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Technologic Innovations for the Prevention of Catheter-Related Bloodstream Infection

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Teleflex®

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Objectives

- Recognize the significance of Catheter Related Bloodstream Infection (CR-BSI) and understand that knowledge of pathogenesis drives prevention efforts
- Describe evidence-based measures to prevent CR-BSI by limiting intraluminal and extraluminal catheter contamination
- Be able to introduce technologic innovations for the prevention of Catheter Related Bloodstream Infection (CR-BSI)

Clinical Significance of CLA-BSI

Clinical Significance of CLA-BSI

- 50% reduction in CLA-BSI between 2008 and 2014 in acute care hospitals in the United States[1]
- CLA-BSI rate in critical care units ranges from 0.0 – 2.9/1000 CVC d[1]
- 30,389 CLA-BSI reported by 3710 hospitals to CDC NHSN in 2021.[2] 12,219 from ICUs, 14,328 Wards, 3,842 NICU.
- CLA-BSI are associated with increased mortality (OR 2.75, CI 1.86-4.07), and attributable cost of $45,814 (CI, $30,919-$65,245)[3]

1.CDC. National HAI Progress Report. 2016. http://www.cdc.gov/HAI/pdfs/progress-report/hai-progress-report.pdf.

2. CDC HAI Progress Report, 2021. https://www.cdc.gov/hai/data/portal/progress-report.html.

3. Zimlichman et al. JAMA Intern Med, 2013. Ziegler et al. Infection . 2015.

Centers for Disease Control and Prevention
National Center for Emerging and Zoonotic Infectious Diseases

COVID-19: Reversal of Trends

	2020 Q1	2020 Q2	2020 Q3	2020 Q4
CLABSI	↓ −11.8%	↑ 27.9%	↑ 46.4%	↑ 47.0%
CAUTI	↓ −21.3%	No Change[1]	↑ 12.7%	↑ 18.8%
VAE	↑ 11.3%	↑ 33.7%	↑ 29.0%	↑ 44.8%
SSI: Colon surgery	↓ −9.1%	No Change[1]	↓ −6.9%	↓ −8.3%
SSI: Abdominal hysterectomy	↓ −16.0%	No Change[1]	No Change[1]	↓ −13.1%
Laboratory-identified MRSA bacteremia	↓ −7.2%	↑ 12.2%	↑ 22.5%	↑ 33.8%
Laboratory-identified CDI	↓ −17.5%	↓ −10.3%	↓ −8.8%	↓ −5.5%

Weiner-Lastinger, et al. ICHE 2021

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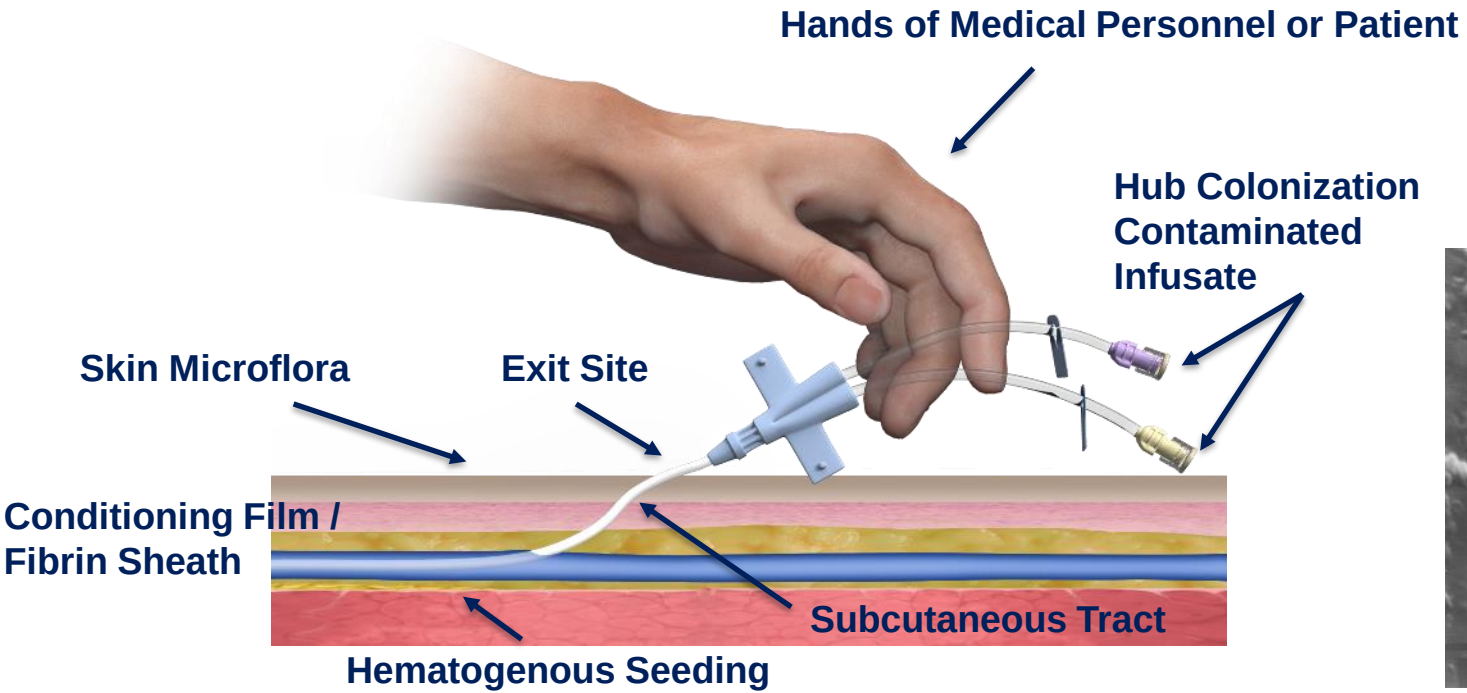
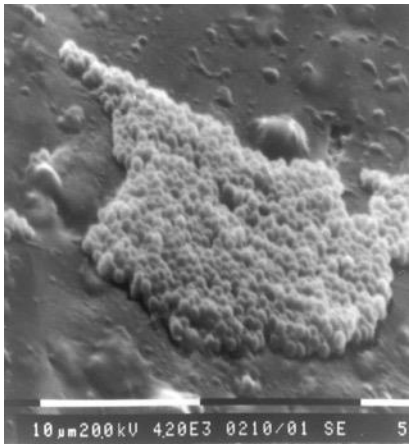
Pathogenesis of CVC-Associated BSI

Pathogenesis of CVC-Associated BSI [4]





4. Safdar N, Maki DG. The pathogenesis of catheter-related bloodstream infection with non cuffed short-term central venous catheters. *Int Care Med*. 2004;30:62-67.

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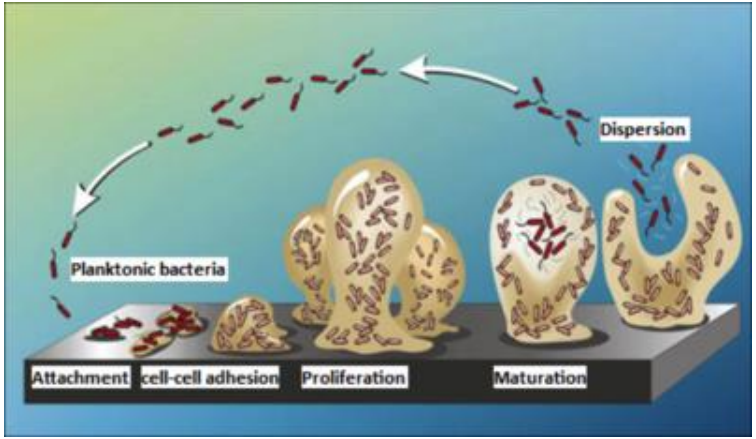
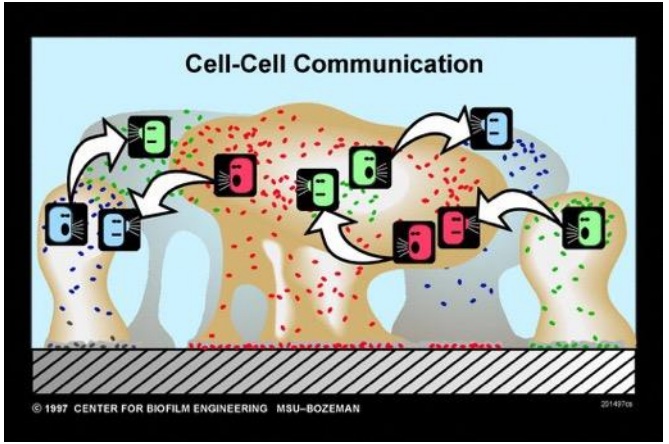
Biofilms: Complex and Dynamic Environment



Biofilm: Structure & Function

Microbial “Community”



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Prevention of CR-BSI

Pre and Peri-CVC Insertion

CR-BSI Prevention Pre and Peri-insertion

Education

- Indications for vascular catheters
- Sterile technique (Sim lab training)

Staffing & personnel

Insertion bundle

- Maximal sterile barriers
- Chlorhexidine + Alcohol skin prep
- Checklist

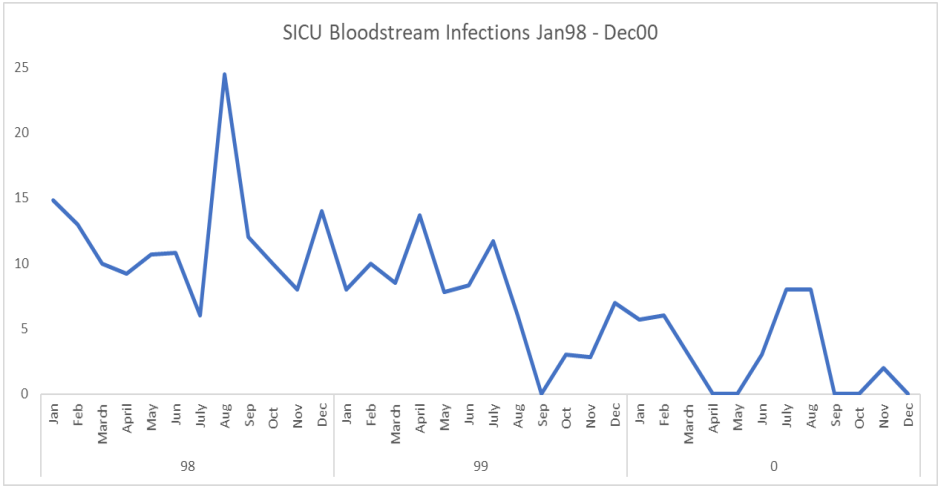
CR-BSI Prevention Pre and Peri-insertion

Surgical ICU

- 10-page self-study module for ICU nurses

Overall BSI rate

- Pre: 10.8/1000 CVC d
- Post: 3.7/1000 CVC d

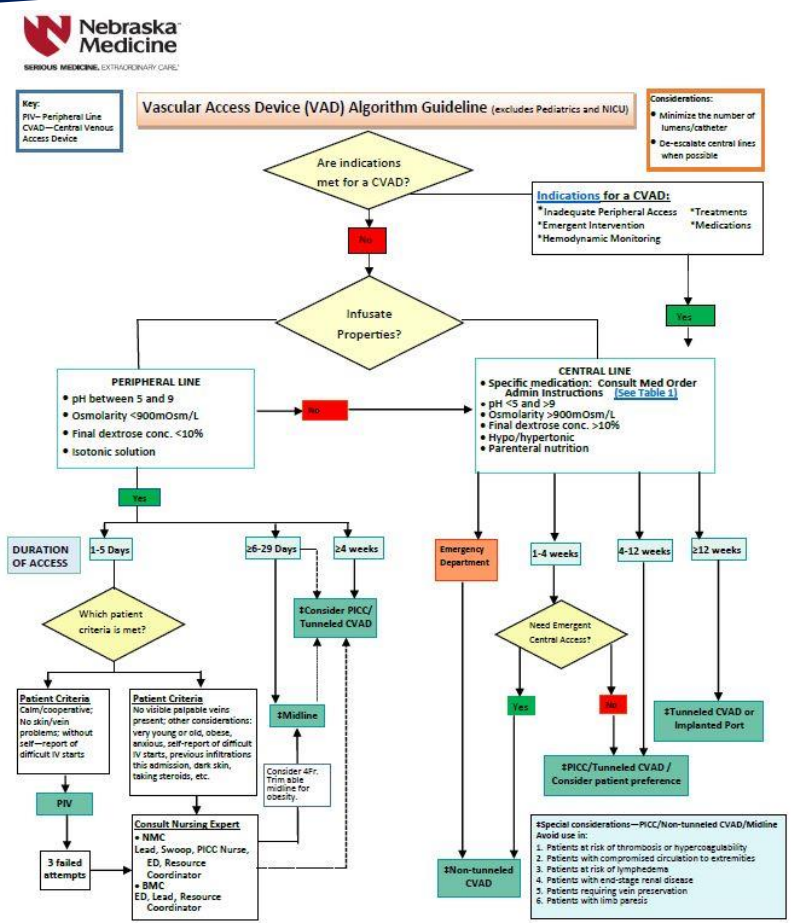


5. Coopersmith CM, et al. Effect of an education program on decreasing catheter-related bloodstream infections in the surgical intensive care unit. Critical Care Med, 2002. Jan;30(1):59-64

CR-BSI Prevention: Catheter Selection Algorithm[6]

Algorithm used at Nebraska Medicine to guide catheter selection decision.

Cawcutt et al. Infect Control Hosp Epidemiol. 2019. https://doi.org/10.1017/ice.2019.49



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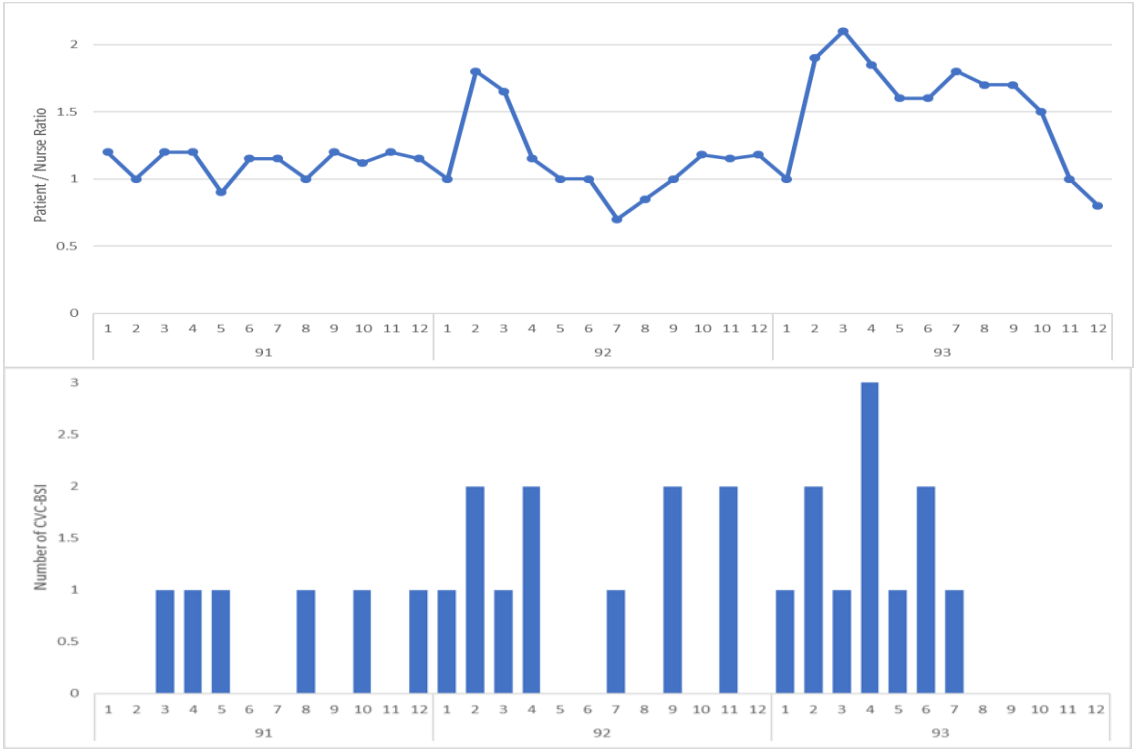
Nurse Ratio and Staffing Levels



Outbreak of CVC BSI associated with higher patient to nurse ratio in an SICU[7]

7. Fridkin SK, et al. The role of understaffing in central venous catheter-associated bloodstream infections. Infection Control Hospital Epidemiology, 1996. Mar;17(3):150-8.

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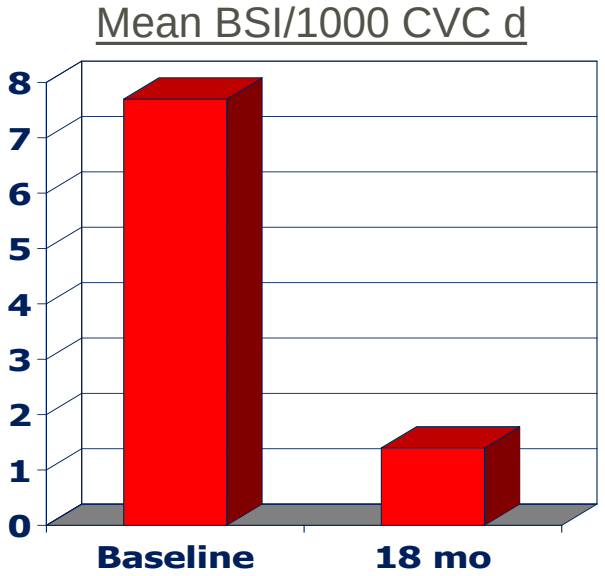
Maximal Sterile Barrier Precautions

Cap, Mask, Sterile Gown, Sterile Gloves, Head-to-toe Sterile Sheet

An Intervention to Decrease Catheter-Related Bloodstream Infections in the ICU[8]

Intervention in 108 ICUs:

- Daily Goals Sheet
- Hand Hygiene
- Full Sterile Barrier Precautions
- Chlorhexidine Antiseptic
- Avoidance of the Femoral Site
- Removal of CVCs as soon as possible



(P<0.002)

8. Peter Pronovost, M.D., Ph.D., Dale Needham, M.D., Ph.D., Sean Berenholtz, M.D et al. An Intervention to Decrease Catheter-Related Bloodstream Infections in the ICU. N Engl J Med 2006; 355:2725-2732. DOI: 10.1056/NEJMoa061115. December 28, 2006

Prevention of CR-BSI

Post Insertion Interventions

Post Insertion CVC Care

- Perform hand hygiene before manipulating the CVC
- Maintain clean and intact dressing
  - CHG impregnated dressing
- “Scrub the Hub” every time the catheter is accessed
  - Passive port protector
- Bathe patients with CHG
- Remove the CVC as soon as it is not needed

10. Buetti N, Marschall J, Drees M, et al. Strategies to prevent central line-associated bloodstream infections in acute-care hospitals: 2022 Update. https://www.cambridge.org/core/journals/infection-control-and-hospital-epidemiology/compendium

Prevention of CR-BSI

Technologic Innovations

Behavioral Change vs. Technology

"If you can choose between education and influencing human behavior or introduction of a gizmo, choose the gizmo every time."

-Bob Weinstein

“It is impossible to make anything foolproof because fools are so ingenious”

-Anonymous

Commercially Available Antimicrobial Central Venous Catheters

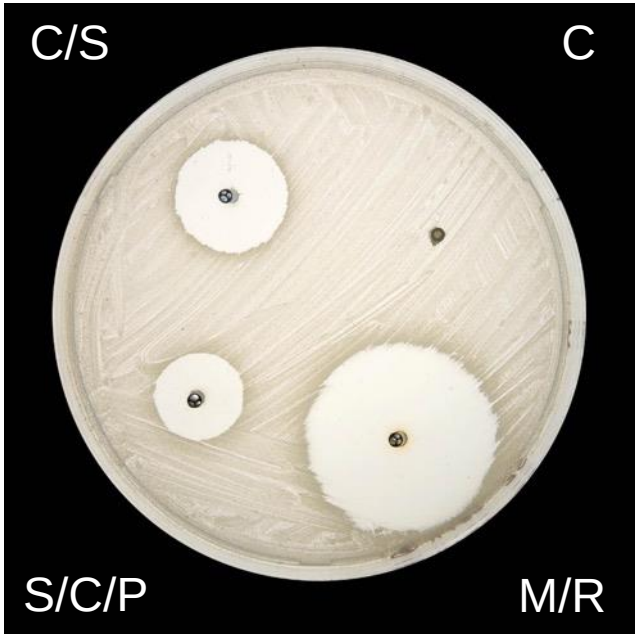
- CHG / SS Chlorhexidine - Silver Sulfadiazine
- Minocycline – Rifampicin
- Silver / Platinum / Carbon
- Miconazole / Rifampicin
- Benzalkonium
- Benzalkonium + Heparin

Compounds used in Coated Catheters[11]

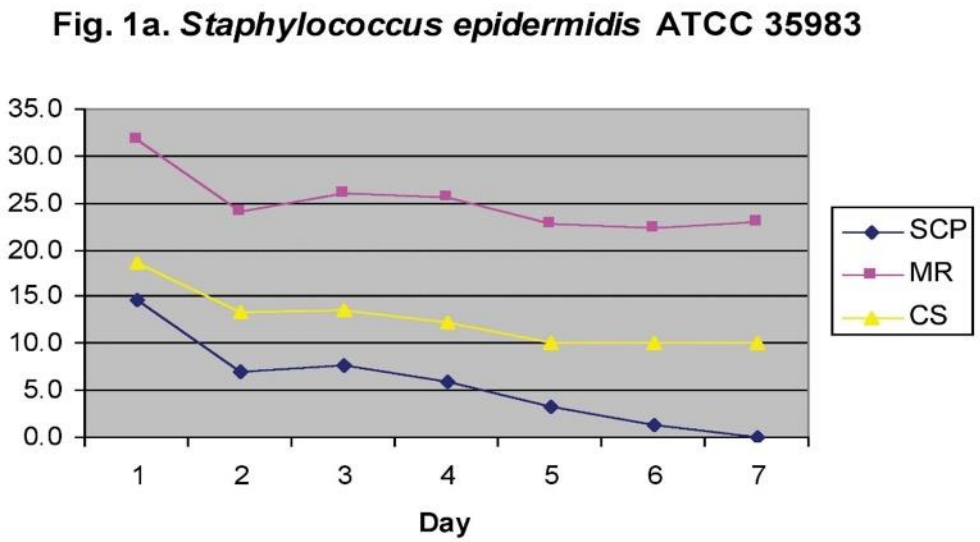
- Chlorhexidine – cationic polybiguanide disinfectant, disrupts cell membranes
- Silver – disinfectant, deactivates enzymes and membrane transport by binding to thiol groups
- Sulfadiazine – antibiotic, inhibits dihydropteroate synthetase
- Rifampin – antibiotic, inhibits bacterial DNA-dependent RNA polymerase
- Minocycline – broad spectrum tetracycline antibiotic, inhibits bacterial protein synthesis

11. Singha, Priyadarshini et al. “A review of the recent advances in antimicrobial coatings for urinary catheters.” *Acta biomaterialia* vol. 50 (2017): 20-40. doi:10.1016/j.actbio.2016.11.070

Spectrum and Duration of Activity of Antimicrobial Catheters[12]



Staphylococcus epidermidis



No correlation between in *vitro/in* vivo testing methods and clinical outcomes have currently been ascertained.

12. Spangler, D., Moss, S. “In-Vitro Assessment of Antimicrobial Activity of Three Commercially Available Central Venous Catheters.” Arrow International, Department of Applied Research, 2007

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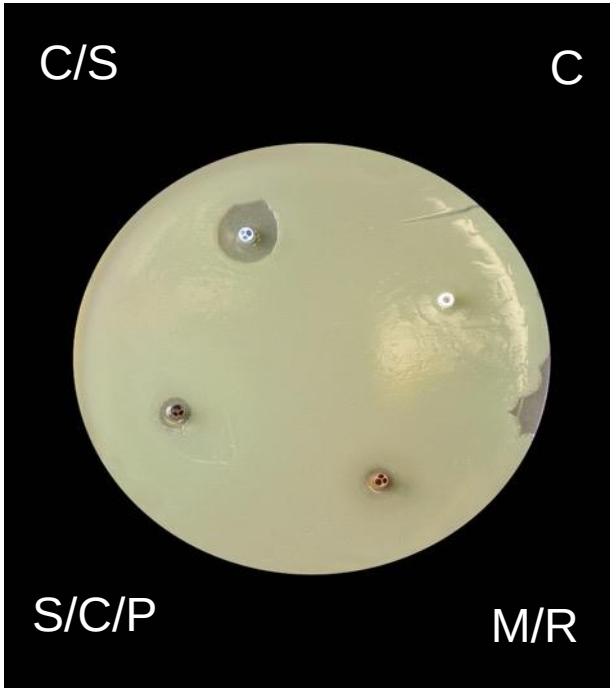
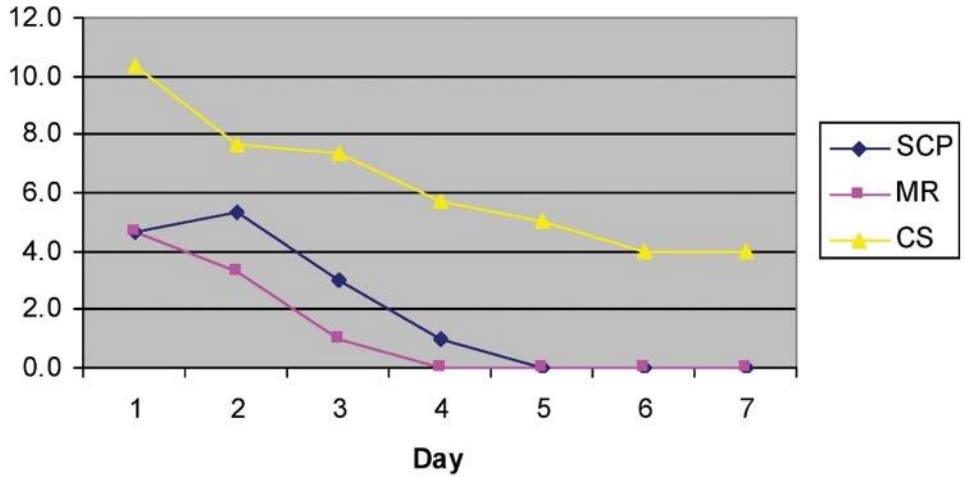
Spectrum and Duration of Activity of Antimicrobial Catheters[12]



Pseudomonas aeruginosa

Fig. 1d. *Pseudomonas aeruginosa* ATCC 27853



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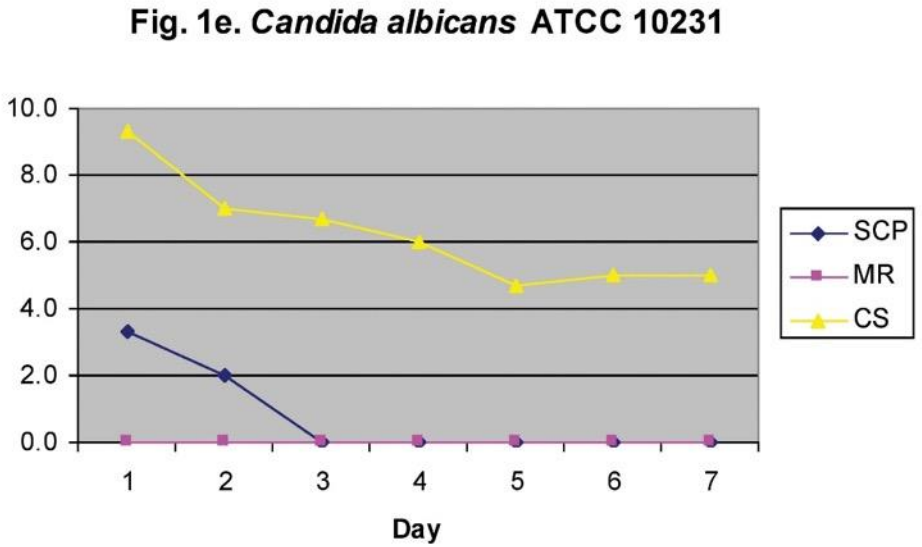
Spectrum and Duration of Activity of Antimicrobial Catheters[12]

Candida albicans



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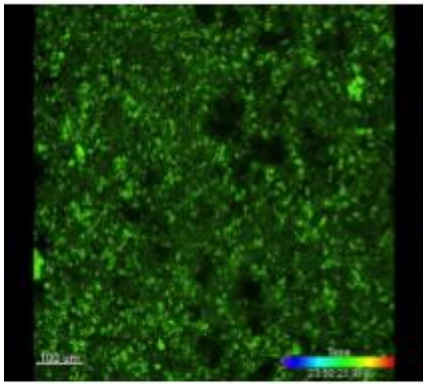
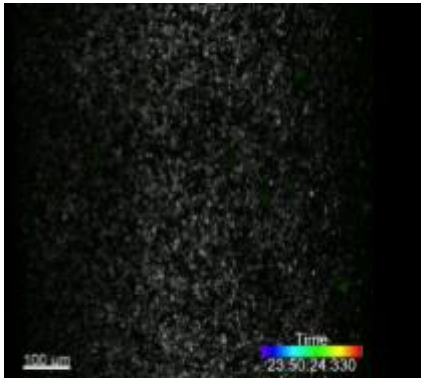
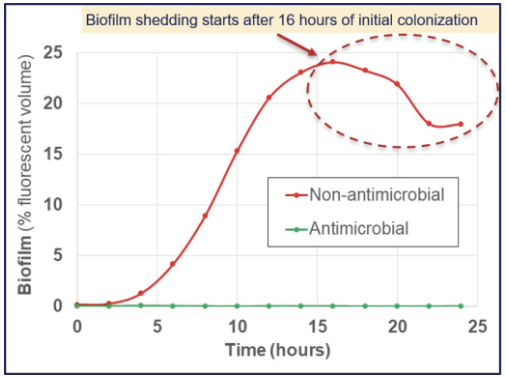
Effect of CH/SS on Adherence and Biofilm Formation







Chlorhexidine treated PICC prevents bacterial adherence and biofilm formation over 24 hour exposure to *GFP-S aureus* in flow cell experiment

13. Real-time evaluation of Chlorhexidine-treated indwelling PICC in reducing bacterial attachment, colonization and biofilm formation
Gupta & Haughton AVA 2019

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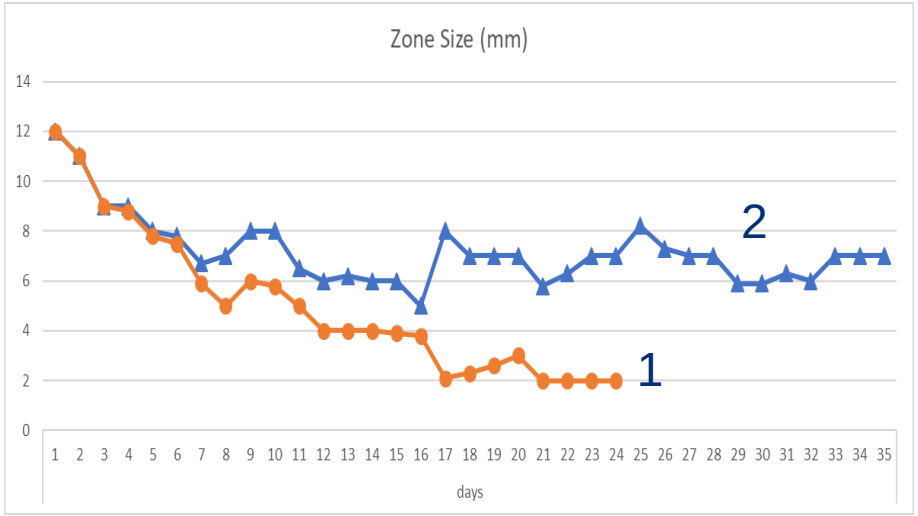
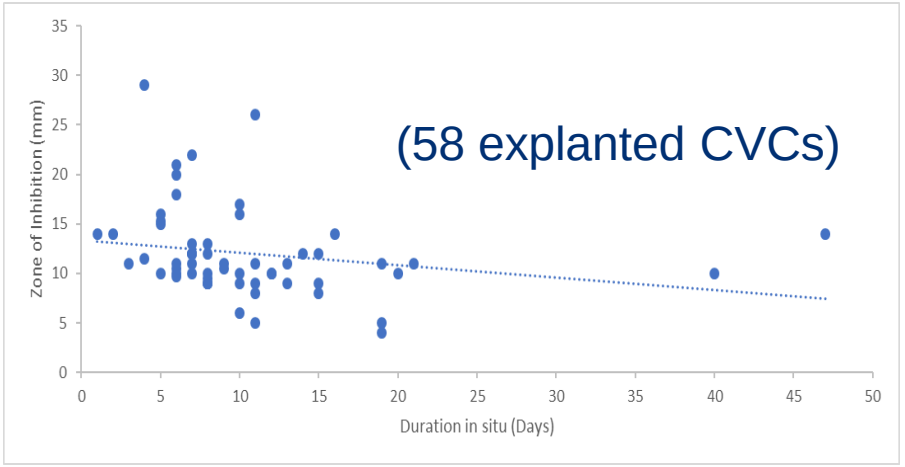
Duration of Activity CH/SS CVC[14,15]

S. aureus
1st & 2nd generation CH/SS CVCs



S. epidermidis
2nd generation CH/SS CVC



14. Bassetti, et al. Prolonged Antimicrobial Activity of a Catheter Containing Chlorhexidine-Silver Sulfadiazine Extends Protection against Catheter Infections In Vivo. ANTIMICROBIAL AGENTS AND CHEMOTHERAPY. DOI: 10.1128/AAC.45.5.1535–1538.2001. May 2001, p. 1535–1538

15. Fey et al. Scientific Report and presentation. 40th Interscience Conference on Antimicrobial Agents and Chemotherapy, Toronto, Canada, 17-20 September 2000.

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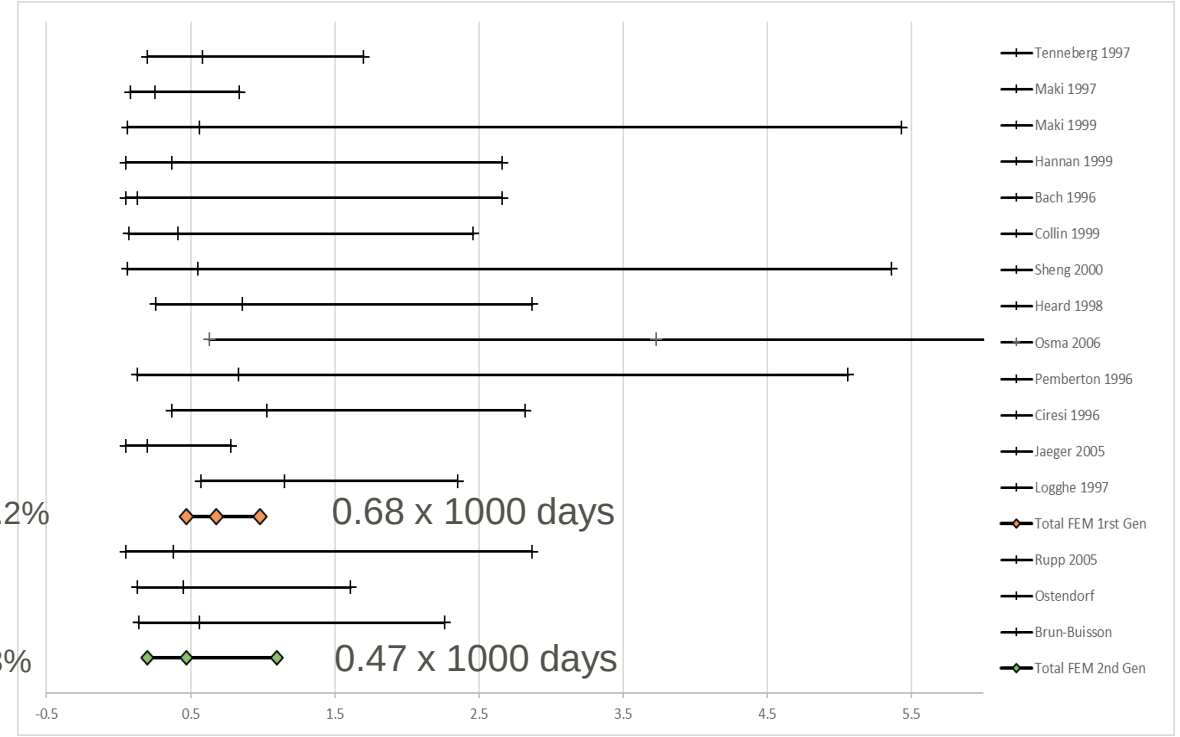
Do antimicrobial-coated catheters prevent BSI?

CSS Catheters



First Generation CSS
Control CVC Infection Rate 4.2%

Second Generation CSS
Control CVC Infection Rate 2.3%

17. Casey AL, et al. Antimicrobial central venous catheters in adults: a systematic review and meta-analysis. Lancet Infectious Disease, Volume 8, ISSUE 12, P763-776, December 01,2008

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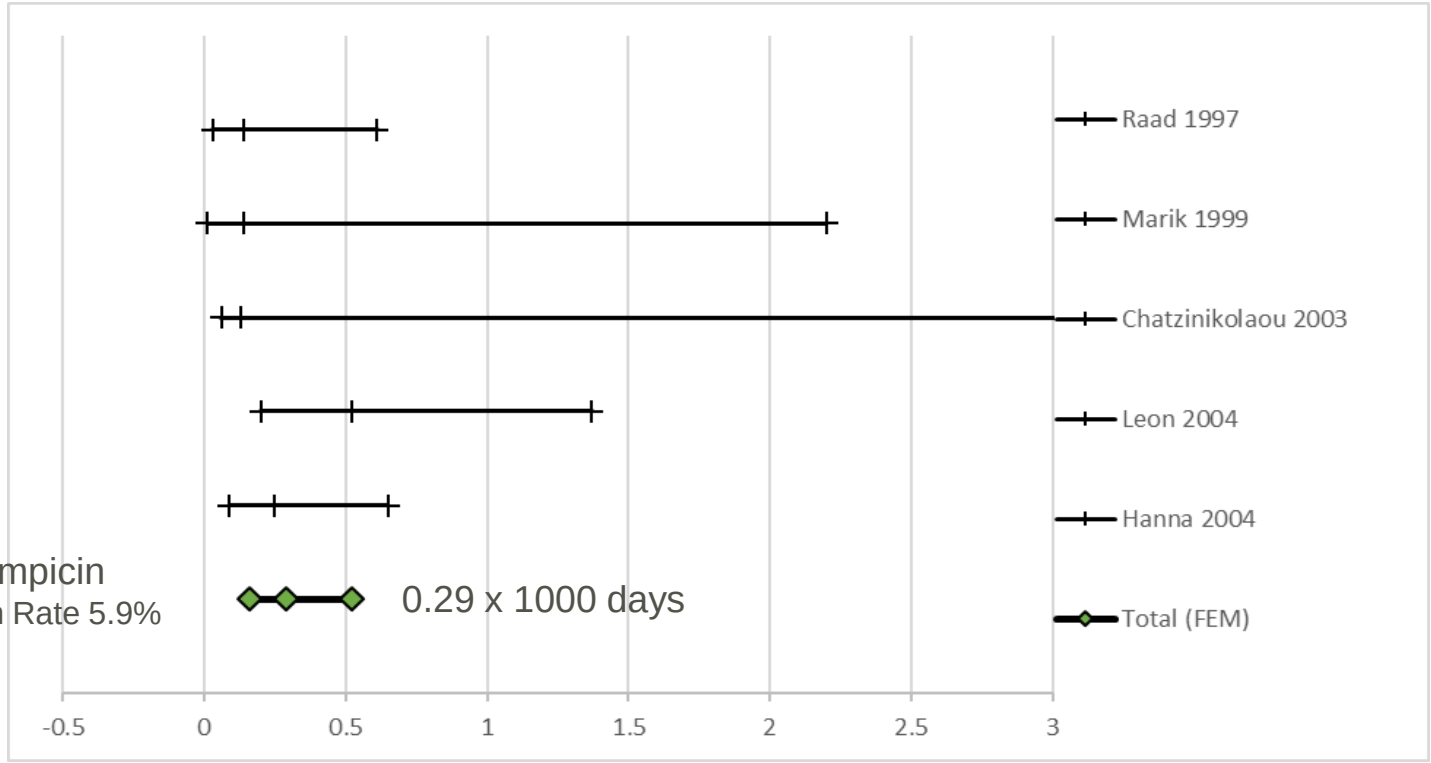
Do antimicrobial-coated catheters prevent BSI?

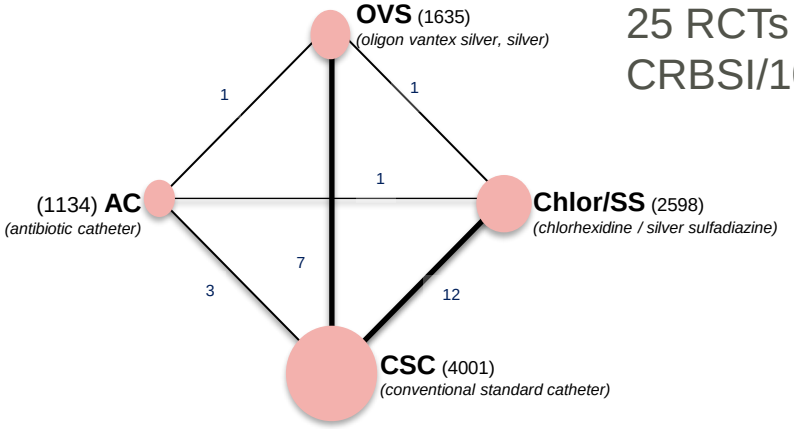
M/R Catheters



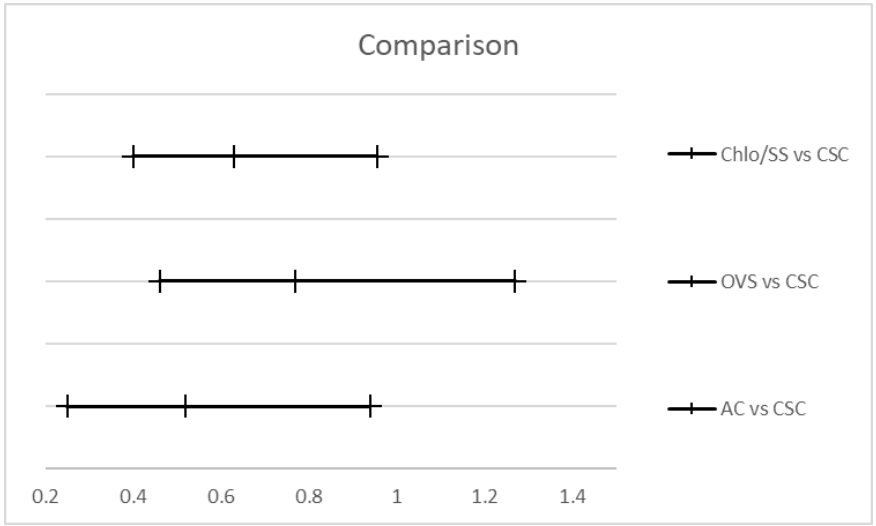
Minocycline – Rifampicin
Control CVC Infection Rate 5.9%

18. Casey AL, et al. Antimicrobial central venous catheters in adults: a systematic review and meta-analysis. Lancet Infectious Disease, Volume 8, ISSUE 12, P763-776, December 01,2008

Effectiveness of antimicrobial-coated central venous catheters for preventing catheter-related blood-stream infections with the implementation of bundles: a systematic review and network meta-analysis[19]



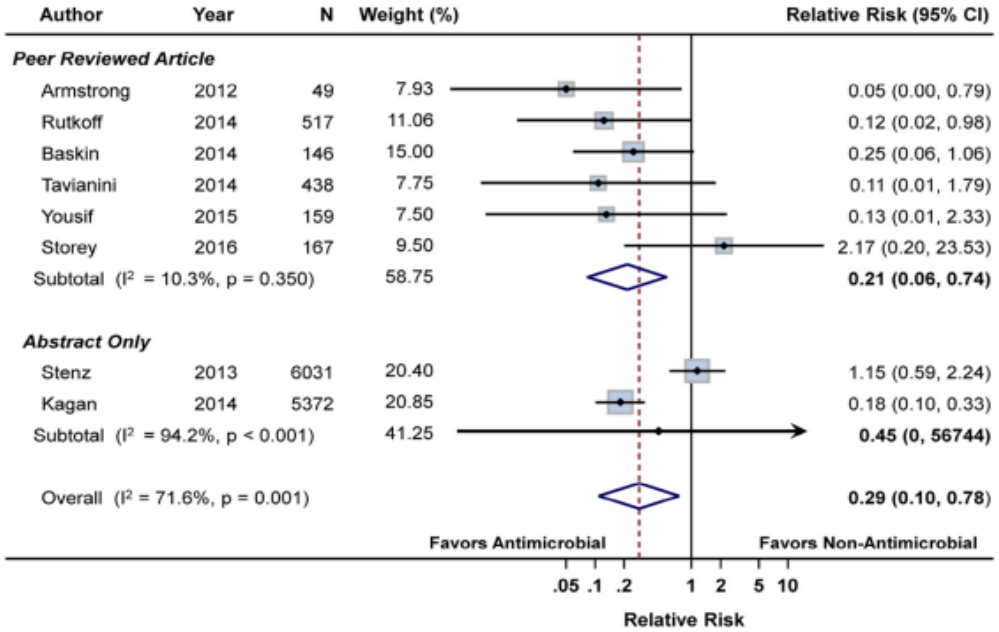
25 RCTs reported
CRBSI/1000 CVC days



CH/SS vs. CSC OR 0.64
AC vs. CSC OR 0.53
OVS vs. CSC OR 0.70

19. Hongliang Wang, et al. Effectiveness of antimicrobial-coated central venous catheters for preventing catheter-related blood-stream infections with the implementation of bundles: a systematic review and network meta-analysis. Ann. Intensive Care (2018) 8:71 https://doi.org/10.1186/s13613-018-0416-

Are antimicrobial peripherally inserted central catheters associated with reduction in central line-associated bloodstream infection? A systematic review and meta-analysis[20]



1476 patients. CLABSI: OR 0.21 (0.06, 0.74)

2.4/1000 PICC d vs 0.26/1000 PICC days (P = 0.014); NNT = 26

No difference between coating type: CHG = 0.31, R/M = 0.27; P= 0.93

20. Rachel D. Kramer BS, Mary A.M. Rogers PhD, Marisa Conte MLIS, Jason Mann MSA, Sanjay Saint MD,MPH, Vineet Chopra MD, MSc. Are antimicrobial peripherally inserted central catheters associated with reduction in central line associated bloodstream infection? A systematic review and meta-analysis American Journal of Infection Control (2016). dx.doi.org/10.1016/j.ajic.2016.07.021

Will antibiotic coated catheters lead to antibiotic resistance?
What about antiseptic coated catheters?

Technologic Innovations

Emergence of Resistance?

In Vitro and in Vivo Efficacy of Catheters Impregnated with Antiseptics or Antibiotics: Evaluation of the of the Risk of Bacterial Resistance to the Antimicrobials in the Catheters[21]

- Serial passage experiments for *S. epidermidis* and *E. coli* in drug or antiseptic containing broth
- Tested explanted catheters (from rats) in zone of inhibition tests against passaged strains.

CONCLUSIONS: Antiseptic and antibiotic catheters exhibit similar efficacy; however, when challenged with a rifampicin resistant strain, the antibiotic catheter appeared to be more susceptible to colonization than antiseptic device

21. Sampath, Lester A., Suhas M. Tambe, and Shanta M. Modak. "In vitro and in vivo efficacy of catheters impregnated with antiseptics or antibiotics: evaluation of the risk of bacterial resistance to the antimicrobials in the catheters." *Infection Control & Hospital Epidemiology* 22.10 (2001): 640-646.

Emergence of Resistance?

In Vitro Exposure of Bacteria to Antimicrobial Impregnated – Central Venous Catheter Does Not Directly Lead to the Emergence of Antimicrobial Resistance[22]

- In-vitro susceptibility testing of isolates of *S. epidermidis, S. aureus, E. faecalis,* and *E. coli* that had been grown next to CVC segments

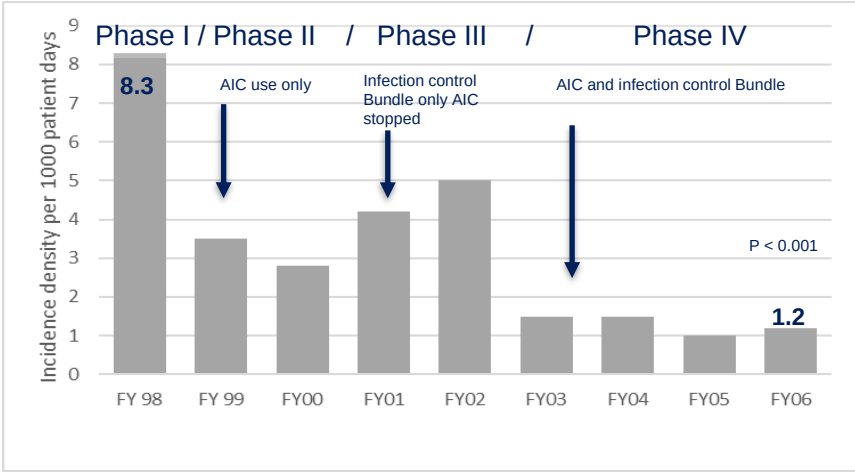
CONCLUSIONS: Our in vitro data suggest that the exposure of Gram-positive cocci to either rifampicin or minocycline can lead to development of resistance. However, exposure of bacteria to these antibiotic in combinations does not directly lead to resistance. Clinical investigations will be required to determine the true risk and implications of the development of resistance.

22. Munson, Erik L., Stephen O. Heard, and Gary V. Doern. "In vitro exposure of bacteria to antimicrobial impregnated-central venous catheters does not directly lead to the emergence of antimicrobial resistance." *Chest* 126.5 (2004): 1628-1635.

Emergence of Resistance?

Clinical Effectiveness and risk of emerging resistance associated with prolonged use of antibiotic – impregnated catheters: More than 0,5 million catheters days and 7 years of clinical experience[23]

- 9200 CVCs; 511,520 CVC days
- CLABSI decreased from 8.3 to 1.2/1000 CVC d
- Resistance of S aureus or CoNS to rifampin or tetracycline remained stable or decreased
- Long term use of R/M CVC not associated with clinical emergence of resistance



23. Ramos et al. Clinical effectiveness and risk of emerging resistance associated with prolonged use of antibiotic-impregnated catheters: More than 0.5 million catheter days and 7 years of clinical experience. Critical care medicine 39(2):245-51 · November 2010.

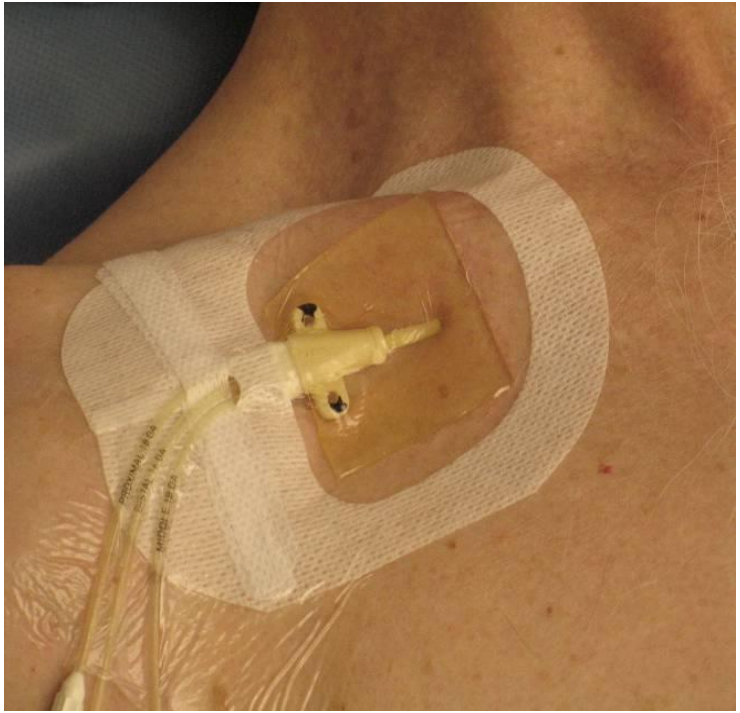
Novel Antimicrobial Coatings

- 5-Fluorouracil
- Rifampin-Miconazole
- Silver Nanoparticles
- Chlorhexidine/Mino-cycline/Rifampin
- Gentian violet/ Chlorhexidine
- Surface Pattern
- Polymeric sulfobetaine (polySB)
- PolyHexaMethylene biguanide
- Gold, Silver, Palladium
- Antimicrobial peptides
- Auranofin

Additional to Catheter

Technologic Innovations

Chlorhexidine Impregnated CVC Dressings



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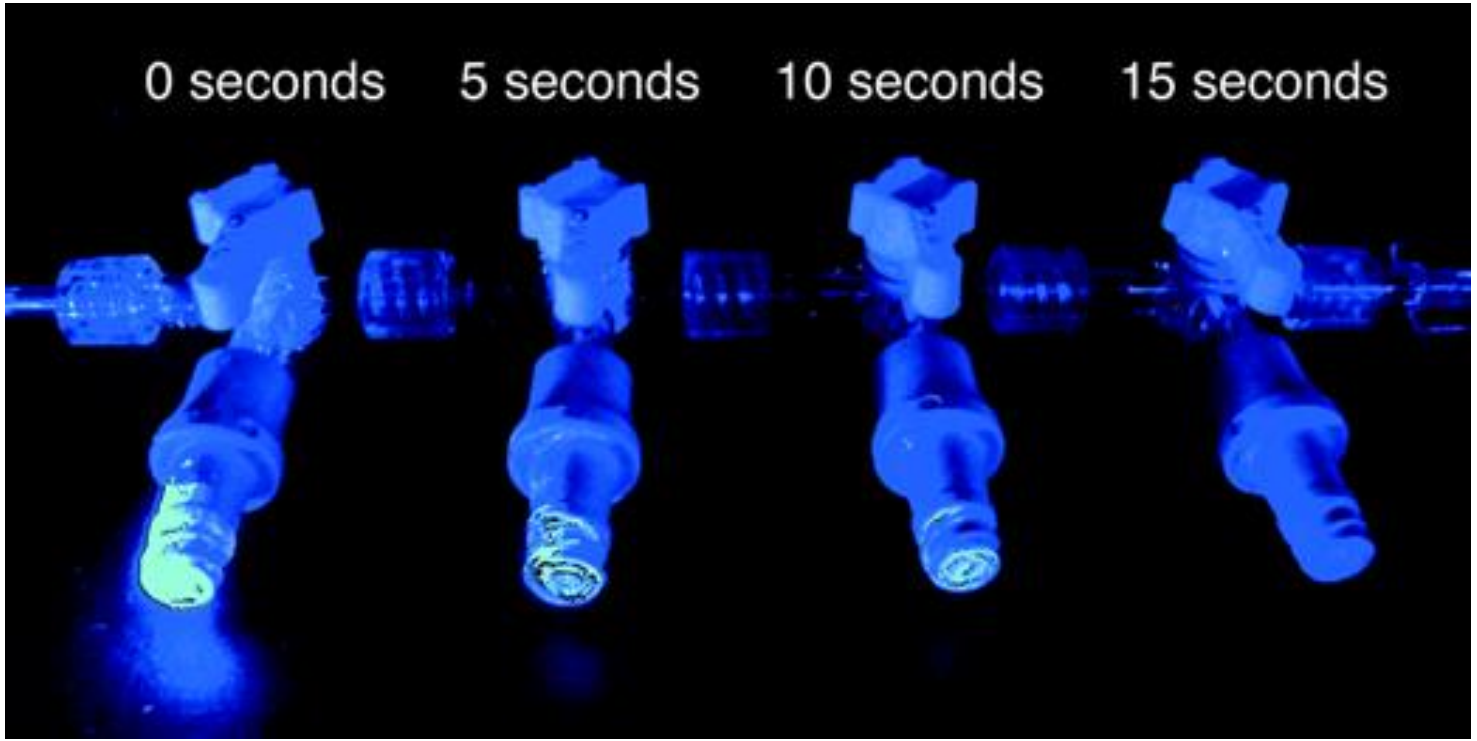
Meta-analysis and systematic reviews on use of CHG Dressings in Prevention of CRBSI

- Ho, et al. J Antimicrob Chemother. 2006. 6 studies, 2446 catheters (OR 0.58)
- Safdar, et al. Crit Care Med. 2014. 9 RCTs, 10,481 catheters (RR 0.6)
- Ullman, et al. Cochrane Review. 2015. 22 studies, 7436 patients (RR 0.65)
- Xing, et al. Iran J Public Health. 2019. 13 RCTs, 7555 patients, 11,931 catheters (RR 0.55)
- Wei, et al. BMC Infect Dis. 2019. 12 RCTs, 6028 patients (OR 0.6)
- Puig-Asensio, et al. Infect Control Hosp Epidemiol. 2020. 20 studies, 15,590 catheters (RR 0.71)

6 meta-analyses all concluded that CHG dressings significantly reduced risk of CRBSI

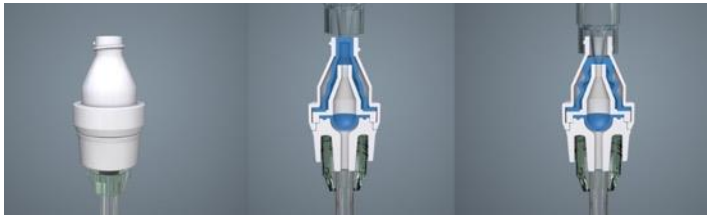
Scrub the Hub!



24. Lockman JL, Heitmiller ES, Ascenzi JA, Berkowitz. Scrub the hub! Catheter needleless port decontamination. Anesthesiology. 2011 Apr;114(4):958

Not All Mechanical Valves are Created Equal

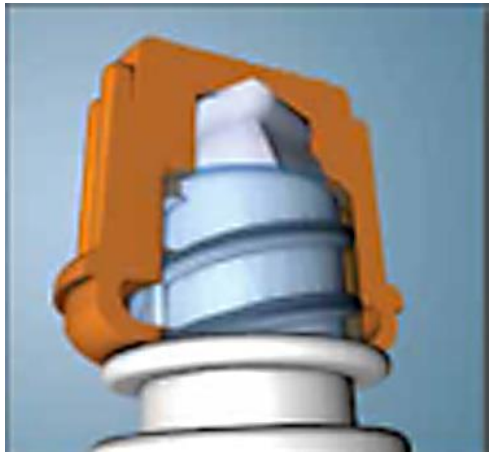
Negative Displacement
Needleless Connector

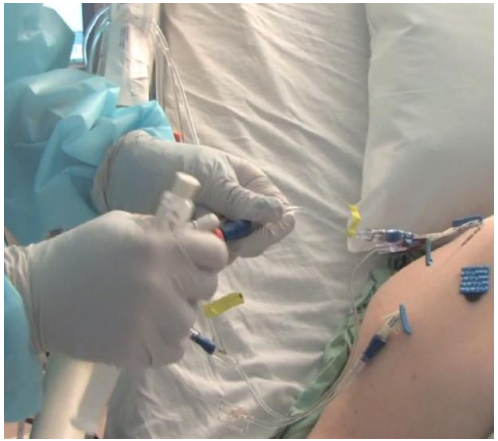


Neutral Displacement
Needleless Connector

Positive Displacement
Needleless Connector

Antiseptic Caps Passive Port Protectors





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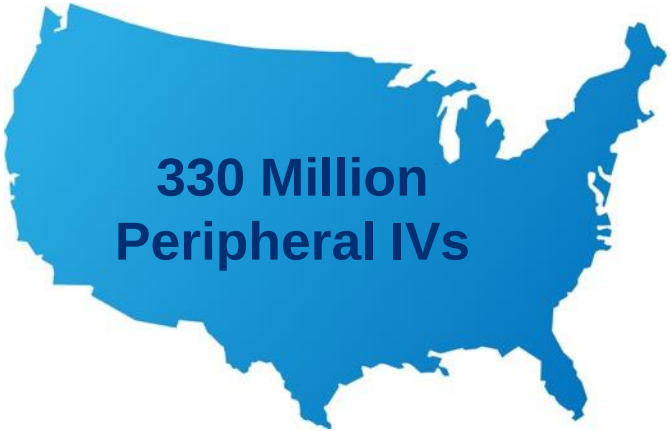
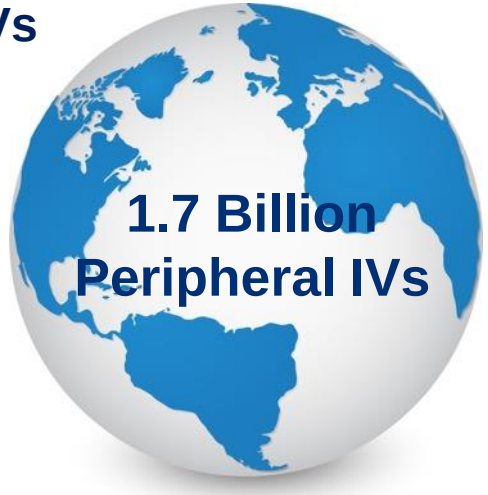
Scope of the Problem

What about Peripheral IVs???

Yearly Use of Peripheral IVs





Little systematic data regarding complications: infection, phlebitis, infiltration, extravasation

28. Webster, Joan, et al. "Clinically-indicated replacement versus routine replacement of peripheral venous catheters." *Cochrane Database of Systematic Reviews* 1 (2019).

The Risk of Bloodstream Infection in Adults With Different Intravascular Devices: A Systematic Review of 200 Published Prospective Studies[29]

- Review of 110 studies, 10,910 catheters
- 0.5 BSI (95% CI 0.2–0.7)/1000 device days
- 9 higher quality studies (microbial concordance between catheter and blood culture): 0.6 BSI/1000 device days
- 1 per 1000 devices x 330 Million/2.25 attempts per successful IV start = 146,000 episodes of BSI

Short-term Peripheral Venous Catheter-Related Bloodstream Infections: A Systematic Review[30]

- BSI 0.18% amongst 85,063 PVCs
- PIVs responsible for 23% of catheter-related BSI

29. Maki, Dennis G., Daniel M. Kluger, and Christopher J. Crnich. "The risk of bloodstream infection in adults with different intravascular devices: a systematic review of 200 published prospective studies." *Mayo Clinic Proceedings*. Vol. 81. No. 9. Elsevier, 2006.

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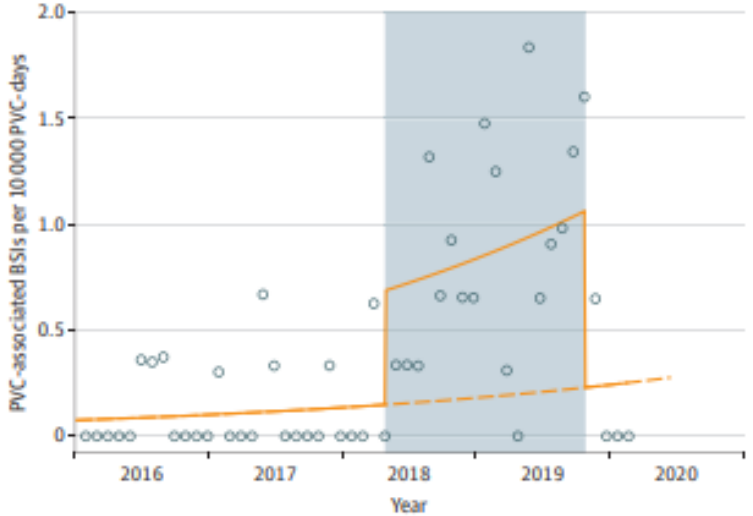
JAMA Internal Medicine | Original Investigation

Comparison of Routine Replacement With Clinically Indicated Replacement of Peripheral Intravenous Catheters

Niccolò Buetti, MD, MSc; Mohamed Abbas, MD, MSc; Didier Pittet, MD, MSc; Marlieke E. A. de Kraker, PhD; Daniel Teixeira, MSc; Marie-Noëlle Chraiti, RN; Valérie Sauvan, RN; Julien Sauser, MSc; Stephan Harbarth, MD, MSc; Walter Zingg, MD

JAMA Intern Med. 2021;181(11):1471-1478. doi:10.1001/jamainternmed.2021.5345

- Observational cohort study at AMC in Switzerland from Jan 2016 to Mar 2020
- 412,631 PIVs in 164,331 pts
- Baseline: PIVs changed every 96 hours (27 mo): Intervention: PIVs changed as needed (18.5 mo); Reversion to baseline (5.5 mo)
- A significant increase in PIV BSI was observed (BSI/10,000 PIV d) 0.128 (baseline) vs 0.894 (intervention) vs 0.287 (reversion). Incidence rate ratio 7.2 (intervention vs baseline), 95% CI (3.65-14.22) vs 1.35 (reversion vs baseline), 95% CI (0.3-6.17).



Monthly incidence density of PIV BSI. Trend lines per Poisson Regression: Solid = observed; dotted = predicted if intervention had not occurred

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What about Midlines?

A comparison of the incidence of midline catheter−associated bloodstream infections to that of central line−associated bloodstream infections in 5 acute care hospitals[31]

- Multi-center retrospective review
- 165,166 CL-days and 26,063 ML-days among all 5 hospitals
- 23 MLABSIs for an overall MLABSI incidence of 0.88 per 1,000 ML-days
- 178 CLABSIs resulting in a CLABSI incidence of 1.10 per 1,000 CL-days
- MLABSI and CLABSI was not statistically significant (*P*=.37)

31. Hogle, Nancy J., et al. "A comparison of the incidence of midline catheter–associated bloodstream infections to that of central line–associated bloodstream infections in 5 acute care hospitals." *American journal of infection control* 48.9 (2020): 1108-1110.

Scope of the Problem

What about Arterial Catheters???

- Arterial catheters (AC) are associated with same risk for BSI as nontunneled CVCs. 1.7 BSI/1000 cath days.[26]
- 8 Million ACs used per year in USA.[31]
- Only 44% of institutions follow CDC recommendations for AC insertion precautions.[32,33]
- ACs should be inserted and cared for with same level of respect as CVCs.[26]

26.Maki et al. The risk of bloodstream infection in adults with different intravascular devices: a systematic review of 200 published prospective studies. Mayo Clin Proc 2006.

31. Safdar et al. Arterial catheter-related bloodstream infection: incidence, pathogenesis, risk factors and prevention. J Hosp Infect 2013.

32. O'Horo et al. Chlorhexidine-impregnated dressing for prevention of catheter-related bloodstream infection: a meta-analysis*. Crit Care Med 2014.

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Infection Control – View for the Future

"There are known knowns. These are things we know that we know. There are known unknowns. That is to say, there are things that we know we don't know. But there are also unknown unknowns. There are things we don't know we don't know."

-Secretary of Defense Donald Rumsfeld

(PS: there are also things that we think we know, but we're wrong)

Any Questions?

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33. Cohen et al. Arterial Catheter Use in the ICU A National Survey of Antiseptic Technique and Perceived Infectious Risk. Crit Care Med 2015.

Rx only

Contraindication: Clinical assessment of the patient must be completed to ensure no contraindications exist. Arrowg+ard Blue Advance® Catheters are contraindicated in the following areas:
• Patients with known hypersensitivity to chlorhexidine
• In presence of device related infections
• In presence of previous or current thrombosis in the intended vessel or along the catheterized vessel pathway.
No correlation between *in vitro/in vivo* testing methods and clinical outcomes have currently been ascertained.

Teleflex®

Thank You

Thank You

Rx only