Optimal timing for peripheral IV replacement? *J Fam Pract*. 2012;62:200-202.

Potential PURL Review Form: Randomized controlled trials

SECTION 1: IDENTIFYING INFORMATION

1. Citation	Rickard CM, Webster J, Wallis MC, et al. Routine versus clinically indicated replacement of peripheral intravenous catheters: a randomised controlled equivalence trial. *Lancet*. 2012;380:1066-1074.
2. Hypertext link to PDF of full article	http://www.ncbi.nlm.nih.gov/pubmed?term=22998716
3. First date published study available to readers	September 22, 2012
4. PubMed ID	22998716
5. Nominated By	Jim Stevermer
6. Institutional Affiliation of Nominator	University of Missouri
7. Date Nominated	September 29, 2012
8. Identified Through	InfoPOEMs
9. PURLS Editor Reviewing Nominated Potential PURL	Kate Rowland
10. Nomination Decision Date	October 19, 2012
11. Potential PURL Review Form (PPRF) Type	Randomized controlled trial
12. Other comments, materials or discussion	
13. Assigned Potential PURL Reviewer	Dionna Brown
14. Reviewer Affiliation	University of Chicago
15. Date Review Due	December 6, 2012
16. Abstract	**BACKGROUND:**

The millions of peripheral intravenous catheters used each year are recommended for 72-96 h replacement in adults. This routine replacement increases health-care costs and staff workload and requires patients to undergo repeated invasive procedures. The effectiveness of the practice is not well established. Our hypothesis was that clinically indicated catheter replacement is of equal benefit to routine replacement.

METHODS:

This multicentre, randomised, non-blinded equivalence trial recruited adults (≥18 years) with an intravenous catheter of expected use longer than 4 days from three hospitals in Queensland, Australia, between May 20, 2008, and Sept 9, 2009. Computer-generated random assignment (1:1 ratio, no blocking, stratified by hospital, concealed before allocation) was to clinically indicated replacement, or third daily routine replacement. Patients, clinical staff, and research nurses could not be masked after treatment allocation because of the nature of the intervention. The primary outcome was phlebitis during catheterisation or within 48 h after removal. The equivalence margin was set at 3%. Primary analysis was by intention to treat. Secondary endpoints were catheter-related bloodstream and local infections, all bloodstream infections, catheter tip colonisation, infusion failure, catheter numbers used, therapy duration, mortality, and costs. This trial is registered with the Australian New Zealand Clinical Trials Registry, number ACTRN12608000445370.

FINDINGS:

All 3283 patients randomised (5907 catheters) were included in our analysis (1593 clinically indicated; 1690 routine replacement). Mean dwell time for catheters in situ on day 3 was 99 h (SD 54) when replaced as clinically indicated and 70 h (13) when routinely replaced. Phlebitis occurred in 114 of 1593 (7%) patients in the clinically indicated group and in 114 of 1690 (7%) patients in the routine replacement group, an absolute risk difference of 0.41% (95% CI -1.33 to 2.15%), which was within the prespecified 3% equivalence margin. No serious adverse events related to study interventions occurred.

INTERPRETATION:

Peripheral intravenous catheters can be removed as clinically indicated; this policy will avoid millions of catheter insertions, associated discomfort, and substantial costs in both equipment and staff workload. Ongoing close monitoring should continue with timely treatment cessation and prompt removal for complications.

SECTION 2: CRITICAL APPRAISAL OF VALIDITY

1. Number of patients starting each arm of the study?	1593 patients randomized to clinically indicated removal and 1690 assigned to routine replacement on day 3 for a total of 3283 randomized patients.
2. Main characteristics of study patients (inclusions, exclusions, demographics, settings, etc.)?	Patients aged at least 18 years with an intravenous (IV) catheter in place and expected treatment of longer than 4 days were eligible. Exclusion criteria were bloodstream infection, planned removal of IV catheter within 24 h, or IV catheter already in situ for more than 72 h. The study permitted IV catheters inserted in any clinical area, including the emergency department and operating room. IV catheters inserted in an emergency were not eligible. IV catheters could be inserted by any nurse or doctor or by an IV insertion team.
3. Intervention(s) being investigated?	The primary outcome was phlebitis during the catheterization or within 48 hours after removal. Secondary end points included catheter-related bloodstream infection, all-cause bloodstream infections, local venous infection, colonization of IV catheter tip with >15 organisms, infusion failure, number of IV catheters needed per patient for the course of treatment, overall duration of IV therapy per patient (h), cost per patient for the course of IV therapy, mortality with IV catheter in situ or within 48 h of removal. It was

	expected that IV catheters would be used >4 days.
4. Comparison treatment(s), placebo, or nothing?	Clinically indicated catheter removal was compared to routine replacement on day 3 to determine if there was any difference in phlebitis or secondary outcomes between the 2 groups.
5. Length of follow-up? Note specified end points, e.g. death, cure, etc.	The patients were followed for 48 hours after removal of the catheter. Patients in the clinically indicated group had their IV catheters removed only for completion of therapy, phlebitis, infiltration, occlusion, accidental removal, or suspected infection. Patients in the routine replacement group had their IV catheters replaced every third calendar day, unless clinical reasons made this impossible (eg, IV catheters failed before day 3, or patient unable to be recannulated). The day 3 resite occurred at about 72 h (48-96 h depending on insertion and removal times).
6. What outcome measures are used? List all that assess effectiveness.	Phlebitis was defined as 2 or more of the following signs or symptoms, present simultaneously: (1) patient-reported pain or tenderness (on questioning, then palpation by the research nurse) with a severity of 2 or more on a 10-point scale; (2) erythema, extending at least 1 cm from the insertion site; (3) swelling, extending at least 1 cm from the insertion site; (4) purulent discharge; or (5) palpable venous cord beyond the IV catheter tip. All items apart from patient-reported pain or tenderness were rated by the research nurse after direct assessment of the patient, and review of clinical data. Phlebitis measures were repeated daily, and at 48 h after removal (by telephone if the patient had been discharged). A structured outcome assessment form was used and inter-rater reliability testing was done. Blood cultures and catheter tip cultures were used to assess catheter-related infections.
7. What is the effect of the intervention(s)? Include absolute risk, relative risk, NNT, CI, p-values, etc.	In the primary analysis, in both groups 7% of patients had phlebitis, with an absolute risk difference (ARD) of 0.41% (95% CI, –1.33 to 2.15), which was within the predefined equivalence margin of 3%. Therefore we accepted the equivalence hypothesis. All comparisons of phlebitis occurrence between study groups were equivalent, including per patient (*P*=.64) and per 1000 catheter days (*P*=.67, table 3), and on survival analysis (*P*=.96). The per-protocol analysis (n=2537) had consistent results with the primary analysis with ARD 0.70% (95% CI, –0.88 to 2.28); this comparison had 90% power (*P*=.05) to detect equivalence (margin 3%) at the recorded occurrence of phlebitis of 5.5%. No patient had a venous (local) infection and groups were equivalent for all-cause bloodstream infections, and catheter colonization. Only one patient had a catheter-related bloodstream infection and this patient was in the routine replacement group.
8. What are the adverse effects of intervention compared with no intervention?	Rates of infiltration, occlusion, accidental removal, total infusion failure, and in-hospital mortality were all equivalent between groups. The groups had equivalent overall duration of IV treatment; however, the clinically indicated group required significantly fewer IV catheters per patient, with significantly reduced hospital costs (both *P*<.0001). No serious adverse events were related to the trial intervention.
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	Adequately addressed Comments: The study stated that the patients and clinical staff could not be kept blinded and the research nurses could not be masked because they had to allocate patients to the treatment group and staff had to be told, of course, not to change the IV as routinely done and to monitor patients for signs of phlebitis. However, the laboratory staff were blinded when assessing for microbacterial infections.
13. Comparison groups are similar at the start of the trial	Well covered Comments: Table 1 showed that the groups were very similar.
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.	Well covered Comments: no major differences between patient and catheter characteristics (Tables 1 and 2).
15. Were all relevant outcomes measured in a standardized, valid, and reliable way?	Well covered Comments: A structured outcome assessment form and inter-rater reliability testing was done for accurately assessing phlebitis. Also a study manager was used to audit the data for accuracy and completeness and also to monitor the nurses for compliance with study procedures.
16. Are patient-oriented outcomes included? If yes, what are they?	Yes, patients would definitely like to receive fewer IV insertions during hospitalization if there is no increased risk of infection compared with the standard of care (routine replacement).
17. What percent dropped out, and were lost to follow up? Could this bias the results? How?	No patient withdrew consent.
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?	Yes, these were 3 sites in university-affiliated government hospitals in Queensland, Australia that held monthly meetings to ensure consistency among the sites.
20. Is the funding for the trial a potential source of bias? If yes, what measures were taken to insure scientific integrity?	No, the Australian National Heath and Medical Research Council funded this study through national grants.
21. To which patients might the findings apply? Include patients in the study and other patients to whom the findings	All adult hospitalized patients who receive IV catheters in a nonemergent setting.

may be generalized.

22. In what care settings might the findings apply, or not apply?	This study could also be applied to nursing homes and long-term care facilities where patients may need IV access.
23. To which clinicians or policy makers might the findings be relevant?	All health care organizations and insurance companies, because this would decrease long-term costs.

SECTION 3: REVIEW OF SECONDARY LITERATURE

1. DynaMed excerpts

2. DynaMed citation/access date	Superficial thrombophlebitis. In: DynaMed [database online]. Available at: www.DynamicMedical.com. Last updated September 28, 2012. Accessed November 29, 2012.
3. Bottom line recommendation or summary of evidence from DynaMed (1-2 sentences)	According to new data, there may be no difference in peripheral IV–associated phlebitis with routine changing of the IV (avg 70 h) vs changing the IV when clinically indicated.

4. UpToDate excerpts

5. UpToDate citation/access date	Prevention of intravascular catheter-related infections. In: Basow DS, ed. UpToDate [database online]. Waltham, Mass: UpToDate; 2012. Available at: http://www.uptodate.com. Last updated November 20, 2012. Accessed December 3, 2012.
6. Bottom line recommendation or summary of evidence from UpToDate (1-2 sentences)	Since it is likely the increase of phlebitis increases with the amount of time that a peripheral IV is in place and with the ease of replacement, it is recommended to change peripheral IV catheters at 4 days.

7. PEPID PCP excerpts
www.pepidonline.com
username: fpinauthor
pw: pepidpcp

8. PEPID citation/access data

9. PEPID content updating	1. Do you recommend that PEPID get updated on this topic? Yes, there is important evidence or recommendations that are missing If yes, which PEPID Topic, Title(s): Prevention of IV catheter-related infections 2. Is there an EBM Inquiry (HelpDesk Answers and Clinical Inquiries) as indicated by the EB icon () that should be updated on the basis of the review? Yes, there is important evidence or recommendations that are missing

	If yes, which Evidence-Based Inquiry (HelpDesk Answer or Clinical Inquiry), Title(s): Prevention of IV catheter-related infections
10. Other excerpts (USPSTF; other guidelines; etc.)	CDC guidelines: 2011 Guidelines for the Prevention of Intravascular Catheter-Related Infections
11. Citations for other excerpts	Replacement of Peripheral and Midline Catheters 1. There is no need to replace peripheral catheters more frequently than every 72-96 hours to reduce risk of infection and phlebitis in adults. Category 1B 2. No recommendation is made regarding replacement of peripheral catheters in adults only when clinically indicated. Unresolved issue. 3. Replace peripheral catheters in children only when clinically indicated. Category 1B 4. Replace midline catheters only when there is a specific indication. Category II
12. Bottom line recommendation or summary of evidence from Other Sources (1-2 sentences)	There are no clear guidelines if replacement when clinically indicated is preferred over routine replacement every 72-96 hours.

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?	This was a nonblinded RCT due to the nature of the study. The authors did use a structured outcome assessment form as well as inter-rater reliability testing to account for this for determining phlebitis. Because the authors did take these measures, I think that the risk for internal bias was reduced. A study manager was in place and monthly meetings were conducted to assess for adherence to protocol.
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.	Definitely all hospitalized patients >18 years old would benefit from fewer peripheral IV placements.

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)	3
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.	I do think that this is a practice change, because this study assessed equivalence and showed no difference in infection rates with routine versus clinically indicated replacement of peripheral IV catheters. However, I'm not sure if this is a strong practice change, because in this study both groups had a similar mean duration of therapy—98 hours for the clinically indicated group and 96 hours for the routine replacement group. Most patients in this study only required an IV catheter for about 4 days of treatment. If more had needed longer durations of therapy, it would have been interesting to see if more infections would have occurred in the clinically indicated group.
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)	1
8. If you coded 4.7 as a 4, 5, 6 or 7, please explain.	Yes, could be done in hospital setting or any place where peripheral IV catheters are placed for at least 4 days.
9. Immediacy of Implementation: Are there major barriers to immediate implementation? Would the	1

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)	
10. If you coded 4.9 as 4, 5, 6, or 7, please explain why.	No barriers. Staff who place peripheral IVs would need to be retrained regarding clinical indications for replacement of the IV to prevent infections.
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
12. If you coded 4.11 as a 4, 5, 6, or 7 please explain why.	Fewer IVs and less pain.
13. In your opinion, is this a Pending PURL? Give one number on a scale of 1 to 7 (1=definitely a Pending PURL; 4=uncertain; 7=definitely not 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	2

in medical care settings and seems different than current practice.

- Applicability in medical setting:
- Immediacy of implementation

14. Comments on your response in 4.13

No difference in infections was found in both groups. This change in practice would save costs for many hospitals and is applicable in many settings. The one concern would be that all staff who place IVs would have to be better trained on recognizing when to appropriately replace an IV, because the IVs would not be replaced on a schedule. This practice could be immediately implementable with hospital protocols that would standardize clinical indications for the replacement of catheters.