

Article details: 2017-0010	
Title	Improved outcomes in a nurse-led peripherally inserted central catheter program: a retrospective cohort study
Authors	Sheryl McDiarmid RN MBA, Nicholas Scrivens BSc, Marc Carrier MD, Elham Sabri MSc, Baldwin Toye MD, Lothar Huebsch MD, Dean Fergusson PhD
Reviewers 1	Lauren Lapointe-Shaw and Donald Redelmeier
Institution	Department of Medicine, University of Toronto, Toronto, Ont.
General comments (author response in bold)	<p>This was mostly a single-center case-series analysis of inpatients (n = 656) receiving a peripherally inserted central catheter (PICC) in Canada. Introduction justifies the study based on the seriousness of the potential risk of PICC - associated bloodstream infections and thromboembolism. Methods consist of measuring rates and confidence intervals for the frequency of adverse events. Results show a risk of 0.61% for PICC bloodstream infection (n = 4) and of 1.52% for PICC thromboembolism (n = 10). Conclusion stresses that complication rates are lower than previously reported.</p> <p>Our largest concern is the novelty of study findings. As the authors mention, the literature already provides much data including systematic reviews for the frequency of each adverse outcome. Further, previous studies have adopted stronger designs that included comparison groups. In addition, the analysis says little about potential alternatives such as earlier discontinuation, different insertion techniques, or central venous options. Finally, the study is based on a single center, may not be generalizable elsewhere, and mostly reinforces a low risk that clinicians already appreciate.</p> <ul style="list-style-type: none"> <li>• <b>Please see comment below. The study is relatively novel because it is reporting much lower risks of PICC-related complications.</b> We agree with the reviewer that the single-center design may decrease generalizability, however, it may be used as a template for other centers to improve quality of care within their institution</li> <li>• <b>All patients are triaged by the expert RN team for necessity of PICC placement.</b> The patients with the greatest number of complications are those with hematological malignancies where early discontinuation is not an option. This group of patients requires reliable central venous access for months of therapy so early discontinuation is not an option.</li> <li>• <b>We have discussed the limitation of a single centre study in the paper.</b></li> </ul> <p>The clinical utility of the findings is also questionable. The authors suggest that their care protocols led to lower complication rates, yet this claim cannot be made in the absence of a comparison group. The observed complication rates reported may be lower than in some other publications, yet the difference in thromboembolism is marginal (3.0% vs 1.52%), particularly after considering the width of the confidence interval in this study (0.83% - 2.78%). Finally, the current results are not directly practice-changing because PICC insertion is already mainstream practice for hospital inpatients.</p> <p>The rationale for conducting this study is to provide evidence that PICCs do not have an unacceptably high complication rate. The outcomes from this study show a very low rate of a composite of clinically important endpoints. PICCs are widely prescribed for administration of intravenous therapy across a broad spectrum of health care facilities including tertiary care, complex continuing care, long term chronic care, and home care. The most influential papers in the field are by Chopra et al., in a very high impact journals (Chopra V, Anand S, Hickner A et al., Risk of venous thromboembolism associated with peripherally inserted central catheters: a systematic review and meta-analysis. Lancet. 2013 Jul 27;382(9889):311-24 doi: 10.1016/S0140-6736(13)60592-9) concludes that although deep vein thrombosis of the arm is infrequent in the general population, the same disorder related to indwelling devices such as PICCs is common. A previous publication by Chopra et al., (Chopra V, O'Horo, J, Rogers A, et al. The risk of bloodstream infection associated with peripherally inserted central catheters compared with central venous catheters in Adults: A systematic Review and Meta-Analysis. Infect Control Hosp Epidemiol. 2013;34(9):908-918.), found the unweighted incidence of PICC-related central line associated bloodstream infection in hospitalized patients was 5.2%. The final publication in the American Journal of Medicine (Chopra V, Anand S, Krein SL et al., Bloodstream infection, venous thrombosis, and peripherally inserted central catheters: reappraising the evidence. Am J Med 2012 Aug;125(8):733-41 doi: 10.1016/j.amjmed.2012.04.010) concluded that there is an unprecedented need for a research agenda examining the benefits and risks related to PICC use after systemic reviews and meta-analysis found that PICCs were associated with greater overall complications than other central venous catheters (17% vs 10%).</p> <p>One more concern relates to sampling bias potentially distorting a case series analysis. In particular, the analysis starts with 8,314 total patients from whom 656 charts were reviewed yielding 14 patients (4 + 10) with an adverse event. Hence, the true risk could be as high as 99.4% <math>[(8,314 - 656 + 14) / 8,314]</math> or as low as 0.2% <math>(14 / 8,314)</math> depending on sampling bias (and whether third-party randomization was conducted and scrutinized). In addition, one could quibble over the cases of Candida bacteremia and Coagulase Negative Staph bacteremia excluded on Table 3.</p> <ul style="list-style-type: none"> <li>• <b>We apologize for the confusion. As described within the Method Section, the cases were identified using random generation and it is unlikely to have led to selection bias..</b></li> <li>• <b>We have cited the attribution of CRBSI by infectious disease specialists as a limitation.</b></li> </ul> <p>Otherwise this paper has several strengths. The writing was clear and well organized. Tables were sensible. The primary and secondary adverse outcomes selected were appropriate and relevant clinical consequences. Follow-up of PICC line complications until line removal ensured thorough outcome reporting. The overall blockage catheter occlusion rate of 11% was impressive. The contrast between single-lumen and double-lumen in rates of catheter occlusion was logical and plausible. The discussion provided a detailed comparison of this study's results to those obtained by others.</p>

	We thank the reviewer for its kind comments.
Reviewer 2	Dr. Balthasar Hug
Institution	Luzerner Kantonsspital, Internal Medicine, Lucerne, Switzerland
General comments (author response in bold)	<p>McDiarmid et al describe a retrospective analysis of 700 PICC lines inserted at Ottawa Hospital and their outcomes regarding infection and venous thrombosis. The paper is interesting to read, timely and well written. All the same, there are some issues that need clarification as outlined below.</p> <p>Abstract</p> <p>1. There is mentioned the first time that this is a nurse-led program. On p.2, lines 5-6 the readers learns that the nurses insert the catheters themselves. In other centers this might be the anesthetist or an interventional radiologist inserting the PICC lines. Later on, in the results, the authors do not discuss this issue any further. Does it matter whether PICC lines are inserted by nurses or other hospital services? Are there studies comparing the quality of these services? The authors should give their view on this point in the paper.</p> <p>• <b>We agree with the reviewers comments and believe that a comprehensive, expert nurse-led team performing insertions and providing care and maintenance improve outcomes. The conclusion has been re-written accordingly.</b></p> <p>Methods</p> <p>2. The authors do not define clearly "primary BSI" and "secondary BSI" in their paper but discuss that this is difficult to do (p. 4, second paragraph and p. 7, lines 23 and following). They should either give the reader a clear definition on p. 4 or cut out the terms primary and secondary in this context (since they are at times not easy to discern).</p> <p>• <b>The terms primary and secondary have been removed and Table 3 has been removed and the organisms identified as catheter related blood stream infections identified in the text.</b></p> <p>Results</p> <p>3. P. 4, second line: one patient had 842 catheter days equaling about two years and three months. This is very unusual. The authors should describe this range of CD and if catheters were changed in this one person etc.</p> <p>• <b>In our setting it is not usual to have PICCs in situ for months to years. Thirty one PICCs were in for greater than 1 year and 6 greater than 2 years. We do not remove or change PICCs based on a time period rather functionality and need for the catheter.</b></p> <p>4. P. 4, line 40: the authors use several times the expression "No thrombolytic was required in 89% of PICCs (95% CI, 86.61-91.39%)." Why not make it easy to understand for the reader with a positive statement like "Thrombolytic therapy was needed in 11% of PICC patients" or the like. See also p. 6, second to last line.</p> <p>• <b>The requested changes have been made.</b></p> <p>Discussion</p> <p>5. P.5, line 38: Here the authors talk about a "mean dwell time of 89 days" but in the abstract and results they report the median of 45 days. The authors should be consistent throughout the paper and use one or the other according to the distribution and skewing of their data. I suppose the median of 45 days would be appropriate looking at the outlier discussed above.</p> <p>• <b>Mean dwell time has been removed in the manuscript and replaced with median days.</b></p> <p>6. P. 6, second paragraph, line 11: "The symptomatic DVT rate in this cohort was lower..." Here the question arises how the authors controlled for DVTs. Did they use ultrasound on a regular basis or only on patient complaint? This is very important because we would suspect to find more DVTs with the former than the latter. The authors should describe this in their methods section on p.3.</p> <p>• <b>Only patients where DVT was suspected were investigated with ultrasound. No screening imaging was performed on asymptomatic patients. This has been added to the methods section.</b></p> <p>7. Minor: P. 6, line 24: "with an incidence of .4/1000 catheter days compared to 0.17/1000 catheter days..." Here the authors should write 0.4/1000 as they did in the rest of the paper.</p> <p>• <b>This has been corrected in the manuscript.</b></p> <p>8. Limitations: This section is fine, but the authors should add that this was a single center study with an accordingly reduced generalizability of their results.</p> <p>• <b>The single center limitation was added to the limitation paragraph.</b></p> <p>Conclusion</p> <p>9. Here again the reader wonders whether the fact that this is a nurse-led program might have an influence on the results? If yes, this should appear in the conclusions.</p> <p>• <b>The conclusion has been re-written to emphasize the fact that we believe a nurse-led program improves outcomes.</b></p> <p>Tables:</p> <p>10. Table 1: please insert the range of the parameter "Age"</p>

	<p>• <b>This has been added to the manuscript.</b></p> <p>11. Table 2: The authors mention that they inserted the PICC lines in 84% on the right arm. Why did they do that? Most people are right-handed and should have a line-free hand on that side. It would be interesting to have a comment of the authors on that.</p> <p>• <b>Published literature has shown an increased risk of deep vein thrombosis associated with PICC insertions on the left side.</b> Most recently a study by T. Marnejon et al., Risk Factors for upper extremity venous thrombosis associated with peripherally inserted central venous catheters JVasc Access 2012; 13(2):231-238) found that left sided PICC line insertion posed a greater risk (P=.026) than right sided insertion. The hypothesis is that there is a more direct route from the right arm to the superior vena cava than the left. In one study as many as two-thirds of thromboses were left sided. We do not place onerous activity related restrictions on patients with PICCs so whether the PICC is on the left or right side it does not interfere with limb movement.</p> <p>12. Table 3: primary and secondary BSI: see comment above about p. 7, lines 23 and following</p> <p>• <b>The table has been removed and the information has been incorporated into the manuscript.</b></p> <p>13. Table 4: Please add percentage of 10 VT per 700 PICC lines=1.4% on top of the table. Please be specific about what "Lung", "Breast" and "Colorectal" mean. Are these diseases in general or cancers only?</p> <p>• <b>I have added 1.52% on top of the table (it is now Table 3) – that is the correct percentage not 1.4%.</b>  • <b>Diagnoses have been clarified.</b></p> <p>14. Table 5: the p-value should be written below the table</p> <p>• <b>That change has been made (it is now Table 4).</b></p>
Reviewer 3	Dr. Sandy L. Widder
Institution	Department of Surgery & Critical Care Medicine, University of Alberta, Edmonton, Alta.
General comments (author response in bold)	<p>A very nice review of how interdisciplinary models of care can improve patient care overall.</p> <p>1. Of the 700 randomly selected patients, 44 were excluded as PICC removal dates (n= 7) were not available or patients were transferred to another facility (n=37). Was there any attempt made to pursue these patients to determine whether or not any complications occurred? Were these patients home on patients?</p> <p>• <b>We did not attempt to pursue the 44 patients who were excluded because removal dates were not available.</b> The care and maintenance protocols for patients transferred to another facility may not have been comparable so they were excluded. I reviewed the source data and none of the 44 patients had a diagnosis of hematological malignancy. Given the complexity of patients with hematological malignancy they are typically followed by the hematology staff at The Ottawa Hospital.</p> <p>2. Would it be possible to perform a retrospective before-after study; specifically looking at patients before the introduction of a specialized nursing team? Could you match patients with another site that does not have a specialized nursing team inserting PICCs, or another site that uses alternate methods, i.e. radiologist insertion?</p> <p>• <b>This specialized nursing team has been in place since 2008.</b> There are many centers where radiologists insert PICC and that would make an interesting comparative study but outside of the scope of this paper.</p> <p>3. Were there any new specific protocols introduced or implemented during the time frame to potentially improve outcomes? Any evidence behind line brands or types? Were there any balancing measures that were looked at? How about costs and wait times for PICC lines, and whether or not there was a trickle down affect to overall LOS and patient outcomes? Are there more health care costs saved when using specialized nursing models of care?</p> <p>• <b>This is a single center study retrospective cohort study without a comparator group so it is not possible to determine which if any of the variables affected the overall low incidence of serious complications related to PICCs in this study.</b> The Bioflo PICC we inserted during the study period is a polyurethane catheter that has been modified by the addition of the Endexo polymer which has been shown in vitro testing to reduce thrombus accumulation however it is not possible to determine the contribution this catheter made to the overall low rate of complications in this cohort.</p> <p>We have a comprehensive database that tracks wait times and ours are &gt;24 – 48 hours for inpatient referrals. There are significant cost savings using nursing models of care particularly when compared with the insertion of PICCs in the radiology suite. Although interesting, it was not the focus of this study but could be for another manuscript.</p>