Studies Included in the Systematic Review and Meta-Analysis (Chronological Order)

1. Boyanova L, Gergova G, Nikolov R, et al. Prevalence and evolution of *Helicobacter pylori* resistance to 6 antibacterial agents over 12 years and correlation between susceptibility testing methods. Diagn Microbiol Infect Dis 2008;60:409–415.
2. Khashei R, Shojaei H, Adibi P, et al. Genetic diversity and drug resistance of *Helicobacter pylori* strains in Isfahan, Iran. Iran J Basic Med Sci 2008;11:174–182.
3. Ndip RN, Malange Takang AE, Ojongokpoko JE, et al. *Helicobacter pylori* isolates recovered from gastric biopsies of patients with gastro-duodenal pathologies in Cameroon: current status of antibiogram. Tropic Med Int Health 2008;13:848–854.
4. Ahmad N, Zakaria WR, Abdullah SA, et al. Characterization of clarithromycin resistance in Malaysian isolates of *Helicobacter pylori*. World J Gastroenterol 2009; 15:3161–3165.
5. Andrzejewska E, Szkaradkiewicz A, Karpinski T. Antimicrobial resistance of *Helicobacter pylori* clinical strains in the last 10 years. Polish J Microbiol 2009; 58:301–305.
6. Horiki N, Omata F, Uemura M, et al. Annual change of primary resistance to clarithromycin among *Helicobacter pylori* isolates from 1996 through 2008 in Japan. Helicobacter 2009;14:86–90.
7. Kuo CH, Hu HM, Kuo FC, et al. Efficacy of levofloxacin-based rescue therapy for *Helicobacter pylori* infection after standard triple therapy: a randomized controlled trial. J Antimicrob Chemother 2009;63:1017–1024.
8. Singh V, Mishra S, Maurya P, et al. Drug resistance pattern and clonality in *H. pylori* strains. J Infect Dev Ctries 2009;3:130–136.
9. Tanuma M, Rimbara E, Noguchi N, et al. Analysis of clarithromycin resistance and CagA status in *Helicobacter pylori* by use of feces from children in Thailand. J Clin Microbiol 2009;47:4144–4145.
10. Tonkic A, Tonkic M, Brnic D. Increasing prevalence of primary clarithromycin resistance in *Helicobacter pylori* strains in Split, Croatia. J Chemother 2009;21: 5984–589.
11. Woo HY, Park DI, Park H, et al. Dual-priming oligonucleotide-based multiplex PCR for the detection of *Helicobacter pylori* and determination of clarithromycin resistance with gastric biopsy specimens. Helicobacter 2009;14:224–228.
12. Wueppenhorst N, Stueger HP, Kist M, et al. Identification and molecular characterization of triple- and quadruple-resistant *Helicobacter pylori* clinical isolates in Germany. J Antimicrob Chemother 2009;63:6484–6653.
13. Xuan SH, Zhou YG, Shao B, et al. Enzymic colorimetry-based DNA chip: a rapid and accurate assay for detecting mutations for clarithromycin resistance in the 23S rRNA gene of *Helicobacter pylori*. J Med Microbiol 2009;58(Pt 11). 14434–1448.
14. Agudo S, Perez-Perez G, Alarcon T, et al. High prevalence of clarithromycin-resistant *Helicobacter pylori* strains and risk factors associated with resistance in Madrid, Spain. J Clin Microbiol 2010;48. 37034–3707.
15. Bago J, Majstorovic K, Belosic-Halle Z, et al. Antimicrobial resistance of H. pylori to the outcome of 10-days vs. 7-days moxifloxacin based therapy for the eradication: a randomized controlled trial. Ann Clin Microbiol Antimicrob 2010;9. 134–118.
16. Boyanova L, Nikolov R, Gergova G, et al. Two-decade trends in primary *Helicobacter pylori* resistance to antibiotics in Bulgaria. Diagn Microbiol Infect Dis 2010; 67:319–326.
17. Farshad S, Alborzi A, Japoni A, et al. Antimicrobial susceptibility of *Helicobacter pylori* strains isolated from patients in Shiraz, Southern Iran. World J Gastroenterol 2010;16:5746–5751.
18. Gao W, Cheng H, Hu F, et al. The evolution of *Helicobacter pylori* antibiotics resistance over 10 years in Beijing, China. Helicobacter 2010;15:460–466.
19. Haghi Tomatari F, Mohabbati Mobarez A, Amini M, et al. *Helicobacter pylori* resistance to metronidazole and clarithromycin in dyspeptic patients in Iran. Iran Red Crescent Med J 2010;12:409–412.
20. Hwang TJ, Kim N, Kim HB, et al. Change in antibiotic resistance of *Helicobacter pylori* strains and the effect of A2143G point mutation of 23S rRNA on the eradication of H. pylori in a single center of Korea. J Clin Gastroenterol 2010;44:536–543.
21. Lins AK, Lima RA, Magalhaes M. Clarithromycin-resistant *Helicobacter pylori* in Recife, Brazil, directly identified from gastric biopsies by polymerase chain reaction. Arq Gastroenterol 2010;47:379–382.
22. Liou JM, Lin JT, Chang CY, et al. Levofloxacin-based and clarithromycin-based triple therapies as first-line and second-line treatments for *Helicobacter pylori* infection: a randomised comparative trial with crossover design. Gut 2010;59:572–578.
23. O'Connor A, Taneike I, Nami A, et al. *Helicobacter pylori* resistance to metronidazole and clarithromycin in Ireland. Eur J Gastroenterol Hepatol 2010;22: 1123–1127.
24. Raymond J, Lamarque D, Kalach N, et al. High level of antimicrobial resistance in French *Helicobacter pylori* isolates. Helicobacter 2010;15:21–27.
25. Romano M, Cuomo A, Gravina AG, et al. Empirical levofloxacin-containing versus clarithromycin-containing sequential therapy for *Helicobacter pylori* eradication: a randomised trial. Gut 2010;59:1465–1470.
26. Siavoshi F, Saniee P, Latifi-Navid S, et al. Increase in resistance rates of *H. pylori* isolates to metronidazole and tetracycline—comparison of three 3-year studies. Arch Iran Med 2010;13:177–187.
27. Sirimontaporn N, Thong-Ngam D, Tumwasorn S, et al. Ten-day sequential therapy of *Helicobacter pylori* infection in Thailand. Am J Gastroenterol 2010;105: 1071–1075.
28. Sun QJ, Liang X, Zheng Q, et al. Resistance of *Helicobacter pylori* to antibiotics from 2000 to 2009 in Shanghai. World J Gastroenterol 2010;16:5118–5121.
29. Vecsei A, Innerhofer A, Binder C, et al. Stool polymerase chain reaction for *Helicobacter pylori* detection and

clarithromycin susceptibility testing in children. Clin Gastroenterol Hepatol 2010;8:309–312.
30. Wang LH, Cheng H, Hu FL, et al. Distribution of gyrA mutations in fluoroquinolone-resistant *Helicobacter pylori* strains. World J Gastroenterol 2010;16:2272–2277.
31. Wu DC, Hsu PI, Wu JY, et al. Sequential and concomitant therapy with four drugs is equally effective for eradication of *H pylori* infection. Clin Gastroenterol Hepatol 2010;8:36–41.
32. Yakoob J, Abid S, Abbas Z, et al. Antibiotic susceptibility patterns of *Helicobacter pylori* and triple therapy in a high-prevalence area. Br J Biomed Sci 2010;67: 197–201.
33. Zevit N, Levy I, Shmuely H, et al. Antibiotic resistance of *Helicobacter pylori* in Israeli children. Scand J Gastroenterol 2010;45:550–555.
34. Zheng Q, Chen WJ, Lu H, et al. Comparison of the efficacy of triple versus quadruple therapy on the eradication of Helicobacter pylori and antibiotic resistance. J Digest Dis 2010;11:313–318.
35. Abadi AT, Taghvaei T, Mobarez AM, et al. Frequency of antibiotic resistance in *Helicobacter pylori* strains isolated from the northern population of Iran. J Microbiol 2011;49:987–993.
36. Agudo S, Perez-Perez G, Alarcon T, et al. Rapid detection of clarithromycin resistant *Helicobacter pylori* strains in Spanish patients by polymerase chain reaction-restriction fragment length polymorphism. Rev Esp Quimioter 2011;24:32–36.
37. Bontems P, Kalach N, Oderda G, et al. Sequential therapy versus tailored triple therapies for *Helicobacter pylori* infection in children. J Pediatr Gastroenterol Nutr 2011;53:646–650.
38. De Francesco V, Giorgio F, Ierardi E, Zotti M, Neri M, Milano A, et al. Primary clarithromycin resistance in *Helicobacter pylori:* the Multicentric Italian Clarithromycin Resistance Observational (MICRO) study. J Gastrointest Liver Dis 2011;20:235–239.
39. Goh KL, Navaratnam P. High *Helicobacter pylori* resistance to metronidazole but zero or low resistance to clarithromycin, levofloxacin, and other antibiotics in Malaysia. Helicobacter 2011;16:241–245.
40. Karczewska E, Wojtas-Bonior I, Sito E, et al. Primary and secondary clarithromycin, metronidazole, amoxicillin and levofloxacin resistance to *Helicobacter pylori* in southern Poland. Pharmacol Rep 2011;63:799–807.
41. Lehours P, Siffre E, Megraud F. DPO multiplex PCR as an alternative to culture and susceptibility testing to detect *Helicobacter pylori* and its resistance to clarithromycin. BMC Gastroenterol 2011;11:112.
42. Liou JM, Chen CC, Chen MJ, et al. Empirical modified sequential therapy containing levofloxacin and high-dose esomeprazole in second-line therapy for *Helicobacter pylori* infection: a multicentre clinical trial. J Antimicrob Chemother 2011;66:1847–1852.
43. Liu G, Xu X, He L, et al. Primary antibiotic resistance of *Helicobacter pylori* isolated from Beijing children. Helicobacter 2011;16:356–362.
44. Miendje Deyi VY, Bontems P, Vanderpas J, et al. Multicenter survey of routine determinations of resistance of *Helicobacter pylori* to antimicrobials over the last 20 years (1990 to 2009) in Belgium. J Clin Microbiol 2011; 49:2200–2209.
45. Vecsei A, Innerhofer A, Graf U, et al. *Helicobacter pylori* eradication rates in children upon susceptibility testing based on noninvasive stool polymerase chain reaction versus gastric tissue culture. J Pediatr Gastroenterol Nutr 2011;53:65–70.
46. Vilaichone RK, Mahacahai V, Tumwasorn S, et al. CagA genotype and metronidazole resistant strain of *Helicobacter pylori* in functional dyspepsia in Thailand. J Gastroenterol Hepatol 2011;26(Suppl 3):46–48.
47. Yakoob J, Jafri W, Abbas Z, et al. Risk factors associated with *Helicobacter pylori* infection treatment failure in a high prevalence area. Epidemiol Infect 2011;139: 581–590.
48. Chung JW, Jung YK, Kim YJ, et al. Ten-day sequential versus triple therapy for *Helicobacter pylori* eradication: a prospective, open-label, randomized trial. J Gastroenterol Hepatol 2012;27:1675–1680.
49. Chung JW, Lee GH, Jeong JY, et al. Resistance of *Helicobacter pylori* strains to antibiotics in Korea with a focus on fluoroquinolone resistance. J Gastroenterol Hepatol 2012;27:493–497.
50. Cuadrado-Lavin A, Salcines-Caviedes JR, Carrascosa MF, et al. Antimicrobial susceptibility of *Helicobacter pylori* to six antibiotics currently used in Spain. J Antimicrob Chemother 2012;67:170–173.
51. Federico A, Nardone G, Gravina AG, et al. Efficacy of 5-day levofloxacin-containing concomitant therapy in eradication of *Helicobacter pylori* infection. Gastroenterology 2012;143:55–61.
52. Hansomburana P, Anantapanpong S, Sirinthornpunya S, et al. Prevalence of single nucleotide mutation in clarithromycin resistant gene of *Helicobacter pylori*: a 32-months prospective study by using hybridization real time polymerase chain reaction. J Med Assoc Thailand 2012;95(Suppl 3):S28–S35.
53. Huang YK, Wu MC, Wang SS, et al. Lansoprazole-based sequential and concomitant therapy for the first-line *Helicobacter pylori* eradication. J Digest Dis 2012; 13:232–238.
54. Karczewska E, Klesiewicz K, Skiba I, et al. Variability in prevalence of *Helicobacter pylori* strains resistant to clarithromycin and levofloxacin in southern Poland. Gastroenterol Res Pract 2012; article ID418010.
55. Khan A, Farooqui A, Manzoor H, et al. Antibiotic resistance and cagA gene correlation: a looming crisis of *Helicobacter pylori*. World J Gastroenterol 2012; 18(18):2245–2452.
56. McNulty CA, Lasseter G, Shaw I, et al. Is *Helicobacter pylori* antibiotic resistance surveillance needed and how can it be delivered? Aliment Pharmacol Ther 2012; 35:1221–1230.
57. Milani M, Ghotaslou R, Akhi MT, et al. The status of antimicrobial resistance of *Helicobacter pylori* in Eastern Azerbaijan, Iran: comparative study according to demographics. J Infect Chemother 2012;18:848–852.
58. Molina-Infante J, Pazos-Pacheco C, Vinagre-Rodriguez G, et al. Nonbismuth quadruple (concomitant)

therapy: empirical and tailored efficacy versus standard triple therapy for clarithromycin-susceptible *Helicobacter pylori* and versus sequential therapy for clarithromycin-resistant strains. Helicobacter 2012;17:269–276.
59. Rajper S, Khan E, Ahmad Z, et al. Macrolide and fluoroquinolone resistance in *Helicobacter pylori* isolates: an experience at a tertiary care centre in Pakistan. J Pak Med Assoc 2012;62:1140–1144.
60. Saracino IM, Zullo A, Holton J, et al. High prevalence of primary antibiotic resistance in *Helicobacter pylori* isolates in Italy. J Gastrointest Liver Dis 2012;21:363–365.
61. Talebi Bezmin Abadi A, Ghasemzadeh A, Taghvaei T, et al. Primary resistance of *Helicobacter pylori* to levofloxacin and moxifloxacine in Iran. Intern Emerg Med 2012;7:447–452.
62. Tay CY, Windsor HM, Thirriot F, et al. *Helicobacter pylori* eradication in Western Australia using novel quadruple therapy combinations. Aliment Pharmacol Ther 2012;36:1076–1083.
63. Tonkic A, Tonkic M, Brnic D, et al. Time trends of primary antibiotic resistance of *Helicobacter pylori* isolates in Southern Croatia. J Chemother 2012;24:182–184.
64. Zhou YQ, Xu L, Wang BF, et al. Modified sequential therapy regimen versus conventional triple therapy for *Helicobacter Pylori* eradication in duodenal ulcer patients in China: a multicenter clinical comparative study. Gastroenterol Res Pract 2012;2012:article ID405425.
65. An B, Moon BS, Kim H, et al. Antibiotic resistance in *Helicobacter pylori* strains and its effect on *H. pylori* eradication rates in a single center in Korea. Ann Lab Med 2013;33:415–419.
66. Binh TT, Shiota S, Nguyen LT, et al. The incidence of primary antibiotic resistance of *Helicobacter pylori* in Vietnam. J Clin Gastroenterol 2013;47:233–238.
67. Cosme A, Montes M, Martos M, et al. Usefulness of antimicrobial susceptibility in the eradication of *Helicobacter pylori*. Clin Microbiol Infect 2013;19:379–383.
68. Georgopoulos SD, Xirouchakis E, Martinez-Gonzalez B, et al. Clinical evaluation of a ten-day regimen with esomeprazole, metronidazole, amoxicillin, and clarithromycin for the eradication of *Helicobacter pylori* in a high clarithromycin resistance area. Helicobacter 2013;18:459–467.
69. Hsiang J, Selvaratnam S, Taylor S, et al. Increasing primary antibiotic resistance and ethnic differences in eradication rates of *Helicobacter pylori* infection in New Zealand—a new look at an old enemy. N Z Med J 2013;126(1384):64–76.
70. Khademi F, Faghri J, Poursina F, et al. Resistance pattern of *Helicobacter pylori* strains to clarithromycin, metronidazole, and amoxicillin in Isfahan, Iran. J Res Med Sci 2013;18:1056–1060.
71. Kupcinskas L, Rasmussen L, Jonaitis L, et al. Evolution of *Helicobacter pylori* susceptibility to antibiotics during a 10-year period in Lithuania. APMIS 2013;121:431–436.
72. Lee JW, Kim N, Kim JM, et al. Prevalence of primary and secondary antimicrobial resistance of *Helicobacter pylori* in Korea from 2003 through 2012. Helicobacter 2013;18:206–214.
73. Liang X, Xu X, Zheng Q, et al. Efficacy of bismuth-containing quadruple therapies for clarithromycin-, metronidazole-, and fluoroquinolone-resistant *Helicobacter pylori* infections in a prospective study. Clin Gastroenterol Hepatol 2013;11:802–807.
74. Liao J, Zheng Q, Liang X, et al. Effect of fluoroquinolone resistance on 14-day levofloxacin triple and triple plus bismuth quadruple therapy. Helicobacter 2013;18:373–377.
75. Liou JM, Chen CC, Chen MJ, et al. Sequential versus triple therapy for the first-line treatment of *Helicobacter pylori:* a multicentre, open-label, randomised trial. Lancet 2013;381(9862):205–213.
76. Loffeld RJ, Werdmuller BF. Changes in antibiotic susceptibility of *Helicobacter pylori* in the course of eight years in the Zaanstreek Region in The Netherlands. Gastroenterol Res Pract 2013;2013:article ID625937.
77. Megraud F, Coenen S, Versporten A, et al. *Helicobacter pylori* resistance to antibiotics in Europe and its relationship to antibiotic consumption. Gut 2013;62:34–42.
78. Molina-Infante J, Romano M, Fernandez-Bermejo M, et al. Optimized nonbismuth quadruple therapies cure most patients with *Helicobacter pylori* infection in populations with high rates of antibiotic resistance. Gastroenterology 2013;145:121–128.
79. Morse AL, Goodman KJ, Munday R, et al. A randomized controlled trial comparing sequential with triple therapy for *Helicobacter pylori* in an Aboriginal community in the Canadian North. Can J Gastroenterol 2013;27:701–706.
80. Murakami K, Furuta T, Ando T, et al. Multi-center randomized controlled study to establish the standard third-line regimen for *Helicobacter pylori* eradication in Japan. J Gastroenterol 2013;48(10):1128–1135.
81. O'Connor A, Taneike I, Nami A, et al. *Helicobacter pylori* resistance rates for levofloxacin, tetracycline and rifabutin among Irish isolates at a reference centre. Irish J Med Sci 2013;182:693–695.
82. Ogata SK, Godoy AP, da Silva Patricio FR, et al. High *Helicobacter pylori* resistance to metronidazole and clarithromycin in Brazilian children and adolescents. J Pediatr Gastroenterol Nutr 2013;56:645–648.
83. Sadeghifard N, Seidnazari T, Ghafourian S, et al. Survey in Iran of clarithromycin resistance in *Helicobacter pylori* isolates by PCR-RFLP. Southeast Asian J Trop Med Public Health 2013;44:89–95.
84. Seck A, Burucoa C, Dia D, et al. Primary antibiotic resistance and associated mechanisms in *Helicobacter pylori* isolates from Senegalese patients. Ann Clin Microbiol Antimicrob 2013;12:3.
85. Su P, Li Y, Li H, Zhang J, et al. Antibiotic resistance of *Helicobacter pylori* isolated in the Southeast coastal region of China. Helicobacter 2013;18:274–279.
86. Trespalacios AA, Otero W, Caminos JE, et al. Phenotypic and genotypic analysis of clarithromycin-resistant *Helicobacter pylori* from Bogota DC, Colombia. J Microbiol 2013;51:448–452.
87. Vekens K, Vandebosch S, De Bel A, et al. Primary antimicrobial resistance of *Helicobacter pylori* in Belgium. Acta Clin Belg 2013;68:183–187.

88. Vilaichone RK, Yamaoka Y, Shiota S, et al. Antibiotics resistance rate of *Helicobacter pylori* in Bhutan. World J Gastroenterol 2013;19:5508–5512.
89. Wueppenhorst N, Stueger HP, Kist M, et al. High secondary resistance to quinolones in German *Helicobacter pylori* clinical isolates. J Antimicrob Chemother 2013; 68:1562–1566.
90. Yula E, Nagiyev T, Kaya OA, et al. Detection of primary clarithromycin resistance of *Helicobacter pylori* and association between cagA (+) status and clinical outcome. Folia Microbiol 2013;58:141–146.
91. Zendedel A, Moradimoghadam F, Almasi V, et al. Antibiotic resistance of *Helicobacter pylori* in Mashhad, Iran. J Pak Med Assoc 2013;63:336–339.
92. Boyanova L, Davidkov L, Gergova G, et al. *Helicobacter pylori* susceptibility to fosfomycin, rifampin, and 5 usual antibiotics for *H. pylori* eradication. Diagn Microbiol Infect Dis 2014;79:358–361.
93. Karamanolis GP, Daikos GL, Xouris D, et al. The evolution of *Helicobacter pylori* antibiotics resistance over 10 years in Greece. Digestion 2014;90:229–231.
94. Keshavarz Azizi Raftar S, Moniri R, Saffari M, et al. *Helicobacter pylori* resistance to ciprofloxacin in Iran. Int J Antimicrob Agents 2014;43:573–574.
95. Kutluk G, Tutar E, Bayrak A, et al. Sequential therapy versus standard triple therapy for *Helicobacter pylori* eradication in children: any advantage in clarithromycin-resistant strains? Eur J Gastroenterol Hepatol 2014; 26:1202–1208.
96. Lee JY, Kim N, Kim MS, et al. Factors affecting first-line triple therapy of *Helicobacter pylori* including CYP2C19 genotype and antibiotic resistance. Digest Dis Sci 2014; 59:1235–1243.
97. Martos M, Bujanda L, Salicio Y, et al. Clarithromycin for first-line treatment of *Helicobacter pylori* infection after culture in high-resistance regions. Eur J Gastroenterol Hepatol 2014;26:1380–1384.
98. Ogata SK, Gales AC, Kawakami E. Antimicrobial susceptibility testing for *Helicobacter pylori* isolates from Brazilian children and adolescents: comparing agar dilution, E-test, and disk diffusion. Braz J Microbiol 2014; 45:1439–1448.
99. Park CS, Lee SM, Park CH, et al. Pretreatment antimicrobial susceptibility-guided vs. clarithromycin-based triple therapy for *Helicobacter pylori* eradication in a region with high rates of multiple drug resistance. Am J Gastroenterol 2014;109:1595–1602.
100. Peretz A, Paritsky M, Nasser O, et al. Resistance of *Helicobacter pylori* to tetracycline, amoxicillin, clarithromycin and metronidazole in Israeli children and adults. J Antibiotics 2014; 67L555–L557.
101. Picoli SU, Mazzoleni LE, Fernandez H, et al. Resistance to amoxicillin, clarithromycin and ciprofloxacin of *Helicobacter pylori* isolated from Southern Brazil patients. Rev Inst Med Trop Sao Paulo 2014;56:197–200.
102. Selgrad M, Tammer I, Langner C, et al. Different antibiotic susceptibility between antrum and corpus of the stomach, a possible reason for treatment failure of *Helicobacter pylori* infection. World J Gastroenterol 2014;20:16245–16251.
103. Wuppenhorst N, Draeger S, Stuger HP, et al. Prospective multicentre study on antimicrobial resistance of *Helicobacter pylori* in Germany. J Antimicrob Chemother 2014;69:3127–3133.
104. Zhao LJ, Huang YQ, Chen BP, et al. *Helicobacter pylori* isolates from ethnic minority patients in Guangxi: resistance rates, mechanisms, and genotype. World J Gastroenterol 2014;20:4761–4770.
105. Zhou L, Zhang J, Chen M, et al. A comparative study of sequential therapy and standard triple therapy for *Helicobacter pylori* infection: a randomized multicenter trial. Am J Gstroenterol 2014;109:535–541.
106. Alsohaibani F, Al Ashgar H, Al Kahtani K, et al. Prospective trial in Saudi Arabia comparing the 14-day standard triple therapy with the 10-day sequential therapy for treatment of *Helicobacter pylori* infection. Saudi J Gastroenterol 2015;21:220–225.
107. Bai P, Zhou LY, Xiao XM, et al. Susceptibility of *Helicobacter pylori* to antibiotics in Chinese patients. J Digest Dis 2015;16:464–470.
108. Boltin D, Ben-Zvi H, Perets TT, et al. Trends in secondary antibiotic resistance of *Helicobacter pylori* from 2007 to 2014: has the tide turned? J Clin Microbiol 2015;53: 522–527.
109. Boyanova L, Evstatiev I, Gergova G, et al. Linezolid susceptibility in *Helicobacter pylori,* including strains with multidrug resistance. Int J Antimicrob Agents 2015; 46:703–706.
110. Caliskan R, Tokman HB, Erzin Y, et al. Antimicrobial resistance of *Helicobacter pylori* strains to five antibiotics, including levofloxacin, in Northwestern Turkey. Rev Soc Bras Med Trop 2015;48:278–284.
111. Cao Z, Chen Q, Zhang W, et al. Fourteen-day optimized levofloxacin-based therapy versus classical quadruple therapy for *Helicobacter pylori* treatment failures: a randomized clinical trial. Scand J Gastroenterol 2015; 50:1185–1190.
112. Chen KY, Lin TJ, Lin CL, et al. Hybrid vs sequential therapy for eradication of *Helicobacter pylori* in Taiwan: a prospective randomized trial. World J Gastroenterol 2015;21:10435–10442.
113. Cheng A, Sheng WH, Liou JM, et al. Comparative in vitro antimicrobial susceptibility and synergistic activity of antimicrobial combinations against *Helicobacter pylori* isolates in Taiwan. J Microbiol Immunol Infect 2015; 48:72–79.
114. Dong F, Ji D, Huang R, et al. Multiple genetic analysis system-based antibiotic susceptibility testing in Helicobacter pylori and high eradication rate with phenotypic resistance-guided quadruple therapy. Medicine 2015; 94(47):e2056.
115. Hsu PI, Kao SS, Wu DC, et al. A randomized controlled study comparing reverse hybrid therapy and standard triple therapy for Helicobacter pylori Infection. Medicine 2015;94(48):e2104.
116. Kalach N, Gosset P, Dehecq E, et al. Usefulness of gastric biopsy-based real-time polymerase chain reaction for the diagnosis of *Helicobacter pylori* infection in children. J Pediatr Gastroenterol Nutr 2015;61: 307–312.

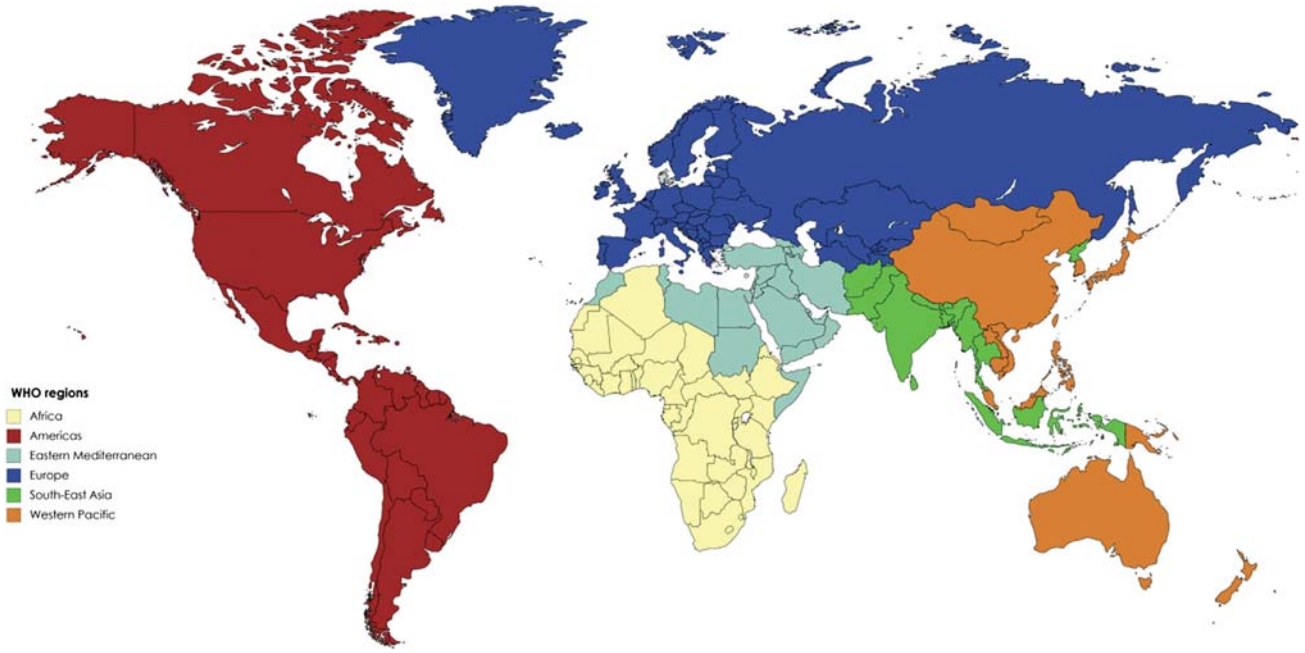
117. Keshavarz Azizi Raftar S, Moniri R, Saffari M, et al. The *Helicobacter pylori* resistance rate to clarithromycin in Iran. Microb Drug Resist 2015;21:69–73.
118. Liou JM, Chang CY, Chen MJ, et al. The primary resistance of *Helicobacter pylori* in Taiwan after the national policy to restrict antibiotic consumption and its relation to virulence factors–a nationwide study. PLoS One 2015; 10(5):e0124199.
119. Liu Q, Qi D, Kang J, et al. Efficacy of real-time PCR-based detection of *Helicobacter pylori* infection and genotypic resistance-guided quadruple therapy as the first-line treatment for functional dyspepsia with *Helicobacter pylori* infection. Eur J Gastroenterol Hepatol 2015;27:221–225.
120. Navarro-Jarabo JM, Fernandez-Sanchez F, Fernandez-Moreno N, et al. Prevalence of primary resistance of *Helicobacter pylori* to clarithromycin and levofloxacin in southern Spain. Digestion 2015;92:78–82.
121. Ontsira Ngoyi EN, Atipo Ibara BI, Moyen R, et al. Molecular detection of *Helicobacter pylori* and its antimicrobial resistance in Brazzaville, Congo. Helicobacter 2015;20:316–320.
122. Peretz A, Paritsky M, Dinisman-Zavulunov E, et al. Susceptibility of *Helicobacter pylori* to levofloxacin and rifampicin in Israel. Microb Drug Resist 2015;21: 448–451.
123. Phan TN, Santona A, Tran VH, et al. High rate of levofloxacin resistance in a background of clarithromycin- and metronidazole-resistant *Helicobacter pylori* in Vietnam. Int J Antimicrob Agents 2015;45:244–248.
124. Prapitpaiboon H, Mahachai V, Vilaichone RK. High efficacy of levofloxacin-dexlansoprazole-based quadruple therapy as a first line treatment for *Helicobacter pylori* eradication in Thailand. Asian Pac J Cancer Prev 2015; 16:4353–4356.
125. Shiota S, Reddy R, Alsarraj A, et al. Antibiotic resistance of *Helicobacter pylori* among male United States Veterans. Clin Gastroenterol Hepatol 2015;13:1616–1624.
126. Shokrzadeh L, Alebouyeh M, Mirzaei T, et al. Prevalence of multiple drug-resistant *Helicobacter pylori* strains among patients with different gastric disorders in Iran. Microb Drug Resist 2015;21:105–110.
127. Tai WC, Liang CM, Lee CH, et al. Seven-day nonbismuth containing quadruple therapy could achieve a grade "A" success rate for first-line *Helicobacter pylori* eradication. BioMed Res Int 2015;2015:articlel D623732.
128. Tong YF, Lv J, Ying LY, et al. Seven-day triple therapy is a better choice for *Helicobacter pylori* eradication in regions with low antibiotic resistance. World J Gastroenterol 2015;21:13073–13079.
129. Tongtawee T, Dechsukhum C, Matrakool L, et al. High prevalence of *Helicobacter pylori* resistance to clarithromycin: a hospital-based cross-sectional study in Nakhon Ratchasima Province, Northeast of Thailand. Asian Pa J Cancer Prev 2015;16:8281–8285.
130. Tsay FW, Wu DC, Kao SS, et al. Reverse sequential therapy achieves a similar eradication rate as standard sequential therapy for *Helicobacter pylori* eradication: a randomized controlled trial. Helicobacter 2015;20: 71–77.
131. Wu IT, Chuah SK, Lee CH, et al. Five-year sequential changes in secondary antibiotic resistance of *Helicobacter pylori* in Taiwan. World J Gastroenterol 2015; 21:10669–10674.
132. Yang JC, Lin CJ, Wang HL, et al. High-dose dual therapy is superior to standard first-line or rescue therapy for *Helicobacter pylori* infection. Clin Gastroenterol Hepatol 2015;13:895–905.
133. Zhang W, Chen Q, Liang X, et al. Bismuth, lansoprazole, amoxicillin and metronidazole or clarithromycin as first-line *Helicobacter pylori* therapy. Gut 2015;64: 1715–17120.
134. Zhang YX, Zhou LY, Song ZQ, et al. Primary antibiotic resistance of *Helicobacter pylori* strains isolated from patients with dyspeptic symptoms in Beijing: a prospective serial study. World J Gastroenterol 2015; 21:2786–2792.
135. Aftab H, Miftahussurur M, Subsomwong P, et al. *Helicobacter pylori* antibiotic susceptibility patterns in Bangladesh: emerging levofloxacin resistance. J Infect Dev Ctries 2016;10:245–253.
136. Ang TL, Fock KM, Ang D, et al. The changing profile of *Helicobacter pylori* antibiotic resistance in Singapore: a 15-year study. Helicobacter 2016;21:261–265.
137. Baradaran Moghaddam A, Alebouyeh M, Farzi N, et al. Sensitivity to nitazoxanide among metronidazole resistant *Helicobacter pylori* strains in patients with gastritis. Med J Islam Repub Iran 2016;30:405.
138. Bouihat N, Burucoa C, Benkirane A, et al. *Helicobacter pylori* primary antibiotic resistance in 2015 in Morocco: a phenotypic and genotypic prospective and multicenter study. Microb Drug Resist 2017;23:727–732.
139. Brennan DE, Omorogbe J, Hussey M, et al. Molecular detection of *Helicobacter pylori* antibiotic resistance in stool vs biopsy samples. World J Gastroenterol 2016; 22:9214–9221.
140. Chen Q, Zhang W, Fu Q, et al. Rescue therapy for *Helicobacter pylori* eradication: a randomized non-inferiority trial of amoxicillin or tetracycline in bismuth quadruple therapy. The Am J Gastroenterol 2016;111:1736–1742.
141. Cosme A, Lizasoan J, Montes M, et al. antimicrobial susceptibility-guided therapy versus empirical concomitant therapy for eradication of *Helicobacter pylori* in a region with high rate of clarithromycin resistance. Helicobacter 2016;21:29–34.
142. Ducournau A, Benejat L, Sifre E, et al. *Helicobacter pylori* resistance to antibiotics in 2014 in France detected by phenotypic and genotypic methods. Clin Microbiol Infect 2016;22:715–718.
143. Georgopoulos SD, Xirouchakis E, Martinez-Gonzales B, et al. Randomized clinical trial comparing ten day concomitant and sequential therapies for *Helicobacter pylori* eradication in a high clarithromycin resistance area. Eur J Intern Med 2016;32:84–90.
144. Ghaith D, Elzahry M, Mostafa G, et al. Mutations affecting domain V of the 23S rRNA gene in *Helicobacter pylori* from Cairo, Egypt. Journal of chemotherapy 2016; 28(5):367–370.
145. Goudarzi M, Heidary M, Azad M, et al. Evaluation of antimicrobial susceptibility and integron carriage in

Helicobacter pylori isolates from patients. Gastroenterol Hepatol Bed Bench 2016;9(Suppl1):S47–S52.

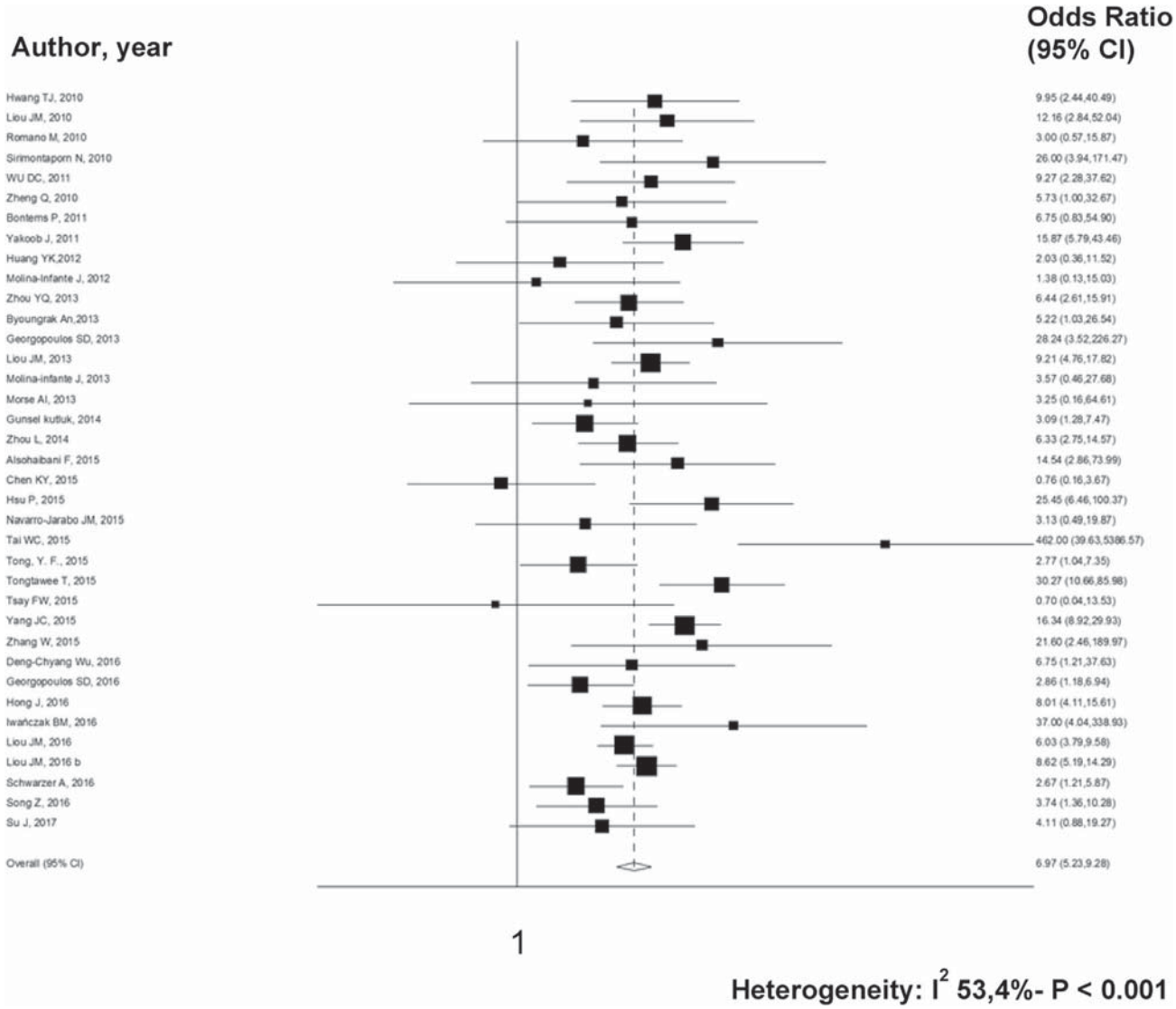
146. Goudarzi M, Seyedjavadi SS, Fazeli M, et al. Identification of a novel cassette array in integronbearing *Helicobacter Pylori* strains isolated from Iranian patients. Asian Pac J Cancer Prev 2016;17:3309–3315.
147. Han R, Lu H, Jiang M-W, et al. Multicenter study of antibiotic resistance profile of *H. pylori* and distribution of CYP2C19 gene polymorphism in rural population of Chongqing, China. Gastroenterol Res Pract 2016;2016: article ID8547686.
148. Hong J, Shu X, Liu D, et al. Antibiotic resistance and CYP2C19 polymorphisms affect the efficacy of concomitant therapies for *Helicobacter pylori* infection: an open-label, randomized, single-centre clinical trial. J Antimicrob Chemother 2016;71:2280–2285.
149. Iwanczak BM, Borys-Iwanicka A, Biernat M, et al. assessment of sequential and standard triple therapy in treatment of *Helicobacter pylori* infection in children dependent on bacteria sensitivity to antibiotics. Adv Clin Exp Med 2016;25:701–708.
150. Ji Z, Han F, Meng F, Tu M, et al. The association of age and antibiotic resistance of *Helicobacter Pylori*: a study in Jiaxing City, Zhejiang Province, China. Medicine 2016; 95(8):e2831.
151. Khashei R, Dara M, Bazargani A, et al. High rate of A2142G point mutation associated with clarithromycin resistance among Iranian *Helicobacter pylori* clinical isolates. APMIS 2016;124:787–793.
152. Kuo CH, Liu CJ, Yang CC, et al. A rapid and accurate method to evaluate *Helicobacter pylori* infection, clarithromycin resistance, and CYP2C19 genotypes simultaneously from gastric juice. Medicine 2016;95(21): e3458.
153. Liou JM, Chen CC, Chang C, et al. Sequential therapy for 10 days versus triple therapy for 14 days in the eradication of *Helicobacter pylori* in the community and hospital populations: a randomised trial. Gut 2016; 65:1784–1792.
154. Liou JM, Fang YJ, Chen CC, et al. Concomitant, bismuth quadruple, and 14-day triple therapy in the first-line treatment of *Helicobacter pylori*: a multicentre, open-label, randomised trial. Lancet 2016;388(10058): 2355–2365.
155. Martins GM, Sanches BS, Moretzsohn LD, et al. Molecular detection of clarithromycin and fluoroquinolones resistance in Helicobacter pylori infection, directly applied to gastric biopsies, in an urban Brazilian population. Arq Gastroenterol 2016;53:113–117.
156. Miftahussurur M, Syam AF, Nusi IA, et al. Surveillance of *Helicobacter pylori* antibiotic susceptibility in Indonesia: different resistance types among regions and with novel genetic mutations. PLoS One 2016;11:e0166199.
157. Park JY, Dunbar KB, Mitui M, et al. *Helicobacter pylori* clarithromycin resistance and treatment failure are common in the USA. Digest Dis Sci 2016;61:2373–2380.
158. Phiphatpatthamaamphan K, Vilaichone RK, Siramolpiwat S, et al. Effect of IL-1 polymorphisms, CYP2C19 genotype and antibiotic resistance on *Helicobacter pylori* eradication comparing between 10-day sequential therapy and 14-day standard triple therapy with four-times-daily-dosing of amoxicillin in Thailand: a prospective randomized study. Asian Pac J Cancer Prev 2016;17:1903–1907.
159. Quek C, Pham ST, Tran KT, et al. Antimicrobial susceptibility and clarithromycin resistance patterns of *Helicobacter pylori* clinical isolates in Vietnam. F1000Res 2016;5:671.
160. Ramzy I, Elgarem H, Hamza I, et al. Genetic mutations affecting the first line eradication therapy of *Helicobacter pylori*-infected Egyptian patients. Rev Inst Med Trop Sao Paulo 2016;58:88.
161. Sanches BS, Martins GM, Lima K, et al. Detection of *Helicobacter pylori* resistance to clarithromycin and fluoroquinolones in Brazil: a national survey. World J Gastroenterol 2016;22:7587–7594.
162. Schwarzer A, Bontems P, Urruzuno P, et al. Sequential therapy for *Helicobacter pylori* infection in treatment-naive children. Helicobacter 2016;21:106–113.
163. Song Z, Suo B, Zhang L, et al. Rabeprazole, minocycline, amoxicillin, and bismuth as first-line and second-line regimens for *Helicobacter pylori* eradication. Helicobacter 2016;21:462–470.
164. Song Z, Zhou L, Zhang J, et al. Levofloxacin, bismuth, amoxicillin and esomeprazole as second-line *Helicobacter pylori* therapy after failure of non-bismuth quadruple therapy. Digest Liver Disease 2016;48: 506–511.
165. Song Z, Zhou L, Zhang J, et al. Hybrid therapy as first-line regimen for *Helicobacter pylori* eradication in populations with high antibiotic resistance rates. Helicobacter 2016;21:382–388.
166. Vannarath S, Vilaichone RK, Rasachak B, et al. Antibiotic resistant pattern of *Helicobacter Pylori* infection based on molecular tests in Laos. Asian Pac J Cancer Prev 2016;17:285–287.
167. Vilaichone RK, Ratanachu-Ek T, Gamnarai P, et al. extremely high prevalence of metronidazole-resistant *Helicobacter pylori* strains in mountain people (Karen and Hmong) in Thailand. Am J Trop Med Hyg 2016; 94:717–720.
168. Wu DC, Kuo CH, Tsay FW, et al. A pilot randomized controlled study of dexlansoprazole MR-based triple therapy for *Helicobacter pylori* infection. Medicine 2016; 95:e2698.
169. Zhou L, Zhang J, Song Z, et al. Tailored versus triple plus bismuth or concomitant therapy as initial *Helicobacter pylori* treatment: a randomized trial. Helicobacter 2016; 21:91–99.
170. Zollner-Schwetz I, Leitner E, Plieschnegger W, et al. Primary resistance of *Helicobacter pylori* is still low in Southern Austria. Int J Med Microbiol 2016;306: 206–211.
171. Boehnke KF, Valdivieso M, Bussalleu A, et al. Antibiotic resistance among *Helicobacter pylori* clinical isolates in Lima, Peru. Infect Drug Resist 2017;10:85–90.
172. Chunlertlith K, Limpapanasit U, Mairiang P, et al. Outcomes of a randomized controlled trial comparing modified high dose omeprazole and amoxicillin triple therapy with standard triple therapy for *Helicobacter*

Pylori eradication. Asian Pac J Cancer Prev 2017; 18:927–932.

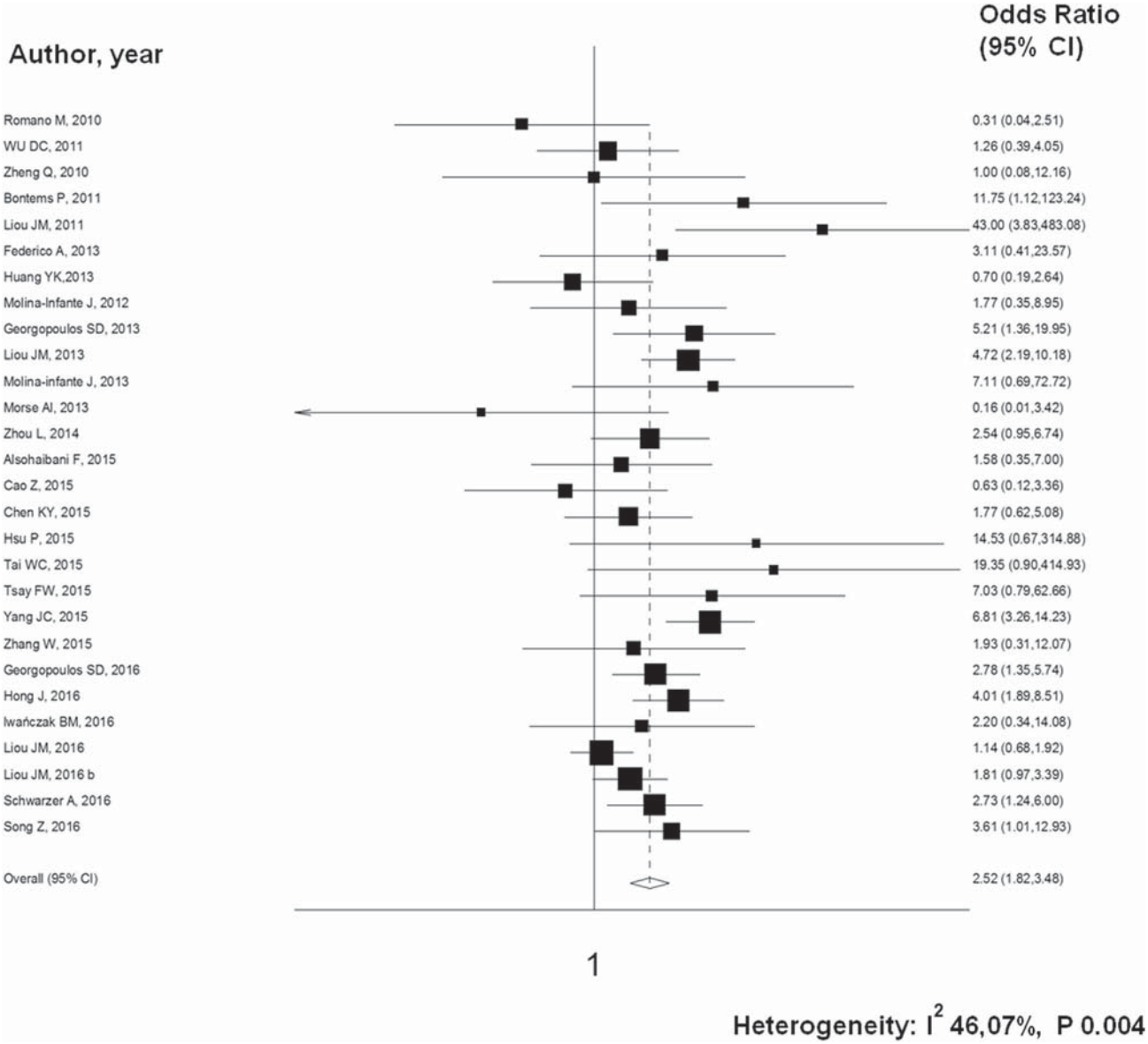
173. Ferenc S, Gnus J, Koscielna M, et al. High antibiotic resistance of *Helicobacter pylori* and its effect on tailored and empiric eradication of the organism in Lower Silesia, Poland. Helicobacter 2017;22(2).
174. Fu W, Song Z, Zhou L, et al. Randomized clinical trial: esomeprazole, bismuth, levofloxacin, and amoxicillin or cefuroxime as first-line eradication regimens for *Helicobacter pylori* infection. Digest Dis Sci 2017; 62:1580–1589.
175. Gunnarsdottir AI, Gudjonsson H, Hardardottir H, et al. Antibiotic susceptibility of Helicobacter pylori in Iceland. Infect Dis 2017:1–8.
176. Su J, Zhou X, Chen H, et al. Efficacy of 1st-line bismuth-containing quadruple therapies with levofloxacin or clarithromycin for the eradication of *Helicobacter pylori* infection: A 1-week, open-label, randomized trial. Medicine 2017;96(7):e5859.
177. Vilaichone RK, Ratanachu ek T, Gamnarai P, et al. High fluoroquinolone resistant strains of *Helicobacter pylori* in the Golden triangle. Asian Pac J Cancer Prev 2017; 18:455–458.
178. Zerbetto De Palma G, Mendiondo N, et al. Occurrence of mutations in the antimicrobial target genes related to levofloxacin, clarithromycin, and amoxicillin resistance in Helicobacter pylori isolates from Buenos Aires City. Microb Drug Resist 2017;23:351–358.



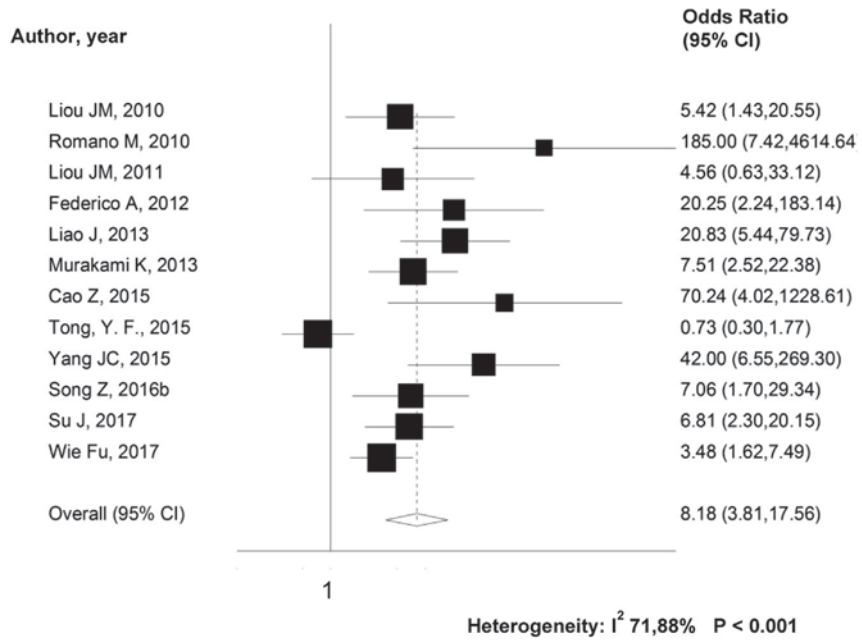
Supplementary Figure 1. Geographical distribution of the 6 WHO regions and member states for each region (alphabetical order). Africa Region (AFR), 47 countries: Algeria, Angola, Benin, Botswana, Burkina Faso, Burundi, Cameroon, Cabo Verde, Central African Republic, Chad, Comoros, Congo, Côte d'Ivoire, Democratic Republic of the Congo, Equatorial Guinea, Eritrea, Ethiopia, Gabon, Gambia, Ghana, Guinea, Guinea-Bissau, Kenya, Lesotho, Liberia, Madagascar, Malawi, Mali, Mauritania, Mauritius, Mozambique, Namibia, Niger, Nigeria, Rwanda, Sao Tome and Principe, Senegal, Seychelles, Sierra Leone, South Africa, South Sudan, Swaziland, Togo, Uganda, United Republic of Tanzania, Zambia, Zimbabwe. Americas Region (AMR), 35 countries: Antigua and Barbuda, Argentina, Bahamas, Barbados, Belize, Bolivia, Brazil, Canada, Chile, Colombia, Costa Rica, Cuba, Dominica, Dominican Republic, Ecuador, El Salvador, Grenada, Guatemala, Guyana, Haiti, Honduras, Jamaica, Mexico, Nicaragua, Panama, Paraguay, Peru, Saint Kitts and Nevis, Saint Lucia, Saint Vincent and the Grenadines, Suriname, Trinidad and Tobago, United States of America, Uruguay, Venezuela. Eastern Mediterranean Region (EMR), 21 countries: Afghanistan, Bahrain, Djibouti, Egypt, Iran (Islamic Republic of), Iran, Jordan, Kuwait, Lebanon, Libya, Morocco, Oman, Pakistan, Qatar, Saudi Arabia, Somalia, Sudan, Syrian Arab Republic, Tunisia, United Arab Emirates, Yemen. Europe Region (EUR), 48 countries Albania; Andorra; Armenia; Austria; Azerbaijan; Belarus; Belgium; Bosnia and Herzegovina; Bulgaria; Croatia; Cyprus; Czech Republic; Denmark; Estonia; Finland; France; Georgia; Germany; Greece; Hungary; Iceland; Ireland; Israel; Italy; Kazakhstan; Kyrgyzstan; Latvia; Lithuania, Luxembourg, Malta, Monaco, Montenegro, Netherlands, Norway, Poland, Portugal, Republic of Moldova, Romania, Russian Federation, San Marino, Serbia, Slovakia, Slovenia, Spain, Sweden, Switzerland, Tajikistan, The former Yugoslav Republic of Macedonia, Turkey, Turkmenistan, Ukraine, United Kingdom, Uzbekistan. South-East Asia Region (SEAR), 10 countries: Bangladesh, Bhutan, Democratic People's Republic of Korea, India, Indonesia, Maldives, Myanmar, Nepal, Sri Lanka, Thailand, Timor-Leste. Western Pacific Region (WPR), 27 countries: Australia, Brunei Darussalam, Cambodia, China, Cook Islands, Fiji, Japan, Kiribati, Lao People's Democratic Republic, Malaysia, Marshall Islands, Micronesia (Federated States of), Mongolia, Nauru, New Zealand, Niue, Palau, Papua New Guinea, Philippines, Republic of Korea, Samoa, Singapore, Solomon Islands, Tonga, Tuvalu, Vanuatu, Viet Nam.



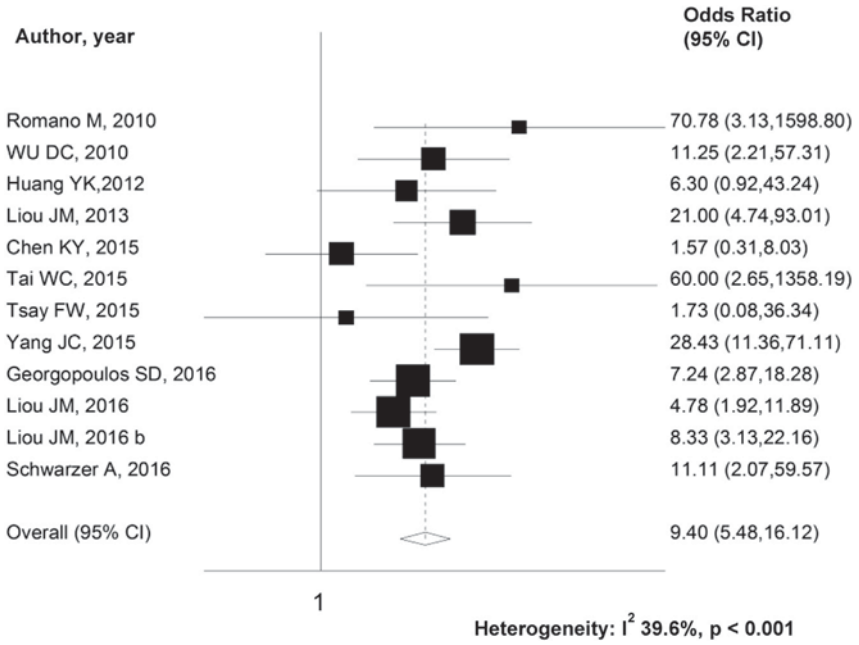
Supplementary Figure 2. Summary forest plot of the odds ratios associating treatment failure and clarithromycin resistance.



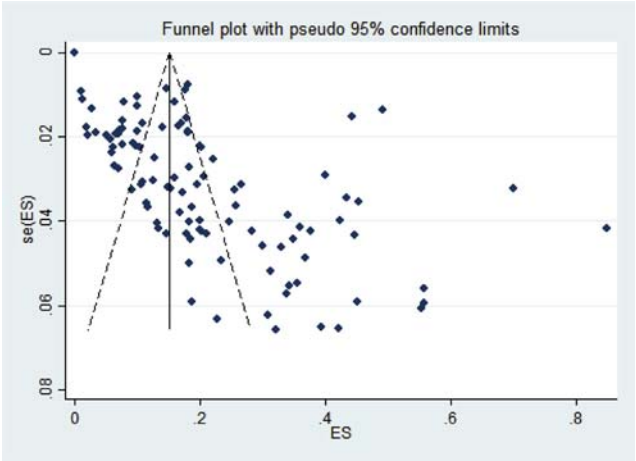
Supplementary Figure 3. Summary forest plot of the odds ratios associating treatment failure and metronidazole resistance.



Supplementary Figure 4. Summary forest plot of the odds ratios for studies associating treatment failure and levofloxacin resistance.



Supplementary Figure 5. Summary forest plot of the odds ratios for studies associating treatment failure and clarithromycin plus metronidazole resistance.



Supplementary Figure 6. Funnel plot of the meta-analysis on overall *Helicobacter pylori* primary resistance to clarithromycin (104 studies included, Egger's test for small study effect $P < .01$). ES, effect size.

Supplementary Table 1. Quality Assessment of Included Studies

1. Was the study's target population a close representation of the target population? Y/N

The target population refers to the group people entities to which the results of the study will be generalized. Studies providing data from several hospitals across the nation can be well representative of the national situation in terms of resistance prevalence.

2. Were the study participants recruited in an appropriate way? Y/N

Prospective consecutive enrollment (no random selection)

3. Was the sample size adequate? Y/N

We considered adequate studies computing their own sample size calculation or, if not mentioned, we deemed as adequate studies including at least 250 isolates. We based this cutoff on the following calculation:

We supposed a prevalence of clarithromycin resistance of 25% (based on results of a previous meta-analysis), with the width of the 95% CI, 0.10, an accuracy of ±0.05.

- The expected isolates proportion $P = .25$
- The desired width of the CI (d) = 0.10
- The confidence level = 95%

$n = 1.962 \times 4\ p\ (1–p) / d2$

$n = 15.37 \times 0.25\ (1–0.25) / 0.10^2$

$n = 288$

4. Were the study subjects' characteristics described in detail? Y/N

The question aims at assessing whether and how the sociodemographic features (age, sex, and race) and clinical features (type and grade of *Helicobacter pylori*–related disease) were reported in the study.

5. Was the data analysis conducted with sufficient coverage of the identified sample? Y/N

Are resistance results provided for all the isolates?

6. Were objective, standard criteria used for the measurement of the condition? Y/N

Several diagnostics tools were used with satisfying sensitivity and specificity % in reporting prevalence data. New and not well-defined diagnostic technique can provide unreliable data.

7. Was the condition measured reliably? Y/N

The type of antimicrobial susceptibility testing (phenotypic and/or genotypic) and the breakpoint systems referred to the definition of resistance should be reported.

8. Are all important confounding factors/subgroups/differences identified and accounted for? Y/N

The type of resistance (primary or secondary) should be reported. Previous administration of antibiotics/anti-acid should be reported. In case of secondary resistance, the previous antibiotic treatment should be provided.

The following points were deemed as redundant for the purpose of this systematic review.

1. Was there appropriate statistical analysis? NA

2. Were subpopulations identified using objective criteria? NA

n, no; NA, not applicable; Y, yes.

Supplementary Table 2. Patients Demographic and Clinical Features

Characteristics	Data
Age, *y*, median (IQR)	48 (43–51)
Male sex, %, mean (SD)	49 (9)
Population type, n (%)	
Pediatrics	2416 (4.5)
Adults	45,021 (84.0)
Both or not specified	6146 (11.5)
Any previous eradication treatment, n (%)	
Naïve patients	29,094 (54.0)
Pretreated patients	5676 (11.0)
Both or not specified	18,813 (35.0)
Endoscopic findings, median (IQR)	
NUD	70.2 (38.5–83.9)
PUD	25.5 (12.9-45.3)

IQR, interquartile range; NUD, non-ulcer dyspepsia; PUD, peptic ulcer disease; SD, standard deviation.

Supplementary Table 3. Pooled Prevalence of Antibiotic Resistance by Country, World Health Organization Region Africa

Antibiotic, country (no. of studies)	Pooled prevalence, %	95% CI
Clarithromycin		
Cameroon (1)	45	36–53
Senegal (1)	1	0–5
Congo (1)	2	0–9
Metronidazole		
Cameroon (1)	93	88–96
Senegal (1)	85	77–91
Levofloxacin		
Senegal (1)	15	9–23
Congo (1)	50	34–66
Amoxicillin		
Cameroon (1)	86	79–91
Senegal (1)	0	0–3
Tetracycline		
Cameroon (1)	44	36–52
Senegal (1)	0	0–3

Supplementary Table 4. Pooled Prevalence of Antibiotic Resistance by Country, World Health Organization Region Americas

Antibiotic, country (no. of studies)	Pooled prevalence, %	95% CI
Clarithromycin		
Argentina (1)	7	4–12
Brazil (6)	16	14–19
Canada (2)	0	0–2
Colombia (2)	6	4–8
Peru (1)	36	26–47
USA (3)	22	7–37
Metronidazole		
Argentina (1)	8	5–12
Brazil (2)	40	33–48
Canada (2)	12	5–19
Peru (1)	62	51–72
USA (2)	20	13–27
Levofloxacin		
Argentina (1)	9	5–13
Brazil (3)	10	5–15
Peru (1)	36	26–47
USA (2)	37	23–39
Amoxicillin		
Argentina (1)	2	1–5
Brazil (3)	7	1–13
Colombia (1)	4	2–9
Peru (1)	33	23–44
Tetracycline		
Peru (1)	4	1–11
CLA+MET		
Canada (1)	3	0–13

CLA+MET, clarithromycin and metronidazole.

Supplementary Table 5. Pooled Prevalence of Antibiotic Resistance by Country, World Health Organization Region Eastern Mediterranean

Antibiotic, country (no. of studies)	Pooled prevalence, %	95% CI
Clarithromycin		
Egypt (2)	56	47–64
Iran (15)	21	15–28
Morocco (1)	25	20–32
Pakistan (6)	40	32–49
Saudi Arabia (1)	23	15–34
Metronidazole		
Egypt (1)	63	51–73
Iran (14)	63	56–71
Morocco (1)	40	33–47
Pakistan (4)	62	51–74
Saudi Arabia (1)	49	37–60
Levofloxacin		
Iran (9)	25	14–37
Morocco (1)	11	7–16
Pakistan (5)	24	0–49
Saudi Arabia (1)	13	4–31
Amoxicillin		
Iran (13)	14	9–19
Morocco (1)	0	0–2
Pakistan (3)	25	0–52
Saudi Arabia (1)	15	6–32
Tetracycline		
Iran (11)	15	9–22
Morocco (1)	0	0–2
Pakistan (3)	12	7–18
CLA+MET		
Iran (6)	14	5–23

CLA+MET, clarithromycin and metronidazole.

Supplementary Table 6. Pooled Prevalence of Antibiotic Resistance by Country, World Health Organization Region Europe

Antibiotic, country (no. of studies)	Pooled prevalence, %	95% CI
Clarithromycin		
Austria (5)	32	12 to 52
Belgium (7)	36	20 to 51
Bulgaria (7)	23	17 to 28
Croatia (2)	14	11 to 17
France (8)	43	28 to 57
Germany (5)	13	6 to 20
Greece (5)	36	27 to 46
Iceland (1)	6	3 to 12
Ireland (3)	31	3 to 59
Israel (12)	47	39 to 56
Italy (7)	15	11 to 20
Multicenter (3)	17	5 to 30
Spain (12)	19	17 to 22
The Netherlands (6)	16	14 to 19
Turkey (4)	28	19 to 36
United Kingdom (1)	36	30 to 42
Metronidazole		
Austria (2)	14	10 to 19
Belgium (7)	40	29 to 51
Bulgaria (7)	28	22 to 35
Croatia (2)	11	8 to 14
France (6)	65	53 to 77
Germany (5)	37	30 to 43
Greece (4)	38	31 to 45
Iceland (1)	1	0 to 5
Ireland (2)	31	25 to 37
Israel (12)	57	48 to 65
Italy (6)	26	22 to 31
Multicenter (3)	32	25 to 39
United Kingdom (1)	57	51 to 63
Poland (7)	38	24 to 51
Turkey (1)	35	26 to 45
The Netherlands (6)	15	11 to 19
Levofloxacin		
Austria (2)	11	6 to 16
Belgium (4)	29	18 to 41
Bulgaria (7)	10	7 to 14
Croatia (1)	2	1 to 5
France (6)	15	12 to 18
Germany (17)	18	15 to 22
Greece (5)	10	6 to 13
Iceland (1)	6	3 to 12
Ireland (2)	11	6 to 16
Israel (10)	5	3 to 7
Italy (6)	5	3 to 7
Multicenter (3)	7	–1 to 16
Poland (5)	8	2–14
Spain (8)	16	14 to 18
Turkey (1)	30	21 to 39
United Kingdom (1)	11	8 to 16
Amoxicillin		
Austria (2)	0	0 to 1
Bulgaria (7)	1	0 to 1
Croatia (1)	0	0 to 3
France (2)	0	0 to 1
Germany (1)	0	0 to 6
Greece (4)	0	0 to 0
Iceland (1)	0	0 to 4
Ireland (2)	0	0 to 4
Israel (2)	4	0 to 8
Italy (2)	0	0 to 1
Multicentre (3)	0	0 to 1
Poland (5)	0	0 to 1
Spain (8)	0	0 to 0
United Kingdom (1)	2	1 to 5
Tetracycline		
Austria (2)	0	0 to 1
Bulgaria (6)	3	1 to 6
France (2)	0	0 to 0
Germany (1)	0	0 to 0
Greece (4)	0	0 to 0
Iceland (1)	0	0 to 4
Ireland (1)	0	0 to 5
Israel (2)	2	0 to 6
Italy (2)	0	0 to 1
Multicenter (3)	0	0 to 1
Poland (2)	0	0 to 1
Spain (6)	0	0 to 0
United Kingdom (1)	2	1 to 4
CLA+MET		
Belgium (1)	4	2 to 8
Bulgaria (4)	15	6 to 24
Germany (4)	3	2 to 5
Greece (4)	13	6 to 21
Iceland (1)	0	0 to 4
Israel (12)	30	16 to 44
Italy (6)	8	4 to 12
Multicenter (1)	3	2 to 7
Poland (5)	8	1 to 4
Spain (1)	10	5 to 18
United Kingdom (1)	31	25 to 37

CLA+MET, clarithromycin and metronidazole.

Supplementary Table 7. Pooled Prevalence of Antibiotic Resistance by Country, World Health Organization Region South-East Asia

Antibiotic, country (no. of studies)	Pooled prevalence, %	95% CI
Clarithromycin		
Bangladesh (1)	39	28–52
Bhutan (1)	0	0–4
India (1)	5	2–13
Indonesia (1)	9	4–18
Thailand (9)	19	2–36
Metronidazole		
Bangladesh (1)	95	85–98
Bhutan (1)	83	75–89
India (1)	100	94–100
Indonesia (1)	47	36–58
Thailand (6)	44	28–60
Levofloxacin		
Bangladesh (1)	66	53–77
Bhutan (1)	5	3–11
Indonesia (1)	31	22–42
Thailand (4)	19	14–23
Amoxicillin		
Bangladesh (1)	4	1–12
Bhutan (1)	0	0–4
India (1)	65	53–76
Indonesia (1)	5	2–13
Thailand (2)	1	0–3
Tetracycline		
Bangladesh (1)	0	0–7
Bhutan (1)	0	0–4
India (1)	0	0–6
Indonesia (1)	3	1–9
Thailand (2)	0	0–1
CLA+MET	6	1–10
Bangladesh (1)	9	4–19
Thailand (1)	4	1–13

CLA+MET, clarithromycin and metronidazole.

Supplementary Table 8. Pooled Prevalence of Antibiotic Resistance by Country, World Health Organization Region Western Pacific

Antibiotic, country (no. of studies)	Pooled prevalence, %	95% CI
Clarithromycin		
Australia (5)	96	92–99
China (47)	37	30–43
Japan (3)	28	25–32
Laos (1)	13	8–20
Malaysia (3)	5	0–10
New Zealand (1)	7	4–12
Singapore (3)	16	12–19
South Korea (7)	18	10–25
Taiwan (38)	26	22–31
Vietnam (5)	63	37–88
Metronidazole		
Australia (5)	68	63–73
China (44)	77	74–79
Malaysia (2)	82	75–88
New Zealand (1)	49	38–61
Singapore (3)	44	39–48
South Korea (7)	40	3–50
Taiwan (37)	31	27–35
Vietnam (5)	58	40–76
Levofloxacin		
Australia (5)	5	3–7
China (31)	33	29–38
Laos (1)	13	8–21
Singapore (3)	13	10–15
South Korea (7)	28	21–35
Taiwan (31)	15	13–17
Vietnam (5)	32	20–43
Amoxicillin		
Australia (5)	0	0–1
China (32)	1	0–1
Malaysia (2)	0	0–1
New Zealand (1)	5	2–13
Singapore (3)	4	2–6
South Korea (7)	4	2–5
Taiwan (38)	1	1–1
Vietnam (5)	2	0–4
Tetracycline		
Australia (5)	0	0–1
China (15)	2	1–3
Malaysia (1)	12	6–24
New Zealand (1)	0	0–5
Singapore (3)	7	5–9
South Korea (7)	4	1–6
Taiwan (18)	2	1–3
Vietnam (5)	17	4–31
CLA+MET		
China (15)	14	11–17
New Zealand (1)	8	4–17
Singapore (3)	4	1–8
South Korea (3)	4	1–8
Taiwan (18)	10	7–13
Vietnam (2)	15	8–23

CLA+MET, clarithromycin and metronidazole.

Supplementary Table 9. Heterogeneity Assessment by Studies' Country

Variable	Country	Pooled prevalence, %	95% CI	I^2 %
Clarithromycin resistance	Australia	96	92–99	61
	Brazil	16	14–19	0
	Italy	15	11–20	66
	Turkey	28	19–36	66
Metronidazole resistance	Australia	68	63–73	0
	Germany	37	30–43	64
	Greece	38	31–45	47
	The Netherlands	15	11–19	60
Levofloxacin resistance	Australia	5	3–7	0
	France	15	12–18	0
	Greece	10	6–13	39
	Italy	5	3–7	16
	Poland	8	2–14	63
	Spain	16	14–18	62
Clarithromycin plus metronidazole resistance	Germany	3	2–5	0
	Italy	8	4–12	61

NOTE. Only pooled prevalence for countries with I^2 value $< 75\%$ are reported.