Cost-effectiveness analysis of clinically-indicated versus routine replacement of peripheral intravenous catheters

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Running title

Cost-effectiveness of clinically-indicated catheter replacement

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Abstract

Background

Millions of peripheral intravenous catheters are used worldwide. The current guidelines recommend routine catheter replacement every 72-96 hours. This practice requires increasing healthcare resources. The clinically-indicated catheter replacement strategy is proposed as an alternative.

Objectives

To assess the cost-effectiveness of clinically-indicated versus routine replacement of peripheral intravenous catheters.

Methods

A cost-effectiveness analysis from the perspective of Queensland Health, Australia, was conducted alongside a randomised controlled trial. Adult patients with an intravenous catheter of expected use longer than four days were randomly assigned to clinically-indicated replacement, or third daily routine replacement group. The primary outcome was phlebitis during catheterisation or within 48 hours after removal. Resource use data were prospectively collected and valued (2010 prices). The incremental net monetary benefit was calculated with uncertainty characterised using bootstrap simulations. Additionally, value of information (VOI) and value of implementation analyses were performed.

Results

The clinically-indicated replacement strategy was associated with cost saving per patient of AU\$7.60 (95%CI: 4.96 to 10.62) and a non-significant difference in phlebitis rate 0.41% (95%CI: (-1.33 to 2.15)). The incremental net monetary benefit was AU\$7.60 (95%CI: 4.96 to 10.62). The expected VOI was zero, whereas the expected value of perfect implementation of the clinically-

indicated replacement strategy was approximately AU\$5 million over five years.

Conclusion

The clinically-indicated catheter replacement strategy is cost-saving compared to routine replacement. It is recommended that healthcare organisations consider changing to a policy whereby catheters are changed only if clinically indicated.

Key points for decision makers

- Routine replacement of peripheral intravenous catheters does not reduce the rate of catheter related complications compared to the clinically-indicated (e.g., due to catheter failure) replacement.
- Replacing catheters only if clinically indicated saves health care costs.
- It is recommended that health care organisations change to a policy whereby peripheral intravenous catheters are replaced when clinically indicated and not routinely.

Introduction

Peripheral venous catheters are commonly used to deliver medications, fluids, blood products, and nutritional supplements intravenously. Up to 70% of patients in acute care hospitals need a short peripheral intravenous catheter; about 330 million are sold each year in the USA alone.(1) The insertion of intravenous catheters is an invasive procedure that can cause discomfort to patients and is associated with complications such as irritation of the vein (phlebitis) in (2.3%-60%) and catheter-related bloodstream infections (CRBSI) in (0.1%) of the cases.(2-4) To reduce the incidence of these adverse events in adult patients, the current guidelines from the USA Centers for Disease Control and Prevention (CDC) recommend routine intravenous catheter replacement no more frequently than every 72–96 hours.(5) This routine replacement is the current practice in most of the hospitals around the world although it subjects patients to repeated invasive procedures and increases health-care costs. (6, 7) Interestingly, recent studies have found no evidence to support the routine replacement of catheters as a measure to mitigate catheter-related complications.(6, 8-10) A recently published trial by Rickard and colleagues(7) tested whether patients who had their peripheral intravenous catheters replaced when clinically indicated would have equivalent rates of phlebitis and other complications but reduced health care resources and costs compared to the patients who had routine catheter replacement every three days. Patients in the clinically indicated group had their intravenous catheters removed only for completion of therapy, phlebitis, infiltration, occlusion, accidental removal, or suspected infection. (7) The aim of this paper is to determine the cost-effectiveness comparing the two approaches of clinically-indicated versus routine replacement of peripheral venous catheters based on the results of the clinical trial of Rickard *et al*(7), within the context of the public health system in Queensland, Australia. In addition, a value of information and value of implementation analyses were undertaken to characterise decision uncertainty and inform if the implementation of the recommended strategy is worthwhile.

Methods

Clinical trial design and results

Full details of the design and results of the clinical trial have been reported elsewhere.(7) Briefly, this was a multicentre, randomised, non-blinded equivalence trial which recruited adult patients with an intravenous catheter of expected use longer than four days from three hospitals in Queensland, Australia, between 2008 and 2009. Computer-generated random assignment was to clinically-indicated replacement or third daily routine replacement. Patients in the clinically-indicated group had their intravenous catheters removed only for completion of therapy, phlebitis, infiltration, occlusion, accidental removal, or suspected infection. (7) The primary outcome was phlebitis during catheterisation or within 48 hours after removal. Primary analysis was by intention to treat. Of the 3379 eligible patients, 3283 were enrolled and they were all included in the analysis (1593 clinically indicated; 1690 routine replacement). Patients' characteristics were comparable across the two groups. Phlebitis occurred in 114 of 1690 (6.75%) patients in the routine replacement group and in 114 of 1593 (7.16%) patients in the clinically-indicated group, an absolute risk difference of 0.41% (95% CI; -1.33 to 2.15%).(7) Catheter-related bloodstream infections were rare in both groups at one per 3,283 (0.03%) patients; no serious adverse events related to study interventions occurred (Table 1).

<<Table 1 goes here>>

Resource use measurement

Health care resource utilisation data were collected alongside the clinical trial for the two study groups. These resources included equipment required for insertion and removal of intravenous catheters and staff time to insert and remove catheters (Table 2). The equipment required for each intervention arm was valued using negotiated hospital supply contract rates (2010) from the

perspective of the State health department, Queensland Health, Australia. Based on observed rates of 14.5 minutes per insertion and 4.5 minutes per removal, the staff time was valued at the fixed industrial award wages in Australia (2010).(7)

<<Table 2 goes here>>

Analysis

1. Cost-effectiveness analysis

The economic evaluation was from the perspective of Queensland Health. The net monetary benefit (NB) approach was used for the cost-effectiveness analysis.(11) The NB for each strategy was calculated by multiplying its effect outcome by the WTP threshold and subtracting cost. The strategy with the maximum mean NB would be the preferred option. The incremental net monetary benefit (INB) is the difference between the NBs of the compared strategies and it represents the net gain from the introduction of the new strategy. Because the primary outcome of the trial was phlebitis rate, which is an adverse event, the effect outcome chosen for the cost-effectiveness analysis was the rate of phlebitis avoided (i.e., 1- phlebitis rate). A willingness to pay (WTP) threshold was set at AU\$0.0 per phlebitis case avoided since the treatment of phlebitis typically consisted only of removal and replacement of the affected intravenous catheter, which was already accounted for in the cost calculations. The 95% non-parametric confidence interval (percentile method) based on 1,000 bootstrap replications was calculated to characterise the uncertainty in the INB.(12) The results of the bootstrap simulation are shown in a cost-effectiveness plane. In addition, a cost-effectiveness acceptability curve (CEAC) was plotted to show the probability of one of the two strategies being cost-effective across a range of possible WTP thresholds.(13)

The clinical trial directly compared the two alternative strategies of catheter replacement and

prospectively captured all relevant outcomes and costs; therefore, an economic evaluation based on the trial data alone was considered sufficient (i.e. there was no need for modelling). Because the time horizon of the analysis was one month, total costs and effect outcomes were not discounted.

2. Value of information analysis

Value of information (VOI) analysis is a systematic approach to measure uncertainty surrounding the results of cost-effectiveness analyses.⁽¹⁴⁾ The analysis would usually start by calculating the expected value of perfect information (EVPI). The EVPI is the difference between the net benefit of a decision given perfect information and the net benefit of the decision based on current information.⁽¹⁴⁾ The population-EVPI would be estimated by multiplying the calculated EVPI by the number of patients expected to benefit from this intervention over a given time horizon. The population that would benefit from the cost-effective strategy in Queensland public hospitals over the coming five years (discounted at 5%) was estimated to be approximately 680,000. This is based on the assumption that one third of the 450,000 overnight admissions per year (150,000) would need catheter placement for more than 3 days.⁽¹⁵⁾ The population-EVPI reflects the magnitude of uncertainty in the results of a cost-effectiveness analysis and represents the maximum (upper bound) value for conducting further research to resolve this uncertainty.⁽¹⁴⁾ If further research appears potentially worthwhile based on the population-EVPI, the value of resolving uncertainty surrounding a particular parameter (e.g., cost, effect) would be estimated by calculating the expected value of perfect parameter information (EVPPI).⁽¹⁴⁾ To inform the value of a proposed future trial design (e.g., sample size) that could reduce uncertainty surrounding our results, the expected value of sample information (EVSI) would be calculated.^(16, 17) If the EVPI was small (approaching zero) then there would be very little uncertainty surrounding the findings of our cost-effectiveness analysis, and there would be no need to estimate the EVPPI or the EVSI.

Our focus on this case should be directed to the implementation of the strategy that was expected to be cost-effective.(18)

Methods to calculate the above VOI measures are described in detail elsewhere.(19-21) In general, VOI analysis was performed using Monte Carlo simulation. Random values for the estimated NBs were sampled repeatedly (10,000 iterations) from the normal distribution of the mean NB of each intervention, based on the central limit theorem.(19) Then, NB for each strategy *at each iteration* was calculated to identify the optimal strategy. Averaging the maximum NBs from all iterations and subtracting from this the mean NB of the preferred strategy (calculated from the cost-effectiveness analysis) would give the EVPI. Assuming that the NB was a linear function of the cost and effect parameters, the same one-level Monte Carlo simulation technique would be used to calculate the EVPPI for the parameters of interest.(19) Similarly, the EVSI for a proposed trial of a given sample size could be calculated by sampling from the updated (using Bayesian updating) distribution of the mean NB for each strategy.(21)

3. Value of implementation analysis

The expected value of perfect implementation (EVPI_m) is the difference between the expected benefit of perfectly implementing the cost-effective strategy and the expected benefit of this strategy with sub-optimal implementation:(18)

$$EVPI_m = NB \text{ of preferred strategy} - (P \times NB \text{ of preferred strategy}) \quad \text{Equation 1}$$

P is the proportion of the eligible population that is currently benefiting from the preferred strategy, which can take values between 0-1. The population-EVPI_m was calculated by multiplying the EVPI_m from the above equation by the number of Queensland Health patients that would benefit from the preferred strategy over the coming five years (i.e., 680,000). The

population-EVPI_m could inform the cost-effectiveness of programs to improve the implementation of the preferred strategy.

Results

Resource use

Table 3 summarises resource utilisation data over the study period. The clinically indicated catheter replacement group had fewer catheters inserted compared to the routine replacement group (1.7(SD1.05) versus 1.9 (SD 1.17)) with a reduction of 0.21 catheter per patient (95% CI: 0.14 to 0.29). In addition, replacing peripheral intravenous catheters only when clinically indicated was associated with a significant reduction in the staff time for the insertion and removal of catheters at 3.08 minutes (95%CI: 1.97 to 4.19) and 0.94 minutes (95%CI: 0.60 to 1.30), respectively.

<<Table 3 goes here>>

Cost

Cost results are reported in Table 4. The routine replacement group incurred equipment cost of AU\$47.80 (SD 30.00) and staff cost of AU\$21.50 (SD14.10). For the clinically-indicated replacement group, the average cost for the equipment and staff was AU\$42.50 (SD \$27.00) and AU\$19.20 (SD \$13.10), respectively. The clinically-indicated replacement group had lower total cost (AU\$61.70; SD \$39.50) versus AU\$69.30; SD \$43.50)) with a statistically significant reduction in total cost at AU\$7.60 (95%CI: 4.96 to 10.62) per patient.

<<Table 4 goes here>>

Cost-effectiveness

At a WTP of AU\$ 0.0, the clinically-indicated catheter replacement strategy was associated with a higher NB compared to the routine-replacement strategy (AU\$ -61.70 versus AU\$ -69.30) indicating that the clinically-indicated replacement is the preferred strategy (Table 5). The INB was AU\$ 7.60 (95%CI: 4.96 to 10.62) in cost saving. Figure 1 presents the INB in AU\$ with 95% uncertainty interval across a range of values for the WTP. From the CEAC, the probability of the clinically-indicated replacement strategy being cost-effective was greater than 95% as long as the WTP threshold was less than AU\$350 per phlebitis case avoided (Figure2).

<<Table 5 goes here>>

<<Figure 1 goes here>>

<<Figure 2 goes here>>

Value of information analysis

The VOI analysis estimated the EVPI to be AU\$0.0 per patient for the proposed WTP threshold of AU\$0.0. Because the EVPI is the upper bound for the cost of uncertainty the EVSI would be also AU\$0.0. The EVPI was found to remain around AU\$0.0 as long as the WTP threshold per phlebitis case avoided was below AU\$350 (Figure 2).

Value of implementation analysis

Assuming that the current implementation of the clinically-indicated catheter replacement is zero, the value of perfectly implementing this strategy (EVPI_m) based on the results of the cost-effectiveness analysis would be the NB of the clinically-indicated replacement strategy. The population-EVPI_m was estimated to be around AU\$5 million (680,000 x AU\$7.6) for Queensland public hospitals over the coming five years.

Discussion

This study presents a cost-effectiveness analysis and VOI based on a multicentre randomised

controlled trial comparing the clinically-indicated versus routine replacement of intravenous peripheral venous catheters. The clinical analysis concluded that the two strategies had the same rate of phlebitis and other complications including bloodstream infections. The cost-effectiveness analysis showed that the clinically-indicated replacement strategy was associated with a significant reduction in health care resources in terms of equipment and staff time, resulting in an average cost reduction of AU\$7.6 per patient. Because patient-level data on cost and effect were available from the clinical trial, the decision was made to conduct a full cost-effectiveness analysis to estimate the joint density of cost and effect differences and present uncertainty on cost-effectiveness acceptability curve. Performing a cost-minimisation analysis based on the equivalence in effect could result in biased estimation of uncertainty surrounding the results.(22) A VOI analysis was also undertaken measure this uncertainty and to assess whether the evidence from the clinical trial is sufficient to change the current practice

The results of the cost-effectiveness analysis suggested that adopting the clinically indicated catheter replacement strategy would result in an INB of AU\$7.6 per patient, the probability of this strategy being cost-effective approached 100% as long as the WTP for phlebitis case avoided was below AU\$350. The EVPI was also approaching zero under this WTP threshold suggesting negligible uncertainty and minimal value for additional research. This is one example of how the VOI analysis can support new strategies when decisions on strategy adoption and the need for further research are taken simultaneously.

Because globally a high number of patients need intravenous catheters, there is significant value of implementing the findings of this study by changing the current guidelines to recommend catheters replacement only if clinically indicated. The EVPI in Queensland public hospitals over the coming five years was approximately AU\$5 million. This benefit of implementation would

amount to higher figures if this strategy was implemented worldwide. For example, of the 37 million patients admitted to hospitals each year in the USA alone,(23) if one-third (12.5 million) needed a catheter for more than 3 days, then a change to clinically-required replacement would prevent around 2.5 million unnecessary intravenous catheter insertions and would save up to 1 million hours of staff time. The expected monetary value of perfectly implementing this strategy in the USA alone over five years would be around US\$400 million in health cost savings. To implement this strategy, hospitals with routine catheter replacement practice already in place need to change current policies and develop protocols to allow regular patient assessment and subsequent catheter removal or replacement for phlebitis, other complications, or when therapy has been completed. Nevertheless, the expected cost of implementation is less likely to exceed the benefits from adopting the proposed strategy.

This study has a number of limitations. First, the analysis was based on a single clinical trial from Australia. However, the clinical trial was multisite with a large sample size (3,283 patients), with high quality methods to eliminate selection, allocation, and detection bias, together with 100% follow-up for the primary endpoint. Furthermore, the results of this study are in line with the findings from previous smaller randomised trials and a recent systematic review.(6, 8, 10) Second, the resources measured included equipment and staff time but excluded other resources such as hospital stay. Nevertheless, patients in the two groups were well matched in their baseline characteristics including the reason of admission, and it is unlikely that the hospital stay would be prolonged due to the complications associated with the compared strategies (e.g., phlebitis). Third, measuring and valuing different resources were from the perspective of one health department, Queensland Health. However, different jurisdictions and organisations can assign local values to relevant resources in order to have more accurate estimate of the magnitude of cost savings. We would expect that the relative costs of the key resources valued in these analyses (e.g., nursing

time, catheter equipment) will be similar in other jurisdictions. The other assumption made was the WTP threshold of AU\$0.0; however, the effect of varying WTP values on the findings of the cost-effectiveness analysis was clearly presented in the results section. Finally, due to the acute nature of this intervention, it was difficult to measure the effect of each strategy on the quality of life of the hospitalised patients and conduct a cost utility analysis. Patients are presumably unlikely to want routine replacement since insertion of an intravenous catheter is painful, requiring piercing of skin, tissue, and vein with a steel needle at least once, or several times for a difficult insertion.(7)

Conclusion

There was no significant difference in the rate of phlebitis or other complications between the clinically-indicated versus the routine peripheral catheter replacement strategies. Changing catheters only when clinically indicated reduces health care resources and saves costs. Health care organisations should consider changing current policies to recommend the clinically indicated replacement of peripheral intravenous catheters.

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Conflict of Interest/Disclosure

The authors declare no conflict of interest.

Author Contributions

All authors made substantial contributions to the writing and the final review of the manuscript.

HT, LG and PS performed the economic analysis. CR, NM, JW, and MW contributed to the acquisition and analysis of the clinical data. HT is the guarantor for the overall content

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Table 1: Trial outcomes per group based on intention-to-treat analysis (7)

	Clinically indicated (n=1593)	Routine replacement (n=1690)	Risk (95%CI)	p value
Primary outcome, intention-to-treat analysis				
Phlebitis per patient, n (%)	114 (7.16%)	114 (6.75%)	RR 1.06 (0.83 to 1.36) ARD 0.41% (-1.33 to 2.15)	0.64
Phlebitis/1000 intravenous catheter days (95% CI)	13.08 (10.68 to 15.48)	13.11 (10.71 to 15.52)	HR 0.94 (0.73 to 1.23)	0.67
Secondary outcomes, n (n per 1000 intravenous catheter days)				
Any infusion failure ^a	670 (76.9)	636 (73.2)	HR 0.99 (0.89 to 1.11)	0.87
Infiltration	279 (32.0)	235 (27.0)	HR 1.06 (0.89 to 1.27)	0.51
Occlusion	344 (39.5)	344 (39.6)	HR 0.92 (0.79 to 1.07)	0.92
Accidental removal	166 (19.0)	159 (18.3)	HR 0.98 (0.79 to 1.23)	0.88
CRBSI ^b	0 (0)	1 (0.11)	..	..
All BSI	4 (0.46)	9 (1.03)	HR 0.46 (0.14 to 1.48)	0.19
Venous (local) infection ^b	0	0	..	..
Mortality, n (%) ^c	4 (<1%)	4 (<1%)	RR 1.06 (0.27 to 4.23)	0.93

ARD =absolute risk difference; BSI=bloodstream infection; CRBSI=catheter-related bloodstream infection;

HR=hazard ratio; IRR=incident rate ratio; RR=relative risk.

^aCombined endpoint of phlebitis, infiltration, occlusion, accidental removal, and CRBSI.

^bRisk and p value inestimable because of 0 incidence in one or both groups.

^cIn all cases, mortality was unrelated to intravenous catheter treatment

Table 2: Unit costs used in the study (2010 AU\$)

Resource item	Unit	Unit cost
Equipment		
Intravenous catheter plus AS, burette, and fluid bag	Per item	AU \$25.13
Intravenous catheter plus AS and fluid bag	Per item	AU \$21.83
Intravenous catheter plus end cap	Per item	AU \$12.73
Gauze and tape for removal	Per item	AU \$00.37
Staff		
Registered nurse	Per hour	AU \$32.93
Junior medical staff	Per hour	AU \$45.96
Senior medical staff	Per hour	AU \$67.16

AS= administration set; AU\$= Australian Dollar

Table 3: Health resource use

Resources	Routine replacement (n=1690)	Clinically indicated (n=1593)	Difference		
	Mean (SD)	Mean (SD)	Mean	95% CI	p value
Equipment					
Catheters inserted	1.90 (1.17)	1.70 (1.05)	-0.21	-0.29,-0.14	<0.0001
<i>Catheter + AS + burette + fluid</i>	98%	97%			
<i>Catheter + AS + fluid</i>	1%	1.5%			
<i>Catheter</i>	1%	1.5%			
Catheters removed	0.90 (1.17)	0.70 (1.05)	-0.21	-0.28,-0.13	<0.0001
<i>Gauze and tape for removal</i>	100%	100%			
Staff time					
Insertion time (min)	27.58 (17.01)	24.50 (15.00)	-3.08	-4.19,-1.97	<0.0001
<i>Registered Nurse</i>	51%	47%			
<i>Junior medical staff</i>	37%	39%			
<i>Senior medical staff</i>	12%	14%			
Removal time (min)	4.07(5.30)	3.13 (4.70)	-0.94	-1.30,-0.60	<0.0001
<i>Registered Nurse</i>	100%	100%			

AS= Administration set

Table 4: Cost comparison between the trial groups (2010 AU\$)

	Routine replacement (n=1690)	Clinically indicated (n=1593)	Difference		
Cost (AU\$)	Mean (SD)	Mean (SD)	Mean	95% CI	p value
Equipment cost	47.80 (30.00)	42.50 (27.00)	-5.30	-7.30 to -3.40	<0.0001
Staff cost	21.50 (14.10)	19.20 (13.10)	-2.30	-3.24 to -1.30	<0.0001
Total cost	69.30 (43.50)	61.70 (39.50)	-7.60	-10.62 to -4.96	<0.0001

AU\$=Australian Dollar

Table 5: Cost-effectiveness analysis

	Routine replacement (n=1690)	Clinically indicated (n=1593)	Difference	
	Mean (SD)	Mean (SD)	Mean	Bootstrap 95% CI
Phlebitis avoided	93.25% (25.10)	92.84% (25.80)	-0.41%	-2.15% to 1.33%
Total cost	AU\$ 69.30 (43.50)	AU\$ 61.70 (39.50)	AU\$ -7.60	-4.96 to -10.62
NB ^a	AU\$ -69.30 (43.50)	AU\$ -61.70 (39.50)	AU\$ 7.60	4.96 to 10.62

NB= net benefit; AU\$=Australian Dollar

^aWillingness to pay threshold= AU\$ 0.0

Figure 1: The INB for the clinically-indicated replacement strategy with 95% uncertainty boundaries^a

INB = incremental net benefit

^a From 1000 bootstraps

Figure 2: Cost-effectiveness acceptability curve (CEAC) and the expected value of perfect information (EVPI)