Minireview Article

Abstract: A review of the intraluminal fluid pathway to prevent catheter related

bloodstream infections and occlusions

4

1

2

3

5 The most common complications associated with vascular access devices are catheter related 6 bloodstream infections (CR-BSI), which occur in acute care patients every minute, and 7 occlusions. This review will address major issues associated with patient care and research associated with vascular access and intravenous connectors including descriptions of different 8 types of connectors, care and maintenance issues such as septum disinfection and flushing, 9 education of students and practitioners, a new framework for research, and relevant questions 10 for healthcare practitioners to ask during patient assessment. This review includes two overall 11 12 strategies to prevent CRBSI's and occlusions;1) prevent the active and passive migration of 13 microorganisms into the fluid pathway and 2) prevent microorganism adhesion to the catheter surface. The connector, which is placed on the end of a catheter, is the gatekeeper to the 14 intraluminal fluid pathway and its design directly impacts the success of strategies to prevent 15 complications. Best practice requires that practitioners have specific knowledge of connector 16 17 technology as well as patient factors for caring for vascular access devices. There is a large gap in the scientific literature and in policies and procedures related to evidenced based 18 decision making associated with care and maintenance of needleless intravenous connectors. 19

22

23

20

21

Key words: CRBSI, sepsis, connectors, nursing care, vascular access, occlusions

A review on connectors is necessary to meld research and practice together for best patient

practices, so the occurrences of CRBSI's and occlusions can be mitigated and eliminated.

24

25

26

A Review of theIntraluminal Fluid Pathway to Prevent Catheter Related Bloodstream

Infections and Occlusions

Background

27

28

29

30

31

32

33

34

35

36

37

38

39

40

41

42

43

44

45

46

47

48

49

50

51

52

A patient obtains a catheter related bloodstream infection every minute and this can lead to a diagnosis of sepsis which is the most costly hospital acquired infection withup to a 50% mortality rate. 2Catheter occlusions result in loss of vascular access, loss of time for treatments and increased length of stay. Any of these negative outcomes causes a poorer quality of life for the patient. The importance of understanding current research on connectors and its association with their care, maintenance and educational needs is imperative to professional best care practices. The intravenous catheter, whether centrally or peripherally placed, is an extension of the venous system to the outside environment. As a result, a hole in the skin referred to as the insertion site (extraluminal) and the hole in the catheter (intraluminal) are entry points for bacteria, yeast and fungus. The role of nursing practice in caring forthe intraluminal pathway is to prevent treatment-related complications so that every vascular access device (VAD) remains safely in place and complication free for the durationthe VAD is needed (brief or prolonged). The two most common complications associated with the intraluminal pathway are CR-BSI³ and occlusion. Best practices for extraluminal care^{4,5} are reported to only prevent 40% of bloodstream infections⁶. Therefore, 60% of CR-BSIs have causes that are intraluminal in nature. Intraluminal CR-BSIs occur when organisms, in particular bacteria, migrate into the fluid pathway and adhere to the pathway wall. Once attached, the bacteria form a colony and develop a protective cover referred to as biofilm. When biofilm is formed it is difficult to eradicate the colony and infection can occur and proliferate. The cost of CR-BSIs has been calculated to be approximately \$33,000-\$35,000 (£20,915-22,183) per episode making it a relevant cost issue^{7,8,9}. Four major pathogens (*Staphylococcus epidermidis*, *Staphylococcus aureus*,

54

55

56

57

58

59

60

61

62

63

64

65

66

67

68

69

70

71

72

73

74

75

76

77

Pseudomonas aeruginosa. Escherichia coli) are responsible for 60% of CR-BSIs at a total cost of \$225 (£ 143) million per year and 200,000 intensive care unit days/year ¹⁰. Occlusions are common¹¹ and under reported and about half are directly related to thrombus formation¹². Occlusion is also related to fluid pathway design with the best design to minimize occlusions being a connector that is short, small, has a straight fluid pathway and minimal reflux on connection and disconnection. Intraluminal reflux related thrombi rates are reported as 5%-25%¹³ and connector use is associated with varying amounts of reflux and thereforethe connector is directly related to intraluminal thrombi¹⁴. Fibrin deposition on the intraluminal surfaces of the intravenous (IV) connector fluid pathway and catheter has been shown to also increase the risk of coagulase-negative staphylococci infection¹⁵. Therefore, through several mechanisms thrombosis has been shown to enhance the risk of infection¹⁶. Interestingly prevention of occlusions may rely heavily on patient assessment and this has not been recognized by healthcare practitioners. **IV Connectors Overview** The IV connector is referred to by many different names such as "hep-locks", "male adaptors", "Luer-locks", "split septums" and "INTs" to name a few. Needleless connectors were developed in the 1990's as a means of preventing needle sticks and decreasing the potential for human immunodeficiency virus transmission. During the last decade research findings have questioned the role of IV connectors by category and as contributors to CR-BSI^{17,18}. In 2010, nine design features were outlined as variables that impacted CR-BSI including: septum surface, septum seal, fluid pathway, dead space, internal mechanism, clamping sequence, visibility, blood reflux and flushing solution¹⁹. All IV connectors available today have four elements in common: an external housing, a septum which is the entry point of the connector, a fluid pathway, and a mechanism for returning

the septum to its original closed position with disconnection. Dead space, which exists in most

78 connectors, refers to areas within the fluid pathway that cannot be cleared when flushing. The 79 designs of these four elements vary greatly from connector to connector. There are three major types of needleless intravenous connectors based on reflux known as 80 negative, positive, and neutral fluid displacement²⁰. Connector designs evolved over a decade 81 82 with changes made to improve usability and to minimize occlusion associated with their use. The first type is negative mechanical valves (NMV). Reflux occurs with disconnection. Total or 83 partial occlusion^{12,14} is associated with NMV reflux. In addition NMVs have been associated with 84 CR-BSI²¹. The second type is positive pressure mechanical valves (PPMV) and with this type 85 reflux occurs with connection. Positive connectors have been associated with increased 86 bloodstream infections^{22,23}. These are under FDA (USA) investigation for possibly causing 87 deaths²⁴. The last and most recent type is neutral. Withneutralconnectors there is no reflux with 88 89 either connection ordisconnection. Several studies reveal that specific connectors are associated with an increased risk of blood stream infections^{21,22,25,26} including positive-pressure 90 connectors 17,27. 91 It is not one design feature that is important in connector design and their associated outcomes, 92 but the combination of all the design features outlined by Dr. Jarvis 19 that will impact 93 94 complication reductions and eliminations. **Care & Maintenance of Connectors** 95 Strategies to prevent intraluminal complications must be two-pronged; 1) prevent the active and 96 passive migration of microorganisms into the intraluminal fluid pathway, and 2) prevent catheter 97 wall adhesion. This approach will prevent bacterial colonization and biofilm formation. 98 Nursing has only two actions for intraluminal care within their domain of practice: swabbing the 99 100 connector septum for disinfection and flushing the fluid pathway to remove residue after use. 101 **Septum Disinfection of Connectors** Septum disinfection is the first action necessary to prevent bacterial migration. Today, 70% 102 103 alcohol alone or Chlorhexidine (CHG) alcohol are the two most commondisinfection agents

105

106

107

108

109

110

111

112

113

114

115

116

117

118

119

120

121

122

123

124

125

126

127

128

129

selected by institutions in the United States. Alcohol biocide activity occurs while wet. It dehydrates the cell surface causing cell destruction. CHG must enter the cell and disrupt the cell contents to cause cell death. So while alcohol is active when wet, CHG must dry to be effective.CHG's greatest benefit is persistence when applied to the skin. There is minimal research associated with its benefits when applied to inanimate objects. Appropriate septum disinfection is a significant part of care. Even with conventional disinfection with 70% alcohol one study of NMVs revealed 67% transmit microorganisms ranging from 442 to 25,000 colonyforming units²⁸ and it is known that greater than 15 colony-forming units can lead to sepsis²⁹. Another studyrevealed a range of colony forming units for different connectors, post 70% alcohol swab using downward pressure and 3 rotations, to range from zero to over 13,500 for 4 different bacteria lending data to the knowledge base that connectors are a significant variable in the development of infections³⁰. The IV connector must be swabbed before each access. Thisprotocol results in three or four(if using heparin as a final flush) separate swabbing procedures with each IV push medication or blood draw. It is common for connectors to be accessed repeatedly during a patient care shift. In the US, there has been an increase in swabbing times to 15-30 seconds in an attempt to improve disinfection. This action has placed the entire burden on the nurse and may not be clinically realistic. Connector design has not been considered even though research has confirmed that complete disinfection of some IV connectors septum's surfaces is difficult and in fact may not be achievable at high rates in the clinical setting^{28, 31}. To increase septum disinfection success, the septum should be made of hydrophobic material and be smooth without irregularities to prevent bacteria from sticking. The septum seal should be tight when not activated so that there are no areas that lie outside disinfectant contact. When relying on research to set the swabbing practice, it is important to remember that generalization of research findings to connectors not included in the study is problematic. Long, complicated swabbing practices are cumbersome and difficult to consistently perform in the clinical setting.

Selecting a connector that can be swabbed easily with > 99% bacterial kill will improve compliance. Ask manufacturers of connectors for independent research in this area and if they have none be weary of using the product. If the manufacturer tells you to follow your hospital policy on scrubbing the hub do NOT accept this as valid as it is not research based and is actually an admission that the manufacturers have no research on their product. This lack of research and evidence does not support evidence based nursing practice and can be detrimental to patient outcomes. Research on one product, Invision-Plus® (RyMed Technologies, Inc., TN, USA), validated through aninvitro study by Nelson laboratories (Salt Lake City, UT) showed that 3-5 twists of swabbing with 70% alcohol pad, like squeezing an orange, removes 100% of bacteria³².

Flushing of Connectors

Fibrin deposition on the intraluminal surfaces of the fluid pathway increases the risk of coagulase-negative staphylococci infection¹⁵ and occlusions. Thrombosis has been shown to enhance the risk of infection¹⁶ and makes flushing difficult or impossible. In order for flushing to be successful, the fluid pathway must be straight. This is because fluid follows the path of least resistance. This means that anything outside this pathway will not come in contact with the flushing solution. These areas outside the pathway continue to have blood and medication residueproviding an environment forbacterial growth. Edminston³⁴ inoculated connector intraluminal fluid pathways and reported that increased intraluminal fluid pathway volume corresponds to higher organism growth rates. With a larger internal volume there was increased area outside the fluid pathway. A small unobstructed, straight fluid pathway provides an area where 100% of the pathway surface comes into contact with the flush. An invitro study showed that a connector designed with a very small priming volume (0.027 mL)and using as little as 1 mL saline flush 99.96% and with 4 mL saline that 100% of microscopic hemoglobin was removed³⁵.

It is practice in some institutions in the US to use a push-pause flushing method. This practice became very popular because it was hypothesized that fluid turbulence enhances the "scrubbing" action of the flush. No research is available to support this practice. Donlan³⁵, a leader in biofilm science, reported in 2002 that turbulent flow actually enhances bacterial adhesion and that a steady flush minimizes adhesion. No research exists that focuses flushing on patient need yet many patients are at high risk for occlusion (see below).

Table 1: Patients At High Risk For Vascular Access Occlusion

Acute Spinal Cord Injury
Advanced Age
Bone Marrow Transplant
Brain Tumor
Catheters Placed via the Left Subclavian Vein
Catheter Tip Location in Subclavian Vein
Chronic Obstructive Pulmonary Disease
Dehydration
Diabetes
High Platelet Levels
History of Deep Vein Thrombosis
Lung Cancer
Major Trauma Gynecologic Malignancies
Malposition of the Catheter
Oral Contraceptive Use
Pregnancy
Renal Failure
Sickle Cell Anemia
Trauma Patients

Performing the identical flushing procedures with all patients may result in uneven outcomes and research is needed in this area. Using a final heparin flush is also problematic. Heparin is a protein derived from pigs. This protein becomes food for bacterial colonies. Also heparin is associated with a serious complication known as heparin induced thrombocytopenia (HIT). Numerous medications are incompatible with heparin and must be completely flushed before heparin is instilled making compliance in care more difficult. Because of certain connector pathway designs, residue remains in the dead space adding to bacterial growth and biofilm formation environments. Hence, we do not recommend the use of heparin as common practice.

172

173

174

175

176

177

178

179

180

181

182

183

184

185

186

187

188

189

190

191

192

193

194

195

196

Negative and positive connectors have reflux associated with usage. Since reflux occurs either with disconnection (NNV) or connection (PPV) mitigating reflux depends on the nurses' ability to identify the connector by type and then apply the correct clamping sequence²⁰ either before disconnection clamping (NNV) or after disconnection(PPV). Additionally, when using the Y-port on anyIV administration tubing a clamping sequence cannot be used and reflux cannot be mitigated. Many institutions stock more than one type of connector necessitating the nurse to visually identify the connector type and then select the correct clamping sequence. The package label usually does not identify the connector type or which clamping sequence to use. This makes the nurse's job more difficult. Using the wrong sequence means that occlusion is more prevalent when using a negative pressure system^{36,37} with reflux occurring with disconnection. Occlusion incidence is much less using one neutral connector³⁸. Selecting one IV connector to be used exclusively enhances education and ultimately improves procedure compliance¹⁷. New research has reported that for flushing ports the nurse needs to make sure that the needle bevel is in an upward/top direction before flushing. This placement improves the fluid flow path, enhancing cleaning³⁹. Knowledge about connector design and associated best flushing practices will help in overcoming CRBSIs and occlusions.

EDUCATION

The prevention of CR-BSIs⁴⁰ and occlusions are possible but requires education of healthcare providers on cause, care and maintenance actions related to the specific IV connector, and continual recent research evaluation with associated implementation of policy and practice changes. Research reveals that 78% of acute care nurses are uninformed about different connector types and their specific, yet opposing, care⁴¹. Forty three percent of nurses could not name 2 complications associated with IV connectors (e.g.: infection, occlusion, thrombosis) and 64% are involved with 4 to 5 hours of IV therapy care and maintenance per 12 hour nursing shift, making IV therapy an important clinical issue and educational necessity⁴¹. However, there are neither courses nor enough lectures in most nursing programs on IV therapy, though

198

199

200

201

202

203

204

205

206

207

208

209

210

211

212

213

214

215

216

217

218

219

220

221

222

information related to science and research has resulted in several books being published in the area of IV therapy. The ability of nurses to collect cues related to IV connector problems begins with education on information that is basic, understandable, differentiating and complete to aid in clinical reasoning. Patient assessment, knowledge of technology and specific nursing care are required to best protect the intraluminal fluid pathway of VADs^{1,42-45}. Without knowledge and appropriate nursing interventions intraluminal protection becomes compromised and there can be an increase in CR-BSI, occlusions, thrombi and potential associated deaths.

Framework for Research

For nursing and medical research associated with VADs the Healthcare AndTechnology Synergy (HATS) framework (Figure 1) is appropriate. This framework ⁴⁶ represents a synergy between three major variables (patient, product, practice) with each one affecting the others and being affected by the others. All of the variables can have an impact on healthcare outcomes. This framework adds a more holistic and comprehensive approach to comparative effectiveness and evidence based practice research and when translating findings to bedside care. Using connectors as an example the patient variables to be considered, though not an exhaustive list, include age, diagnosis, comorbidities, therapeutic regimens, projected length of stay, physical assessment, mental health status, transcultural beliefs, finances, and length of treatment including current needs and recurring needs. Product variables may include the following: intravenous connectors categorized on the basis of reflux as well as bacterial and biofilm growth as previously discussed, connector septum design including septum seal tightness, fluid pathway design, type of VAD, insertion site, and number of catheter lumens. Practice variables may include connector septum disinfection practice, dressing management, clamping sequence, flushing practice including solution(s) and time frequency (eg: 10 mL normal saline every 6 hours), the education and skill levels of the nurse specific to vascular access, availability of specialized vascular access teams, and nurse-patient staffing ratios. Research in some of these areas have already been implemented, presented and/or published^{41, 42, 47-52}.

223 **Patient IV Connector Assessment** What type of connector does my patient have? Is it negative, positive orneutral? 224• Do I have the materials, skills and knowledge to correctly implement scrubbing the hub and 225• 226 flushing? 227• Do I have the knowledge to implement appropriate disconnection? How often should I change the connector? This time frame should be specifically stated by 228• 229 the manufacturer as "follow your usual hospital policy" is meaningless to nursing care. Does my patient have a three way stop cock? The use of stop cocks increased bloodstream 230• infections when compared to disinfectable needlefree-connectors⁵³. 231 Summary 232 Connector design and category impact occlusion and CR-BSI rates 233• 234• Connector design impacts nursing disinfection and flushing practice success 235• Best practice requires that health care professionals have specific knowledge of connector technology aswell as patient factors for caring for vascular access devices. 236 The more desirable design features a connector has included in its final product the more user 237• friendly the connectorwill be and the less complications you will encounter. 238 239• Without specific knowledge regarding connector technology there is an increase in the potential 240 for sepsis, catheter occlusion and death. When the connector surface is not properly disinfected, flushed, and/or disconnected 241• thenbacteria can enter the intraluminal fluid pathway, adhere to the internal surface, 242 243 colonize and develop biofilm increasing the risk for patient infection and sepsis. Healthcare providers should demand that manufactured connector devices be developed 244• with fail-safe engineering advances aimed at further mitigation of risk of infection in the 245 246 complex hospital environment and devices that include ease of use by the nurse. The 247 addition of alcohol caps is another step for nurses to implement and one that should not be necessarywith a properly designed connector. Additional steps also increase human error. 248

249•	Instituting the "Healthcare And Technology Synergy (HATS)" framework that includes "Patient,
250	Practice, Product", into intravenous practice settings and within research is paramount to a
251	better understanding of intraluminalvascular access infections.
252•	The frequent usage and care of connectors in all healthcare settings makes connectors
253	significantvariables for practice and comparative effectiveness and outcomesresearch.
254•	There are large gaps in the scientific literature, policies and procedures in regards to unbiased
255	evidenced based decision making, care and maintenance related to needleless connectors.
256	CONCLUSIONS
257	An increased knowledge of connector design and evidence based practice can prevent CRBSI's
258	and occlusions through preventing the active and passive migration of microorganisms into the
259	fluid pathway and preventing microorganism adhesion to the catheter surface. The connector,
260	as the gatekeeper to the intraluminal fluid pathway, plays a significant and vital role in the
261	prevention of patient complications, including death. CRBSIs are related to septum design and
262	fluid pathway design of connectors and occlusions are related to fluid pathway design of
263	connectors. The best designed connector should have all design features 19 not just zero reflux.
264	Best practice requires utilization of research in the development and implementation of policy
265	and procedures associated with needleless intravenous connector care and maintenance. Also,
266	the potential of value enhanced purchasing can best be accomplished through inclusion of
267	evidence. Through a combination of research and education there could be a very significant
268	decrease in 'one every minute' CRBSI's and vascular access catheter occlusions.
269	
270	
271	
272	
273	
274	

References

275

- 1. Macklin D. Catheter management. Seminars in Oncology Nursing. 2010;26(2):113-
- 277 20.DOI:10.1016/j.soncn.2010.02.002
- 278 2. Angus DC, Linde-Zwirble WT, Lidicker J, Clermont G, Carcillo J, Pinsky MR. Epidemiology of
- 279 severe sepsis in the United States: analysis of incidence, outcome, and associated costs of
- 280 care. Crit Care Med. 2001; 29(7):1303-10.
- 3. Jones CA. Central venous catheter infection in adults in acute hospital settings. Brit J
- 282 <u>Nurs.</u>2006;15(7):362,364-68.
- 4. Pronovost PJ, Marsteller JA, Goeschel CA. Preventing bloodstream infections: A measurable
- rational success story in quality improvement. Health Affairs.2011;30(4):628-34.doi:
- 285 10.1377/hlthaff.2011.0047.
- 5. Pronovost P, Needham D, BerenholtzS, Sinopoli D, Chu H, Cosgrove S, et al. An intervention
- to decrease catheter-related bloodstream infections in the ICU.N Engl J Med.
- 288 2006;355(26):2725-32.
- 6. Rosado V, Romanelli RM de C, Camargos PAM. Risk factors and preventive measures for
- catheter-related bloodstream infections. Jornal de pediatria (Brazil). 2011;87(6):469-
- 291 77.doi:10.2223/JPED.2134.
- 7. Arnow PM, Quimosing EM, Beach M. Consequences of intravascular catheter
- 293 sepsis.ClinInfec Dis. 1993;16(6):778-84.
- 8. Pittet D, Tarara D, Wenzel RP. Nosocomial bloodstream infections in critically ill patients:
- Excess length of stay, extra costs and attributable mortality. JAMA.1994; 271(20):1598-1601.
- 9. Rello J, Ochogavia A, Sabanes E, Roque M, Mariscal D, Reynaga E, et al. Evaluation of
- 297 outcome of intravenous catheter-related infections in critically ill patients. Am J RespirCrit Care
- 298 Med. 2000;162(3 Pt 1):1027-30.
- 10. Tacconelli E, Smith G, Hieke K, Lafuma A, Bastide P. Epidemiology, medical outcomes and
- 300 costs of catheter-related bloodstream infections in intensive care units of four European

- 301 countries: Literature- and registry-based estimates. J Hosp Infect. 2009;72(2):97-103. doi:
- 302 10.1016/j.jhin.2008.12.012.
- 11. Baskin JL, Pui CH, Reiss U, Wilimas JA, Metzger ML, Ribeiro RC, et. al. Management of
- occlusion and thrombosis associated with long-term indwelling central venous catheters.
- 305 Lancet;2009;374(9684):159-69. doi: 10.1016/S0140-6736(09)60220-8.
- 12. Rummel MA, Donnelly PJ, Fortenbaugh CC. Clinical evaluation of a positive pressure
- device to prevent central venous catheter occlusion: Results of a pilot study. Clin J OncNurs.
- 308 2001;5(6):261–5.
- 13. Rosovsky RP, Kuter DJ.Catheter-related thrombosis in cancer patients: pathophysiology,
- diagnosis, and management. HematolOnc Clinic North Amer.2005;19(1):183–202.
- 14. Garland JS, Alex CP, Sevallius JM, Murphy DM, Good MJ, Volberding AM, et al. Cohort
- 312 study of the pathogenesis and molecular epidemiology of catheter-related bloodstream infection
- in neonates with peripherally inserted central venous catheters. Infect Control HospEpidemiol.
- 314 2008;29(3):243-49.<u>http://dx.doi.org/10.1086/526439</u>
- 15. van Rooden CJ, Schippers EF, Guiot HF, Barge RM, Hovens MM, van der Meer FJ, et al.
- 316 Prevention of coagulase-negative staphylococcal central venous catheter-related infection using
- urokinase rinses: a randomized double-blind controlled trial in patients with hematologic
- 318 malignancies. J ClinOncol.2008;26(3):428-33.doi: 10.1200/JCO.2007.11.7754.
- 16. Jacobs BR. Central venous catheter occlusion and thrombosis. Crit Care
- 320 Clinic.2003;19(3):489-514.
- 17. Jarvis WM, Murphy C, Hall KK, Fogle PJ, Karchmer TB, Harrington G, et al. Healthcare-
- associated bloodstream infections associated with negative- or positive-pressure or
- displacement mechanical valve needleless connectors. Clin Infect Dis. 2009;49(12):1821-27.
- 18. Maragakis LL, Bradley KL, Song X, Beers C, Miller MR, Cosgrove SE, et al. Increased
- catheter-related bloodstream infection rates after the introduction of a new mechanical valve
- intravenous access port. Infect Control HospEpidemiol. 2006;27(1):67-70.

- 19. Jarvis WR. Choosing the best design for intravenous needleless connectors to prevent
- 328 bloodstream infections.2010. Retrieved on 07/15/2010 from
- 329 http://www.infectioncontroltoday.com
- 20. Chernecky C, Macklin D, Casella L, Jarvis E. Caring for patients with cancer through
- nursing knowledge of IV connectors. Clin J OncolNurs. 2009;13(6):630-33.
- 21. Field K, McFarlane C, Cheng AC, Hughes PJ, Jacobs E, Styles K, et al. Incidence of
- catheter-related bloodstream infection among patients with a needleless, mechanical valve-
- based intravenous connector in an Australian hematology-oncology unit. Infect Control
- 335 HospEpidemiol. 2007;28(5):610-13.
- 22. Rupp ME, Sholtz LA, Jourdan DR, Marion ND, Tyner LK, Fey PD et al. Outbreak of
- bloodstream infection temporally associated with the use of an intravascular needleless valve.
- 338 Clin Infect Dis. 2007;44(11):1408-14.
- 23. Jarvis W, Sheretz R, Peri T, Bradley K, Giannetta E. Increased central venous catheter-
- associated bloodstream infection rates temporally associated with changing from a split-septum
- to a luer-access mechanical valve device: A nationwide outbreak? In: Program and abstracts of
- the 32nd Annual Educational Conference and International Meeting of the Association of
- Professionals in Infection Control and Epidemiology, June 20-23, 2005: Baltimore, MD.
- 24. Food & Drug Administration. Letter to Infection Control Practitioners Regarding Positive
- Displacement Needleless Connectors, July 2010. Retrieved September 31, 2010 from
- 346 http://www.fda.gov/MedicalDevices/Safety/AlertsandNotices/ucm220459.htm
- 25. Karchmer TB, Cook E, Palavecino E, Ohl C, Sherertz R. Needleless valve ports may be
- associated with a high rate of catheter-related bloodstream infection [abstract 307].
- 349 2005(04/09/2005 04/12/2005); In Proceedings of the 15th Annual Scientific Meeting of the
- 350 Society for Healthcare Epidemiology of America, Los Angeles, CA.
- 351 26. Rosenthal K. Do needleless connectors increase bloodstream infection risk? Nurs
- 352 Management.2006;3*7*(4):78-80.

- 27. Marschall J, Mermel LA, Classe D, Arias KM, Podgorny K, Anderson DJ, et al. Strategies to
- prevent central line-assocaited bloodstream infections inacute care hospitals. Infect Control
- 355 HospEpidemiol. 2008;29(Suppl 1):S22-30. Doi: 10.1086/591059
- 28. Menyhay SZ, Maki DG. Disinfection of needleless catheter connectors and access ports
- with alcohol may not prevent microbial entry: The promise of a novel antiseptic-barrier cap.
- Infect Control HospEpidemiol. 2006;27(1): 23-7.
- 29. Maki DG, Weise CE, Sarafin HW. A semiquantitative culture method for identifying
- intravenous-catheter-related infection.N Engl J Med.1977;296(23):1305-09.
- 30. Chernecky C, Waller J. In Vitro Comparisons of two Antimicrobial intravenous
- 362 Connectors.ClinNurs Res: An Internat J.2011;20(1):101-09.
- 363 31. ArduinoMJ, Bland LA, Danzig LE, McAllister SK, Aguero SM. Microbiologic evaluation of
- needleless and needle-access devices. Am J Infect Control. 1997;25(5):377-80.
- 365 32. RyMed Technologies, Inc. Disinfection swabbing study for the Invision-Plus® with neutral
- advantage™ technology. Nelson Laboratories, Inc, Nos. 395445 and 398575.Retrieved
- December 16, 2013 fromhttp://rymedtech.com/assets/files/InVision-
- 368 Plus%20Swabbing%20Disinfection%20Study.pdf, 2009a.
- 33. RyMed Technologies, Inc. Blood Clearing Study for the InVision-Plus® with Neutral
- 370 Advantage[™]Technology. Nelson LaboratoriesInc, No.458652. Personal communication P.
- 371 Blackburn, RyMed Technologies, Inc, December 16, 2013,2009b.
- 372 34. Edmiston CE, Markina V. Reducing the risk of infection in vascular access patients: An in
- 373 vitro evaluation of an antimicrobial silver nanotechnology luer activated device. Am J Infect
- 374 Control. 2010;38(6):421-23.doi:10.1016/j.ajic.2009.09.010
- 35. Donlan RM.Bioflms: Microbial life on surfaces. Emerg Infect Dis. 2002;8(9):881-90.
- 36. Jacobs BR, Schilling S, Doellman D, Hutchinson N, Rickey M, Nelson S. Central venous
- catheter occlusion: A prospective, controlled trial examining the impact of a positive-pressure
- valve device. JPEN: J Parenteral Enteral Nutrition. 2004;28(2):113-18.

- 37. Casell, L. Jarvis E. Save a patient's line with positive pressure. Acute & Critical Care
- Special Interest Group Newsletter; 2007. Oncology Nursing Society, Pittsburgh, PA., pp. 3-4.
- 38. Caillouet B. The evolution of the injection cap-combining staff safety and patient safety: An
- 382 M.D. Anderson research study. Presented at the 22nd Annual Association for Vascular Access
- Conference, September 11, Savannah, GA; 2008.
- 39. GuiffantG, Durussel JJ, Flaud P, Vigier JP, Merckx J. Flushing parts of totally implantable
- venous access devices, and impact of the Huber point needle bevel orientation: Experimental
- tests and numerical computation. Medical Devices: Evidence and Research. 2012; 5(1):31-
- 37.DOI: http://dx.doi.org/10.2147/MDER.S30029
- 40. Harnage S. Achieving zero catheter related blood stream infections: 15 months success in
- a community based medical center. JAVA.2007;12(4):218-24.
- 41. Chernecky C, Casella L, Jarvis E, Macklin D, Rosenkoetter M. Nurses' knowledge of
- intravenous connectors.J Res Nurs;2010;15 (5):405-16.
- 42. Chernecky C, Jarvis WR, Waller JL, Macklin D. Clinical comparisons of split septum,
- 393 positive and negative mechanical valve intravenous connectors to an intraluminal protection
- connector on infection rates. Poster, The 2011 Council for the Advancement of Nursing Science
- 395 Special Topics Conference, Washington DC, October 12, 2011.
- 396 43. Chernecky C, Macklin D. Improving hospital acquired infections with a practice bundle.
- Podium, World Congress on Vascular Access. Amsterdam, Netherlands June 27-29, 2012.
- 398 44. Cook D, Meyer T. Luer activate device priming volume as a predictor of biofilm
- formation in an in vitro assay. Poster presentation at the Society for Healthcare Epidemiology
- 400 of America, Baltimore, MD, 2007.
- 401 45. Macklin D. The impact of IV connectors on clinical practice and patient outcomes. JAVA
- 402 2010;15(3):126-39.

403 46. Chernecky C, Zadinsky J, Macklin D, Maeve MK. The healthcare and technology 404 synergy (HATS) model for comparative effectiveness research as part of evidence based practice in vascular access. JAVA;2013;18(3):169-74.doi: 10.1016/j.java.2013.05.001 405 406 47. Chernecky C, Waller J, Jarvis W. In-vitro Study Assessing the Antibacterial Activity of Three 407 Silver-Impregnated/Coated Mechanical Valve Needleless Connectors after Blood Exposure.Am J Infect Control. 2012;41(3):278-80. doi:10.1016/j.ajic.2012.03.020 408 409 48. Macklin D, Chernecky C, Jarvis WR, Waller J. Clinical comparisons of split septum, positive and negative mechanical valve intravenous connectors to an intraluminal protection device on 410 infection rates.2011; Poster, Association for Professionals in Infection Control and 411 Epidemiology, Inc. conference, Baltimore, MD. 412 49. Chernecky C, Waller J, Macklin D, Caillouet B. Comparative effectiveness of intravenous 413 414 catheter connectors.2011; Poster, National Teaching Institute, Chicago, IL. 415 50. Chernecky C, Waller J. Comparative evaluation of five needleless intravenous connectors. J Advanced Nurs. 2011;67(7):1601-13. 416 417 51. CherneckyC. In-vitro connector research (letter). Clin Infect Dis; 2010:51(12):1463. 418 52. Chernecky C, Waller J. Comparison of bacterial CFUs in five intravenous connectors. 419 ClinNurs Res: An Internat J.2010;19(4):416-28. 53. Yébenes JC, Vidaur L, Serra-Prat M, Sirvent JM, Batile J, Motje M, et al. Prevention of 420 421 catheter-related bloodstream infection in critically ill patients using a disinfectable, needle-free connector: A randomized controlled trial. Am J Infect Control. 2004;32(5):291-422 95.doi:10.1016/j.ajic.2003.12.004 423 424 425 426 427 428

Figure 1: Healthcare And Technology Synergy (HATS) Framework

