Sequential therapy boosts *H pylori* eradication rates. *J Fam Pract*. 2008;57:651-654.
Potential PURL Review Form: Systematic Reviews and Meta-Analyses
SECTION1: IDENTIFYING INFORMATION FOR NOMINATED PURL

1.0 Citation	Jafri NS, Hornung CA, Howden CW. Meta-analysis: sequential therapy appears superior to standard therapy for *Helicobacter pylori* infection in patients naive to treatment. *Ann Intern Med*. 2008;148:923-931.
1.3 Hypertext link to PDF of full article	http://www.annals.org/cgi/content/full/148/12/923
1.4 First date published study available to readers	5/19/08
1.5 PubMed ID	18490667
1.6 Nominated By	Sarah-Anne Schumann
1.7 Institutional Affiliation of Nominator	University of Chicago
1.8 Date Nominated	6/3/08
1.9 Identified Through	*Annals of Internal Medicine*
1.10 PURLS Editor	Bernard Ewigman
1.11 Nomination Decision Date	6/10/08
1.12 Potential PURL Review Form (PPRF) type	PPRF Systematic Reviews/Meta-Analyses
1.14 Assigned Potential PURL Reviewer	Mike Mendoza
1.15 Reviewer Affiliation	University of Chicago
1.16 Date Review Due	6/26/08

1.17 Abstract	BACKGROUND: Standard proton-pump inhibitor-based therapy for *Helicobacter pylori* infection fails in up to one quarter of patients. Sequential therapy may be more efficacious. PURPOSE: To compare sequential therapy with standard triple therapy for *H pylori* infection. DATA SOURCES: MEDLINE, EMBASE (1981 to October 2007), the Cochrane Central Register of Controlled Trials, and Google Scholar. PubMed and Ovid were the search engines used. STUDY SELECTION: Randomized, controlled trials (RCTs) comparing sequential and standard triple therapies in treatment-naive patients with documented *H pylori* infection. DATA EXTRACTION: 3 reviewers independently assessed trial eligibility and quality and extracted data on eradication. DATA SYNTHESIS: The crude rates of *H pylori* eradication in 10 RCTs involving 2747 patients were 93.4% (95% CI, 91.3%-95.5%) for sequential therapy (n=1363) and 76.9% (CI, 71.0%-82.8%) for standard triple therapy (n=1384) (relative risk reduction, 71% [CI, 64%-77%]; absolute risk reduction, 16 percentage points [CI, 14 to 19 percentage points]). The median rates of adherence were 97.4% (range, 90.0%-98.9%) for sequential therapy and 96.8% (range, 93.0%-100%) for standard therapy. Sequential therapy appeared superior in prespecified sensitivity (subgroup) analyses stratified by trial quality; smoking status; diagnosis (ulcer disease or nonulcer dyspepsia); resistance to clarithromycin, imidazoles, or both; duration of triple therapy; and method of diagnosis. Both treatments had similar side effect profiles. Limitations: Only 1 study was double-blinded. Most patients were from Italy. There was clear evidence of publication bias. CONCLUSIONS: Sequential therapy appears superior to standard triple therapy for eradication of *H pylori* infection. If RCTs in other countries confirm these findings, 10-day sequential therapy could become a standard treatment for *H pylori* infection in treatment-naive patients.
SECTION 2: DETAILED STUDY DESCRIPTION	
2.1 What types of studies are included in this review?	RCTs. Inclusion criteria: RCT, *H pylori* treatment naïve, no PPI, ranitidine, H2RA, or antibiotics in previous month. Diagnosed by histologic evaluation, urease biopsy, fecal antigen, urea breath test. Eradication defined as negative on any of the above. Excluded: non-RCTs, abstracts with insufficient details
2.2 What is the key question addressed by this review? Summarize the main conclusions and any strengths or weaknesses.	Is sequential therapy for *H pylori* preferable to standard triple therapy for treatment-naïve patients? The authors concluded that sequential therapy appears superior to standard triple therapy for *H pylori* eradication. Outcomes: 1) Eradication rates 93.4% (95% confidence interval [CI], 91.3-95.5 for sequential) vs 76.9% (95% CI, 71.0-82.8 for standard). RRR 71%, ARR 16 percentage points. Number needed to treat [NNT] = 1/.16 = 6.25

	Major Weaknesses: Publication bias, all RCTs were conducted in Italy, although 2 of them recruited US patients
SECTION 3: INTERNAL VALIDITY	
3.1 Study addresses an appropriate and clearly focused question	Well addressed
3.2 A description of the methodology used is included.	Well addressed. Cochrane and QUOROM
3.3 The literature search is sufficiently rigorous to identify all the relevant studies.	Well addressed
3.4 Study quality is assessed and taken into account.	Well addressed. When only high-quality studies were analyzed, their conclusion was the same.
3.5 There are enough similarities between selected studies to make combining them reasonable.	Well addressed. 9 RCTs compared sequential therapy with PPI containing triple therapy. 1 compared sequential therapy with a ranitidine bismuth citrate–containing triple therapy. 1 RCT only kids.
3.6 Are patient oriented outcomes included? If yes, what are they?	No. Eradication rate only. Adherence = patients who “completed treatment” or “compliant”
3.7 Is funding a potential source of bias? If yes, what measures (if any) were taken to insure scientific integrity?	No external funding.
SECTION 4: EXTERNAL VALIDITY	
4.1 To which patients might the findings apply? Include patients in the meta-analysis and other patients to	Italian treatment-naïve *H pylori*–positive adults and children. Suspect no problem generalizing to non-Italian adults and children.

whom the findings may be generalized.	
4.2 In what care settings might the findings apply, or not apply?	Primary care
4.3 To which clinicians or policy makers might the findings be relevant?	Primary care
SECTION 5: REVIEW OF SECONDARY LITERATURE	
5.1 DynaMed excerpts	DynaMed notes the findings from multiple RCTs of sequential therapy for *H pylori* and states that it "may be more effective" than 7-day triple therapy and 10-day standard therapy based on evidence summarized from the following references: *Lancet*. 2007 Sep 22;370(9592):1010. *Can J Gastroenterol*. 2006 Feb;20(2):113 *Ann Intern Med*. 2007 Apr 17;146(8):556, commentary can be found in *ACP J Club* 2007 Sep-Oct;147(2):40, *Ann Intern Med*. 2007 Sep 18;147(6):434 *Aliment Pharmacol Ther*. 2005 Jun 15;21(12):1419, commentary can be found in *ACP J Club* 2006 Jan-Feb;144(1):2 *Gastroenterology*. 2005 Nov;129(5):1414
5.2 DynaMed citation/access date	http://dynaweb.ebscohost.com/Detail.aspx?id=114484&sid=5e653c0d-c888-4eb6-bd68-400b47dfec73@sessionmgr8 Accessed July 2008
5.3 UpToDate excerpts	UpToDate states that "Sequential triple therapy using three antibiotics may improve eradication rates, especially with clarithromycin resistant stains….. However, before recommending this therapy as first line treatment, studies confirming its utility from the United States and other non-European countries are needed."
5.4 UpToDate citation/access date	Accessed July 2008
5.5 PEPID PCP excerpts	Nothing on sequential therapy
SECTION 6: CONCLUSIONS	
6.1 How well does the meta-analysis minimize sources of internal bias and maximize internal validity? Give one	2

number on a scale of 1 to 7 (1=extremely well; 4=neutral; 7=extremely poorly)	
6.2 If 6.1 was coded as 4 or greater, please describe the potential bias and how it could affect the study results. Specifically, what is the likely direction in which potential sources of internal bias might affect the results?	
6.3 Are the results of this review relevant to the health care needs of patients cared for by "full scope" family physicians, general internists, general pediatricians, or general OB/GYNs? Without significant change in programs or policies such as the organization or financing of practice? Give one number on a scale of 1 to 7 (1=absolutely relevant; 4=neutral; 7=not at all relevant)	1
6.4 Please explain your response to item 6.3.	High-prevalence condition in primary care.
6.5 What is the main recommendation for change in practice, if any? Include a description of the change in practice, the indication(s), and the target population.	Use sequential therapy instead of standard triple therapy for treatment naïve patients with documented *H pylori* infection.
SECTION 7: EDITORIAL DECISIONS	
7.1 FPIN PURLs editorial decision (select one)	PURL—Forward to JFP Editor for interest in JFP publication
7.2 FPIN PURLS Editor	Bernard Ewigman
7.3 Date of decision	June 26, 2008

7.4 Brief summary of decision	Sequential therapy improves eradication
7.5 Survey question	Question for PURLs Instant Poll: Do you use sequential therapy for *H pylori* infection (PPI plus 5 days of 1 antibiotic followed by 5 days of 2 different antibiotics): ___Always ___Sometimes ___Never After reading this PURL, how likely are you to use sequential therapy for *H pylori*? ___Very unlikely ___Unlikely ___Likely ___Very likely What barriers do you anticipate (or have you experienced) in using sequential therapy for *H pylori*?
7.6 JFP Interest in Publication	Interested and date of publication set for October 2008