



Los IBPs no tienen riesgo



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Youtube “William otero gastroenterologo”

Hani

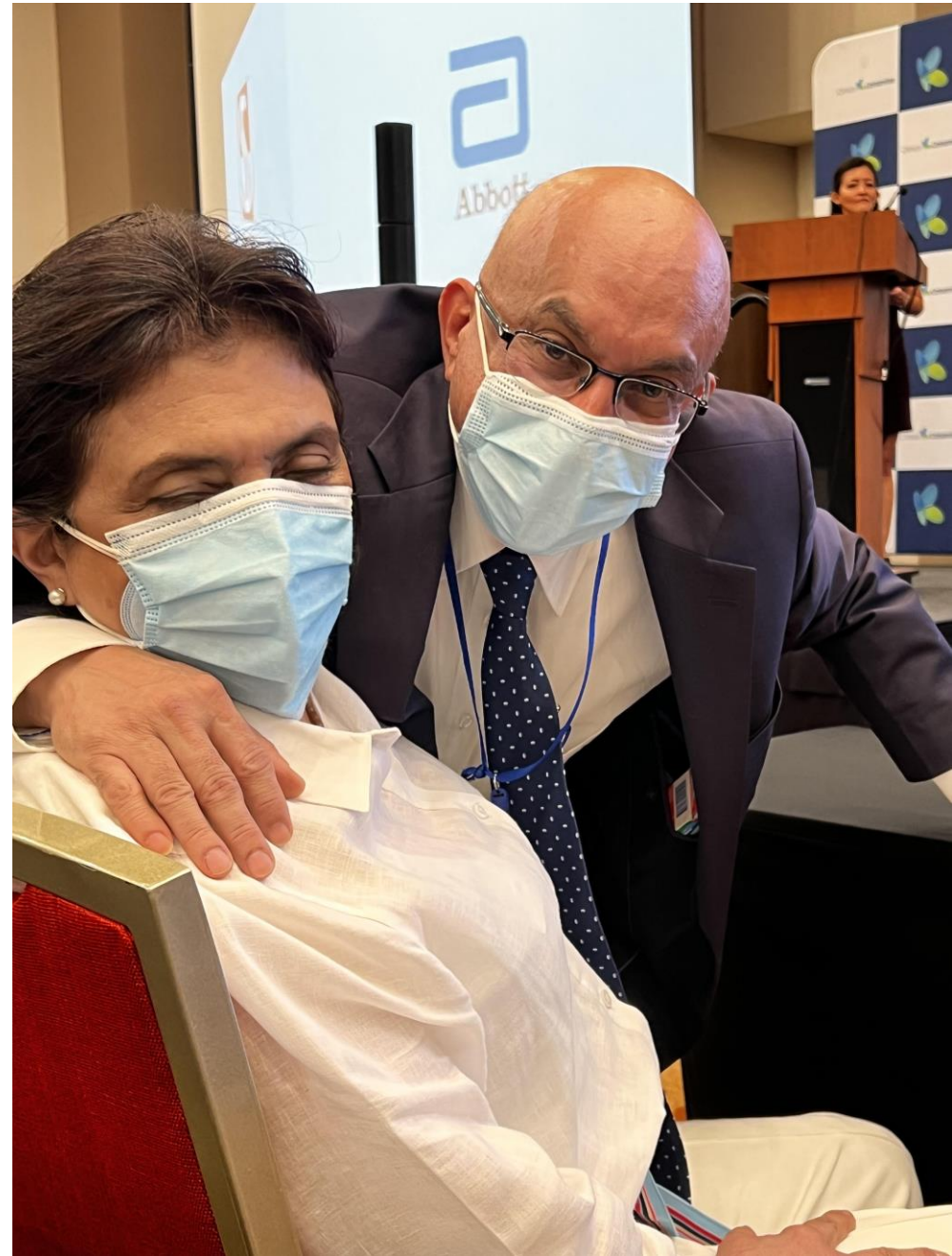


Otero

Hani



Otero



Si

No

*La comunidad científica
está dividida: Unos dicen
que los IBP hacen daño
y otros dicen que no*



CLINICAL PRACTICE UPDATE

AGA Clinical Practice Update on De-Prescribing of Proton Pump Inhibitors: Expert Review

Laura E. Targownik,¹ Deborah A. Fisher,² and Sameer D. Saini^{3,4}

Indicaciones correctas de los IBPs



**Por períodos
Cortos <12 semanas**

Erradicación *H.pylori*
Úlceras pépticas
Úlcera péptica sangrante
Profilaxis úlceras estrés
Dispepsia funcional (“**Gastritis**”)
Esofagitis eosinofílica sin
respuesta



**Por períodos
Indefinidos**

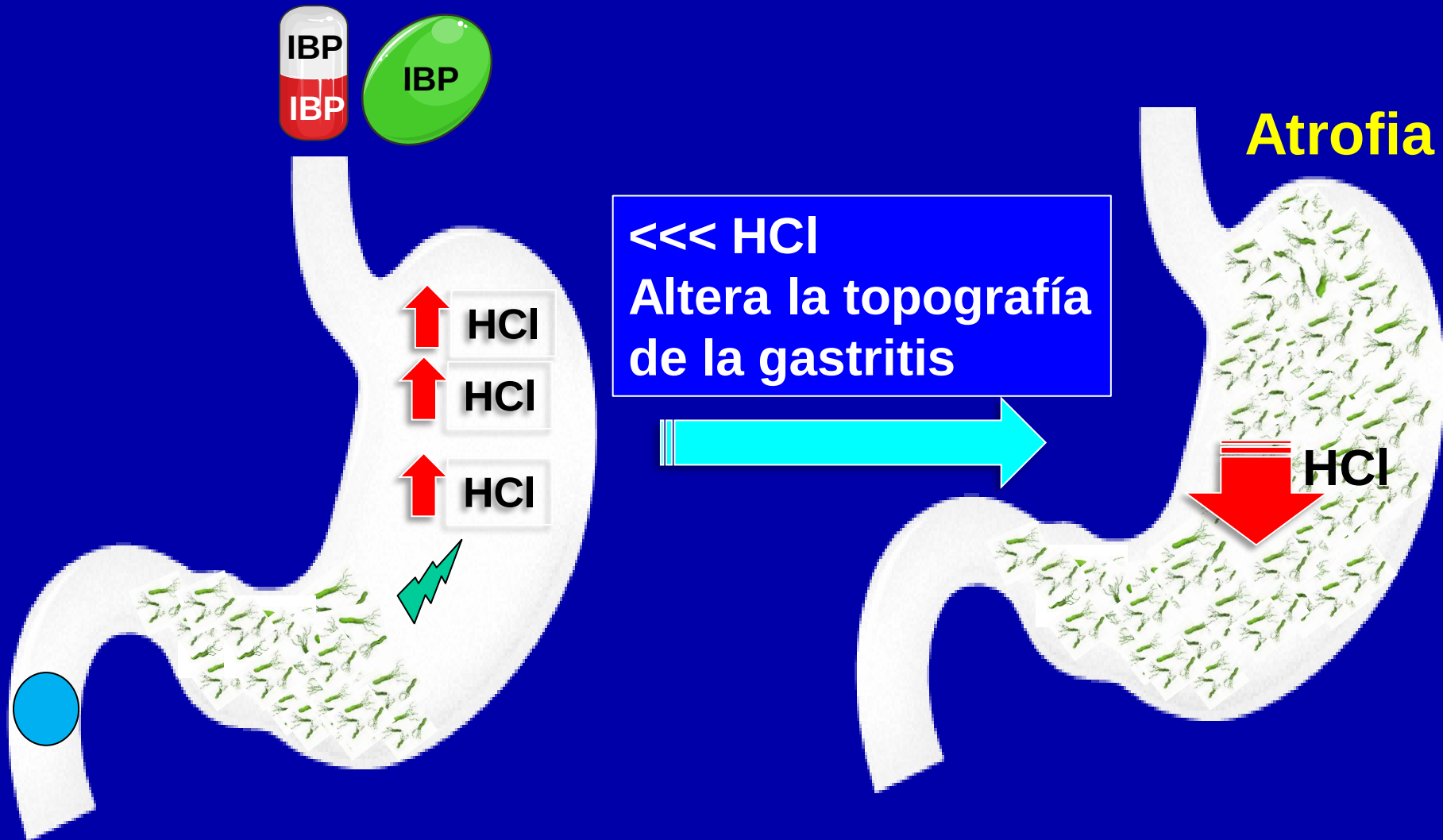
Esofagitis C y D
Esófago de Barrett
Úlcera péptica idiopática
Profilaxis AINES
Profilaxis antiplaquetarios
Esofagitis eosinofílica (+)
Fibrosis Pulmonar
Zollinger Ellison

Herszényi L, Dig Dis 2020;38:104-11

Targownik LE, Gastroenterology 2022;162:1334-42

IBP realidades

IBP y Hpylori



Kuipers EJ, Am J Gastroenterol 1995;90:1401-6
Kuipers EJ, N Engl J Med 1996;334:1018-22
Lundell L, Alim Pharmacol Ther 2006;23:639-47

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

Helicobacter 2018;23:e12475

Wen Zhong Liu¹ | Yong Xie² | Hong Lu¹ | Hong Cheng³ | Zhi Rong Zeng⁴ | Li Ya Zhou⁵ | Ye Chen⁶ | Jiang Bin Wang⁷ | Yi Qi Du⁸ | Nong Hua Lu²  | on behalf of Chinese Society of Gastroenterology, Chinese Study Group on *Helicobacter pylori* and Peptic Ulcer

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 Gasbarrini¹⁰ Richard H Hunt^{11,12} Marcis Leja ^{13,14} Colm O’Morain¹⁵ 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

Gut 2022 online agosto 8

Statement 11: Long-term treatment with PPIs alters the topography of *H. pylori* gastritis.

Agreement 94% Grade A1

Statement 12: *H. pylori* eradication improves gastritis in long- term PPI users.

Agreement 97% Grade A1

IBP largos
Períodos

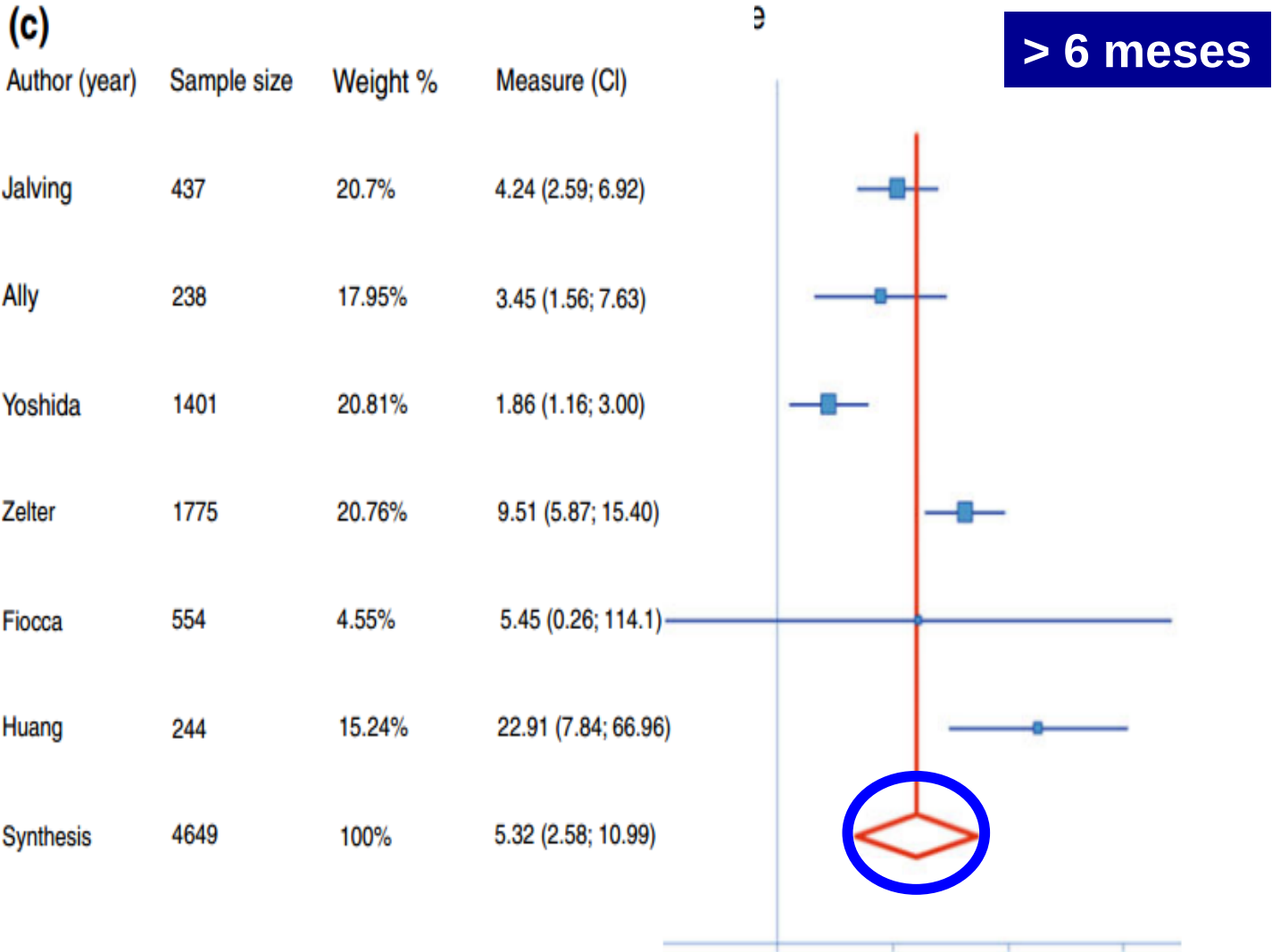


Erradicación
H.pylori

Systematic review with meta-analysis: fundic gland polyps and proton pump inhibitors

Aliment Pharmacol Ther 2016,Online Sept 21

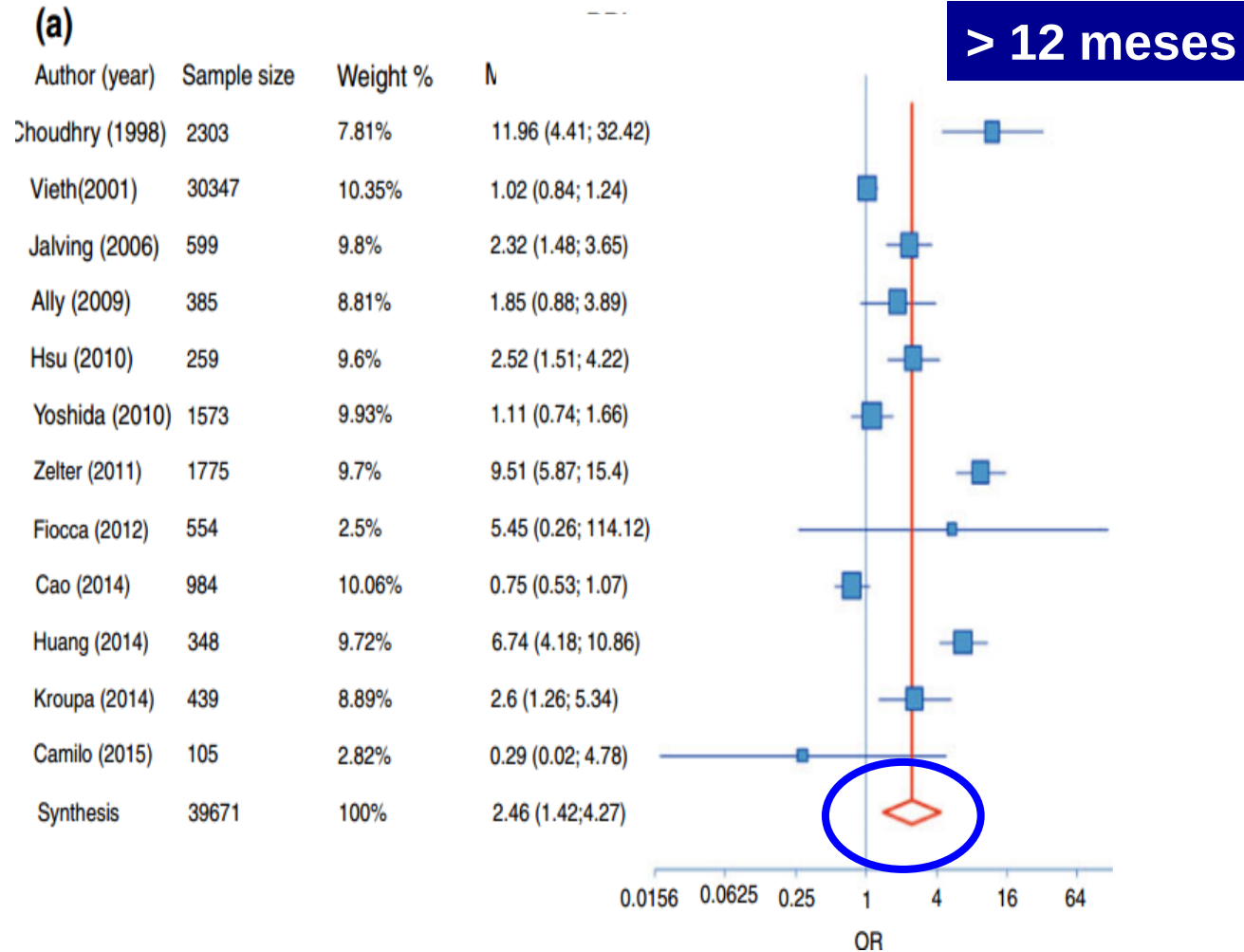
F. C. Martin*, G. Chenevix-Trench† & N. D. Yeomans*,‡



Systematic review with meta-analysis: fundic gland polyps and proton pump inhibitors

Aliment Pharmacol Ther 2016,Online Sept 21

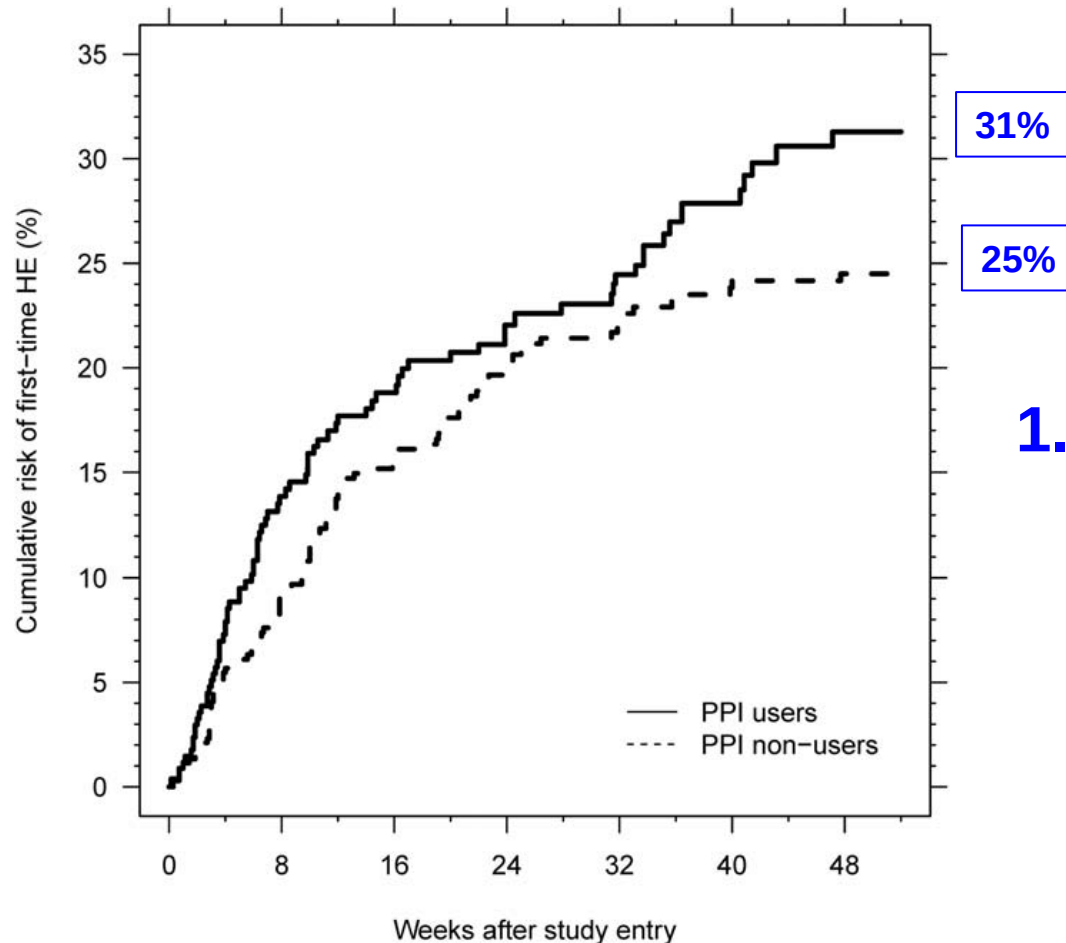
F. C. Martin*, G. Chenevix-Trench[†] & N. D. Yeomans ^{*,‡}



Cirrosis

Proton Pump Inhibitors as a Risk Factor for Hepatic Encephalopathy and Spontaneous Bacterial Peritonitis in Patients With Cirrhosis With Ascites

Gitte Dam,¹ Hendrik Vilstrup,¹ Hugh Watson,² and Peter Jepsen^{1,3}

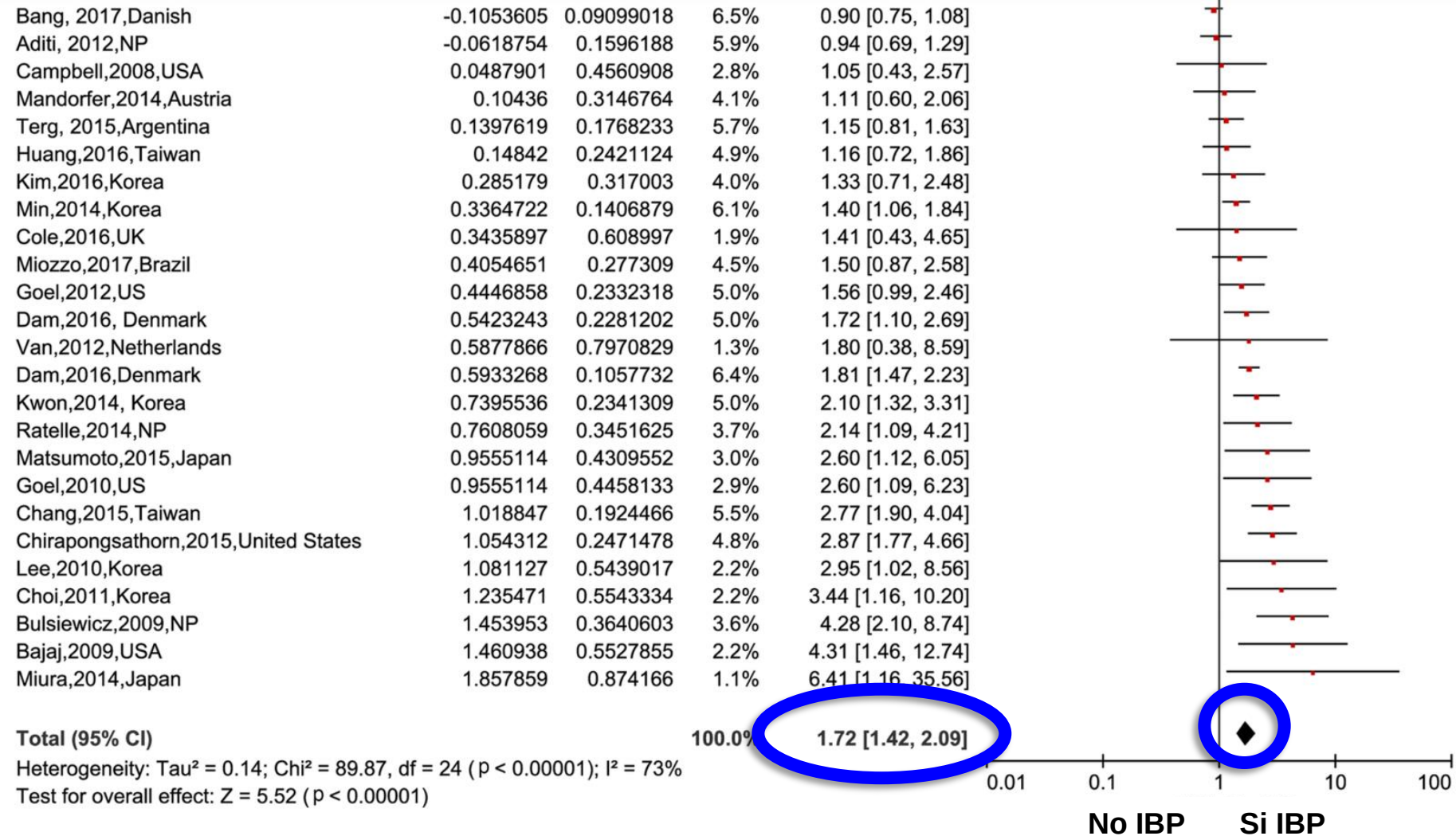


1.72 (IC 95% 1.10-2.69).

Adverse outcomes of proton pump inhibitors in chronic liver disease: a systematic review and meta-analysis

Junna Wang^{1,2} · Yangpeng Wu³ · Qiu Bi⁴ · Xianglong Zheng⁵ · Jingtao Zhang⁶ · Wenxiang Huang⁵

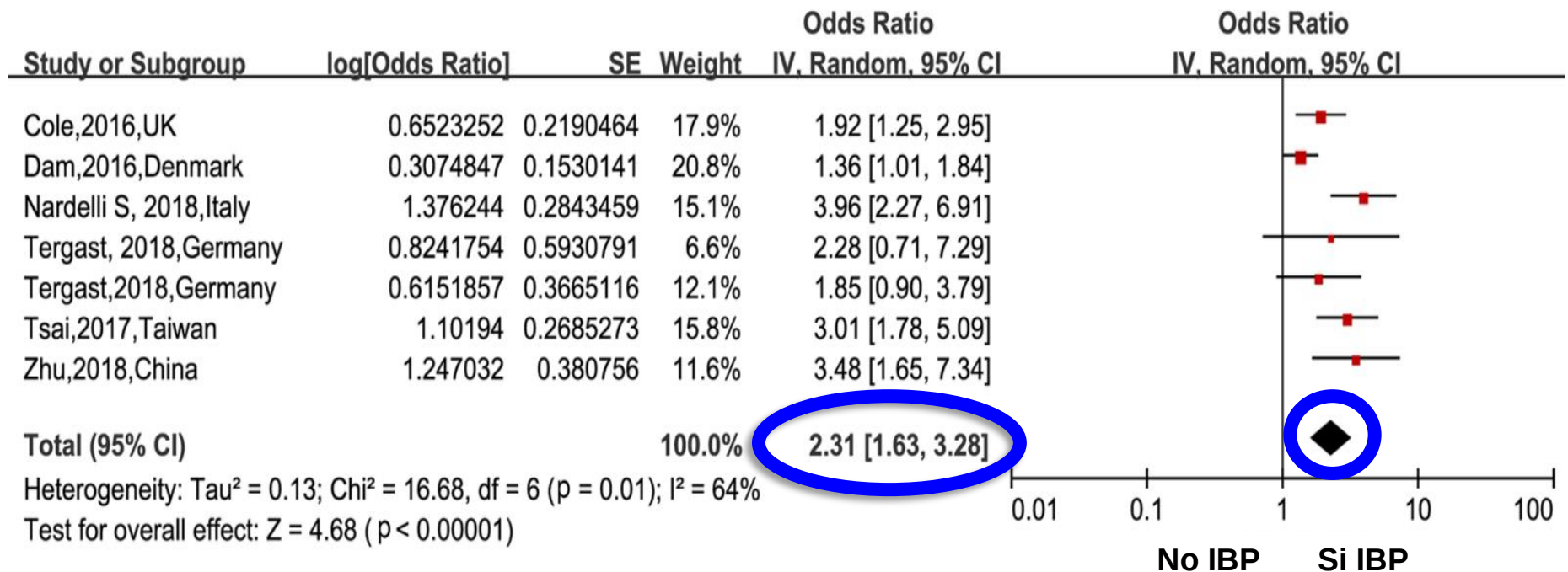
Peritonitis Bacteriana Espontánea



Adverse outcomes of proton pump inhibitors in chronic liver disease: a systematic review and meta-analysis

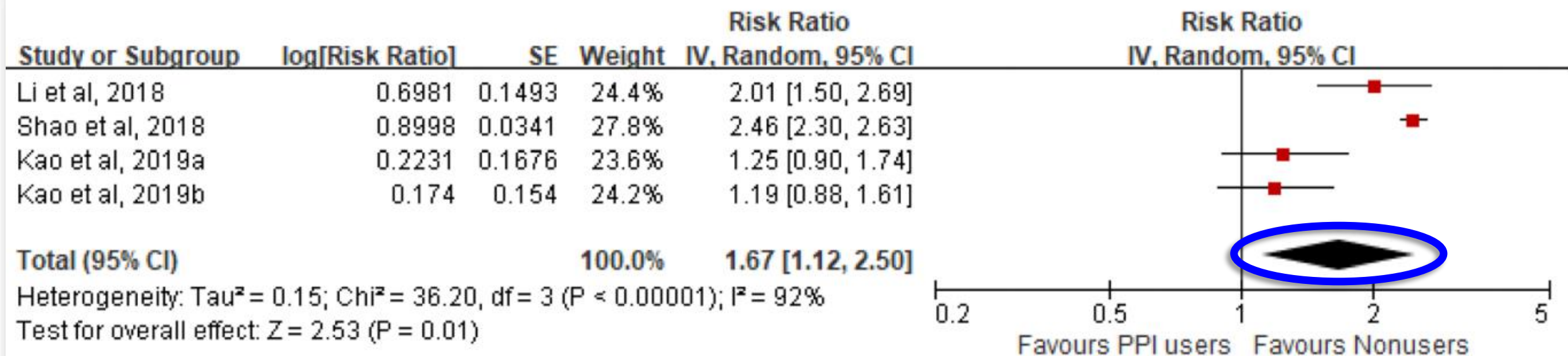
Junna Wang^{1,2} · Yangpeng Wu³ · Qiu Bi⁴ · Xianglong Zheng⁵ · Jingtao Zhang⁶ · Wenxiang Huang⁵

Encefalopatía

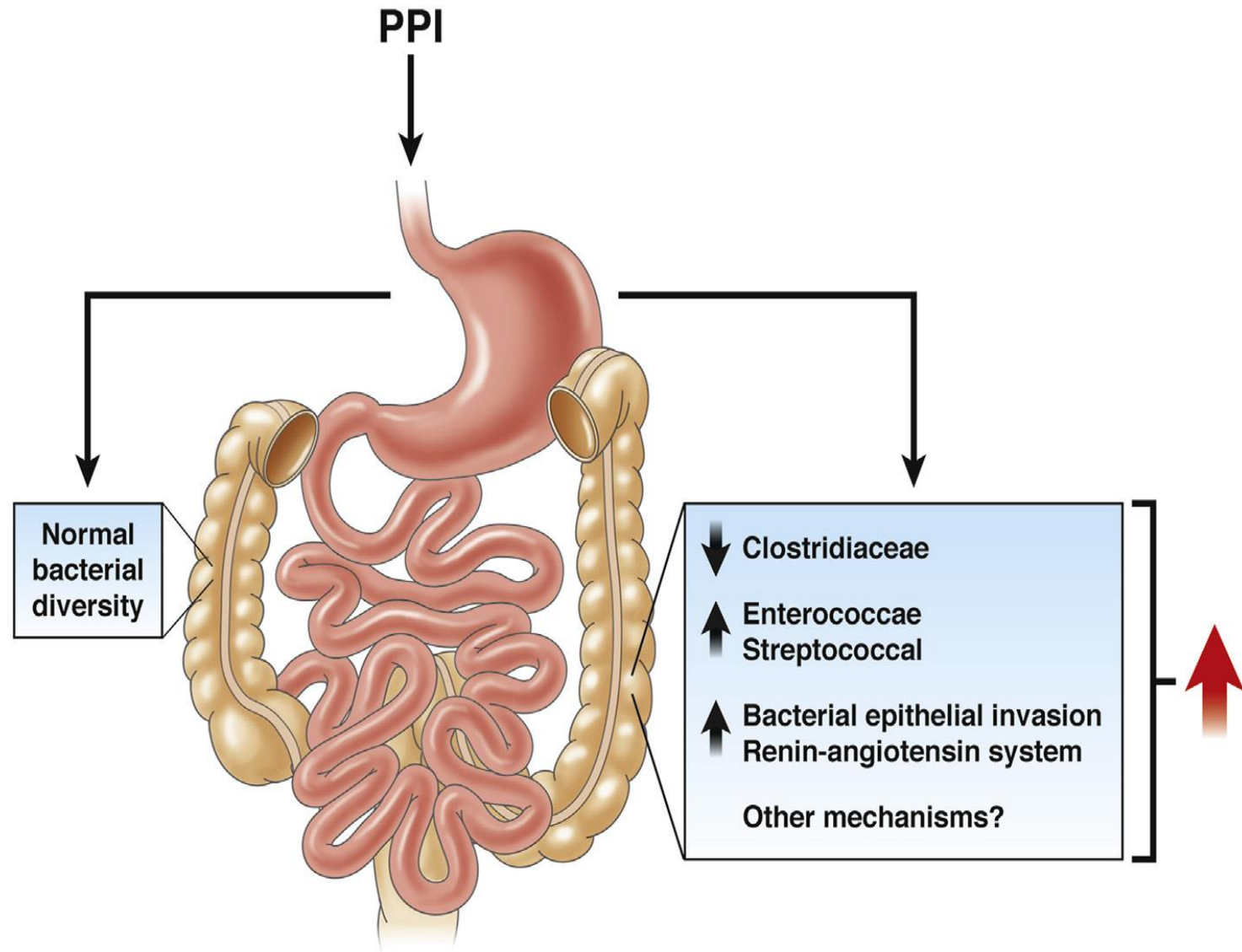


Proton pump inhibitors and risk of liver cancer and mortality in patients with chronic liver disease: a systematic review and meta-analysis

Hyun Jin Song^{1,2}  • Xinyi Jiang¹ • Linda Henry¹ • Mindie H. Nguyen³ • Haesuk Park¹ 



Song HJ, et al. Eur J Clin Pharmacol. 2020;76:851-66



Melgar S, Gastroenterology 2015;149:848–863

ORIGINAL ARTICLE

Imhann F, et al. Gut 2016;65:740–748

Proton pump inhibitors affect the gut microbiome

Floris Imhann,¹ Marc Jan Bonder,² Arnau Vich Vila,¹ Jingyuan Fu,² Zlatan Mujagic,³ Lisa Vork,³ Ettje F Tigchelaar,² Soesma A Jankipersadsing,² Maria Carmen Cenit,² Hermie J M Harmsen,⁴ Gerard Dijkstra,¹ Lude Franke,² Ramnik J Xavier,⁵ Daisy Jonkers,³ Cisca Wijmenga,² Rinse K Weersma,¹ Alexandra Zhernakova²

ORIGINAL ARTICLE

Jackson MA, et al. Gut 2016;65:749–75

Proton pump inhibitors alter the composition of the gut microbiota

Matthew A Jackson,¹ Julia K Goodrich,^{2,3} Maria-Emanuela Maxan,⁴ Daniel E Freedberg,⁵ Julian A Abrams,⁵ Angela C Poole,^{2,3} Jessica L Sutter,^{2,3} Daphne Welter,^{2,3} Ruth E Ley,^{2,3} Jordana T Bell,¹ Tim D Spector,¹ Claire J Steves¹

Proton Pump Inhibitors Alter Specific Taxa in the Human Gastrointestinal Microbiome: A Crossover Trial



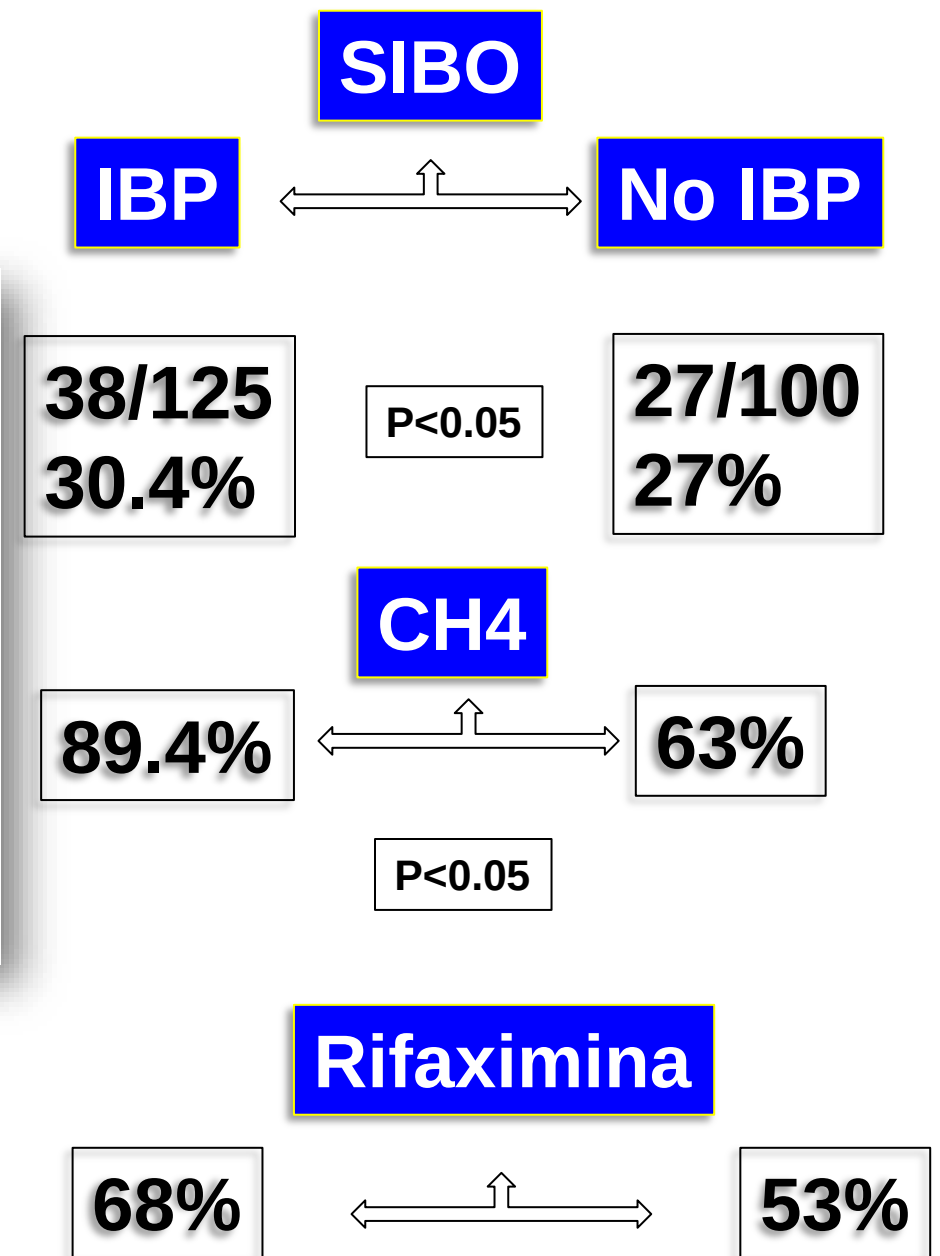
Daniel E. Freedberg,¹ Nora C. Toussaint,² Sway P. Chen,³ Adam J. Ratner,⁴ Susan Whittier,⁵ Timothy C. Wang,¹ Harris H. Wang,^{5,6,§} and Julian A. Abrams^{1,§}

Gastroenterology 2015;149:883–885

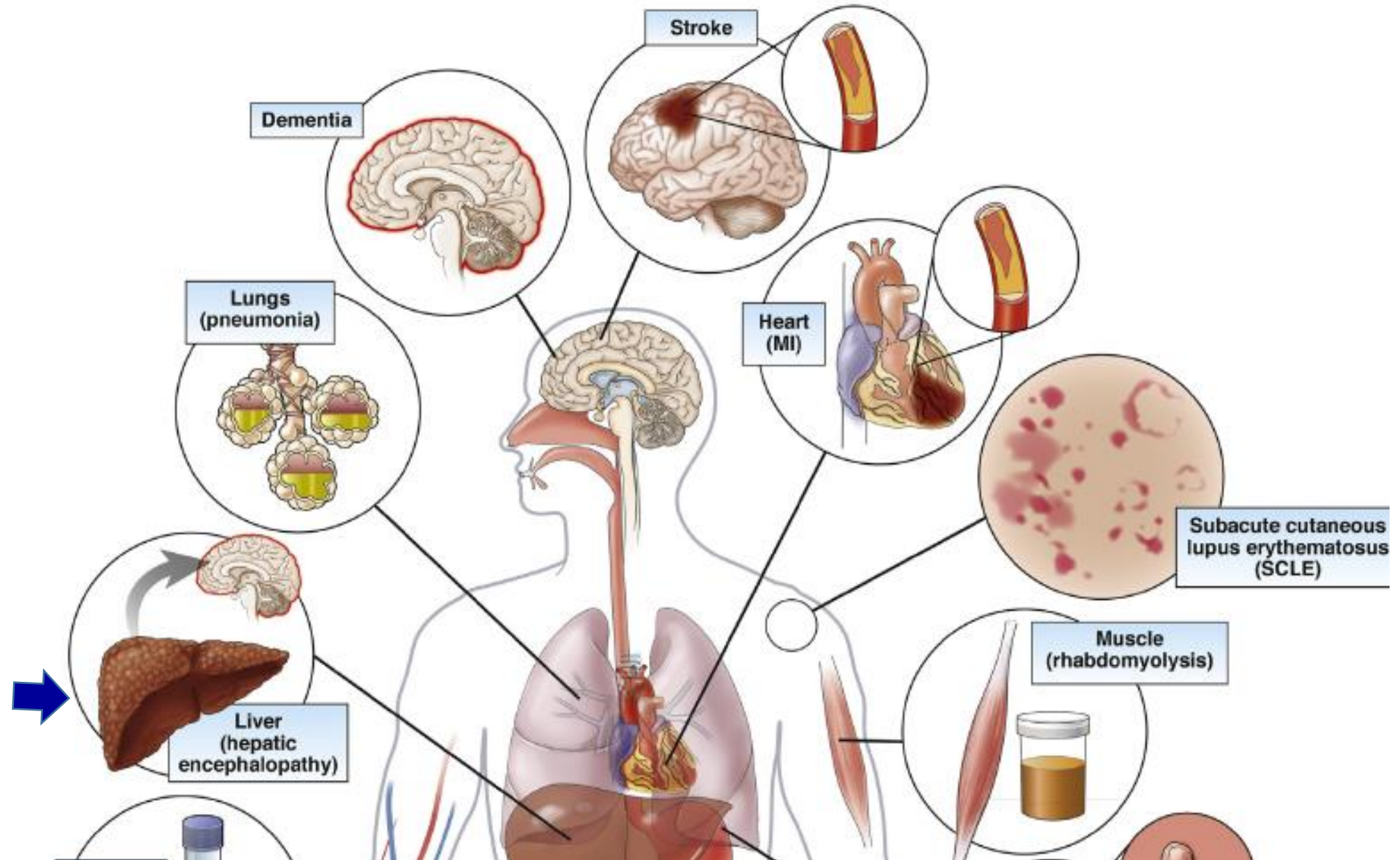
Assessment of small intestinal bacterial overgrowth and methane production in patients on chronic proton-pump inhibitor treatment: prevalence and role of rifaximin in its management in primary care

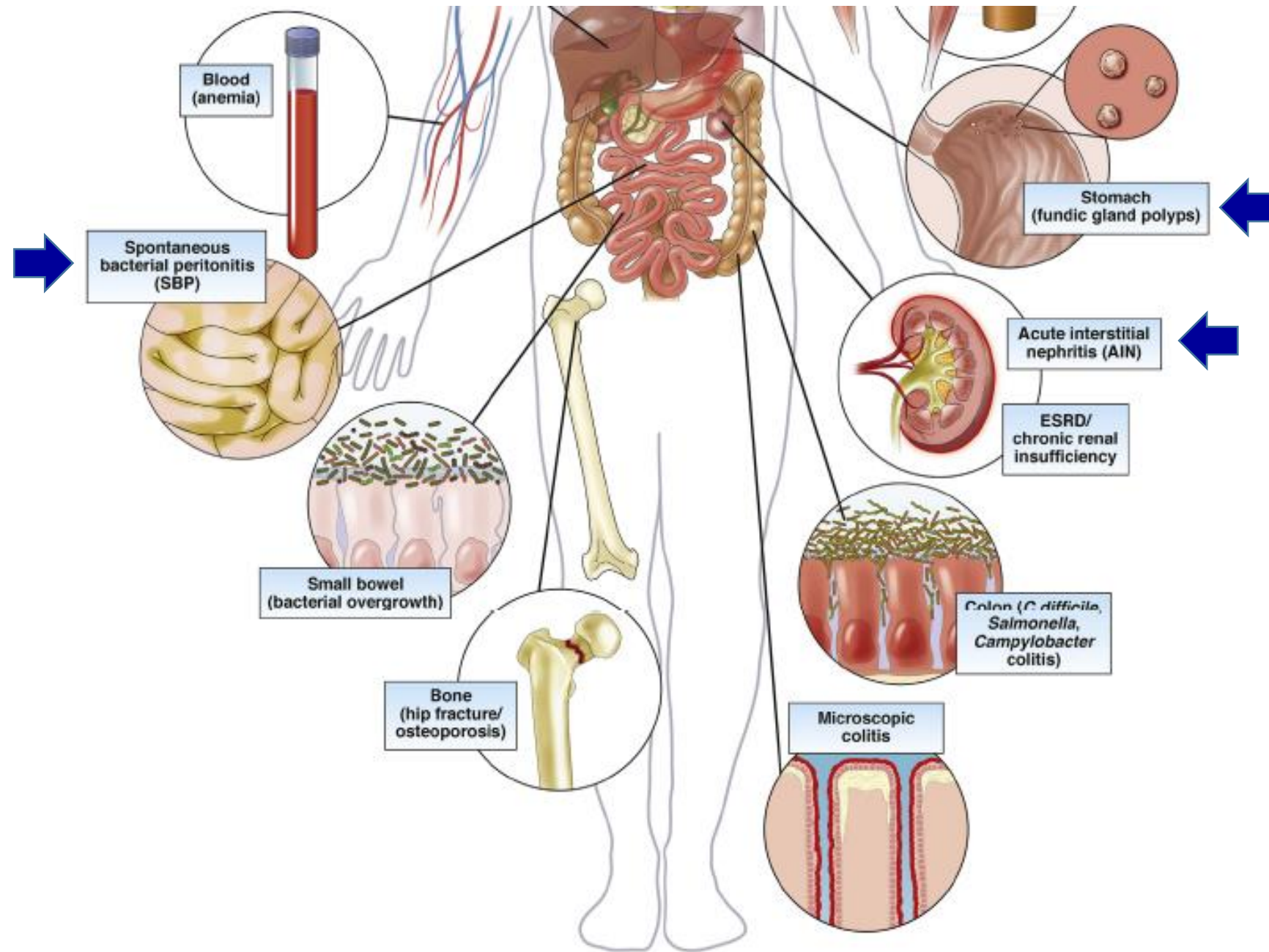
Rudi DE Bastiani ¹, Loris R Lopetuso ^{2 3 4 5}, Marco DE Bastiani ¹, Paolo Bacchin ⁶, Edoardo Benedetto ¹, Laura Boscariolo ⁷, Rosanna Caneve ⁸, Fabio Chesani ⁹, Francesco Chiumeo ¹⁰, Zinaida Civic ⁷, Antonio Dainese ¹¹, Manuela DE Polo ¹, Giuseppe Disclafani ¹, Ignazio Grattagliano ¹, Ornella Mana ⁹, Maurizio Mancuso ¹, Tecla Mastronuzzi ¹, Antonino Pati ¹, Enzo Pirrotta ¹, Maurizio Salandini ⁹, Guido Sanna ¹, Riccardo Scoglio ¹, Pietro Severino ⁹, Cesare Tosetti ¹, Leyla Turnava ¹, Maria Zamparella ¹, Walter Elisei ¹², Antonio Gasbarrini ², Antonio Tursi ^{13 14}

Minerva Gastroenterol (Torino) 2023 On line Marzo 21



Efectos colaterales “Temidos”





Proton Pump Inhibitor Use and Risk of Gastric, Colorectal, Liver, and Pancreatic Cancers in a Community-Based Population

Jeffrey K. Lee, MD, MPH^{1,2}, Sophie A. Merchant, MPH², Jennifer L. Schneider, MPH², Christopher D. Jensen, PhD, MPH², Bruce H. Fireman, MA², Charles P. Quesenberry, PhD² and Douglas A. Corley, MD, PhD^{1,2}

IBP 2 o màs años

Càncer Gàstrico
OR 1.07 (IC95%0.8-1.1)

Càncer Colo-Rectal
OR 1.05 (IC95%0.99-1.12)

Càncer Hígado
OR 1.14 (IC95%0.91-1.42)

Càncer Pàncreas
OR 1.22 (IC95%0.89-1.67)

Lee JK, Am J Gastroenterol 2020;115:706-15

Meta-analysis: Use of proton pump inhibitors and risk of gastric cancer in patients requiring gastric acid suppression

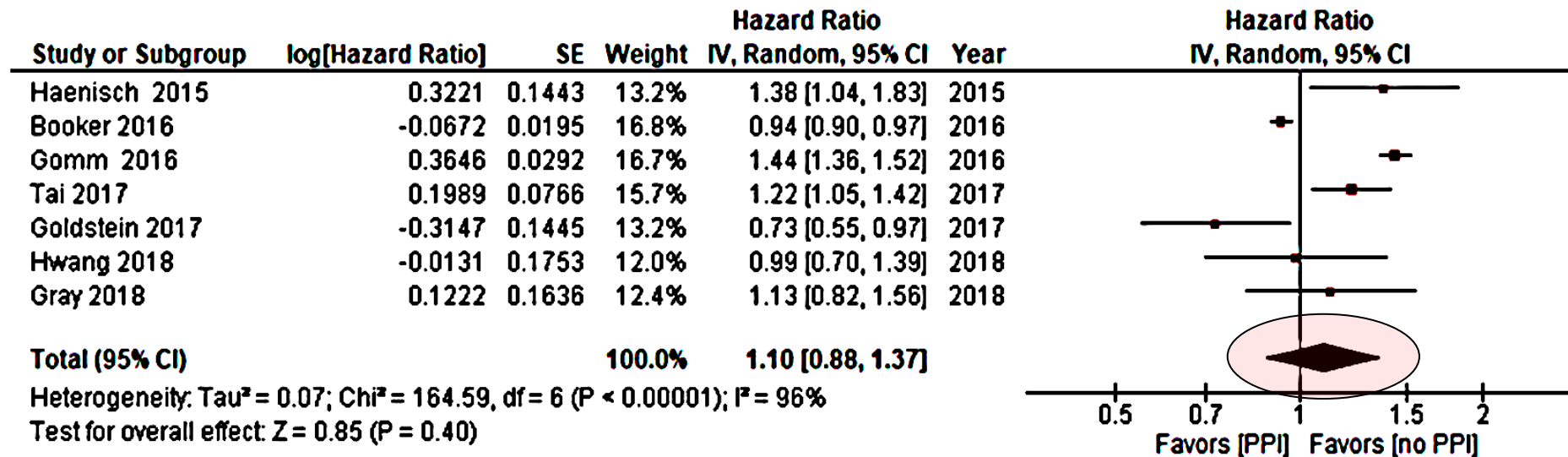
Daniele Piovani^{1,2}  | Andreas G. Tsantes^{3,4}  | Holger J. Schünemann^{1,5,6}  |
Stefanos Bonovas^{1,2} 

Results: Of 8375 records, 12 NRS (>6 million patients; 11,554 gastric cancers) and two randomised clinical trials (498 patients; 1 gastric cancer) fulfilled the eligibility criteria. Randomised evidence was very imprecise and provided very-low certainty evidence. Meta-analysis of six NRS providing a comprehensive adjustment for confounding (2.5 million patients; 7372 gastric cancers) did not show any association between PPIs and gastric cancer ($RR_{\text{random}} = 1.07, 0.97-1.19$; $RR_{\text{fixed}} = 1.05, 0.98-1.12$). The certainty of the evidence was low. No convincing evidence of dose-response, or increased risk with long-term use, was found. Lack of or minimal adjustment for confounding was associated with larger effect sizes.

Conclusions: We found no association between PPIs and gastric cancer in NRS having adequately controlled for confounding. Published studies may suffer residual

No Association Linking Short-Term Proton Pump Inhibitor Use to Dementia: Systematic Review and Meta-analysis of Observational Studies

Muhammad Ali Khan, MD^{1,2}, Yuhong Yuan, MD, PhD³, Umair Iqbal, MD⁴, Sehrish Kamal, MD¹, Mubeen Khan, MD², Zubair Khan, MD⁵, Wade M. Lee, MLIS⁵ and Colin W. Howden, MD, FACG²

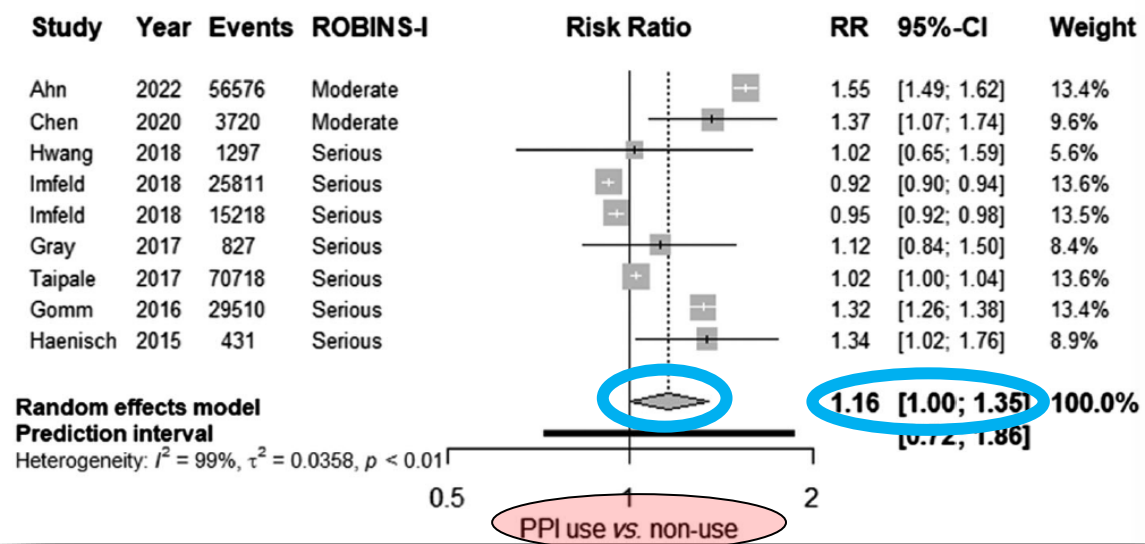


Do proton pump inhibitors increase the risk of dementia? A systematic review, meta-analysis and bias analysis

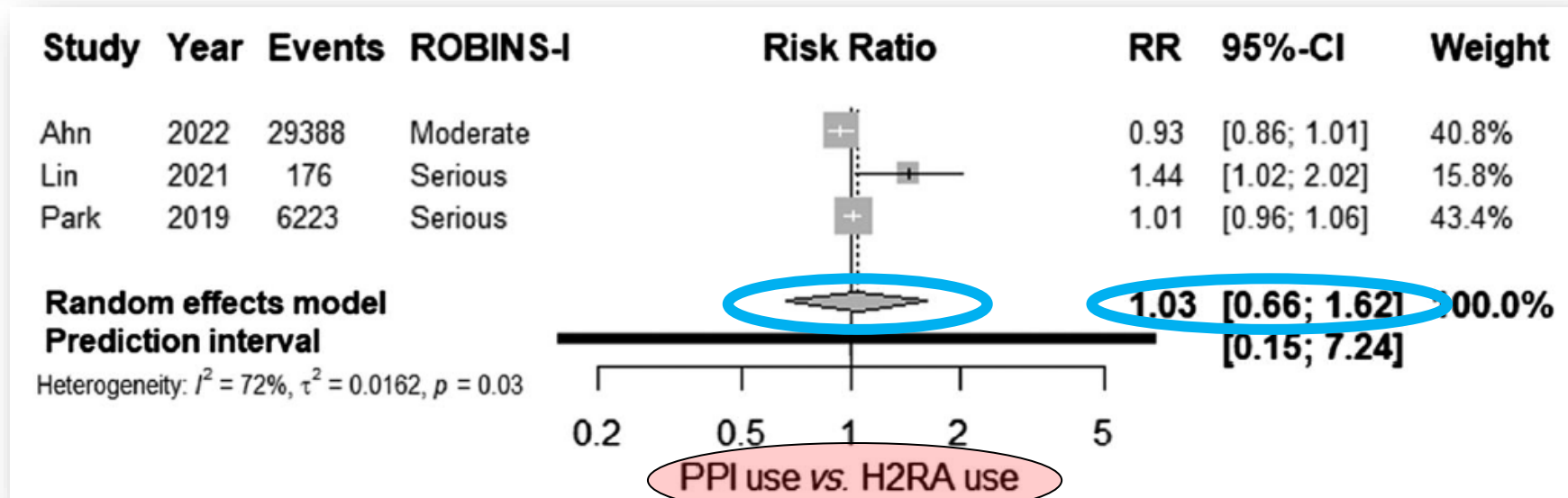
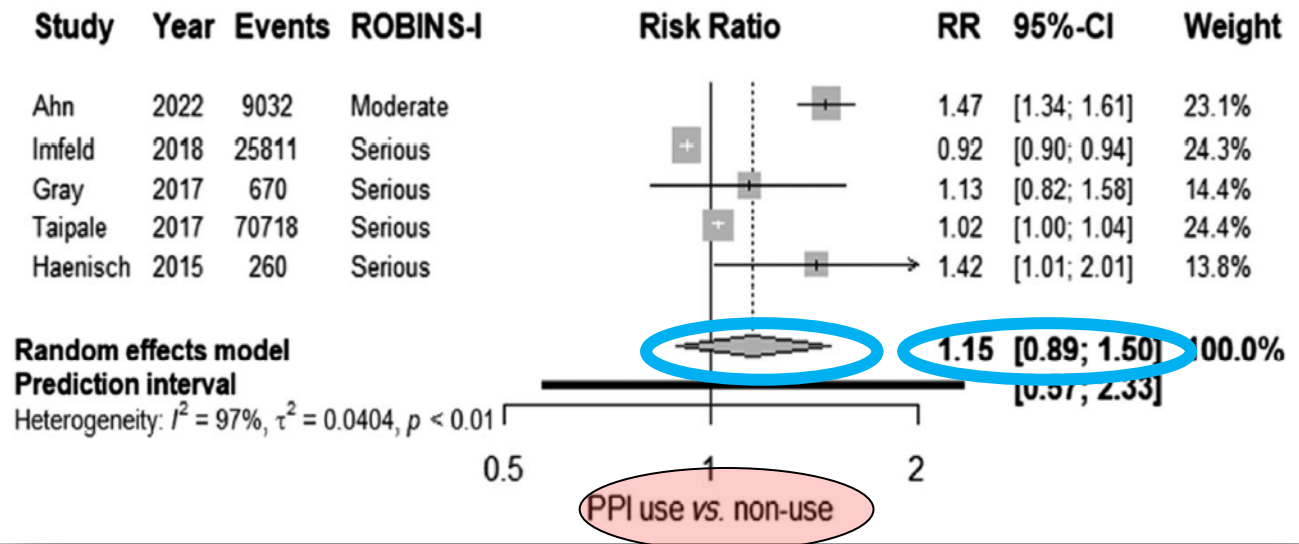
Nayeon Ahn^{1,2}  | Michael Nolde^{1,2}  | Evamaria Krause³ | Florian Güntner⁴ |
Alexander Günter⁴ | Martin Tauscher⁵ | Roman Gerlach⁵ | Christa Meisinger² |
Jakob Linseisen^{1,2} | Sebastian-Edgar Baumeister⁶ | Ina-Maria Rückert-Eheberg^{1,2}

Ahn N, Br J Clin Pharmacol. 2023;89:602-16.

Demencia



Demencia-Alzheimer

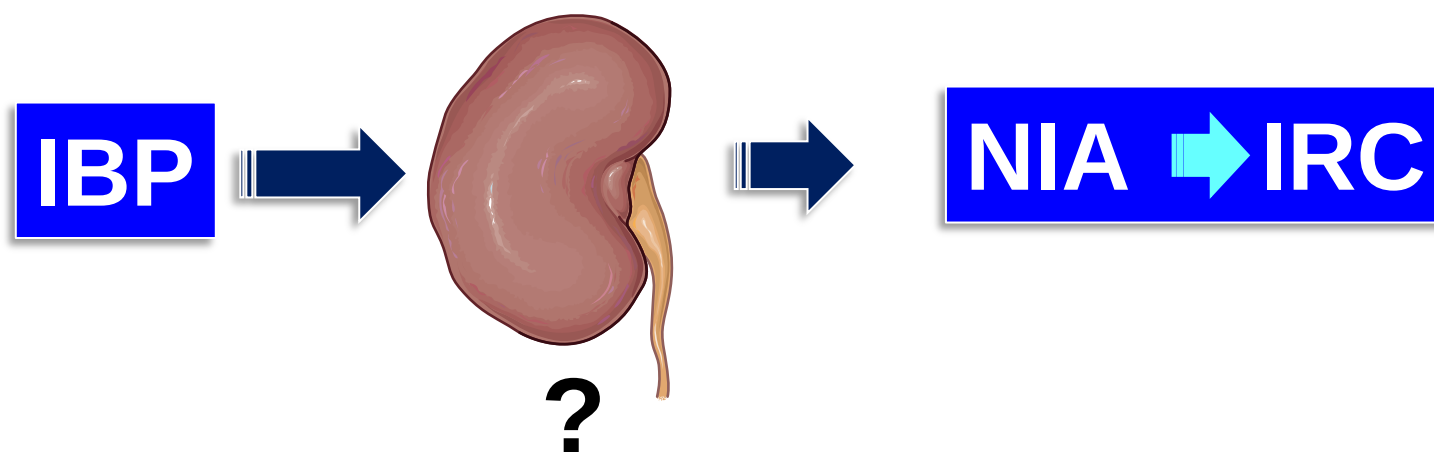
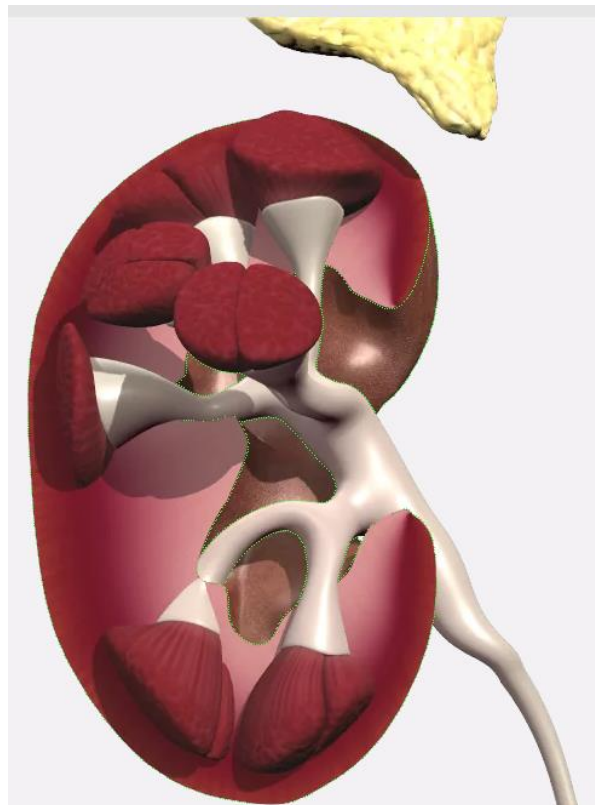


Proton Pump Inhibitors Do Not Increase Risk for *Clostridium difficile* Infection in the Intensive Care Unit

Table 3. Final multivariable model of risk factors for health-care facility-onset *Clostridium difficile* infection in the ICU

Risk factors	Adjusted HR (95% CI)
<i>ICU type</i>	
Medical	Ref.
Surgical	1.05 (0.76–1.46)
Cardiac	0.89 (0.60–1.31)
Neurological	1.50 (1.01–2.23)
Creatinine (per mg/dl increase)	1.09 (1.02–1.16)
Albumin (per g/dl increase)	0.93 (0.77–1.12)
<i>Charlson comorbidity index</i>	
0–2	Ref.
3+	1.34 (1.00–1.79)
Mechanical ventilation	1.31 (0.96–1.77)
Hemodialysis	1.14 (0.79–1.64)
Proton pump inhibitors	1.29 (0.62–2.70)
Antibiotics	2.79 (1.50–5.19)

IBP y daño renal



Hipomagnesemia
>Daño vascular hemodialisis?
(Mg inhibe calcificación)

Xie Y, Kidney Internat 2017;91,:1482–1494
Lazarus B, JAMA Intern Med 2016;176:238-46

Nefritis Intersticial Aguda



1/12.500 pacientes/año

Simpson IJMM, Nephrology 2006;11:381-5

Risk of bias in non-randomized observational studies assessing the relationship between proton-pump inhibitors and adverse kidney outcomes: a systematic review

Pradeep Rajan, Kristy Iglay, Thomas Rhodes, Cynthia J. Girman, Dimitri Bennett  and Kamyar Kalantar-Zadeh

Conclusion: Using ROBINS-I, we found that non-randomized observational studies suggesting kidney harm by PPIs have moderate to serious risk of bias, making it challenging to establish causality. Additional high-quality, real-world evidence among generalizable populations are needed to better understand the relation between PPI treatment and acute and chronic kidney outcomes, accounting for the effects of varying durations of PPI treatment, self-treatment with over-the-counter PPIs, and potential critical confounders.



W

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*World Journal of
Transplantation*

Submit a Manuscript: <https://www.f6publishing.com>

World J Transplant 2019 June 28; 9(2): 35-47

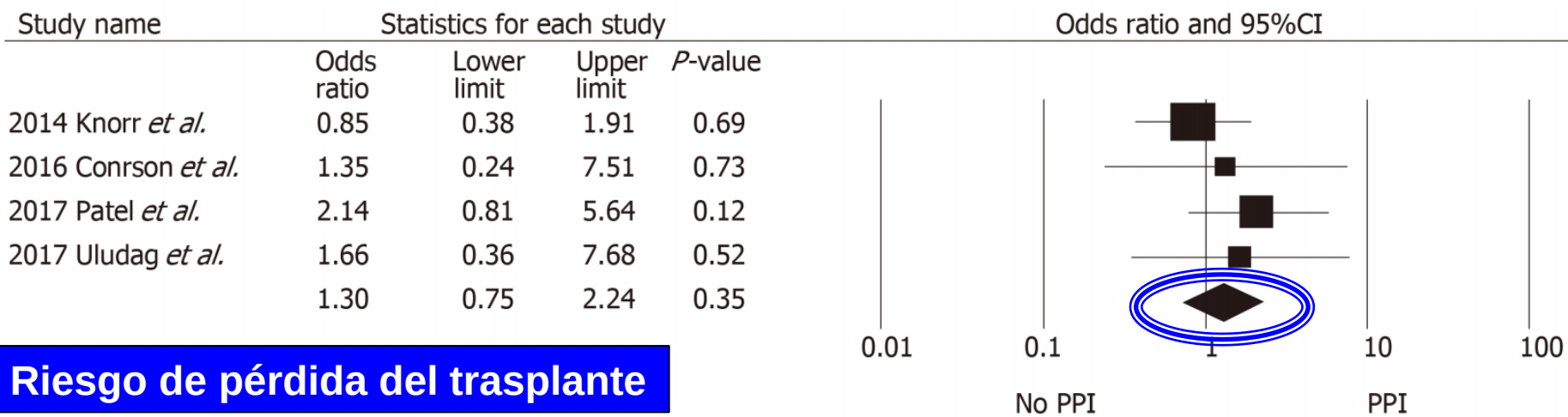
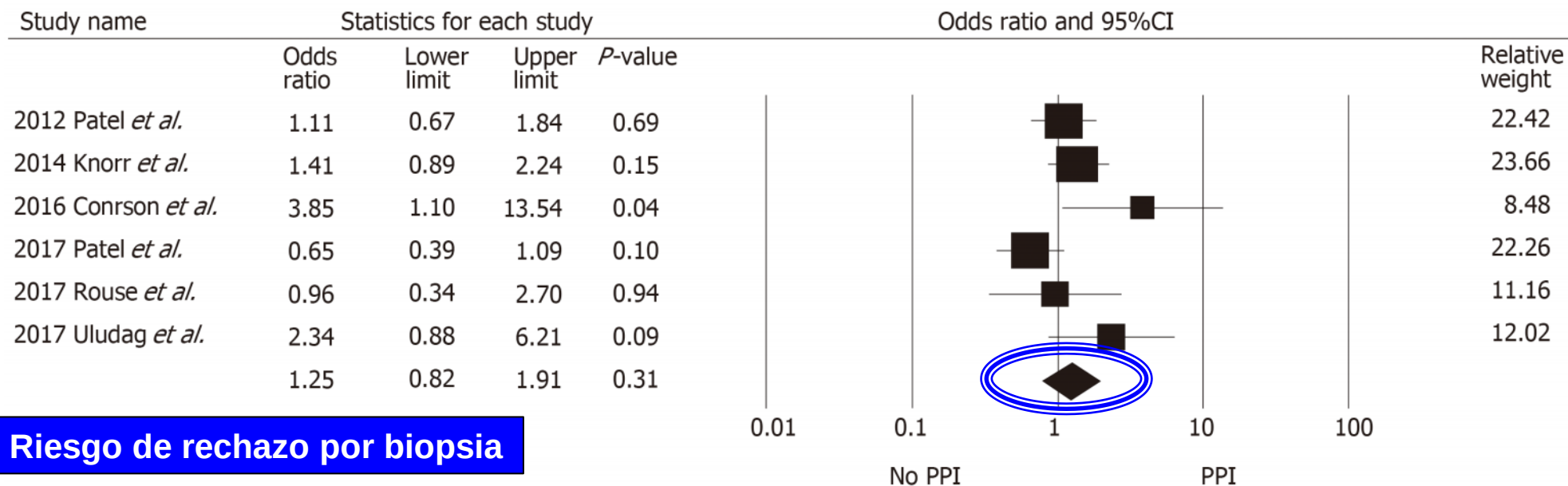
DOI: [10.5500/wjt.v9.i2.35](https://doi.org/10.5500/wjt.v9.i2.35)

ISSN 2220-3230 (online)

META-ANALYSIS

Proton pump inhibitors and adverse effects in kidney transplant recipients: A meta-analysis

Boonpheng B, et al World J Transplant 2019;9:35-47



Asociación no es causalidad

Analogía: Exposiciones similares dan el efecto

Gradiente biológico: A mayor dosis > efecto

Coherencia: El hallazgo no contradice lo demostrado

Especificidad: otras causas no están presentes

Temporalidad: precede al efecto

Fuerza de la asociación: Tamaño del OR, RR

Consistencia: siempre se encuentra lo mismo

Plausibilidad biológica: Fisiopatología

Experimento clínico: evidencia definitiva

Efecto adverso	Plausibilidad biológica	Fuerza de la asociación OR	Consistencia de la asociación	Implicación clínica
Riesgo de fractura	Incierto	Débil < 2	Contradictoria	Utilizar el IB si hay indicación
Deficiencia de B12	Hipoclorhidria disminuye disociación B12	Desconocido	Contradictoria	Vigilar niveles B12 en ancianos
Deficiencia de calcio	Hipoclorhidria disminuye liberación de Ca ionizado	Desconocido	Contradictoria	NO vigilancia
Neumonía	<< HCl favorece bacterias en estómago, broncoaspiración	Débil <2	Contradictoria	Utilizar el IBP si hay indicación
Enfermedad Renal Crónica	Incierta	Débil <2	Contradictoria	Utilizar el IBP si hay indicación
Demencia	Incierta	Débil <2	Contradictoria	Utilizar el IBP si hay indicación
Infecciones entéricas	<< HCl evita destrucción de microorganismos	Moderado 2-4	Consistente consistente	Utilizar la dosis mínima necesaria

Vaezi MF, Gastroenterology 2017;153:35-48

Savarino V, Dig Liv Dis 2016;48:851-9

Origen de las alarmas

**Estudios observacionales
Retrospectivos
Base de datos analizados con
Propósitos Administrativos**

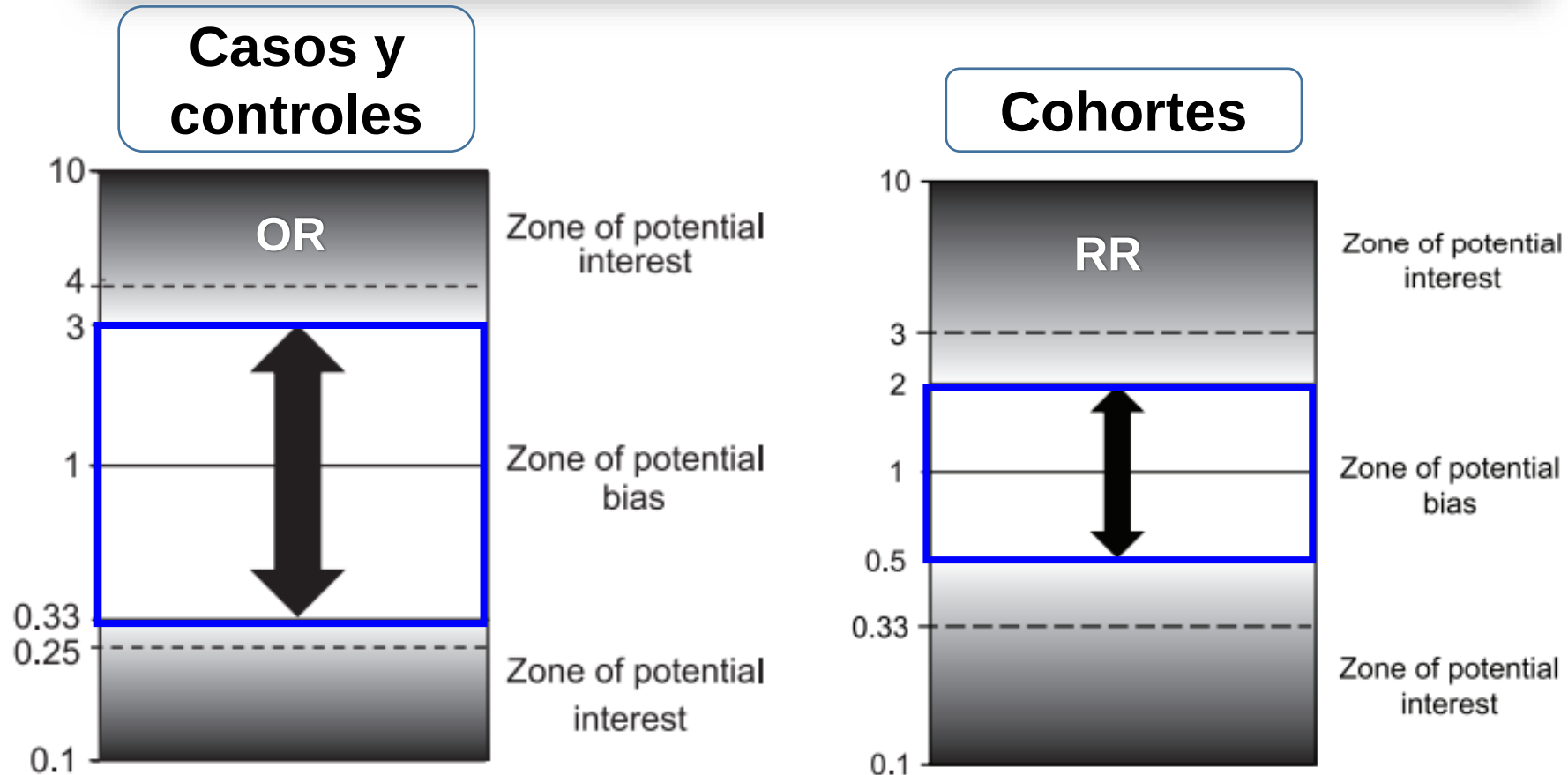


**No hay aleatorización:
Exposición a IBP vs No exposición
Análisis multivariado no puede eliminar
Variables de confusión no controladas**

False Alarms and Pseudo-Epidemics

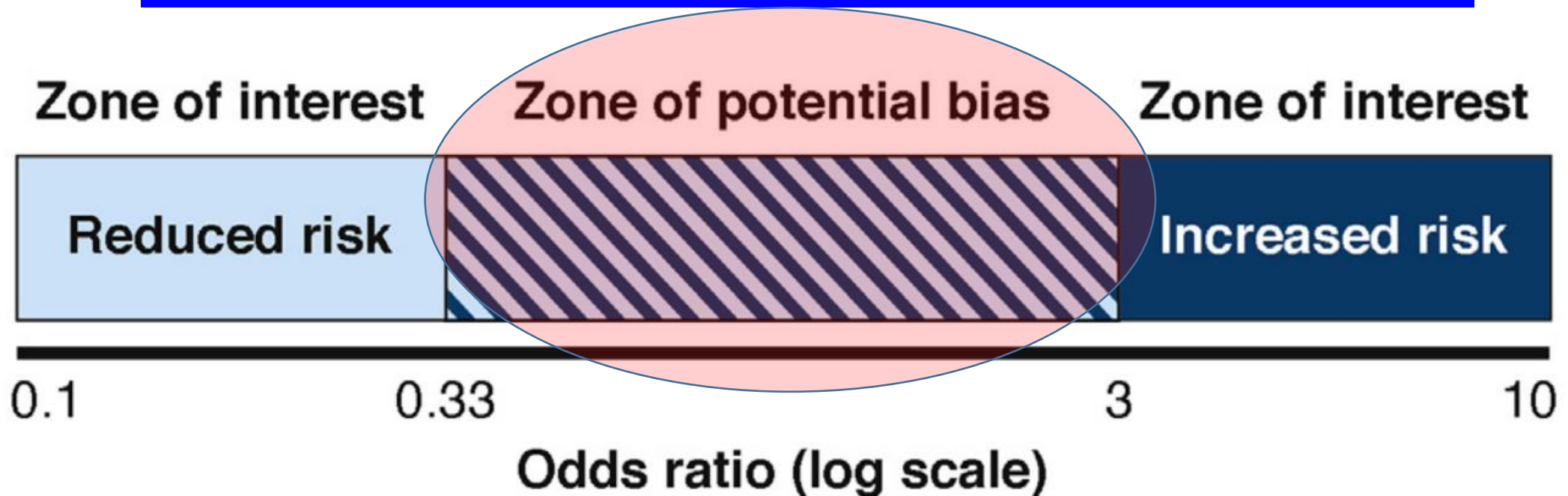
The Limitations of Observational Epidemiology

David A. Grimes, MD, and Kenneth F. Schulz, PhD, MBA



IBP y efectos adversos serios

Los estudios OBSERVACIONALES, tienen alto riesgo de variables no controladas



Safety of Proton Pump Inhibitors Based on a Large, Multi-Year, Randomized Trial of Patients Receiving Rivaroxaban or Aspirin



Paul Moayyedi,¹ John W. Eikelboom,¹ Jackie Bosch,¹ Stuart J. Connolly,¹ Leanne Dyal,¹ Olga Shestakovska,¹ Darryl Leong,¹ Sonia S. Anand,¹ Stefan Störk,² Kelley R. H. Branch,³ Deepak L. Bhatt,⁴ Peter B. Verhamme,⁵ Martin O'Donnell,⁶ Aldo P. Maggioni,⁷ Eva M. Lonn,¹ Leopoldo S. Piegas,⁸ Georg Ertl,² Matyas Keltai,⁹ Nancy Cook Bruns,¹⁰ Eva Muehlhofer,¹⁰ Gilles R. Dagenais,¹¹ Jae-Hyung Kim,¹² Masatsugu Hori,¹³ P. Gabriel Steg,¹⁴ Robert G. Hart,¹ Rafael Diaz,¹⁵ Marco Alings,¹⁶ Petr Widimsky,¹⁷ Alvaro Avezum,¹⁸ Jeffrey Probstfield,¹⁹ Jun Zhu,²⁰ Yan Liang,²⁰ Patricio Lopez-Jaramillo,²¹ Ajay K. Kakkar,²² Alexander N. Parkhomenko,²³ Lars Ryden,²⁴ Nana Pogosova,²⁵ Antonio L. Dans,²⁶ Fernando Lanus,²⁷ Patrick J. Commerford,²⁸ Christian Torp-Pedersen,²⁹ Tomek J. Guzik,^{30,31} Dragos Vinereanu,³² Andrew M. Tonkin,³³ Basil S. Lewis,³⁴ Camilo Felix,³⁵ Khalid Yusoff,³⁶ Kaj P. Metsarinne,³⁷ Keith A. A. Fox,³⁸ and Salim Yusuf,¹ for the COMPASS Investigators

8, 18 Brazil
21 Colombia
27 Chile
35 Ecuador

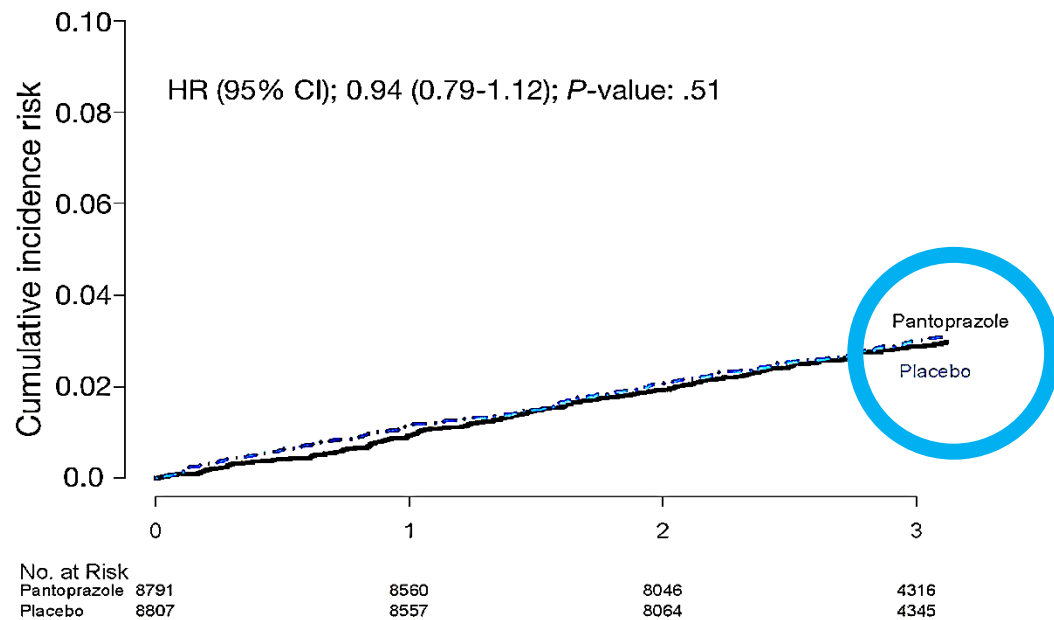
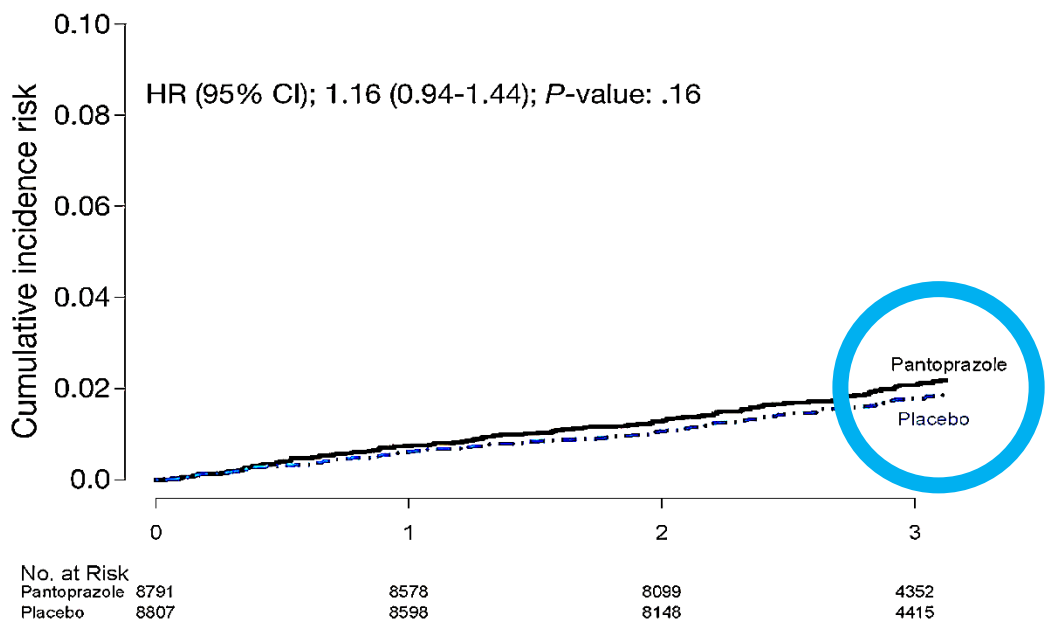
**Primer ensayo clínico prospectivo
aleatorizado evaluando efectos adversos
Multicéntrico – 3 años – 17598 pacientes**

23%

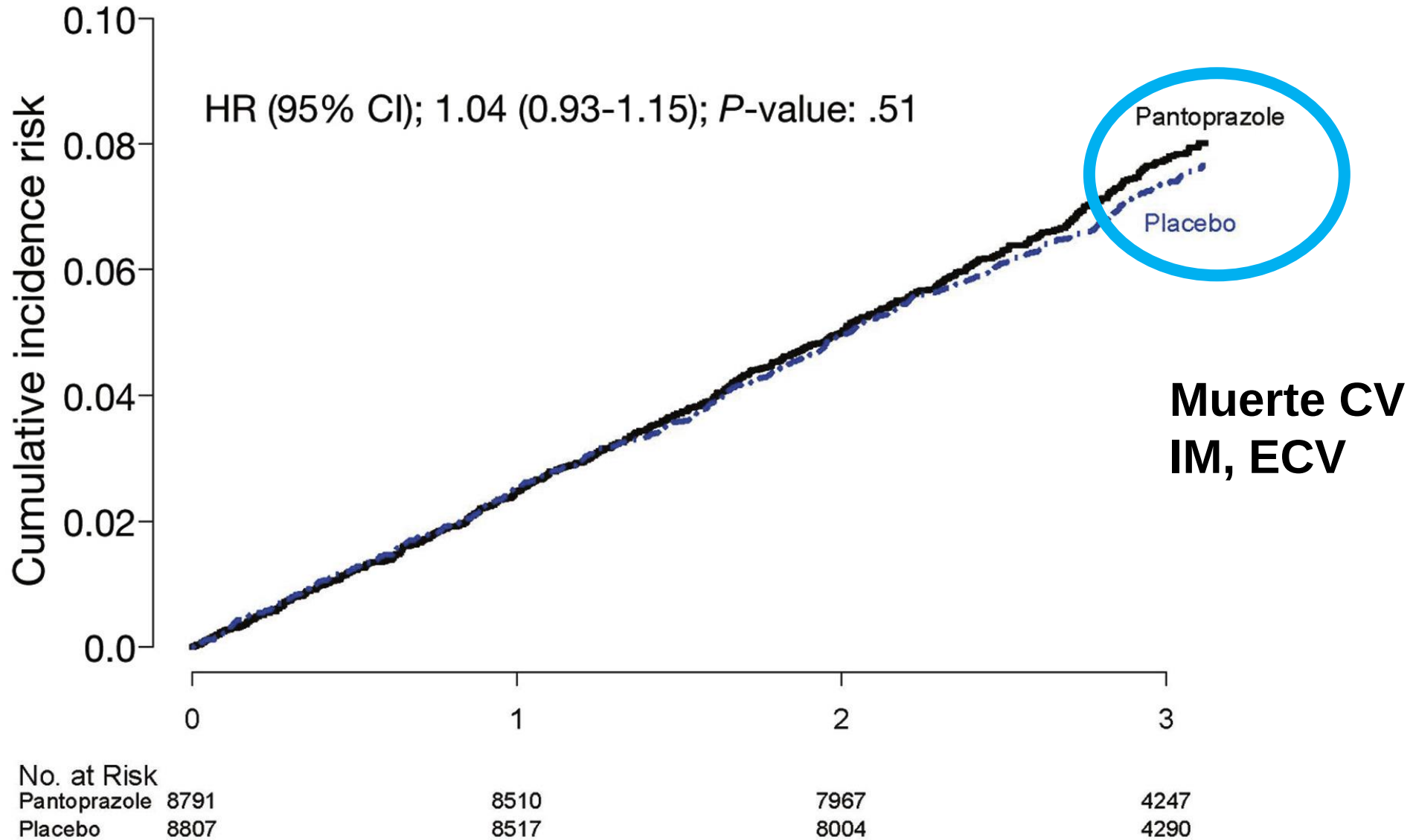
Moayyedi P, et al. Gastroenterology 2019;157:682–691

A**Myocardial Infarction**

Moayyedi P, et al. Gastroenterology 2019;157:682–691

**Infarto del miocardio****B****Stroke****ECV**

CV Death, MI, Stroke



Moayyedi P, et al. Gastroenterology 2019;157:682–691

ACG Clinical Guideline for the Diagnosis and Management of Gastroesophageal Reflux Disease

Philip O. Katz, MD, MACG¹, Kerry B. Dunbar, MD, PhD^{2,3}, Felice H. Schnoll-Sussman, MD, FACG¹, Katarina B. Greer, MD, MS, FACG⁴, Rena Yadlapati, MD, MSHS⁵ and Stuart Jon Spechler, MD, FACG^{6,7}

Regarding the safety of long-term PPI usage for GERD, we suggest that patients should be advised as follows: “PPIs are the most effective medical treatment for GERD. Some medical studies have identified an association between the long-term use of PPIs and the development of numerous adverse conditions including intestinal infections, pneumonia, stomach cancer, osteoporosis-related bone fractures, chronic kidney disease, deficiencies of certain vitamins and minerals, heart attacks, strokes, dementia, and early death. Those

studies have flaws, are not considered definitive, and do not establish a cause-and-effect relationship between PPIs and the adverse conditions. High-quality studies have found that PPIs do not significantly increase the risk of any of these conditions except intestinal infections. Nevertheless, we cannot exclude the possibility that PPIs might confer a small increase in the risk of developing these adverse conditions. For the treatment of GERD, gastroenterologists generally agree that the well-established benefits of PPIs far outweigh their theoretical risks.”

2. Switching PPIs can be considered for patients who experience minor PPI side effects including headache, abdominal pain, nausea, vomiting, diarrhea, constipation, and flatulence.

3. For patients with GERD on PPIs who have no other risk factors for bone disease, we do not recommend that they raise their intake of calcium or vitamin D or that they have routine monitoring of bone mineral density.

4. For patients with GERD on PPIs who have no other risk factors for vitamin B12 deficiency, we do not recommend that they raise their intake of vitamin B12 or that they have routine monitoring of serum B12 levels.

5. For patients with GERD on PPIs who have no other risk factors for kidney disease, we do not recommend that they have routine monitoring of serum creatinine levels.

6. For patients with GERD on clopidogrel who have LA grade C or D esophagitis or whose GERD symptoms are not adequately controlled with alternative medical therapies, the highest quality data available suggest that the established benefits of PPI treatment outweigh their proposed but highly questionable cardiovascular risks.

7. PPIs can be used to treat GERD in patients with renal insufficiency with close monitoring of renal function or consultation with a nephrologist.

Katz PO, Am J Gastroenterol. 2022;117:27-56

Mensajes para la casa

**Los IBPs Tienen indicaciones concretas
Prescripciones incorrectas son la mayoría
Contraindicados en cirrosis avanzada
Nefritis intersticial idiosincrática NNT 12500
Efectos adversos temidos no hay evidencia
Asociación menor a 3 no es causalidad
Los médicos son influidos por la prensa
Los pacientes doctor Google, “memes”**

Estudios observacionales

No todo lo que parece ser es!



Muchas gracias!

