Health Care–Associated Bloodstream Infections Associated with Negative- or Positive-Pressure or Displacement Mechanical Valve Needleless Connectors

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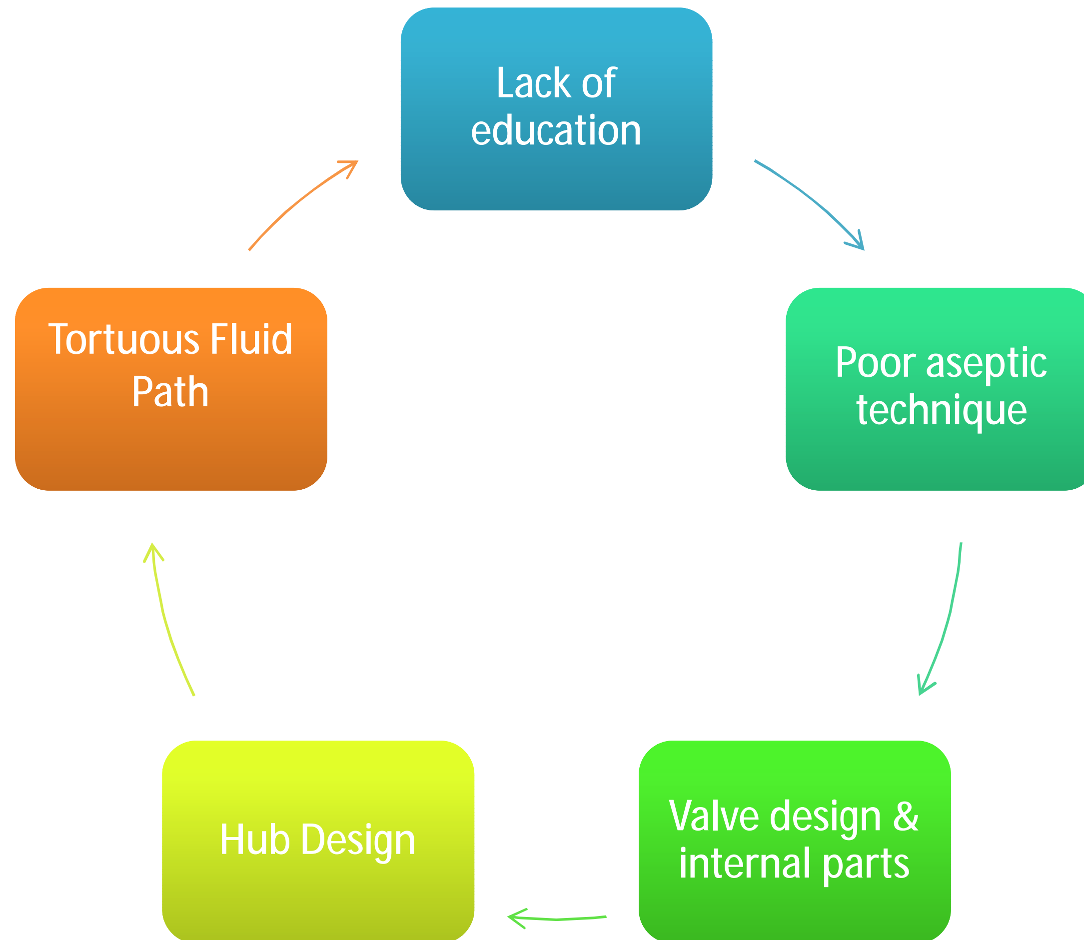
Assoc Prof Cathryn Murphy is a casual consultant to MayoHealthcare.

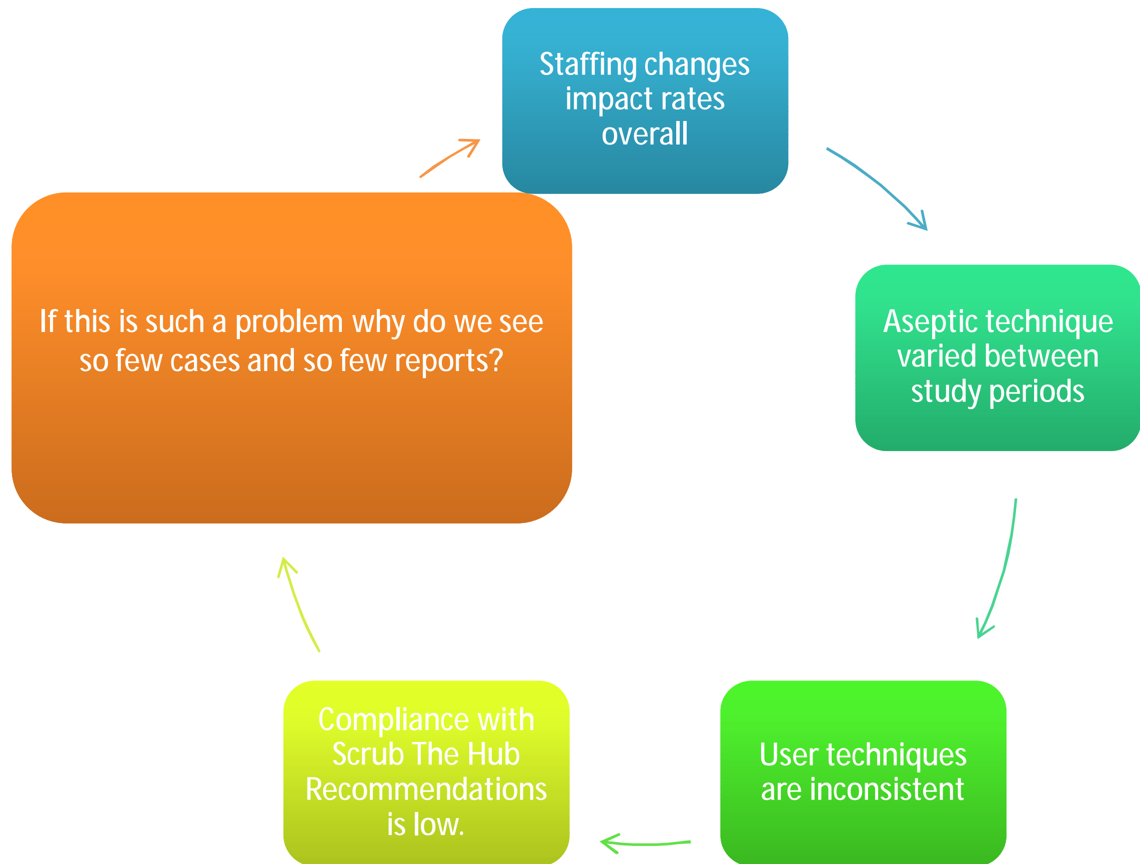
Objectives

- Highlight the significance of this paper
- Provide an overview of the key points made in the paper and detail methods
- Suggest ways in which clinicians may use this paper in guiding IV practice in their clinical settings.

Evolving Thinking on Connectors and CR-BSI



Evolving Thinking on Connectors and No Risk of CR-BSI



The Significance of This Paper

Significance of This Paper

- Additional evidence of negative patient outcomes associated with mechanical valve technology
- Largest study and first multi-national study
- Increases noted in a range of clinical settings
- Both +ve and –ve pressure valves are implicated

Significance of This Paper

- Bloodstream infection prevention practices and surveillance methods were studied and no anomalies reported that may have affected reported increases
- Raises questions about the likelihood of additional problems in other countries where MVs are commonly used
- Expands the list of mechanical valves now implicated

Key Points

Background

- Prior to this paper there have been 4 outbreaks <u>temporally associated</u> with positive-pressure mechanical valve (MV) use:
  - Maragakis – from CLAVE™ to Smartsite Plus ™
  - Salgado - Smartsite ™
  - Rupp – Smartsite Plus ™
  - Field – CLAVE ™ & CLC 2000 ™
- The true impact of mechanical valves remains undefined
- This paper included reports of increased healthcare care-associated catheter-related bloodstream infections (HA-BSIs) associated with negative and positive MVs
- This is the first multi-country paper

Participant Details

Table 2. Participants Split Septum (SS) and Mechanical Valve (MV) Needleless Connectors and Use Periods.

Hospital	Country	SS/needle used	Duration SS use, months	MV used	Duration of MV use, months	Post-MV device used	Duration post-MV period, months
A	United States	Interlink	18	UltraSite	39	Q-Syte	8
B	United States	Interlink	24	Clearlink	21	Interlink	5
C	United States	Interlink	18	Clearlink	11	Interlink	18
D	Australia	Interlink	12	SmartSite	12	Not available	Not available
E	Australia	Needles	6	SmartSite	11	Not available	Not available

Patients and Methods

- Quasi-experimental design was used to identify additional institutions
  - This design is used when a subjects cannot be randomly assigned to treatment conditions. The researcher does manipulate the independent variable (MV) and exercises certain controls to enhance the internal validity (the degree of inference that MVs rather than uncontrolled factors caused the observed effects) of the results.
- Forums, scientific meetings were used to identify other cases as there were no international or national networks or mechanisms available

Patients and Methods
Data Collection and Quality

- All data had been obtained before the focus group meetings so independent of those proceedings
  - Active
    - Actively identify infections using multiple data sources
  - Patient-based
    - Identify individual risk factors and patient care procedures in addition to laboratory data
  - Prospective
    - Monitor patients for infection during their hospitalization when possible

Sources of Data for Finding CLABSI

- Microbiology reports
- Infection control rounds on monitored units
- Pharmacy reports for antimicrobial use
- Networking with nursing staff
- Temperature chart
- List of patients with central lines

Reproduced from http://www.cdc.gov/nhsn/PDFs/slides/NHSN_training_CLABSI_revised_April_08_Slides.pdf Accessed 01/10/10

How CLABSI Denominator Data for ICU Was Collected

- At the same time each day, counted
- –# patients (i.e., patient days)
- –# patients with one or more central lines (i.e., central line-days)
- Enter the totals within 30 days of the end of the month

Collection of Denominator Data – CVC Days

*Facility ID# 10000 *Month: Feb *Year: 2005 *Location Code: MSICU

Date	*Number of patients	**Number of patients with 1 or more central lines	**Number of patients with a urinary catheter	**Number of patients on a ventilator
1	6	6		
2	8	6		
3	6	4		
4	7	7		
5	6	6		
6	8	6		
7				
8				
9				
10				
11				
31	//	//		
*Totals	151	138		
	Patient-days	Central-line days	Urinary catheter-days	Ventilator-days

Patients and Methods: Calculating Rate To Determine Infections per 1000 CVC Days

$$\text{CLABSI Rate*} = \frac{\text{\# CLABSIs identified}}{\text{\# central line days}} \times 1000$$

Patients and Methods: Study Periods

- The pre-MV-NC, MV-NC and post-MV-NCs are clearly defined, differentiated and identified.
  - Pre-MV-NC – (Range 6-24 months, median 18, mean 15.6)
  - MV-NC – (Range 11-39 months, median 12, mean 18.8)
  - Post MV-NCs – (Range 5-18 months, median 8, mean 10.3)
- Australian hospitals did not provide data on post-MV device use
- <u>HA-BSI prevention practices were assessed to control for confounders</u>

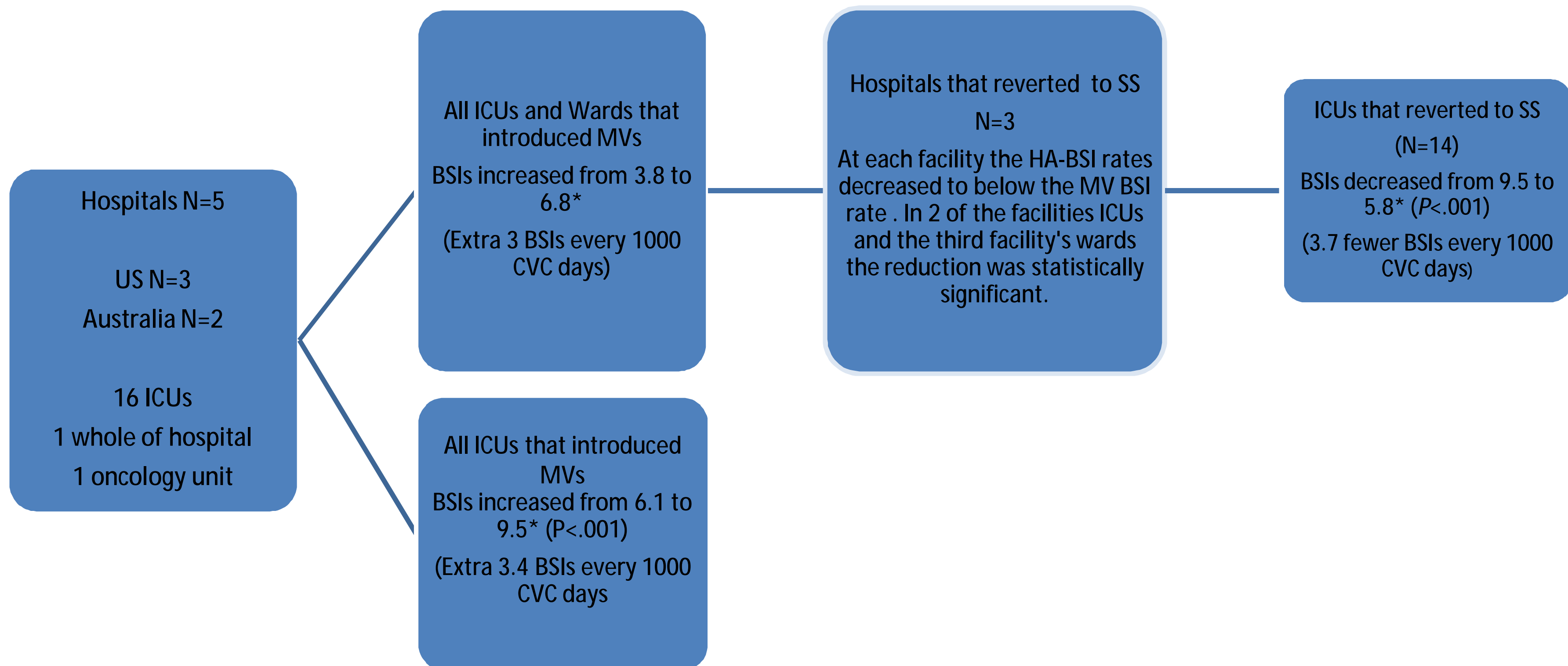
Results

- Prevention practices were similar for all hospitals
- During or between the periods there were no changes in:
  - Surveillance methods
  - Clinical practices
  - Patient populations or culturing
  - Nurse to patient ratios or infection prevention staff

Results

- 3 MVs implicated:
  - Clearlink (Baxter) – negative pressure – 2 US hospitals
  - Ultrasite (B. Braun) – positive pressure 1 US hosp
  - Smartsite (CareFusion) – positive pressure – 2 Aussie hospitals

How Are The Results Presented?



* All mean values expressed as BSIs per 1000 CVC days

Results

Table 3. Participating Hospital Bloodstream Infection (BSI) Rates during Split Septum (SS) and Mechanical Valve (MV) Needleless Device Use Period.

Hospital, unit/ward	SS BSI rate[a]	MV BSI rate	Relative risk (95%CI)	*P*	Post-MV-BSI rate	Relative risk (95%CI)	*P*
A: Adult ICUs (*n* = 4)	8.47	9.84	1.16 (0.94–1.44)	.16	6.10	1.61 (1.18–2.22)	.003
B: Adult ICUs (*n* = 6)	3.09	8.82	2.85 (2.15–3.65)	<.001	5.29	1.67 (1.12–2.48)	.008
C							
Adult wards	2.48	3.41	1.38 (0.98–1.93)	.05	2.29	1.49 (1.04–2.11)	.02
Adult ICUs (*n* = 4)	3.15	3.47	1.10 (0.67–1.46)	.67	2.89	1.20 (.74–1.95)	.43
D							
Adult ICU	0	4.30	NC (0.03–999)	.60			
Adult oncology ward	2.70	6.20	2.30 (2.09–2.71)	.04			
E: Adult ICU	6.80	11.8	1.79 (1.24–2.56)	.001			
A–E: Adult ICUs (*n* = 16)	6.15	9.49	1.54 (1.37–1.74)	<.001	5.77[b]	1.65 (1.38–1.96)	<.001

NOTE. CI, confidence interval; ICU, intensive care unit; NC, not calculated.

[a] Rates are based on health care–associated BSIs per 1000 central venous catheter–days for all except hospital C, which used 1000 patient-days for the adult ward health care–associated BSI rate that includes the entire hospital.

[b] Includes 3 hospitals with 14 adult ICUs. Post-MV rate includes the health care–associated BSI rate only in facilities changing from MV needleless connectors to SS needleless connectors.

Interpreting The Results

- Statistical significance: Statistical methods allow an estimate to be made of the probability of the observed or greater degree of association between factors. From this estimate, in a sample of given size, the statistical "significance" of a result can be stated. A number that expresses the probability that the result of a given experiment or study could not have occurred purely by chance.

University of Ottowa. McLaughlin Center For Population Health Risk Assessment. http://www.rfcom.ca/glossary/index.shtml Accessed 7th January 2010

Interpreting The Results

- P Value: the probability of observing CR-BSI as extreme or more extreme than the one actually observed from chance alone
- Lets us decide whether to reject or accept the null hypothesis (that there is no increased risk of BSI with needleless connector use)
  - $P > 0.05$ Not significant
  - $P = 0.01$ to 0.05 Significant
  - $P = 0.001$ to 0.01 Very significant
  - $P < 0.001$ Extremely significant

Results

Highly significant increase when I6 ICUs introduced MVs

Highly significant reduction when I4 ICUs MVs were discontinued and SS reintroduced

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[a] Rates are based on health care–associated BSIs per 1000 central venous catheter–days for all except hospital C, which used 1000 patient-days for the adult ward health care–associated BSI rate that includes the entire hospital.

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There are a few other significant results but concentrate on highly significant and larger sample size and trends.

Relative Risk

- The ratio of the risk of disease in the exposed group (MVs) compared to the risk of disease in the unexposed group (SS)
- Also referred to as Risk Ratio
- Values of RR range from 0 to infinity

Relative Risk

- Measures the magnitude of the association between the disease among those with exposure (MV) compared to the those without the exposure (SS)
  - RR = 1, no association
  - RR > 1, positive association
  - 0 < RR < 1, negative association

Interpreting The Results

- What is a Confidence interval?:
  - A range of values for a variable of interest e.g., a rate, constructed so that this range has a specified probability of including the true value of the variable.
- What is 95% Confidence Interval?
  - RR 1.54 (95% CI 1.37 - 1.74). This means that the estimated risk of BSI in the ICUs where MVs were in use was 1.54, and there is a 95% probability that the "true" risk (if that could be ascertained) is within the range 1.37 - 1.74.

Table 3. Participating Hospital Bloodstream Infection (BSI) Rates during Split Septum (SS) and Mechanical Valve (MV) Needleless Device Use Period.

Hospital, unit/ward	SS BSI rate[a]	MV BSI rate	Relative risk (95% CI)	P	Post-MV BSI rate	Relative risk (95% CI)	P
A: Adult ICUs (n = 4)	6.47	9.64	1.18 (0.94–1.44)	.16	6.10	1.61 (1.18–2.22)	.003
B: Adult ICUs (n = 6)	3.09	6.62	2.05 (2.15–3.65)	<.001	5.29	1.67 (1.12–2.48)	.006
C							
Adult wards	2.46	3.41	1.39 (0.99–1.93)	.05	2.29	1.49 (1.04–2.11)	.02
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E: Adult ICU	6.20	11.8	1.79 (1.24–2.58)	.001			
A–E: Adult ICUs (n = 19)	6.15	9.49	1.54 (1.37–1.74)	<.001	5.77[b]	1.65 (1.38–1.96)	<.001

NOTE. CI, confidence interval; ICU, intensive care unit; NC, not calculated.

[a] Rates are based on health care–associated BSIs per 1000 central venous catheter-days for all except hospital C, which used 1000 patient-days for the adult ward health care–associated BSI rate that includes the entire hospital.

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University of Ottowa. McLaughlin Center For Population Health Risk Assessment. http://www.rfcom.ca/glossary/index.shtml Accessed 7th January 2010

What Scientific Claims Can We Make From This Data?

- Temporal relationship has been shown to exist but not clear causation
- Temporal refers to the timing of the relationship between a factor (MV) and an outcome (BSI). It is one of the criteria used to assign causality to a relationship.
- In this temporal relationship the problem (BSI) appears when exposure occurs (MVs) and disappears (or does not occur) when the exposure is not present
- Confounding: The distortion of an apparent effect of an exposure on risk, brought about by the association with other factors that can influence the outcome.

University of Ottowa. McLaughlin Center For Population Health Risk Assessment. http://www.rfcom.ca/glossary/index.shtml Accessed 7th January 2010

Jarvis, W. 2010. Personal communication. 10th January.

Extrapolating The Results

- In our study in various settings we know the increased rate of BSIs per 1000 CVC days when MVs were introduced.
- We also know the decreased rate per 1000 CVC days when MVs were removed.
- In a 2006 landmark study of 103 ICUs in Michigan, Pronovost reported that the mean number of catheter-days per month in an ICU ranged from 4757 to 5469.
- If we assume that this is the typical number of catheter days in US and Aussie ICUs hospitals we can estimate excess cases, potential reductions and costs (in $USD) of both
- Assume the average increased cost of care for a patient with a CR-BSIs ranges from $USD 29-45k per episode.

Estimated Impact on BSIs Per Month if MVs Introduced or Removed in An ICU

Mean CVC Days Per Month as per Pronovost Study (2006)*	Estimated Extra ICU BSIs Per Month If MVs Introduced & Assuming Increase is 3.4 extra per 1000 CVC Days	Estimated Reduction in ICU BSIs Per Month If MVs Removed & SS Introduced and Assuming Reduction is 3.7 fewer per 1000 CVC Days
4757	16	18
5469	19	20

*Pronovost, P., D. Needham, et al. (2006). "An Intervention to Decrease Catheter-Related Bloodstream Infections in the ICU." The New England Journal of Medicine **355(26): 2725.**

Estimated Extra ICU BSIs Per Month If MVs Introduced & Assuming Increase is 3.4 extra per 1000 CVC Days	Estimated Additional Monthly Cost @ $ USD 29k	Estimated Additional Monthly Cost @ $ USD 45k	Estimated Reduction in ICU BSIs Per Month If MVs Removed & SS Introduced and Assuming Reduction is 3.7 fewer per 1000 CVC Days	Estimated Monthly Saving @ $ USD 29k	Estimated Monthly Saving @ $ USD 45k
16	$464,000	$720, 000	18	$522,000	$810, 000
19	$551,000	$855, 000	20	$580,000	$900, 000

Pronovost, P., D. Needham, et al. (2006). "An Intervention to Decrease Catheter-Related Bloodstream Infections in the ICU." The New England Journal of Medicine **355(26): 2725.**

Results

- Pathogens attributed to HA-BSI:
  - Coagulase-negative staphylococci
  - Staphylococcus aureus
  - Yeast
  - Enterococcus
  - Other gram-negative and gram-positive organisms
- ? Indicates that valves (design) susceptible to contamination and/or inadequate disinfection

Discussion – Unique Aspects

- Demonstrates the problem in multiple and different environments (13 wards or units in 4 hospitals, 1 entire hospital and in 2 countries)
- Reductions noted only when reverted to SS
  - Largest, comprehensive evaluation of its type
  - First study to compare types (+ve/-ve & SS)
  - Systematic evaluation of prevention practices
  - Evaluated reasons for change
  - Used focus group methodology

Discussion

- Demonstrates that prevention efforts were equivalent or superior in the MV-use periods yet increases occurred
- Therefore increases cannot be attributed to poor infection control
- No hospital achieved rates as low as SS rates when MVs were in use

Hypotheses

- When MVs are used there is an increased impact of deviating from good infection controls
- Clinicians may not be aware of the different practice requirements between MVs
- Connection problems, leakage, fluid accumulation
- Insufficient or inadequate MV disinfection
- Opacity precluding visualisation of flush

Limitations

- None explicitly described in the paper but some possible:
  - Small sample size;
  - Self-selection of participants;
  - Study design weak compared to a RCT
  - Authors' consultancy relationship with manufacturer of split-septum technology;
  - Duplication of previously published data – e.g. Salgado

Ways In Which Clinicians May Use This Paper In Guiding IV Practice In Their Clinical Settings.

(Including Its Relationship To Existing Guiding Documents and Competitors' Current Marketing Claims)

S22 INFECTION CONTROL AND HOSPITAL EPIDEMIOLOGY OCTOBER 2008, VOL. 29, SUPPLEMENT 1

SUPPLEMENT ARTICLE: SHEA/IDSA PRACTICE RECOMMENDATION

Strategies to Prevent Central Line–Associated Bloodstream Infections in Acute Care Hospitals

3. Do not routinely use positive-pressure needleless connectors with mechanical valves before a thorough assessment of risks, benefits, and education regarding proper use (B-II).[88-91]

   a. Routine use of the currently marketed devices that are associated with an increased risk of CLABSI is not recommended.

Marschall J, Mermel LA, Classen D, Arias KM, Podgorny K, Anderson DJ, Burstin H, Calfee DP, Coffin SE, Dubberke ER, Fraser V, Gerding DN, Griffin FA, Gross P, Kaye KS, Klompas M, Lo E, Nicolle L, Pegues DA, Perl TM, Saint S, Salgado CD, Weinstein RA, Wise R, Yokoe DS. Strategies to prevent central line-associated bloodstream infections in acute care hospitals. Infect Control Hosp Epidemiol. 2008;29: S22-3 0.

LETTERS TO THE EDITOR

Does the Evidence Support the SHEA-IDSA Recommendation on the Use of Positive-Pressure Mechanical Valves?

To the Editor—Few, if any, issues related to bloodstream infections and invasive devices have inspired such divergent opinions as that of needleless access connectors (ie, mechanical valves [MVs]). In a situation in which product choice is often decided on the basis of recommendations of societies such as the Society for Healthcare Epidemiology of America (SHEA) and the Infectious Diseases Society of America (IDSA), the obligation to ensure that such recommendations find support in empirical studies is paramount.

ommendation used negative-pressure devices (Figure). Thus, the recommendation summarized the evidence incorrectly.

Each of the 4 studies identifies deficits related to the design of the MV that may be associated with an increase in the rate of catheter-related bloodstream infection (CRBSI). The following quotations from each of the 4 studies describes these specific design deficits:

> MV devices have intricate access surfaces that are more difficult to disinfect than simpler split-septum models. The fluid path in the MV devices has moving parts, and at least 1 of the MV devices has internal corrugations that may serve as reservoirs and foster the growth of microbial contaminates....Some of the devices have been noted by healthcare personnel to have incomplete flushing of blood from the fluid channel, and some are opaque, so that this would not be readily apparent to the user.[2(p69)]

Edgar KJ. Does the evidence support the SHEA-IDSA recommendation on the use of positive-pressure mechanical valves? Infect Control Hosp Epidemiol. 2009 Apr;30(4):402-3; author reply 3-4.

http://wwwn.cdc.gov/publiccomments/comments/guidelines-for-the-prevention-of-intravascular-catheter-related-infections.aspx

Guidelines for the Prevention of Intravascular Catheter-Related Infections

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DRAFT

Centers for Disease Control and Prevention

Public Comments

Home · Open Documents

Guidelines for the Prevention of Intravascular Catheter-Related Infections

Read Draft Document

Date	From	Subject	Comment
12-03-2009	[illegible]		Read
12-03-2009	[illegible]		Read
12-02-2009	Jeff Goble		Read
[illegible]	Jeff Goble		Read
12-03-2009	Lisa Ovington		Read
12-03-2009	Erin O'Malley		Read
12-02-2009	Erin O'Malley		Read
12-03-2009	[illegible]		Read
12-03-2009	Cathryn Murphy		Read
12-03-2009	Cathryn Murphy		Read

Contact Us:
Centers for Disease Control and Prevention
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24 Hours/Every Day

Current Language As Per CDC Draft

- Lines 1077-1079, p.48.
  - Use a needleless system to access IV tubing. Category 1C
  - When needleless systems are used, the split septum valve is preferred over the mechanical valve due to increased risk of. Category II
- Optimistic that this language will remain unchanged – public submissions vary in response to it

Summary

- Long awaited publication that provides useful additional tool to draw clinicians' attention to the temporal relationship between use of MVs and increased CR BSI
- The strong aspects of the study are its design, size, multinational component and confirmation of previous studies
- Given that this paper is yet another example of the relationship between MVs and CR-BSI as advocates of better patient safety around the world we need to ensure that this paper is used in upcoming redrafting of guidance documents locally and internationally.

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