Rethinking antibiotics for sinusitis—again. *J Fam Pract*. 2012;61:610-612.	
Potential PURL Review Form: Randomized controlled trials	
SECTION 1: IDENTIFYING INFORMATION	
1. Citation	Garbutt JM, Banister C, Spitznagel E, et al. Amoxicillin for acute rhinosinusitis: a randomized controlled trial. *JAMA*. 2012;307:685-692.
2. Hypertext link to PDF of full article	http://www.ncbi.nlm.nih.gov/pubmed/22337680
3. First date published study available to readers	February 15, 2012
4. PubMed ID	22337680
5. Nominated By	Kate Rowland
6. Institutional Affiliation of Nominator	University of Chicago
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9. PURLS Editor Reviewing Nominated Potential PURL	Kate Rowland
10. Nomination Decision Date	February 23, 2012
11. Potential PURL Review Form (PPRF) Type	Randomized controlled trial
12. Other comments, materials or discussion	
13. Assigned Potential PURL Reviewer	Kate Rowland
14. Reviewer Affiliation	University of Chicago
15. Date Review Due	March 22, 2012
16. Abstract	**CONTEXT:** Evidence to support antibiotic treatment for acute rhinosinusitis is limited, yet antibiotics are commonly used. **OBJECTIVE:** To determine the incremental effect of amoxicillin treatment over symptomatic treatments for adults with clinically diagnosed acute rhinosinusitis. **DESIGN, SETTING, AND PARTICIPANTS:** A randomized, placebo-controlled trial of adults with uncomplicated, acute rhinosinusitis recruited from 10 community practices in Missouri between November 1, 2006, and May 1, 2009. **INTERVENTIONS:** Ten-day course of either amoxicillin (1500 mg/d) or placebo administered in 3 doses per day. All patients received a 5- to 7-day supply of symptomatic treatments for pain, fever, cough, and nasal congestion to use as needed. **MAIN OUTCOME MEASURES:** The primary outcome was improvement in disease-specific quality of life after 3 to 4 days of treatment assessed with the Sinonasal Outcome Test-16 (minimally important difference of 0.5 units on a 0-3 scale). Secondary outcomes included the patient's retrospective assessment of change in sinus symptoms and functional status, recurrence or relapse, and satisfaction with and adverse effects of treatment. Outcomes were assessed by telephone interview at days 3, 7, 10, and 28. **RESULTS:** A total of 166 adults (36% male; 78% white race) were randomized to amoxicillin (n = 85) or placebo (n = 81); 92% concurrently used 1 or more symptomatic

	treatments (94% for amoxicillin group vs 90% for control group; *P* = .34). The mean change in Sinonasal Outcome Test-16 scores was not significantly different between groups on day 3 (decrease of 0.59 in the amoxicillin group and 0.54 in the control group; mean difference between groups of 0.03 [95% CI, -0.12 to 0.19]) and on day 10 (mean difference between groups of 0.01 [95% CI, -0.13 to 0.15]), but differed at day 7 favoring amoxicillin (mean difference between groups of 0.19 [95% CI, 0.024 to 0.35]). There was no statistically significant difference in reported symptom improvement at day 3 (37% for amoxicillin group vs 34% for control group; *P* = .67) or at day 10 (78% vs 80%, respectively; *P* = .71), whereas at day 7 more participants treated with amoxicillin reported symptom improvement (74% vs 56%, respectively; *P* = .02). No between-group differences were found for any other secondary outcomes. No serious adverse events occurred. **CONCLUSION:** Among patients with acute rhinosinusitis, a 10-day course of amoxicillin compared with placebo did not reduce symptoms at day 3 of treatment. **TRIAL REGISTRATION:** clinicaltrials.gov. Identifier: NCT00377403.
SECTION 2: CRITICAL APPRAISAL OF VALIDITY	
1. Number of patients starting each arm of the study?	85 patients in the treatment group, 81 in the control group.
2. Main characteristics of study patients (inclusions, exclusions, demographics, settings, etc.)?	Ages 18-70 years, who met CDC diagnostic criteria with moderate, severe, or very severe symptoms. Diagnosis required history of maxillary pain or tenderness in the face or teeth, purulent nasal secretions, rhinosinusitis symptoms for ≥7 days and ≤28 days that were not improving or worsening, or rhinosinusitis symptoms lasting for <7days that had significantly worsened after initial improvement. Patients were excluded if they had allergy to penicillin, prior antibiotic treatment within 4 weeks, complications, or comorbidity that may impair immune response or needed a concurrent antibiotic, were pregnant, or had mild or very mild symptoms. Patients were recruited from 10 primary care offices in Missouri, group characteristics were similar, median age 32 years, approx. 70% female, white non-Hispanic. From a diverse range of socioeconomic status.
3. Intervention(s) being investigated?	Amoxicillin 1500 mg TID for 10 days
4. Comparison treatment(s), placebo, or nothing?	Placebo
5. Length of follow-up? Note specified end points e.g. death, cure, etc.	28 days
6. What outcome measures are used? List all that assess effectiveness.	Primary outcome: SNOT-16 (Sinonasal Outcome Test-16) score to assess disease-specific quality of life. Secondary outcome: retrospective assessment of change in sinus symptoms, functional status, recurrence or relapse, and satisfaction/adverse effects related to treatment.
7. What is the effect of the intervention(s)? Include absolute risk, relative risk, NNT, CI, p-values, etc.	SNOT-16 has been noted to have a minimally important difference of 0.5 units on a scale of 0 to 3 points. SNOT-16 scores*: Day 0: 1.71 in amoxicillin vs 1.70 in control Day 3: 1.12 vs 1.14, *P*=.69 Day 7: 0.65 vs 0.84, *P*=.02 Day10: 0.48 vs 0.49, *P*=.85 Self-reported improvement since day 0*: Amoxicillin vs control: Day 3: 37% vs 34%, *P*=.67 Day 7: 74% vs 56%, *P*=.02, NNT 6

	Day 10: 78% vs 80%, *P*=.71 **P* values provided are for comparisons between the 2 groups. Time missed from work, time unable to do usual activities, relapse and recurrence rates, as well as satisfaction were similar between the 2 groups.
8. What are the adverse effects of intervention compared with no intervention?	Headache: (22% for amoxicillin group and 23% for control group; *P*=.96) Excessive tiredness: (11% for amoxicillin group and 21% for control group; *P*=.12). Few patients had nausea (7%), diarrhea (9%), abdominal pain (5%), or vaginitis (6% of women), with no differences by study group.
9. Study addresses an appropriate and clearly focused question - ***select one***	Well covered
10. Random allocation to comparison groups	Well covered
11. Concealed allocation to comparison groups	Well covered
12. Subjects and investigators kept “blind” to comparison group allocation	Well covered
13. Comparison groups are similar at the start of the trial	Well covered
14. Were there any differences between the groups/arms of the study other than the intervention under investigation? If yes, please indicate whether the differences are a potential source of bias.	Adequately addressed Comments: More smokers in the control group: 21(26%) compared to 11(13%) in the amoxicillin group.
15. Were all relevant outcomes measured in a standardized, valid, and reliable way?	Well covered
16. Are patient-oriented outcomes included? If yes, what are they?	All outcome measures were patient oriented.
17. What percent dropped out, and were lost to follow up? Could this bias the results? How?	14% dropped out. Loss to follow-up was minimal and similar to clinical practice. I do not see any overt bias.
18. Was there an intention-to-treat analysis? If not, could this bias the results? How?	Yes
19. If a multi-site study, are results comparable for all sites?	Site specifics were not reported.

20. Is the funding for the trial a potential source of bias? If yes, what measures were taken to insure scientific integrity?	NIH funded.
21. To which patients might the findings apply? Include patients in the study and other patients to whom the findings may be generalized.	The results are widely generalizable. Although most patients were white women, given the preponderance of data that suggests acute sinusitis will resolve spontaneously, I imagine neither race nor sex plays a role. Patients with overt complications, pregnancy, and very mild or mild symptoms should be excluded.
22. In what care settings might the findings apply, or not apply?	Primary care, may also be relevant for ENT and other specialists.
SECTION 3: REVIEW OF SECONDARY LITERATURE	
1. DynaMed excerpts	
2. DynaMed citation/access date	
3. Bottom line recommendation or summary of evidence from DynaMed (1-2 sentences)	
4. UpToDate excerpts	
5. UpToDate citation/access date	
6. Bottom line recommendation or summary of evidence from UpToDate (1-2 sentences)	
7. PEPID PCP excerpts www.pepidonline.com username: fpinauthor pw: pepidpcp	**Therapeutics** 1. Antibiotics have little if any positive effects on severity and duration of symptoms 2. Viral rhinosinusitis (VRS): Sx treatment o Analgesics, antipyretics ▪ NSAIDs o First-generation antihistamines ▪ Diphenhydramine o Oral decongestants preferred ▪ Pseudoephedrine 60 mg PO q6h or 120 mg SR q12h ▪ Mucolytic: guaifenesin (no proven benefit) o Topical decongestants controversial ▪ Do not use for >3 days to avoid rebound vasodilation ▪ Oxymetazoline 2 sprays q12h

- Phenylephrine (Afrin) 2 sprays q4h
- Home self-care
  - Rest
  - Hydration (6-10 glasses/day)
  - Steamy shower
  - Apply warm facial packs
  - Saline irrigation lavage
  - Sleep w/ head elevated
  - Avoid cigarette smoke

3. Uncomplicated - acute bacterial rhinosinusitis (ABRS)
   - Mild pain, temp <101°F
     - Observation w/o antibiotics
     - Symptomatic relief (see above)
     - F/u assurance
4. Complicated - ABRS
   - Temp >102°F, history of severe symptoms, HA, upper teeth/facial pain, anatomical blockage
   - Reoccur symptoms, colored nasal drainage, poor nasal decongestant response
   - Antibiotics
     - Amoxicillin
       - 500 mg TID or 875 mg BID x 10-14 days (1st-line therapy)
       - May be better than placebo for acute sinusitis in adults
     - If beta-lactam allergy
       - TMP-SMX 5 mg/kg; 1 tab PO BID x 10 days or
       - Fluoroquinolones (as below) or
       - Doxycycline 100 mg q12h x 1 day, then 50 mg q12h x 9 days
   - Moderately severe symptoms, recent antibiotic use, or no response to Tx in 72 hours:
     - Amoxicillin-clavulanate potassium (Augmentin) 500 mg q8h, OR 875 mg q12h
     - Or fluoroquinolones (Note: *S pneumoniae* resistance increasing)
       - Levofloxacin 500 mg qD x 10 d, or
       - Gatifloxacin 400 mg qD x 10 d, or
       - Ciprofloxacin 500 mg q12h x 10 d, or
       - Moxifloxacin 400 mg qD x 10 d
   - Intranasal steroids
     - More effective than amoxicillin for treating patients with mild/moderate

	acute sinusitis − Adding an intranasal steroid to an antibiotic is more effective than an antibiotic alone
8. PEPID citation/access data	Khan S, Merel S. Acute sinusitis. In: PEPID [database online]. Available at: http://www.pepidonline.com. Accessed March 15, 2012.
9. PEPID content updating	

SECTION 4: CONCLUSIONS	
1. Validity: How well does the study minimize sources of internal bias and maximize internal validity? Give one number on a scale of 1 to 7 (1=extremely well; 4=neutral; 7=extremely poorly)	1
2. If 4.1 was coded as 4, 5, 6, or 7, 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?	
3. Relevance: Are the results of this study generalizable to and relevant to the health care needs of patients cared for by "full scope" family physicians? Give one number on a scale of 1 to 7 (1=extremely well; 4=neutral; 7=extremely poorly)	1
4. If 4.3 was coded as 4, 5, 6, or 7, please provide an explanation.	
5. Practice-changing potential: If the findings of the study are both valid and relevant, does the practice that would be based on these findings represent a change from current practice? Give one number on a scale of 1 to 7 (1=definitely a change from current practice; 4=uncertain; 7=definitely not a change from current practice)	2
6. If 4.5 was coded as 1, 2, 3, or 4, please describe the potential new practice recommendation. Please be specific about what should be done, the target patient population and the expected benefit.	
7. Applicability to a Family Medical Care Setting: Is the change in practice recommendation something that	1

could be done in a medical care setting by a family physician (office, hospital, nursing home, etc), such as a prescribing a medication, vitamin or herbal remedy; performing or ordering a diagnostic test; performing or referring for a procedure; advising, educating or counseling a patient; or creating a system for implementing an intervention? Give one number on a scale of 1 to 7 (1=definitely could be done in a medical care setting; 4=uncertain; 7=definitely could not be done in a medical care setting)	
8. If you coded 4.7 as a 4, 5, 6, or 7, please explain.	
9. Immediacy of Implementation: Are there major barriers to immediate implementation? Would the cost or the potential for reimbursement prohibit implementation in most family medicine practices? Are there regulatory issues that prohibit implementation? Is the service, device, drug or other essentials available on the market? Give one number on a scale of 1 to 7 (1=definitely could be immediately applied; 4=uncertain; 7=definitely could not be immediately applied)	2
10. If you coded 4.9 as 4, 5, 6, or 7, please explain why.	Alternative strategies, such as delay in prescribing and suggestion to reevaluate in several days, may be unattractive options for patients, given the cost of follow-up compared with the cost of amoxicillin.
11. Clinical meaningful outcomes or patient-oriented outcomes: Are the outcomes measured in the study clinically meaningful or patient oriented? Give one number on a scale of 1 to 7 (1=definitely clinically meaningful or patient oriented; 4=uncertain; 7=definitely not clinically meaningful or patient oriented)	1