4%	1.04 [0.86, 1.26]
Choi 2019	48	50	98	104	9.3%	1.02 [0.95, 1.10]
Choi 2021	91	110	88	107	6.9%	1.01 [0.89, 1.14]
Cosme 2016	98	104	103	118	8.8%	1.08 [0.99, 1.17]
Dong 2015	41	45	33	45	4.1%	1.24 [1.02, 1.52]
Molina-Infante 2012	69	87	182	209	7.0%	0.91 [0.81, 1.03]
Ong 2019	164	201	169	196	8.7%	0.95 [0.87, 1.03]
Pan 2020	238	310	100	157	6.4%	1.21 [1.06, 1.38]
Zhou 2016	282	318	545	700	10.3%	1.14 [1.08, 1.20]
Zhuo 2015	281	313	405	500	10.2%	1.11 [1.05, 1.17]
Total (95% CI)		**2074**		**2455**	**100.0%**	**1.04 [0.99, 1.09]**
Total events	1786		2005			

Heterogeneity: Tau² = 0.01; Chi² = 42.74, df = 12 (P < 0.0001); I² = 72%

Test for overall effect: Z = 1.51 (P = 0.13)



Nyssen OP,et al. Front Microbiol 2022;13:Art 913436.

Segunda Línea

Tercera Línea

Todas rescate

1.5.2 Second-line

Avidan 2001	5	5	5	5	1.2%	1.00 [0.71, 1.41]	2001
Lamouliatte 2003	84	113	83	172	2.4%	1.54 [1.28, 1.86]	2003
Miwa 2003	31	38	36	39	2.6%	0.88 [0.74, 1.05]	2003
Marzio (b) 2006	50	51	26	32	2.7%	1.21 [1.02, 1.43]	2006
Bonoso(b) 2021	8	9	6	6	1.3%	0.92 [0.66, 1.28]	2021
Subtotal (95% CI)		**216**		**254**	**10.2%**	**1.10 [0.85, 1.41]**	
Total events	178		156				

Heterogeneity: Tau² = 0.07; Chi² = 25.15, df = 4 (P < 0.0001); I² = 84%

Test for overall effect: Z = 0.73 (P = 0.47)

1.5.3 Third-line

Liou (a) 2018	17	21	12	20	0.9%	1.35 [0.89, 2.04]	2018
Liou (b) 2018	160	205	148	205	3.5%	1.08 [0.97, 1.21]	2018
Bonoso (c) 2021	1	1	2	4	0.1%	1.50 [0.46, 4.91]	2021
Subtotal (95% CI)		**227**		**229**	**4.5%**	**1.10 [0.99, 1.23]**	
Total events	178		162				

Heterog

Test for

1.5.4 All

Avidan 2

Miwa 20

Lamouli

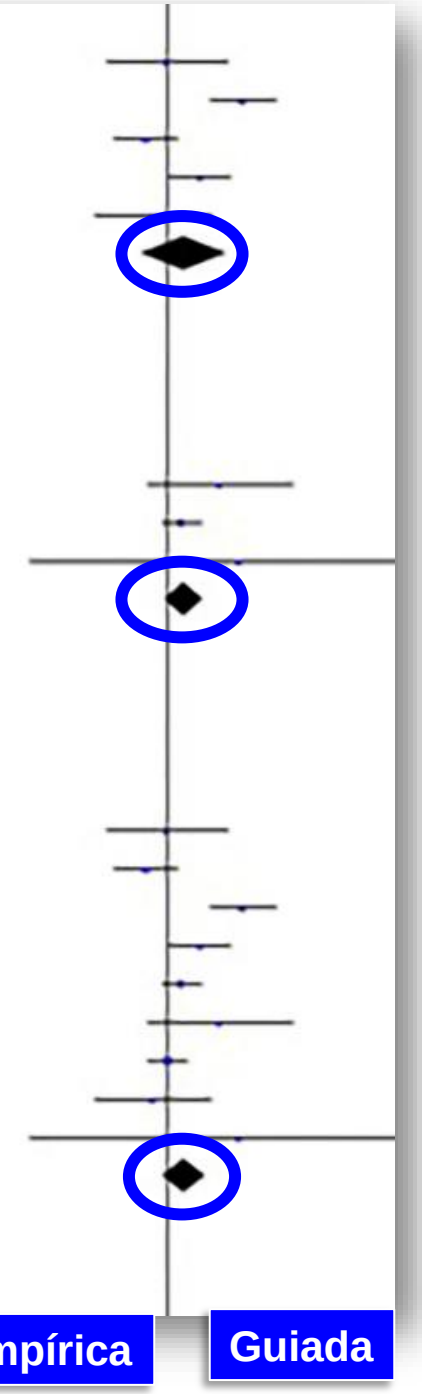
Marzio (b) 2006 50 51 26 32 2.7% 1.21 [1.02, 1.43] 2006

Liou (b) 2018	160	205	148	205	3.5%	1.08 [0.97, 1.21]	2018
Liou (a) 2018	17	21	12	20	0.9%	1.35 [0.89, 2.04]	2018
Ji 2020	164	220	156	210	3.5%	1.00 [0.90, 1.12]	2020
Bonoso(b) 2021	8	9	6	6	1.3%	0.92 [0.66, 1.28]	2021
Bonoso (c) 2021	1	1	2	4	0.1%	1.50 [0.46, 4.91]	2021
Subtotal (95% CI)		**663**		**693**	**18.2%**	**1.10 [0.97, 1.25]**	
Total events	520		474				

Heterogeneity: Tau² = 0.02; Chi² = 25.47, df = 8 (P = 0.001); I² = 69%

Test for overall effect: Z = 1.54 (P = 0.12)

El beneficio de las terapias Guiadas no fue demostrado



Empírica

Guiada

Nyssen OP,et al. Front Microbiol 2022;13:Art 913436.

Empirical rescue therapy after *Helicobacter pylori* treatment failure: a 10-year single-centre study of 500 patients

J. P. GISBERT, J.-L. GISBERT, S. MARCOS, I. JIMENEZ-ALONSO, R. MORENO-OTERO & J. M. PAJARES

500 pacientes

Primera línea	**70% (65–75%)**
Segunda línea	**74% (66 – 81%)**
Eficacia acumulada	**99.5% (98.2-99.8%)**

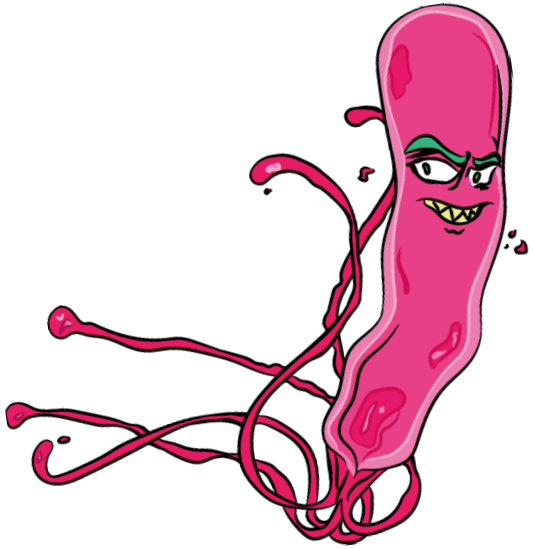
En cada región o país se desearía Conocer cuál sería la secuencia exitosa!

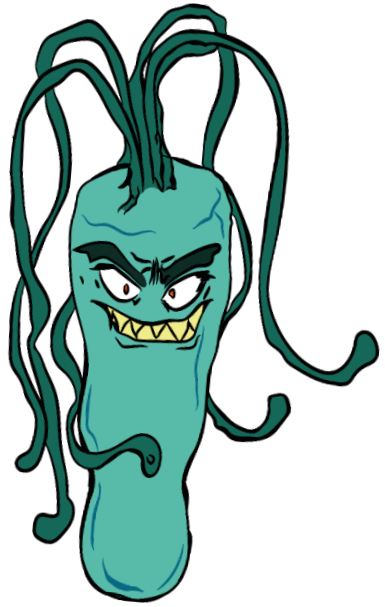
Aliment Pharmacol Ther 2008;27, 346–354

Mensajes para la casa

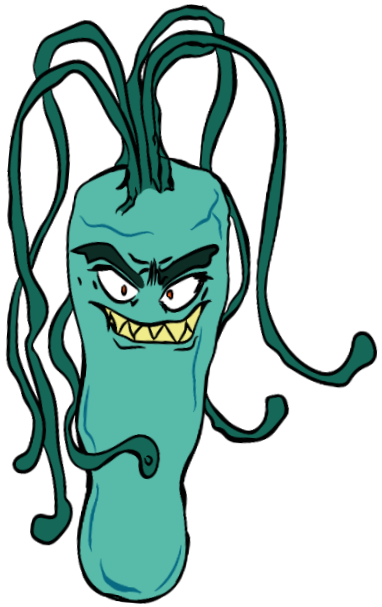
Tratamiento por 14 dìas
IBP mas 3 antibiòticos excepto dual
No hay esquema universal
Cada país estudiarà sus esquemas
Eficacia exigida ITT 90% PP 95%
Investigar tratamientos basados susceptibilidad

Hasta ahora ningùn *Helicobacter* es bueno!





H.pylori encontrado



H. pylori tratado

Sugano K, Kyoto Consensus. Gut 2015;65:1353-67

Muchas gracias !