



# Inherent and modifiable risk factors for peripheral venous catheter failure during cancer treatment: a prospective cohort study

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## Abstract

**Purpose** To identify modifiable and non-modifiable risk factors for peripheral intravenous catheter (PIV) failure among patients requiring intravenous treatment for oncology and haematology conditions.

**Methods** A single-centre prospective cohort study was conducted between October 2017 and February 2019. Adult in-patients requiring a PIV for therapy were prospectively recruited from two cancer units at a tertiary hospital in Queensland, Australia. The primary outcome was a composite of complications leading to PIV failure (local and bloodstream infection; occlusion; infiltration/extravasation; leakage; dislodgement; and/or phlebitis). Secondary outcomes were (i) PIV dwell time; (ii) insertion and (iii) failure of a CVAD; (iv) adverse events; (v) length of hospital stay. Outcomes were investigated using Bayesian multivariable linear regression modelling and survival analysis.

**Results** Of 200 participants, 396 PIVs were included. PIV failure incidence was 34.9%; the most common failure type was occlusion/infiltration ( $n = 74$ , 18.7%), then dislodgement ( $n = 33$ , 8.3%), and phlebitis ( $n = 30$ , 7.6%). While several patient and treatment risk factors were significant in univariable modelling, in the final multivariable model, only the use of non-sterile tape (external to the primary dressing) was significantly associated with decreased PIV dislodgement (hazard ratio 0.06, 95% confidence interval 0.01, 0.48;  $p = 0.008$ ).

**Conclusion** PIV failure rates among patients receiving cancer treatment are high, the sequelae of which may include delayed treatment and infection. Larger studies on risk factors and interventions to prevent PIV failure in this population are needed; however, the use of secondary securements (such as non-sterile tape) to provide further securement to the primary PIV dressing is particularly important.

**Trial registration** Study methods were registered prospectively with the Australian New Zealand Clinical Trials Registry on the 27<sup>th</sup> March 2017 (ACTRN12617000438358); <https://www.anzctr.org.au/Trial/Registration/TrialReview.aspx?id=372191&isReview=true>

**Keywords** Peripheral venous · Vascular access · Oncology · Haematology

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## Introduction

Patients receiving treatment for cancer (both solid tumours and haematological malignancies) are highly dependent upon intravenous (IV) infusions such as chemotherapies and antibiotics [1]. Within this setting, central venous access devices (CVADs) are recommended for long-term and vesicant treatments (i.e. infusates harmful to peripheral vasculature), and peripheral intravenous (PIV) catheters for short-term and non-vesicant treatments [2]. Studies have highlighted drawbacks of PIV use in cancer treatment (compared with CVADs), including the frequency and pain associated with frequent venepuncture, inability to draw blood (a regular requirement during treatment), and subsequent vein exhaustion [3, 4]. Despite this, CVAD use is, in some cases, impractical for reasons such as the recency of bloodstream infection (BSI) [5] or short-term IV treatment; and PIVs remain a necessary tool in cancer care. Little evidence exists, however, to establish the prevalence and characteristics of PIV use specifically in the cancer setting, despite studies highlighting this as a key area of concern [1, 6]. Moreover, recent studies have identified alarmingly high rates of PIV failure (resulting from occlusion, infiltration, dislodgement, phlebitis, and infection) in medical and surgical care populations (33–69%) [7, 8]. However, similar outcome rates have yet to be confirmed in cancer-specific populations as, traditionally, PIV studies in cancer populations have focused upon the incidence and treatment of vesicant extravasation injuries, specifically [9, 10]; to date, there have been no prospective studies which have reported the incidence of *all-cause* PIV failure.

There are inherent differences in the population of patients with cancer which would lead clinicians to believe the rate and characteristics of PIV failure would differ to medical and surgical populations (e.g. regular administration of vesicant therapies, limbs affected by lymphoedema, and long-term treatment requirements) [11]. The aim of this prospective observational cohort study was to investigate the use and outcomes of PIV (and subsequent use- and failure- of CVAD) among cancer care inpatients from hospital admission through to discharge and to determine both inherent and modifiable risk factors for PIV failure.

## Methods

### Study design and setting

We conducted a single-centre prospective, observational cohort study at a large teaching and referral hospital in Queensland, Australia (approximately 3000 in-patient

admissions per year for cancer). Participants were prospectively enrolled between the 20<sup>th</sup> of October 2017 and 3<sup>rd</sup> of February 2019 from two haematology (including bone marrow transplant (BMT)) and oncology (medical, radiation) in-patient units. Study methods were registered prospectively with the Australian New Zealand Clinical Trials Registry on the 27<sup>th</sup> of March 2017 (ACTRN12617000438358).

### Participants

All adult patients ( $\geq 18$  years) admitted to a haematology/bone marrow transplant or oncology (medical, radiation) units at the recruiting hospital were eligible for participation if they (i) were able to provide informed consent and (ii) had a PIV inserted within the previous 48 h (first PIV this admission). Exclusion criteria were (i) patients receiving end-of-life care and (ii) those from a non-English speaking background without a suitable interpreter. Patients with previous enrolment in the study were also excluded, as patients may present with the same inherent risk factors each admission, potentially influencing findings. The Research Nurses (ReNs) reviewed admission lists for the recruiting wards three times weekly (Monday, Wednesday, Friday) and further screened for the presence of a PIV, before liaising with the treating nurse/team for patient appropriateness to participate. Eligible patients were provided with a participant information sheet and consent form; signed informed consent was required prior to enrolment.

### PIV insertion procedures

Standard PIV insertion and maintenance policies and procedures were in place throughout the duration of the project and applied to both the haematology/bone marrow transplant and oncology (medical, radiation) units. Skin preparation was 2% chlorhexidine gluconate (CHG) in alcohol 70% for skin preparation (SoluPrep™; 3M, St Paul, USA); and PIVs were BD Insyte™ Autoguard™ blood control catheters (Becton Dickinson, Utah, USA). PIVs were recommended to be dressed with a bordered polyurethane dressing, Tegaderm™ 1635 (3M, St. Paul, USA); however, small variations in selected dressings were common in these units. Due to the nature of the study, compliance was not monitored or enforced.

### Outcomes

The primary outcome was all-cause PIV failure; a composite measure of any one of the following five events: infection

(suspected or laboratory-confirmed local or bloodstream infection [12]); occlusion (device will not infuse) [13]; infiltration (infusate leaking into the interstitial tissue; if with vesicant, this was considered *extravasation*) [14]; leakage (external); dislodgement (complete or partial removal from the vein); or phlebitis (defined as pain alone ( $\geq 2/10$ ); or  $\geq 2$  signs/symptoms of (i) pain/tenderness, (ii) erythema, (iii) swelling, and/or (iv) palpable cord) [15].

Secondary outcomes were (i) PIV dwell time; (ii) insertion and (iii) failure of a CVAD; (iv) adverse events (including BSI and mortality); and (v) length of hospital stay.

### Data sources/measurement

All data was entered on the Research Electronic Data Capture (REDCap) web-based platform (Vanderbilt University) [16], hosted on a secure internal server (Griffith University).

**Participant characteristics** Upon enrolment, the ReN collected baseline data including age; gender; height; weight; skin integrity (good, fair, poor) [17]; dominant hand; number of comorbidities (0, 1, 2, 3, > 3); primary admitting diagnosis and treatment duration; presence and type of current infections or wounds; blood type; and history of PIV and/or CVAD insertion.

**Device characteristics** Data were collected for every PIV inserted during the patients' admission including inserter; place of insertion (e.g. ward, emergency); PIV size/gauge; anatomical location; insertion side; number of insertion attempts required; insertion pain experienced (11-point Likert scale, 0 (no pain) to 10 (worst pain)) 7; primary PIV dressing and additional securements; and the patients' hydration status at device insertion. Three-times weekly, the ReN further collected data with a standardized tool including IV treatments administered, administration set attachments, primary dressing and additional securement changes, and phlebitis assessment (requiring both a visual assessment and insertion site palpation). Signs and symptoms of phlebitis included pain and/or tenderness (each, collected on an 11-point Likert scale, 0 (no pain) to 10 (worst pain)); erythema, swelling, palpable cord, or vein streak (each, in cm); purulence (with or without ulceration); and warmth/heat, skin hardness, or itch (any, at the insertion site).

**Device and patient outcomes** Data collected included reason for device removal (including complications); signs and symptoms of phlebitis; and dwell time. Discharged patients were contacted by phone to establish outcomes (within 72 h). Data relating to subsequent CVAD details were collected including type, gauge, insertion side, inserting clinician, and reason for removal (including complications). Patient outcomes (mortality, infection), occurring between enrolment

and 48 h after patient removal (from the study), were entered once available. Infection outcomes (catheter-associated local and bloodstream infection) were determined by a qualified infectious diseases physician.

### Study size

The sample size was determined by calculating the number of anticipated failure events, to ensure a minimum of ten events per variable (twenty possible risk factors) used in model development [18]; this practice is recommended for observational studies in cancer research employing multivariable modelling. Based on previous studies conducted locally, a 40% PIV failure rate was anticipated [15, 19], with an average of 2.5 devices per participant (pp) predicted ( $n = 500$  PIVs, 200 failure events).

### Statistical methods

Data were exported into Stata Statistical Software [20] for analysis. Continuous data are presented as means (and standard deviations), or medians (and inter-quartile ranges), where appropriate; categorical data are presented as frequency (percentage). Incidence rates for failure per 1000 catheters days were calculated using Poisson regression with the natural logarithm of days-at-risk included in the model as an offset. Failure was coded into three failure types including (i) dislodgement (partial, complete); (ii) infiltration/occlusion/extravasation; and (iii) phlebitis. The association between patient characteristics and failure was investigated using univariable and multivariable Cox regression models. Effect estimates are presented as hazard ratio (HR) with a 95% confidence interval (CI). The best multivariable model was selected based on the Bayesian information criterion (BIC). The best model for a fixed number of explanatory variables was identified as the model with the lowest BIC value. When adding another explanatory variable to the model, the new model was defined to be superior if the BIC decreased by 2 units or more when determining the best multivariable model.  $p$  value < 0.05 was considered statistically significant. Kaplan-Meier curves were used to evaluate time-to-PIV failure for the three failure types. Data was censored either when the device was removed or at 5 days, whichever occurred first. No data were imputed; where missing data exists, altered sample sizes are provided.

## Results

### Participants

Overall,  $n = 280$  eligible patients were considered for inclusion ( $n = 79$  met exclusion criteria) with a total of  $n = 201$

enrolled (Fig. 1). One participant subsequently withdrew all consent, leaving a final sample of  $n = 200$  included in the analysis.

## Descriptive data

Participants had a median age of 64 years (IQR, 54; 71), and the majority were male ( $n = 132$ , 66%) (Table 1). Most participants were being treated for a haematological malignancy ( $n = 123$ , 62%), and 60% ( $n = 119$ ) had two or more underlying comorbidities. The presence of a wound was uncommon ( $n = 20$ , 10%); however, there was a high prevalence of patients with current infections ( $n = 84$ , 42%). Length of hospital stay (follow-up time from study entry) was a median of 5 days (IQR, 3; 10).

On average, participants required 2 PIVs each during their hospital admission, with a total of  $n = 396$  PIVs analysed (957 PIV days) (Table 2). These PIVs were most commonly a 22-gauge catheter ( $n = 194/362$ , 54%), inserted by a ward nurse ( $n = 263/375$ , 70%), into the forearm ( $n = 191/385$ , 50%); ultrasound was seldom used ( $n = 6/396$ , 2%). Secondary dressing use was common, with 46% ( $n = 136/293$ ) of PIVs dressed with at least one piece of non-sterile tape (outside of the primary dressing), with or without additional elasticised tubular bandaging, used on 45% ( $n = 131/293$ ) of PIVs. CVADs were placed following PIV removal for  $n = 19$  (9.5%) participants (total  $n = 34$  CVADs); these were most commonly peripherally inserted central catheters ( $n = 24/34$ , 71%).

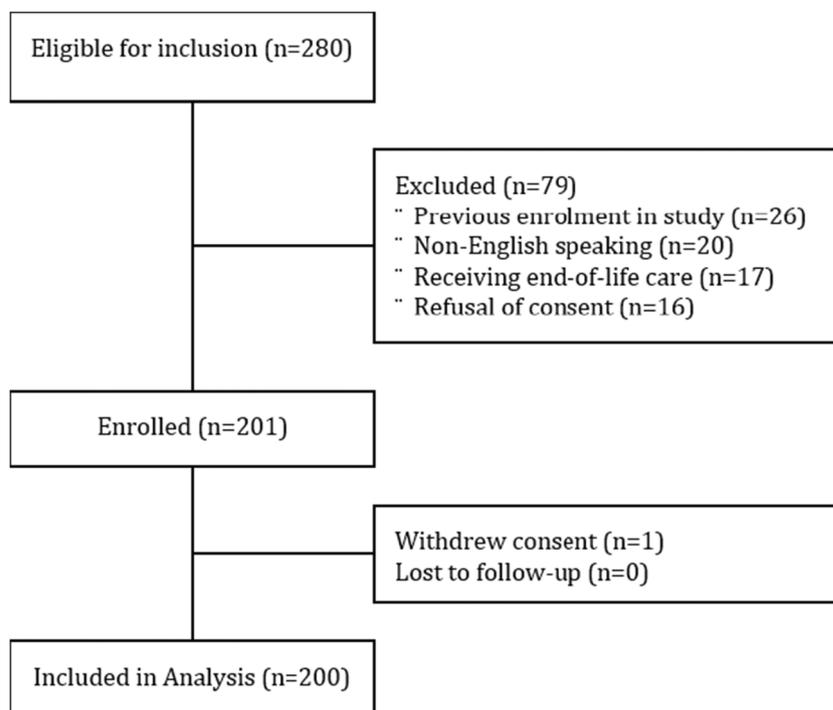
## Outcome data

PIV failure occurred in 34.9% of all PIVs (130.7/1000 catheter days, 95%CI 109.7, 155.7). The most common failure type was occlusion/infiltration ( $n = 74$ , 18.7%; 7.4/1000 catheter days, 95%CI 61.6, 97.1), followed by dislodgement ( $n = 33$ , 8.3%; 3.4/1000 catheter days, 95%CI 24.5, 48.5) and phlebitis ( $n = 30$ , 7.6%; 3.1/1000 catheter days, 95%CI 21.9, 44.9); there were no cases of extravasation. The median dwell time was 2.3 days (IQR 1.1–3.2); a Kaplan-Meier survival analysis (risk of PIV failure by dwell time) was plotted to 5 days (Fig. 2). The need for subsequent PIV insertions was high, with 55% ( $n = 109$ ) of participants requiring a second device, with a further 22% ( $n = 44$ ) and 10% ( $n = 20$ ) requiring third, and fourth PIVs, respectively. Further, 12% ( $n = 23$ ) of participants required five or more PIVs during their admission.

## Univariable modelling

In univariable Cox regression analysis (Table 3), the 20-gauge PIVs (HR 2.38, 95%CI 1.01; 5.63,  $p = 0.049$ ) were significantly associated ( $p < 0.05$ ) with an increase in PIV failure by dislodgement. Three or more attempts at PIV insertion were also significantly associated with an increased risk of occlusion/infiltration/leakage (HR 2.13, 95%CI 1.05; 4.32;  $p = 0.037$ ). PIVs were significantly less likely to present with phlebitis with each increase in age (by decade) (HR 0.78, 95%CI 0.61; 0.99,  $p = 0.043$ ), if the patient had three or more comorbidities (HR 0.36, 95%CI 0.13; 0.98,  $p = 0.045$ ), and if

**Fig. 1** Participant flow diagram [21]



**Table 1** Participant (non-modifiable) characteristics by failure mode

| Variable                     | Failure type   |               |                                    |               |
|------------------------------|----------------|---------------|------------------------------------|---------------|
|                              | Total          | Dislodgement  | Occlusion/infiltration/<br>leakage | Phlebitis     |
| Group size                   | <i>n</i> = 200 | <i>n</i> = 17 | <i>n</i> = 39                      | <i>n</i> = 16 |
| Age (years) <sup>a</sup>     | 64 (54,71)     | 65 (59,74)    | 65 (55,71)                         | 62 (45,69)    |
| Male gender                  | 132 (66)       | 9 (53)        | 23 (59)                            | 9 (56)        |
| Body mass index <sup>a</sup> | 28 (24, 32)    | 28 (24, 32)   | 25 (21, 28)                        | 26 (22, 28)   |
| Skin integrity               |                |               |                                    |               |
| Good                         | 83 (42)        | 4 (24)        | 12 (31)                            | 8 (50)        |
| Fair                         | 77 (39)        | 8 (47)        | 21 (54)                            | 6 (38)        |
| Poor                         | 40 (20)        | 5 (29)        | 6 (15)                             | 2 (13)        |
| Comorbidities                |                |               |                                    |               |
| Zero                         | 46 (23)        | 0 (0)         | 12 (31)                            | 6 (38)        |
| One                          | 35 (18)        | 6 (35)        | 3 (8)                              | 3 (19)        |
| Two                          | 36 (18)        | 3 (18)        | 5 (13)                             | 3 (19)        |
| Three+                       | 83 (42)        | 8 (47)        | 19 (49)                            | 4 (25)        |
| Discipline                   |                |               |                                    |               |
| Haematology                  | 123 (62)       | 11 (65)       | 24 (62)                            | 8 (50)        |
| Oncology                     | 77 (39)        | 6 (35)        | 15 (39)                            | 8 (50)        |
| Current infection            | 84 (42)        | 11 (65)       | 16 (41)                            | 5 (31)        |
| Blood type ( <i>n</i> = 155) |                |               |                                    |               |
| O+                           | 66 (43)        | 5 (38)        | 10 (32)                            | 5 (36)        |
| A+                           | 46 (30)        | 3 (23)        | 11 (36)                            | 4 (29)        |
| Other                        | 43 (28)        | 5 (38)        | 10 (32)                            | 5 (36)        |
| Wound present                | 20 (10)        | 2 (12)        | 3 (8)                              | 3 (19)        |
| History of CVAD              | 151 (76)       | 4 (24)        | 7 (18)                             | 5 (31)        |
| Hospital stay length         | 5 (3, 10)      | 6 (4,12)      | 5 (3,10)                           | 6 (4,19)      |

*n* = 200 participants unless otherwise noted; <sup>a</sup>Median (inter-quartile range)

the patient was receiving IV antibiotics (HR 0.25, 95%CI 0.08; 0.73, *p* = 0.011). The administration of IV fluids was significantly associated with a reduced risk of PIV dislodgement (HR 0.29, 95%CI 0.13; 0.62, *p* = 0.002), occlusion/infiltration (HR 0.45, 95%CI 0.26; 0.77, *p* = 0.003), and phlebitis (HR 0.31, 95%CI 0.14; 0.71, *p* = 0.005), and the use of secondary non-sterile adhesive tape was significantly associated with reduced risk of PIV dislodgement (HR 0.04, 95%CI 0.01; 0.31, *p* = 0.002) and occlusion/infiltration (HR 0.46, 95%CI 0.25; 0.84, *p* = 0.012).

### Multivariable modelling

Multivariable modelling demonstrated the use of secondary application of non-sterile tape to the primary dressing was significantly associated with less PIV failure by dislodgement (HR 0.06, 95%CI 0.01; 0.48, *p* = 0.008) (Table 4).

### Adverse events

There was one case of confirmed PIV-related BSI [12] (*Proteus mirabilis*). The patient, who was febrile and

displaying symptoms of delirium day 4 PIV dwell (102 h) had a recent history of local PIV infection (*Staphylococcus aureus*) and presented with a tender PIV site (3/10), with erythema (1 cm length) and purulence at the insertion site.

There were two confirmed catheter local infections (*n* = 1 *Enterobacter cloacae*; *n* = 1 unconfirmed organism):

- *Case 1* was admitted to the emergency department 5 days post-discharge with fevers and PIV site local infection (purulence); 5-day admission requiring IV antibiotics (piperacillin tazobactam; vancomycin). The patient was subsequently discharged home on oral antibiotics (ciprofloxacin, flucloxacillin).
- *Case 2* developed signs and symptoms of local infection day 1 (24 h) of PIV dwell (erythema < 0.5 cm; swelling/induration < 0.5 cm; purulence); the infection resolved post-removal without intervention.

Mortality occurred in 4% (*n* = 16/200) of the population; no cases were related to vascular access devices.

**Table 2** Peripheral intravenous catheter (PIV) modifiable characteristics by failure mode

| Variable  | Failure type   |               |                                    |               |
|---|----------------|---------------|------------------------------------|---------------|
|   | Total          | Dislodgement  | Occlusion/infiltration/<br>leakage | Phlebitis     |
| Group size  | <i>n</i> = 396 | <i>n</i> = 33 | <i>n</i> = 74                      | <i>n</i> = 30 |
| Inserted by ( <i>n</i> = 375)                           |                |               |                                    |               |
| Nurse   | 263 (70)       | 21 (68)       | 48 (71)                            | 17 (61)       |
| Doctor  | 92 (25)        | 8 (26)        | 17 (22)                            | 10 (36)       |
| Other   | 20 (5)         | 2 (7)         | 3 (4)                              | 1 (4)         |
| Size/gauge ( <i>n</i> = 362)                            |                |               |                                    |               |
| 16/18 g   | 15 (4)         | 0 (0)         | 2 (3)                              | 3 (11)        |
| 20 g  | 145 (40)       | 17 (61)       | 32 (47)                            | 11 (39)       |
| 22 g  | 194 (54)       | 10 (36)       | 33 (49)                            | 14 (50)       |
| Other   | 8 (2)          | 1 (4)         | 1 (2)                              | 0 (0)         |
| Device location—position on arm ( <i>n</i> = 385)       |                |               |                                    |               |
| Upper arm   | 5 (1)          | 0 (0)         | 0 (0)                              | 1 (3)         |
| Antecubital fossa                                       | 101 (26)       | 11 (34)       | 19 (27)                            | 6 (20)        |
| Forearm   | 191 (50)       | 12 (38)       | 37 (52)                            | 14 (47)       |
| Wrist   | 53 (14)        | 3 (9)         | 11 (16)                            | 5 (17)        |
| Hand  | 35 (9)         | 6 (19)        | 4 (6)                              | 4 (13)        |
| Multiple attempts ( <i>n</i> = 367)                     |                |               |                                    |               |
| One   | 271 (74)       | 19 (63)       | 45 (71)                            | 20 (69)       |
| Two   | 53 (14)        | 7 (23)        | 5 (8)                              | 6 (21)        |
| Three or more   | 43 (12)        | 4 (13)        | 13 (21)                            | 3 (10)        |
| Hydration status ( <i>n</i> = 396)                      |                |               |                                    |               |
| Nil by mouth  | 24 (6)         | 2 (6)         | 2 (3)                              | 3 (10)        |
| Altered fluid intake                                    | 74 (19)        | 7 (21)        | 16 (22)                            | 9 (30)        |
| None of the above                                       | 298 (75)       | 24 (73)       | 56 (76)                            | 18 (60)       |
| Administration set in place ( <i>n</i> = 293)           | 211 (72)       | 11 (65)       | 33 (73)                            | 9 (56)        |
| Medications administered <sup>a</sup> ( <i>n</i> = 396) |                |               |                                    |               |
| IV fluids   | 221 (56)       | 13 (39)       | 36 (49)                            | 13 (43)       |
| IV antibiotics  | 138 (35)       | 12 (36)       | 25 (34)                            | 6 (20)        |
| Blood products  | 54 (14)        | 2 (6)         | 8 (11)                             | 4 (13)        |
| Chemotherapy  | 19 (5)         | 0 (0)         | 3 (4)                              | 2 (7)         |
| Antivirals/antifungals                                  | 1 (0)          | 1 (3)         | 0 (0)                              | 0 (0)         |
| Secondary dressings <sup>a</sup> ( <i>n</i> = 293)      |                |               |                                    |               |
| Non-sterile tape  | 136 (46)       | 4 (12)        | 18 (24)                            | 9 (30)        |
| Elasticised tubular bandage                             | 131 (45)       | 6 (18)        | 26 (35)                            | 8 (27)        |
| No additional dressing/s                                | 87 (30)        | 5 (15)        | 10 (14)                            | 1 (3)         |
| Other   | 31 (11)        | 3 (9)         | 3 (4)                              | 3 (10)        |

<sup>a</sup>> 100% where multiple options could be selected

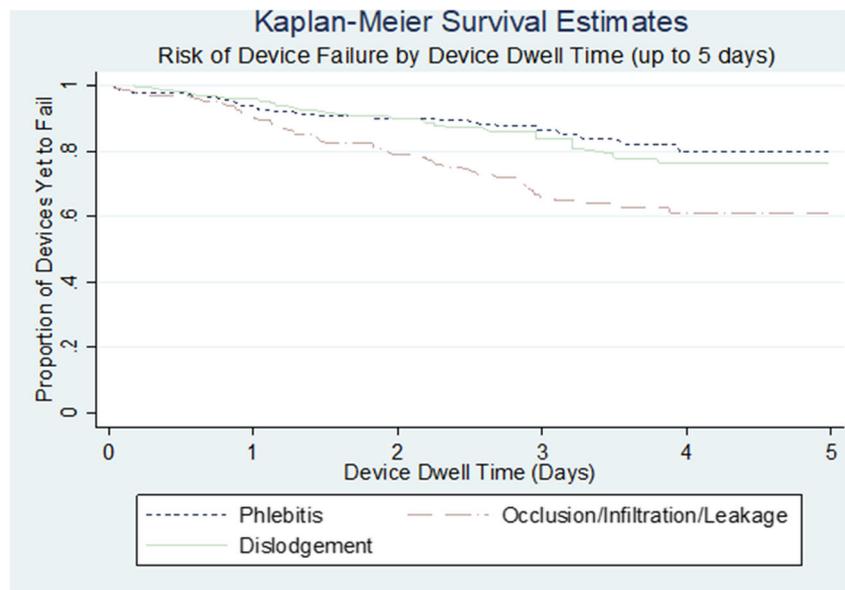
## Discussion

This observational study confirmed an unacceptably high PIV failure rate among patients receiving treatment for cancer (34.9%). This failure rate was comparable with other prospective studies, which found similar rates (and higher) in medical and surgical populations [8, 19, 22]. PIVs most commonly failed from complications associated with occlusion or infiltration (*n* = 74, 18.7%). To date, PIV research has overwhelmingly focused upon extravasation injuries among patients with cancer [9, 10, 23, 24]; however, there were no cases of extravasation reported in

our study. We postulate this may be a result of a low incidence of chemotherapy administration (*n* = 19, 5%) and a high proportion of CVAD use (70%) based on a point-prevalence audit conducted in this population [25]. PIVs were instead more likely to be placed for the administration of hydrocolloid fluids (*n* = 221, 56%), antibiotics (*n* = 138, 35%), and/or blood products (*n* = 54, 14%).

In univariable modelling, several non-modifiable patient and treatment-related factors were associated with a reduction in PIV failure by phlebitis (increase in age,  $\geq 3$  comorbidities, and IV antibiotics). Increase in age related to a decrease in phlebitis was similarly found in a large multivariate

**Fig. 2** Kaplan-Meier curve of dislodgement (a), occlusion/infiltration (b), phlebitis (c)



analysis (HR 0.99; 95%CI 0.98; 0.99,  $p < 0.001$ ) [26]. However, while our study found  $\geq 3$  comorbidities and the use of IV antibiotics reduced the risk of phlebitis, this contradicts evidence from other studies which found higher rates of phlebitis with the use of several IV antibiotics [27] and a higher rate of phlebitis among patients with comorbidities such as diabetes mellitus [28, 29]; these factors were not significant in multivariable modelling. Occlusion/infiltration and dislodgement were associated with modifiable (PIV-related) risk factors such as 20-g PIVs (dislodgement), and  $\geq 3$  attempts at PIV insertion (occlusion/infiltration). In contrast, 20-g PIVs have previously demonstrated a lower incidence of dislodgement compared with 22 g (HR 1.29; 95%CI 1.02, 1.61,  $p = 0.03$ ) [26]. The administration of IV fluids was associated with less failure from all three failure modes; the nature of this association is not clear as the mode of administration (e.g. flush or slow infusion) was not collected; IV fluids alone have not previously been shown as protective in risk factor studies.

Multivariable modelling identified a single protective factor for the prevention of PIV dislodgement alone, the application of the non-sterile tape, secondary to the primary dressing (HR 0.06, 95%CI 0.01, 0.48,  $p = 0.008$ ). This finding is consistent with previous studies which similarly demonstrated the benefits of using secondary tapes and securements, to prevent PIV failure [19, 30]. A large RCT which recently compared novel dressing and securement methods to prevent PIV failure, such as tissue adhesive and external securement devices, found that while simple (un-bordered) polyurethane dressings performed equally to these novel options, the use of additional non-sterile tapes and secondary securements (e.g. bandaging) was common and may have influenced the results [15]. Consequently, we agree with recommendations

[15, 31] for the development of improved secondary dressings and securements to decrease PIV failure, specifically dislodgement.

Regrettably, multiple ( $\geq 2$ ) insertion attempts prior to PIV placement were common (26%) and, in univariable modelling, were associated with occlusion and infiltration ( $\geq 3$  attempts, HR 2.13, 95%CI 1.05, 4.32;  $p = 0.037$ ). Improved technology (e.g. ultrasound guidance) to prevent multiple needlesticks, particularly prior to the administration of chemotherapy, is recommended to ensure best possible outcomes for patients [32]. However, in our study, ultrasound was seldom used ( $n = 6/396$ ) which likely contributed to the incidence of multiple insertion attempts, given there is strong evidence of its efficacy, with a recent systematic review ( $n = 1660$ ) finding insertion success significantly higher with ultrasound use (81%) than without (70%) (95%CI 1.37–4.52,  $p = 0.003$ ) [33].

It was also observed that 76% of participants ( $n = 151$ ) had previously required a CVAD for treatment (any admission); this was unsurprising due to the chronic nature of cancer and the regular administration of vesicant and irritant infusates [1]. However, in our study, patients who commenced treatment with PIVs rarely had CVAD placement following PIV failure ( $n = 19, 10\%$ ), despite 22% ( $n = 44$ ) of participants requiring three or more PIVs during their admission. Improved device selection (based on expected treatments and duration) may reduce the number of patients requiring multiple PIVs during their stay; alternative options may include long-dwell or mid-line catheters [34], where CVADs are deemed inappropriate due to risks of thrombosis and/or infection [35]. This further supports the need for wide implementation of ultrasound technologies, to enable the insertion of devices unsuitable for blind puncture insertion [36]. Furthermore, as antibiotic use was

**Table 3** Cox univariable regression by failure mode

| Variable                              | Hazard ratio (95% CI) <i>p</i> value            |   |   |
|---------------------------------------|---|---|---|
|                                       | Failure type                                    |   |   |
|                                       | Dislodgement                                    | Occlusion/infiltration/leakage                  | Phlebitis                                       |
| Age (per decade)                      | ^   | ^   | 0.78 (0.61, 0.99) <i>p</i> = 0.043 <sup>a</sup> |
| Comorbidities (ref. none)             |   |   |   |
| Three+                                | ^   | ^   | 0.36 (0.13, 0.98) <i>p</i> = 0.045 <sup>a</sup> |
| Inserted by (ref. nurse)              |   |   |   |
| Doctor                                | ^   | ^   | 2.30 (0.96, 5.40) <i>p</i> = 0.061 <sup>b</sup> |
| Size/gauge (ref. 22 g)                |   |   |   |
| 20 (pink)                             | 2.38 (1.01, 5.63) <i>p</i> = 0.049 <sup>a</sup> | ^   | ^   |
| Multiple attempts (ref. no)           |   |   |   |
| Two                                   | 2.26 (0.88, 5.80) <i>p</i> = 0.089 <sup>b</sup> | ^   | ^   |
| Three or more                         | ^   | 2.13 (1.05, 4.32) <i>p</i> = 0.037 <sup>a</sup> | ^   |
| Medications administered (ref. no)    |   |   |   |
| IV fluids                             | 0.29 (0.13, 0.62) <i>p</i> = 0.002 <sup>a</sup> | 0.45 (0.26, 0.77) <i>p</i> = 0.003 <sup>a</sup> | 0.31 (0.14, 0.71) <i>p</i> = 0.005 <sup>a</sup> |
| IV antibiotics                        | ^   | 0.60 (0.33, 1.06) <i>p</i> = 0.079 <sup>b</sup> | 0.25 (0.08, 0.73) <i>p</i> = 0.011 <sup>a</sup> |
| Blood products                        | ^   | ^   | ^   |
| Chemotherapy                          | ^   | ^   | ^   |
| Secondary dressings applied (ref. no) |   |   |   |
| Non-sterile tape                      | 0.04 (0.01, 0.31) <i>p</i> = 0.002 <sup>a</sup> | 0.46 (0.25, 0.84) <i>p</i> = 0.012 <sup>a</sup> | 0.45 (0.19, 1.09) <i>p</i> = 0.077 <sup>b</sup> |
| Elasticised tubular bandage           | 0.46 (0.19, 1.14) <i>p</i> = 0.093 <sup>b</sup> | ^   | ^   |
| No additional dressing/s              | ^   | 0.48 (0.22, 1.07) <i>p</i> = 0.072 <sup>b</sup> | 0.14 (0.02, 1.03) <i>p</i> = 0.054 <sup>b</sup> |
| Other                                 | ^   | ^   | ^   |

<sup>a</sup>*p* < 0.05; <sup>b</sup>*p* < 0.1; ^*p* > 1.0 (not presented); ref = reference

common (*n* = 138, 35%), oral alternatives may be considered; recent evidence suggests IV antibiotic administration may be substituted for oral delivery, with equivalent efficacy, in low-risk patients with neutropenia and fever [37]. Improvements such as these are necessary, to reduce PIV failure, as the sequelae of PIV complications is not merely limited to the need for PIV re-insertion; it can result in further negative outcomes such as venous depletion and morbidity/mortality associated with critical complications (e.g. catheter-related BSI) [38]. Moreover, the resulting pain, discomfort, and anxiety associated with PIV re-insertion can be severe, particularly for patients requiring multiple re-insertion attempts [39, 40].

Due to recent advancements in treatments, increased awareness, and early cancer detection methods (particularly for solid tumours) [41], the estimated number of cancer survivors is expected to grow (approximately 30%, 2016 to 2026) [42]. As a result, a growing number of oncology and haematology patients are likely to require long-term therapy, to maintain interruption of disease progression and for treatment of secondary chronic illnesses [43]. It is imperative that improvements are made for PIV insertion, care/maintenance, and removal among patients with cancer to ensure long-term vessel health and preservation [44], and ensure compliance with the *Access Device Standards of Practice for Oncology Nursing* [45].

**Table 4** Cox multivariable regression by failure mode

| Variable             | Hazard ratio (95% CI) <i>p</i> value            |                                    |                                    |
|----------------------|---|------------------------------------|------------------------------------|
|                      | Failure type                                    |                                    |                                    |
|                      | Dislodgement                                    | Occlusion/infiltration/leakage     | Phlebitis                          |
| Hospital stay length | 1.00 (0.94, 1.06) <i>p</i> = 0.983              | 1.01 (0.97, 1.05) <i>p</i> = 0.613 | 1.03 (0.99, 1.07) <i>p</i> = 0.100 |
| Current infection    | ^   | ^                                  | 0.45 (0.15, 1.37) <i>p</i> = 0.162 |
| Non-sterile tape     | 0.06 (0.01, 0.48) <i>p</i> = 0.008 <sup>a</sup> | ^                                  | ^                                  |

<sup>a</sup>*p* < 0.05; ^Not included in multivariable modelling

## Limitations

This study had several limitations. First, the sample size was smaller than required, based on the 10-events per-variable rule; fewer PIVs (2 per person) were studied than expected (2.5 per person). This may have influenced the final results as risk factors identified as significant in the univariable model may have been significant in the multivariable model, if a larger sample was studied. Second, this observational cohort study was conducted in cancer units (only) at a single tertiary hospital in Australia; the findings may not be externally valid to other clinical settings (disciplines, hospitals). Third, reasons for CVAD insertion were not assessed; therefore, their insertion may relate to treatment needs rather than as a result of PIV failure. Despite these limitations, this was the first-ever observational cohort study designed to determine risk factors for PIV failure in a cancer cohort; and findings can now inform future research and priorities in this area.

## Conclusions

In conclusion, this study highlighted a high rate of PIV failure in an oncology and haematology population. This confirms findings from other patient cohorts (e.g. medical, surgical), demonstrating similar associations between PIV failure and risk factors, with the strongest association found between the use of non-sterile tape securement and significantly reduced PIV dislodgement.

## Compliance with ethical standards

Human Research Ethics Committee (HREC) approval was obtained from the Royal Brisbane and Women's Hospital (HREC/17/RBWH/7) and Griffith University (NRS/2017/154).

## References

- Bertoglio S, van Boxtel T, Goossens GA, Dougherty L, Furtwangler R, Lennan E, Pittiruti M, Sjøvall K, Stas M (2017) Improving outcomes of short peripheral vascular access in oncology and chemotherapy administration. *J Vasc Access* 18(2):89–96. <https://doi.org/10.5301/jva.5000668>
- Gallieni M, Pittiruti M, Biffi R (2008) Vascular access in oncology patients. *CA Cancer J Clin* 58(6):323–346. <https://doi.org/10.3322/CA.2008.0015>
- Chernecky C (2001) Satisfaction versus dissatisfaction with venous access devices in outpatient oncology: a pilot study. *Oncol Nurs Forum* 28(10):1613–1616
- Freytes CO (1997) Vascular access problems revisited: the Multinational Association of Supportive Care in Cancer (MASCC) experience. *Support Care Cancer* 6(1):13–19. <https://doi.org/10.1007/s005200050126>
- Daneman N, Downing M, Zagorski BM (2012) How long should peripherally inserted central catheterization be delayed in the context of recently documented bloodstream infection? *J Vasc Interv Radiol* 23(1):123–125. <https://doi.org/10.1016/j.jvir.2011.09.024>
- Leal A, Kadakia K, Looker S, Hilger C, Sorgatz K, Anderson K, Jacobson A, Grendahl D, Seisler D, Hobday T (2014) Fosaprepitant-induced phlebitis: a focus on patients receiving doxorubicin/cyclophosphamide therapy. *Support Care Cancer* 22(5):1313–1317. <https://doi.org/10.1007/s00520-013-2089-8>
- Webster J, Clarke S, Paterson D, Hutton A, Sv D, Gale C, Hopkins T (2008) Routine care of peripheral intravenous catheters versus clinically indicated replacement: randomised controlled trial. *Br Med J* 337(7662):157–160. <https://doi.org/10.1136/bmj.a339>
- Bausone-Gazda D, Lefaiver CA, Walters S (2010) A randomized controlled trial to compare the complications of 2 peripheral intravenous catheter-stabilization systems. *J Infus Nurs* 33(6):371–384. <https://doi.org/10.1097/NAN.0b013e318185be2>
- Schulmeister L (2011) Extravasation Management: Clinical Update. *Semin Oncol Nurs* 27(1):82–90. <https://doi.org/10.1016/j.soncn.2010.11.010>
- Ener RA, Meglathery SB, Styler M (2004) Extravasation of systemic hemato-oncological therapies. *Ann Oncol* 15(6):858–862. <https://doi.org/10.1093/annonc/mdh214>
- Wells S (2008) Venous access in oncology and haematology patients: part one. *Nurs Stand* 22(52):39–46. <https://doi.org/10.7748/ns2008.09.22.52.39.c6649>
- Centers for Disease Control and Prevention National Healthcare Safety Network. (2019) Bloodstream Infection Event (Central Line-Associated Bloodstream Infection and Non-central Line Associated Bloodstream Infection) Chapter 17:1-30.
- Helm RE, Klausner JD, Klemperer JD, Flint LM, Huang E (2019) Accepted but unacceptable: peripheral IV catheter failure. *J Infus Nurs* 42(3):151–164. <https://doi.org/10.1097/NAN.0000000000000326>
- Doellman D, Hadaway L, Bowe-Geddes LA, Franklin M, LeDonne J, Papke-O'Donnell L, Pettit J, Schulmeister L, Stranz M (2009) Infiltration and extravasation: update on prevention and management. *J Infus Nurs* 32(4):203–211. <https://doi.org/10.1097/NAN.0b013e3181aac042>
- Rickard CM, Marsh N, Webster J, Runnegar N, Larsen E, McGrail MR, Fullerton F, Bettington E, Whitty JA, Choudhury MA (2018) Dressings and securements for the prevention of peripheral intravenous catheter failure in adults (SAVE): a pragmatic, randomised controlled, superiority trial. *Lancet* 392(10145):419–430. [https://doi.org/10.1016/S0140-6736\(18\)31380-1](https://doi.org/10.1016/S0140-6736(18)31380-1)
- Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG (2009) Research electronic data capture (REDCap)—a metadata-driven methodology and workflow process for providing translational research informatics support. *J Biomed Inform* 42(2):377–381. <https://doi.org/10.1016/j.jbi.2008.08.010>
- Ullman AJ, Mihala G, O'Leary K, Marsh N, Woods C, Bugden S, Scott M, Rickard CM (2019) Skin complications associated with vascular access devices: a secondary analysis of 13 studies involving 10,859 devices. *Int J Nurs Stud* 91:6–13. <https://doi.org/10.1016/j.ijnurstu.2018.10.006>
- Mallett S, Royston P, Dutton S, Waters R, Altman DG (2010) Reporting methods in studies developing prognostic models in cancer: a review. *BMC Med* 8(1):20. <https://doi.org/10.1186/1741-7015-8-20>
- Marsh N, Webster J, Larson E, Cooke M, Mihala G, Rickard CM (2018) Observational study of peripheral intravenous catheter outcomes in adult hospitalized patients: a multivariable analysis of peripheral intravenous catheter failure. *J Hosp Med* 13(2):83–89. <https://doi.org/10.12788/jhm.2867>
- StataCorp (2017) Stata Statistical Software: Release 15. StataCorp LLC, College Station

21. von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP (2007) The Strengthening of Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *Lancet* 370(9596):1453–1457. [https://doi.org/10.1016/s0140-6736\(07\)61602-x](https://doi.org/10.1016/s0140-6736(07)61602-x)
22. Martínez J, Piazuolo M, Almela M, Blecuá P, Gallardo R, Rodríguez S, Escalante Z, Robau M, Trilla A (2009) Evaluation of add-on devices for the prevention of phlebitis and other complications associated with the use of peripheral catheters in hospitalised adults: a randomised controlled study. *J Hosp Infect* 73(2):135–142. <https://doi.org/10.1016/j.jhin.2009.06.031>
23. Fidalgo JP, Fabregat LG, Cervantes A, Margulies A, Vidal C, Roila F (2012) Management of chemotherapy extravasation: ESMO–EONS clinical practice guidelines. *Ann Oncol* 23:viii167–viii173. <https://doi.org/10.1093/annonc/mds294>
24. Kassner E (2000) Evaluation and treatment of chemotherapy extravasation injuries. *J Pediatr Oncol Nurs* 17(3):135–148. <https://doi.org/10.1053/jpon.2000.8063>
25. Russell E, Chan RJ, Marsh N, New K (2013) A point prevalence study of cancer nursing practices for managing intravascular devices in an Australian tertiary cancer center. *Eur J Oncol Nurs* 18(3):231–235. <https://doi.org/10.1016/j.ejon.2013.11.010>
26. Wallis MC, McGrail M, Webster J, Marsh N, Gowardman J, Playford EG, Rickard CM (2014) Risk factors for peripheral intravenous catheter failure: a multivariate analysis of data from a randomized controlled trial. *Infect Control Hosp Epidemiol* 35(1):63–68. <https://doi.org/10.1086/674398>
27. Salgueiro-Oliveira A, Parreira P, Veiga P (2012) Incidence of phlebitis in patients with peripheral intravenous catheters: the influence of some risk factors. *Aust J Adv Nurs* 30(2):32–39
28. Nassaji-Zavareh M, Ghorbani R (2007) Peripheral intravenous catheter-related phlebitis and related risk factors. *Singap Med J*: 733–736
29. Furtado LCR (2011) Incidence and predisposing factors of phlebitis in a surgery department. *Br J Nurs* 20(Sup7):S16–S25. <https://doi.org/10.12968/bjon.2011.20.Sup7.S16>
30. Miliani K, Taravella R, Thillard D, Chauvin V, Martin E, Edouard S, Astagneau P (2017) Peripheral venous catheter-related adverse events: evaluation from a multicentre epidemiological study in France (the CATHEVAL Project). *PLoS One* 12(1). <https://doi.org/10.1371/journal.pone.0168637>
31. Corley A, Ullman AJ, Marsh N, Larsen EN, Mihala G, Harris PNA, Rickard CM (2019) SECURE -ment bundles to prevent peripheral vascular access device failure – The SECURE -PVAD trial: Study protocol for a pilot randomized control trial. *Vasc Access* 13(3):6–14
32. Pagnutti L, Bin A, Donato R, Di Lena G, Fabbro C, Fornasiero L, Gerratana A, Rigon L, Gonella S, Palese A (2015) Difficult intravenous access tool in patients receiving peripheral chemotherapy: a pilot-validation study. *Eur J Oncol Nurs* 20:58–63. <https://doi.org/10.1016/j.ejon.2015.06.008>
33. Van Loon F, Buise M, Claassen J, Dierick-van Daele A, Bouwman AJ, Bjoa (2018) Comparison of ultrasound guidance with palpation and direct visualisation for peripheral vein cannulation in adult patients: a systematic review and meta-analysis. *Br J Anaesth* 121(2): 358–366. <https://doi.org/10.1016/j.bja.2018.04.047>
34. Chopra V, Flanders SA, Saint S, Woller SC, O'Grady NP, Safdar N, Trerotola SO, Saran R, Moureau N, Wiseman S (2015) The Michigan Appropriateness Guide for Intravenous Catheters (MAGIC): results from a multispecialty panel using the RAND/UCLA appropriateness method. *Ann Intern Med* 163(Sup6):S1–S40. <https://doi.org/10.7326/M15-0744>
35. Chopra V, Anand S, Krein SL, Chenoweth C, Saint S (2012) Bloodstream infection, venous thrombosis, and peripherally inserted central catheters: reappraising the evidence. *Am J Med* 125(8):733–741. <https://doi.org/10.1016/j.amjmed.2012.04.010>
36. Infusion Nurses Society (2016) *Infusion Therapy Standards of Practice*, pp S1–S159
37. Freifeld A, Marchigiani D, Walsh T, Chanock S, Lewis L, Hiemenz J, Hiemenz S, Hicks JE, Gill V, Steinberg SM (1999) A double-blind comparison of empirical oral and intravenous antibiotic therapy for low-risk febrile patients with neutropenia during cancer chemotherapy. *N Engl J Med* 341(5):305–311. <https://doi.org/10.1056/NEJM199907293410501>
38. Armenteros-Yeguas V, Gárate-Echenique L, Tomás-López MA, Cristóbal-Domínguez E, Moreno-de Gusmão B, Miranda-Serrano E, Moraza-Dulanto MI (2017) Prevalence of difficult venous access and associated risk factors in highly complex hospitalised patients. *J Clin Nurs* 26(23-24):4267–4275. <https://doi.org/10.1111/jocn.13750>
39. Larsen E, Keogh S, Marsh N, Rickard C (2017) Experiences of peripheral IV insertion in hospital: a qualitative study. *Br J Nurs* 26(19):S18–S25. <https://doi.org/10.12968/bjon.2017.26.19.S18>
40. Fink RM, Ellen Hjort RNN, Barbara Wenger R, Mary Cunningham R, Aimee Orf R, Wendy Pare R, Jennifer Zwink R (2009) The impact of dry versus moist heat on peripheral IV catheter insertion in a hematology-oncology outpatient population. *Oncol Nurs Forum* 36(4):E198–E204. <https://doi.org/10.1188/09.ONF.E198-E204>
41. Byers T, Wender RC, Jemal A, Baskies AM, Ward EE, Brawley OW (2016) The American Cancer Society challenge goal to reduce US cancer mortality by 50% between 1990 and 2015: results and reflections. *CA Cancer J Clin* 66(5):359–369. <https://doi.org/10.3322/caac.21348>
42. Miller KD, Siegel RL, Lin CC, Mariotto AB, Kramer JL, Rowland JH, Stein KD, Alteri R, Jemal A (2016) Cancer treatment and survivorship statistics, 2016. *CA Cancer J Clin* 66(4):271–289. <https://doi.org/10.3322/caac.21349>
43. Richards M, Corner J, Maher J (2011) The National Cancer Survivorship Initiative: new and emerging evidence on the ongoing needs of cancer survivors. *Br J Cancer* 105(1):S1–S4. <https://doi.org/10.1038/bjc.2011.416>
44. Hallam C, Weston V, Denton A, Hill S, Bodenham A, Dunn H, Jackson T (2016) Development of the UK Vessel Health and Preservation (VHP) framework: a multi-organisational collaborative. *J Infect Prev* 17(2):65–72. <https://doi.org/10.1177/1757177415624752>
45. Camp-Sorrell D, Matey L (2017) Access device standards of practice for oncology nursing. *Oncology Nursing Society*.

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