Title: This antiemetic may help kids skip that trip to the hospital. *J Fam Pract.* 2009;58:85-88.
Potential PURL Review Form: Meta-analysis – systematic review
SECTION 1: IDENTIFYING INFORMATION FOR NOMINATED POTENTIAL PURL

1. Citation	DeCamp LR, Byerley JS, Doshi N, Steiner MJ. Use of antiemetic agents in acute gastroenteritis: a systematic review and meta-analysis. *Arch Pediatr Adolesc Med.* 2008;162:858-865.
2. Hypertext link to PDF of full article	http://www.ncbi.nlm.nih.gov/entrez/utils/fref.fcgi?PrId=3051&itool=AbstractPlus-def&uid=18762604&db=pubmed&url=http://archpedi.ama-assn.org/cgi/pmidlookup?view=long&pmid=18762604
3. First date published study available to readers	September 2008
4. PubMed ID	18762604
5. Nominated By	Sarah-Anne Schumann
6. Institutional Affiliation of Nominator	University of Chicago
7. Date Nominated	
8. Identified Through	*BMJ* online
9. PURLS Editor Reviewing Nominated Potential PURL	Bernard Ewigman
10. Nomination Decision Date	
11. Potential PURL Review Form (PPRF) Type	Meta-analysis
12. Other comments, materials or discussion	
13. Assigned Potential PURL Reviewer	Sarah-Anne Schumann
14. Reviewer Affiliation	University of Chicago
15. Date Review Due	
16. Abstract	OBJECTIVE: To perform a systematic review and meta-analysis to determine whether taking antiemetic drugs reduces vomiting and decreases the need for further intervention in children with gastroenteritis without causing significant adverse effects.

DATA SOURCES: Computerized databases, reference lists, and expert recommendations.
STUDY SELECTION: Prospective controlled trials evaluating medication use in children with vomiting from gastroenteritis.
INTERVENTION: Antiemetic drug therapy.
MAIN OUTCOME MEASURES: Emesis cessation, use of intravenous (IV) fluid for rehydration, hospital admission, return to care, and medication adverse effects.
RESULTS: The 11 articles that met the inclusion criteria evaluated various antiemetic agents: ondansetron (n = 6), domperidone (n = 2), trimethobenzamide (n = 2), pyrilamine-pentobarbital (n = 2), metoclopramide (n = 2), dexamethasone (n = 1), and promethazine (n = 1). Meta-analysis of 6 randomized, double-masked, placebo-controlled trials of ondansetron demonstrated decreased risk of further vomiting (5 studies; relative risk [RR], 0.45; 95% confidence interval [CI], 0.33-0.62, number needed to treat [NNT] = 5); reduced need for IV fluid (4 studies; RR, 0.41; 95% CI, 0.28-0.62, NNT = 5),;and decreased risk of immediate hospital admission
(5 studies; RR, 0.52; 95% CI, 0.27-0.95, NNT = 14). Diarrheal episodes increased in ondansetron-treated patients in 3 studies. Ondansetron use did not significantly affect return to care (5 studies; RR, 1.34; 95% CI, 0.77-2.35).
CONCLUSIONS: Ondansetron therapy decreases the risk of persistent vomiting, the use of IV fluid, and hospital admission in children with vomiting due to gastroenteritis. Future treatment guidelines should incorporate ondansetron therapy for select children with gastroenteritis.

SECTION 2: CRITICAL APPRAISAL OF VALIDITY

1. What types of studies are included in this review?	RCT; other: prospective controlled trials
2. What is the key question addressed in this review? Summarize the main conclusions and any strengths and weaknesses.	Do antiemetic drugs reduce vomiting and decrease the need for further intervention in children with gastroenteritis without causing significant adverse effects? Included 11 studies of multiple medications, but the 6 ondansetron studies were of the highest quality and showed the most effect vs placebo; ondansetron reduced risk of further vomiting, need for IV fluid, and risk of immediate hospitalization (see abstract above

for RR, CI, NNT); 3 ondansetron studies reported an increase in diarrhea, but didn't seem to be clinically significant as there was no difference in return to care; study did not support the use of any other agents/

3. Study addresses an appropriate and clearly focused question - ***select one***

- ☒ Well covered
- ☐ Adequately addressed
- ☐ Poorly addressed
- ☐ Not addressed
- ☐ Not reported
- ☐ Not applicable

4. A description of the methodology used is included.

- ☒ Well covered
- ☐ Adequately addressed
- ☐ Poorly addressed
- ☐ Not addressed
- ☐ Not reported
- ☐ Not applicable

5. The literature search is sufficiently rigorous to identify all the relevant studies.

- ☒ Well covered
- ☐ Adequately addressed
- ☐ Poorly addressed
- ☐ Not addressed
- ☐ Not reported
- ☐ Not applicable

6. Study quality is assessed and taken into account.

- ☒ Well covered
- ☐ Adequately addressed
- ☐ Poorly addressed
- ☐ Not addressed
- ☐ Not reported
- ☐ Not applicable

7. There are enough similarities between selected studies to make combining them

- ☐ Well covered
- ☒ Adequately addressed
- ☐ Poorly addressed
- ☐ Not addressed

reasonable.	☐ Not reported ☐ Not applicable Comments: The researchers separated the studies by medication type, and focused on the ondansetron studies as there were more of them, they were of higher quality, and they had positive results.
8. Are patient-oriented outcomes included? If yes, what are they?	Yes: reduction of vomiting, less need for IV fluid, and fewer hospital admissions
9. Is the funding for the trial a potential source of bias? If yes, what measures were taken to insure scientific integrity?	Not of the meta-analysis, but the authors mention that all of the primary ondansetron studies included funding from the pharmaceutical company that manufactures ondansetron under the trade name Zofran, which could favor positive results. However, the medication is now available in a generic form.
10. To which patients might the findings apply? Include patients in the study and other patients to whom the findings may be generalized.	Children with vomiting due to gastroenteritis and mild to moderate dehydration; all the studies were in ERs or inpatient settings; it is unclear whether the findings apply to outpatients with similar symptoms, but the outcomes are likely generalizable.
11. In what care settings might the findings apply, or not apply?	ER, primary care
12. To which clinicians or policy makers might the findings be relevant?	Primary care doctors, ER doctors, insurance companies, Medicaid (people who decide on coverage of medication)

SECTION 3: REVIEW OF SECONDARY LITERATURE

1. DynaMed excerpts	Efficacy: -Ondansetron (Zofran) may decrease the need for IV hydration in children with acute gastritis/gastroenteritis (level 2 [mid-level] evidence) based on randomized trial without allocation concealment -106 patients ages 1-10 years with acute gastritis/gastroenteritis who failed oral rehydration in emergency department randomized to ondansetron (0.15 mg/kg) vs. placebo -Endpoints were IV hydration (primary), hospital admission, subsequent episodes of emesis and diarrhea, return visit to emergency department -21.6% ondansetron patients required IV hydration vs. 54.5% in placebo group ($p < 0.001$) -

2. DynaMed citation/access date	Reference: Ann Emerg Med. 2008;52:22.
3. Bottom line recommendation or summary of evidence from DynaMed (1-2 sentences)	Includes recent RCT in ED showing that ondansetron reduces need for IV hydration and hospital admission.
4. UpToDate excerpts	No recommendation before IVH. In children with gastroenteritis and vomiting, we recommend a single dose of ondansetron because it reduces vomiting, facilitates the administration of oral rehydration therapy (ORT), and decreases the need to intervene with intravenous fluids (Grade 2B). (See "Vomiting" above). In children with vomiting, a single oral dose of ondansetron reduces vomiting and facilitates the administration of ORT [41] . This was illustrated in a randomized controlled study of children (6 months to 10 years of age) treated in a pediatric emergency department for gastroenteritis and dehydration with1 reported episode of nonbilious vomiting. Patients who received oral ondansetron, compared with placebo-treated patients, were less likely to vomit (14 versus 35 percent), vomited less often (mean number of episodes per child 0.18 versus 0.65), had a greater intake of oral fluids (239 versus 196 mL), and were less likely to receive intravenous fluids (14 versus 31 percent). In this study, the dosing for ondanestron was: •2 mg for children weighing 8 to 15 kgs •4 mg for children weighing >15 to 30 kgs •8 mg for children weighing >30 mg The increased use of ondansetron in children with gastroenteritis and vomiting may lead to improved success of ORT and a decreased need to intervene with intravenous fluids.
5. UpToDate citation/access date	Oral ondansetron for gastroenteritis in a pediatric emergency department. Au: Freedman SB, Adler M, Seshadri R, et al. *N Engl J Med*. 2006;354:1698-1705
6. Bottom line recommendation or summary of evidence from UpToDate (1-2 sentences)	Recommends single dose of ondansetron in children with gastroenteritis and vomiting to reduce further vomiting and need for IV fluids.

7. PEPID PCP excerpts

No recommendations for gastroenteritis.

Pediatric Dosing

- CINV, prophylaxis
- Oral:

  4-11 yo: 4 mg PO, start 30 min before chemo, then 4 and 8 hr after first dose, then q8h x 1-2 d after chemo; >12 yo: 8 mg PO, start 30 min before chemo, then q12h x 1-2 d after chemo
- IV:

  >6 mo: same as adult IV dosing
- PONV, Prophylaxis

  1 mo-12 yo: >40 kg: 4 mg IV x1;<40 kg: 0.1 mg/kg IV x1

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8. PEPID citation/access data

9. PEPID content updating

1. Do you recommend that PEPID get updated on this topic?

2. Is there an EBM Inquiry (HelpDesk Answers and Clinical Inquiries) as indicated by the EB icon (EB) that should be updated on the basis of the review?

If yes, which Evidence Based Inquiry(HelpDesk Answer or Clinical Inquiry), Title(s):

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)

3

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 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.	In children with vomiting and mild to moderate dehydration who have failed attempts at oral rehydration, give 1 dose of oral ondansetron and a repeat trial of oral rehydration to decrease further vomiting, IV fluids, and need for hospital admission.

7. Applicability to a Family Medical Care Setting: Is the change in practice recommendation something that 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	3 Yes, but it might require more time in clinic for observation.
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	2 IL Medicaid covers the medication, so presumably it can be easily obtained by most patients.

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

10. If you coded 4.9 as 4, 5, 6, or 7, please explain why.

11. Clinically 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

12. If you coded 4.11 as a 4, 5, 6, or 7, please explain why.

13. In your opinion, is this a Pending PURL?
Criteria for a Pending PURL:

- Valid: Strong internal scientific validity; the findings appears to be true.
- Relevant: Relevant to the practice of family medicine.

- Practice changing: There is a specific identifiable new practice recommendation that is applicable to what family physicians do in medical care settings and seems different than current practice.
- Applicability in medical setting.
- Immediacy of implementation.

Give one number on a scale of 1 to 7 (1=definitely a Pending PURL; 4=uncertain; 7=definitely not a Pending PURL)

SECTION 5: EDITORIAL DECISIONS

1. FPIN PURLs editorial decision	Pending PURL
2. Follow-up issues for Pending PURL Reviewer	
3. FPIN PURLS Editor making decision	Bernard Ewigman
4. Date of decision	
5. Brief summary of decision	Well-done meta-analysis showing ondansetron to be effective in preventing IV hydration and hospitalization in children with vomiting/GI illness. We believe these findings are relevant in the outpatient setting as well.