Update su *Helicobacter pylori*

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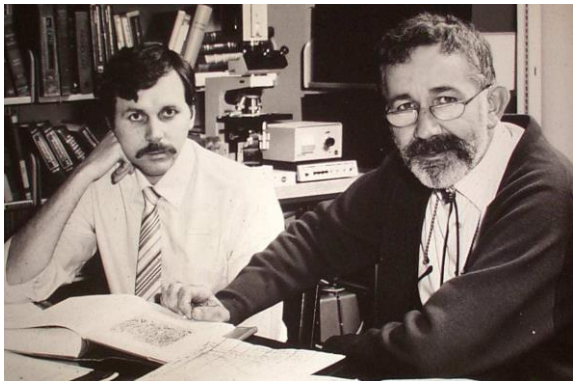
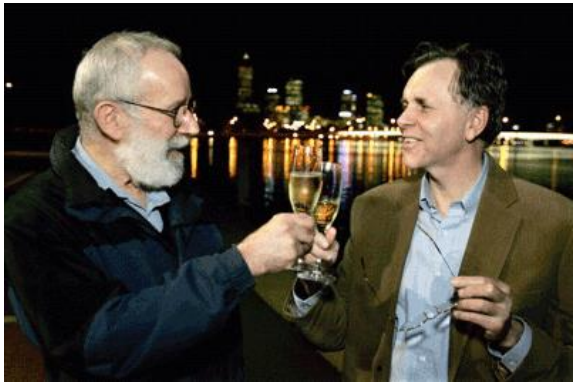
Gastroenterologia ed Endoscopia Digestiva
ASST-Rhodense
Garbagnate Milanese-Rho

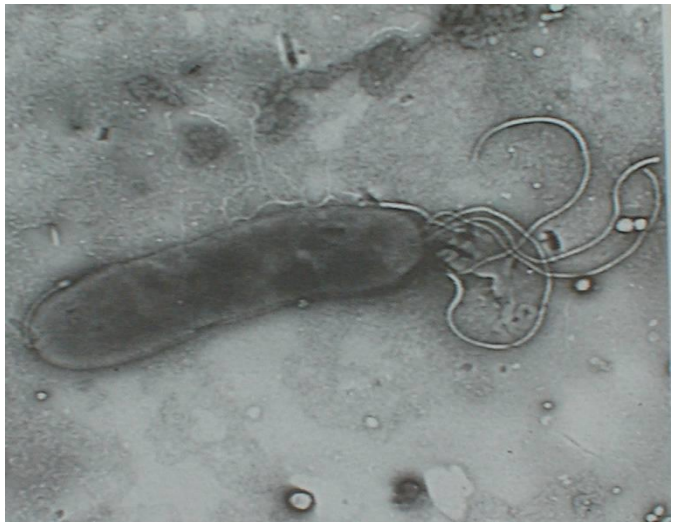
UNIDENTIFIED CURVED BACILLI ON GASTRIC EPITHELIUM IN ACTIVE CHRONIC GASTRITIS





Warren JR and Marshall BJ *Lancet 1983;i:1273 (letter)*

Helicobacter pylori



Spiraliforme

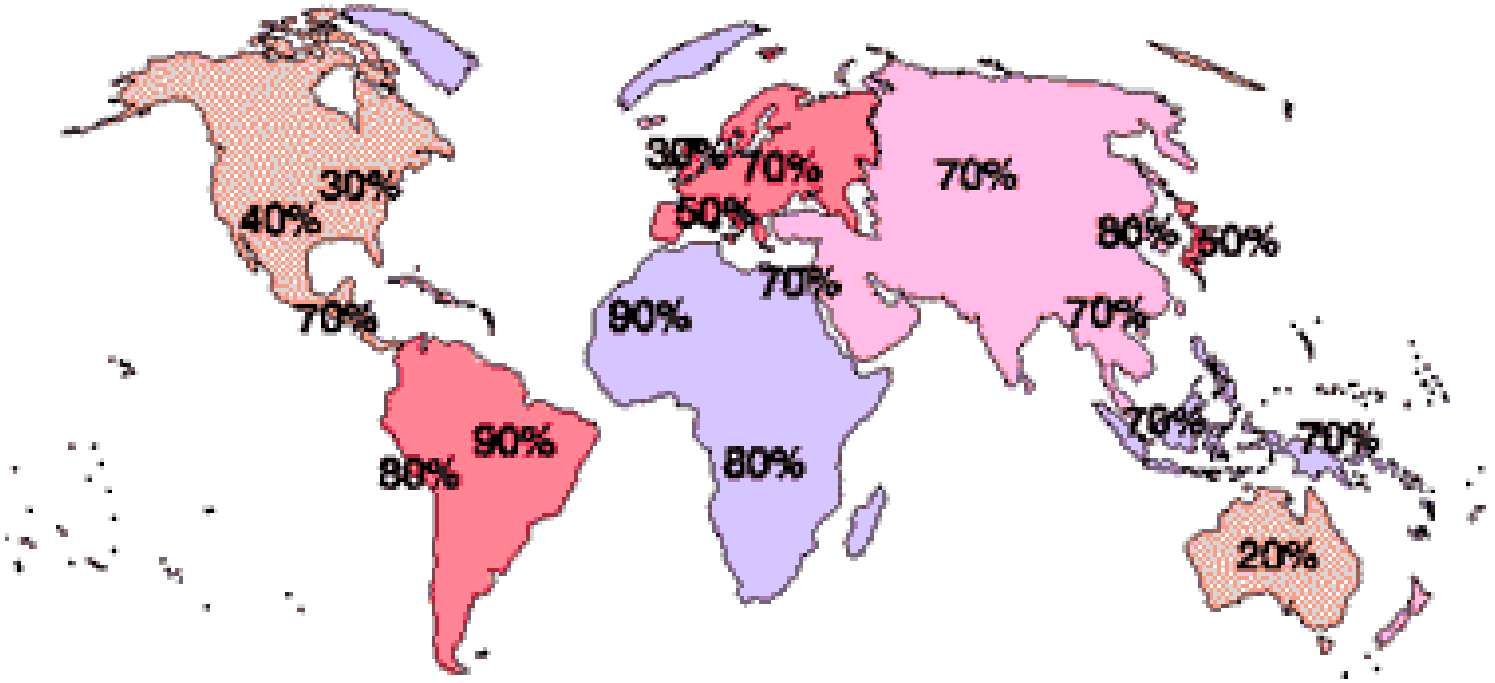
Gram negativo

Flagellato

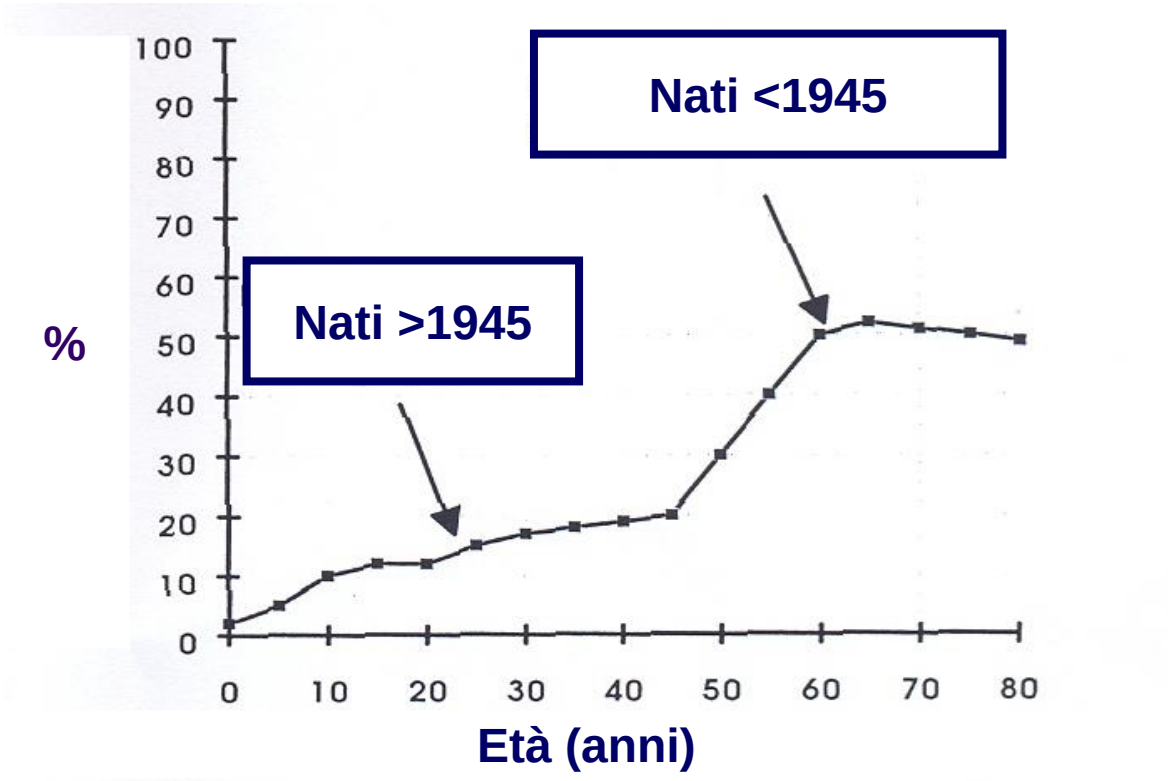
Microaerofilo

Ureasi positivo

Goodwin CS ***Int J Syst Bacteriol 1989;39:397-405***

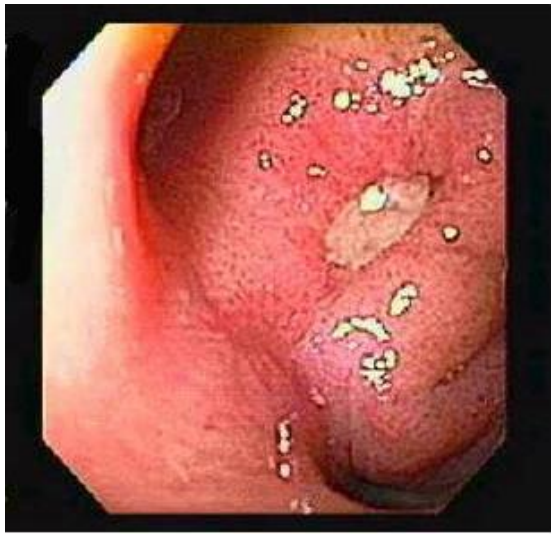


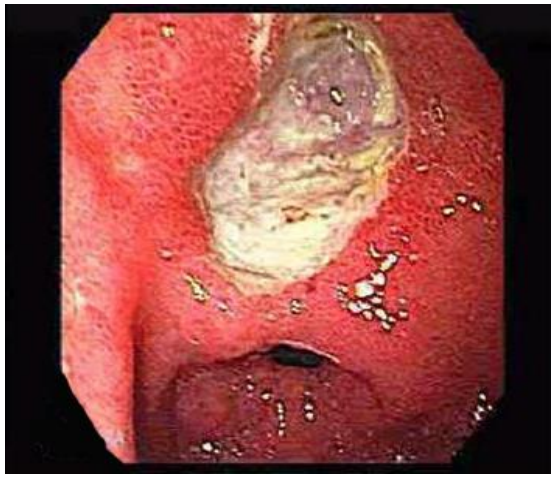
Worldwide prevalence of *H. Pylori*	
United States and Canada	30%-40%
Mexico and Central/South America	70%-90%
Western Europe	30%-50%
Eastern Europe	70%
Africa	70%-90%
Asia	70%-80%
Australia	20%



Marshall BJ. ***Am J Gastroenterol 1994***

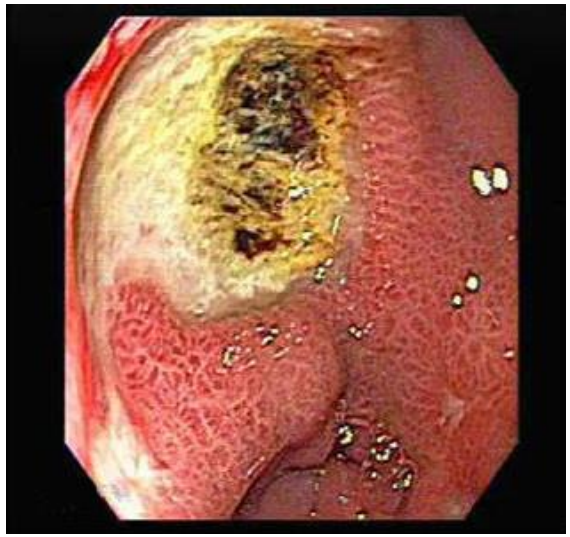
CLINICA

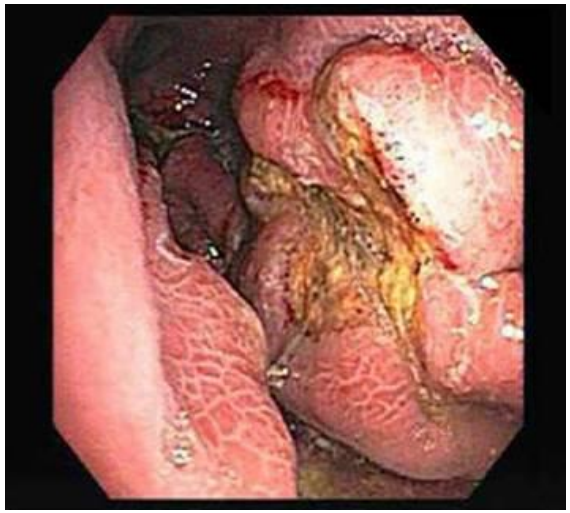




H. pylori

- Ulcera duodenale
- Ulcera gastrica
- Dispepsia non ulcerosa
- Interazione con FANS
- Piastrinopenia autoimmune
- Anemia sideropenica
- Carenza di vitamina B12
- Linfoma MALT
- Cancro gastrico
- Gastrite cronica attiva



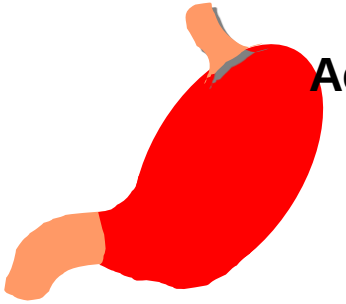


CLINICA

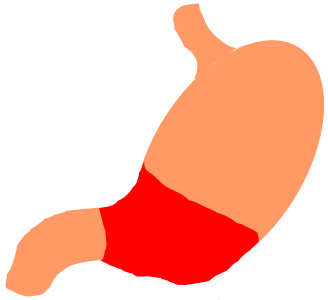
- **Reflusso gastro-esofageo**
- **Malattia coronarica**
- **Patologie autoimmuni (tiroidite, LES, ecc.)**
- **Allergie**
- **Cefalea**
- **Acne rosacea**
- **Encefalopatia epatica nel cirrotico**
- ***ecc…!***

1

***H.pylori* infection**

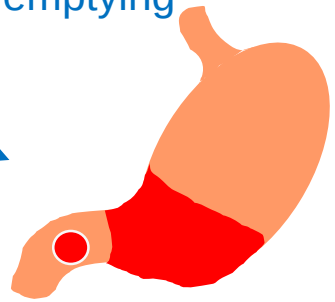


Acute gastritis



Chronic active gastritis

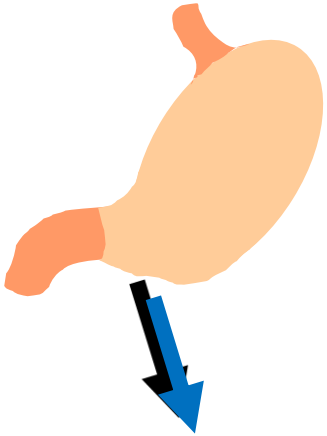
gastrin
acid secretion
gastric emptying



Duodenal ulcer

drugs
age
nutrition
smoking
genetic factors

Pangastritis



Intestinal metaplasia and atrophy

Vit C
nitrosamine
carcinogens
genetic factors

Gastric cancer

Gastric ulcer

Storia clinica: *H. pylori, genetica ed* Ambiente

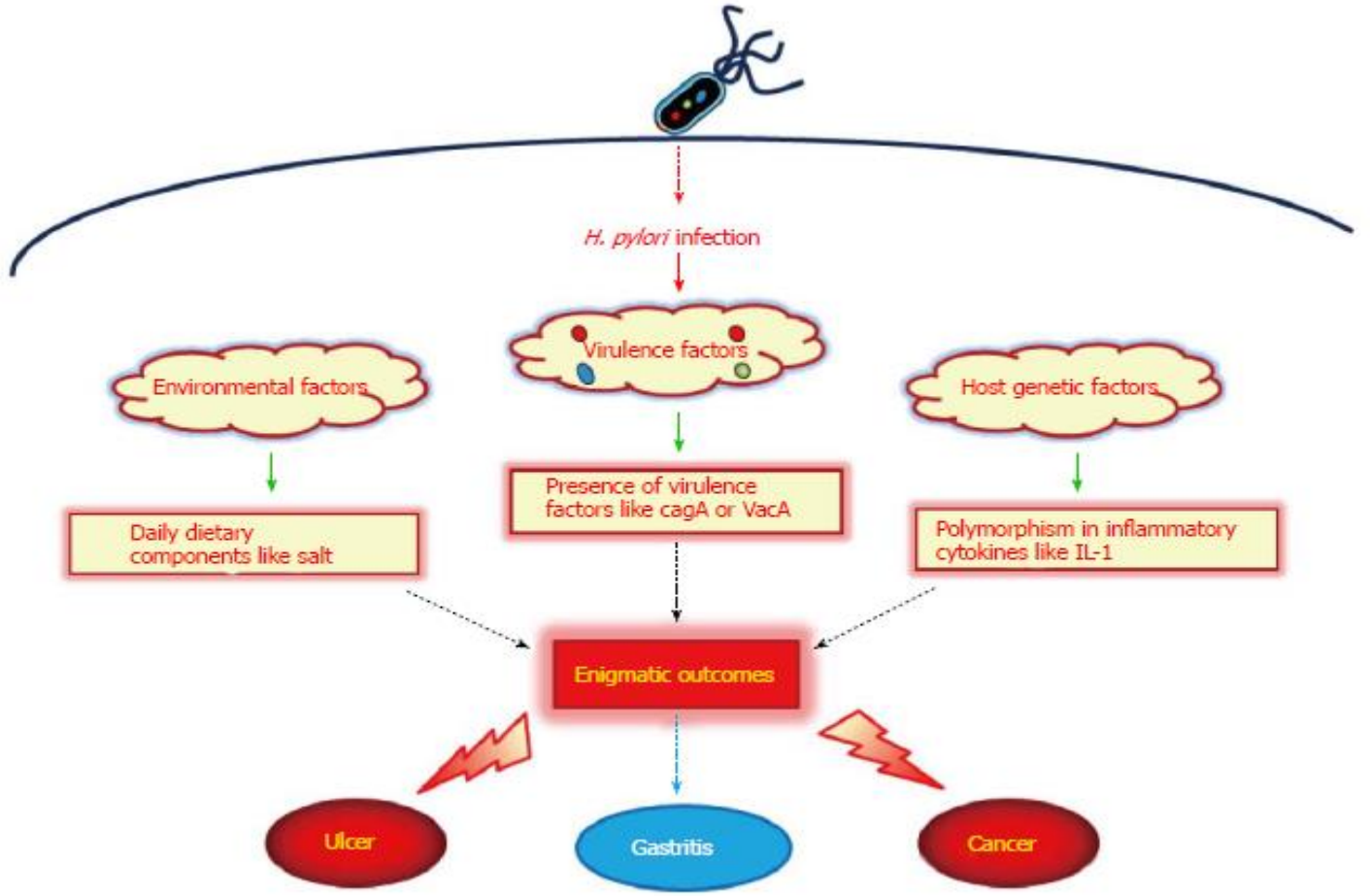


Figure 1 Three main factors behind *Helicobacter pylori* associated enigma namely: (1) Bacterial virulence factors; (2) Host genetic factors; and (3) Environmental factors. *H. pylori*: *Helicobacter pylori*; cagA: Cytotoxin associated gene-A; VacA: Vacuolating cytotoxin A; IL-1: Interleukin-1.

Zaidi SF, WJGO 2016 April 15; 8(4):341-356

2

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

H. pylori e gastrite

Statement 1: H. pylori gastritis is an infectious disease irrespective of symptoms and complications.

Level of evidence: 1B **Grade of recommendation: A**

- L' eradicazione dell' infezione da *H. pylori:*
  - determina la guarigione della mucosa infiammata, che potrebbe tornare normale;
  - previene le complicanze severe come ulcera peptica e cancro gastrico

Malfertheiner P, *et al. Gut* 2017;**66**:6–30. doi:10.1136/gutjnl-2016-312288

Since all patients with a positive test of active infection with *H. pylori* should be offered treatment, the critical issue is which patients should be tested for the infection (strong recommendation, quality of evidence: not applicable),

QUESTION 2: WHAT ARE THE INDICATIONS TO TEST FOR, AND TO TREAT, *H. PYLORI* INFECTION?

Recommendations

Since all patients with a positive test of active infection with *H. pylori* should be offered treatment, the critical issue is which patients should be tested for the infection (strong recommendation, quality of evidence: not applicable),

All patients with active peptic ulcer disease (PUD), a past history of PUD (unless previous cure of *H. pylori* infection has been documented), low-grade gastric mucosa-associated lymphoid tissue (MALT) lymphoma, or a history of endoscopic resection of early gastric cancer (EGC) should be tested for *H. pylori* infection. Those who test positive should be offered treatment for the infection (strong recommendation, quality of evidence: high for active or history of PUD, low for MALT lymphoma, low for history of endoscopic resection of EGC).

In patients with uninvestigated dyspepsia who are under the age of 60 years and without alarm features, non-endoscopic testing for *H. pylori* infection is a consideration. Those who test positive should be offered eradication therapy (conditional recommendation, quality of evidence: high for efficacy, low for the age threshold).

ACG Clinical Guideline: Treatment of *Helicobacter pylori* Infection

Am J Gastroenterol 2017; 112:212–238

3

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

H. pylori e dispepsia

Statement 5: *H. pylori* gastritis is a distinct entity and causes dyspeptic symptoms in some patients. *H. pylori* eradication produces long-term relief of dyspepsia in about 10% of patients in comparison to placebo or acid suppression therapy.

Level of evidence: moderate **Grade of recommendation: strong**

Statement 6: *H. pylori* gastritis has to be excluded before a reliable diagnosis of functional dyspepsia can be made.

Level of evidence: high **Grade of recommendation: high**

Malfertheiner P, *et al. Gut* 2017;**66**:6–30. doi:10.1136/gutjnl-2016-312288

H. pylori e dispepsia

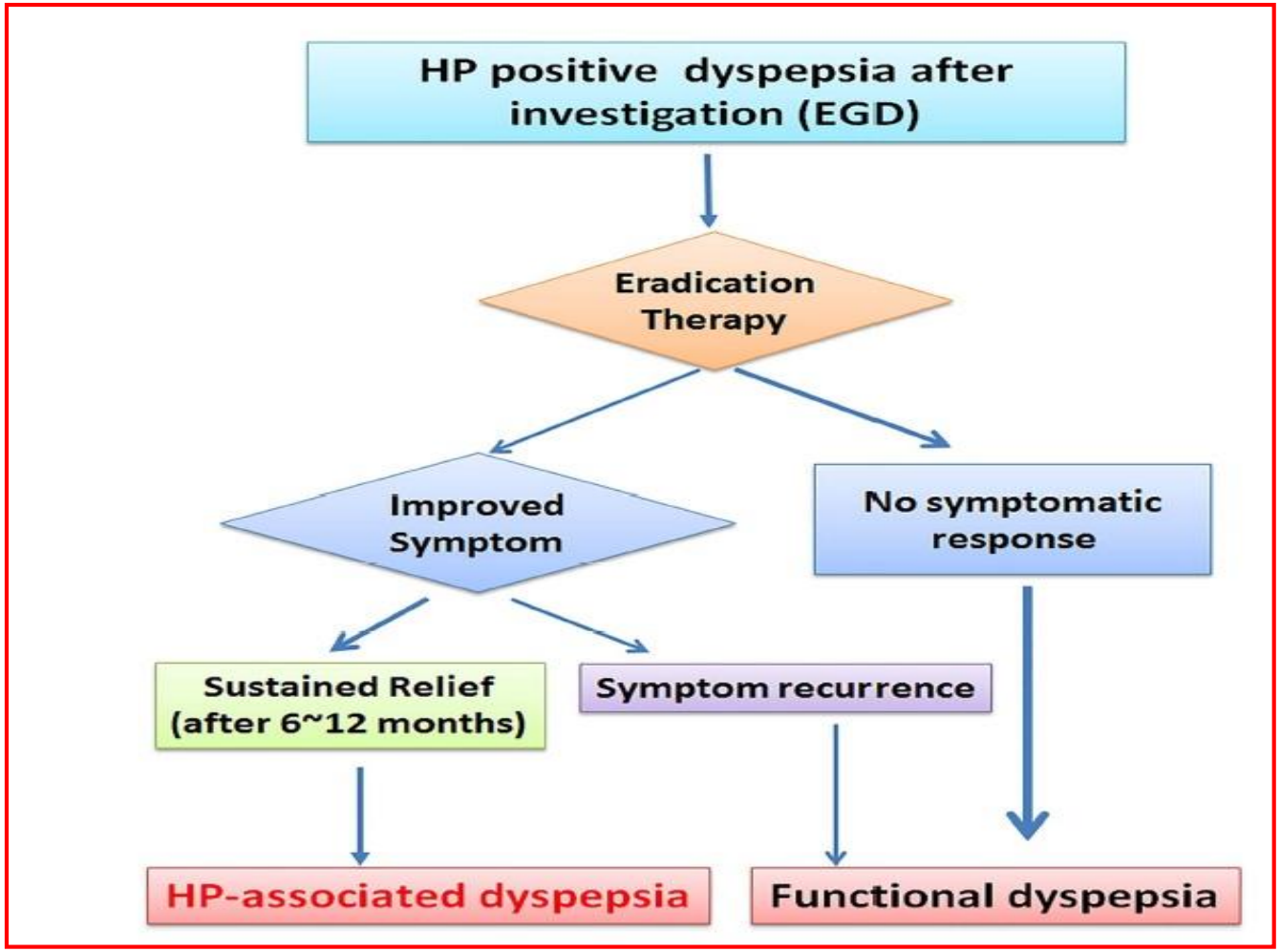
Fattori di rischio della dispepsia funzionale: studio multicentrico condotto sulla popolazione cinese

Fattori demografici	Odds ratio (95% CI)
Sesso femminile	2.01 (1.16-3.47)
NSAIDs consumo	6.60 (3.13-13.9)
Disturbi del sonno	1.71 (1.09-2.73)
Ansia	3.41 (2.01-5.77)
Depressione	1.92 (1.10-3.33)
IBS	6.89 (3.41-13.94)
Helicobacter pylori	**1.60** (1.03-2.48)

NSAID: Anti-infiammatori non steroidei
IBS: Sindrome dell'intestino irritabile

Fang YJ, et al. GUT 2015

ALGORITMO DIAGNOSTICO: DISPEPSIA ASSOCIATA
a H. pylori



Kyoto Global Consensus Report on Helicobacter pylori Gastritis. Sugano K et al. GUT 2015

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

H. pylori e dispepsia

Statement 2: A test-and-treat strategy is appropriate for uninvestigated dyspepsia. This approach is subject to regional *H. pylori* prevalence and cost-benefit considerations. It is not applicable to patients with alarm symptoms or older patients.

Level of evidence: high **Grade of recommendation: strong**

Statement 3: An endoscopy-based strategy should be considered in patients with dyspeptic symptoms, particularly in low prevalence *H. pylori* populations.

Level of evidence: very low **Grade of recommendation: weak**

Malfertheiner P, *et al. Gut* 2017;**66**:6–30. doi:10.1136/gutjnl-2016-312288

Helicobacter pylori "Test and Treat" or Endoscopy for Managing Dyspepsia: An Individual Patient Data Meta-analysis

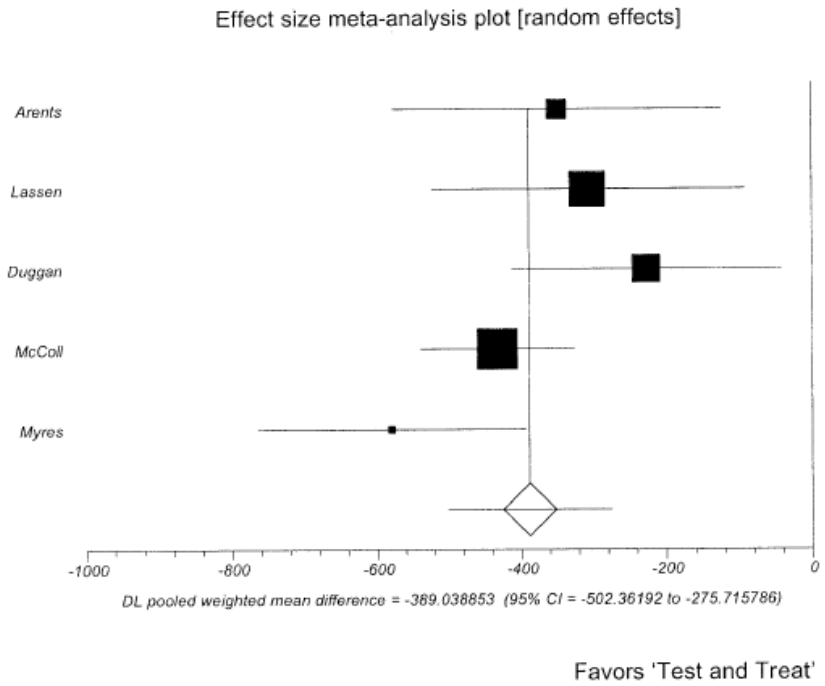


Figure 3. Weighted mean difference in total cost at 12 months for prompt endoscopy compared with "test and treat." ■, Individual RCT effect (area proportional to study size); ◇, pooled effect.

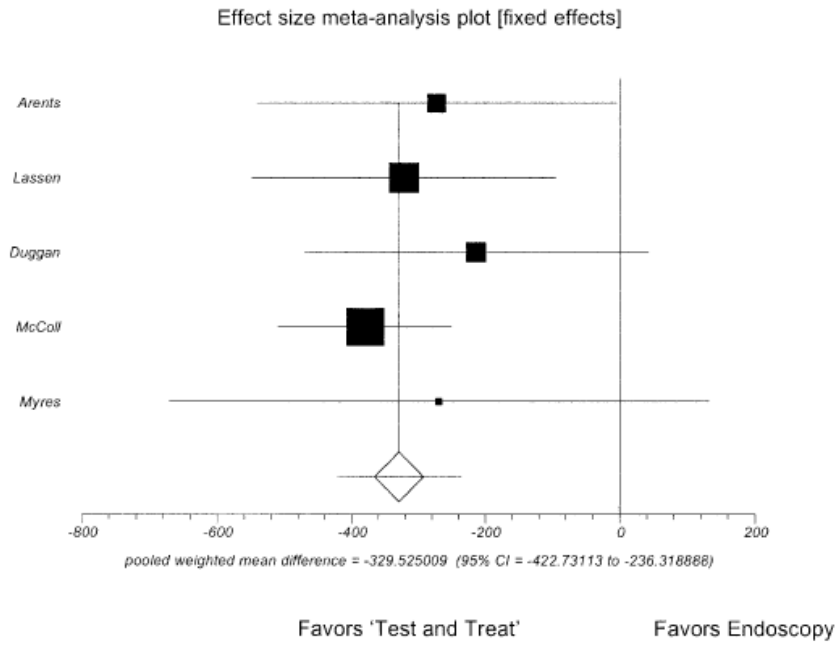
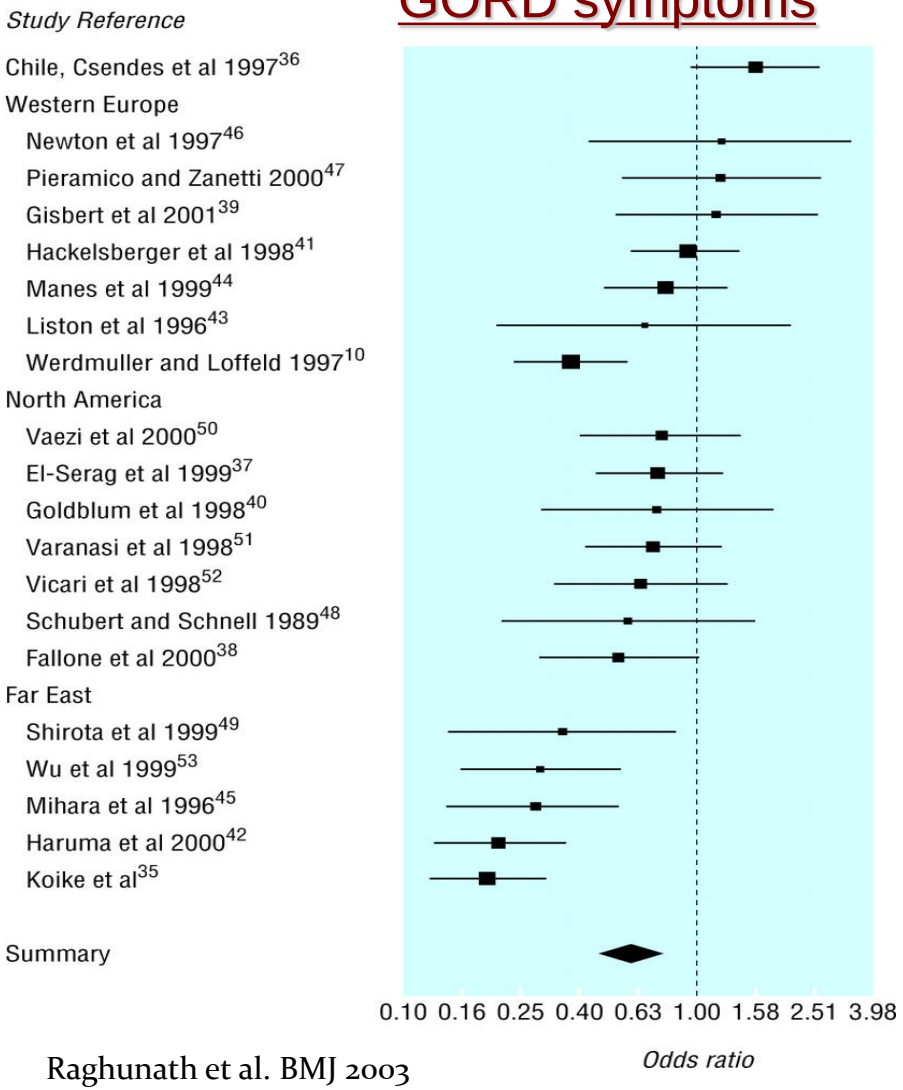


Figure 4. Weighted mean difference in net benefit for prompt endoscopy vs "test and treat" at a willingness to pay of $1000. ■, Individual RCT effect (area proportional to study size); ◇, pooled effect.

GASTROENTEROLOGY 2005;128:1838–1844

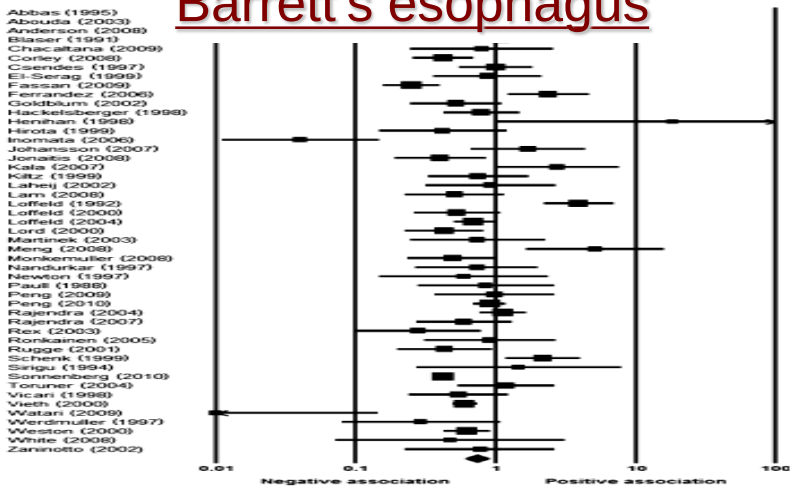
H. pylori e malattia da reflusso gastro-esofageo

GORD symptoms



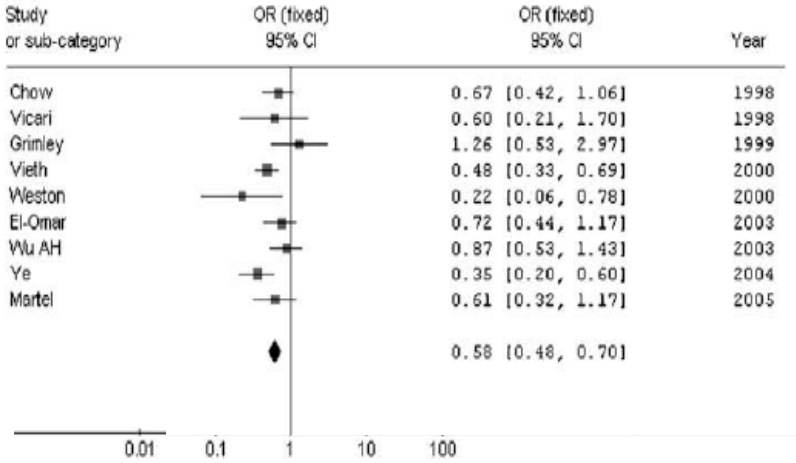
Raghunath et al. BMJ 2003

Barrett's esophagus



Fischbach et al. Helicobacter 2012

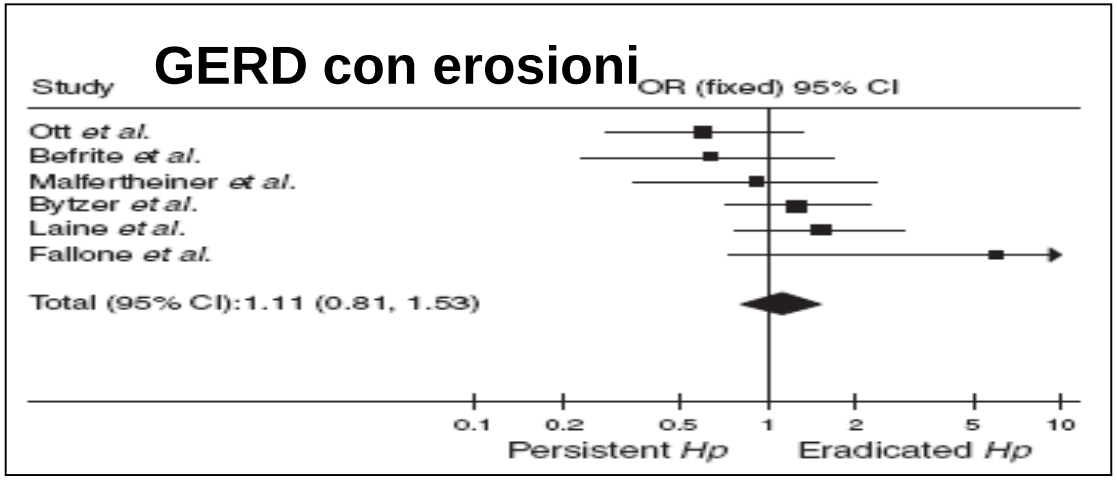
Esophageal adenocarcinoma

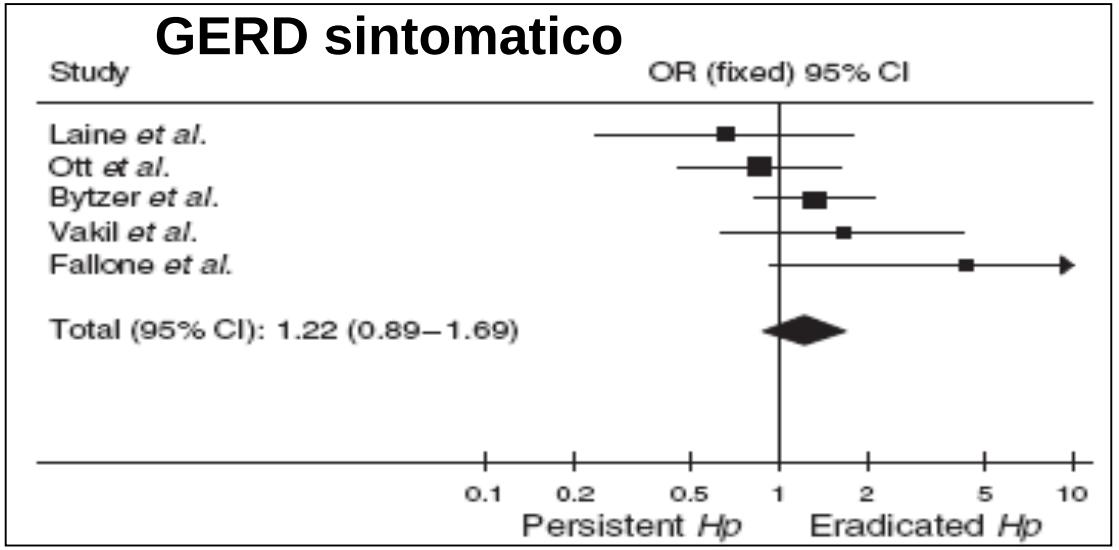


Zhou et al. Clin Oncol 2008

H. pylori e malattia da reflusso gastro-esofageo

Non c'è associazione tra eradicazione dell'infezione da *H. pylori* e sviluppo di nuovi casi di GERD





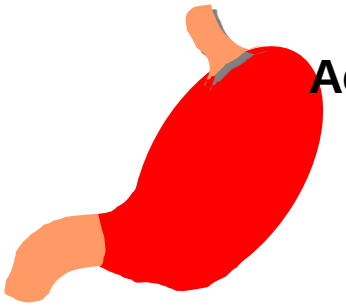
Yaghoobi M et al. AJG 2010

GORD: reflusso gastro-esofageo

4

H.pylori infection

top ten in gastroenterologia 10° EDIZIONE
8 e 9 MARZO 2019
BERGAMO
HOTEL EXCELSIOR SAN MARCO
Piazza della Repubblica, 5
Responsabile Scientifico: Fabio Pace



Acute gastritis

Chronic active gastritis

gastrin
acid secretion
gastric emptying

Intestin
an

Statement 4: *H. pylori* gastritis may increase or decrease acid secretion. Treatment may reverse or partially reverse these effects.

Level of evidence: high

Grade of recommendation: high

lcer

Pangastritis

Vit C
nitrosamine
carcinogens
genetic factors

Gastric cancer

Gastric ulcer

5

H. pylori e uso cronico di NSAIDs/ASA

top ten in gastroenterologia
10ª EDIZIONE
8 e 9 MARZO 2019
BERGAMO
HOTEL EXCELSIOR SAN MARCO
Piazza della Repubblica, 6
Responsabile Scientifico: Fabio Pace

Statement 7: The use of aspirin and non-steroidal anti-inflammatory drugs (NSAIDs) increases the risk of ulcer disease in *H. pylori* infected subjects. Anticoagulants (aspirin, coumarines, new oral anticoagulants) increase the risk of bleeding in patients with peptic ulcer.

Level of evidence: high **Grade of recommendation: strong**

Statement 8: Testing for *H. pylori* should be performed in aspirin and NSAIDs users with a history of peptic ulcer.

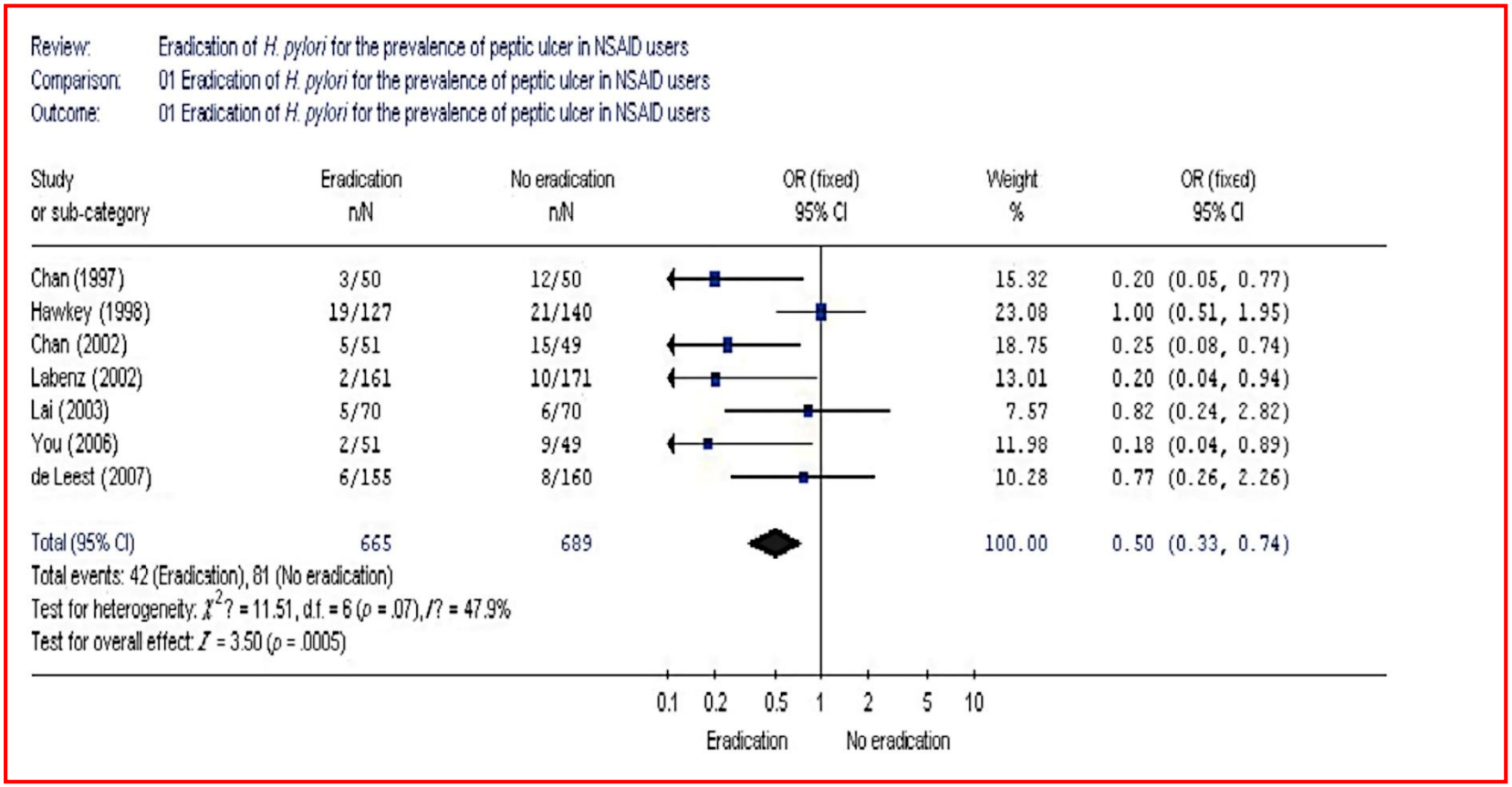
Level of evidence: moderate **Grade of recommendation: high**

In patients taking long-term, low-dose aspirin, testing for *H. pylori* infection could be considered to reduce the risk of ulcer bleeding. Those who test positive should be offered eradication therapy to reduce the risk of ulcer bleeding (conditional recommendation; moderate quality of evidence).

Patients initiating chronic treatment with a non-steroidal anti-inflammatory drug (NSAID) should be tested for *H. pylori* infection. Those who test positive should be offered eradication therapy (Strong recommendation; Moderate quality of evidence). The benefit of testing and treating *H. pylori* in a patient already taking an NSAID remains unclear (conditional recommendation; low quality of evidence).

H. pylori e uso cronico di NSAIDs/ASA

L'eradicazione dell'infezione da *H. pylori*, riduce l'incidenza di ulcera peptica in pazienti che assumono NSAIDs



NSAIDs: farmaci anti-infiammatori non steroidei

Tang C et al, Helicobacter 2012

DIAGNOSI

Test invasivi

Esame istologico
Test rapido all'ureasi
Esame colturale

Test non invasivi

Urea breath test
Antigene fecale
Sierologia

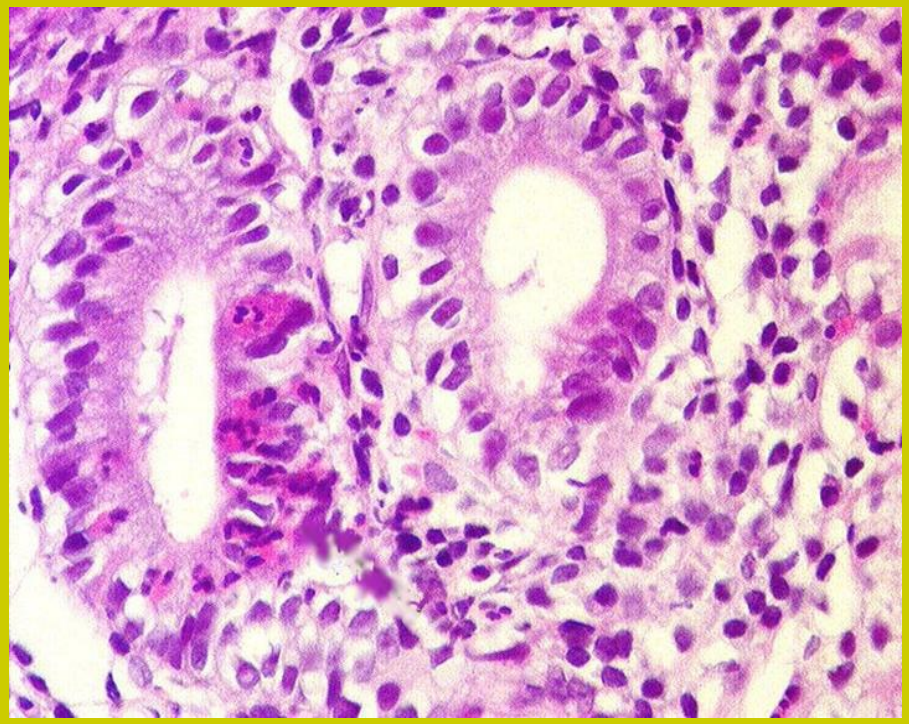
Statement 2: PPI should be discontinued at least 2 weeks before testing for *H. pylori* infection. Antibiotics and bismuth compounds should be discontinued at least 4 weeks before the test.

Level of evidence: 2b Grade of recommendation: B

DIAGNOSI

Esame istologico

L'esame istologico è il gold-standard!



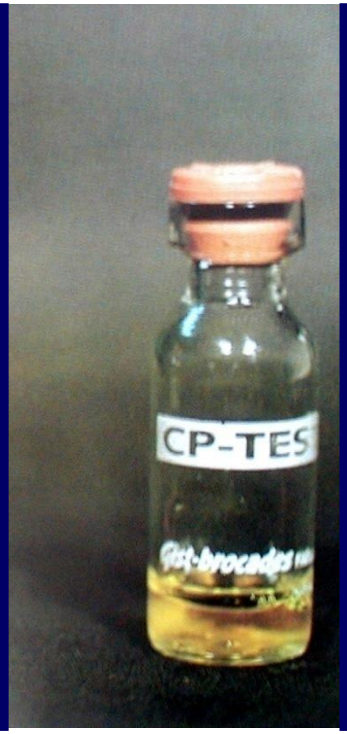
DIAGNOSI

Test rapido all'ureasi

Urea

+

Indicatore di pH



H. pylori

ureasi

NH3

Lettura entro 30 minuti

A comparison amongst three rapid urease tests to diagnose *Helicobacter pylori* infection in 375 consecutive dyspeptic

Dino Vaira · Luigi Gatta · Chiara Ricci · Federico Perna · Ilaria Saracino · Giulia Fiorini · Valentina Castelli · John Holton

Intern Emerg Med (2010) 5:41–47

Table 2 Sensitivity, specificity, likelihood ratios and AUCs for UFT 300

	Sensitivity (95% CI)	Specificity (95% CI)
UFT at 1 min	90.3% (87.6–93)	100% (99.3–100)
UFT at 5 min	94.5% (92.4–96.6)	100% (99.3–100)
UFT at 60 min	96.2% (94.5–98)	100% (99.3–100)
UFT at 24 h	97.4% (95.9–98.8)	100% (99.3–100)

Statement 3: In clinical practice when there is an indication for endoscopy, and there is no contraindication for biopsy, the rapid urease test (RUT) is recommended as a first-line diagnostic test. In the case of a positive test, it allows immediate treatment. One biopsy should be taken from the corpus and one from the antrum. RUT is not recommended as a test for *H. pylori* eradication assessment after treatment.

Level of evidence: 2b Grade of recommendation: B

DIAGNOSI

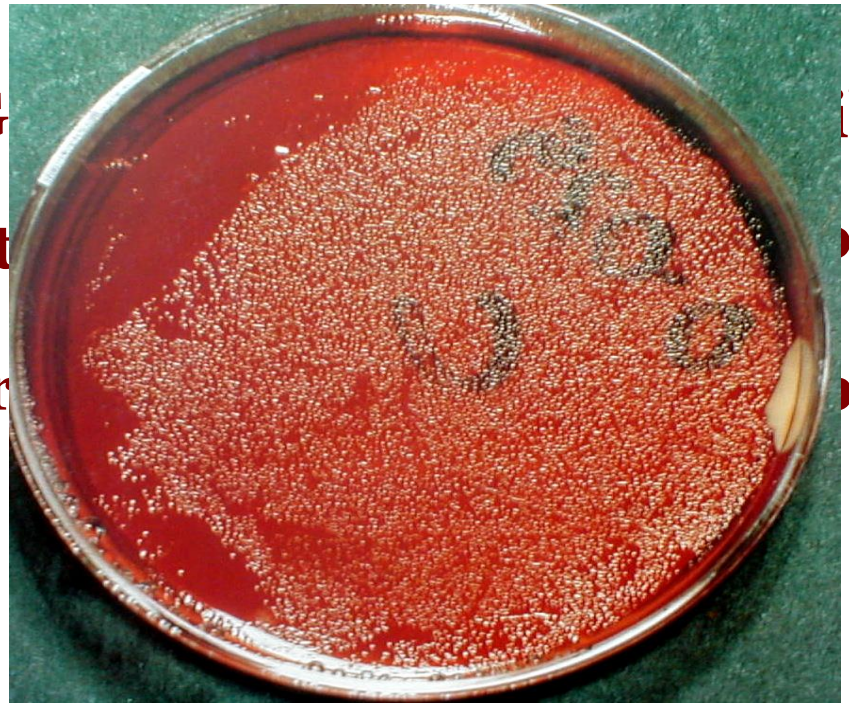
Esame colturale

A clinical practice viewpoint: to culture or not to culture *Helicobacter pylori*?

A. Zullo*, C. Hassan, R. Lorenzetti, S. Winn, S. Morini

Gastroenterology and Digestive Endoscopy, 'Nuovo Regina Margherita' Hospital, Via E. Morosini 30, 00156 Rome, Italy

Digestive and Liver Disease 35 (2003) 357–361



- **Nuova EG** **ilità 50-90%**
- **Mezzo di t** **ogramma**
- **Laborator** **panza *vitro/vivo***

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

Statement 15: After failure of second-line treatment, culture with susceptibility testing or molecular determination of genotype resistance is recommended in order to guide treatment.

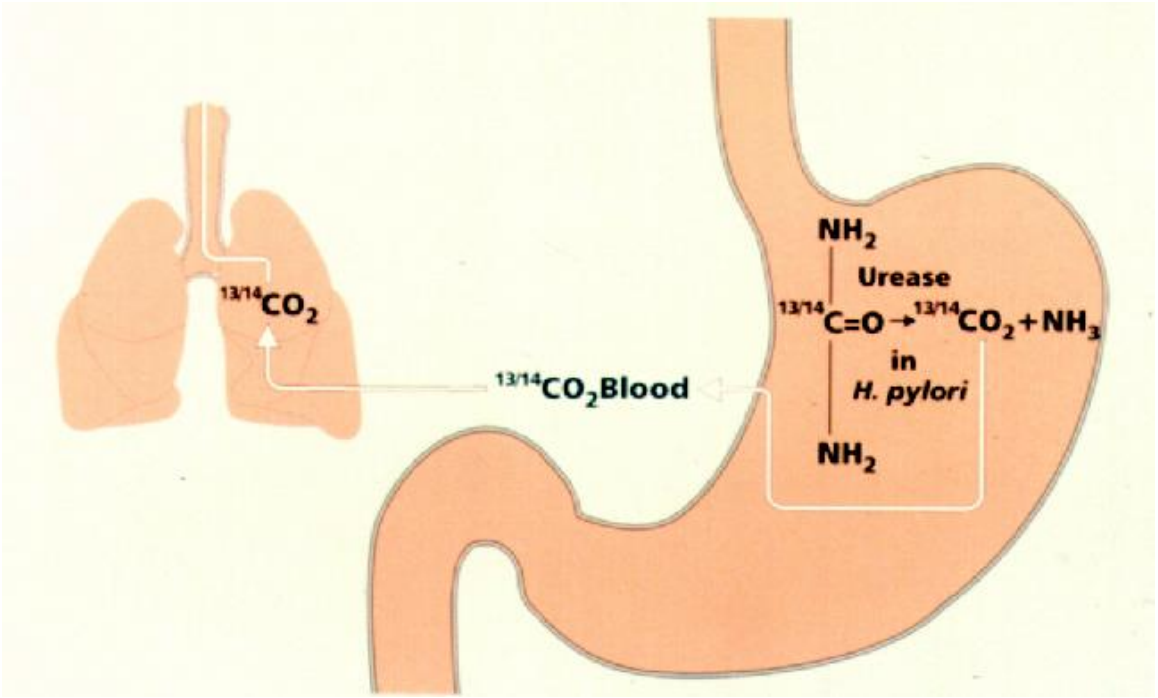
Level of evidence: very low **Grade of recommendation: weak**

Statement 7: After a first failure, if an endoscopy is carried out, culture and standard antimicrobial susceptibility testing (AST) are recommended to tailor the treatment, except if a bismuth-based quadruple therapy is considered.

Level of evidence: weak **Grade of recommendation: strong**

DIAGNOSI

Urea Breath test



SENSIBILITA' E SPECIFICITA'

PRE-TRATTAMENTO = 98-100%

POST-TRATTAMENTO= 98-100%

DIAGNOSI

Ricerca antigeni fecali

TEST	SENSIBILITA'	SPECIFICITA'
Policlonale		
- pre-terapia	91	93
- post-terapia	86	92
Monoclonale		
- pre-terapia	96	97
- post-terapia	96	97

DIAGNOSI
Sierologia

Statement 8: Serological tests presenting high accuracy, and locally validated, can be used for non-invasive *H. pylori* diagnosis.

Level of evidence: 2a **Grade of recommendation: B**

Serological tests can be used only after validation. Rapid ('office') serology tests using whole blood should be avoided in this regard.

Level of evidence: 2a **Grade of recommendation: B**

Non usare la sierologia dopo una terapia eradicante: il test può rimanere positivo per mesi!

La terapia

TERAPIA

Gli inibitori della pompa protonica

- **Omeprazolo 20 mg**
- **Lansoprazolo 30 mg**
- **Pantoprazolo 40 mg**
- **Rabeprazolo 20 mg**
- **Esomeprazolo 20 mg**

½ ora prima di colazione

½ ora prima di cena

TERAPIA

Gli antibiotici

- **Amoxicillina 1 g**
- **Claritromicina 500 mg**
- **Metro/Tinidazolo 500 mg**
- **Levofloxacina 250 mg**

Appena dopo colazione

Appena dopo cena

- **Tetraciclina**
- **Sali di Bismuto**
- **Furazolidone**
- **Rifabutina**

Schemi terapeutici

- Duplice terapia:
  - IPP, Amo per 14 gg
- Triplici terapie classiche:
  - IPP, Amo/Cla/Met per 7-14 gg
- Quadruplice con bismuto:
  - IPP, Tetra-Met-Bism per 10-14 gg
- Quadruplici terapie senza bismuto:
  - Concomitante: IPP, Amo-Cla-Met per 10-14 gg
  - Sequenziale: IPP, Amo per 5 gg =>IPP, Cla-Met per 5 gg
  - Ibrida: IPP, Amo per 5 gg => IPP, Cla-Met-Amo per 5 gg

TERAPIA

Le triplici terapie

- **IPP** **b.i.d**
- **Claritromicina 500 mg** **b.i.d**
- **Amoxicillina 1 g** **b.i.d**

- **IPP** **b.i.d**
- **Claritromicina 500 mg** **b.i.d**
- **Tinidazolo 500 mg** **b.i.d**

Per 7-14 giorni

Come aumentare la efficacia della terapia eradicante?

- Aumentare la dose del PPI => + 6-10%
- Aumentare la durata del trattamento a 10-14 giorni => + 5%
- Sostituire l'amoxicillina con il metronidazolo ?
- Aggiungere degli adiuvanti alla terapia
- Considerare i fattori clinici
  - Obesità
  - Fumo
  - Dispepsia

top ten
in gastroenterologia
10ª EDIZIONE
8 e 9 MARZO 2019
BERGAMO
HOTEL EXCELSIOR SAN MARCO
Piazza della Repubblica, 6
Responsabile Scientifico: Fabio Pace

Statement 1: *H. pylori* resistance rates to antibiotics are increasing in most parts of the world.

Level of evidence: moderate Grade of recommendation: strong

Prevalenza di ceppi resistenti in Italia

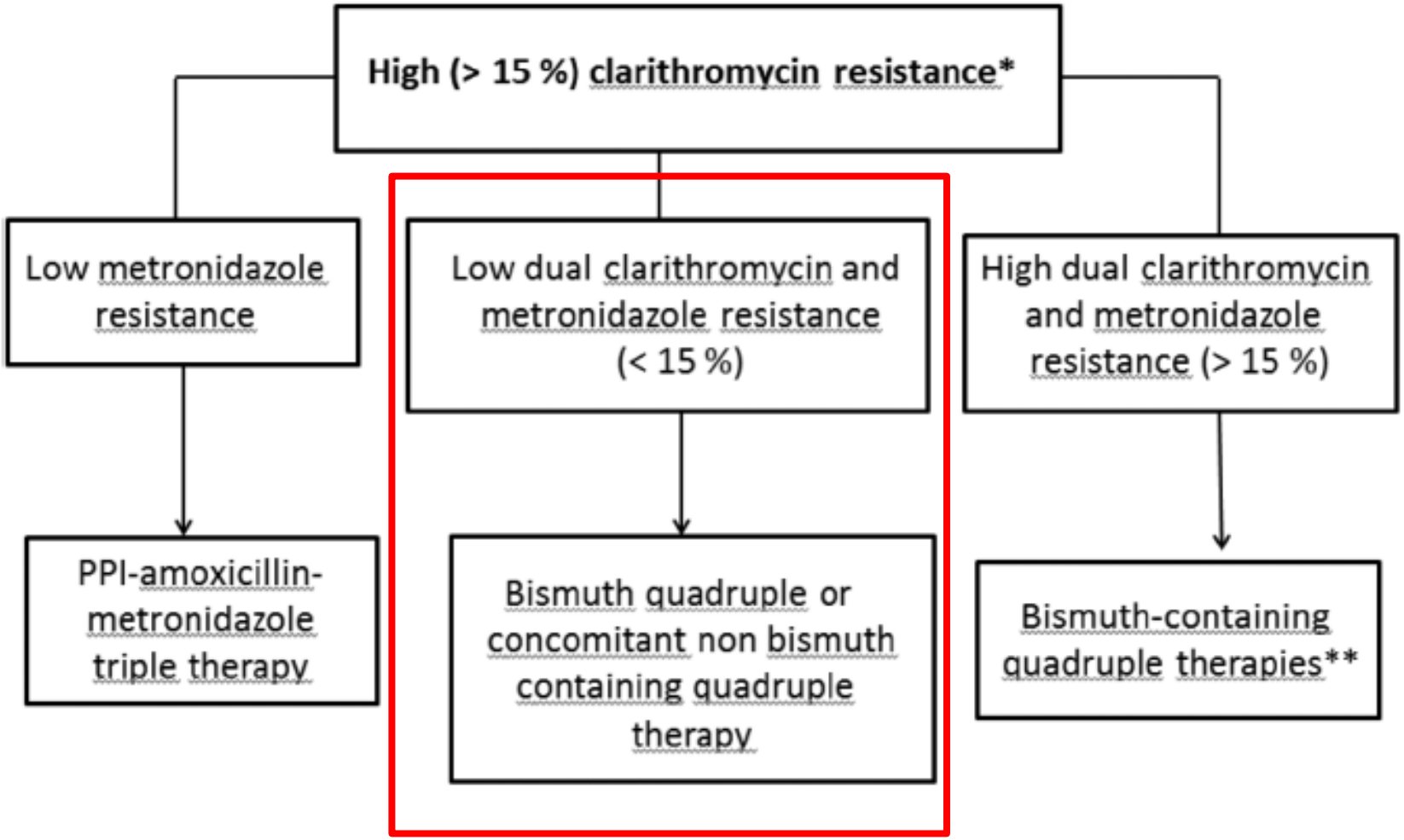
- Claritromicina = 30%

- Metronidazolo < 40%

- Dual resistance < 15%

Statement 2: PPI-clarithromycin-containing triple therapy without prior susceptibility testing should be abandoned when the clarithromycin resistance rate in the region is more than 15%.

Level of evidence: very low **Grade of recommendation: weak**



La quadruplice terapia con bismuto

IPP b.d

Met 500 mg t.d

Tet 500 mg q.d

Bismuto q.d

10-14 giorni

La terapia sequenziale

IPP b.d

AMO 1g b.d

Prima di colazione e cena

Dopo colazione e cena

5 giorni

più

IPP b.d

CLA 500 b.d

TIN 500 b.d

Prima di colazione e cena

Dopo colazione e cena

5 giorni

Zullo A. *Aliment Pharmacol Ther 2000;14:715-8.*

The sequential therapy regimen for *Helicobacter pylori* eradication: a pooled-data analysis

Gut 2007;**56**:1353–1357.

Angelo Zullo, Vincenzo De Francesco, Cesare Hassan, Sergio Morini, Dino Vaira

Table 1 Overall eradication rate following sequential therapy at intention to treat (ITT) and per protocol (PP) analysis

Author (reference)	Year	Centres involved	Patients enrolled	Patients cured	ITT (%)
Zullo *et al*[32]	2000	1	52	51	98
De Francesco *et al*[32]	2001	2	63	61	93.8
Focareta *et al*[33]	2002	1	94	90	95.7
Zullo *et al*[34]	2003	8	522	481	92
Hassan *et al*[35]	2003	1	152	142	93.4
Focareta *et al*[36]	2003	1	174	166	95.4
De Francesco *et al*[37]	2004	1	162	151	93.2
De Francesco *et al*[38]	2004	2	45	43	95.5
De Francesco *et al*[39]	2004	2	116	110	94.8
Francavilla *et al*[40]	2005	1	38	36	94.7
Zullo *et al*[41]	2005	3	89	84	94.4
Zullo *et al*[42]	2005	1	40	38	95
Scaccianoce *et al*[43]	2005	2	72	68	94.4
Francavilla *et al*[40]	2006	1	40	33	82.5
Vaira *et al*[45]	2007	2	[illegible]	133	[illegible]
Total			1805	1687	93.5

Annals of Internal Medicine | Volume 148 • Number 12 | 17 June 2008 | Review

Meta-analysis: Sequential Therapy Appears Superior to Standard Therapy for *Helicobacter pylori* Infection in Patients Naive to Treatment

Nadim S. Jafri, MD, MSc; Carlton A. Hornung, PhD, MPH; and Colin W. Howden, MD

Analysis (References)	Participants, *n*	Studies, *n*	Eradication Rate with Sequential Therapy, %	Eradication Rate with Triple Therapy, %
All studies	2747	10	93.4	76.9
High-quality studies (Jadad score ≥3) (23, 24, 26–28)	841	5	92.8	79.1
Outcome: ulcer healing (19, 22, 25)	497	3	97.2	84.4
Diagnosis: peptic ulcer disease (19, 22–24)	416	4	97.5	79.8
Diagnosis: nonulcer dyspepsia (19, 22–24)	1083	4	91.9	73.2
Adults only (19–25, 27, 28)	2417	9	93.2	76.7
Smokers only (23, 24)	169	2	93.8	75.0
Clarithromycin-resistant strains (28, 29)	186	2	82.2	40.6
Imidazole-resistant strains (22, 28)	130	2	95.8	78.0
Standard treatment duration >5 d (20–28)	2620	9	93.2	77.4
10-d sequential therapy vs 7-d standard triple therapy (20–22, 24–27)	2207	7	93.7	75.5
10-d sequential therapy vs 10-d standard triple therapy (23, 24, 27, 28)	772	4	92.7	79.4

La terapia “concomitante”

Update on non-bismuth quadruple (concomitant) therapy for eradication of *Helicobacter pylori*

Javier P Gisbert[1]
Xavier Calvet[2]

Clinical and Experimental Gastroenterology
13 March 2012

O 20 mg bid + A 1 g bid +
C 500 mg bid + T 500 mg bid

→ 3, 4, 5, 7, 10 o 14 gg

Eradicazione: 63-96%

La terapia “concomitante”

Sequential and Concomitant Therapy With Four Drugs Is Equally Effective for Eradication of *H pylori* Infection

CLINICAL GASTROENTEROLOGY AND HEPATOLOGY 2010;8:36–41

DENG–CHYANG WU,[*,‡,§] PING–I HSU,[‖] JENG–YIH WU,[*,‡] ANTONE R. OPEKUN,[¶] CHAO–HUNG KUO,[‡,#] I–CHEN WU,[*] SOPHIE S. W. WANG,[*] ANGELA CHEN,[§,**] WEN–CHUN HUNG,[§,**] and DAVID Y. GRAHAM[¶]

Table 2. The Outcomes of Concomitant and Sequential Therapies

	Concomitant therapy	Sequential therapy	*P* value
Eradication rate			
Intention-to-treat	107/115 (93%)	108/117 (92.3%)	.83
Per-protocol	107/115 (93%)	108/116 (93.1%)	.99
Compliance	113/115 (98.2%)	112/117 (95.7%)	.26
Side effect	31/115 (26.9%)	36/117 (30.7%)	.40

La terapia “ibrida”

Modified Sequential *Helicobacter pylori* Therapy: Proton Pump Inhibitor and Amoxicillin for 14 Days with Clarithromycin and Metronidazole added as a Quadruple (Hybrid) Therapy for the Final 7 Days

Ping-I. Hsu,[*] Deng-Chyang Wu,[†] Jeng-Yih Wu[†,‡] and David Y. Graham[§]

Helicobacter **16:** 139–145 2011

Table 2 The major outcomes of 14-day hybrid therapy

Parameters of outcomes	Hybrid therapy (n = 117)
Eradication rate	
Per-protocol	99.1% (108/109)(97.3–100.0%)[a]
Intention-to-treat	97.4% (114/117)(94.5–100.0%)
Adverse events	14.5% (17/117)(8.1–20.9%)
Compliance	94.9% (111/117)(91.0–98.8%)

Quale terapia di prima linea?

Caratteristiche delle diverse terapie di prima linea in Italia.

Terapia	Durata (giorni)	Numero di cpr	Costo (euro)*
Sequenziale	10	50	26
Concomitante	14	112	61
Ibrida	14	84	41.4
Triple (Amox)	14	84	40.6
Triple (Tin)	14	84	49.5

*Costo calcolato con farmaci generici.

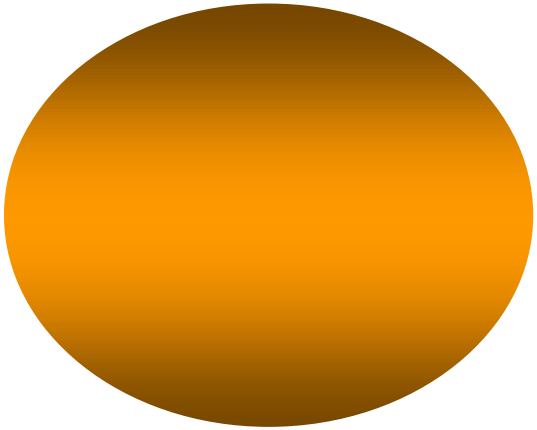
La quadruplice terapia con bismuto

PPI +

Metronidazolo 125 mg

Tetraciclina cloridrato 125 mg

Bismuto subcitrato 140 mg



La quadruplice terapia con bismuto

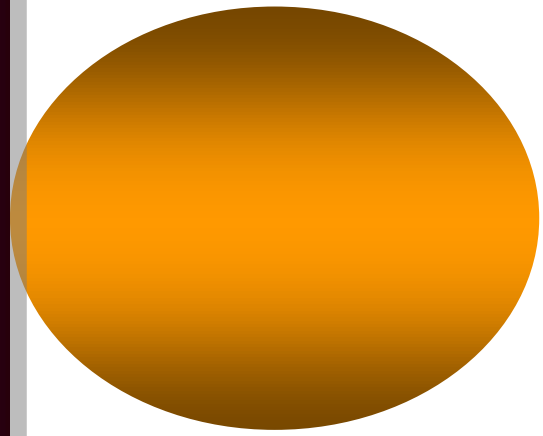
PPI x 2 prima di colazione e cena

Pylera 3 cp x 4 volte al giorno

dopo colazione, pranzo e cena e

subito prima di andare a letto

per 10 giorni



Razionale

- Non contiene antibiotici a cui Hp è resistente (Cla e Levo)
- Il bismuto non è un antibiotico ma un antisettico
- Hp è raramente resistente a Tetraciclina
- La resistenza a Metro è poco importante e viene superata con l'uso di elevate dosi del farmaco (riduzione eradicazione del 14%)

Possibili vantaggi

- **Contiene antibiotici poco usati in altre infezioni**
- **Elevate percentuali di eradicazione**
- **Minimizzato rischio di infezione da *clostridium difficile***
- **Semplice da ricordare nelle diverse condizioni**
- **Terapia standardizzata**

Helicobacter pylori eradication with a capsule containing bismuth subcitrate potassium, metronidazole, and tetracycline given with omeprazole versus clarithromycin-based triple therapy: a randomised, open-label, non-inferiority, phase 3 trial

Lancet 2011; 377: 905–13

Peter Malfertheiner, Franco Bazzoli, Jean-Charles Delchier, Krysztof Celiński, Monique Giguère, Marc Rivière, Francis Mégraud, for the Pylera Study Group

	Quadruple therapy		Standard therapy	
Eradication rate by baseline metronidazole resistance*				
Baseline metronidazole resistance	Yes	No	Yes	No
Eradication	38/42 (91%); 77·4–97·3	98/103 (95%); 89·0–98·4	28/41 (68%); 51·9–81·9	64/90 (71%); 89·0–98·4
p value	0·283	..	0·837	..
Eradication rate by baseline clarithromycin resistance*				
Baseline clarithromycin resistance	Yes	No	Yes	No
Eradication	30/33 (91%); 75·7–98·1	106/112 (95%); 88·8–98·0	2/25 (8%); 1·0–26·0	90/106 (85%); 76·6–91·1
p value	0·426	..	<0·0001	..
Eradication rate by baseline combined metronidazole and clarithromycin resistance*				
Baseline combined metronidazole and clarithromycin resistance	Yes	No	Yes	No
Eradication	11/12 (92%); 61·5–99·8	125/133 (94%); 88·5–97·4	2/10 (20%); 2·5–55·6	90/121 (74%); 65·6–81·9
p value	0·551	..	0·001	..

Data ate n/N (%); 95% CI unless otherwise indicated. Quadruple therapy is omeprazole, bismuth, metronidazole, and tetracycline. Standard therapy is omeprazole, amoxicillin, and clarithromycin. PP=per protocol.
*Percentages are based on the number of patients with both baseline and post-baseline resistance data in the PP population; not all cultures provided resistance or sensitivity data.

Table 3: **Eradication rates and antibiotic resistance in the PP population**

Use of a combination formulation of bismuth, metronidazole and tetracycline with omeprazole as a rescue therapy for eradication of *Helicobacter pylori*

J. C. Delchier*, P. Malfertheiner† & R. Thieroff-Ekerdt‡

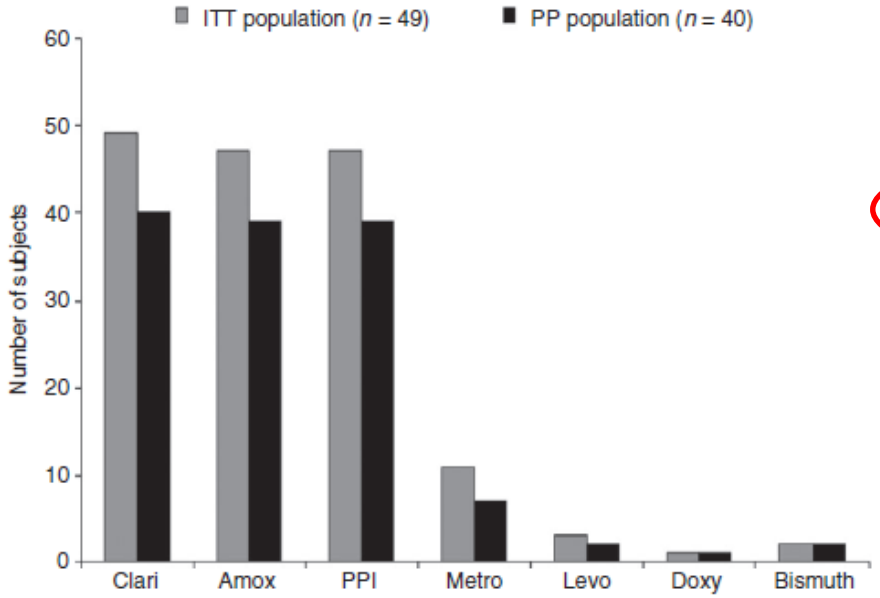


Table 2 | *Helicobacter pylori* eradication rate in ITT and PP populations

	ITT population (n = 49)	PP population (n = 40)
Number with ^{13}C-UBT 28–56 days following the last day of treatment	44	38
Number (%) eradicated	41 (93.2)	36 (94.7)
95% confidence interval	81.3, 98.6	82.3, 99.4
Number with ^{13}C-UBT ≥28 days following the last day of treatment	47	40
Number (%) eradicated	44 (93.6)	38 (95.0)
95% confidence interval	82.5, 98.7	83.1, 99.4
Number with ^{13}C-UBT following the last day of treatment	48	40
Number (%) eradicated	45 (93.8)	38 (95.0)
95% confidence interval	82.8, 98.7	83.1, 99.4

^{13}C-UBT, 13C-urea breath test.

10

Pylera and sequential therapy for first-line *Helicobacter pylori* eradication: a culture-based study in real clinical practice

Giulia Fiorini[a], Angelo Zullo[b], Ilaria M. Saracino[a], Luigi Gatta[c], Matteo Pavoni[a] and Dino Vaira[a]

Table 2. Eradication rates at intention-to-treat and per protocol analyses according to the antibiotic resistance patterns

	Sequential therapy [*n* (%)]		Bismuth-quadruple therapy with Pylera [*n* (%)]		
	ITT analysis	PP analysis	ITT analysis	PP analysis	*P* value (ITT)
C_RM_R	28/33 (85)	28/30 (93)	34/40 (85)	34/38 (89)	0.6
C_RM_S	16/20 (80)	16/17 (94)	32/33 (97)	32/32 (100)	0.061
C_SM_R	26/28 (93)	26/28 (93)	27/29 (93)	27/27 (100)	0.7
C_SM_S	96/105 (91)	96/101 (95)	84/90 (93)	84/85 (99)	0.6
Not available	64/64 (100)	64/64 (100)	46/53 (87)	46/48 (96)	0.003
Total	230/250 (92)	230/240 (96)	223/245 (91)	223/230 (97)	–

C_R, clarithromycin resistant; C_S, clarithromycin sensitive; ITT, intention-to-treat; M_R, metronidazole resistant; M_S, metronidazole sensitive; PP, per protocol.

European Journal of Gastroenterology & Hepatology 2018, 30:621–625

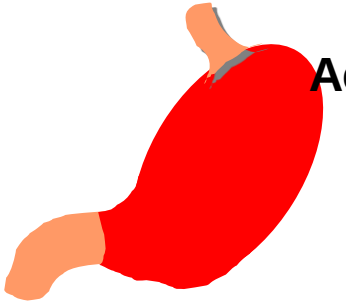
La terapia di seconda linea

•Dopo un primo fallimento di una terapia con Cla la possibilità che H.pylori sia resistente a Cla è del 60-70%
•Mai ripetere la stessa terapia dopo un fallimento

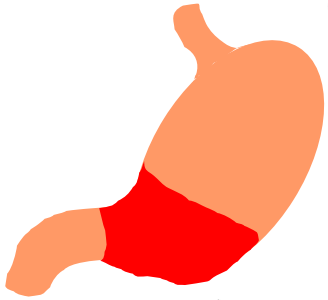
• Quadruplice	10-14 giorni
• Quadruplice con Levoflox	10-14 giorni
• IPP + Levoflox 250 mg + Amox 1 g b.i.d	14 giorni
• Eso 40 mg + Amox 1 g t.i.d	14 giorni
• IPP + Rifabutina 150 mg + Amox 1 g b.i.d	10 giorni

1

***H.pylori* infection**

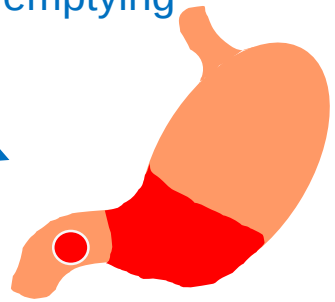


Acute gastritis



Chronic active gastritis

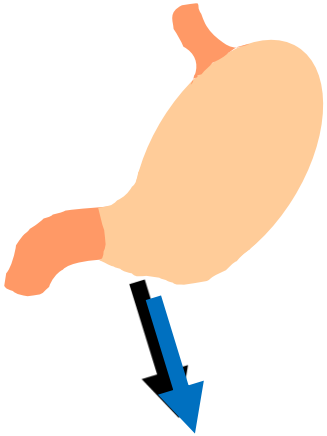
gastrin
acid secretion
gastric emptying



Duodenal ulcer

drugs
age
nutrition
smoking
genetic factors

Pangastritis



Intestinal metaplasia and atrophy

Vit C
nitrosamine
carcinogens
genetic factors

Gastric cancer

Gastric ulcer

2

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

H. pylori e gastrite

Statement 1: H. pylori gastritis is an infectious disease irrespective of symptoms and complications.

Level of evidence: 1B **Grade of recommendation: A**

- L' eradicazione dell' infezione da *H. pylori:*
  - determina la guarigione della mucosa infiammata, che potrebbe tornare normale;
  - previene le complicanze severe come ulcera peptica e cancro gastrico

Malfertheiner P, *et al. Gut* 2017;**66**:6–30. doi:10.1136/gutjnl-2016-312288

3

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

H. pylori e dispepsia

Statement 5: *H. pylori* gastritis is a distinct entity and causes dyspeptic symptoms in some patients. *H. pylori* eradication produces long-term relief of dyspepsia in about 10% of patients in comparison to placebo or acid suppression therapy.

Level of evidence: moderate **Grade of recommendation: strong**

Statement 6: *H. pylori* gastritis has to be excluded before a reliable diagnosis of functional dyspepsia can be made.

Level of evidence: high **Grade of recommendation: high**

Malfertheiner P, *et al. Gut* 2017;**66**:6–30. doi:10.1136/gutjnl-2016-312288

4

H.pylori infection

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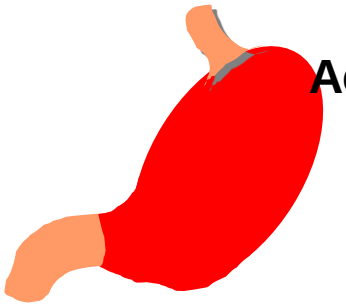

Acute gastritis

Chronic active gastritis

gastrin
acid secretion
gastric emptying

Intestin
an

Statement 4: *H. pylori* gastritis may increase or decrease acid secretion. Treatment may reverse or partially reverse these effects.

Level of evidence: high

Grade of recommendation: high

lcer

Pangastritis

Vit C
nitrosamine
carcinogens
genetic factors

Gastric cancer

Gastric ulcer

5

H. pylori e uso cronico di NSAIDs/ASA

Statement 7: The use of aspirin and non-steroidal anti-inflammatory drugs (NSAIDs) increases the risk of ulcer disease in *H. pylori* infected subjects. Anticoagulants (aspirin, coumarines, new oral anticoagulants) increase the risk of bleeding in patients with peptic ulcer.

Level of evidence: high **Grade of recommendation: strong**

Statement 8: Testing for *H. pylori* should be performed in aspirin and NSAIDs users with a history of peptic ulcer.

Level of evidence: moderate **Grade of recommendation: high**

In patients taking long-term, low-dose aspirin, testing for *H. pylori* infection could be considered to reduce the risk of ulcer bleeding. Those who test positive should be offered eradication therapy to reduce the risk of ulcer bleeding (conditional recommendation; moderate quality of evidence).

Patients initiating chronic treatment with a non-steroidal anti-inflammatory drug (NSAID) should be tested for *H. pylori* infection. Those who test positive should be offered eradication therapy (Strong recommendation; Moderate quality of evidence). The benefit of testing and treating *H. pylori* in a patient already taking an NSAID remains unclear (conditional recommendation; low quality of evidence).

Guidelines for the management of *H. Pylori* infection in Italy. Zagari RM et al. Dig Liver Dis 2015

DIAGNOSI

Test invasivi

Esame istologico
Test rapido all'ureasi
Esame colturale

Test non invasivi

Urea breath test
Antigene fecale
Sierologia

Statement 2: PPI should be discontinued at least 2 weeks before testing for *H. pylori* infection. Antibiotics and bismuth compounds should be discontinued at least 4 weeks before the test.

Level of evidence: 2b Grade of recommendation: B

Schemi terapeutici

- Duplice terapia:
  - IPP, Amo per 14 gg
- Triplici terapie classiche:
  - IPP, Amo/Cla/Met per 7-14 gg
- Quadruplice con bismuto:
  - IPP, Tetra-Met-Bism per 10-14 gg
- Quadruplici terapie senza bismuto:
  - Concomitante: IPP, Amo-Cla-Met per 10-14 gg
  - Sequenziale: IPP, Amo per 5 gg =>IPP, Cla-Met per 5 gg
  - Ibrida: IPP, Amo per 5 gg => IPP, Cla-Met-Amo per 5 gg

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Statement 1: *H. pylori* resistance rates to antibiotics are increasing in most parts of the world.

Level of evidence: moderate Grade of recommendation: strong

Prevalenza di ceppi resistenti in Italia

- Claritromicina = 30%

- Metronidazolo < 40%

- Dual resistance < 15%

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IPP b.d

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Prima di colazione e cena

Dopo colazione e cena

5 giorni

più

IPP b.d

CLA 500 b.d

TIN 500 b.d

Prima di colazione e cena

Dopo colazione e cena

5 giorni

Zullo A. *Aliment Pharmacol Ther 2000;14:715-8.*

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C_SM_R	26/28 (93)	26/28 (93)	27/29 (93)	27/27 (100)	0.7
C_SM_S	96/105 (91)	96/101 (95)	84/90 (93)	84/85 (99)	0.6
Not available	64/64 (100)	64/64 (100)	46/53 (87)	46/48 (96)	0.003
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European Journal of Gastroenterology & Hepatology 2018, 30:621–625