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Indwell times, complications and costs of open vs closed safety peripheral intravenous catheters: a randomized study[☆]

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SUMMARY

Background: Catheter-related infections (CRIs) caused by peripheral intravenous catheters (PIVCs) are an increasingly common iatrogenic complication. To prevent this, recommended timelines for routine replacement of PIVCs have increased from 48 h to 72 h and subsequently to 96 h, despite a lack of supporting scientific evidence.

Aim: To compare closed-system (COS) PIVCs with open-system (MOS) PIVCs.

Methods: This prospective, randomized controlled trial compared the indwell time of COS PIVCs without complications with that of MOS PIVCs, removed only by clinical indication. In total, 1199 PIVCs (642 inpatients) were randomized and 283 PIVCs were cultured. Sixteen catheters (11 patients) were lost to the study after randomization.

Findings: In total, 104,469 catheter-hours (54,173 h in 584 COS and 50,296 h in 599 MOS) were recorded. The median dwell time was 137.1 h for COS PIVCs and 96 h for MOS PIVCs ($P = 0.001$). Among PIVCs in place for ≥ 24 h, the median dwell time was 144.5 h for COS PIVCs [95% confidence interval (CI) 123.4–165.6] and 99 h for MOS PIVCs (95% CI 87.2–110.8). Use of COS PIVCs reduced phlebitis rates by 29% (31 vs 45 cases/1000 catheter-days; $P = 0.004$). The probability that a MOS PIVC would last for 96 h was 79.9%, and the probability that a COS PIVC would last for 144 h was 80.4%. There were no significant differences in rates of bacterial colonization per 1000 catheter-days (51.1 COS vs 54.1 MOS) or CRI (5.76 COS vs 6.65 MOS). Nevertheless, there was a 20% relative risk reduction in CRI.

Conclusion: Use of COS PIVCs reduced episodes of phlebitis and risk of infection at a cost of only €0.09/day. When PIVCs are replaced based on clinical indication, COS PIVCs last for up to 144 h and MOS PIVCs last for up to 96 h without increased risk and with significant cost savings (€786,257/year/1000 beds).

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Introduction

Peripheral intravenous catheters (PIVCs) are the most commonly used invasive devices (150 million/year in the USA).¹ In Spain, nearly 50% of inpatients receive an intravenous catheter, almost 95% of which are peripheral. PIVCs have been recognized as a source of *Staphylococcus aureus* bacteraemia in 12–50% of all catheter-related bloodstream infections (CRBSI),^{2,3} and are the cause of considerable morbidity and mortality, prolonged hospital stay and an increased cost^{4,5} of up to €3700 per episode.⁶

It has been reported that nearly half of PIVC-related bacteraemias are associated with phlebitis,^{3,7} which is the most important complication of PIVCs⁴ (approximately 20% of patients).^{7–9}

Catheter-related complication (CRC) rates are thought to be associated with the length of time that the catheter remains in the vein (indwell time). The timelines for routine replacement have been the subject of controversy and uncertainty. Over the years, they have increased from 48 h to 72 h^{10,11} and, most recently, to 96 h.¹² However, such recommendations are based primarily on dated studies (1975,¹⁰ 1987¹¹ and 1998¹²) that did not take recent manufacturing changes in PIVC technology into account.

Safety PIVCs, which reduce the risk of sharps injury, have been introduced recently. Needleless connectors create 'closed systems' that have lower rates of microbial contamination compared with three-way 'stopcocks'.^{13,14} However, safety devices cost more than conventional devices, and 'integrated closed devices'¹⁵ cost even more than open ones. To the authors' knowledge, this is the first study to compare open and closed safety PIVCs.

Methods

Objectives and definitions

The COSMOS study was a randomized controlled trial to investigate the clinical performance of two state-of-the-art safety PIVC systems: a 'compact' closed system (COS) and a 'mounted' open system (MOS), both of which should only be removed from patients when clinically indicated. The two systems were compared in terms of effectiveness (insertion success, maintenance, utility), efficacy (indwell time without complications), safety for professionals and patients against accidental needlestick injury or CRC rates (phlebitis, pain, painful haematoma, infiltration/extravasation, occlusion, bacterial colonization, suspicion of infection by unexplained fever, catheter-related infection) and efficiency (cost analysis).

Catheter-related infection (CRI) was defined as the growth of more than 15 colony-forming units of the same species in semiquantitative culture of catheter tips removed as a result of phlebitis, pain or the suspicion of infection due to unexplained fever, or by defervescence within 24 h of catheter removal.^{5,16,17}

Study design and sample

This prospective, open label, parallel-group randomized control trial was conducted in three medical (61 beds) and surgical (154 beds) wards at the Hospital Clínico 'San Carlos', a 1000-bed tertiary university hospital in Madrid, Spain, for 108

days between March and July 2008. The 126 nurses who comprised the staff of the three wards participated as field researchers. PIVCs were inserted and maintained in accordance with the guidelines of the US Centers for Disease Control and Prevention (CDC),⁵ except for routine replacement recommendations (i.e. catheters were only removed when clinically indicated). The needleless connector was replaced routinely every eight days (after up to 64 activations), which is less than the 70 activations reported by Adams *et al.*¹⁸

All patients aged ≥ 18 years needing a PIVC for at least 24 h were evaluated for inclusion in the study. Informed consent was obtained and enrolled patients were randomized into the COS or MOS PIVC group. Patients were excluded if they were participating in another study, had a PIVC placed under emergency conditions, had a synchronous catheter (PIVC, intravenous midline, peripherally inserted central catheter or central venous catheter) or had a fever of ≥ 38 °C.

The sample size was calculated on the assumption of a phlebitis rate of 15% in the MOS group at 72 h, a 5% reduction in the COS group, alpha error of 0.045 and beta error of 0.20. Phlebitis was chosen as the endpoint because it is the most common complication associated with CRI and PIVC removal.^{4,5} The minimum calculated accrual number was 435 catheters in each arm of the study.

After the first 420 patients were enrolled, an interim analysis revealed that nurses had been less familiar with COS PIVCs than MOS PIVCs at study initiation (17.2% vs 82.8% of nurses; respectively), because MOS PIVCs had been used in the hospital for years while COS PIVCs had only been introduced recently. This led the investigators to increase the target sample size to 1200 catheters so that the learning curve would have no impact on clinical outcomes.

At least 141 catheters from each group were selected at random and cultured to determine baseline colonization rates. This sample size assumed a 9.5% rate of catheter contamination¹⁷ with a 95% confidence level and a false-positive sample error rate of 3%. The size of the sample was adequate to detect a difference in the frequency of colonization between the systems of 10%, with an alpha error of 0.05 and a power of 80% (beta error 0.20). Catheters were evaluated using Maki's semiquantitative culture technique.¹⁶ Laboratory technicians and microbiologists who cultured the catheter tips were blinded to the study group assignment.

Randomization was computer generated.¹⁹ Study variables and their definitions have been described elsewhere.²⁰

Materials

The COS PIVC (Figure 1) used in this study was the Nexiva closed intravenous catheter system with a Q-Syte luer access split-septum connector (BD, Franklin Lakes, NJ, USA). The catheter is made of Vialon (a proprietary polyurethane) with integrated extension tubing, a stabilization platform (wings) and a passive needle shielding mechanism. A second Q-Syte was added in order to close the Y-connector completely.

The MOS PIVC (Figure 1) used in this study was the Vasocan safety catheter (B. Braun, Melsungen, Germany), made of polytetrafluoroethylene (PTFE). This catheter has wings and a passive safety mechanism. A three-way tap ('stopcock') with 10 cm of extension tubing (BD Connecta) with a luer/luer-lock Sollner cap (Amebil, Basauri, Spain) was added.

3M Tegaderm 1633 intravenous dressing (3M Healthcare, St. Paul, MN, USA) was used for both groups. Following the manufacturer's recommendations, dressings were changed every seven days, or sooner if necessary. Seventy percent alcohol was used for skin antisepsis and disinfection of access ports.

Statistical analysis

It was hypothesized that, for the intention-to-treat (ITT) population, the COS group would have a 5% reduction in efficacy and safety compared with the MOS group. Qualitative variables were compared using Chi-squared or Fisher's exact tests. Quantitative variables were analysed using Student's *t*-test.

The rate of events was calculated in relation to catheter-hours and catheter-days. This analysis was performed using Kaplan–Meier survival curves to allow for intra-individual variability in patients who were randomized to more than one catheter. The conditional hazard ratio was determined using Cox's proportional hazards regression by generalized estimation equation models, both univariate and with adjusted analysis for confounding variables.

Statistical analysis was performed using the ITT population, which included all catheters, and the 'modified' ITT

population, which included catheters with at least one assessment (i.e. in place for ≥ 24 h). This parameter takes into account the fact that many catheters are inserted for brief periods of time, and are removed for reasons unrelated to catheter performance or complications.

In all analyses, the level of statistical significance was assumed to be 0.05. The post-hoc power of the study was 97% (Granmo 7.11: Program to calculate the sample size and power of contrast hypothesis. Consortion URLEC, Institut Hospital del Mar d'Investigacions Mèdiques, Barcelona, Spain).

Cost analysis

Primary direct cost calculations were based on 20 min of nursing time for insertion, as measured at the study centre and supported by similar studies,^{21,22} plus the cost of materials used in the insertion and maintenance of catheters with a daily saline flushing. These calculations allow the extrapolation of potential savings. The material costs are those paid by the hospital in 2012, according to its accounting system.

The trial protocol is reported in accordance with the CONSORT 2010 statement,²³ and is registered on ClinicalTrials.gov (NCT00665886). All statistical analyses were undertaken using

Closed system (COS)



Open system (MOS)



Figure 1. Composition of the closed and open system peripheral intravenous catheters.

Statistical Package for the Social Sciences Version 15.0 (SPSS Inc, Chicago, IL, USA) and Data Analysis and Statistical Software Version 9.0 (Stata Corp., College Station, TX, USA).

Results

Of 1294 catheters evaluated in 694 inpatients, 95 PIVCs in 52 patients were considered ineligible. After early loss of 16 PIVCs, the ITT population was composed of 1183 catheters (631 inpatients), and the modified ITT population was composed of 952 catheters (513 patients). With a mean age of 71.5 years, patients were similar in both groups in terms of sex, race, hypertension, obesity, diabetes and mortality ($P =$ not significant); the only significant difference was morbid obesity ($P = 0.006$). All analyses were controlled for this parameter (conditional Cox model) and the outcome measures were not affected. In addition, there were no differences between the groups in terms of the presence of surgical wounds and drains, urinary catheters, frequency of healthy vein or repeated punctures, gauge or length of catheter, frequency of insertion site (hand/forearm), use of the right vs left arm, or specific vein cannulated (basilic/cephalic/median-cubital).

Both systems were analysed by insertion success (Table I), and all catheters with a successful or failed insertion were included in the ITT analysis. MOS PIVCs were significantly more likely to be inserted with fewer attempts ($P = 0.001$) due to the previous experience of nurses with this system. There were no significant differences relative to catheter use. When evaluated by number of patient exposure-days to each type of intravenous infusion listed in Table I (antibiotics, chemotherapy, lipids), there was no difference between the two groups. However, there was a difference in the use of infusion pumps (6% COS vs 3.5% MOS; $P = 0.049$), which is considered a risk factor for the occurrence of phlebitis²⁴ and CRI.²⁵

Indwell times

In total, 104,469 catheter-hours (54,173 hours in 584 COS PIVCs and 50,296 hours in 599 MOS PIVCs) were recorded. The maximum indwell time was 40.5 days in a patient with a COS PIVC.

The mean and median dwell times in the ITT population were 206.4 h and 114.3 h, respectively. The large difference between these values is due to the broad range of dwell times (0–972 h). As shown in Table II, the median time to any adverse event was significantly higher for the COS group than the MOS group ($P = 0.003$).

Survival curves until the onset of CRC for both groups are shown in Figure 2. The curves begin to separate between 24 and 48 h, and remain separated beyond 240 h at a statistically significant level ($P = 0.001$). When these results are adjusted for morbid obesity, the outcomes are unchanged [adjusted conditional hazard ratio 0.752; 95% confidence interval (CI) 0.635–0.891]. Use of COS PIVCs provides a relative risk reduction (RRR) of 25% of CRC in the ITT population. At 120 h, the number needed to treat is 8.3, meaning that one catheter-related complication is avoided for every eight COS PIVCs used. Figure 3 shows the stratified analysis of the main effect of CRC in categories of baseline variables.

For the catheters that remained in place for ≥ 24 h (Table II), the median dwell time was 144.5 h for COS PIVCs, which

provides a RRR of 29% of CRC compared with MOS PIVCs (conditional hazard ratio 0.707; 95% CI 0.590–0.848; $P < 0.001$) with a number needed to treat at 144 h (sixth day) of 9.4.

Complication rates

Reasons for catheter removal are summarized in Table I. There were 70 cases of phlebitis in the COS group (12%, 31 cases/1000 catheter-days) compared with 101 cases in the MOS group (16.9%, 45 cases/1000 catheter-days). Use of COS PIVCs led to a reduction in the phlebitis rate of 29% ($P = 0.004$).

Table III presents the CRC rates according to their frequency per 1000 catheter-hours and catheter-days, showing a significant reduction in the rate of phlebitis (grade 2 or higher, 36%), CRC (25%) and infiltration (24%) in the COS group, associated with RRR for painful haematoma (49%), occlusion (24%), pain (22%) and CRI (20%). However, there was no significant difference in the cumulative incidence (22.6% COS vs 21.3% MOS) or in the incidence density rates per 1000 catheter-days (51.1 COS vs 54.1 MOS) for bacterial colonization, and no statistical significance could be found between the CRI rates of the COS (2.2%) and MOS (2.5%) groups.

In this study, *Staphylococcus epidermidis* was responsible for 45.7% of colonization and 52.4% of CRI. *S. aureus* was isolated in two of 21 cases of CRI (9.5%), one in each study arm. Although more cases of bacterial colonization were detected in the COS group ($n = 37$) than in the MOS group ($n = 33$), only nine cases of CRI were confirmed in the COS group, compared with 12 cases in the MOS group.

Finally, no needlestick injuries occurred to healthcare workers in either group, proving that both MOS and COS PIVCs are passive safety devices.

Cost analysis

The cost analysis is summarized in Table IV. Using the costs and clinical practices of the study hospital, it was estimated that the implementation of a protocol for the use of COS PIVCs in catheterizations lasting >72 h with replacement every 144 h would save €88,605.24/year in the cost of devices, and up to €274,714.27/year in total intravenous therapy costs. Likewise, it was estimated that the use of MOS PIVCs in catheterizations lasting ≤ 72 h with replacement every 96 h would decrease costs by €80,104.87 and €511,542.78, respectively.

Discussion

This study shows the clear superiority of COS PIVCs over MOS PIVCs. Indwell times were significantly longer for COS PIVCs, and phlebitis and infiltration rates were significantly lower, with an RRR for CRI, for only €0.09/day.

Colonization rates of properly disinfected access ports did not show significant differences,²⁶ despite reports by other authors.¹⁴ A previous study found that the use of needleless connectors showed a reduction in the CRI rate, but this did not reach statistical significance.¹³ No other authors have found these results when comparing needleless connectors with three-way 'stopcocks' in central venous catheters.²⁷ On the other hand, although it has been reported that a dwell time of more than 72 h increases the risk of *S. aureus* bacteraemia,^{28,29} this survey showed that only 9.5% of CRI were caused by

Table I
Insertion success, utility and catheter withdrawal for intention-to-treat population

		Assigned system				P-value
		Closed		Open		
		No. of cases	%	No. of cases	%	
<i>Insertion parameters</i>						
Successful insertion	Yes	529	95.0	563	98.1	0.004
	No	28	5.0	11	1.9	
Successful puncture	First	363	66.0	437	76.3	0.001
	Second	129	23.5	99	17.3	
	Third	58	10.5	37	6.5	
Reason why procedure unsuccessful	Vasculature anatomy	3	30.0	4	44.4	0.041
	Absence of blood reflux	0	0.0	0	0.0	
	Difficulty advancing catheter	5	50.0	0	0.0	
	Kinking	0	0.0	0	0.0	
	Other	2	20.0	5	55.6	
Nurse assessment of difficulty of catheter puncture	1 Minimum	242	41.8	262	44.5	0.180
	2	171	29.5	159	27.0	
	3	106	18.3	93	15.8	
	4	44	7.6	45	7.6	
	5 Maximum	16	2.8	30	5.1	
Nurse assessment of difficulty of insertion	1 Minimum	152	26.3	220	37.4	<0.001
	2	171	29.5	161	27.4	
	3	132	22.8	123	20.9	
	4	70	12.1	58	9.9	
	5 Maximum	54	9.3	26	4.4	
Nurse assessment of difficulty of fixation	1 Minimum	234	41.8	273	46.7	0.266
	2	175	31.3	176	30.1	
	3	100	17.9	94	16.1	
	4	34	6.1	32	5.5	
	5 Maximum	17	3.0	9	1.5	
Pain felt by patient	Visual analogue scale from 0 to 10					0.378
Rupture of vein during procedure	Yes	69	12.0	26	4.4	<0.001
Timing of rupture	At puncture	18	26.5	9	36.0	0.266
	At insertion	50	73.5	16	64.0	
<i>Use of catheters</i>						
Maintenance fluids		159	27.0	186	31.1	0.138
Antibiotics		354	63.0	380	64.7	0.538
Chemotherapy		0	0.0	1	0.2	0.322
Lipids		23	4.1	18	3.1	0.349
Transfusions		14	2.5	25	4.3	0.098
Blood draws		68	12.1	72	12.3	0.931
<i>Catheter withdrawal</i>						
Success						
End of treatment		98	16.8	81	13.5	0.118
Patient discharge		162	27.7	135	22.5	0.039
Lost catheters						
Insertion unsuccessful		28	4.8	11	1.8	0.004
Accidental loss of intravenous line		65	11.1	61	10.2	0.598
Study losses						
Transfer of patient		18	3.1	19	3.2	0.929
Catheter-related complications						
Catheter occlusion		42	7.2	51	8.5	0.398
Infiltration/extravasation		123	21.1	151	25.2	0.091
Phlebitis		70	12.0	101	16.9	0.017
Persistent pain		46	7.9	55	9.2	0.422
Painful haematoma		6	1.0	11	1.8	0.242
Catheter-related infection suspected		13	2.2	11	1.8	0.635
Total catheters removed because of complications		248	42.6	306	51.1	0.004

Table II
Indwell time analysis for intention-to-treat (ITT) and modified ITT populations

Assigned system	Event median ITT (N = 1183)			Event median modified ITT (N = 952)			Interquartile range (N = 952)		
	Survival (h)	SE	95% CI	Survival (h)	SE	95% CI	Closed ^a	Open ^b	
Closed	137.0	8.7	120.1–154.0	144.5	10.8	123.4–165.6	25	48.50	44.50
Open	96.0	4.3	87.5–104.5	99.0	6.0	87.2–110.8	50	79.00	70.25
Total	114.3	6.0	102.6–126.0	125.0	6.8	111.7–138.3	75	141.75	116.92
	<i>P</i> = 0.003			<i>P</i> < 0.001			<i>P</i> = 0.016		

SE, standard error; CI, confidence interval.

^a Range: 24–972.

^b Range: 24–602.

S. aureus compared with 23.7% in patients with central venous catheters in non-ICU settings (i.e. on hospital wards).^{30,31}

However, in light of the current economic crisis, the main finding of this study was the identification of indwell times for safe and effective routine replacement of PIVCs, thus saving on consumption and costs. Furthermore, passive safety devices have 100% effectiveness in eliminating needlestick injuries.

Study limitations

The first limitation of this study was the impossibility of blinding due to the obvious differences in the two device types.

Nevertheless, microbiological analysis was blinded. Secondly, variability in the experience and technique of nurses was addressed through intensive training before they joined the research team, although this measure could not eliminate the unsuccessful insertion of COS PIVCs (5% vs 1.9%; *P* = 0.004). This limitation actually penalized the COS group. In fact, the cost of COS PIVCs may be even lower once overcome by the learning curve. Thirdly, COS and MOS PIVCs are made of different materials. However, this has little relevance in this study as the two types of PIVCs that were available at the study hospital at the beginning of the study were compared (a closed and integrated system with a polyurethane cannula and an open system

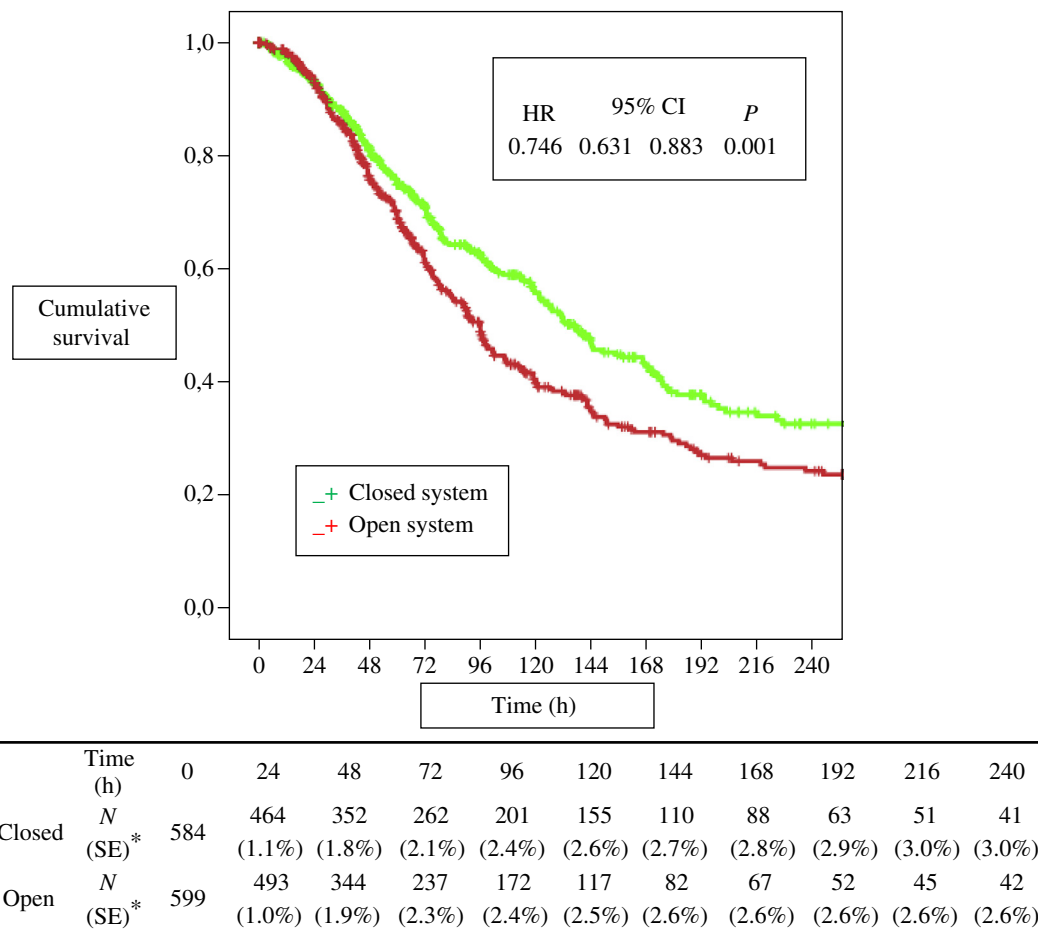
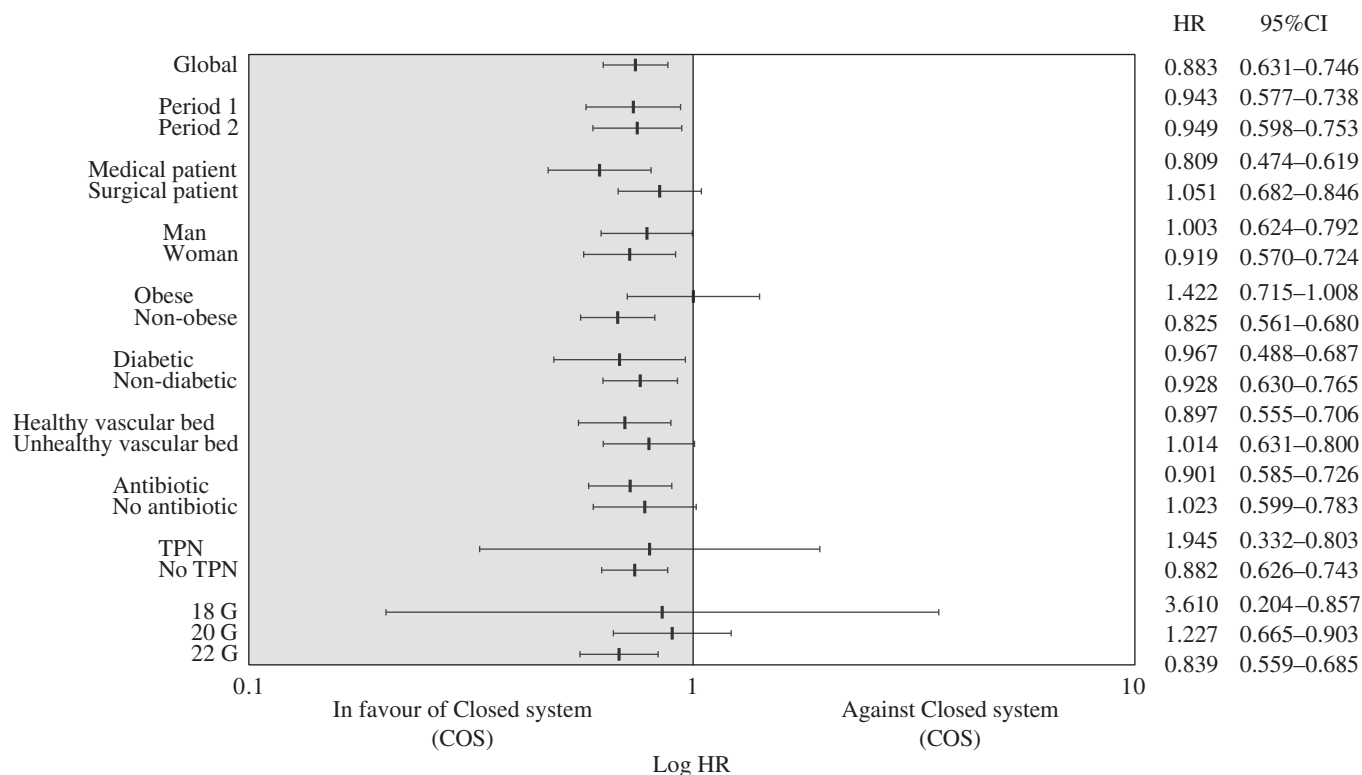


Figure 2. Kaplan–Meier survival curve to the onset of complications (intention-to-treat population). HR, hazard ratio; CI, confidence interval.



Data expressed as Hazard Ratio (Cox model) and error lines are 95% confidence interval.

Figure 3. Stratified analysis of the main effect of catheter-related complications in categories of baseline variables. HR, hazard ratio; CI, confidence interval; TPN, total parenteral nutrition.

that was assembled manually and had a PTFE cannula). Both were only replaced when clinically indicated (patient discharge, in-hospital end of treatment, catheter-related complication or death). The dwell times of these different types of PIVCs (which are used in clinical practice around the world) were studied for complications associated with extended periods of use. Lastly, blood cultures to confirm CRBSI were not performed as this would have required a much larger sample.

On the other hand, although it has been shown that polyurethane decreases the risk of phlebitis,^{7,32,33} Maki and

Ringer⁷ found a trend in CRBSI that was somewhat higher in the Vialon group than in the Teflon group, without achieving statistical significance, in contrast to the results of the present study.

Clinical and economic implications

Increased dwell times without increased risks have important implications for PIVC-replacement protocols, such as catheter removal every 72 h, which is the current practice in the study hospital and in the majority of hospitals, despite the

Table III
Rates of catheter-related complications (intention-to-treat population)

Catheter-related complication	Closed system		Open system		Rate ratio ^a	95% CI	P-value ^a
	Rate per 1000 catheter-hours	Rate per 1000 catheter-days	Rate per 1000 catheter-hours	Rate per 1000 catheter-days			
Hours/catheter	54,173		50,296				
Days/catheter	2257		2096				
Occlusion	0.75	18.61	1.01	22.59	0.76	0.50–1.17	0.199
Infiltration/extravasation	2.27	54.49	3.00	66.90	0.76	0.59–0.97	0.021
Phlebitis grade 2 or higher	1.29	31.01	2.01	44.75	0.64	0.47–0.88	0.004
Persistent pain	0.85	20.38	1.09	24.37	0.78	0.51–1.17	0.210
Painful haematoma	0.11	2.66	0.22	4.87	0.51	0.15–1.49	0.183
Catheter-related infection	0.24	5.76	0.30	6.65	0.80	0.35–1.81	0.572
Total complications	4.58	109.87	6.08	135.57	0.75	0.63–0.89	<0.001

CI, confidence interval.

^a Compare rates per 1000 catheter-hours.

Table IV
Cost analysis (intention-to-treat population)

Concept	Closed system ^a (N = 584)		Open system ^b (N = 599)	
	Unit cost (€)	Total cost (€)	Unit cost (€)	Total cost (€)
Closed system with two needleless connectors	3.495	2041.08	–	–
Safety PIVC	–	–	0.925	554.08
Stopcock	–	–	0.396	394.02
Luer/luer-lock cap	–	–	0.042	220.08
Cost of system	3.495	2041.08	1.363	1168.18
Non-sterile gloves	0.032	18.69	0.032	19.17
Sterile gauze	0.090	52.56	0.090	53.91
Transparent dressing	0.434	377.41	0.434	386.96
Infusion line	0.163	117.69	0.163	126.65
Flushing catheter	0.275	1284.80	0.275	1317.80
Nursing time (20 min)	6.347	3706.65	6.347	3801.85
Total study cost ^c	10.836	7598.88	8.704	6874.52
Cost/day (€)		3.37		3.28

PIVC, peripheral intravenous catheter.

Savings by protocol change:

- In 2012, the Hospital Clínico 'San Carlos' used 230,475 PIVCs using a protocol of replacing catheters every 72 h, extended to 96 h for closed systems (Nexiva™).
- Of all catheters, 25% [57,619 PIVCs — 16% lost catheters (see Table I) × 96 h = 4,646,400 catheter-hours] were long term (>72 h) and 75% [172,856 PIVCs — 12% lost catheters (see Table I) × 72 h = 10,952,136 catheter-hours] were short term (≤72 h).
- Applying a simple calculation, one can determine how many Nexiva could be saved in catheterizations >72 h with a change protocol every 144 h, and the number of open catheters that could be saved in catheterizations ≤72 h with a change protocol every 96 h:
 - Closed system: 4,646,400 catheter-hours/144 h = 32,267 catheters.
57,619 – 32,267 = 25,352 PIVCs saved × €3.495 = €88,605.24/year saving in cost of devices. Also 25,352 PIVCs saved × €10.836 = €274,714.27/year saving in intravenous therapy costs.
 - Open system: 10,952,136 catheter-hours/96 h = 114,085 catheters.
172,856 – 114,085 = 58,771 PIVCs saved × €1.363 = €80,104.87/year saving in cost of devices. Also 58,771 PIVCs saved × €8.704 = €511,542.78/year saving in intravenous therapy costs.

^a Catheterization-days: 2257.2.

^b Catheterization-days: 2095.7.

^c All prices paid by hospital in 2012 (VAT included).

fact that phlebitis was not observed on the third day in >90% of COS PIVCs and 86% of MOS PIVCs.

Although the duration of catheterization has been considered to be the most important predictor of phlebitis,^{7,10,28} and has led to worldwide protocols of routine resiting every 48–96 h, this recommendation has been questioned because the evidence suggests that the risk of complications, especially phlebitis, increases until approximately 48 h but then remains more or less constant until the sixth day (144 h).^{8,10}

The 2011 guidelines of the CDC³⁴ recommending catheter removal at 72–96 h are based on three relatively dated studies.^{7,12,28} In the most recent of these studies, Lai recommended prolonging the indwell time from 72 to 96 h, with a saving of US\$61,200/year for a hospital with 375 beds.¹² However, this study had important limitations; it was non-randomized, there were no cultures of catheter tips, and the sample size of catheters lasting >96 h was very small (N = 32). The present study showed that COS PIVCs had a probability of phlebitis-free survival of 80.4% at 144 h. The probability of survival of MOS PIVCs to 96 h (79.9%) confirms, with an adequate sample size, the safety of prolonging the dwell time of PIVCs, even with Teflon cannulae, up to 96 h, as suggested by Lai.¹²

Using the 'San Carlos' Hospital perspective, the application of these findings to clinical practice may involve savings in intravenous therapy of up to €786,257.05/year/1000 beds with no increase in risk.

Other studies have shown that catheter replacement only when clinically indicated is a safe strategy^{35,36} and reduces costs.³⁵ A 2010 Cochrane review concluded that clinical management could be as effective as scheduled catheter exchange.³⁷ Recently, Rickard *et al.*³⁸ tested whether the policy of routine replacement after a set dwell time reduces complications vs replacement purely on clinical grounds. In their study, the mean dwell time was 99 h when catheters were replaced when clinically indicated but only 70 h when replaced routinely. This study, unlike the present study, was not testing catheter dwell times *per se*. In the present study, the mean indwell time for the total sample was 206.4 h, which is more than double the mean indwell time reported by Rickard *et al.* but proves similar points, namely that routine replacement does not reduce complications but causes many unnecessary invasive procedures, and that costs can be driven down without compromising on patient outcomes by allowing the catheter to remain in place for as long as clinically indicated.

Finally, recommendations for optimal dwell times of PIVCs should be re-evaluated, and may differ depending on whether a COS or MOS device is being used. The implementation of a protocol to use COS PIVCs in catheterizations that are expected to remain in place for >72 h, with replacement every 144 h, and MOS PIVCs in catheterizations expected to remain in place for ≤72 h, with replacement every 96 h, will significantly reduce the cost of intravenous therapy without increasing the risk. This constitutes good news, from a clinical, economic and environmental point of view, for healthcare systems. It reduces risks and discomfort to patients, while decreasing intravenous therapy costs and biohazard waste.

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Conflict of interest statement

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References

- Mermel LA, Farr BM, Sherertz RJ, et al. Guidelines for the management of intravascular catheter-related infections. *Clin Infect Dis* 2001;32:1249–1272.
- Pujol M, Hornero A, Saballs M, et al. Clinical epidemiology and outcomes of peripheral venous catheter-related bloodstream infections at a university-affiliated hospital. *J Hosp Infect* 2007;67:22–29.
- Trinh TT, Chan PA, Edwards O, et al. Peripheral venous catheter-related *Staphylococcus aureus* bacteremia. *Infect Control Hosp Epidemiol* 2011;32:579–583.
- Pearson ML. The Hospital Infection Control Practices Advisory Committee. Guideline for prevention of intravascular device-related infections. *Am J Infect Control* 1996;24:262–293.
- O'Grady NP, Alexander M, Dellinger EP, et al. Healthcare Infection Control Practices Advisory Committee (HICPAC). Guidelines for the prevention of intravascular catheter-related infections. *Infect Control Hosp Epidemiol* 2002;23:759–769.
- Maki DG, Kluger DM, Crnich CJ. The risk of bloodstream infection in adults with different intravascular devices: a systematic review of 200 published prospective studies. *Mayo Clin Proc* 2006;81:1159–1171.
- Maki DG, Ringer M. Risk factors for infusion-related phlebitis with small peripheral venous catheters. A randomized controlled trial. *Ann Intern Med* 1991;114:845–854.
- Bregenzer T, Conen D, Sakman P, Widmer AF. Is routine replacement of peripheral intravenous catheters necessary? *Arch Intern Med* 1998;158:151–156.
- Tagalakis V, Kahn SR, Libman M, et al. The epidemiology of peripheral vein infusion thrombophlebitis: a critical review. *Am J Med* 2002;113:146–151.
- Collin J, Collin C, Constable FL, Johnston IDA. Infusion thrombophlebitis and infection with various cannulas. *Lancet* 1975;2:150–153.
- Maki DG, Botticelli JT, LeRoy ML, Thielke TS. Prospective study of replacing administration sets for intravenous therapy at 48- vs. 72-hour intervals. 72 hours is safe and cost-effective. *JAMA* 1987;258:1777–1781.
- Lai KK. Safety of prolonging peripheral cannula and IV tubing use from 72 hours to 96 hours. *Am J Infect Control* 1998;26:66–70.
- Bouza E, Muñoz P, López-Rodríguez J, et al. A needleless closed system device (CLAVE™) protects from intravascular catheter tip and hub colonization: a prospective randomized study. *J Hosp Infect* 2003;54:279–287.
- Casey AL, Burnell S, Whinn H, Worthington T, Faroqui MH, Elliott TS. A prospective clinical trial to evaluate the microbial barrier of a needleless connector. *J Hosp Infect* 2007;65:212–218.
- Van Zundert A. New closed IV catheter system. *Acta Anaesthesiol Belg* 2005;56:283–285.
- Maki DG, Weise CE, Sarafin HW. A semiquantitative culture method for identifying intravenous catheter related infection. *N Eng J Med* 1977;296:1305–1309.
- Aygun G, Yasar H, Yilmaz M, et al. The value of gram staining of catheter segments for rapid detection of peripheral venous catheter infections. *Diag Microbiol Infect Dis* 2006;54:165–167.
- Adams D, Karpanen T, Worthington T, Lambert P, Elliott TSJ. Infection risk associated with a closed luer access device. *J Hosp Infect* 2006;62:353–357.
- Saghaei M. Random allocation software for parallel group randomized trials. *BMC Med Res Methodol* 2004;4:26.
- González López JL, Fernández del Palacio E, Benedicto Martí C, Olivares Corral J, Herrera Portal P, Arribi Vilela A. COSMOS: a study comparing peripheral intravenous systems. *Br J Nurs* 2009;18:844–853.
- Webster J, Clarke S, Paterson D, et al. Routine care of peripheral intravenous catheters versus clinically indicated replacement: randomised controlled trial. *BMJ* 2008;337:157–160.
- Rickard CM, McCann D, Munnings J, McGrail MR. Routine resite of peripheral intravenous devices every 3 days did not reduce complications compared with clinically indicated resite: a randomised controlled trial. *BMC Med* 2010;8:53.
- Schulz KF, Altman DG, Moher D, for the CONSORT Group. CONSORT 2010 statement: updated guidelines for reporting parallel group randomised trials. *BMJ* 2010;340:c332.
- Uslusoy E, Mete S. Predisposing factors to phlebitis in patients with peripheral intravenous catheters: a descriptive study. *J Am Acad Nurse Pract* 2008;20:172–180.
- Curran ET, Coia JE, Gilmore H, et al. Multi-centre research surveillance project to reduce infection/phlebitis associated with peripheral vascular catheters. *J Hosp Infect* 2000;46:194–202.
- Arduino MJ, Bland LA, Danzig LE, McAllister SK, Agüero SM. Microbiologic evaluation of needleless and needle-access devices. *Am J Infect Control* 1997;25:377–380.
- Esteve F, Pujol M, Limón E, et al. Bloodstream infections related to catheters connections: a prospective trial of two connections systems. *J Hosp Infect* 2007;67:30–34.

28. Tager IB, Ginsberg MB, Ellis SE, et al. An epidemiologic study of the risks associated with peripheral intravenous catheters. *Am J Epidemiol* 1983;118:839–851.
29. Soifer NE, Borzak S, Edlin BR, Weinstein RA. Prevention of peripheral venous catheter complications with an intravenous therapy team: a randomized controlled trial. *Arch Intern Med* 1998;158:473–477.
30. Wisplinghoff H, Bischoff T, Tallent SM, Seifert H, Wenzel RP, Edmond MB. Nosocomial bloodstream infections in US hospitals: analysis of 24,179 cases from a prospective nationwide surveillance study. *Clin Infect Dis* 2004;39:309–317.
31. Gaynes R, Edwards JR. Overview of nosocomial infections caused by Gram-negative bacilli. *Clin Infect Dis* 2005;41:848–854.
32. Gaukroger PB, Roberts JG, Manners TA. Infusion thrombophlebitis: a prospective comparison of 645 Vialon and Teflon cannulae in anesthetic and postoperative use. *Anesth Intens Care* 1988;16:265–271.
33. McKee JM, Shell JA, Warren TA, Campbell VP. Complications of intravenous therapy: a randomised prospective study – Vialon vs Teflon. *J Intraven Nurs* 1989;129:288–295.
34. O’Grady NP, Alexander M, Burns LA, et al. Healthcare Infection Control Practices Advisory Committee (HICPAC). Guidelines for the prevention of intravascular catheter-related infections. *Clin Infect Dis* 2011;52:e162–e193.
35. Webster J, Lloyd S, Hopkins T, Osborne S, Yaxley M. Developing a research base for intravenous peripheral cannula re-sites (DRIP trial). A randomised controlled trial of hospital in-patients. *Int J Nurs Stud* 2007;44:664–671.
36. Van Donk P, Rickard CM, McGrail MR, Doolan G. Routine replacement versus clinical monitoring of peripheral intravenous catheters in a regional hospital in the home program: a randomized controlled trial. *Infect Control Hosp Epidemiol* 2009;30:915–917.
37. Webster J, Osborne S, Rickard C, Hall J. Clinically-indicated replacement versus routine replacement of peripheral venous catheters. *Cochrane Database Syst Rev* 2010;3:CD007798.
38. 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.