Supplementary Material

Table A: Risk bias assessment of RCTs included into systematic review and meta-analysis

	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data	Selective reporting	Other sources of bias
Zullo *et al.* (2003) [6]							
Focareta *et al.* (2003) [15]							
De Francesco *et al.* (2004) [16]							
De Francesco *et al.* (2004) [17]							
Zullo *et al.* (2005) [18]							
Scaccianoce *et al.* (2006) [19]							
Vaira *et al.* (2007) [7]							
Choi *et al.* (2008) [20]							
Ma *et al.* (2008) [21]							
Wu *et al.* (2008) [22]							
Hu *et al.* (2009) [23]							
Park *et al.* (2009) [24]							
Zhao *et al.* (2009) [25]							
Paoluzi *et al.* (2010) [26]							

Legend: Green = Low Risk of Bias; Yellow = Unclear Risk of Bias; Red = High Risk of Bias.

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Table A: Risk bias assessment of RCTs included into systematic review and meta-analysis *(continued).*

	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data	Selective reporting	Other sources of bias
Aminian *et al.* (2010) [27]							
Liang *et al.* (2010) [28]							
Molina-Infante *et al.* (2010) [29]							
Song *et al.* (2010) [30]							
Wu *et al.* (2010) [31]							
Romano *et al.* (2010) [32]							
Gao *et al.* (2010) [33]							
Greenberg *et al.* (2011) [34]							
Kim *et al.* (2011) [35]							
Gatta *et al.* (2011)[36]							
Wu *et al.* (2011) [37]							
Franceschi *et al.* (2012)[38]							
Choi HS *et al.* (2012)[39]							

Legend: **Green** = Low Risk of Bias; **Yellow** = Unclear Risk of Bias; **Red** = High Risk of Bias.

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Table A: Risk bias assessment of RCTs included into systematic review and meta-analysis *(continued).*

	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data	Selective reporting	Other sources of bias
Fakheri *et al.* (2012)[40]							
Huang *et al.* (2012) [41]							
Oh *et al.* (2012) [42]							
Park *et al.* (2012) [43]							
Chung *et al.* (2012) [44]							
Kalapothakos *et al.* (2012) [45]							
Singh *et al.*(2012) [46]							
Qian *et al.*(2012) [47]							
Lahbabi *et al.*(2012)[48]							
Harmandar *et al.*(2012) [49]							
Liou *et al.* (2012) [50]							
Javid *et al.* (2013) [51]							

Legend: **Green** = Low Risk of Bias; **Yellow** = Unclear Risk of Bias; **Red** = High Risk of Bias.

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Table A: Risk bias assessment of RCTs included into systematic review and meta-analysis *(continued).*

	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data	Selective reporting	Other sources of bias
Seddik *et al.* (2013)[52]							
Yep-Gamarra *et al.* (2013)[53]							
Sardarian *et al.* (2013)[54]							
McNicholl *et al.*[55]							
Liu *et al.*[56]							
Ang *et al.*[57]							
Zullo *et al.*[58]							

Legend: **Green** = Low Risk of Bias; **Yellow** = Unclear Risk of Bias; **Red** = High Risk of Bias.

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Table B. Sub-group analysis in studies comparing sequential treatment to triple therapy lasting 7 days.

	Number of studies	Number of patients	RR of eradication with ST (95% CI)	I^2	Q for difference in RR	p value for Q
Country of origin						
China	6	722	1.17 (1.09 to 1.26)	0%		
Italy	8	2578	1.23 (1.19 to 1.28)	0%		
South Korea	5	1011	1.16 (1.08 to 1.26)	0%		
Malaysia	1	100	0.86 (0.71 to 1.04)	0%		
Morocco	2	604	1.26 (1.17 to 1.36)	0%	16.824	0.002
Use of tinidazole						
ST without tinidazole	6	1283	1.13 (1.01 to 1.27)	69.8%		
ST with tinidazole	16	3732	1.22 (1.18 to 1.26)	0%	1.724	0.189
Type of publication						
Article	16	3937	1.23 (1.19 to 1.27)	0%		
Abstract	6	1078	1.13 (1.01 to 1.26)	65.5%	2.144	0.143
*Type of PPI**						
Esomeprazole	5	998	1.22 (1.15 to 1.28)	0%		
Lansoprazole	1	200	1.32 (1.07 to 1.64)	0%		
Omeprazole	5	832	1.18 (1.10 to 1.27)	0%		
Pantoprazole	1	120	1.24 (1.01 to 1.53)	0%		
Rabeprazole	8	2491	1.16 (1.07 to 1.26)	66.6%	1.950	0.745

*, two studies not included as full data on PPI used were not reported;[24,48] ST, sequential therapy; RR, relative risks; PPI, proton pump inhibitors.

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Table C. Sub-group analysis in studies comparing sequential treatment to triple therapy lasting 10 days.

	Number of studies	Number of patients	RR of eradication with ST (95% CI)	I^2	Q for difference in RR	p value for Q
Country of origin						
China	1	106	1.44 (1.13 to 1.82)	0%		
Greece	1	270	1.15 (1.01 to 1.32)	0%		
India	1	272	1.22 (1.04 to 1.44)	0%		
Iran	1	214	0.88 (0.79 to 0.99)	0%		
Italy	4	772	1.16 (1.10 to 1.23)	0%		
Peru	1	261	1.01 (0.88 to 1.16)	0%		
Singapore	1	179	0.99 (0.91 to 1.07)	0%		
South Korea	3	442	1.07 (0.95 to 1.19)	45.6%		
Spain	1	230	1.18 (1.00 to 1.40)	0%	34,06	0.000
Use of tinidazole						
ST without tinidazole	6	1158	1.06 (0.96 to 1.16)	77 %		
ST with tinidazole	8	1588	1.14 (1.05 to 1.22)	32%	1.370	0.241
Type of publication						
Article	10	1983	1.14 (1.06 to 1.22)	68.3%		
Abstract	4	763	1.03 (0.92 to 1.16)	22%	1.868	0.172
Risk of bias						
Low risk of bias	2	572	1.10 (1.02 to 1.18)	0%		

High or unclear of bias	12	2174	1.17 (1.07 to 1.27)	67.5%	0.076	0.783
*Type of PPI**						
Esomeprazole	1	143	1.15 (0.93 to 1.43)	0%		
Lansoprazole	1	159	1.29 (0.97 to 1.71)	0%		
Omeprazole	3	705	1.00 (0.88 to 1.14)	75.9%		
Pantoprazole	2	572	1.18 (1.00 to 1.38)	0%		
Rabeprazole	4	665	1.17 (1.04 to 1.31)	55.3%	4.575	0.334

*, three studies not included as full data on PPI used were not reported;[24, 45, 57] ST, sequential therapy; RR, relative risks; PPI, proton pump inhibitors.

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Table D. Sub-group analysis in studies comparing sequential treatment to triple therapy lasting 14 days.

	Number of studies	Number of patients	RR of eradication with ST (95% CI)	I^2	Q for difference in RR	p value for Q
Country of origin						
Chile°	1	139	0.98 (0.82 to 1.18)	0%		
China	1	103	1.00 (0.80 to 1.24)	0%		
Colombia°	1	140	0.95 (0.78 to 1.17)	0%		
Costa Rica°	1	140	1.03 (0.87 to 1.22)	0%		
Honduras°	1	141	0.866 (0.72 to 1.02)	0%		
Mexico°	2	282	0.862 (0.72 to 1.02)	0%		
Nicaragua°	1	132	0.94 (0.73 to 1.22)	0%		
South Korea	3	694	1.02 (0.93 to 1.12)	54.8%		
Taiwan	1	600	1.07 (0.92 to 1.25)	0%		
Turkey	1	80	1.32 (1.08 to 1.69)	0%	8.768	0.459
Use of tinidazole						
ST without tinidazole	4	2063	0.99 (0.91 to 1.07)	65.7%		
ST with tinidazole	3	388	0.99 (0.89 to 1.10)	0%	0.005	0.941
Type of publication						
Article	5	2316	0.97 (0.90 to 1.03)	49.1%		
Abstract	2	135	1.12 (0.95 to 1.22)	58.5%	2.266	0.132
*Type of PPI**						

Esomeprazole	1	103	1.02 (0.80 to 1.24)	0%		
Lansoprazole	2	1574	0.96 (0.86 to 1.14)	83%		
Pantoprazole	2	489	1.14 (0.93 to 1.40)	0%		
Rabeprazole	1	230	0.94 (0.82 to 1.08)	0%	1.802	0.614

°, sub-groups of the same study;[34] *, one study not included as full data on PPI used were not reported;[24] ST, sequential therapy; RR, relative risks; PPI, proton pump inhibitors.

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Table E. Sub-group analysis in studies comparing sequential treatment to non-bismuth quadruple therapy.

	Number of studies	Number of patients	RR of eradication with ST (95% CI)	I^2	Q for difference in RR	p value for Q
Country of origin						
Chile°	1	140	1.28 (1.05 to 1.56)	0%		
Colombia°	1	141	0.97 (0.82 to 1.15)	0%		
Costa Rica°	1	140	1.16 (1.05 to 1.35)	0%		
Honduras°	1	143	0.94 (0.82 to 1.09)	0%		
Italy	1	180	1.06 (0.95 to 1.18)	0%		
México°	2	279	0.94 (0.80 to 1.11)	0%		
Nicaragua°	1	132	1.05 (0.82 to 1.34)	0%		
Singapore	1	176	0.95 (0.89 to 1.02)	0%		
Spain	1	338	0.93 (0.85 to 1.02)	0%		
Taiwan	2	401	0.97 (0.91 to 1.03)	24.4%	16.6	0.04
Risk of bias						
Low risk of bias	1	338	0.93 (0.83 to 1.04)	0%		
High risk of bias	5	1732	0.99 (0.93 to 1.05)	32.7%	0.369	0.544
*Type of PPI**						
Lansoprazole	2	1144	0.90 (0.78 to 1.05)	67.0%		
Omeprazole	2	518	0.99 (0.92 to 1.06)	69.6%		
Esomeprazole	1	232	0.99 (0.92 to 1.06)	0%	2.128	0.345

Duration of NBQT						
Duration of 10 days	4	915	0.91 (0.91 to 1.00)	0%		
Duration of 5 days	2	1155	1.04 (0.98 to 1.11)	32.2%	5.597	0.098
Type of publication						
Article	5	1894	0.97 (0.92 to 1.04)	38.4%		
Abstract	1	176	0.99 (0.91 to 1.08)	0%	0.138	0.710
Use of tinidazole						
ST without tinidazole	5	1890	0.97 (0.93 to 1.02)	25.8%		
ST with tinidazole	1	180	1.06 (0.94 to 1.19)	0%	1.850	0.174

°, sub-groups of the same study;[34] *, one study not included as full data on PPI used were not reported;[57] ST, sequential therapy; RR, relative risks; PPI, proton pump inhibitors.

Supplementary Material

Table F. Eradication rates in strains with primary resistance to clarithromycin.

	Strains resistant to clarithromycin			
Studies	Eradication Rate ST (n=33)	*vs.* Eradication Rate TT-7 (n=34)		Difference
Zullo *et al.* (2003)[6] Gatta *et al.* (2011)[36]	87.8% (95% CI: 71.9 to 96.5)	38.2% (95% CI: 22.1 to 56.4)		49.6% (95% CI: 27.7 to 66.9)
	Eradication Rate ST (n= 17)	*vs.* Eradication Rate TT-10 (n=30)		Difference
Vaira *et al.* (2007)[7] Chung *et al*. (2012)[44]	76.4% (95% CI: 50.1 to 93.1)	26.6% (95% CI: 12.2 to 45.8)		49.8% (95% CI: 20.3 to 70.5)
	Eradication Rate ST (n= 17)	*vs.* Eradication Rate TT-14 (n=20)		Difference
Liou *et al.* (2012)[50]	58.8% (95% CI:32.9 to 81.5)	55% (95% CI: 31.5 to 76.9)		3.8% (95% CI: -27.5 to 34.1)
	Eradication Rate ST (n= 12)	*vs.* Eradication Rate NBQT (n= 7)		Difference
Wu *et al.* (2010)[31] Huang *et al.*(2012)[41]	58.3% (95% CI: 27.6 to 84.8)	85.7% (95% CI: 42.1 to 99.6)		-27.4% (95% CI: -59.9 to 18.4)
	Eradication Rate ST (n=12)	*vs. ST-Levo 250[(a)] (n=13)*	*ST Levo 500[(b)] (n=14)*	Difference
Romano *et al.*(2010)[32]	75% (95% CI: 42.8 to 94.5)	100% (95% CI: 75.2 to 100)	100% (95% CI: 76.3 to 100)	[(a)]: -25% (95% CI: -53.7 to 1.6) [(b)]: -25% (95% CI: -53.7 to 0.19)

ST, sequential therapy; TT-7, triple therapy lasting 7 days; TT-10, triple therapy lasting 10 days; NBQT, non-bismuth quadruple therapy; (a), 250 two times daily; (b), 500 two times daily.

Supplementary Material

Table G. Eradication rates in strains with primary resistance to metronidazole.

	Strains resistant to metronidazole			
Studies	Eradication Rate ST (n=36)	*vs.* Eradication Rate TT-7 (n=37)		Difference
Zullo *et al.* (2003)[6]	94.4% (95% CI: 81.3 to 99.3)	70.2% (95% CI: 53 to 84.1)		24.2% (95% CI: 7.2 to 41.3)
	Eradication Rate ST (n=50)	*vs.* Eradication Rate TT-10 (n=44)		Difference
Vaira *et al.* (2007)[7] Chung *et al.* (2012)[44]	92% (95% CI: 80.7 to 97.7)	75% (95% CI: 59.6 to 86.8)		17% (95% CI: 2.1 to 32.7)
	Eradication Rate ST (n=44)	*vs.* Eradication Rate TT-14 (n=46)		Difference
Liou *et al.* (2012)[50]	72.7% (95% CI:57.2 to 85)	89.1% (95% CI: 76.4 to 96.3)		-16.4% (95% CI: -32.8 to -0.14)
	Eradication Rate ST (n=48)	*vs.* Eradication Rate NBQT (n=42)		Difference
Wu *et al.* (2010)[31] Huang *et al.* (2012)[41]	85.4% (95% CI: 72.2 to 93.9)	95.2% (95% CI: 83.3 to 99.4)		-9.8% (95% CI: -23.3 to 3.2)
	Eradication Rate ST (n=14)	*vs.* *ST-Levo 250[(a)] (n=19)*	*ST Levo 500[(b)] (n=17)*	Difference
Romano *et al.*(2010)[32]	92.8% (95% CI: 66.1 to 99.8)	100% (95% CI: 82.3 to 100)	100% (95% CI: 80.4 to 100)	[(a)]: -7.2% (95% CI: -31.9 to 10.8) [(b)]: -7.2% (95% CI: -31.9 to 12.5)

ST, sequential therapy; TT-7, triple therapy lasting 7 days; TT-10, triple therapy lasting 10 days; NBQT, non-bismuth quadruple therapy; (a), 250 two times daily; (b), 500 two times daily.

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Table H. Eradication rates in strains with primary resistance to clarithromycin and metronidazole.

	Strains resistant to clarithromycin and metronidazole			
Studies	Eradication Rate ST (n=10)	*vs.* Eradication Rate TT-7 (n=5)		Difference
Zullo *et al.* (2003)[6]	80% (95% CI: 44.3 to 97.4)	40% (95% CI: 5.2 to 85.3)		40% (95% CI: -11.3 to 76.5)
	Eradication Rate ST (n=7)	*vs.* Eradication Rate TT-10 (n=13)		Difference
Vaira *et al.* (2007)[7] Chung *et al*. (2012)[44]	14.2% (95% CI: 0.3 to 57.8)	15.3% (95% CI: 1.9 to 45.5)		-1.1% (95% CI: -33 to 40.1)
	Eradication Rate ST (n=7)	*vs.* Eradication Rate TT-14 (n=4)		Difference
Liou *et al.* (2012)[50]	42.8% (95% CI:9.8 to 81.5)	50% (95% CI: 6.7 to 93.2)		-7.2% (95% CI: -58.7 to 47.5)
	Eradication Rate ST (n=7)	*vs.* Eradication Rate NBQT (n=6)		Difference
Wu *et al.* (2010)[31] Huang *et al.*(2012)[41]	42.8% (95% CI: 9.8 to 81.5)	83.3% (95% CI: 35.8 to 99.5)		-40.5 (95% CI: -76 to 14.7)
	Eradication Rate ST (n=3)	*vs.* *ST-Levo 250[(a)] (n=4)*	*ST Levo 500[(b)] (n=4)*	Difference
Romano *et al.*(2010)[32]	0% (95% CI: 0 to 0.70)	100% (95% CI: 39.7to 100)	100% (95% CI: 39.7to 100)	[(a & b)]: -100% (95% CI: -100 to -23.1)

ST, sequential therapy; TT-7, triple therapy lasting 7 days; TT-10, triple therapy lasting 10 days; NBQT, non-bismuth quadruple therapy; (a), 250 two times daily; (b), 500 two times daily.

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Table I. Eradication rates in strains with primary resistance to levofloxacin.

	Strains resistant to levofloxacin			
	Eradication Rate ST (n=2)	*vs.* *ST-Levo 250[(a)] (n=2)*	*ST Levo 500[(b)] (n=3)*	Difference
Romano *et al.*(2010)[32]	50% (95% CI: 1.2 to 98.7)	50% (95% CI: 1.2 to 98.7)	66.6% (95% CI: 9.4 to 90.5)	[(a)]: 0 % (95% CI:-74.9 to 74.9) [(b)]: -16.6% (95% CI: -78.6 to 60.1)

ST, sequential therapy; TT-7; (a), 250 two times daily; (b), 500 two times daily.