中文題目：比較相繼式治療與三合一治療在幽門桿菌第一線藥物之療效與成本效益分析–一項多中心之隨機分派試驗

英文題目：Sequential therapy versus triple therapy in the first line treatment of Helicobacter pylori infection- a multicenter rRandomized trial and cost-effectiveness analysis

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前言(Background): Sequential therapy appeared to be more effective than triple therapy in the first line treatment of *Helicobacter pylori* infection in Italy, but controversial results were reported in Asia and Latin American. The contradictory results might be attributed to the different prevalence of antibiotic resistance in different geographic regions, but the exact mechanisms remain unproven because susceptibility tests were performed in few of the previously clinical trials. Besides, whether extending the treatment duration of sequential therapy from 10 days to 14 days would be more effective than triple therapy for 14 days has not been reported. Whether sequential therapy is more cost-effective than triple therapy also remains unknown. Therefore, we aimed to compare the cost-effectiveness of sequential therapy for 10 days and 14 days versus triple therapy for 14 days in the first line treatment with sensitivity analysis according to the prevalence of clarithromycin and metronidazole resistance within a randomized trial.

材料及方法(Materials and Methods): Adult patients who had upper gastrointestinal symptoms and asymptomatic subjects who underwent gastric cancer screening with documented *Helicobacter* infection (*n*=900) were randomized in this multicentre, open-label trial to receive

sequential therapy for 14 days (S-14) or 10 days (S-10) or triple therapy for 14 days (T-14). Susceptibility test and genotypic resistance (23S rRNA and *gyrA* mutation) were also determined. A decision model was constructed based on the choice of antibiotic treatment and the pattern of antimicrobial susceptibility. The relative cost-effectiveness between regimens was expressed with the incremental cost-effectiveness ratio (ICER), *i.e.*, the incremental cost divided by the incremental effectiveness to cure one additional *H. pylori* carrier. Deterministic and probabilistic sensitivity analyses were performed to investigate the effects of changes in the prevalence rates of the clarithromycin-resistant and the metronidazole-resistant strains across a wide range of assumptions.

結果（Results): The eradication rates for S-14, S-10, and T-14 were 90·7% (272/300, 95% CI 87·4%-94·0%), 87·0% (261/300, 95% CI 83·2%-90·8%), and 82·3% (247/300, 95% CI 78·0%-86·6%) in the ITT analysis, respectively. S-14 was superior to T-14 in both the ITT (number needed to treat 12, 95% CI 7·2-34·5, p=0·003) and PP analyses (number needed to treat 13·7, 95% CI 8·3-40, p=0·003). Their efficacies were all affected by clarithromycin resistance, but not by host CYP2C19 polymorphism or bacterial virulence factors. The efficacies of S-14 and S-10 were affected by metronidazole resistance. The base-case analysis showed that sequential therapies were more effective and less costly than the T-14. Deterministic sensitivity analyses showed that the efficacies of S-14, S-10, and T-14 decreased with increasing prevalence rates of clarithromycin resistance. S-14 appeared to be more effective than S-10 and T-14 in areas with different prevalence of metronidazole resistance. S-10 appeared to be more effective

than T-14 only in areas where the metronidazole resistance was lower than 40%. In the two-way analyses, S-14 was the most effective regimen in all areas, except in areas with very low (<5%) clarithromycin resistance and very high (>80%) metronidazole resistance when all regimens were compared (Figure 2). S-10 also appeared to be more effective than T-14, except in areas with low clarithromycin and high metronidazole resistance. Probability sensitivity analyses showed that a low possibility of being cost-effective for the T-14 with a chance of less than 5%. The S-10 was the most cost-effective across a wide range of ceiling ratios while the S-14 could be an alternative choice when the ceiling ratio was higher than US $410.

結論（Conclusion): Sequential therapy appeared to be more effective and cost-effective than triple therapy for 14 days, except in areas with concomitant high metronidazole and low clarithromycin resistance. (**ClinicalTrials.gov.ID**: NCT01042184)

Keywords: *Helicobacter pylori*, sequential therapy, triple therapy, levofloxacin, and duration