The Incidence Rate and Determinants of Thrombotic Occlusion of Power Injectable Peripherally Inserted Central Catheters at the WRHA Community Intravenous Infusion Clinics in Winnipeg, Manitoba

by

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Abstract

Power-injectable peripherally inserted catheters (PI PICCs) have been used frequently in community settings as they provide a reliable central venous access to infuse intravenous (IV) infusates. However, these catheters can occlude. Thrombotic occlusion is the most frequent complication of PICCs, which causes catheter dysfunction and health-related problems for community-based IV infusion patients, and brings the additional economic cost to the health care system. A retrospective cohort study was conducted to investigate the incidence rate and the determinants of PI PICCs at the Winnipeg Regional Health Authority (WRHA) Community IV Program (CIVP) IV Infusion Clinics in Winnipeg, Manitoba.

Data was extracted from electronic patient charts housed in Accuro Electronic Medical Record (EMR) at the WRHA CIVP IV Infusion Clinics. Survival analysis methods were used to analyze data. Cox proportional hazards models were used to assess the association between thrombotic occlusion and certain socio-demographic, clinical, insertion and PI PICC-related characteristics.

The incidence rate of thrombotic PI PICC occlusion was 32 per 1,000 person-weeks (95% CI: 25-43). After adjusting for IV antimicrobials, ambulatory drug delivery pump use, the tip location of PI PICCs, and the number of PI PICC lumens, the hazard of thrombotic occlusion for those PI PICCs which received IV vancomycin was 5.8 times greater (95% CI: 2.8-12.3). The hazard of thrombotic occlusion was 5.1 times greater (95 % CI: 2.8-9.1) when multiple-lumen PI PICCs used.

To reduce the incidence rate of thrombotic occlusion, single-lumen PI PICCs should be used whenever possible. Heparin lock may be used to lock multiple-lumen PI PICCs and when IV vancomycin is infused. Further research with a greater sample size is needed to validate the findings of this study.

Keywords: power injectable peripherally inserted catheters, peripherally inserted catheters, thrombotic occlusion, withdrawal occlusion, community-based IV infusion clinic.

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List of Abbreviations

CI	Confidence Interval
CIVP	Community Intravenous Program
CVAD	Central Venous Access Device
EMR	Electronic Medical Record
Fr	French
G	Gauge
HR	Hazard Ratio
ICU	Intensive Care Unit
IV	Intravenous
IVSC	IV Self Care
MCHP	Manitoba Centre for Health Policy
NS	Normal Saline
OR	Odds Ratio
PASV	Pressure Activated Safety Valve
PHIN	Personal Health Identification Number
PICC	Peripherally Inserted Central Catheter
PI PICC	Power Injectable Peripherally Inserted Central Catheter
RN	Registered Nurse
SEFI-2	Socio-economic Factor Index 2
SES	Socio-economic Status
TPA	Tissue Plasminogen Activator
WRHA	Winnipeg Regional Health Authority

Chapter 1: Introduction

PICCs, including PI PICCs, are widely used to provide central venous access for patients requiring IV infusions as they are easy to insert with fewer complications compared with other central venous access devices (CVADs) and easy to maintain by community-based nurses and caregivers (Alport et al., 2012; Bard Access Systems, 2016; Camp-Sorrell et al., 2011; Lyons & Phalen, 2014; Shrestha et al., 2016). With appropriate nursing care a PICC may remain in place for up to one year (Dougherty & Lamb, 2009; Gabriel, 2011; Gorski & Czaplewski, 2004; Hamilton & Bodenham, 2009). The first PICC was made from silicone and introduced on the healthcare market in 1975(Hoshal, 1975). However, PI PICCs have been available on the healthcare market since 2007 (Sandrucci, 2014). PI PICCs are made from polyurethane and have more burst and tensile strength in comparison with silicone PICCs (Sandrucci, 2014).

Although PICCs provide a reliable central venous access for infusing IV infusates, they can occlude. Thrombotic occlusion is the most frequent complication of PICCs and causes catheter dysfunction (Hardy & Ball, 2005; Moureau et al., 2002). Thrombotic PICC occlusion has a significant negative impact on patients and their families, and it contributes to rising health care costs (Bartock, 2010; Hardy & Ball, 2005; Hitchcock, 2016; Lyons & Phalen, 2014; Moureau et al., 2002). Thrombotic occlusion is defined as obstruction of CVADs due to fibrin deposits in the catheter lumen or at the tip, or around the external surface of these devices hampering drawing blood and infusing IV infusates (Alexander et al., 2010; Gorski, 2003; Gorski. et al., 2016; Mattox, 2017; Weinstein, 2014). Thrombotic occlusion is responsible for catheter dysfunction, which leads to unexpected hospital stays, emergency room visits, premature removal and replacement of PICCs (Moureau et al., 2002; Rihn, 2001; van Miert et al., 2012).

Additional economic cost to the health care systems associated with the treatment of thrombotic occlusions and PICC replacements are other negative consequences of thrombotic occlusions (Baskin et al., 2012; Moureau et al., 2002; O'Brien et al., 2013).

PI PICCs are frequently used at the WRHA CIVP IV Infusion Clinics in Winnipeg, Manitoba, to provide IV antimicrobial infusion therapies to community-based IV infusion patients through home visits and two community-based IV infusion clinics, namely Access Transcona and Lions Place IV Infusion Clinics (Hoy, 2009). Lions Place IV Infusion Clinic was renamed as the Misericordia IV Infusion Clinic as of October 2018. The WRHA CIVP receives patient referrals from the inpatient units of the hospitals, emergency rooms and the offices of infectious diseases specialists in Winnipeg, Manitoba.

Because thrombotic occlusion is a major cause for PICC dysfunction, and it is associated with negative health consequences and additional economic cost to the health care systems, it is important to understand the magnitude of the thrombotic occlusion problem and its determinants in order to develop appropriate and cost-effective occlusion management and prevention methods. Such information can result in improved clinical and system-wide interventions to reduce thrombotic occlusion of PI PICCs.

The incidence rate of thrombotic occlusion of PI PICCs at the WRHA CIVP IV Infusion Clinics has not been studied yet, and little is known about the clinical and other determinants of thrombotic PI PICC occlusions. This study addresses this gap by estimating the incidence rate and investigating the determinants of thrombotic PI PICC occlusions at the WRHA CIVP IV Infusion Clinics in Winnipeg, Manitoba.

Study Objectives

The purpose of this study is to estimate the incidence rate of thrombotic PI PICC occlusion and to identify its determinants in adults aged 18 years and older who had a PI PICC inserted and underwent IV antimicrobial infusion therapies at the WRHA CIVP IV Infusion Clinics, Access Transcona and Lions Place Clinics, between January 1, 2015 and December 31, 2017.

The specific objectives of this study are:

1. To estimate the incidence rate of thrombotic PI PICC occlusions at the WRHA CIVP IV Infusion Clinics.
2. To understand socio-demographic, clinical, insertion and PI PICC-related determinants of thrombotic PI PICC occlusions.

Summary and Organization of this Thesis

The information provided in this thesis is organized into five chapters. The introduction is provided in chapter one. The literature review is provided in chapter two. Chapter three describes the methods used in this research. Chapter four presents the results. A discussion of the results, future research directions and policy recommendations are provided in the chapter 5.

Chapter 2: Literature Review

Articles published in English were collected by searching the computerized databases of Medline (Ovid), Embase (Ovid), CINAHL, Scopus, Cochrane Library, Pubmed and Google Scholar. Hand search of the bibliography of the selected articles was completed. The keywords used for search were "power injectable peripherally inserted central catheters", "power injectable picc", "power piccs", peripherally inserted central catheters", "power injectable peripherally inserted catheter occlusions", "picc occlusions", thrombotic picc occlusion" and "central venous catheter". The basic details of the reviewed studies are provided in Table 1 in Appendix B.

The majority of the reviewed studies were randomized clinical trials (Alport et al., 2012; Bowers et al., 2008; Deitcher et al., 2002; Lyons & Phalen, 2014; Ng et al., 2004; Pittiruti et al., 2014; Ponec et al., 2001). Six of the reviewed studies were retrospective cohort studies (Barr et al., 2012; Moureau et al., 2002; Pittiruti et al., 2012; Shrestha et al., 2016; Smith et al., 2017; Williams, 2018), and two of them were prospective cohort studies (Grau et al., 2017; O'Brien et al., 2013).

The majority of the reviewed studies were conducted in the USA (Bowers et al., 2008; Deitcher et al., 2002; Lyons & Phalen, 2014; Moureau et al., 2002; Ng et al., 2004; Ponec et al., 2001; Shrestha et al., 2016; Smith et al., 2017; Williams, 2018). Two of the studies were conducted in the UK (Barr et al., 2012; van Miert et al., 2012), two of the studies were conducted in Italy (Pittiruti et al., 2012; Pittiruti et al., 2014), and one of the studies was conducted in France (Grau et al., 2017). Only two of the studies were conducted in Canada (Alport et al., 2012; O'Brien et al., 2013).

The majority of the studies were conducted among adults aged 18 years and older (Alport et al., 2012; Barr et al., 2012; Grau et al., 2017; Lyons & Phalen, 2014; Pittiruti et al., 2014;

Shrestha et al., 2016; Smith et al., 2017). However, some of the studies were conducted in both pediatric and adult populations (Moureau et al., 2002; Pittiruti et al., 2012; Williams, 2018).

Use of PI PICCs

PI PICCs have been on the healthcare market since 2007 (Alport et al., 2012; Sandrucci, 2014). They are made from polyurethane and have more burst and tensile strength in comparison with silicone PICCs (Bard, 2018; Poli et al., 2016; Sandrucci, 2014; Seckold et al., 2015). PI PICCs are available as single and multiple-lumen catheters in different sizes such as 4 Fr, 5 Fr and 6 Fr (Alexander et al., 2010; Bard, 2018). Some of those PI PICCs are designed with an intrinsic pressure-activated safety valve (PASV) technology, which prevents air flow into patients' venous circulatory system (Alexander et al., 2010; Bard, 2018). For example, Bard PowerPICC SOLO®^{2} has three internal PASVs in the proximal hub of the device (Alport et al., 2012). The larger PASV opens with minimal positive pressure during IV infusion whereas the smaller two valves open with negative pressure during blood aspiration (Alport et al., 2012). If PI PICCs are not in use, those PASVs remain closed and prevent air from entering into the venous circulation (AngioDynamics, 2017). There are also PI PICCs that have no intrinsic valves in them, such as the Cook Turbo-Ject, so they need to be clamped to prevent air flow into the venous circulation (Alport et al., 2012).

PI PICCs were initially introduced for use with high-pressure pumps or power injectors, for infusing high-velocity contrast media in computed tomography scan and for other radiological diagnostic procedures (Alport et al., 2012; Pittiruti et al., 2012). High-pressure pumps can generate pressures as high as 300 psi (Pittiruti et al., 2012). PI PICCs can tolerate that much pressure whereas silicon PICCs cannot tolerate it (Pittiruti et al., 2012).

Today, PI PICCs are commonly used to infuse IV infusion therapies such as IV antimicrobial infusions, chemotherapy, blood products and total parenteral nutrition (TPN) (Alport et al., 2012; Grau et al., 2017; Lim & Balasubramaniam, 2013). In addition to that, PI PICCs are also used for blood sampling and infusing high-velocity contrast media in computed tomography scan (Alport et al., 2012; Pittiruti et al., 2012). In community settings, PI PICCs are widely used in patients who need short and long term IV antimicrobial infusion therapies as well as for blood sampling to perform laboratory tests and for computed tomography with contrast media infusion (Gorski. et al., 2016; Lyons & Phalen, 2014).

Efficacy of PI PICCs

The literature review has shown that there were no studies conducted at community-based IV infusion clinics in regards to efficacy and use of PI PICCs. However, there were studies conducted in hospitals and in outpatient units of hospitals. For instance, a prospective randomized clinical trial comparing complication rates of two different brands of PI PICCs, Cook Turbo-Ject and Bard PowerPICC Solo2, in surgical patients of a hospital in Saskatchewan, Canada, showed that they were effective and safe to use in patients who needed long term venous access for administering IV infusions (Alport et al., 2012).

In addition, a retrospective cohort study regarding PI PICC use in intensive care units in Italy indicated that PI PICCs were safe to use for infusing high-flow IV infusions > 1000 ml/hour through an infusion pump as well as for infusing the contrast media for computed tomography scan (Pittiruti et al., 2012). However, a prospective randomized controlled clinical study investigating clinical performance of three different PI PICCs including Bard Solo2, Xcela and ProPICC in oncology patients of a hospital outpatient unit in Italy reported that three catheter ruptures had occurred in Bard Solo2 group, (n=61), during IV chemotherapy infusion through an infusion pump (Pittiruti et al., 2014).

Outpatient IV Infusion Model

Alternative models for inpatient IV infusion therapy, specifically for parenteral antimicrobial therapy, have become a necessity since the last quarter of the twentieth century due to increased health care costs and decreased number of hospital beds (Baker, 2016; Bernard et al., 2001; Mitchell et al., 2017). The outpatient IV infusion model has been broadly accepted in countries such as Canada, Australia, the UK and USA (Mitchell et al., 2017; Paladino & Poretz, 2010). Outpatient IV antimicrobial infusion therapy has been done successfully in patients' homes in the USA and Canada, including Winnipeg (Alexander et al., 2010; Stiver et al., 1978). In addition to home care, community-based IV infusion clinics, hospital-based outpatient clinics and physician offices are also alternative sites for providing IV antimicrobial infusion therapies to patients who have infections such as cellulites, osteomyelitis, diabetic foot ulcers, urinary tract infections, septic arthritis and pseudomonas infections (Owen, 2016).

In the past, IV infusion therapy was exclusively done by physicians in inpatient units of hospitals (Alexander et al., 2010). However, this changed in 1940, and RNs became responsible for initiating short peripheral IV lines and IV infusion therapies, blood transfusions and venipuncture (Alexander et al., 2010). Today, IV infusion therapy is an essential part of RN's clinical practice including PICC insertion and maintenance, PICC removal, and restoring the patency of PICCs (Alexander et al., 2010; Gorski, 2003; Gorski. et al., 2016).

Epidemiology of Thrombotic PI PICC Occlusion

Thrombotic PI PICC Occlusion

Thrombotic occlusion can be classified as withdrawal (partial) occlusion, and complete occlusion (Alexander et al., 2010; Bartock, 2010; Baskin et al., 2012; Gorski. et al., 2016). Withdrawal (partial) occlusion occurs if blood withdrawal is not possible from the CVAD due to fibrin deposits at the catheter tip or in the catheter lumen after ruling out mechanical causes of occlusion such as kinked or clamped tubing (Alexander et al., 2010; Gorski. et al., 2016; Hitchcock, 2016; Weinstein, 2014). When withdrawal occlusion is present, there is no blood return from the CVAD when it is aspirated, but the catheter lumen may still be flushed, and IV infusates may still be infused (Alexander et al., 2010; Gorski. et al., 2016; Weinstein, 2014). If the catheter lumen completely occluded, flushing the catheter lumen and infusing IV infusates are not possible, and this situation is defined as complete occlusion (Alexander et al., 2010; Bowers et al., 2008; Gabriel, 2011; Gorski. et al., 2016).

Thrombotic occlusion of PI PICCs can lead to significant health problems among community-based IV infusion patients (Lyons & Phalen, 2014; Moureau et al., 2002). For instance, if fibrin deposit forms around the external surface of the catheter and coats its entire exterior wall as a sheath, IV infusates may flow retrograde along this sheath leading to tissue necrosis or damage (Alexander et al., 2010). Thrombotic occlusion can also cause pulmonary embolism and deep venous thrombosis (Chopra et al., 2013; Grau et al., 2017; Hamilton & Bodenham, 2009; Hardy & Ball, 2005; Lyons & Phalen, 2014; van Miert et al., 2012). Repeated PICC insertions related to premature loss of those catheters due to thrombotic occlusion may cause vascular damage and scar tissues in the veins (Gonsalves et al., 2003). Thrombotic occlusion also increases the risk of acquiring catheter-related blood stream infections (Rihn, 2001; Williams, 2018). Delays and interruptions in IV treatment as a

consequence of thrombotic occlusion also increase the risk of further morbidity and can cause significant emotional stress to the patients and their families (Hoffer et al., 1999; van Miert et al., 2012). Thrombotic PICC occlusion also impairs patients' quality of life due to prolonged IV treatments and may cause anxiety (Bolton, 2013; Dougherty & Lamb, 2009). These occlusions may lead to emergency room visits and unscheduled hospitalizations if the catheter function cannot be restored (Moureau et al., 2002). In addition, IV antimicrobial infusion and blood sampling for laboratory tests may not be possible when thrombotic occlusion is present (Alexander et al., 2010; Gorski. et al., 2016).

Thrombotic occlusion is a major cause for catheter dysfunction (Moureau et al., 2002; van Miert et al., 2012). Repeated emergency room and hospital visits, PICC replacements, and interruptions in IV treatments due to thrombotic PICC occlusions create financial burden for patients and their families (Bartock, 2010).

Thrombotic occlusion is treated by instilling a fibrinolytic agent such as tissue plasminogen activator (TPA) in PICC lumens (Baskin et al., 2012; Deitcher et al., 2002; Ponec et al., 2001). TPA binds to the fibrin and converts plasminogen to plasmin to activate fibrinolysis (Baskin et al., 2012; Deitcher et al., 2002; Ponec et al., 2001). A typical intraluminal dose of TPA is 2mg/ 2 ml (Alexander et al., 2010; Baskin et al., 2012; Deitcher et al., 2002; Ponec et al., 2001). TPA treatment can be safely used in community setting (Gorski, 2003). If catheter lumen cannot be cleared, a second dose of 2 mg/ml may be administered (Baskin et al., 2012; Deitcher et al., 2002; Ng et al., 2004; Ponec et al., 2001). If the catheter patency cannot be restored, it needs to be replaced (Moureau et al., 2002). Restoring patency and reinsertion of PICCs brings additional economic cost to the health care systems (Moureau et al., 2002; O'Brien et al., 2013; van Miert et al., 2012). There was no Canadian study found in the literature evaluating TPA cost, but

administering a typical treatment dose of 2 mg of TPA to restore catheter patency costs $ 80-116 in the USA (Baskin et al., 2012). If PI PICCs get multiple thrombotic occlusions, TPA cost will consequently increase. Although, there was no study found in the literature regarding cost of PICC insertion in Manitoba, the total cost of a PICC insertion at McGill University Health Centre in Quebec is $ 582.97 (O'Brien et al., 2013). Therefore, reinsertion of PICCs brings additional costs of $ 582. 97 to the hospital and the provincial health care system (O'Brien et al., 2013). When this cost is adjusted for the year of 2020, the cost of the insertion a PICC is $ 650. This calculation of the price adjustment is based on the consumer price index in Canada between 2014 and October 2020 (Statistics Canada, 2020).

In addition to the TPA use and the reinsertion of PICCs, thrombotic PICC occlusion-related emergency room visits and hospitalizations bring extra economic cost to the provincial health care systems. For example, in Manitoba, the average cost of an emergency department visit was 403 $ in 2017 (Bernstein et al., 2019). The average cost of a hospitalization related to an infection except viral meningitis was 4, 500 $ per case, and the average cost of cellulites was 2,373 $ per case between 2005/06 in Manitoba (Finlayson et al., 2009).

Incidence Rate of Thrombotic PI PICC

To the best of my knowledge, the incidence rate and determinants of thrombotic PI PICC occlusion at community-based IV infusion clinics have not been studied yet. However, several retrospective cohort studies were conducted in the USA among home IV infusion patients who had a PICC inserted for receiving IV infusion therapies. One of these studies reported that the incidence rate of thrombotic PICC occlusion was 0.40 per 1,000 catheter-days in patients who received their IV infusions at home (Moureau et al., 2002). However, PI PICCs were not

included in this study, and both pediatrics and adult patients were included in this study (Moureau et al., 2002).

Another retrospective cohort study conducted in the USA found that the incidence rate of PICC occlusion was 2.46 per 1,000 outpatient parenteral antimicrobial therapy-days in community-based IV self-care (IVSC) patients (Shrestha et al., 2016). However, researchers did not report if they included PI PICCs in this study (Shrestha et al., 2016). Occurrence of thrombotic PICC occlusion is expected to increase in the future since PICC use has been steadily increasing for administering IV infusion therapies (Lyons & Phalen, 2014; Williams, 2018).

Predictors of Thrombotic PI PICC Occlusion

Studies have shown that several predictors were associated with thrombotic PICC occlusion. For example, a retrospective cohort study conducted in the USA showed that insertion of PICCs in the right arm was associated with smaller odds of thrombotic occlusion (Odds Ratio [OR] = 0.82, 95 % CI= 0.72-0.94) compared to the left arm (Smith et al., 2017). Placing the tip of PICCs at the cavoatrial junction was associated with reduction in thrombotic PICC occlusion (OR= 0.75, 95 % CI= 0.61-0.92) (Smith et al., 2017).

Smaller PICC gauge size was associated with greater odds of thrombotic occlusion in bivariate analyses, but as a result of high collinearity with the number of lumens, only the number of PICC lumens was included in multivariate analyses in the retrospective cohort study conducted in the USA (Smith et al., 2017). This study also found that compared with single-lumen PICCs, double and triple-lumen PICCs were associated with greater odds of thrombotic occlusion (OR= 3.12, 95 % CI= 2.56-3.79; OR= 3.81, 95 % CI= 2.94-4.94, respectively) (Smith et al., 2017).

Infusing IV vancomycin (OR= 1.81, 95 % CI= 1.57-2.07), piperacillin/tazobactam (OR=1.21, 95 % = 1.02-1.44) and cefepime (OR= 1.45, 95% CI=1.23-1.70) were associated with greater odds of thrombotic PICC occlusion in the retrospective cohort study conducted in the USA (Smith et al., 2017). A retrospective cohort study conducted in the UK fond that IV flucloxicillin was a strong predictor of central line events including thrombotic occlusion (OR= 3) (Barr et al., 2012), however, the researchers did not report if PI PICCs were included in this study.

Two randomized clinical trials conducted in the USA found that using normal saline (NS) flush only to lock PICCs was one of the predictors of thrombotic occlusion (Bowers et al., 2008; Lyons & Phalen, 2014), but this association was not statistically significant (Bowers et al., 2008; Lyons & Phalen, 2014). In one of these studies, the saline-only flush group had the highest percentage of thrombotic occlusion (25%) requiring fibrinolytic agent administration compared to the high and low-heparin lock groups (9.4%, 10% respectively) (Lyons & Phalen, 2014). In addition, the saline-only flush group had the highest percentage of additional nursing visits to assess PICC occlusions (32.1%) compared to the high and low-heparin lock groups (15.6%, 13.3% respectively), and there were 17 of PI PICCs included in this study (n=90) (Lyons & Phalen, 2014). A secondary data analysis of this study showed that a longer PICC dwell time was associated with thrombotic occlusion (Lyons & Phalen, 2014). In another randomized clinical study conducted in the USA three PICC occlusions occurred in the NS flush group compared to the heparin lock group (NS= 6%, HS= 0%), but this association was not statistically significant (Bowers et al., 2008). A retrospective cohort study conducted in the USA found that locking PICCs with 3 ml of heparin following a 10 ml of NS flush was associated with significantly lower odds of thrombotic occlusion (OR= 0.53, 95% CI: 0.32-0.88) , and NS flush was not associated with thrombotic occlusion in this study (Smith et al., 2017).

Using split-septum neutral-displacement needleless connectors was also a predisposing factor for thrombotic occlusion according to a retrospective cohort study conducted in the USA (Williams, 2018). The incidence rate of thrombotic PICC occlusion was greater (Incidence Rate [IR]: 1.46, 95 % CI= 0.35-1.25) when split-septum neutral-displacement needleless connectors were used compared with solid-surface neutral-reflux needleless connectors (Williams, 2018). A prospective cohort study conducted in France found that age > 65 was associated with increased risk of thrombotic PICC occlusion (Grau et al., 2017).

Summary

In summary, PI PICCs have been widely used in community-based IV infusion patients who need a central venous access for short and long-term IV antimicrobial infusion therapies as those catheters provide a reliable central venous access (Alport et al., 2012; Camp-Sorrell et al., 2011; Weinstein, 2014). With careful nursing care, PICCs can achieve a dwell time for up to one year (Gabriel, 2011; Gallieni et al., 2008; Gorski & Czaplewski, 2004; Weinstein, 2014).

Although PI PICCs provide a reliable central venous access to infuse IV antimicrobials for community-based IV infusion patients, thrombotic occlusion remains as a common problem associated with their use. Literature review has shown that there was no study conducted to investigate the incidence rate and determinants of thrombotic PI PICC occlusion at the community-based IV infusion clinics. Therefore, this study will provide baseline thrombotic occlusion data related to PI PICC use in adult population at the community-based IV infusion clinics.

Chapter 3: Methods

Study Design

A retrospective cohort study design was conducted using data obtained through a chart review from the electronic patient charts housed in the WRHA CIVP Accuro EMR with the approval of the University of Manitoba Research Ethics Board and the WRHA Research Access and Approval Committee. The retrospective cohort study design was suitable for this study as historical data related to PI PICCs was available in Accuro EMR. In addition, a cohort study allows the measurement of incidence rates (Gordis, 2014; Young, 2004).

Enrollment Period

The enrollment period was from January 1, 2015 to December 31, 2017. This enrollment period was chosen to obtain the necessary number of patients for adequately-powered analysis. A priori, the study sample was calculated as minimum of 246 subjects to get enough power for this study.

Inclusion Criteria

Patients residing in Winnipeg, Manitoba, who were 18 years of age and over at the index date and who had a PI PICC inserted to receive an IV antimicrobial infusion therapy at the WRHA CIVP IV Infusion Clinics between January 1, 2015 and December 31, 2017 were included in this study. The index date was the date of insertion of a PI PICC. In total, 383 electronic patient charts received from the WRHA Community Services Information System Unit. Of these, 97 patients were excluded from the study as they did not meet the inclusion criteria. Details regarding reasons for exclusion from the study are presented in Table 2 in Appendix B. For example, 45 of the home IV patients excluded from this study because they had paper-based

charts in their homes, and this study was based on reviewing electronic patient charts housed in the WRHA CIVP Accuro EMR. As a result, 286 patients were included in the analysis.

Data Sources

Electronic patient charts housed in the WRHA CIVP Accuro EMR were used as the data source. Accuro EMR has been widely used in community-based and outpatient clinics in Canada and elsewhere (Accuro Electronic Medical Records, 2020; Canada Health Infoway, 2013), and it is a useful tool for conducting research as it holds recent and past patient medical records (Canada Health Infoway, 2013; Ghany & Keshavjee, 2015). On the other hand, data quality and the validity of nursing and other documents entered in the WRHA CIVP Accuro EMR have not been studied yet. However, nursing resource coordinators at the WRHA CIVP have been performing regular nursing chart audits to evaluate quality and completeness of the clinical nursing data.

Healthcare professionals at the WRHA CIVP IV Infusion Clinics including RNs, infectious diseases specialists and clinical pharmacists have been using Accuro EMR since 2013 to document patient care. Accuro EMR captures patient demographics including age, sex and postal codes in the demographics section (Accuro EMR User Guide, 2019). Clinical assistants enter information related to the patient demographics and their clinic appointments in Accuro EMR.

Daily nursing clinical flow sheets are housed in Accuro EMR and contain rich information related to PI PICC characteristics including their type, number of lumens, gauge size, tip location, vein and arm used for PI PICC placement, number of NS flushes used to flush PI PICCs and their removal date. Those clinical flow sheets also have a standard vascular access device assessment section, which is filled out by RNs when they provide patient care. Those nursing clinical flow sheets also contain information regarding ambulatory drug delivery pumps, if IV infusions administered by RNs or patients themselves and blood withdrawal from

the PI PICCs for laboratory tests. They also contain data regarding thrombotic PI PICC occlusion including the type of those occlusions. In addition to the clinical flow sheets, nursing clinical notes also contain information regarding PI PICC occlusions.

Vascular access details forms housed in Accuro EMR contain information regarding PI PICC characteristics and their insertion dates. These forms are filled out by RNs who insert PI PICCs at the hospitals and are faxed to the WRHA CIVP.

Nursing health assessment forms are also housed in Accuro EMR and contain medical history of patients including current diagnosis and co-morbidities.

Type, dose, frequency and duration of the current and past IV antimicrobial infusion therapies are found in the medication section housed in Accuro EMR. When RNs administer IV infusion therapies, they sign off for the related medication in the medication section.

Data Extraction

The candidate extracted the following information from 286 electronic patient charts housed in Accuro EMR using a custom Microsoft Access Database.

Socio-demographic Data

Including the date of birth, sex, and the six-digit postal codes were extracted from the demographics section. The postal codes were not recorded in the data extraction form as they were only used to find out the corresponding socio-economic factor index-2 (SEFI-2) scores from the MCHP-based SEFI-2 list (Manitoba Centre for Health Policy, 2019).

Co-morbidity

Data pertaining to diabetes mellitus was extracted from nursing health assessment forms. These forms are standard nursing forms and are completed using information provided by the patients during initial health assessment.

Clinical Data

The type and frequency of IV antimicrobial infusions administered to the patients were extracted from medication sections; however, data was not collected related to the type of the infections. Frequency of blood withdrawal, information regarding IV infusion administration (RNs vs. patient administration), the number of NS flushes and information regarding ambulatory pump use were extracted from daily nursing clinical flow sheets. Data related to thrombotic PI PICC occlusion was extracted from daily nursing clinical flow sheets and the nursing notes.

PI PICC-related Data

The number of lumens, the gauge size and the tip location were extracted from nursing daily flow sheets and from vascular access details forms. Information regarding line maintenance of PI PICCs was extracted from the nursing clinical flow sheets. The insertion date of PI PICCs was extracted from vascular access details forms, and the removal date of them was extracted from the nursing clinical flow sheets. The insertion and removal date of PI PICCs were used to calculate the total dwell time of PI PICCs.

PI PICC Insertion-related Data

Vein and arm used for PI PICC placement, and the tip location of PI PICCs were extracted from the daily nursing clinical flow sheets and the vascular access details forms.

Outcome: Thrombotic PI PICC Occlusion

Thrombotic PI PICC occlusion was identified if it was documented in daily nursing flow sheets or in nursing clinical notes as “withdrawal occlusion” or “complete occlusion.” When a patient had more than one thrombotic PI PICC occlusion, only the first event was counted.

Covariates

The following covariates were selected for the analyses based on the literature review and biological plausibility.

Socio-demographic Covariates

A retrospective cohort study evaluating complications of different types of vascular access devices in IVSC patients in the USA showed that younger age and female sex were associated with more vascular access device complications including device occlusions (Shrestha et al., 2016). A prospective cohort study conducted among hospital patients in France found that age > 65 was associated with thrombotic PICC occlusion (Grau et al., 2017). Therefore, age and sex were included in this study as covariates to be assessed.

The association between socio-economic status (SES) of individuals and their health has been well established in the literature, and SES is one of the important social determinants of health (Ecob & Davey Smith, 1999; Mustard et al., 1997; Wilkinson & Marmot, 2003; World Health Organization, 2008). It has been widely accepted that people's health status is related to their SES (Government of Canada, 2006; Marmot & Allen, 2014; World Health Organization, 2008). For instance, men who have a higher income live six years longer than men who have low incomes in Canada (Government of Canada, 2006). In addition, men in higher income groups can have fourteen more disability-free years compared to men in lower income groups; and women in higher income groups are expected to have eight more disability-free years compared to women in lower income groups in Canada (Government of Canada, 2006). Furthermore, people in low-income groups are more likely to have poor health compared to people in higher income groups (Government of Canada, 2006). Therefore, SES was included in this study as a

covariate to be assessed. To the best of my knowledge, the association between SES and thrombotic PI PICC occlusion was not assessed in the literature.

Neighbourhood-based SEFI-2 scores were used for this study as a proxy measure of SES. The SEFI-2 was developed and validated at the Manitoba Centre for Health Policy (MCHP) (Manitoba Centre for Health Policy, 2019). The SEFI-2 is defined as "a factor score derived from Canadian Census data that reflects non-medical social determinants of health and used as a proxy measure of SES" (Manitoba Centre for Health Policy, 2019). SEFI-2 < 0 indicates more favourable socioeconomic conditions and SEFI-2 > 0 indicates less favourable conditions (Manitoba Centre for Health Policy, 2019). The MCHP-based SEFI-2 list was obtained from the MCHP, which contains the postal codes and corresponding SEFI-2 scores. However, the limitation of this list is that it does not contain new postal codes (C. Burchill, personal communication, March 21, 2019).

Co-morbidity

Diabetes mellitus was included in this research to assess if it was associated with thrombotic PI PICC occlusion because the current literature shows that diabetes is associated with increased activation of platelets, clotting factors and denser fibrin clots (Carr, 2001; Dunn et al., 2005; Schafer, 1985; Vazzana et al., 2012). In addition to that, the incidence and prevalence of diabetes mellitus is higher among First Nations in Manitoba compared to all other Manitobans (Manitoba Centre for Health Policy, 2020). The risk of having type 2 diabetes is 3.5 times higher among First Nations in Manitoba compared to all other Manitobans (Manitoba Centre for Health Policy, 2020).

According to the Canadian census in 2016, Winnipeg has the largest Indigenous population in Canada including First Nations (Statistics Canada, 2016). Although we don't have the proportion of First Nations who receive IV antimicrobial infusion therapies at WRHA CIVP on hand, they receive IV antimicrobial therapies at the program. Therefore, it is important include diabetes in the analyses as a covariate. The current literature shows that there is also association between obesity and thrombotic events (Blokhin & Lentz, 2013; Samad & Ruf, 2013). However, obesity was not included as covariate in this research because the height of the patients in this cohort was not available in the patient charts for the body mass index calculation.

To the best of my knowledge, the association between diabetes mellitus and thrombotic PI PICC occlusion at the community-based IV infusion clinics was not assessed in the literature.

Clinical Covariates

Type of IV Antimicrobial Agents. IV antimicrobial agents including antibiotics, antifungals and antiviral agents were included in this study as the existing literature demonstrates that IV antimicrobial infusions including antibiotics, antifungals and antiviral infusions are associated with vascular access device occlusions among community-based IVSC patients (Barr et al., 2012; Smith et al., 2017). Thus this variable was also included in this study.

To the best of my knowledge, the association between IV antimicrobials and thrombotic PI PICC occlusion at the community-based IV infusion clinics was not assessed in the literature.

For this study, type of IV antimicrobial agents identified if the prescription of an IV antimicrobial was found in the medication section housed in Accuro EMR.

Frequency of Blood Withdrawal from PI PICC. Deposition of the blood components in a CVAD lumen can lead to thrombotic occlusion (Alexander et al., 2010; Dougherty & Lamb, 2009; Lyons & Phalen, 2014). Therefore, this variable was included in this study to assess if the

frequency of blood withdrawal was associated with thrombotic PI PICC occlusions. The routine blood work is done once a week at the WRHA IV infusion clinics to review the complete blood count, the kidney function and the serum levels of IV antimicrobials such as vancomycin trough. To the best of my knowledge, the association between the frequency of blood withdrawal from PI PICCs and thrombotic occlusions at the community-based IV infusion clinics was not assessed in the literature.

For this study, the frequency of blood withdrawal from PI PICCs was identified if the weekly blood withdrawal was documented in the daily nursing clinical flow sheets housed in Accuro EMR.

Number of NS Flushes. A randomized clinical trial comparing flushing protocols in community-based patients who had PICCs showed that when PICCs were locked with the NS flush only, they had a higher incidence of thrombotic occlusion requiring a fibrinolytic treatment when compared the PICCs locked with heparin (Lyons & Phalen, 2014), but this association was not statistically significant.

The NS flush in this study refers to the 10 ml syringe of sterile pre-filled preservative free NS flush. It is used to flush PI PICC lumens before, after and between IV infusions, and after drawing blood from PI PICCs for laboratory tests. For this study, if the PI PICCs were flushed with only one 10 ml syringe of NS is counted as one flush. If the multiple flushes were used to flush the PI PICCs, it is recorded in the spread sheet accordingly.

Method of IV Infusion Administration. In the UK, there was no association found between IVSC and thrombotic occlusions among community-based IVSC patients (Barr et al., 2012). However, the association between RN versus IVSC administration of IV antimicrobials and the

thrombotic PI PICC occlusion at the community-based IV infusion clinics was not assessed in the literature. Therefore, this variable was also included in this study to be assessed.

RNs provide IV antimicrobial infusion therapies to the patients at the WRHA CIVP IV Infusion Clinics. In addition to that, patients or their caregivers may administer IV antimicrobial infusions in their homes after they get trained by the RNs at the IV infusion clinics. When the patients or their caregivers administer IV infusions in their homes, those patients are classified as IVSC patients. For this study, IVSC was identified if it was documented in the daily nursing clinical flow sheets or in nursing notes that the patients or their caregivers had received training from the RNs and were sent home with their IV antimicrobial medications and IV supplies.

When the RNs provide IV antimicrobial infusion therapy at the IV infusion clinics, they sign off for that specific IV antimicrobial medication in the medication section and fill out a new daily nursing flow sheet in Accuro EMR. For this study, if the RNs signed off the medication section and filled out the daily nursing flow sheets, it was identified that the RNs had infused the IV antimicrobial infusions.

Ambulatory Drug Delivery Pump Use. To the best of my knowledge, the association between ambulatory drug delivery pump use and the thrombotic PI PICC occlusion was not assessed in the literature. Therefore, this variable was included in this study. Nurse clinicians at the WRHA IV Infusion Clinics observe thrombotic PI PICC occlusions when IV antimicrobials are infused through ambulatory pumps, especially when IV Cloxacillin is infused. Thus, it is important to include ambulatory drug delivery pump use in the study as a covariate.

Ambulatory drug delivery pumps are used to deliver continuous IVantimicrobial infusions to the patients at the WRHA IV Infusion Clinics. These pumps are connected to the patients'

PI PICCs until the course of IV antimicrobial infusion therapy is completed. Patients carry their pumps with them when they are on continuous IV infusion therapies. Those PI PICCs which are connected to the ambulatory drug delivery pumps are flushed only once a day after IV bag change, and they are also flushed after drawing blood from them for the laboratory tests.

For this study, ambulatory drug delivery pump use was identified if it was documented in the nursing daily flow sheets that the patients were using ambulatory drug delivery pumps to receive their IV antimicrobial infusions.

PI PICC Related Covariates

Number of Lumens and Gauge Size. The current literature demonstrated that double and triple-lumen PICCs were associated with thrombotic occlusions compared with single-lumen PICCs (Smith et al., 2017). Hence, number of lumens was also included in this study to be assessed.

Gauge size is defined as external diameter of a PICC (Alexander et al., 2010; Dougherty & Lamb, 2009). The external diameter can be expressed as gauge or French such as 23 gauge or 2 French. For this study, French sizes were used to express the gauge size of PI PCCs.
The number of PI PICC lumens was identified if they were documented in daily nursing clinical flow sheets and vascular access details forms.

Dwell Time. In the secondary data analysis of a randomized clinical study in the USA demonstrated that longer catheter dwell time was associated with thrombotic PICC occlusion (Lyons & Phalen, 2014). Hence, dwell time of the PI PICCs was also included in this study to be assessed. For this study, dwell time of PI PICCs was defined as the total number of days that PI PICCs remained in patients' central vein until they were removed. The insertion and removal date of PI PICCs were used to calculate the dwell time of PI PICCs in this study.

Line Maintenance. To the best of my knowledge, the association between line maintenance and thrombotic PI PICC occlusion was not assessed in the literature. Hence, line maintenance was also included in this study. When the course of an IV antimicrobial infusion therapy is completed at the WRHA CIVP, a PI PICC may be kept in place for up to 90 days for potential use again (WRHA, 2013). This situation was described as line maintenance in the WRHA Nursing Procedures Manual (WRHA, 2013). For this study, line maintenance was identified if it was documented in daily nursing clinical flow sheets or in nursing notes.

Insertion-related Covariates

Vein Used for PI PICC Placement. To the best of my knowledge, the association between vein used for PI PICC placement and thrombotic occlusion was not assessed in the literature. Hence, this variable was also included in this study to be assessed. The common veins used for PICC insertion are the cephalic, the basilic or the median cubital veins of the antecubital fossa (Dougherty & Lamb, 2009; Gorski. et al., 2016; Hamilton & Bodenham, 2009). Vein used for PI PICC placement was identified if it was documented in daily nursing clinical flow sheets and in vascular access details forms.

Arm Used for PI PICC Placement. When the right arm was used for PICC insertion, it was associated with decreased odds of thrombotic occlusion compared with the left arm (Smith et al., 2017). Hence, this covariate is also included in this study. Arm used for PI PICC placement was identified if it was documented in daily nursing clinical flow sheets and in vascular access details forms.

Tip Location of PI PICC. The tip of a PICC can be located at the superior or inferior vena cava, or at the cavoatrial junction (Gorski. et al., 2016; Hamilton & Bodenham, 2009). The existing literature showed that tip location other than cavoatrial junction was associated with

thrombotic occlusion (Smith et al., 2017). Hence, this variable was also included in this study to investigate if there is an association. Tip location of PI PICCs in this study was identified if it was documented in daily nursing flow sheets and in vascular access details forms.

Statistical Methods

The follow-up time for the study cohort was measured from the index date to the date at which thrombotic PI PICC occlusion or discharge from the IV infusion clinics occurs, or until the study end date. The discharge reasons from the WRHA CIVP IV Infusion Clinics were as follows: Patients completed the course of IV antimicrobial therapy, patients were transferred to their homes to receive their IV infusion therapies from a visiting RN, patients were transferred to the hospitals or to the CancerCare Manitoba, and patients were lost to follow-up. The discharge date for the patients who were lost to follow-up was established according to the date of their last IV clinic visit.

All statistical analyses were conducted by using Stata® version 16 statistical software. The descriptive analyses were conducted first to identify characteristics of the cohort and study variables. The incidence rate of thrombotic PI PICC occlusion was calculated as per 1,000 person-weeks.

10% cut off was used for missing data because if missing data are greater than 10%, the results of the statistical analyses may be biased (Bennett, 2001; Dong & Peng, 2013), and for this reason, the dwell time of PI PICCs was excluded from the Cox proportional-hazards analyses as the amount of missing data related to this variable was 21 %. In order to calculate the dwell time, the insertion and removal date of the PI PICCs are needed. However, the insertion and removal date of the PI PICCs were not in the patients' charts due to following reasons: The insertion and removal dates of PI PICCs were not recorded in the patients' charts, patients were transferred to

their homes to receive their IV infusion therapies from a visiting RN, patients were transferred to the hospitals or to the CancerCare Manitoba, and patients were lost to follow-up.

Survival analysis methods were used for data analyses. Cox multivariate proportional-hazards analysis was conducted to assess the association between thrombotic PI PICC occlusion and certain socio-demographic, clinical, insertion and PI PICC-related characteristics.

The Kaplan-Meier survival curves were generated to estimate the median survival time of PI PICCs. The interaction analyses were also conducted to identify the potential effect modifiers; however, due to small sample size of the study these analyses could not be performed.

Adjustment for Confounding

The multivariate stratified Cox proportional-hazards models were used to adjust for the potential confounders. A causal directed acyclic graph (DAG) was used to choose variables to include in the final model. The DAG approach especially used to choose variables for including in the final model because it reduces biased estimate (Shrier & Platt, 2008).

Based on the DAG, the following variables were included in the final model to adjust for potential confounding: IV antimicrobials, ambulatory drug delivery pump use, the tip location of PI PICCs and the number of PI PICC lumens.

Statistical Power and Sampling

A priori sample size calculation was conducted by using the Epitools epidemiological calculator (*Epitools-Epidemilogical Calculators*, 2019). This calculation was based on the sample size of 246. With the sample size of 246 cases and assuming a Type I error rate = 0.05, the study would have sufficient power (80 %) to measure the incidence of thrombotic occlusion of PI PICCs. A two- tailed significance test method was used. The statistical significance was defined as $p < 0.05$.

The convenience sampling method was used to select patients for this retrospective chart review study. The convenience sampling method is the most common and practical method used in retrospective chart review studies, and it is especially suitable for the smaller sample sizes (Gearing et al., 2006; Matt & Matthew, 2013). In convenience sampling method, patients are selected over a specific time period (Gearing et al., 2006; Worster & Haines, 2004). Patients who received the IV antimicrobial infusion therapies at the WRHA CIVP IV Infusion Clinics between January 1, 2015 and December 31, 2017 were selected for this study.

Ethical Considerations

This research received ethics approval by the University of Manitoba Health Research Ethics Board (HREB) and the WRHA Research Access and Approval Committee, (Ethics # HS22585, H 2019:067). The documents of the ethical approvals are presented in Appendix A.

There was no individual and institutional conflict of interest to be disclosed to the ethics boards. During the data extraction process, the PHINs, the postal codes, the first names and last names of the patients were not collected. The patients were not contacted or interviewed. Patient consent was not needed as this study was based on the electronic chart review. De-identified patient data was retained in the secure environment of the University of Manitoba Vaccine and Drug Evaluation Centre.

Chapter 4: Results

Descriptive Analyses

Characteristics of the Cohort and Covariates

Socio-demographic Characteristics. The characteristics of the cohort are presented in Table 3 in Appendix B. The average age of the patients was 52 years (standard deviation (SD) 16), and the median age was 54 years. Most patients were males (52%) and had less favorable SEFI-2 scores, (SEFI > 0), (55%). About 35% of the patients had diabetes mellitus.

Clinical Characteristics. The most frequently used IV antimicrobial agent was IV ceftriaxone (51%) followed by ertapenem (22%) and vancomycin (13%). A smaller proportion of the patients (9%) received other IV antimicrobial infusions as follows: acyclovir, amikacin, cefazolin, ceftazidim, Cipro, Daptomycin, flucanazole, foscarnet, meropenem, micafungin, tobramycin, penicillin and piperacillin/tazobactam.

About 97% of the patients had blood withdrawal done once a week for laboratory tests. The majority of the patients received IV antimicrobial infusions from RNs (81%). All of the IVSC patients infused their IV antimicrobial infusions by themselves. Only a smaller proportion of the patients received their IV antimicrobial infusions through an ambulatory drug delivery pump (6%).

About 95% of PI PICCs were flushed with 10 millilitres of NS before administering IV infusions whereas about 92% of them were flushed with 10 millilitres of NS after IV infusions. A smaller proportion of PI PICCs received more than one NS flushes after IV infusions (8%). About 97% of PI PICCs were flushed with two syringes of 10 millilitres of NS after withdrawing blood from them.

Insertion-related Characteristics. The majority of PI PICCs was inserted in the right arm (68%) and in the basilic vein (75%). Missing data related to these characteristics was only 1%. More than half of the catheter tips were located at the cavoatrial junction (53%), and only 2% of the data was missing related to the tip location of PI PICCs.

PI PICC-related Characteristics. The majority of PI PICCs were single-lumen catheters (84%), and their gauge size was 4, which is the larger size. The rest of the PI PICCs were multiple-lumen catheters (16%) with the gauge size of 5. All of the PI PICCs' brand name was Bard PowerPICC Solo, which has three internal pressure-activated safety valves in it.

40% of PI PICCs had the dwell time < 40 days whereas 39% of them had longer dwell time, and 21% of the dwell time was unknown. About 24 % of the PI PICCs had line maintenance.

Outcome

Thrombotic PI PICC Occlusion. Details of thrombotic PI PICC occlusion are presented in Table 3 in Appendix B. A total of 51 (18%) of the PI PICCs which were placed in patients developed thrombotic occlusion. The average age of these patients was 51.5 years (SD: 15) while the median age was 54 years. The proportion of thrombotic occlusion was smaller (14%) in patients aged ≥ 65 compared to the other age groups. A greater proportion of males (19%) had thrombotic occlusion compared to females (16%). The proportion of thrombotic occlusion did not differ significantly in patients who had more or less favorable SEFI-2 scores (18 %, 17% respectively). Only 2% of the SEF-2 scores were missing as those were belonged to the recently built areas in Winnipeg, Manitoba. About 19% of diabetic patients had thrombotic occlusion.

Half of the patients who received IV cloxacillin infusion developed thrombotic PI PICC occlusion. About 43% of the patients received IV vancomycin developed thrombotic occlusion

followed by ertapenem (16%). The proportion of thrombotic PI PICC occlusion was significantly lower (9%) in patients received IV ceftriaxone.

About 18% of the patients who had blood withdrawal from their PI PICCs had thrombotic occlusion. IVSC patients had a higher proportion of thrombotic occlusion (22 %) compared to the patients received their IV infusions from RNs (17%). Half of the PI PICCs connected to the ambulatory pumps had thrombotic occlusion.

About 62% of the PI PICCs had thrombotic occlusion when they were not flushed with 10 milliliters of NS before IV antimicrobial infusions, and these PI PICCs were connected to the ambulatory pumps for continuous IV infusions. However, only 16% of them occluded when they were flushed with one or more 10 milliliters of NS before infusions. When the PI PICCs were flushed with one 10 milliliters of NS after infusion, only 14 % of them occluded. About 31% of the PI PICCs occluded when they were flushed with two of 10 milliliters of NS between infusions. 18% of the PI PICCs occluded when they were flushed with two of 10 milliliters of NS after blood withdrawal. Only 16% of PI PICCs occluded when they were on line maintenance.

When the left arm was used for insertion, 20 % of PI PICCs occluded compared to the right arm (17%). A greater proportion of the PI PICCs occluded when the brachial vein was used for insertion (24%) compared to the basilic (17%) and the cephalic vein (16%). A higher proportion of PI PICCs occluded (24%) when their tips were located at the cavoatrial junction compared to the superior vena cava (12 %).

The majority of multiple-lumen PI PICCs (53%) occluded compared to the single-lumen PI PICCs (11%). A greater proportion of the PI PICCs (31%) occluded when the dwell time of the PI PICCs > 40 days compared to the dwell time <40 days (7 %).

Incidence Rate of Thrombotic PI PICC Occlusion

The stratified incidence rates are presented in Table 4 in Appendix B. A total of 51 PI PICCs developed thrombotic occlusion, and the total follow-up time was 1,573 person-weeks. Almost all of the thrombotic occlusions were withdrawal occlusions; there was only one complete occlusion. The incidence rate of thrombotic PI PICC occlusions was 32/1,000 person-weeks (95% CI: 25-43).

The incidence rate of thrombotic PI PICC occlusion was higher among 51-64 year-olds (Incidence rate [IR]: 39/1,000; 95% CI: 25-61) whereas it was the lowest among patients ≥ 65 years (IR: 21/1,000; 95% CI: 11-39). Males had higher incidence rate (IR: 38/1,000; 95% CI: 26-54) compared to females (IR: 27/1,000; 95% CI: 18-42). The incidence rate did not significantly differ in patients who had more or less favorable SEFI-2 scores, in diabetics and non-diabetics.

Some of the IV antimicrobials had the highest incidence rate of thrombotic PI PICC occlusion. For example, the incidence rate for IV cloxacillin was 163/1,000; (95% CI: 78-341) followed by vancomycin (IR: 133/1,000; 95% CI: 82-218). However, the incidence rate was lower for IV ceftriaxone (IR: 18/1,000; 95% CI: 10-30) and ertapenem (IR: 19/1,000; 95% CI: 10-35).

The incidence rate remained higher when PI PICCs were connected to the ambulatory pumps (IR: 151/1,000; 95% CI: 75-301) and when RNs provided IV antimicrobial infusions (IR: 34/1,000; 95% CI: 25-47).

The incidence rate of thrombotic occlusion was higher when the left arm and the brachial vein were used for PI PICC insertion (IR: 40/1,000; 95% CI: 25-63) and (IR: 55/1,000; 95% CI: 29-106), respectively.

When the tip of the PI PICCs was located at the cavoatrial junction the incidence rate was greater (IR: 42/1,000; 95% CI: 30-58) compared with the superior vena cava (IR: 23/1,000; 95% CI: 14-38).

Multiple-lumen PI PICCs had a higher incidence rate of thrombotic occlusion (IR= 89/1,000; 95% CI: 60-131) compared with single-lumen PI PICCs (IR=20/1,000; 95% CI: 14-30). When PI PICCs were on line maintenance the incidence rate remained lower (IR= 19/1,000; 95% CI: 11-35) compared with the PI PICCs which were not on line maintenance (IR= 40/1,000; 95% CI: 29-54).

Survival Time of the PI PICCs

The survival time of the PI PICCs are presented in the Kaplan-Meier curves in Appendix B. The median survival time of the PI PICCs was about 8 weeks for IV vancomycin and was 5 weeks for cloxacillin. The survival curves of IV vancomycin and cloxacillin crossed over, but it is difficult to assess the significance of this finding due to the small number of events (see Figure 1 in Appendix B).

The median survival time of the single-lumen PI PICCs was longer (39 weeks) compared with multiple-lumen catheters (4 weeks). The survival time of PI PICCs was shorter (4 weeks) when they were connected to the ambulatory drug delivery pumps for continuous IV infusions. In addition, the survival time of the PI PICCs was shorter (21 weeks) when their tips were located at the cavoatrial junction compared with the superior vena cava.

Univariate Cox Proportional Hazards Analysis

Association between Certain Socio-economical, Clinical, Insertion and PI PICC-related Characteristics and Thrombotic PI PICC Occlusion

The crude hazard ratios are presented in Table 5 in Appendix B. Without adjustment for other covariates, IV cloxacillin and vancomycin, multiple-lumen PI PICCs, cavoatrial junction and ambulatory drug delivery pump use were associated with thrombotic PI PICC occlusion.

The hazard of thrombotic occlusion for those PI PICCs which received IV cloxacillin was about 7.3 times higher (95% CI: 2.9-18.3) compared with IV ceftriaxone. For IV vancomycin the hazard of thrombotic occlusion was 6.8 times higher (95%CI: 3.3-14.1) compared with ceftriaxone.

Multiple-lumen PI PICCs had about 6.2 times greater hazard (95% CI: 3.6-10.8) compared to single-lumen PI PICCs. The hazard of thrombotic occlusion for those PI PICCs which were connected to ambulatory drug delivery pumps was 3.9 times higher (95% CI: 1.8-8.3) compared with PI PICCs which were not connected to the pumps. Compared with the superior vena cava, the hazard of thrombotic occlusion was about 2.2 times higher (95% CI: 1.2-4) when the tip of PI PICCs were located at the cavoatrial junction.

Adjusted Cox Proportional Hazards Analysis

Association between Certain Clinical, Insertion and PI PICC-related Characteristics and Thrombotic PI PICC Occlusion

After adjustment for select confounders, the adjusted hazard ratios of thrombotic PI PICC occlusion are presented in Table 6 in Appendix B. IV vancomycin and the multiple-lumen

PI PICCs were associated with thrombotic PI PICC occlusion after adjusting for select confounders including IV antimicrobials, ambulatory drug delivery pump use, tip location and number of lumens. The hazard of thrombotic occlusion for those PI PICCs received IV vancomycin was 5.8 times higher (95% CI: 2.8-12.3), and for multiple-lumen PI PICCs it was 5.1 times higher (95% CI: 2.8-9.1).

Infusion of IV cloxacillin, (HR: 3.3, 95% CI: 0.4-28.5), ambulatory pump use (HR: 1.3, 95% CI: 0.2-8.9), and the tip location of cavoatrial junction (HR: 1.8, 95% CI: 1.0-3.5) was associated with a higher hazard of thrombotic PI PICC occlusion, but these associations were not statistically significant.

Chapter 5: Discussion

In the present retrospective cohort study, IV vancomycin and multiple-lumen PI PICCs were associated with thrombotic PI PICC occlusion. These findings are consistent with the existing literature as the same associations found in a retrospective cohort study examining factors associated with PICC occlusions among hospitalized adults in the USA (Smith et al., 2017). In that USA study, the tip position of PICCs at the cavoatrial junction was associated with a lower risk of thrombotic occlusion (Smith et al., 2017). Conversely, in the present study, the cavoatrial junction was associated with a higher hazard of thrombotic occlusion, but this association was not statically significant. The majority of the PICCs were power injectable in that study (91.1%), and the sample size of their study was greater, which was 13, 408 (Smith et al., 2017). However, their cohort consisted of hospitalized adult patients who were receiving care at intensive care units and general medicine wards (Smith et al., 2017). Hospitalized patients are different from community-based patients. For example, patients who receive care at intensive care units are critically ill patients and their care needs are complex (Goodridge et al., 2010).They may need multiple IV fluid therapies, IV blood transfusions, and thrombolytics (Cathala, 2018; Goodridge et al., 2010). On the other hand, community-based patients are well enough to stay home and ambulate to IV infusion clinics to receive their IV infusion therapies. Thus, different findings between the present study and the other studies conducted among hospitalized patients could be related to the difference between the hospitalized and community-based patients.

In the UK, a retrospective cohort study investigating predictors of IV access device complications among community-based IVSC and clinic patients found that IV flucloxicillin was associated with greater odds of thrombotic PICC occlusion, however, these researchers did not

report if PI PICCs were included in this study (Barr et al., 2012). Similarly, in the present study, IV cloxacillin was associated with a higher hazard of thrombotic occlusion, but this association was not statistically significant. However, at the WRHA IV Infusion Clinics nurses frequently observe thrombotic PI PICC occlusions when IV cloxacillin is infused through an ambulatory drug delivery pump. IV flucloxacillin and cloxacillin are both penicillinase-resistant agents (Lilley et al., 2005).

In France, a prospective cohort study examining PICC-related complication rates in hospital and outpatient settings found that age > 65 years was associated with thrombotic PICC occlusion (Grau et al., 2017). However, those researchers did not report if PI PICCs were included in that study. Conversely, in the present study, there was no association found between age and thrombotic occlusion. Those researchers included IV chemotherapy, TPN, and blood transfusions as covariates in their study. However, the present study assessed only IV antimicrobial infusions if they were associated with thrombotic PI PICC occlusion. The sample size of their study consisted of 192 PICCs, which is smaller than the sample size of the present study.

In the present study, there was no association found between the SES, line maintenance, vein used for PI PICC insertion, ambulatory drug delivery pump use and thrombotic PI PICC occlusion. To the best of my knowledge, the previous studies in the literature did not assess these covariates.

In the present study, there was no association found between sex, diabetes mellitus, arm used for PI PICC insertion, and thrombotic occlusion. Similarly, there was no association found between sex, diabetes mellitus, and thrombotic occlusion of PICCs in the existing literature. However, in the USA, insertion of PICCs in the right arm was associated with smaller odds of

thrombotic occlusion in a retrospective cohort study examining factors associated with PICC occlusion (Smith et al., 2017).

In the present study, the incidence rate of thrombotic PI PICC occlusion was 32/1,000 person-weeks (4.6/1,000 person-days). This incidence rate was higher compared with other studies in the literature. For example, in the USA, the incidence rate of thrombotic occlusion of PICCs reported as 0.40/1,000 catheter-days in community-based patients (Moureau et al., 2002). On the other hand, this incidence rate in that USA study was not based on PI PICCs as those devices were not available in the market when that study was conducted. In addition to that, their study cohort was different from the present study's cohort as it consisted of both pediatric and adult patients. Another USA study investigating vascular access complications during IV antimicrobial therapy in community-based IVSC patients reported that the incidence rate of PICC occlusions was 2.46/1,000 outpatient parenteral antimicrobial therapy-days (Shrestha et al., 2016). However, the researchers did not report if PI PICCs were included in their study (Shrestha et al., 2016).

Strengths and Limitations

To the best of my knowledge, the present study is the first study to explore the incidence rate and determinants of thrombotic PI PICC occlusion at the community-based IV infusion clinics. Thus, the present study fills a gap in the literature and provides baseline thrombotic occlusion data related to PI PICC use in the adult population at the community-based IV infusion clinics. This study has provided findings that enhance our understanding related to the determinants of thrombotic PI PICC occlusion at the community-based IV infusion clinics. This is especially important as the use of PICCs has been steadily increasing to infuse IV infusion therapies in the community-based settings (Moureau et al., 2002; Williams, 2018).

Another strength of this study is that the study subjects had already been assembled in Accuro EMR. Consequently, it was less time consuming to conduct this study. The majority of the patient and PI PICC-related data were available in Accuro EMR. Potential confounding bias was controlled by using the Cox multivariable proportional-hazards analysis model.

Despite the present study's strengths and its important contribution to the literature, it has some limitations. For example, the retrospective design can be a source of bias. For instance, a chart review containing the past EMRs was done to collect data. However, these records were not originally documented for research purposes. Thus, information in the electronic patient charts may be not accurate, and this situation can lead to the recall bias which is a common problem in observational studies. There is also no randomization was involved at the design stage of this study. For instance, allocation of exposures was not random in this study. Although multivariable data analysis approach was used to control confounding, without randomization there is still a possibility of confounding bias in this study.

There is also limitation related to the sampling strategy. The convenient sampling method, which is the most common sampling method for the chart review studies, was used to select the electronic patient charts. For example, the patients' charts between January 1, 2015 and December 31, 2017 were selected as they were easily available. However, this method may cause bias as not every chart had an equal chance to be selected (i.e. charts between 2008 and 2017).

In addition, the losses to follow-up may introduce bias if their exposures differ from those patients' who remained in the study. Another potential source of bias is the SEFI-2 scores. The SEFI-2 scores are not the individual level data; they are based on the geographical areas.

Therefore, using the SEFI-2 scores a proxy measure of the SES may cause residual confounding and bias. Due to the amount of missing information, the dwell time could not be included in the analyses. Therefore, the missing dwell time may also be a source of residual confounding and bias. Split-septum neutral-displacement needleless connectors are among the predictors of thrombotic occlusion of PICCs. Because the type of the needleless connectors is not documented at the patients' charts, no data was collected on this potential confounder. Thus, there might be residual confounding in the study.

Another limitation of this study is that its small sample size, which was 286. Therefore, the estimates of the present study may be less reliable than the studies based on a larger sample size.

All of the PI PICCs in this study consisted of Bard PowerPICC Solo, which has pressure-activated safety valves in it. Therefore, the study results may be generalizable to all PI PICCs which have pressure-activated safety valves in them. However, the study sample consisted of Manitoba population, which may limit the generalizability of the study findings.

Policy Recommendations

Despite some limitations of this research, the study results allow policymakers to develop the evidence-based interventions to reduce the incidence rate of thrombotic PI PICC occlusion. For example, multiple-lumen PI PICCs were associated with thrombotic occlusions in the present study and the literature. Thus, single-lumen PI PICCs should be inserted for the community-based IV infusion patients whenever possible. There is currently no hospital policy indicating insertion of single or multiple-lumen PICCs for the community-based IV infusion patients in Winnipeg, Manitoba. Sometimes the decision regarding single or multiple-lumen PICC insertion is based on the PICC supply on hand. Hence, policy change should be made to guide nurses to insert single-lumen PI PICCs for those community-based IV infusion patients.

Some of the previously hospitalized patients are admitted to the WRHA CIVP IV Infusion Clinics with their multiple-lumen PI PICCs inserted. Because multiple-lumen PI PICCs were associated with thrombotic occlusions in the present study and in the current literature, a policy change regarding heparin lock use for multiple-lumen PI PICCs may be considered to prevent further thrombotic PI PICC occlusions as the current literature indicates that using a heparin lock following a NS flush was clinically significant to reduce thrombotic PICC occlusions (Bowers et al., 2008; Lyons & Phalen, 2014). For instance, a policy change may be done to use 300 units of heparin for locking multiple-lumen PI PICCs as a previous randomized clinical trial conducted among hospitalized patients in the USA showed that there was no PICC occlusion occurred when PICCs were locked with 300 units of heparin, however, this association was not statistically significant (Bowers et al., 2008). Similarly, another randomized clinical trial conducted among community-based IV infusion patients in the USA found that when PICCs were locked with 300 units of heparin, the number of RN visits to assess thrombotic PICC occlusions and fibrinolytic use to restore the patency of these devices decreased, however, this association was not statistically significant (Lyons & Phalen, 2014). In addition, the heparin lock may also be used whenever IV vancomycin is infused through PI PICCs as IV vancomycin was also associated with thrombotic occlusions in the present study and current literature.

Currently, PI PICCs are locked with only NS at the WRHA CIVP, and there is no nursing policy to use heparin lock following a NS flush. Only non valved tunneled central venous catheters and implanted ports are locked with 300 to 500 units of heparin at the WRHA CIVP.

Implementing these policies will lead to improved health outcomes for community-based IV infusion patients and provide economical benefits for the provincial health care system in Manitoba. For instance, the risk of tissue damage due to retrograde flow of IV infusates, the risk

of pulmonary embolism and the deep vein thrombosis may decrease. In addition, the risk of vascular damage and scar tissues related to repeated PICC insertions and the risk of acquiring catheter-related blood stream infections may decrease. The risk of further morbidity related to delayed and interrupted IV antimicrobial treatments may decline as well. Patient anxiety related to delayed, prolonged and the interrupted IV treatments may decline, and the quality of life of the patients may improve as well.

In addition, the healthcare costs related to the repeated hospital visits to see a PICC nurse for TPA administrations and replacing PI PICCs may decrease when we implement those policies which were mentioned above. For instance, the current literature indicates that the cost a typical treatment dose of 2 mg of TPA to restore catheter patency is $ 80-116 in the USA, and the total cost of a PICC insertion at McGill University Health Centre in Quebec is 582.97 Canadian Dollars. To the best of my knowledge, there is no study in the literature with regards to evaluating the cost of a TPA administration in Canada and a PICC insertion in Manitoba.

Future Research Directions

To the best of my knowledge, this study is the first to investigate the incidence rate and determinants of thrombotic PI PICC occlusion at the community-based IV infusion clinics. Although this study contributes to the existing literature, further research with a greater sample size is needed to validate the findings of this study and to assess why IV vancomycin is associated with thrombotic PI PICC occlusion.

List of References

Accuro Electronic Medical Records. (2020). *Manitoba EMR*. https://accuroemr.com/manitoba/

Accuro EMR User Guide. (2019). *Demographics Tab*. http://services.optimedsoftware.com/Manual/2016.02/1915.htm

Alexander, M., Corrigan, A., Gorski, L., Hankins, J., & Perucca, R. (2010). *Infusion nursing : an evidence-based approach* (3rd ed.. ed.). St. Louis, MO : Saunders/Elsevier.

Alport, B., Burbridge, B., & Lim, H. (2012). Bard PowerPICC Solo2 vs Cook Turbo-Ject: A Tale of Two PICCs. *Canadian Association of Radiologists journal = Journal l'Association canadienne des radiologistes., 63*(4), 323-328.

AngioDynamics. (2017). *BioFlo PICC*. Retrieved November 29, 2017 from http://www.angiodynamics.com/products/bioflopicc

Baker, A. (2016). IV antibiotic therapy in the community: clinically effective and cost effective. *British journal of nursing : BJN., 25*(sup2), S4.

Bard. (2018). *Nursing PICCS*. http://www.bardaccess.com/products/nursing/powerpicc

Bard Access Systems, I. (2016). <Power PICC, The Universal PICC Catheter. http://www.bardaccess.com/assets/literature/0741196_PowerPICC_FT_RN_IFU_Web.pdf

Barr, D., Semple, L., & Seaton, R. (2012). Self-administration of outpatient parenteral antibiotic therapy and risk of catheter-related adverse events: a retrospective cohort study. *European journal of clinical microbiology & infectious diseases, 31*(10), 2611-2619.

Bartock, L. (2010). An Evidence-Based Systematic Review of Literature for the Reduction of PICC Line Occlusions. *Journal of the Association for Vascular Access, 15*(2), 58-63. https://doi.org/10.2309/java.15-2-3

Baskin, J. L., Reiss, U., Wilimas, J. A., Metzger, M. L., Ribeiro, R. C., Pui, C.-H., & Howard, S. C. (2012). Thrombolytic therapy for central venous catheter occlusion. *Haematologica., 97*(5), 641-650.

Bennett, D. A. (2001). How can I deal with missing data in my study? *Australian and New Zealand journal of public health, 25*(5), 464-469.

Bernard, L., El-Hajj, B., Pron, A., Lotthé, V., Gleizes, F., Signoret, P., Denormandie, J. L., Gaillard, C., & Perronne, C. (2001). Outpatient parenteral antimicrobial therapy (OPAT) for the treatment of osteomyelitis: evaluation of efficacy, tolerance and cost. *Journal of Clinical Pharmacy and Therapeutics, 26*(6), 445-451. https://doi.org/10.1046/j.1365-2710.2001.00380.x

Bernstein, C. N., Nugent, Z., Targownik, L. E., Singh, H., Snider, C., & Witt, J. (2019). The Cost of Use of the Emergency Department by Persons With Inflammatory Bowel Disease Living in a Canadian Health Region: A Retrospective Population-Based Study. *Journal of the Canadian Association of Gastroenterology, 3*(3), 135-140. https://doi.org/10.1093/jcag/gwz001

Blokhin, I. O., & Lentz, S. R. (2013). Mechanisms of thrombosis in obesity. *Current opinion in hematology, 20*(5), 437.

Bolton, D. (2013). Preventing occlusion and restoring patency to central venous catheters. *British journal of community nursing., 18*(11), 539-540, 542. https://doi.org/10.12968/bjcn.2013.18.11.539

Bowers, L., Speroni, K. G., Jones, L., & Atherton, M. (2008). Comparison of occlusion rates by flushing solutions for peripherally inserted central catheters with positive pressure Luer-activated devices. *Journal of Infusion Nursing, 31*(1), 22-27 26p. http://uml.idm.oclc.org/login?url=http://search.ebscohost.com/login.aspx?direct=true&db=c8h&AN=105816581&site=ehost-live

Camp-Sorrell, D., Cope, D. G., & Oncology Nursing, S. (2011). *Access device guidelines : recommendations for nursing practice and education* (3rd ed.. ed.). Pittsburgh, PA : Oncology Nursing Society.

Canada Health Infoway. (2013). *The emerging benefits of electronic medical record use in community based care : executive summary*. Retrieved April 1 from https://www.infoway-inforoute.ca/en/component/edocman/resources/reports/benefits-evaluation/1225-the-emerging-benefits-of-electronic-medical-record-use-in-community-based-care-executive-summary

Carr, M. E. (2001). Diabetes mellitus: a hypercoagulable state. *Journal of Diabetes and its Complications, 15*(1), 44-54.

Cathala, X. (2018). Selecting IV fluids to manage fluid loss in crtically ill patients. *Nursing Times, 114*(12), 41-44.

Chopra, V., O'Horo, J. C., Rogers, M. A., Maki, D. G., & Safdar, N. (2013). The risk of bloodstream infection associated with peripherally inserted central catheters compared with central venous catheters in adults: a systematic review and meta-analysis. *Infection Control & Hospital Epidemiology, 34*(9), 908-918.

Deitcher, S. R., Fesen, M. R., Kiproff, P. M., Hill, P. A., Li, X., McCluskey, E. R., & Semba, C. P. (2002). Safety and efficacy of alteplase for restoring function in occluded central venous catheters: results of the cardiovascular thrombolytic to open occluded lines trial. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology., 20*(1), 317-324. https://doi.org/10.1200/JCO.2002.20.1.317

Dong, Y., & Peng, C.-Y. J. (2013). Principled missing data methods for researchers. *SpringerPlus, 2*(1), 222.

Dougherty, L., & Lamb, J. (2009). *Intravenous therapy in nursing practice*. John Wiley & Sons.

Dunn, E., Ariëns, R., & Grant, P. (2005). The influence of type 2 diabetes on fibrin structure and function. *Diabetologia, 48*(6), 1198-1206.

Ecob, R., & Davey Smith, G. (1999, 1999/03/01/). Income and health: what is the nature of the relationship? *Social Science & Medicine, 48*(5), 693-705. https://doi.org/https://doi.org/10.1016/S0277-9536(98)00385-2

Epitools-Epidemilogical Calculators. (2019). http://epitools.ausvet.com.au/content.php?page=SampleSize

Finlayson, G., Reimer, J., Dahl, M., Stargardter, M., & McGowan, K. (2009). *The Direct Cost of Hospitalizations in Manitoba, 2005/06. Winnipeg, MB*. Manitoba Centre for Health Policy
http://mchp-appserv.cpe.umanitoba.ca/referenceSearch.php?search=Deliverables-Costs&referenceSendbackID=

Gabriel, J. (2011). Vascular device occlusion: causes, prevention and management. *Nursing Standard, 25*(44), 49-55. http://uml.idm.oclc.org/login?url=http://search.ebscohost.com/login.aspx?direct=true&db=c8h&AN=104659175&site=ehost-live

Gallieni, M., Pittiruti, M., & Biffi, R. (2008). Vascular access in oncology patients. *CA: a cancer journal for clinicians, 58*(6), 323-346.

Gearing, R. E., Mian, I. A., Barber, J., & Ickowicz, A. (2006). A methodology for conducting retrospective chart review research in child and adolescent psychiatry. *Journal of the Canadian Academy of Child and Adolescent Psychiatry, 15*(3), 126.

Ghany, A., & Keshavjee, K. (2015). A Platform to Collect Structured Data from Multiple EMRs. *Studies in health technology and informatics., 208*, 142-146.

Gonsalves, C. F., Eschelman, D. J., Sullivan, K. L., DuBois, N., & Bonn, J. (2003). Incidence of central vein stenosis and occlusion following upper extremity PICC and port placement. *Cardiovascular and interventional radiology., 26*(2), 123-127.

Goodridge, D., Goldsworthy, S., Lewis, S. M., & Barry, M. (2010). *Medical-surgical nursing in Canada : assessment and management of clinical problems* (2nd Canadian ed.. ed.). Toronto : Mosby/Elsevier.

Gordis, L. (2014). *Epidemiology*. Philadelphia, PA: Saunders.

Gorski, L. A. (2003). Central Venous Access Device Occlusions: Part:1 : Thrombotic causes and Treatment. *Home health care nurse, 21*(2). Retrieved January 22, 2018, from

Gorski, L. A., & Czaplewski, L. M. (2004). Peripherally inserted central & midline catheters for the home care nurse. *Home healthcare nurse., 22*(11), 758-771.

Gorski., Hadaway, L., Hagle, M., McGoldrick, M., Mayer, B., & Orr, M. (2016). *Policies and procedures for infusion therapy* (5th ed.).

Government of Canada. (2006). *Achieving Health for All: A Framework for Health Promotion*. Retrieved January 23, 2019 from https://www.canada.ca/en/health-canada/services/health-care-system/reports-publications/health-care-system/achieving-health-framework-health-promotion.html

Grau, D., Clarivet, B., Lotthé, A., Bommart, S., & Parer, S. (2017). Complications with peripherally inserted central catheters (PICCs) used in hospitalized patients and outpatients: a prospective cohort study. *Antimicrobial Resistance & Infection Control, 6*(1), 18.

Hamilton, H., & Bodenham, A. (2009). *Central venous catheters*. Wiley-Blackwell.

Hardy, G., & Ball, P. (2005). Clogbusting: time for a concerted approach to catheter occlusions? *Current opinion in clinical nutrition and metabolic care., 8*(3), 277-283. Retrieved January 23, 2108., from

Hitchcock, J. (2016). Preventing intraluminal occlusion in peripherally inserted central catheters. *British journal of nursing : BJN., 25*(19), S12.

Hoffer, E. K., Borsa, J., Santulli, P., Bloch, R., & Fontaine, A. B. (1999). Prospective randomized comparison of valved versus nonvalved peripherally inserted central vein catheters. *AJR, American journal of roentgenology., 173*(5), 1393-1398. https://doi.org/10.2214/ajr.173.5.10541127

Hoshal, V. L. (1975). Total intravenous nutrition with peripherally inserted silicone elastomer central venous catheters. *Archives of surgery., 110*(5), 644-646.

Hoy, L. (2009). Practice spotlight: community intravenous program, winnipeg regional health authority. *The Canadian journal of hospital pharmacy = Le journal canadien de la pharmacie hospitalière*. --, *62*(3), 243-244.

Lilley, L. L., Harrington, S., & Snyder, J. S. (2005). *Pharmacology and the Nursing Process* (4th ed.). Mosby.

Lim, B. K., & Balasubramaniam, B. S. (2013). *Dislodgement of a power-injectable peripherally inserted central catheter after power injection: a case report* (1552-8855) https://www.sciencedirect.com/science/article/abs/pii/S1552885512001808

Lyons, M. G., & Phalen, A. G. (2014). A randomized controlled comparison of flushing protocols in home care patients with peripherally inserted central catheters. *Journal of Infusion Nursing, 37*(4), 270-281.

Manitoba Centre for Health Policy. (2019). *Concept: Socioeconomic Factor Index (SEFI) Version 2 (SEFI-2)*. http://mchp-appserv.cpe.umanitoba.ca/viewConcept.php?conceptID=1387

Manitoba Centre for Health Policy. (2020). *Type 2 Diabetes in Manitoba*. Retrieved November 23, 2020 from http://mchp-appserv.cpe.umanitoba.ca/reference/T2DM_Summary_web.pdf

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Matt, V., & Matthew, H. (2013). The retrospective chart review: important methodological considerations. *Journal of educational evaluation for health professions, 10*.

Mattox, E. A. (2017). Complications of Peripheral Venous Access Devices: Prevention, Detection, and Recovery Strategies. *Critical Care Nurse, 37*(2), e1-e14. https://doi.org/10.4037/ccn2017657

Mitchell, E. D., Czoski Murray, C., Meads, D., Minton, J., Wright, J., & Twiddy, M. (2017). Clinical and cost-effectiveness, safety and acceptability of community intravenous antibiotic service models: CIVAS systematic review. *BMJ Open, 7*(4). https://doi.org/10.1136/bmjopen-2016-013560

Moureau, N., Poole, S., Murdock, M. A., Gray, S. M., & Semba, C. P. (2002). Central venous catheters in home infusion care: outcomes analysis in 50,470 patients. *Journal of vascular and interventional radiology : JVIR., 13*(10), 1009-1016.

Mustard, C. A., Derksen, S., Berthelot, J.-m., Wolfson, M., & Roos, L. L. (1997, 1997/08/01/). Age-specific education and income gradients in morbidity and mortality in a Canadian province. *Social Science & Medicine, 45*(3), 383-397. https://doi.org/https://doi.org/10.1016/S0277-9536(96)00354-1

Ng, R., Li, X., Tu, T., & Semba, C. P. (2004). Alteplase for treatment of occluded peripherally inserted central catheters: safety and efficacy in 240 patients. *Journal of Vascular and Interventional Radiology, 15*(1), 45-49.

O'Brien, J., Paquet, F., Lindsay, R., & Valenti, D. (2013). Insertion of PICCs with minimum number of lumens reduces complications and costs. *Journal of the American College of Radiology : JACR., 10*(11), 864-868. https://doi.org/10.1016/j.jacr.2013.06.003

Owen, K. (2016). Setting up and running a community IV therapy clinic. *Journal of community nursing., 30*(1), 53.

Paladino, J. A., & Poretz, D. (2010). Outpatient parenteral antimicrobial therapy today. *Clinical infectious diseases : an official publication of the Infectious Diseases Society of America, 51 Suppl 2*, S198. https://doi.org/10.1086/653520

Pittiruti, M., Brutti, A., Celentano, D., Pomponi, M., Biasucci, D. G., Annetta, M. G., & Scoppettuolo, G. (2012). Clinical experience with power-injectable PICCs in intensive care patients. *Critical care : the official journal of the Critical Care Forum., 16*(1), R21.

Pittiruti, M., Emoli, A., Porta, P., Marche, B., DeAngelis, R., & Scoppettuolo, G. (2014). A prospective, randomized comparison of three different types of valved and non-valved peripherally inserted central catheters. *The journal of vascular access., 15*(6), 519-523.

Poli, P., Scocca, A., Di Puccio, F., Gallone, G., Angelini, L., & Calabrò, E. M. (2016). A Comparative Study on the Mechanical Behavior of Polyurethane PICCs. *The Journal of Vascular Access, 17*(2), 175-181. https://doi.org/10.5301/jva.5000452

Ponec, D., Irwin, D., Haire, W. D., Hill, P. A., Li, X., McCluskey, E. R., & Investigators, C. (2001). Recombinant tissue plasminogen activator (alteplase) for restoration of flow in occluded central venous access devices: a double-blind placebo-controlled trial—the Cardiovascular Thrombolytic to Open Occluded Lines (COOL) efficacy trial. *Journal of Vascular and Interventional Radiology, 12*(8), 951-955.

Rihn, T. L. (2001). Fibrinolytic therapy in central venous catheter occlusion. *Journal of Infusion Nursing, 24*(3S), S9-S12. https://scholar.google.ca/scholar?hl=en&as_sdt=0%2C5&q=rihn+2001+fibrinolytic+therapy&oq=rihn+2001+fibrinolytic+

Samad, F., & Ruf, W. (2013). Inflammation, obesity, and thrombosis. *Blood, The Journal of the American Society of Hematology*, *122*(20), 3415-3422.

Sandrucci, S. (2014). *Peripherally Inserted Central Venous Catheters*. Dordrecht : Springer.

Schafer, A. I. (1985). The hypercoagulable states. *Annals of Internal Medicine, 102*(6), 814-828.

Seckold, T., Walker, S., & Dwyer, T. (2015). A comparison of silicone and polyurethane PICC lines and postinsertion complication rates: a systematic review. *The journal of vascular access., 16*(3), 167-177.

Shrestha, N. K., Shrestha, J., Everett, A., Carroll, D., Gordon, S. M., Butler, R. S., & Rehm, S. J. (2016). Vascular access complications during outpatient parenteral antimicrobial therapy at home: a retrospective cohort study. *Journal of antimicrobial chemotherapy, 71*(2), 506-512. https://doi.org/10.1093/jac/dkv344

Shrier, I., & Platt, R. W. (2008, 2008/10/30). Reducing bias through directed acyclic graphs. *BMC Medical Research Methodology, 8*(1), 70. https://doi.org/10.1186/1471-2288-8-70

Smith, S., Moureau, N., Vaughn, V. M., Boldenow, T., Kaatz, S., Grant, P. J., Bernstein, S. J., Flanders, S. A., & Chopra, V. (2017). Patterns and predictors of peripherally inserted central catheter occlusion: the 3P-O study. *Journal of Vascular and Interventional Radiology, 28*(5), 749-756. e742.

Statistics Canada. (2016). *Aboriginal Peoples: Fact Sheet for Manitoba*. Retrieved November 24, 2020 from https://www150.statcan.gc.ca/n1/pub/89-656-x/89-656-x2016008-eng.htm

Statistics Canada. (2020, 2020, November 19). *Consumer price index portal*. Retrieved 2020, November 21 from https://www.statcan.gc.ca/eng/subjects-start/prices_and_price_indexes/consumer_price_indexes

Stiver, H. G., Telford, G. O., Mossey, J. M., Cote, D. D., van Middlesworth, E. J., Trosky, S. K., McKay, N. L., & Mossey, W. L. (1978). Intravenous antibiotic therapy at home. *Annals of internal medicine., 89*(5 Pt 1), 690-693.

van Miert, C., Hill, R., & Jones, L. (2012). Interventions for restoring patency of occluded central venous catheter lumens. *The Cochrane database of systematic reviews.*(4), CD007119.

Vazzana, N., Ranalli, P., Cuccurullo, C., & Davì, G. (2012). Diabetes mellitus and thrombosis. *Thrombosis research, 129*(3), 371-377.

Weinstein, S. (2014). *Plumer's principles & practice of infusion therapy* (Ninth edition.. ed.). Philadelphia : Wolters Kluwer Health.

Wilkinson, R. G., & Marmot, M. (2003). *Social determinants of health: the solid facts*. World Health Organization.

Williams, A. (2018). Catheter Occlusion in Home Infusion: The Influence of Needleless Connector Design on Central Catheter Occlusion. *Journal of infusion nursing . 41*(1), 52-57. https://doi.org/10.1097/NAN.0000000000000259

World Health Organization. (2008). *Closing the gap in generation:health equity through action on the social determinants of health. Final Report of the Commission on Social Determinants of Health.*

Worster, A., & Haines, T. (2004). Advanced statistics: understanding medical record review (MRR) studies. *Academic Emergency Medicine, 11*(2), 187-192.

WRHA. (2013). *WRHA-Home Care Nursing Procedures Manual*.

Young, T. K. (2004). *Population health: concepts and methods*. Oxford University Press.

Appendix A: Letter of Approvals

UNIVERSITY OF MANITOBA | Research Ethics and Compliance

Research Ethics - Bannatyne
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HEALTH RESEARCH ETHICS BOARD (HREB)
CERTIFICATE OF FINAL APPROVAL FOR NEW STUDIES
Delegated Review

PRINCIPAL INVESTIGATOR:	INSTITUTION/DEPARTMENT:	ETHICS #:
[redacted]	U of M/Community Health Sciences	HS22585 (H2019:067)
APPROVAL DATE: February 1, 2019	**EXPIRY DATE:** **February 1, 2020**	
STUDENT PRINCIPAL INVESTIGATOR SUPERVISOR (If applicable): [redacted]		

PROTOCOL NUMBER:	PROJECT OR PROTOCOL TITLE;
NA	Thrombotic Occlusion of Power Injectable Peripherally Inserted Central Catheters at the WRHA Community Ambulatory IV Infusion Clinics in Winnipeg, Manitoba
SPONSORING AGENCIES AND/OR COORDINATING GROUPS: NA	

Submission Date of Investigator Documents:	HREB Receipt Date of Documents:
January 16, 2019	January 30, 2019

THE FOLLOWING ARE APPROVED FOR USE:

Document Name	Version(if applicable)	Date
Protocol: Protocol and Bannatyne Campus Research Ethics Board Retrospective Records Review Form dated January 16, 2019	V. 1.1	28-Jan-2019
Consent and Assent Form(s):		
Other: Data Capture Sheet (Undated) provided Unique ID is added to this form		submitted January 16, 2019
Master List (Undated)		submitted January 16, 2019

CERTIFICATION
The above named research study/project has been reviewed in a ***delegated manner*** by the University of Manitoba (UM) Health Research Board (HREB) and was found to be acceptable on ethical grounds for research involving human participants. The study/project and documents listed above was granted final approval by the Chair or Acting Chair, UM HREB.

HREB ATTESTATION
The University of Manitoba (UM) Research Board (HREB) is organized and operates according to Health Canada/ICH Good Clinical Practices, Tri-Council Policy Statement 2, and the applicable laws and regulations of Manitoba. In respect to clinical trials, the HREB complies with the membership requirements for Research Ethics Boards defined in Division 5

of the Food and Drug Regulations of Canada and carries out its functions in a manner consistent with Good Clinical Practices.

QUALITY ASSURANCE
The University of Manitoba Research Quality Management Office may request to review research documentation from this research study/project to demonstrate compliance with this approved protocol and the University of Manitoba Policy on the Ethics of Research Involving Humans.

CONDITIONS OF APPROVAL:

1. The study is acceptable on scientific and ethical grounds for the ethics of human use only. ***For logistics of performing the study, approval must be sought from the relevant institution(s).***
2. This research study/project is to be conducted by the local principal investigator listed on this certificate of approval.
3. The principal investigator has the responsibility for any other administrative or regulatory approvals that may pertain to the research study/project, and for ensuring that the authorized research is carried out according to governing law.
4. **This approval is valid until the expiry date noted on this certificate of approval. A Bannatyne Campus Annual Study Status Report** must be submitted to the HREB within 15-30 days of this expiry date.
5. Any changes of the protocol (including recruitment procedures, etc.), informed consent form(s) or documents must be reported to the HREB for consideration in advance of implementation of such changes on the **Bannatyne Campus Research Amendment Form.**
6. Adverse events and unanticipated problems must be reported to the HREB as per Bannatyne Campus Research Boards Standard Operating procedures.
7. The UM HREB must be notified regarding discontinuation or study/project closure on the **Bannatyne Campus Final Study Status Report**.

Sincerely,

[redacted]

Winnipeg Regional Health Authority / Office régional de la santé de Winnipeg
Caring for Health / À l'écoute de notre santé

George and Fay Yee Centre for Healthcare Innovation
4th Floor, Chown Building
753 McDermot Avenue, Winnipeg, Manitoba, R3E 0T6

May 17, 2019

[redacted]
Vaccine and Drug Evaluation Centre
339 Apotex Centre – 750 McDermot Avenue
Winnipeg, MB R3E 0T5

Dear Ms. [redacted]

Re: Letter of Approval – "Incidence and Determinants of Thrombotic Occlusion of Power Injectable Peripherally Inserted Central Catheters at the WRHA Ambulatory IV Infusion Clinics in Winnipeg, Manitoba"

Reference No: RAAC 2019-011 **UofM REB: HS22585(H2019:067)**

We are pleased to inform you that your request for the above-named study has been approved by the Winnipeg Regional Health Authority (WRHA) Research Access and Approval Committee (RAAC).

Access and approval are pending confirmation that the following conditions are met or agreed to:

1. In compliance with the *Personal Health Information Act, [Sec 24(4)]*, we receive a fully executed Researcher Agreement (attached for your signature) between yourself (the PI), the University of Manitoba and the WRHA;
   - This letter of approval, along with the 'Data Capture Sheet' and the 'WRHA Data Access and Disclosure Plan' constitutes Schedule 'B' of the Researcher Agreement.
   - Once signed, please return the Researcher Agreement to Judy Dyrland, Research Coordinator, George and Fay Yee Centre for Healthcare Innovation, 4th Floor, Chown Building, 753 McDermot Avenue, Winnipeg, MB R3E 0T6.
   - The WRHA RAAC office will forward a fully executed copy of the Researcher Agreement once signed by all parties.
2. All U of M PHIA Pledges of Confidentiality for research team are up-to-date and current (completed every three years);
3. Submit any significant changes in your proposal prior to implementation, or any significant changes during the course of the study;
4. You agree to be accountable for the appropriate storage, disposal and/or destruction of material, as stipulated in the Researcher Agreement;
5. Appropriately acknowledge the role of the WRHA and/or affiliated organizations in any peer-reviewed publications resulting from this study;
6. Submit a summary of the final results of the study to the WRHA and provide the RAAC with a copy of any publications arising from the study;
7. Give the WRHA (facility, program, and RAAC) at least thirty (30) calendar days prior notice (including a draft document) for every intended publication in learned journals or thesis presentation; and at least ten (10) calendar days prior notice is required for every poster or oral presentation.

Thank you for selecting the Winnipeg Regional Health Authority as the site to conduct your research. Please let us know should you encounter any difficulties during the course of your study.

We extend best wishes for successful completion of your study.

Yours sincerely,

[redacted]

cc. [redacted]

Attachment – Researcher Agreement & Appendices

Appendix B: Tables and Figures

Table 1
Thrombotic PI PICC Occlusion Literature Basic Study Details

Author(s)	Study Objective	Number of Patients	Study Setting	Study Location	Study Design	Study Population
Ponec et al.(2001)	To assess efficacy of Alteplase in CVADs	150	Hospital	USA	RCT	Adults
Deitcher et al, (2002)	To assess safety and efficacy of Alteplase in CVADs	997	Multicenter	USA	RCT	Pediatrics, Adults
Moureau et al. (2002)	To investigate complications CVADs	50,470	Community	USA	Retrospective Cohort	Pediatrics, Adults
Ng et al. (2004)	To assess safety and efficacy of Alteplase in PICCs	995	Multicenter	USA	RCT	Pediatrics, Adults
Bowers et al. (2008)	To compare occlusion rates by flushing solutions	102	Hospital	USA	RCT	Adults
Alport et al. (2012)	To compare PICC complications	53	Hospital	Canada	RCT	Adults
Barr et al. (2012)	To investigate complications CVADs	830	Community IVSC and Clinic	UK	Retrospective Cohort	Adults

Note. CVAD = Vascular access device; IVSC = Intravenous self care; PICC = Peripherally inserted central catheters; RCT= Randomized clinical trial.

Table 1 (Continued)
Thrombotic PI PICC Occlusion Literature Basic Study Details

Author(s)	Study Objective	Number of Patients	Study Setting	Study Location	Study Design	Study Population
van Miert et al. (2012)	To review efficacy of fibrinolytic agents	632	Single and Multicenter	UK	SR & MA	Pediatrics, Adults
Pittiruti et al. (2012)	To assess complications of PI PICCs	89	Intensive Care Unit	Italy	Retrospective Cohort	Pediatrics, Adults
O'Brien et al. (2013)	To compare complications in single and double-lumen PICCs, cost analysis	4,030 PICCs	Hospital and Outpatient	Canada	Prospective Cohort	Not reported
Lyons & Phalen. (2014)	To compare flushing protocols	90	Community	USA	RCT	Adults
Pittiruti et al. (2014)	To compare valved and non-valved PI PICCs	180	Hospital	Italy	RCT	Adults
Shresta et al. (2016)	To investigate vascular access complications	1,461	Community	USA	Retrospective Cohort	Adults
Grau et al. (2017)	To assess PICC-related complications	192 PICCs	Hospital	France	Prospective Cohort	Adults
Smith et al. (2017)	To assess PICC occlusions	13,408	Hospital, Multicenter	USA	Retrospective Cohort	Adults
Williams (2018)	To compare PICC occlusions associated with needless connectors	720	Community	USA	Retrospective Cohort	Pediatrics, Adults

Note. PICC = Peripherally inserted central catheter; PI PICC = Power injectable peripherally inserted central catheters; RCT = Randomized clinical trial; SR&MA = Systematic review and meta analysis.

Table 2

Reasons for Exclusion from the Study

Reason for Exclusion from the Study	Number of Excluded
Receiving IV Infusion at Home	45
Not PI PICC	7
Short Peripheral IV Line	3
Line Maintenance at the Index Date	7
Patient Did not Attend	3
Patients Younger than 18 Years	11
Not Residing in Winnipeg	10
Admitted in 2014	4
Never Admitted	3
Thrombotic Occlusion During Admission	4
Total Excluded	97

Note. PI PICC = Power injectable peripherally inserted central catheter;
Line maintenance = PI PICC is not in use for administering IV antimicrobial infusion.

Table 3

Study Covariates

Socio-demographic Covariates
Age
Sex
SEFI-2
Co-morbidity
Diabetes Mellitus
Clinical Covariates
IV Antimicrobials
Frequency of Blood Withdrawal
Number of NS Flushes
IV Infusion Administration (RN vs. IVSC)
Ambulatory Drug Delivery Pump Use
Insertion-related Covariates
Vein Used for PI PICC Placement
Arm Used for PI PICC Placement
Tip Position of PI PICC
PI PICC-related Covariates
Number of Lumens and Gauge Size
Dwell time of PI PICCs
Line Maintenance

Table 4

Number (%) of Thrombotic PI PICC Occlusions According to Certain Socio-economic, Clinical, Insertion and PI PICC-related Characteristics

	Cohort		Thrombotic PI PICC Occlusion	
	Number	**%**	**Number**	**%**
Overall	286	100%	51	18%
Age (years)				
18-50	120	42%	21	18%
51-64	96	34%	20	21%
≥65	70	24%	10	14%
Mean (SD)	52 (16)		51.5 (15)	
Median (Q1-Q3)	54 (40-64)		54 (39-63)	
Sex				
Male	150	52%	29	19%
Female	136	48%	22	16%
SEFI-2				
More Favorable	123	43%	22	18%
Less Favorable	157	55%	27	17
Unknown	6	2%	2	33%
Diabetes	99	35%	19	19%
Intravenous Antimicrobials				
Ceftriaxone	146	51%	13	9%
Ertapenem	64	22%	10	16%
Vancomycin	37	13%	16	43%
Cloxacillin	14	5%	7	50%
Other	25	9%	5	20%
Frequency of Blood Work				
Once a Week	276	97%	51	18%
Blood work Not Done	10	3%	0	0%
IV Infusion Administration				
Registered Nurse	231	81%	39	17%
Patient	55	19%	12	22%
Ambulatory Pump Use	16	6%	8	50%
NS Before Infusion				
One or More Flushes	273	95%	43	16%
No Flush	13	5%	8	62%

Note. PI PICC = Power injectable peripherally inserted central catheter; SD = Standard deviation; Q1-Q3 = The first and third Interquartile range; SEFI-2 = Socio-economic factor index-2; IV = Intravenous; Other IV Antimicrobials = Acyclovir, Amikacin, Cefazolin, Ceftazidime, Cipro, Daptomycin, Flucanazole, Foscarnet, Meropenem, Micafungin, Penicillin, Piperacillin/Tazobactam, Tobramycin; NS = Normal saline.

Table 4 *(Continued)*

Number (%) of Thrombotic PI PICC Occlusions According to Certain Socio-economic, Clinical, Insertion and PI PICC-related Characteristics

	Cohort		Thrombotic PI PICC Occlusion	
	Number	**%**	**Number**	**%**
Overall	286	100%	51	18%
NS Flush After Infusion				
One Flush	263	92%	38	14%
Other	22	8%	12	55%
Unknown	1	0%	1	100%
NS Flush Between Infusions				
Two Flushes	39	14%	12	31%
No Flush	247	86%	39	16%
NS Flush After Blood Work				
Two Flushes	277	97%	51	18%
Unknown	9	3%		0%
PI PICC Maintenance	68	24%	11	16%
Arm Used				
Right	194	68%	33	17%
Left	90	31%	18	20%
Unknown	2	1%	0	0%
Vein Used				
Basilic Vein	215	75%	37	17%
Brachial Vein	37	13%	9	24%
Cephalic Vein	32	11%	5	16%
Unknown	2	1%	0	0%
Tip Location				
Superior Vena Cava	128	45%	15	12%
Cavoatrial Junction	151	53%	36	24%
Unknown	7	2%	0	0%
Number of Lumens				
Single (Gauge 4, Larger)	239	84%	26	11%
Multiple (Gauge 5, Smaller)	47	16%	25	53%
Dwell Time (Days)				
<40	114	40%	8	7%
≥40	111	39%	34	31%
Unknown	61	21%	9	15%

Note. PI PICC = Power injectable peripherally inserted central catheter; NS = Normal saline; PI PICC Maintenance = PI PICC is not in use for intravenous infusion anymore; Dwell time = Total time since insertion in which PI PICC remained in patient's vein; NS flush after infusion other= 2, 3 or 5 flushes; Dwell Time Unknown = Due to following reasons the dwell time could not be calculated: The insertion and removal dates of PI PICCs were unknown, patients were transferred to their homes to receive their IV infusion therapies from a visiting RN, patients were transferred to the hospitals or to the CancerCare Manitoba, and patients were lost to follow-up.

Table 5

Number and Incidence Rate (per 1,000 person-weeks) of Thrombotic PI PICC Occlusion by Certain Socio-economic, Clinical, Insertion and PI PICC-related Characteristics

	Number	**Total person-weeks**	**Incidence Rate (95% CI)**
Overall	51	1,573	32 (25-43)
Age (years)			
18-50	21	593	35 (23-54)
51-64	20	508	39 (25-61)
≥65	10	472	21 (11-39)
Sex			
Male	29	772	38 (26-54)
Female	22	801	27 (18-42)
SEFI- 2			
More Favorable	22	684	32 (21-49)
Less Favorable	27	874	31 (21-45)
Diabetes			
No	32	974	33 (23-46)
Yes	19	599	32 (20-50)
IV Antimicrobials			
Ceftriaxone	13	740	18 (10-30)
Ertapenem	10	526	19 (10-35)
Vancomycin	16	120	133 (82-218)
Cloxacillin	7	43	163 (78-341)
Other	5	145	34 (14-83)
IV Infusion Administration			
Registered Nurse	39	1,143	34 (25-47)
Patient	12	430	28 (16-49)
Ambulatory Pump Use			
No	43	1,520	28 (21-38)
Yes	8	53	151 (75-301)
PI PICC Maintenance			
No	40	1,008	40 (29-54)
Yes	11	565	19 (11-35)

Note. PI PICC = Power injectable peripherally inserted central catheter; IV = Intravenous, CI = Confidence interval; SEFI-2 = Socio-economic factor index-2, IV Antimicrobials Other = Acyclovir, Amikacin, Cefazolin, Ceftazidime, Cipro, Daptomycin, Flucanazole, Foscarnet, Meropenem, Micafungin, Penicillin, Piperacillin/Tazobactam, Tobramycin;
PI PICC Maintenance = PI PICC is not in use anymore for intravenous infusion.

Table 5 (*Continued*)

Number and Incidence Rate (per 1,000 person-weeks) of Thrombotic PI PICC Occlusion by Certain Socio-economical, Clinical, Insertion and PI PICC-related Characteristics

	Number	**Total person-weeks**	**Incidence Rate (95% CI)**
Arm Used			
Right	33	1,112	30 (21-42)
Left	18	456	40 (25-63)
Vein Used			
Basilic Vein	37	1,296	29 (21-39)
Brachial Vein	9	163	55 (29-106)
Cephalic Vein	5	109	46 (19-110)
Tip Location			
Superior Vena Cava	15	657	23 (14-38)
Cavoatrial Junction	36	857	42 (30-58)
Number of Lumens			
Single (Gauge 4, Larger)	26	1,292	20 (14-30)
Multiple (Gauge 5, Smaller)	25	281	89 (60-131)

Note. PI PICC = Power injectable peripherally inserted central catheter; CI = Confidence interval.

Table 6

Crude Hazard Ratio (95% confidence interval) of the Association between Certain Socio-economic, Clinical, Insertion and PI PICC-related Characteristics and Thrombotic PI PICC Occlusion

	HR (95% CI)	**p-value**
Age (years)		
18-50	ref.	
51-64	1.1 (0.6-2.1)	0.663
≥65	0.7 (0.3-1.5)	0.374
Sex		
Male	ref.	
Female	0.9 (0.5-1.5)	0.594
SEFI-2		
More Favorable	ref.	
Less Favorable	1.1 (0.6-1.8)	0.861
Diabetes		
No	ref.	
Yes	0.9 (0.5-1.7)	0.841
IV Antimicrobials		
Ceftriaxone	ref.	
Ertapenem	1.4 (0.6-3.3)	0.412
Vancomycin	6.8 (3.3-14.1)	<0.001
Cloxacillin	7.3 (2.9-18.3)	<0.001
Other	2.2 (0.8-6.3)	0.138
IV Infusion Administration		
Registered Nurse	ref.	
Patient	0.9 (0.5-1.8)	0.840
Ambulatory Pump Use		
No	ref.	
Yes	3.9 (1.8-8.3)	<0.001

Note. PI PICC = *P*ower injectable peripherally inserted catheter; IV = Intravenous, IV Antimicrobials Other = Acyclovir, Amikacin, Cefazolin, Ceftazidime, Cipro, Daptomycin, Flucanazole, Foscarnet, Meropenem, Micafungin, Penicillin, Piperacillin/Tazobactam, Tobramycin; SEFI-2 = Socio-economic factor index 2.

$p < 0.05$.

Table 6 *(Continued*

Crude Hazard Ratio (95% confidence interval) of the Association between Certain Socio-economical, Clinical, Insertion and PI PICC-related Characteristics and Thrombotic PI PICC Occlusion

	HR (95% CI)	**p-value**
PI PICC Maintenance		
Yes	ref.	
No	1.8 (0.9-3.5)	0.102
Arm Used		
Right	ref.	
Left	1.2 (0.7-2.1)	0.541
Vein Used		
Basilic Vein	ref.	
Brachial Vein	1.7 (0.8-3.4)	0.179
Cephalic Vein	1.1 (0.4-2.9)	0.815
Tip Location		
Superior Vena Cava	ref.	
Cavoatrial Junction	2.2 (1.2-4.0)	0.011
Number of Lumens		
Single (Gauge 4, Larger)	ref.	
Multiple (Gauge 5, Smaller)	6.2 (3.6-10.8)	<0.001

*Note. PI PICC = P*ower injectable peripherally inserted catheter; PI PICC Maintenance = PI PICC is not in use for IV infusion anymore.

$p < 0.05$.

Table 7

Adjusted[a] Hazard Ratio (95% confidence interval) of the Association between Certain Clinical, Insertion and PI PICC-related Characteristics and Thrombotic PI PICC Occlusion

	HR (95% CI)	**p-value**
IV Antimicrobials		
Ceftriaxone	ref.	
Ertapenem	1.0 (0.4-2.5)	0.924
Vancomycin	5.8 (2.8-12.3)	<0.001
Cloxacillin	3.3 (0.4-28.5)	0.272
Other	1.9 (0.6-5.9)	0.268
Ambulatory Pump Use		
No	ref.	
Yes	1.3 (0.2-8.9)	0.822
Tip Location		
Superior Vena Cava	ref.	
Cavoatrial Junction	1.8 (1.0-3.5)	0.067
Number of Lumens		
Single (Gauge 4, Larger)	ref.	
Multiple (Gauge 5, Smaller)	5.1 (2.8-9.1)	<0.001

*Note. PI PICC = P*ower injectable peripherally inserted catheter; IV = Intravenous.
[a] Adjusted by the covariates listed in the table.

$p < 0.05$.

Figure 1

Survival Time of PI PICCs by the type of IV Antimicrobials

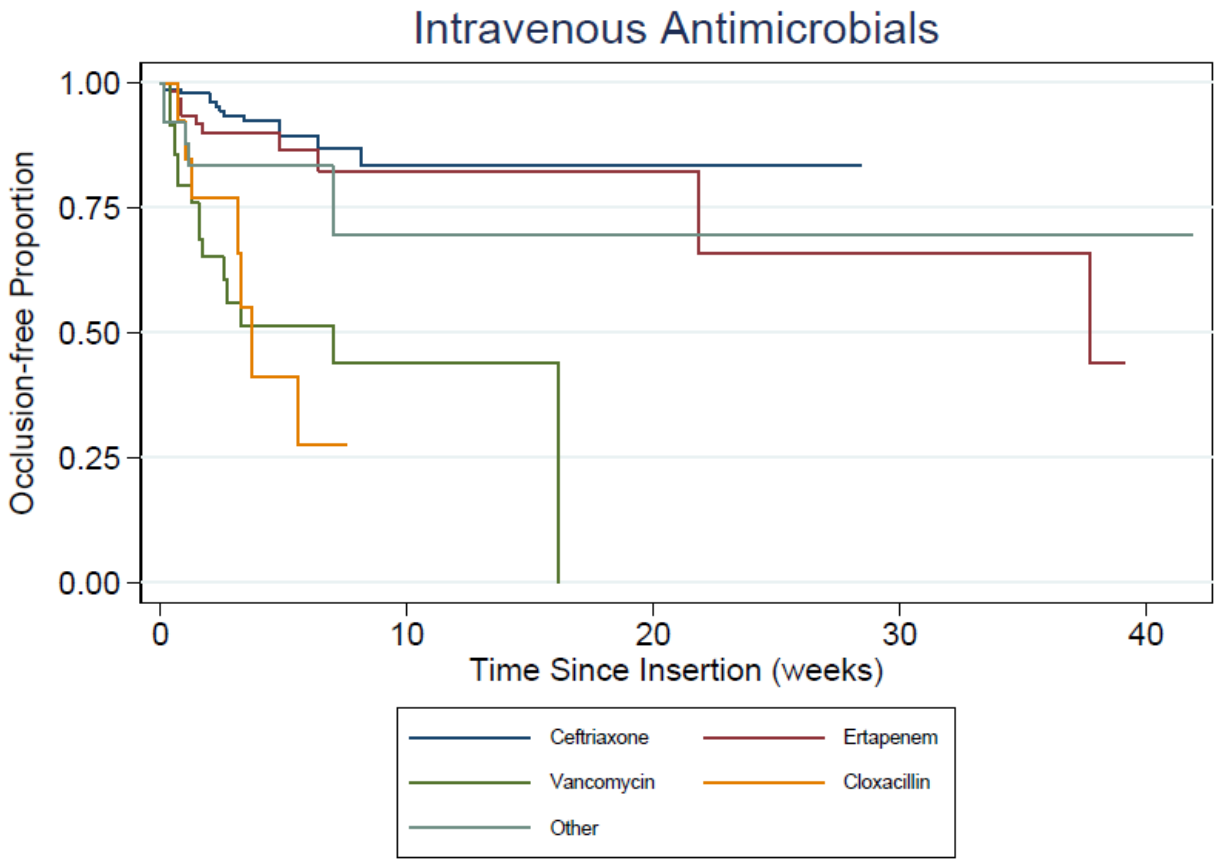

Figure 2

Survival Time of PI PICCs by Ambulatory Pump Use

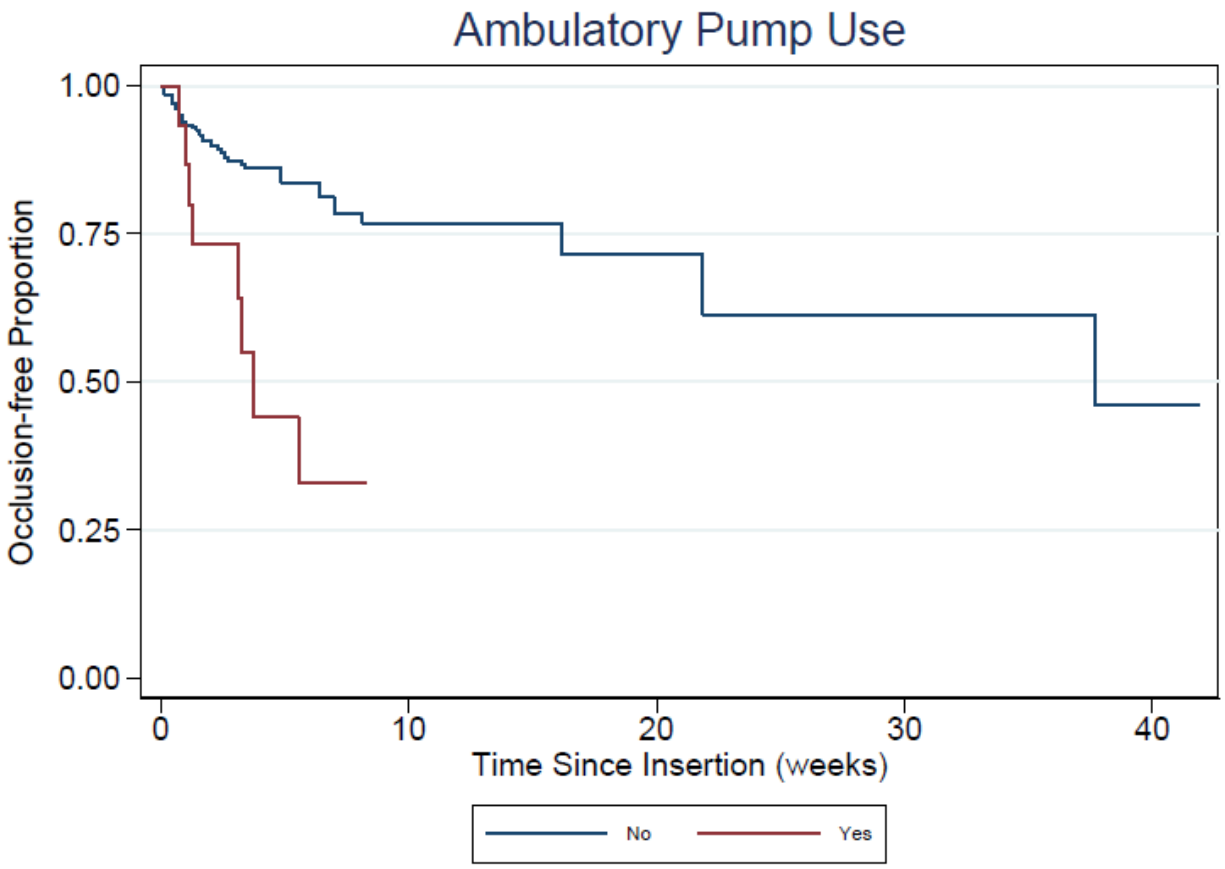

Figure 3

Survival Time of PI PICCs by the Tip Location

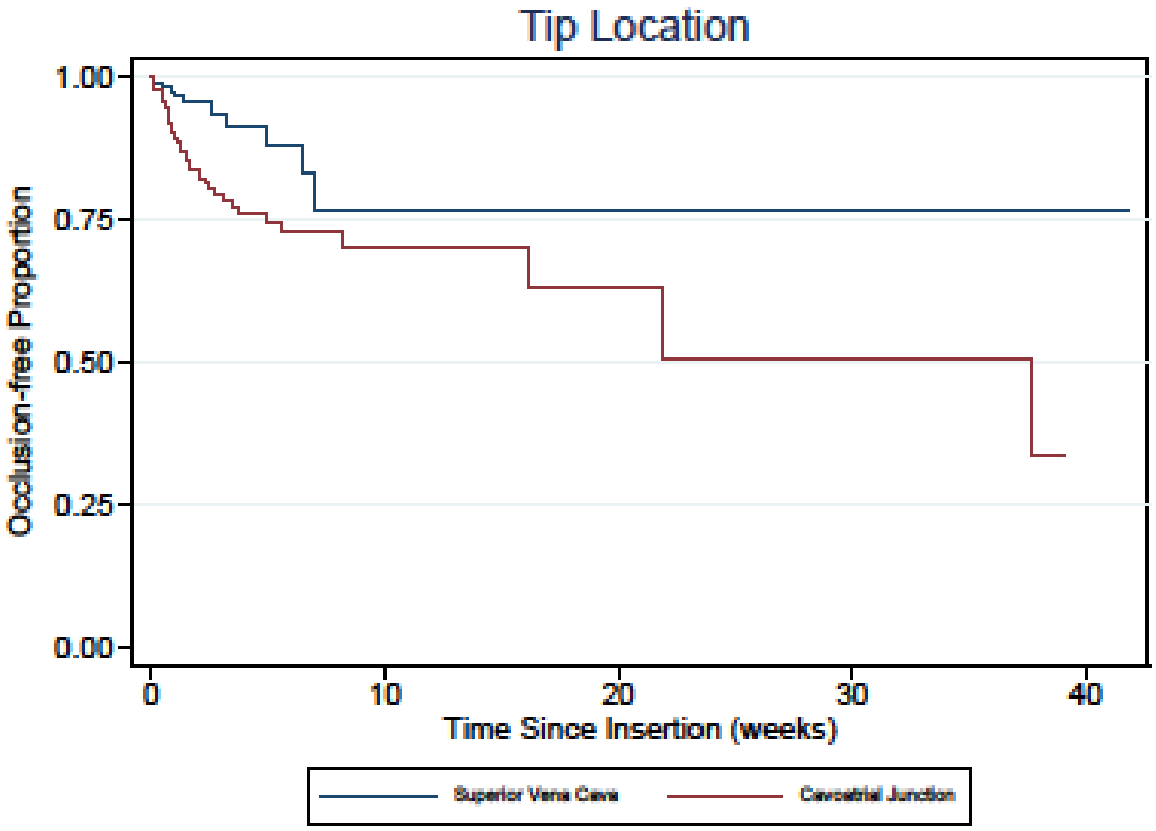

Figure 4

Survival Time of PI PICCs by the Number of PI PICC Lumens