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Integrated versus nonintegrated peripheral intravenous catheter in hospitalized adults (OPTIMUM): A randomized controlled trial

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Abstract

Background: One-third of peripheral intravenous catheters (PIVCs) fail from inflammatory or infectious complications, causing substantial treatment interruption and replacement procedures.

Objectives: We aimed to compare complications between integrated PIVCs (inbuilt extension sets, wings, and flattened bases) and traditional nonintegrated PIVCs.

Designs, Settings and Participants: A centrally randomized, controlled, superiority trial (with allocation concealment until study entry) was conducted in three Australian hospitals. Medical–surgical patients (one PIVC each) requiring intravenous therapy for >24 h were studied.

Main Outcome Measures: The primary outcome was device failure (composite: occlusion, infiltration, phlebitis, dislodgement, local, or bloodstream infection). Infection endpoints were assessor-masked. The secondary outcomes were: failure type, first-time insertion success, tip colonization, insertion pain, dwell time, mortality, costs, health-related quality of life, clinician, and patient satisfaction.

Results: Out of 1759 patients randomized (integrated PIVC, $n = 881$; nonintegrated PIVC, $n = 878$), 1710 (97%) received a PIVC and were in the modified intention-to-treat analysis (2269 PIVC-days integrated; 2073 PIVC-days nonintegrated). Device failure incidence was 35% (145 per 1000 device-days) nonintegrated, and 33% (124 per 1000 device-days) integrated PIVCs.

Intervention: Integrated PIVCs had a significantly lower failure risk (adjusted [sex, infection, setting, site, gauge] hazard ratio [HR]: 0.82 [95% confidence interval, CI: 0.69–0.96], $p = .015$). The per-protocol analysis was consistent (adjusted HR: 0.80 [95% CI: 0.68–0.95], $p = .010$). Integrated PIVCs had significantly longer dwell (top quartile ≥ 95 vs. ≥84 h). Mean per-patient costs were not statistically different.

Conclusions: PIVC failure is common and complex. Significant risk factors include sex, infection at baseline, care setting, insertion site, catheter gauge, and catheter type. Integrated PIVCs can significantly reduce the burden of PIVC failure on patients and the health system.

INTRODUCTION

Peripheral intravenous catheters (PIVCs) are a quick and cost-effective method of vascular access for many hospitalized patients.[1] However, they are often problematic, with one in three failing from phlebitis, occlusion, dislodgement, infiltration, or less commonly from soft-tissue or bloodstream infections.[1,2] In recent years, the longstanding culture of tolerance for these complications has begun to be acknowledged as "accepted but unacceptable."[3,4]

As a foreign body, PIVCs irritate the endothelium of the venous tunica intima, triggering thrombi.[5] Minimizing catheter movement within the vein reduces irritation and resultant infiltration, inflammation, occlusion, dislodgement, and pistoning of skin flora that could lead to infection.[6] Dressings partially assist with securement, but frequently become loose.[7] Traditional PIVCs comprise a cylindrical tube affixed against the flat skin surface overlaying the vein and are "nonintegrated," that is, they require additional attachment of extension tubing, needleless connectors, and/or three-way stopcocks. Integrated PIVCs are "all-in-one" catheters with inbuilt extension tubing, needleless connectors, and a flattened base including "wings" designed to provide a platform for stabilization.[8] Theoretically, these minimize catheter movement within the vein by ensuring clinicians manipulate the device distal to the catheter hub and by providing better affixation to the skin and reduced vein compression under the catheter barrel.[6] Because extension tubing is built-in and exits the hub at approximately 45° angle (rather than at 0°), there may be reduced tension during manipulation for attachment and therapy and less risk of accidental disconnection and manual contamination.[9]

In previous clinical trials, integrated PIVCs had fewer securement-related complications,[10] reduced catheter replacements,[6] and prolonged functional dwell time[11,12] than nonintegrated PIVCs, but the effect on overall PIVC failure has not been studied.[10] Limitations of these trials included quasirandomization[6] or testing of a "bundle" also including prefilled saline flushes, positive displacement needleless connectors, and disinfecting caps.[12] Although prior researchers concluded integrated catheters would achieve cost savings, a formal economic evaluation was not conducted.[6,10–12] Current guidelines make no recommendation regarding integrated PIVCs, although they do emphasize the importance of adequate securement, and avoiding add-on devices to avoid manipulation, accidental disconnection, and infection risk.[8]

The last decade has seen PIVC removal criteria change to clinical assessment and need, rather than routine 3–4 daily removal, and many centers now use PIVCs for longer periods.[8,13,14] However, PIVC failure remains highly prevalent, leading to delayed treatments, additional procedures, patient pain/discomfort, clinician workload, and costs; hence, new technologies need testing, and if clinically and cost-effective, they should be implemented.[3] Despite promising prior trials, a large definitive trial of integrated PIVCs is lacking. We aimed to compare the clinical- and cost-effectiveness as well as the acceptability of integrated PIVC systems to prevent catheter failure and inform health system decision-making.

MATERIALS AND METHODS

Trial design

The OPTIMUM trial (Integrated vs. nonintegrated peripheral intravenous catheters: which is the most effective system for peripheral intravenous catheter management? [OPTIMUM randomized controlled trial in hospitalized adults]) is a two-arm, multicenter, superiority randomized controlled trial (RCT) comparing integrated and nonintegrated PIVCs to prevent PIVC failure. It was approved by three Hospital Human Research Ethics Committees (HREC/16/QRBW/527; Griffith/2017/002; MetroSouth/2016-239). Written informed consent to participate was obtained from participants.[15] The Consolidated Standards of Reporting Trials (CONSORT) reporting guideline was followed, and the trial was prospectively registered (Australian New Zealand Clinical Trial Registry ACTRN12617000089336). Nil protocol changes were made after trial commencement, and the protocol is published (see Supporting Information).[16]

Participants and setting

The trial was undertaken at three metropolitan university-affiliated hospitals in Brisbane, QLD, Australia. The inclusion criteria were as follows: ≥18 years or older, PIVC required ≥ 24 h, and informed written consent. Exclusion criteria included PIVC placed under emergency conditions with an inappropriate aseptic technique, laboratory-confirmed bloodstream infection within the prior 48 h, presence of a coexistent vascular catheter, end-of-life care, cognitive or language barrier (no suitable interpreter) to consent, or previous enrollment. Patients were consecutively recruited by Research Nurses (ReNs) typically during office hours.

Randomization and interventions

Patients were randomized in a 1:1 ratio with varying block sizes and stratified by the hospital using a web-based service (https://randomisation.griffith.edu.au). ReNs advised clinical staff, patients, and families about allocation, and monitored protocol compliance. It was not possible to blind patients and clinical staff because of the nature of the intervention. However, the microbiologist, infectious disease physician, and data analyst were blinded.

Study (integrated) and control (nonintegrated) catheters (Supporting Information: Figure 1) were inserted by hospital credentialled inserters (registered medical or nursing professionals), not specialized teams. The integrated PIVC was the Nexiva™ Closed IV Catheter System Dual Port with SmartSite needleless connectors (BD). The nonintegrated PIVC was the B Braun Introcan Safety 3 Catheter (B Braun), Connecta 10 cm extension set (BD), and Smartsite needleless connector (BD), as per local hospital standard care. PIVC inserters received pretrial training and simulated practice from researchers and manufacturer-provided educators, and PIVC care was standardized as per local state-wide policy. One PIVC was studied per patient.

Data collection

ReNs entered data into REDCap software (Research Electronic Data CAPture, Vanderbilt).[17] At recruitment, patient and PIVC characteristics were collected and PIVCs were assessed daily for use and complications. Treating clinicians, independent of researchers, made decisions about PIVC removal, and any diagnostic testing. Patients were followed for 48 h after PIVC removal for infection outcomes and serious adverse events.[18] Reliability of outcome assessments was promoted with extensive education before and during the study, monitored by a trial manager, and standard operating procedures.

Due to the lack of validated PIVC-specific patient-reported outcome and experience measures, we applied brief, generic instruments. The EuroQol 5-dimension 5-level questionnaire (EQ-5D-5L), a validated patient-completed survey of health status comprising five domains (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression) was collected from a subsample of patients pre-PIVC insertion.[19] The EQ-5D-5L was repeated at the end of treatment (24–60 h after PIVC insertion) to assess for changed status. The Functional Assessment of Chronic Illness Therapy-Treatment Satisfaction-General (FACIT-TS-G) survey of treatment satisfaction, an established generic patient-reported experience measure with eight items, was collected contemporaneously with the second EQ-5D-5L.[20] A simple researcher-constructed clinician satisfaction survey was distributed to 100 nurses who had experience in caring for both devices.

A detailed list of resource utilization included consumables, replacement devices, and ultrasound use (Supporting Information: Table 1), which was collected during the trial for all participants. Insertion time and the number of insertion attempts were measured in a consecutive subset (n = 170, for whom PIVC insertion coincided with ReNs being available to observe), observed from the opening of the insertion kit until the dressing was applied, using local costs.

Outcomes

The primary outcome, PIVC failure, as used previously,[7,12] was a composite of occlusion (inability to infuse fluids or medications[3]), infiltration/extravasation (inadvertent permeation of intravenous fluid [nonvesicant or vesicant solution] into the interstitial compartment, causing swelling[21,22]), phlebitis/thrombophlebitis (patient-reported pain [≥2 on a 0–10 scale of increasing severity] alone or with tenderness, erythema, swelling, warmth, palpable cord, venous streak, or purulent drainage, within 24 h prior to device removal[23]), dislodgement (movement of the catheter out of the vein [complete dislodgement] or leaking [partial dislodgement]),[23] local infection (without bloodstream infection, using the localized arterial or venous infection [Cardiovascular System infection-arterial or venous infection] criteria of the US National Healthcare Safety Network [NHSN]),[18] and peripheral line-associated bloodstream infection (laboratory-confirmed primary bloodstream infection using CDC NHSN criteria [in brief]:

- a recognized pathogen or two matching commensals within 2 days,
- not related to another infection,
- ≥1 symptom of infection (e.g., fever), and
- confirmed by a blinded infectious disease physician).[18]

The secondary outcomes were individual failure types, first-time insertion success, PIVC tip colonization (>15 colony-forming units; semiquantitative culture), patient-reported pain during insertion (0–10 scale of increasing severity), PIVC dwell time, mortality (on trial), direct costs (including catheters, consumables, staff time to insert and replace products, additional devices, and imaging guidance [ultrasound]), health-related quality of life utility score (EQ-5D-5L, with Australian utility scoring algorithm anchored to 0 for death and 100 for perfect health),[19] clinician satisfaction/confidence with PIVC (overall, scale of 0 [not easy] to 10 [very easy]), and patient satisfaction with PIVC (FACIT-TS-G; eight questions on effectiveness, side effects, and satisfaction).[20]

Sample size

We hypothesized 17% reduction in PIVC failure based on prior research[11] requiring 780 participants per group for 80% power (1560 total). An independent data safety monitoring committee (DSMC) reviewed recruitment, blinded aggregate primary event rate (prepared by blinded statistician), and adverse event data at 50% recruitment (no interim analysis and no stopping rules). The DSMC had no safety concerns but recommended increasing the sample size to 2200 due to

the higher-than-predicted aggregate event rate). We continued recruitment until available funding was expended at $N = 1759$.

Statistical analysis

Data were checked for outliers and missing values and corrected (without imputation) where possible before importation into Stata (StataCorp (2019), Release 16; StataCorp LLC).[17] Patients were the unit of measurement. All randomized patients were analyzed as modified intention-to-treat (mITT) (excluding only those who never had a PIVC inserted, since they were not at risk of PIVC failure). Group characteristics were compared at baseline for clinical comparability. Incidence rates of the primary outcome per 1000 PIVC-hours and their ratios between groups were calculated. Kaplan—Meier survival curves and log-rank tests compared group failure over dwell time, with Cox regression to test the effect of group on failure, adjusted for significant patient, device, and clinical variables. The functional form of continuous variables was checked with Martingale residuals. Covariables (multivariable model) were shortlisted using PIVC risk factors from prior studies and guided by $p < .20$ on univariable analysis. Correlations between covariables were tested and considered during the multivariable model building. The final model was derived by manual stepwise removal of variables at $p \geq .05$ and confirmed with forward variable selection. The proportional-hazards assumption was checked (univariable analyses and for the final model). The "goodness of fit" of

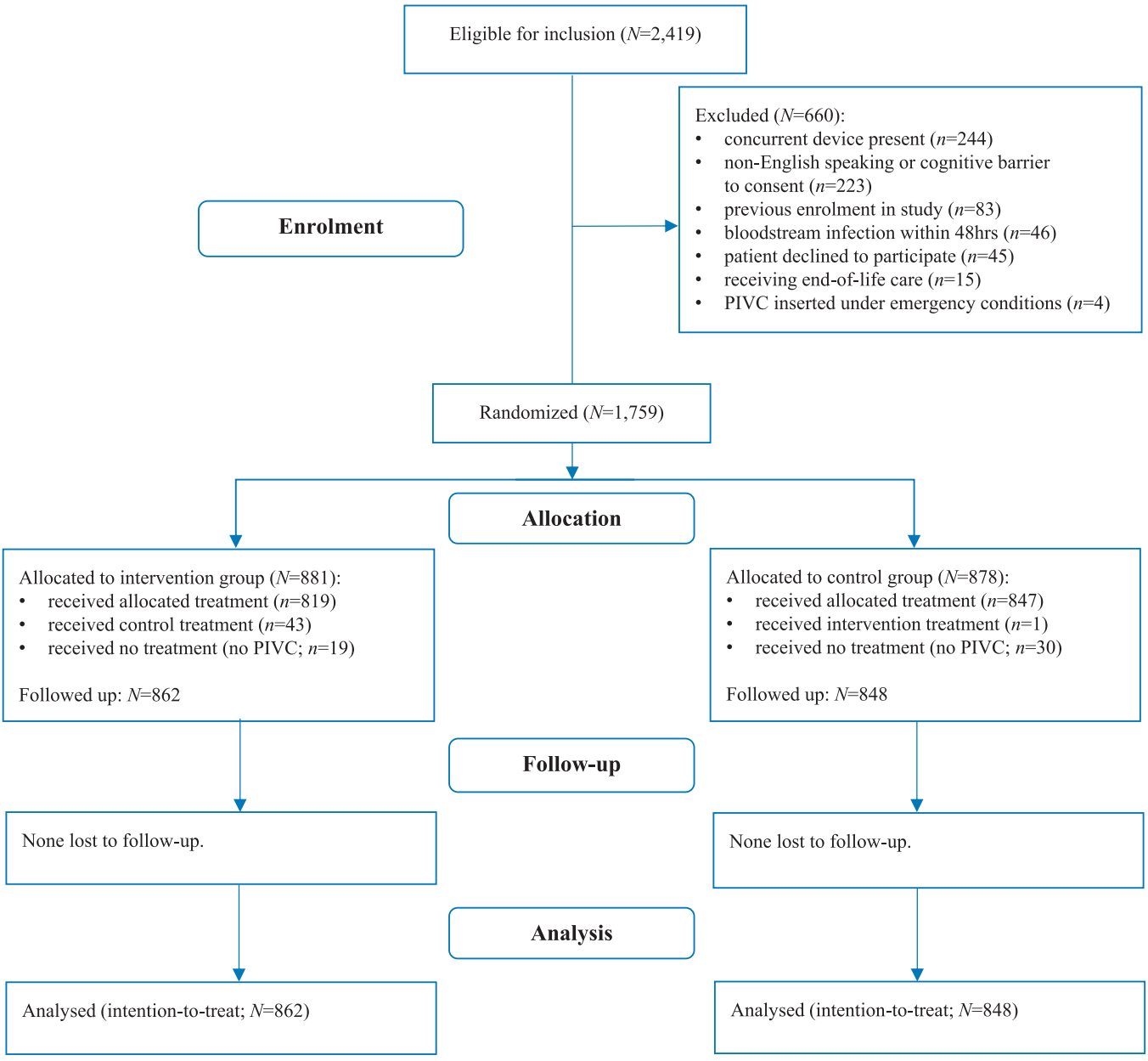

FIGURE 1 CONSORT (Consolidated Standards of Reporting Trials) flowchart.

the final model was checked using Cox–Snell residuals. Secondary endpoints were compared between groups by calculating absolute (risk difference) and relative (risk/rate ratio [RR]) measures of differences. A per-protocol analysis considered only patients who had the randomized PIVC inserted. The mean cost per patient was compared using *t*-test after assessing data distribution. Two-tailed *p* values of <.05 were considered significant.

Economic analysis

A within-trial cost analysis was conducted from the perspective of the hospital based on the mITT analysis. The mean cost per successful insertion was estimated for both study groups based on Queensland Health's (2020 Australian dollar) purchase costs and wages. Staffing costs were included to account for the opportunity cost of clinician time and assess for differences in time, numbers, and skill level for insertion.[7,24] We accounted for additional costs of replacement PIVCs when PIVCs failed, by applying the mean insertion cost by site and group allocation. The observation period for each participant was less than 1 year (with no long-term consequences). As such, all outcomes were observed in the current period, and there was no need to discount failure consequences.[25] The Australian EQ-5D-5L scoring algorithm was used to generate utility scores in this study. Responses from the instrument are used to calculate a utility value, where 1 is "perfect health" and 0 is "death."[26] A linear mixed-effect regression estimated change in the health utility score from the baseline.[27] Due to the paucity of universally accepted minimal, clinically important difference for PIVC interventions, a change of >5 out of 100 in the EQ-5D utility score, was considered clinically significant. One-way sensitivity analyses were conducted first by excluding the staff cost of staff time and then by excluding the ultrasound cost. Finally, mean costs per successful insertion were estimated, including the cost of attempted insertions for those excluded from the mITT analysis.

Microbiological substudy

A subset of PIVC tips (distal 2 cm) was collected by ReNs and analyzed using the semiquantitative culture method.[28] The sample was determined by research staff availability at PIVC removal.

RESULTS

After screening 2419 patients, 1759 patients met all inclusion criteria and no exclusion criteria and were randomized between July 24, 2017 and December 19, 2019 (Figure 1). There were 49 randomized patients (integrated PIVC, 19 patients [2%] vs. nonintegrated, 30 patients [3%]) whose insertion was canceled or unsuccessful (therefore had no primary outcome). The remaining 1710 patients were included in the mITT analysis. Of the 1710, 819 of 862 (95%) integrated PIVC patients received the allocated device, and 847 of 848 (99%) nonintegrated patients. Baseline patient and device characteristics were similar between groups (Tables 1 and 2). There were 15 integrated PIVC and 9 nonintegrated PIVC patients whose study endpoint was recorded at transfer to another hospital. Overall, 4342 PIVC-days were studied (2269 integrated vs. 2073 nonintegrated).

PIVC failure occurred in 33% integrated PIVCs and 35% nonintegrated PIVCs (risk difference: 2.8% [95% confidence interval, CI: −1.7 to 7.3], risk ratio: 0.92 [95% CI: 0.81–1.05]). Failure rates per 1000 days were lower in integrated PIVCs (124 vs. 145, rate difference: 21 [95% CI: −1 to 43], RR: 0.86 [95% CI: 0.72–1.01]), which was significantly different in the per-protocol analysis (RR: 0.83 [95% CI: 0.70–0.98], two-sided $p = .024$) (Table 3 and Figure 2). Survival analysis found that integrated PIVCs had significantly a lower risk of failure (hazard ratio [HR]: 0.85 [95% CI: 0.72–1.00], two-sided $p = .046$), a finding that was consistent with the multivariate analysis (HR: 0.82 [95% CI: 0.69–0.96], two-sided $p = .015$) adjusted for gender, infection at baseline, gauge size, insertion department, and insertion site, and with the per-protocol analysis (HR: 0.80 [95% CI: 0.68–0.95], two-sided $p = .010$) (Table 4 and Figure 2).

Failure was most commonly phlebitis (17%) and dislodgement/leaking (12%). Dislodgement/leaking occurred significantly less in the

TABLE 1 Participant characteristics at randomization

	Nonintegrated (*n* = 878)	Integrated (*n* = 881)	Total (*N* = 1759)
Hospital			
RBWH	454 (52%)	460 (52%)	914 (52%)
PAH	312 (36%)	313 (36%)	625 (36%)
QEII	112 (13%)	108 (12%)	220 (13%)
Age (years)[a]	59.7 (17.3)	60.5 (17.4)	60.1 (17.4)
Gender: males	527 (60%)	527 (60%)	1054 (60%)
Reason for admission			
Surgical	595 (68%)	636 (72%)	1231 (70%)
Medical	241 (27%)	211 (24%)	452 (26%)
Other	42 (5%)	34 (4%)	76 (4%)
Comorbidities			
None	131 (15%)	117 (13%)	248 (14%)
One	139 (16%)	143 (16%)	282 (16%)
Two	120 (14%)	140 (16%)	260 (15%)
Three	99 (11%)	101 (11%)	200 (11%)
Four or more	389 (44%)	380 (43%)	769 (44%)
Infection	134 (15%)	125 (14%)	259 (15%)

Abbreviations: PAH, Princess Alexandra Hospital; QE II, Queen Elizabeth II Hospital; RBWH, Royal Brisbane and Women's Hospital.

[a]Mean (standard deviation).

TABLE 2 Insertion, device, and therapy characteristics

	N	Nonintegrated	Integrated	Total
Successfully inserted[a]	1759	848 (97%)	862 (98%)	1710 (97%)
PIVC-days	1710	2073	2269	4342
Per-protocol device used[a]	1710	847 (>99%)	819 (95%)	1666 (97%)
Device number: Subsequent[b]	1710	751 (89%)	752 (87%)	1503 (88%)
Inserting department	1710			
Ward		762 (90%)	767 (89%)	1529 (89%)
Emergency		75 (9%)	79 (9%)	154 (9%)
Other		11 (1%)	16 (2%)	27 (2%)
Inserted by	1706			
Advanced practice nurse		409 (48%)	420 (49%)	829 ((49%)
Registered nurse		406 (48%)	404 (47%)	810 (47%)
Medical doctor		23 (3%)	31 (4%)	54 (3%)
Catheter size	1710			
22/24 G		514 (61%)	514 (60%)	1028 (60%)
20 G		326 (38%)	336 (39%)	662 (39%)
16/18 G		8 (1%)	12 (1%)	20 (1%)
Device location	1710			
Posterior lower forearm		365 (43%)	346 ((40%)	711 (42%)
Anterior upper forearm		160 (19%)	177 (21%)	337 (20%)
Wrist		103 (12%)	102 (12%)	205 (12%)
Cubital fossa		84 (10%)	97 (11%)	181 (11%)
Hand		58 (7%)	49 (6%)	107 (6%)
Posterior upper forearm		45 ((5%)	55 (6%)	100 (6%)
Anterior upper arm		17 (2%)	20 (2%)	37 (2%)
Other		16 (2%)	16 (2%)	32 (2%)
Insertion on dominant side[a]	1710	384 (45%)	423 (49%)	807 (47%)
Vein quality	1709			
Excellent		144 (17%)	173 (20%)	317 (19%)
Good		233 (28%)	216 (25%)	449 (26%)
Fair		391 (46%)	389 (45%)	780 (46%)
Poor		79 (9%)	84 (10%)	163 (10%)
Ultrasound for insertion[a]	1709	86 (10%)	78 (9%)	164 (10%)
Dressing dirty/wet/damaged (ever)[a]	1229	47 (8%)	46 (7%)	93 (8%)
Nonsterile tape (ever)[a]	1710	119 (14%)	125 (14%)	244 (14%)
Tubi-grip (ever)[a]	1710	558 (66%)	552 (64%)	1110 (65%)
Hyperfix/Mefix/Fixomull (ever)[a]	1710	46 (5%)	72 (8%)	118 (7%)
Another securement device (ever)[a]	1710	31 (4%)	31 (4%)	62 (4%)
No additional securement (ever)[a]	1710	222 (26%)	237 (27%)	459 (27%)
Open connection manipulated	888	22 (3%)	3 (7%)	25 (3%)

(Continued)

TABLE 2 (Continued)

	N	Nonintegrated	Integrated	Total
Closed connection manipulated	819	-	8 (1%)	-
Another vascular device (ever)	1291	98 (15%)	108 (17%)	206 (16%)
IV administration set (ever)	1710	407 (48%)	405 (47%)	812 (47%)
Blood in extension tubing (ever)	1291	77 (12%)	103 (16%)	180 (14%)
IV antibiotics (ever)	1710	470 (55%)	465 (54%)	935 (55%)
IV fluids (ever)	1710	392 (46%)	405 (47%)	797 (47%)
IV antiemetic/gastric protection (ever)	1710	194 (23%)	187 (22%)	381 (22%)
IV radiological contrast (ever)	1710	20 (2%)	26 (3%)	46 (3%)
IV blood product (ever)	1710	46 (5%)	56 (6%)	102 (6%)
IV electrolytes (ever)	1710	105 (12%)	100 (12%)	205 (12%)
IV analgesia (ever)	1710	181 (21%)	192 (22%)	373 (22%)
IV sedation (ever)	1710	115 (14%)	113 (13%)	228 (13%)
Heparin infusion (ever)	1710	64 (8%)	61 (7%)	125 (7%)
IV insulin (ever)	1710	17 (2%)	11 (1%)	28 (2%)
Chemotherapy (ever)	1710	1 (<1%)	2 (<1%)	3 (<1%)
Other IV therapy (ever)	1710	195 (23%)	227 (26%)	422 (25%)
No IV therapy	1710	68 (8%)	78 (9%)	146 (9%)

Abbreviations: IV, intravenous; max, maximum.

[a]Row for "no" responses omitted.

[b]Row for "first" omitted.

integrated group (39 vs. 53 per 1000 device-days, RR: 0.74 [95% CI: 0.55–0.99], two-sided $p = .034$; Table 3). Occlusion and phlebitis both had approximately 5 less events per 1000 device-days lower in integrated PIVCs (not statistically different; Table 3). PIVC dwell time was significantly longer (mean difference: 4.5 h [95% CI: 0.4–8.6], $p = .031$) in the integrated group with the top quartile lasting ≥95 versus ≥84 h for nonintegrated devices (Table 3 and Supporting Information: Figure 2). First-time insertion success, tip colonization, and pain at insertion were comparable between groups. There were no catheter-associated bloodstream infections, and between-group length of stay was equivalent. There were five deaths, all nonattributable to PIVCs.

The direct hospital cost, quality of life, and patient satisfaction were similar between groups (Tables 3 and 5). There were no PIVC infections in either group; thus, treatment costs were not included. For other complications (e.g., phlebitis), no additional treatments were required other than PIVC replacement (a cost already considered in the model). The mean cost per successful insertion was not statistically different (Table 5). The main determinant of cost difference was the additional cost of the integrated PIVC, accompanied by somewhat reduced ultrasound use in this group. In sensitivity analyses, the mean cost was statistically significantly higher in the integrated group when the ultrasound costs were excluded (mean difference: $4.15 [95% CI: 3.20–5.10], two-sided $p < .001$), but the difference was not statistically significant if those excluded from the mITT analysis were included. There was no clinically meaningful gain in health-related quality of life utility scores between groups (Table 3). Patient and clinician satisfaction were generally high for both devices, but clinician satisfaction was statistically higher with integrated PIVCs (mean difference: 1.4; two-sided $p < .001$) (Table 3).

DISCUSSION

This large, multicenter trial found 21 less integrated PIVCs failed per 1000 device-days than nonintegrated PIVCs—this difference was not statistically significant in the mITT analysis (RR: 0.86 [95% CI: 0.72–1.01]) but was significant on per-protocol analysis (RR: 0.83 [95% CI: 0.70–0.98]). Survival analysis and Cox regression indicated that integrated PIVCs had a 15% significantly reduced relative risk of failure, or an 18% reduction on multivariate analysis with adjusted HR of 0.82 (95% CI: 0.69–0.96). These results build upon single-site trials, which reported reduced failure with integrated PIVCs.[11,12,29] Most hospitalized patients require PIVCs, and PIVC failure is highly prevalent reflecting a complex interplay of patient, device, therapy, and provider factors.[2–4,7,30] PIVC design has changed little in several decades, and integrated PIVCs are a cost-effective strategy to reduce PIVC failure.

TABLE 3 Study outcomes (incidences and rates) and relative/absolute differences between study groups

	N	Nonintegrated	Integrated	RD (95% CI)	RR (95% CI)
Primary endpoint					
Failure	1710	300 (35%)	281 (33%)	−2.8% (−7.3 to 1.7)	0.92 (0.81–1.05)
Failure (per-procotol)	1666	299 (35%)	260 (32%)	−3.6% (−8.1 to 1.0)	0.90 (0.79–1.03)
Failure rate[a]	1710	145 (129–162)	124 (110–139)	−20.8 (−42.7 to 1.0)	0.86 (0.72–1.01)
Failure rate[a] (per-protocol)	1666	144 (129–162)	119 (106–135)	**−25.1 (−46.9 to −3.2)**	**0.83 (0.70–0.98)**
Secondary endpoints					
Occlusion	1710	43 (5%)	36 (4%)	−0.9% (−2.9 to 1.1)	0.82 (0.53–1.27)
Occlusion rate[a]	1710	20.7 (15.4–28.0)	15.9 (11.4–22.0)	−4.9 (−13.0 to 3.2)	0.77 (0.48–1.22)
Infiltr./extravasation/tissued	1710	68 (8%)	82 (10%)	1.5% (−1.2 to 4.2)	1.18 (0.87–1.61)
Infiltr./extravasation/tissued rate[a]	1710	32.8 (25.9–41.6)	36.1 (29.1–44.9)	3.3 (−7.7 to 14.4)	1.10 (0.79–1.54)
Phlebitis	1710	146 (17%)	149 (17%)	0.1% (−3.5 to 3.7)	1.00 (0.82–1.24)
Phlebitis rate[a]	1710	70.4 (59.9–82.8)	65.7 (55.9–77.1)	−4.7 (−20.3 to 10.8)	0.93 (0.74–1.18)
Dislodgement/leaking	1710	109 (13%)	88 (10%)	−2.6% (−5.7 to 0.4)	0.79 (0.61–1.03)
Dislodgement/leaking rate[a]	1710	52.6 (43.6–63.4)	38.8 (31.5–47.8)	**−13.8 (−26.6 to −1.0)**	**0.74 (0.55–0.99)**
Local infection	1710	1 (<1%)	0 (0%)	−0.1% (−0.3 to 0.1)	n/c
Local infection rate[a]	1710	0.5 (0.1–3.4)	0.0 (n/c)	−0.5 (−1.4 to 0.5)	0.0 (0.00–35.7)
CABSI	1710	0 (0%)	0 (0%)	0.0% (0.0–0.0)	n/c
CABSI rate[a]	1710	0.0 (n/c)	0.0 (n/c)	n/c	n/c
First-time insertion success	1703	672 (79%)	672 (78%)	−1.0% (−4.9 to 2.9)	0.99 (0.94–1.04)
Tip colonization	172	1 (1%)	1 (1%)	−0.3% (−3.6 to 3.0)	0.76 (0.05–11.9)
Pain at insertion[b]	1690	2 (1–4)	2 (1–4)	−0.04 (−0.25 to 0.18)[c]	n/c
Dwell time (h)[b]	1710	49.8 (26.1–84.1)	51.6 (27.1–94.9)	**4.49 (0.40–8.58)**[c]	n/c
Mortality	1710	3 (<1%)	2 (<1%)	−0.1% (−0.6 to 0.4)	0.66 (0.11–3.92)
Mortality rate[a]	1710	1.4 (0.5–4.5)	0.9 (0.2–3.5)	−0.6 (−2.6 to 1.5)	0.61 (0.05–5.32)
QoL at baseline (max. 100)[d]	685[e]	54.7 (35.4)	54.0 (34.7)	n/c	n/c
QoL change[c]	526[e]	0.57 (−3.13 to 4.28)	3.25 (−0.48 to 6.98)	n/c	n/c
Clinician overall satisfaction[b]	100	**8 (7–10)**[f]	**10 (8–10)**[f]	n/c	n/c
Patient overall treatment rating	265	3 (2–4)[b]	3 (2–3)[b]	−0.18 (−0.42 to 0.05)[c]	n/c

Note: Bold values indicate statistical significance at $p < .05$.

Abbreviations: CABSI, catheter-associated bloodstream infection; infiltr., infiltration; n/c, cannot be calculated; PIVC, peripherally inserted venous catheter; QoL, quality of life; RD, risk difference; RR, risk/rate ratio.

[a]Per 1000 device-days (95% confidence interval).

[b]Median (25th and 75th percentiles).

[c]Mean difference (95% confidence interval).

[d]Mean (standard deviation).

[e]Baseline surveys completed by 685 patients (nonintegrated: 337; integrated: 348) with 526 completed at follow-up (nonintegrated: 266; integrated: 260).

[f]*t*-Test.

The integrated design appeared to improve PIVC stability, leading to significantly less dislodgement and leakage. The integrated catheter's level base and wings likely provided greater surface area and durability for the dressing. Previous integrated PIVC trials also supposed this mechanism of effect, in addition to reduced PIVC kinking, and extravasation.[6,12] A recent large RCT of three novel dressing and securement options found no effect in reducing the failure of nonintegrated PIVCs, supporting the concept that catheter design is an important element in achieving effective securement.[7]

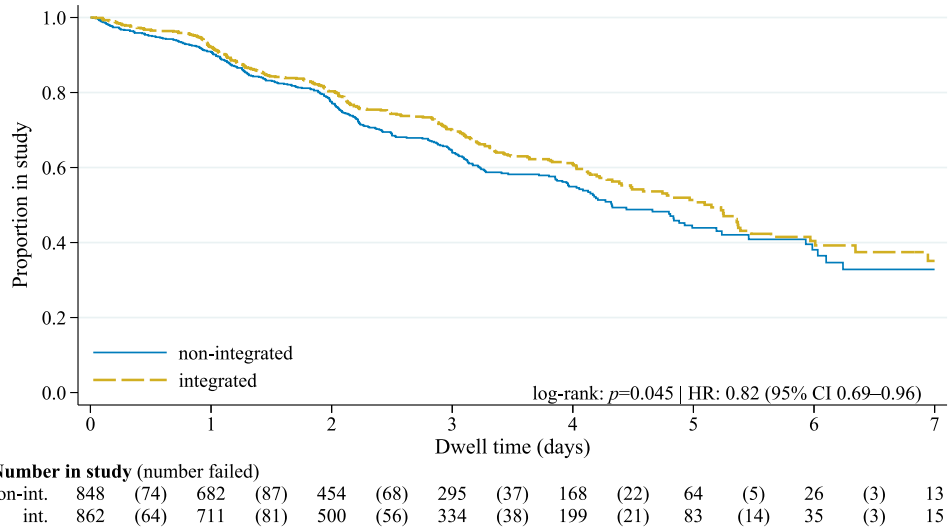

FIGURE 2 Kaplan–Meier survival curves. CI, confidence interval; HR, hazard ratio.

TABLE 4 Risk factors of PIVC failure (Cox regression)

	Hazard ratios (95% CI)		
	Unadjusted mITT (*N* = 1710)	Adjusted mITT (*N* = 1710)	Adjusted per-protocol (*N* = 1666)
Integrated study group (ref.: nonintegrated)	**0.85 (0.72–1.00)**	**0.82 (0.69–0.96)**	**0.80 (0.68–0.95)**
Age group (10-year increment)	0.96 (0.92–1.01)	[a]	
Female gender (ref.: male)	**1.55 (1.31–1.82)**	**1.30 (1.10–1.53)**	**1.30 (1.09–1.54)**
Medical admission (ref.: surgical)	**1.79 (1.50–2.14)**	[a]	
Comorbidity category (increment of 1)	0.99 (0.93–1.04)	[b]	
Infection at baseline (ref.: no)	**1.98 (1.61–2.42)**	**1.56 (1.26–1.92)**	**1.59 (1.28–1.97)**
Subsequent device (ref.: initial device)	**0.45 (0.35–0.56)**	[a]	
Another inserting department (ref.: ward)	**3.95 (3.14–4.96)**	**2.51 (1.92–3.30)**	**2.36 (1.76–3.15)**
Inserted by a doctor (ref.: nurse/APN)	**1.86 (1.28–2.70)**	[a]	
16/18/20 G catheter (ref.: 22/24 G)	**1.63 (1.38–1.92)**	**1.30 (1.09–1.56)**	**1.28 (1.06–1.54)**
Location (ref.: post. lower forearm)			
Upper ant. forearm/upper post. forearm	**1.78 (1.44–2.21)**	**1.61 (1.30–2.01)**	**1.61 (1.29–2.01)**
Hand/wrist	**2.41 (1.92–3.02)**	**2.13 (1.69–2.68)**	**2.10 (1.66–2.65)**
Cubital fossa	**3.36 (2.59–4.36)**	**1.91 (1.42–2.58)**	**1.97 (1.45–2.69)**
Other	**1.73 (1.15–2.60)**	1.28 (0.85–1.94)	1.23 (0.79–1.90)
Insertion on dominant side (ref.: no)	1.09 (0.93–1.28)	[b]	
Vein quality category (decrease of 1)	1.06 (0.97–1.16)	[b]	
Multiple insertion attempts (ref.: single)	**1.24 (1.02–1.51)**	[a]	
Ultrasound guidance used (ref.: not used)	1.10 (0.84–1.44)	[b]	

Note: Bold values indicate statistical significance at $p < .05$.

Abbreviations: ant., anterior; APN, advanced practice nurse; CI, confidence interval; HR, hazard ratio; mITT, modified intention to treat; post., posterior; ref., reference category.

[a]Dropped at $p \geq .05$.

[b]Ineligible at univariable $p \geq .20$.

TABLE 5 Mean cost per patient by study group (assuming failed PIVCs replaced with randomized PIVCs)

	N	Nonintegrated	Integrated	Difference	*p* Value[a]
Insertion costs	1710	$24.15 (21.45–26.86)	$26.24 (23.64–28.83)	$2.08 (−1.66 to 5.83)	.275
Device costs[b]	1710	$1.89 (1.82–1.97)	$5.28 (5.12–5.43)	**$3.39 (3.21–3.56)**	<.001
Labor costs[c]	1710	$2.81 (2.70–2.91)	$2.94 (2.82–3.05)	$0.13 (−0.02 to	.099
Dressing and procedure consumable costs	1710	$6.02 (5.85–6.19)	$5.91 (5.71–6.11)	−$0.11 (−0.37–0.15)	.404
Ultrasound costs	1710	$13.44 (10.73–16.15)	$12.12 (9.54–14.70)	−$1.32 (−5.06 to 2.42)	.489
Maintenance costs[d]	1710	$5.25 (4.89–5.61)	$5.14 (4.79–5.50)	−$0.11 (−0.61 to 0.39)	.666
Replacement device insertions and dressing costs	1710	$8.70 (7.87–9.53)	$8.61 (7.77–9.44)	$0.09 (−1.09 to 1.27)	.881
Total cost	1710	$38.10 (35.20–41.00)	$40.00 (37.20–42.77)	$1.88 (−2.13 to 5.90)	.358
Sensitivity analysis 1: Labor cost excluded	1710	$34.28 (31.43–37.14)	$36.07 (33.35–38.80)	$1.79 (−2.15 to 5.74)	.373
Sensitivity analysis 2: Ultrasound cost excluded	1710	$20.02 (19.41–20.63)	$24.17 (23.44–24.89)	**$4.15 (3.20–5.10)**	<.001
Sensitivity analysis 3: By patients randomized[e]	1710	$38.91 (35.95–41.86)	$40.43 (37.63–43.22)	$1.52 (−2.54 to 5.58)	.463

Note: Australian dollars (2020) and 95% confidence intervals are shown, unless otherwise noted. Bold values indicate statistical significance at $p < .05$.
Abbreviation: PIVC, peripheral intravenous catheter.

[a]*t*-Test.

[b]Nonintegrated included the catheter, short extension tubing, and connector, while integrated included all of these items in the one product.

[c]Mean time for catheter insertion (from opening of equipment to dressing application) was 2.83 and 2.27 min for the integrated and nonintegrated group, respectively.

[d]Included any subsequent dressing and securements required and infusion sets.

[e]Estimated as the total cost per group (mean cost per person estimated for all those randomized multiplied by the total number of persons randomized) divided by the number of successful insertions per group.

Integrated PIVCs were the only identified significant protective factor against PIVC failure in the multivariate analysis, but there were several significant risk factors consistent with prior work.[1,31–34] Females were at higher risk as were patients with any infection at baseline (e.g., respiratory), although heterogeneous antibiotics were not significant. Emergency department-inserted PIVCs were 2.5 times more likely to fail, affirming more efforts are needed in this setting and during interdepartmental transfer. PIVC insertion in areas of flexion (hand/wrist, antecubital fossa) or upper/posterior forearm had significantly more failure. The lower forearm provides added securement via the bone "splint" and is optimal for other than very short-term (procedural) PIVCs. Consistent with the guidelines,[8] recommending preferential smaller gauge PIVCs, we found 20 G or larger devices had significantly more failure.

Insertion of integrated PIVCs requires a lower hand angle than for traditional catheters, which has been suggested to potentiate insertion failure.[6] Although we observed 4% lower protocol compliance in integrated patients, this reflected inserters who chose the non-randomized catheter rather than insertion difficulties, as there was almost identical (79%/78%) first-time insertion success between groups. Another previously reported concern with integrated PIVCs is blood backflow into infusion tubing,[6] but we observed a slightly lower incidence with integrated catheters. This may reflect our successful education regarding the correct PIVC clamping sequence *before* disconnecting syringes (as required by integrated needleless connector).

The strengths of this study were its large, multicenter RCT design, including both clinical and cost-effectiveness outcomes. Generalizability was maximized by the pragmatic approach, with PIVCs inserted and cared for by clinicians, not specialist intravenous teams or researchers. A limitation was the inability to blind patients and clinical staff, although infection outcomes and the analyst were blinded. Our inclusion criteria required planned PIVC use >24 h, so our results are not generalizable to very short-term PIVCs. We followed up PIVCs until 48 h post-PIVC removal[7,12]; however, longer follow-up may have detected additional late failure. It was impractical to observe all PIVC insertions and therefore our results on timing and resources used may not be completely generalizable. We observed no PIVC infections, in the context of well-established infection prevention and surveillance practices, which have been shown to keep such infections at close to zero.[35–37]

Implementation of new healthcare products can have purchase cost as a barrier even if overall cost-effectiveness is improved. Integrated PIVC device purchase cost was higher but was offset by reduced costs required for add-on equipment and device replacement, consistent with a previous study.[6] Our hospitals did not have intravenous teams, therefore initial investment in education for many inserters was required. Health-related quality of life has not previously been measured in PIVCs, and we demonstrated negligible impact on this outcome, potentially due to a lack of sensitivity in the generic instrument, which calls for further research. Patients in our study were largely satisfied with both PIVCs, with clinicians significantly favoring the integrated PIVC.

Current guidelines recommend PIVC removal only when there is clinical justification (e.g., completed therapy) but with the proviso

that staff regularly assess and respond to complications.[14,38] This justifies greater focus on more durable PIVC designs. PIVC failure remains highly prevalent worldwide, leading to delayed treatments, additional insertions, patient pain and anxiety, increased clinician workload, and healthcare costs—new technologies if clinically and cost-effective, should be consistently implemented.[3] This multicenter RCT has resolved uncertainty about the relative merit of integrated and nonintegrated PIVCs, showing a cost-effective significant reduction in device failure with integrated PIVCs. These results can inform device choice decisions at the patient and institutional levels.

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CONFLICT OF INTEREST

Claire M. Rickard reports investigator-initiated research grants and speaker fees provided to her employer (Griffith University of The University of Queensland) from 3M, BD-Bard, Cardinal Health, Eloquest, and ITL Biomedical unrelated to this project. Emily Larsen reports Griffith University has received, on her behalf, an investigator-initiated research grant from Cardinal Health (formerly Medtronic); and a conference scholarship attendance supported by Angiodynamics, unrelated to this project. Rachel M. Walker reports investigator-initiated research grants provided to Griffith University from vascular access product manufacturer Becton, Dickinson and Company (BD), unrelated to this project. Joshua Byrnes reports investigator-initiated research and educational grants provided to Griffith University from Becton Dickinson, and Navi Technologies, unrelated to this project. Marie Cooke reports investigator-initiated research grants and speaker fees provided to her employer from vascular access product manufacturers Becton, Dickinson and Company (BD), unrelated to this project. Peter J. Carr reports speaker fees provided to him from 3M and BD-Bard. Nicole Marsh reports investigator-initiated research grants or speaker fees provided to Griffith University or University of Queensland on her behalf from Becton Dickinson, 3M, and Cardinal Health and Eloquest, and a consultancy payment for expert advice from Becton Dickinson, unrelated to the current project. The remaining authors declare no conflict of interest.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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