

Give vitamin C to avert lingering pain after fracture, *J Fam Pract* 2008; 58:86–89

Potential PURL Review Form: Randomized controlled trial

SECTION 1: IDENTIFYING INFORMATION	
1.1 Citation	Zollinger PE, Tuinebreijer WE, Breederveld RS, Kreis RW. Can vitamin C prevent complex regional pain syndrome in patients with wrist fractures? A randomized, controlled, multicenter dose-response study. <i>J Bone Joint Surg Am</i> 2007; 89:1424–1431.
1.2 PubMed ID	17606778
1.3 Nominated by	Bernard Ewigman, MD, MPSH, Department of Family Medicine, University of Chicago
1.4 Date nominated	August 14, 2007
1.5 Identified through	
1.6 Decision	Potential PURL—assign reviewer
1.7 PURLS Editor	Bernard Ewigman, MD, MPSH
1.7 Nomination decision date	
1.8 Initial status	
1.9 Comments	
1.10 Assigned reviewer	
1.11 Reviewer affiliation	
1.12 Date review due	
SECTION 2: DETAILED STUDY DESCRIPTION	
2.1 Number of patients starting each arm of the study?	99 placebo 96 200 mg vitamin C 114 500 mg vitamin C <u>118 1500 mg vitamin C</u>

	427 total fractures (416 patients)
2.2 Main characteristics of study patients (inclusions, exclusions, demographics, settings, etc)?	Inclusion: >18 years, wrist fracture, presenting to emergency department (ED), in multiple sites in the Netherlands Exclusion: None Demographics: Mean age 61.4 to 62.8 years, ± 15.0 to 18.3
2.3 Intervention(s) being investigated?	Vitamin C as above
2.4 Comparison treatment(s), placebo, usual care, and/or no treatment?	Placebo compared with 3 dosages of vitamin C
2.5 Length of follow up? (Note specified endpoints, eg, death, cure, etc)	One year. Endpoint was occurrence of complex regional pain syndrome
2.6 What outcome measures are used? (List all measures used to assess effectiveness)	Above
2.7 What is the effect of the intervention(s)? (Include absolute risk, relative risk, NNT, CI, <i>P</i> values, etc)	Logistic regression: Vitamin C 200 mg: odds ratio [OR]=0.38 (95% confidence interval [CI], 0.11–0.30) Vitamin C 500 mg: OR=0.14 (95% CI, 0.03–0.68) Vitamin C 1500 mg: OR=0.16 (95% CI, 0.03–0.77)
SECTION 3: INTERNAL VALIDITY	
3.1 Study addresses an appropriate and clearly focused question	Well addressed
3.2 Random allocation to comparison groups	Well addressed
3.3 Concealed allocation to comparison groups	Well addressed
3.4 Subjects and investigators kept “blind” to comparison group allocation	Well addressed
3.5 Comparison groups are similar at the start of the trial	Well addressed
3.6 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	Well addressed
3.7 Were all relevant outcomes measured in a	Well addressed

standardized, valid, and reliable way?	
3.8 Are patient-oriented outcomes included? If yes, what are they?	Yes, presence or absence of complex regional pain syndrome as a proxy for pain
3.9 What percent dropped out, and were lost to follow-up? Could this bias the results? How?	None, compliance reported to be 100%
3.10 Was there an intention-to-treat analysis? If not, could this bias the results? How?	N/A (see above)
3.11 If a multisite study, are results comparable for all sites?	Yes, same protocol followed in all sites
3.12 Is the funding for the trial a potential source of bias? If yes, what measures were taken to insure scientific integrity?	No. Not-for-profit foundation with no agenda other than to improve care
SECTION 4: EXTERNAL VALIDITY	
4.1 To which patients might the findings apply? (Include patients in the study and other patients to whom the findings may be generalized)	Older females (over 60 years of age) who experience fracture of the wrist. No males got CRPS (of 75 total). Could be related to the power of the study. No biological reason to think that males would not benefit from vitamin C, but this is an unknown.
4.2 In what care settings might the findings apply, or not apply?	All settings. No reason to think that this applies only to patients presenting to the ED.
4.3 To which clinicians or policy makers might the findings be relevant?	All clinicians involved in the management of older females with wrist fractures. USPSTF.
SECTION 5: REVIEW OF SECONDARY LITERATURE	
5.1 DynaMed excerpts	None
5.2 DynaMed citation/access date	
5.3 UpToDate excerpts	None
5.4 UpToDate citation/access date	
5.5 PEPID PCP excerpts	None
5.6 PEPID citation/access data	

5.7 Other excerpts (USPSTF; other guidelines; etc)	
5.8 Citations for other excerpts	
SECTION 6: CONCLUSIONS	
6.1 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)	2
6.2 If 6.1 was coded as 4 or below, 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?	N/A
6.3 Are the results of this study relevant to the health care needs of patients cared for by “full scope” family physicians, general internists, general pediatricians, or general ob/gyns? Are they applicable without significant change in programs or policies such as the organization or financing of practice? Give one number of a scale of 1 to 7 (1=absolutely relevant; 4=neutral; 7=not at all relevant)	3
6.4 Please explain your response to item 6.3.	Many wrist fractures are cared for by emergency physicians and orthopedists without involvement of family physicians, internists or ob/gyns
6.5 What is the main recommendation for change in practice, if any? Include a description of the change in practice, the indications, and the target population	Females older than 60 years of age who suffer a wrist fracture should be started on vitamin C 500 mg daily for 50 days to prevent complex regional pain syndrome
SECTION 7: EDITORIAL DECISIONS	
7.1 FPIN PURLs editorial decision	PURL
7.2 FPIN PURLS Editor	Bernard Ewigman, MD