

METHODOLOGICAL APPENDIX

Guideline for Inpatient Diagnosis and Treatment of Central Vascular Catheter (CVC) Infections, 2016

Literature Review Methods and Results

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Section 1. Overview

This document details the methods and results of the systematic literature review performed for the 2016 UMHS clinical guideline for Inpatient Diagnosis and Treatment of Central Vascular Catheter (CVC) Infections.

A systematic search to check for best evidence was provided by the informationists at the Taubman Health Sciences Library, University of Michigan, which reviewed evidence from January 2008 to April 2014. The search included publications:

- Indexed in the Medline (Ovid) database and the Cochrane Database of Systematic Reviews
- Addressing humans and in the English language
- Categorized as clinical guidelines, controlled trials or meta-analyses, and cohort studies
- From 1/1/08 – 4/7/14

The searched addressed 23 topics. The topics are listed in Section II. The detailed search specifications are listed in Section III. This search was supplemented by the literature review results included in the IDSA Clinical Practice Guidelines for the Diagnosis and Management of Intravascular Catheter-Related Infection 2009: Update by the Infectious Diseases Society of America.

Section IV lists the number of publications identified by topic and type of publication. Additional articles were identified by searching references in retrieved publications. Very recent publications known to expert members of the guideline team were also considered. The search identified a total of 674 potentially relevant publications.

Members of the guideline team reviewed these publications, excluding those found not to be relevant to our population or topic (e.g., study population, measures/outcomes) or not to be the best evidence (e.g., studies with better methodology already available). This process is summarized in Section V.

The review process resulted in 35 studies identified as presenting best evidence on a topic. For each topic for which “best evidence” was identified, the evidence was synthesized in an evidence table was prepared that describes for each article the key aspects of methods, results, and issues (e.g., benefits and harms). The 5 evidence tables are presented in Section VI.

Section II. Search Framework and Topics

Presented below is the outline for a systematic search on specific topics relevant to the diagnosis and treatment of for Central Vascular Catheter (CVC) Infections in the inpatient care setting. For each topic, searches were performed for (a) guidelines, (b) controlled trials and meta-analyses, and (c) cohort studies. The searches are not mutually exclusive. This approach assumes that each topic will be reviewed independently and that the search on a topic must include all references relevant to it.

Recent Systematic Search and Review

We performed a systematic search and review of literature concerning the diagnosis and treatment of Inpatient Central Vascular Catheter (CVC) Infections in preparing the Clinical Practice Guideline for the Inpatient Diagnosis and Treatment of Central Vascular Catheter (CVC) Infections. December 2016. Inclusion/exclusion criteria are listed below.

Inclusion and Exclusion Criteria for Systematic Search of More Recent Literature

To search perform a search of relevant literature published we developed the following framework of inclusion and exclusion criteria.

| Domain | Inclusion | Exclusion |
|---------------------------|---|--|
| Language: | English | Not written in English |
| Time frame | Literature search included articles published from January 1, 2008 – April 7, 2014. | Studies published previous to or following these dates unless within categories noted in section (2) below |
| Study type/design | Meta-analyses, controlled trials, cohort studies, guidelines | Opinion, letter, commentary |
| Study population | Adult, pediatric, inpatient | Not inpatient, non-human |
| Medical condition | Central Line Infection | Central line maintenance, prevention |
| Setting | Inpatient | Ambulatory care, population health |
| Interventions/ indicators | <p><u>Diagnosis</u></p> <p>1. Laboratory tests/culture: Blood cultures (peripheral blood cultures, catheter blood cultures), blood culture contamination/contaminants, central cultures, quantitative blood cultures, time to culture positivity, catheter tip cultures, microbiology</p> <p><u>Treatment:</u></p> <p>2. Treatment/management (approach): Catheter removal, change over guidewire, catheter salvage, vein-sparing, antibiotics, antibiotic locks, line holiday/catheter holiday, suppurative thrombophlebitis, endocarditis, vascular infection</p> <p><u>Consultation:</u></p> <p>3. ID consultation</p> | <p>Training in proper insertion techniques, educational interventions for prevention of infection;</p> <p>Interventions/indications that are out of scope for guideline.</p> |
| Outcomes | <ul style="list-style-type: none"> • For diagnosis test, studies that report sensitivity / specificity of diagnostic test or procedure | |

| | | |
|--|---|---|
| | <ul style="list-style-type: none"> • For treatment, studies that report cure rate, infection rate rate, or time to improvement. • For other studies: Any quantitative outcomes reported in studies meeting our other inclusion criteria | |
| Relative quality of evidence available | | Articles are excluded if other articles within retrieved literature are deemed methodologically superior, e.g. have more representative relevant population; larger sample size; stronger methodological design, superior execution of study. |

Additional sources considered to supplement our search were:

- Results of a systematic review of literature from January 2001 to June 2008 prepared as part of the IDSA, and published as part of the guideline Clinical Practice Guidelines for the Diagnosis and Management of Intravascular Catheter-Related Infection: 2009 Update by the Infectious Diseases Society of America.
- References cited in articles identified by the literature search from June 2008 through April 2014 (section 1, described above).
- Publications (meta-analyses, controlled trials, cohort studies, and guidelines) since the literature search, though December 2016, known to members to the guideline team.

Search of Literature from 1/1/08 – 4/7/14

An initial search was performed for the time period from 1/1/08 – 4/7/14.

The general specifications for the search are outlined below. The detailed search terms and specifications are reproduced in Section III.

Within the Medline (Ovid) database, Central venous catheter or catheterization was searched as a major descriptor. Central venous/ or (central line or central lines or (central venous and (catheter or line or lines)) and peripherally inserted central and line or lines or port or ports or catheter were also searched in titles of articles to pick up articles about central vascular catheter infections that weren't indexed with the central venous catheter subject heading. The search was not limited to adults because adult was not routinely used in indexing relevant articles. The MEDLINE In-Process database was also searched, using a keyword search. The strategy is available in Section III.

The Cochrane Database of Systematic Reviews was searched using the terms listed in Section III.

Overall specification terms

- Major topic area: central venous catheters
- Time frame: 1/1/08 – 4/7/14
- Population: humans
- Language: English

Content terms for specific searches

- A. Diagnosis: Laboratory tests/cultures
 - a. Blood cultures (peripheral blood cultures, catheter blood cultures)
 - b. Blood culture contamination/contaminants
 - c. Central cultures
 - d. Quantitative blood cultures

- e. Time to culture positivity
- f. Catheter tip cultures
- g. Microbiology
- h. All diagnosis not in a-g
- B. Treatment: Treatment/Management (approach)
 - a. Catheter removal
 - b. Change over guidewire
 - c. Catheter salvage
 - d. Vein-sparing
 - e. Antibiotics
 - f. Antibiotic locks
 - g. Line holiday/catheter holiday
 - h. Suppurative thrombophlebitis
 - i. Endocarditis
 - j. Vascular infection
 - k. All treatment/management not in a-j
- C. Consultation: ID Consultation
- D. **Other: All central line infection not in 1-3 above*

Note: The "other" search in italics was performed to check for articles not adequately labeled with specific key words.]

Section III. Detailed Search Terms and Strategy

The searches were performed by informationists at the Taubman Health Sciences Library, University of Michigan.

Overall searches were performed for the period from 1/1/08 – 4/7/14.

The search strategies are listed below.

Central Line Infection Main Search (NOTE: Referred to throughout strategies as Main)

1. *Central Venous Catheters/ or *Catheterization, Central Venous/ or (central line or central lines or ("central venous" and (catheter* or line or lines)) or "central line associated" or "catheter related").ti.
2. ("peripherally inserted central" and (line or lines or port or ports or catheter*)).mp. or (PICC or PICCS).ti,ab. or *catheters, indwelling/
3. 1 or 2
4. Cross Infection/ or exp *Sepsis/ or exp *Catheter-Related Infections/ or exp *Bacterial Infections/ or *infection/ or *Prosthesis-Related Infections/
5. 3 and 4
6. (CLABSI* or CRBSI* or CR-BSI*).ti,ab.
7. 5 or 6
8. limit 7 to (english language and yr="2008 -Current")
9. animals/ not (animals/ and humans/)
10. 8 not 9
11. remove duplicates from 10

Central Line Infection Main 1 Search (NOTE: Referred to throughout strategies as Main1, used only for 2.h-j)

1. *Central Venous Catheters/ or *Catheterization, Central Venous/ or (central line or central lines or ("central venous" and (catheter* or line or lines)) or "central line associated" or "catheter related").ti.
2. ("peripherally inserted central" and (line or lines or port or ports or catheter*)).mp. or (PICC or PICCS).ti,ab. or *catheters, indwelling/
3. 1 or 2

Clinical Trials Search Hedge

1. randomized controlled trial/ or controlled clinical trial/ or multicenter study/ or meta-analysis/ or clinical trial, phase iv/
2. clinical trial/
3. limit 2 to humans
4. 1 or 3

Cohort Studies Search Hedge

1. randomized controlled trial/ or controlled clinical trial/ or multicenter study/ or meta-analysis/ or clinical trial, phase iv/
2. clinical trial/
3. limit 2 to humans
4. 1 or 3
5. exp cohort studies/ not 4

Guideline Search Hedge

1. clinical protocols/ or physician's practice patterns/ or algorithms/ or "Outcome and Process Assessment (Health Care)"/ or consensus development conference, nih/ or consensus development conference/ or practice guideline/ or guideline/
 2. randomized controlled trial/ or controlled clinical trial/ or multicenter study/ or meta-analysis/ or clinical trial, phase iv/
 3. clinical trial/

4. limit 3 to humans
5. 2 or 4 or exp cohort studies/
6. 1 not 5

Diagnosis

1. Laboratory tests/cultures

- a. Blood cultures (peripheral blood cultures, catheter blood cultures)
 1. blood cultur*.ti. or *specimen handling/ or exp *blood specimen collection/ or exp *cell culture techniques/ or exp *hematologic tests/ or exp *Culture Media/
 2. exp *Bacterial Infections/bl, di or exp *sepsis/bl, di or exp *toxemia/bl, di or exp *Prosthesis-Related Infections/bl, di or exp *Catheter-Related Infections/bl, di or exp *Infection/bl, di or exp *Bacteria/ip or exp *fungi/ip
 3. 1 or 2
 4. 3 and Main
- b. Blood culture contamination/contaminants
 1. blood cultur*.ti. or *specimen handling/ or exp *blood specimen collection/ or exp *cell culture techniques/ or exp *hematologic tests/ or exp *Culture Media/
 2. exp *Bacterial Infections/bl, di or exp *sepsis/bl, di or exp *toxemia/bl, di or exp *Prosthesis-Related Infections/bl, di or exp *Catheter-Related Infections/bl, di or exp *Infection/bl, di or exp *Bacteria/ip or exp *fungi/ip
 3. 1 or 2
 4. 3 and Main
- c. Central cultures
 1. exp *Blood Specimen Collection/
 2. 1 and Main
- d. Quantitative blood cultures
 1. exp *Bacteria/ip or exp colony count, microbial/ or (quantif* or quantit*).ti,ab.
 2. 1 and Main
- e. Time to culture positivity
 1. (time and positivity).ti. or (time and positivity).ab.
 2. 1 and Main
- f. Catheter tip cultures
 1. catheter tip*.ti,ab.
 2. 1 and Main
- g. Microbiology
 1. *Central Venous Catheters/mi or *Catheterization, Central Venous/mi or exp *bacteria/gd, ip or *blood/mi or exp *Microbiological Techniques/
 2. Cross Infection/mi or exp *Sepsis/mi or exp *Catheter-Related Infections/mi or exp *"bacterial infections and mycoses"/mi or *infection/mi or *Prosthesis-Related Infections/mi
 3. 1 or 2
 4. 3 and Main
- h. All diagnosis not in a-g
 1. blood cultur*.ti. or *specimen handling/ or exp *blood specimen collection/ or exp *cell culture techniques/ or exp *hematologic tests/ or exp *Culture Media/
 2. exp *Bacterial Infections/bl, di or exp *sepsis/bl, di or exp *toxemia/bl, di or exp *Prosthesis-Related Infections/bl, di or exp *Catheter-Related Infections/bl, di or exp *Infection/bl, di or exp *Bacteria/ip or exp *fungi/ip
 3. blood cultur*.ti. or *specimen handling/ or exp *blood specimen collection/ or exp *cell culture techniques/ or exp *hematologic tests/ or exp *Culture Media/
 4. exp *Bacterial Infections/bl, di or exp *sepsis/bl, di or exp *toxemia/bl, di or exp *Prosthesis-Related Infections/bl, di or exp *Catheter-Related Infections/bl, di or exp *Infection/bl, di or exp *Bacteria/ip or exp *fungi/ip
 5. 3 or 4

6. "contaminated blood".ti. or "contaminated blood cultur*".ti,ab. or ((blood or cultur*) and contamina*).ti. or ((blood or cultur*) and contamina*).ab. or equipment contamination/
7. 5 and 6
8. exp *Blood Specimen Collection/ or exp *Bacteria/ip or exp colony count, microbial/ or (quantif* or quantit*).ti,ab. or (time and positivity).ti. or (time and positivity).ab. or catheter tip*.ti,ab.
9. *Central Venous Catheters/mi or *Catheterization, Central Venous/mi or exp *bacteria/gd, ip or *blood/mi or exp *Microbiological Techniques/
10. Cross Infection/mi or exp *Sepsis/mi or exp *Catheter-Related Infections/mi or exp *"bacterial infections and mycoses"/mi or *infection/mi or *Prosthesis-Related Infections/mi
11. 1 or 2 or 7 or 8 or 9 or 10
12. false negative reactions/ or false positive reactions/
13. likelihood functions/ or exp "sensitivity and specificity"/
14. exp diagnosis/ or di.xs. or du.fs.
15. (sensitivity or specificity or predictive value).af.
16. or/12-15
17. 16 not 11
18. 17 and Main

Treatment

2. Treatment/Management (approach)

- a. Catheter removal
 1. Device Removal/ or (catheter* adj6 remov*).ti,ab.
 2. 1 and Main
- b. Change over guidewire
 1. ("guide wire*" or guidewire*).mp.
 2. 1 and Main
- c. Catheter salvage
 1. ((line or lines or catheter*) and salvag*).ti,ab.
 2. 1 and Main
- d. Vein-sparing
 1. (vein\$ and (spare* or sparing)).ti,ab.
 2. 1 and Main
- e. Antibiotics
 1. exp anti-infective agents/ or antibiotic prophylaxis/
 2. 1 and Main
- f. Antibiotic locks
 1. lock*.ti,ab.
 2. 1 and Main
- g. Line holiday/catheter holiday
 1. (line holiday or catheter holiday or "time off" or catheter free or holiday*).ti,ab.
 2. 1 and Main
- h. Suppurative thrombophlebitis
 1. thrombosis/ or exp thrombophlebitis/
 2. 1 and suppurat*.mp.
 3. 2 and Main1
- i. Endocarditis
 1. exp Endocarditis/
 2. 1 and Main1
- j. Vascular infection
 1. vascular infection*.mp.
 2. exp Vascular Diseases/ and (exp infection/ or exp *Sepsis/ or exp Catheter-Related Infections/ or exp Bacterial Infections/ or Prosthesis-Related Infections/)
 3. 1 or 2
 4. 3 and Main1

k. Treatment/management not in 2.a-2.j

1. Device Removal/ or (catheter* adj6 remov*).ti,ab.
2. ("guide wire*" or guidewire*).mp.
3. ((line or lines or catheter*) and salvag*).ti,ab.
4. (vein\$ and (spare* or sparing)).ti,ab.
5. exp anti-infective agents/ or antibiotic prophylaxis/
6. lock*.ti,ab.
7. (line holiday or catheter holiday or "time off" or catheter free or holiday*).ti,ab.
8. thrombosis/ or exp thrombophlebitis/
9. 8 and suppurat*.mp.
10. exp Endocarditis/
11. vascular infection*.mp.
12. exp Vascular Diseases/ and (exp infection/ or exp *Sepsis/ or exp Catheter-Related Infections/ or exp Bacterial Infections/ or Prosthesis-Related Infections/)
13. 11 or 12
14. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 9 or 10 or 13
15. (tu or th).xs. or exp therapeutics/
16. 15 not 14
17. 16 and Main

Consultation

3. ID Consultation

1. exp "Referral and Consultation"/ or Infectious Disease Medicine/
2. (consult or consults or consultation).ti,ab.
3. 1 or 2
4. 3 and Main

Other

4. All central line infection, not in 1-3

1. blood cultur*.ti. or *specimen handling/ or exp *blood specimen collection/ or exp *cell culture techniques/ or exp *hematologic tests/ or exp *Culture Media/
2. exp *Bacterial Infections/bl, di or exp *sepsis/bl, di or exp *toxemia/bl, di or exp *Prosthesis-Related Infections/bl, di or exp *Catheter-Related Infections/bl, di or exp *Infection/bl, di or exp *Bacteria/ip or exp *fungi/ip
3. blood cultur*.ti. or *specimen handling/ or exp *blood specimen collection/ or exp *cell culture techniques/ or exp *hematologic tests/ or exp *Culture Media/
4. exp *Bacterial Infections/bl, di or exp *sepsis/bl, di or exp *toxemia/bl, di or exp *Prosthesis-Related Infections/bl, di or exp *Catheter-Related Infections/bl, di or exp *Infection/bl, di or exp *Bacteria/ip or exp *fungi/ip
5. 3 or 4
6. "contaminated blood".ti. or "contaminated blood cultur*".ti,ab. or ((blood or cultur*) and contamina*).ti. or ((blood or cultur*) and contamina*).ab. or equipment contamination/
7. 5 and 6
8. exp *Blood Specimen Collection/ or exp *Bacteria/ip or exp colony count, microbial/ or (quantif* or quantit*).ti,ab. or (time and positivity).ti. or (time and positivity).ab. or catheter tip*.ti,ab.
9. *Central Venous Catheters/mi or *Catheterization, Central Venous/mi or exp *bacteria/gd, ip or *blood/mi or exp *Microbiological Techniques/
10. Cross Infection/mi or exp *Sepsis/mi or exp *Catheter-Related Infections/mi or exp *"bacterial infections and mycoses"/mi or *infection/mi or *Prosthesis-Related Infections/mi
11. 1 or 2 or 7 or 8 or 9 or 10
12. false negative reactions/ or false positive reactions/
13. likelihood functions/ or exp "sensitivity and specificity"/
14. exp diagnosis/ or di.xs. or du.fs.
15. (sensitivity or specificity or predictive value).af.
16. or/12-15

17. 11 or 16
18. Device Removal/ or (catheter* adj6 remov*).ti,ab.
19. ("guide wire*" or guidewire*).mp.
20. ((line or lines or catheter*) and salvag*).ti,ab.
21. (vein\$ and (spare* or sparing)).ti,ab.
22. exp anti-infective agents/ or antibiotic prophylaxis/
23. lock*.ti,ab.
24. (line holiday or catheter holiday or "time off" or catheter free or holiday*).ti,ab.
25. thrombosis/ or exp thrombophlebitis/
26. 25 and suppurat*.mp.
27. exp Endocarditis/
28. vascular infection*.mp.
29. exp Vascular Diseases/ and (exp infection/ or exp *Sepsis/ or exp Catheter-Related Infections/ or exp Bacterial Infections/ or Prosthesis-Related Infections/)
30. 28 or 29
31. 18 or 19 or 20 or 21 or 22 or 23 or 24 or 26 or 27 or 30
32. (tu or th).xs. or exp therapeutics/
33. 31 or 32
34. exp "Referral and Consultation"/ or Infectious Disease Medicine/
35. (consult or consults or consultation).ti,ab.
36. 34 or 35
37. 17 or 33 or 36
38. Main not 37

MEDLINE In-Process

1. (central line or central lines or ("central venous" and (catheter* or line or lines)) or "central line associated" or "catheter related").ti.
2. ("peripherally inserted central" and (line or lines or port or ports or catheter*)).mp. or (PICC or PICCS).ti,ab.
3. 1 or 2
4. (infection* or thrombosis or thrombophlebitis or bacteri* or endocarditis or "vascular infection*").ti,ab.
5. 3 and 4
6. (CLABSI* or CRBSI* or CR-BSI*).ti,ab.
7. 5 or 6
8. (ureter* or bladder or urin*).ti,ab.
9. 7 not 8
10. limit 9 to (english language and yr="2008 -Current")

Search hedges used for MEDLINE In-Process

Clinical Trials

1. ((randomi?ed adj7 trial*) or (controlled adj3 trial*) or (clinical adj2 trial*) or ((single or doubl* or tripl* or treb*) and (blind* or mask*))).ti,ab.

Cohort Studies

1. (cohort or longitudinal or prospective or retrospective).ti,ab.

Practice Guidelines

1. guideline*.ti. or ((practice adj3 parameter*) or guidance or care pathway* or (clinical adj3 pathway*)).ti,ab.

Cochrane

- | | |
|----|---|
| ID | Search |
| #1 | MeSH descriptor: [Central Venous Catheters] this term only |
| #2 | MeSH descriptor: [Catheterization, Central Venous] explode all trees |
| #3 | MeSH descriptor: [Catheters, Indwelling] explode all trees |
| #4 | (central line or central lines or ("central venous" and (catheter* or line or lines)) or "central line associated" or "catheter related"):ti (Word variations have been searched) |

- #5 "peripherally inserted central" and (line or lines or port or ports or catheter*):ti,ab,kw (Word variations have been searched)
- #6 PICC or PICCS
- #7 #1 or #2 or #3 or #4 or #5 or #6
- #8 MeSH descriptor: [Cross Infection] explode all trees
- #9 MeSH descriptor: [Sepsis] explode all trees
- #10 MeSH descriptor: [Prosthesis-Related Infections] explode all trees
- #11 MeSH descriptor: [Catheter-Related Infections] explode all trees
- #12 MeSH descriptor: [Bacterial Infections] explode all trees
- #13 MeSH descriptor: [Infection] explode all trees
- #14 #8 or #9 or #10 or #11 or #12 or #13
- #15 #7 and #14
- #16 CLABSI* or CRBSI* or CR-BSI*
- #17 #15 or #16 Publication Date from 2008 to 2014

Section IV. Number of Search Results by Topic and Type of Publication

The search (literature published 1/1/08 through 4/7/14) identified 617 unique indexed publications in Medline, listed as the “Base search” and 25 Cochrane reviews.

The results by topic and type of publication are drawn from this base search, and summarized below. Note that a publication may be relevant to more than one topic, so the sum of entries by topic is greater than the number of unique publications overall.

Results for Search, 1/1/08 – 4/7/14

| | Guidelines (-GDL) | Clinical Trials (-Trials) | Cohort Studies (-Cohort) |
|--|----------------------|------------------------------|-----------------------------|
| Base Numbers (for MEDLINE only): | 28 | 187 | 402 |
| <u>DIAGNOSIS</u> | | | |
| 1. Laboratory tests/cultures | | | |
| a. Blood cultures (peripheral blood cultures, catheter blood cultures) | 3 | 14 | 65 |
| b. Blood culture contamination/contaminants | 0 | 4 | 13 |
| c. Central cultures | 1 | 2 | 3 |
| d. Quantitative blood cultures | 1 | 22 | 52 |
| e. Time to culture positivity | 2 | 2 | 11 |
| f. Catheter tip cultures | 1 | 13 | 30 |
| g. Microbiology | 3 | 26 | 102 |
| h. All diagnosis not in a-g | 7 | 34 | 92 |
| <u>TREATMENT</u> | | | |
| 2. Treatment/Management (approach) | | | |
| a. Catheter removal | 2 | 42 | 89 |
| b. Change over guidewire | 0 | 4 | 7 |
| c. Catheter salvage | 0 | 3 | 15 |
| d. Vein-sparing | 0 | 0 | 0 |
| e. Antibiotics | 8 | 79 | 117 |
| f. Antibiotic locks | 0 | 34 | 44 |
| g. Line holiday/catheter holiday | 0 | 0 | 0 |
| h. Suppurative thrombophlebitis | 0 | 0 | 0 |
| i. Endocarditis | 0 | 0 | 6 |
| j. Vascular infection | 1 | 23 | 45 |
| k. All treatment/management not in a-j | 18 | 71 | 189 |
| <u>CONSULTATION</u> | | | |
| 3. ID Consultation | 0 | 0 | 1 |
| <u>OTHER</u> | | | |
| 4. All central line infection not in 1-3 above | 1 | 1 | 9 |
| MEDLINE In-Process database | 5 | 17 | 74 |
| <u>Cochrane</u> | | 25 reviews | |

Section V. Evidence Review and Identification of Best Evidence

Criteria for Best Evidence

In order to identify best evidence, team members were assigned topics, then team members reviewed publications to identify studies that had the overall best methods (“best evidence”) taking into consideration:

Study setting: reflects care and care settings that are similar to inpatient care in the U.S.

Study population and sample(s): represents adult patients typically seen related to central vascular catheter (CVC) infections care seen inpatient in the U.S.

Study design: strength of design in the ability to identify causal relationships using the following categories.

A = systematic reviews of randomized controlled trials with or without meta-analysis,

B = randomized controlled trials,

C = systematic review of non-randomized controlled trials or observational studies, non-randomized controlled trials, group observation studies (cohort, cross-sectional, case-control),

D = individual observation studies (case study/case series),

E = expert opinion regarding benefits and harm

Size of study sample: larger size generally reflecting more stable results

Variables: Extent to which the variables studied matched topics of interest in the inclusion criteria

Measures: Extent to which the measures likely reflected the conceptual variables

Data collection: Extent to which data collection procedures were likely to collect data appropriate for the measures

Intervention appropriateness: Extent to which an intervention was likely to produce the desired condition

Intervention execution: Extent to which interventions were carried out as planned

Analysis appropriateness: Appropriateness of analyses to address the questions of interest

Clarity of description: Extent to which the above information was communicated to readers

Best Evidence Identified and Organized into Evidence Tables

Section VI presents the synthesis of the best evidence identified. It is organized into 5 evidence tables that include a total of 35 publications.

Section VI. Evidence Synthesis: Tables Describing Best Evidence

Evidence identified by the literature review for the Clinical Practice Guideline on Inpatient Central Vascular Catheter (CVC) Infections (2016) was carried forward as best evidence unless the subsequent search for this guideline identified better evidence.

| Topic | Page |
|---|-------------|
| A. CVC Treatment | 14 |
| B. CVC Clinical presentation | 19 |
| C. CVC Diagnostic procedures and considerations | 20 |
| D. CVC Removal vs salvage | 24 |
| E. Additional considerations in CVC diagnosis and treatment | 25 |

*For all evidence tables, level of evidence rating is noted as follows:

A = systematic reviews of randomized controlled trials with or without meta-analysis,

B = randomized controlled trials,

C = systematic review of non-randomized controlled trials or observational studies, non-randomized controlled trials, group observation studies (cohort, cross-sectional, case-control),

D = individual observation studies (case study/case series),

E = expert opinion regarding benefits and harm

Topic A. Treatment

| Reference Citation | Study Design * | Patient Population <ul style="list-style-type: none"> • Description • Total N of patients • If systematic review, N of studies | Description of <ul style="list-style-type: none"> • Study group (n) • Comparison group (n) | Summary of Results for Relevant Main Outcome(s) <ul style="list-style-type: none"> • Effect size • Statistical significance) | Reviewer notes <ul style="list-style-type: none"> • Methodological issues, • Noteworthy harms • Other |
|--|----------------|---|--|---|--|
| <p>Fowler, V. G., Jr, Justice, A., Moore, C., Benjamin, D. K., Jr, Woods, C. W., Campbell, S., Peacock, S. J. (2005). Risk factors for hematogenous complications of intravascular catheter-associated staphylococcus aureus bacteremia. <i>Clinical Infectious Diseases: An Official Publication of the Infectious Diseases Society of America</i>, 40(5), 695-703. doi:CID34862 [pii] PMID: 15714415</p> | C | <p>Consecutive patients with intravascular catheter-associated <i>S. aureus</i> bacteremia were prospectively recruited over a 91-month period n=324</p> | <p>Corresponding bloodstream isolates were examined for the presence of 35 putative virulence determinants. Hematogenous complications (HCs) (i.e., septic arthritis, vertebral osteomyelitis, or endocarditis) were defined. HC occurred in 42 (13%) of 324 patients.</p> | <p>Patient characteristics at diagnosis that were associated with HC included: Community onset (relative risk [RR], 2.25; 95% confidence interval [CI], 1.24-4.07; P=.007), Increased symptom duration (odds ratio for each day, 1.14; 95% CI, 1.06-1.2; P<.001), Presence of a long-term intravascular catheter or noncatheter prosthesis (RR, 4.02; 95% CI, 1.74-9.27; P<.001), Hemodialysis dependence (RR, 3.84; 95% CI, 2.08-7.10; P<.001), and higher APACHE II score (P=.02). On multivariable analysis, symptom duration, hemodialysis dependence, presence of a long-term intravascular catheter or a noncatheter device, and infection with MRSA remained significantly associated with HC. Subsequent failure to remove a catheter was also associated with HC (RR, 2.28; 95% CI, 1.22-4.27; P=.011).</p> | N/A |
| <p>Fowler, V. G., Jr, Miro, J. M., Hoen, B., Cabell, C. H., Abrutyn, E., Rubinstein, E., ICE Investigators. (2005). <i>Staphylococcus aureus</i> endocarditis: A consequence of medical</p> | C | n=1779 | <p>Prospective observational cohort study set in 39 medical centers in 16 countries. Participants were a population of patients with definite infective</p> | <p><i>S aureus</i> was the most common pathogen (558 patients, 31.4%). Health care-associated infection was the most common form of</p> | N/A |

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| <p>progress. JAMA, 293(24), 3012-3021. doi:293/24/3012 [pii] PMID: 15972563</p> | | | <p>endocarditis (IE).</p> | <p>S aureus IE (218 patients, 39.1%). Most patients with health care-associated S aureus IE (131 patients, 60.1%) acquired the infection outside of the hospital. MRSA IE was more common in the United States (37.2%) Persistent bacteremia was independently associated with MRSA IE (odds ratio, 6.2; 95% confidence interval, 2.9-13.2). Patients in the United States were most likely to be hemodialysis dependent, to have diabetes, to have a presumed intravascular device source, to receive vancomycin, to be infected with MRSA, and to have persistent bacteremia (P<.001 for all comparisons).</p> | |
| <p>Chee L, Brown M, Sasadeusz J, MacGregor L, Grigg AP. Gram-negative organisms predominate in hickman line-related infections in non-neutropenic patients with hematological malignancies. <i>J Infect.</i> 2008;56(4):227-233. PMID: 18342947</p> | D | <p>n=273 patients from investigating hospital</p> | <p>All patients with hematological malignancies who had a double catheter fulfilling the definition of CRSBI episode. 273 screened, 61 developed CRSBI on 70 occasions.</p> | <p>There was a predominance of gram-negative infections (68%). The majority (73%) of initial CRBSI episodes required catheter removal within 7 days of onset. Vancomycin and cefepime was the most common initial antibiotic regimen used.</p> | N/A |
| <p>Rodriguez-Creixems M, Alcala L, Munoz P, Cercenado E, Vicente T, Bouza E. Bloodstream infections: Evolution and trends in the microbiology workload, incidence, and etiology, 1985-2006. <i>Medicine (Baltimore).</i> 2008;87(4):234-249. PMID: 18626306</p> | C | <p>27,419 episodes of significant BSI in 22,626 patients</p> | <p>Prospective study of patients with BSI to evaluate workload trends and the incidence and etiology of BSI during the last 22 years, including the acquired immunodeficiency syndrome (AIDS) era.</p> | <p>BSI incidence evolved from 16.0 episodes to 31.2/1000 admissions showing an annual increase of 0.83 episodes/1000 admissions (95% confidence interval, 0.61-1.05; p < 0.0001)..Gram positives 8.2 to 15.7/1000 admissions and 66.8 to 138.3/100,000 population; Gram negatives 7.8 to 16.2/1000 admissions and 63.5 to 141.9/100,000</p> | N/A |

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| | | | | population; anaerobes 0.5 to 1.3/1000 admissions and 4.1 to 11.7/100,000 population; and fungi 0.2 to 1.5/1000 admissions and 1.7 to 12.5/100,000 population. | |
| Pappas PG, Kauffman CA, Andes DR, et al. Executive summary: Clinical practice guideline for the management of candidiasis: 2016 update by the infectious diseases society of america. <i>Clin Infect Dis</i> . 2016;62(4):409-417. PMID: 18626306 | Guideline | N/A | N/A | N/A | Guideline document. Relevant evidence cited from original source material. See evidence tables in source. |
| Reboli AC, Rotstein C, Pappas PG, et al. Anidulafungin versus fluconazole for invasive candidiasis. <i>N Engl J Med</i> . 2007;356(24):2472-2482 PMID: 17568028 | A | 245 adults with invasive candidiasis | Adults with invasive candidiasis were randomly assigned to receive either: <ul style="list-style-type: none"> • intravenous anidulafungin (200 mg on day 1 and then 100 mg daily), n=127 • intravenous fluconazole(800 mg on day 1 and then 400 mg daily), n=118 | Treatment was successful in 75.6% of patients treated with anidulafungin, as compared with 60.2% of those treated with fluconazole (difference, 15.4 percentage points; 95% confidence interval [CI], 3.9 to 27.0). success rates at the end of intravenous therapy were 73.2% in the anidulafungin group and 61.1% in the fluconazole group (difference, 12.1 percentage points; 95% CI, -1.1 to 25.3). The frequency and types of adverse events were similar in the two groups. The rate of death from all causes was 31% in the fluconazole group and 23% in the anidulafungin group. | N/A |
| Kuse ER, Chetchotisakd P, da Cunha CA, et al. Micafungin versus liposomal amphotericin B for candidaemia and invasive candidosis: A phase III randomised double-blind trial. <i>Lancet</i> . 2007;369(9572):1519-1527. PMID: 17482982 | A | 264 individuals with candidaemia and invasive candidosis | Patients were treated with either: <ul style="list-style-type: none"> • micafungin (100 mg/day) n=202. • liposomal amphotericin B (3 mg/kg per day) n=190. | Success was observed for 181 (89.6%) patients treated with micafungin and 170 (89.5%) patients treated with liposomal amphotericin B. The difference in proportions, after stratification by neutropenic status at baseline, was 0.7% (95% CI -5.3 to 6.7). Efficacy was | N/A |

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| | | | | independent of the <i>Candida</i> spp and primary site of infection, as well as neutropenic status, APACHE II score, and whether a catheter was removed or replaced during the study. There were fewer treatment-related adverse events--including those that were serious or led to treatment discontinuation--with micafungin than there were with liposomal amphotericin B. | |
| Kuhn DM, George T, Chandra J, Mukherjee PK, Ghannoum MA. Antifungal susceptibility of candida biofilms: Unique efficacy of amphotericin B lipid formulations and echinocandins. <i>Antimicrob Agents Chemother.</i> 2002;46(6):1773-1780. PMID: 12019089 | C | Invitro examination of <i>Candida albicans</i> and <i>Candida parapsilosis</i> biofilms grown on a bioprosthetic model | Examined antifungal susceptibilities of <i>Candida albicans</i> and <i>Candida parapsilosis</i> biofilms grown on a bioprosthetic model. Examined both conventional agents and new antifungal agents (triazoles, amphotericin B lipid formulations, and echinocandins). | Susceptibility testing of fluconazole, nystatin, chlorhexidine, terbinafine, amphotericin B (AMB), and the triazoles voriconazole (VRC) and ravuconazole revealed resistance in all <i>Candida</i> isolates examined. In contrast, lipid formulations of AMB (liposomal AMB and AMB lipid complex [ABLC]) and echinocandins (caspofungin [Casp] and micafungin) showed activity against <i>Candida</i> biofilms. Preincubation of <i>C. albicans</i> cells with sub-MIC levels of antifungals decreased the ability of cells to subsequently form biofilm (measured by DW; $P < 0.0005$). | In vitro study of agents |
| Rex JH, Bennett JE, Sugar AM, et al. A randomized trial comparing fluconazole with amphotericin B for the treatment of candidemia in patients without neutropenia. candidemia study group and the national institute. <i>N Engl J Med.</i> 1994;331(20):1325-1330. PMID: 7935701 | B | 206 patients positive for candida | Patients were randomly assigned to receive either: <ul style="list-style-type: none"> • amphotericin B (0.5 to 0.6 mg per kilogram of body weight per day). • fluconazole (400 mg per day). | There was no statistically significant difference in outcome: of the 103 patients treated with amphotericin B, 81 (79 percent) were judged to have been treated successfully, as were 72 of the 103 patients treated with fluconazole (70 percent $P =$ | N/A |

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| | | | | <p>0.22; 95 percent confidence interval for the difference, -5 to 23 percent). The bloodstream infection failed to clear in 12 patients in the amphotericin group and 15 in the fluconazole group; the species most commonly associated with failure was <i>Candida albicans</i>. There were 41 deaths in the amphotericin group and 34 deaths in the fluconazole group (P = 0.20). Intravascular catheters appeared to be the most frequent source of candidemia. There was less toxicity with fluconazole than with amphotericin B.</p> | |
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* For study design notation, see legend on first page of appendix

Topic B. Clinical Presentation

| Reference Citation | Study Design * | Patient Population • Description • Total N of patients • If systematic review, N of studies | Description of • Study group (n) • Comparison group (n) | Summary of Results for Relevant Main Outcome(s) • Effect size • Statistical significance) | Reviewer notes • Methodological issues, • Noteworthy harms • Other |
|--|-------------------|--|--|---|---|
| Dellinger RP, Levy MM, Rhodes A, et al. Surviving sepsis campaign: International guidelines for management of severe sepsis and septic shock: 2012. Crit Care Med. 2013;41(2):580-637. | Guideline | N/A | N/A | N/A | Guideline Document. Relevant evidence cited from original source material. See evidence tables in source. |
| Luft D, Schmoor C, Wilson C, et al. Central venous catheter-associated bloodstream infection and colonisation of insertion site and catheter tip. what are the rates and risk factors in haematology patients? Ann Hematol. 2010;89(12):1265-1275. PMID: 23353941 | C | Patients in 2 university hospitals with identified risk factors for skin colonisation, for CVC-tip colonisation and for bloodstream infection (BSI) n=219 patients with haematological malignancies and inserted CVC (with a total of 5,501 CVC-days and 4,275 days at risk) | Quantitative skin cultures were obtained from the insertion site before CVC placement and at regular intervals afterwards. CVC-tip cultures were taken on CVC removal and data collection was performed: • prior to CVC placement (baseline colonization) and • within 10 days after CVC insertion (subsequent colonisation) | Prior to CVC placement Age was an independent risk factor for colonisation (baseline colonisation). Independent risk factors for subsequent colonisation were baseline colonisation and male gender. High level of skin colonisation at the insertion site was a predictor of CVC-tip colonisation, and a predictor of BSI. | Sustained reduction of bacterial growth at the CVC insertion site is indispensable. Male patients are at particular risk for skin colonisation and may be a target population for additional insertion-site care before and during catheterization. |
| Lundgren IS, Zhou C, Malone FR, McAfee NG, Gantt S, Zerr DM. Central venous catheter repair is associated with an increased risk of bacteremia and central line-associated bloodstream infection in pediatric patients. Pediatr Infect Dis J. 2012;31(4):337-340. PMID: 22146741 | C | Pediatric patients 1 month to 21 years of age with CVC breakages that underwent a first-time repair n= 81 children who underwent a first CVC repair procedure Retrospective case-crossover study | Compared rates of bacteremia and CLABSI. 30 days pre-repair (control period). 30 days post-repair (exposure period). | Repair of a broken CVC was associated with a 2- to 4-fold higher risk of developing CLABSI within 30 days of repair in pediatric patients. | NA |

* For study design notation, see legend on first page of appendix

Topic C. Diagnostic Procedures and Considerations

| Reference Citation | Study Design * | Patient Population | Description of | Summary of Results for Relevant Main Outcome(s) | Reviewer notes |
|--|----------------|---|--|--|----------------|
| <p>Bouza, E., Alvarado, N., Alcala, L., Sanchez-Conde, M., Perez, M. J., Munoz, P., Rodriguez-Creixems, M. (2005). A prospective, randomized, and comparative study of 3 different methods for the diagnosis of intravascular catheter colonization. <i>Clinical Infectious Diseases: An Official Publication of the Infectious Diseases Society of America</i>, 40(8), 1096-1100. doi: CID34759 [pii]. PMID: 15791507</p> | B | <p>1000 catheter tips Prospectively compared Maki's semi-quantitative technique and the quantitative methods of sonication and vortexing for the detection of colonization of intravascular catheter tips and catheter-related bloodstream infections</p> | <p>Prospectively compared:</p> <ul style="list-style-type: none"> • Semi-quantitative, Maki's technique with breakpoint of ≥ 15 CFU <ul style="list-style-type: none"> ○ Sonication ○ Vortexing • Quantitative with breakpoint of ≥ 100 CFU • Quantitative with breakpoint of ≥ 1000 CFU | <p>329 (32.9%) had positive results for at least 1 of the 3 techniques when a breakpoint of ≥ 100 colony-forming units (cfu)/catheter segment was used for the quantitative techniques and a breakpoint of ≥ 15 cfu was used for Maki's technique. Eighty-two of the catheter tips for which results were positive were from patients with catheter-related bloodstream infections. For each technique, the likelihood of detection decreased progressively depending on the order in which the technique was performed. The likelihood of detection of catheter colonization for each technique, when the technique was performed first and when 2 breakpoints (≥ 100 cfu/catheter segment and ≥ 1000 cfu/catheter segment) were used for the quantitative techniques and a breakpoint of ≥ 15 cfu was used for Maki's technique, was as follows: 99.1% and 100% for Maki's technique, 95.1% and 92.9% for sonication, and 93.1% and 72.8% for vortexing (for criteria B and A, respectively). No inferiority of Maki's technique could be demonstrated when results were compared according to whether catheter placement was short term (i.e., ≤ 7 days), either for the detection of colonization or for the detection of catheter-related bloodstream infections.</p> | N/A |
| <p>Finkelstein, R., Fusman, R., Oren, I., Kassis, I., & Hashman, N. (2002). Clinical and epidemiologic significance of coagulase-negative staphylococci bacteremia in a tertiary care university israeli hospital. <i>American Journal of Infection Control</i>, 30(1), 21-25. doi: S0196655302901719 [pii]. PMID: 11852412</p> | C | 137 positive blood cultures | <p>Prospective cohort study, 41 (30%) were considered as true infection. Twenty-seven of 119 episodes associated with only 1 blood culture positive for CNS (23%) met the definition of infection as compared with 14 of 18 episodes (78%) associated with 2 or more blood</p> | <p>Methicillin resistance was significantly more frequent among Staphylococcus epidermidis isolates of episodes of true bacteremia than of episodes of contamination (15 of 22 [68%] vs. 11 of 33 [33%], respectively; $P = .02$). S hominis was isolated only in episodes considered as contamination ($P = .01$). It was estimated that CNS represents 24% of all nosocomial bloodstream pathogens. When CNS were isolated in the first 48 hours of hospitalization, an intravascular device was more frequently associated with episodes of true</p> | N/A |

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| | | | cultures positive for CNS (P <.001). | bacteremia than in those considered as contamination (7 of 7 [100%] vs. 10 of 57 [18%], respectively; P <.001). The mortality rate among patients with true CNS bacteremia was 16%. | |
| Flynn, L., Zimmerman, L. H., Rose, A., Zhao, J., Wahby, K., Dotson, B., Tennenberg, S. (2012). Vascular catheter tip cultures for suspected catheter-related blood stream infection in the intensive care unit: A tradition whose time has passed? <i>Surgical Infections</i> , 13(4), 245-249. PMID: 22792865 | C | 1,391 CTCs were obtained | Reviewed retrospectively all positive (>15 colony forming units/roll) vascular catheter tip cultures (CTCs) documented over a four-year period in the ICUs of two hospitals. A CR-BSI was defined as matching positive blood and catheter cultures. The time interval between catheter removal and blood culture was recorded. | 468 (34%) were positive and 143 (31% of the positive cultures) were associated with a diagnosis of CR-BSI. In 133 of these 143 cases (93%), the positive blood culture was obtained before or within 24 h after catheter removal and dictated antibiotic therapy. In only 10 of 143 cases (7%) did catheter removal and culture significantly (>1 day) precede the positive blood culture. In 55% of the CR-BSI cases, the catheter was removed empirically and close to the time of blood culture (-1.3+19.0 h). In the remaining 45%, the catheter was removed clinically (after a blood culture was positive), and this action was more remote in time (23.6+19.4 h; p<0.001 vs. empiric removal). | N/A |
| Franklin, J. A., Gaur, A. H., Shenep, J. L., Hu, X. J., & Flynn, P. M. (2004). In situ diagnosis of central venous catheter-related bloodstream infection without peripheral blood culture. <i>The Pediatric Infectious Disease Journal</i> , 23(7), 614-618. doi:00006454-200407000-00005 [pii]. PMID: 15247598 | D | 136 episodes of positive blood cultures | Computerized search of patient records identified all positive blood culture results. | 136 episodes of bacteremia that were evaluable for alternative definition 1 and 241 episodes that were evaluable for alternative definition 2. In patients with a double lumen CVC, CRBI can be diagnosed by a > or = 5-fold difference in colony-forming units/mL between the 2 lumens (alternative definition 1) with sensitivity, specificity, PPV and likelihood ratio of 61.8, 93.3, 92.2 and 9.22, respectively. In patients with a single or double lumen CVC, CRBI can be diagnosed when the CVC culture yields > or = 100 colony-forming units/mL (alternative definition 2) with sensitivity, specificity, PPV and likelihood ratio of 75.5, 69.1, 79.3, and 2.44. | N/A |
| Guembe, M., Rodriguez-Creixems, M., Sanchez-Carrillo, C., Martin-Rabadan, P., & Bouza, E. (2012). Differential time to positivity (DTTP) for the diagnosis of catheter-related bloodstream infection: Do we need to obtain one or more peripheral vein blood cultures? <i>European Journal of Clinical Microbiology & Infectious Diseases</i> , 31(7), 1367-1372. PMID: 22015990 | C | 60 episodes of proven CLABSI | Patients with proven CLABSI in which catheter lumens and two or more PV blood cultures were taken simultaneously. | If one PV culture had been eliminated in patients with two or three PV blood cultures, documented 91.8% (p=0.362) and 96.9% (p>0.999) of episodes, respectively. Eliminated two PV blood cultures in patients with three PV blood cultures, 90.8% (p>0.999) of episodes would have been documented. When performing the DTTP technique to confirm CLABSI, a single paired PV blood culture was not associated with a significant number of missed CLABSI episodes. | N/A |
| Guembe, M., Rodriguez-Creixems, M., Sanchez-Carrillo, C., Perez-Parra, A., Martin-Rabadan, P., & Bouza, E. (2010). How many lumens should be cultured in | C | 171 episodes proven CRBSI | Patients with microbiologically proven CRBSI in which all available catheter lumens (those that did not contain | If one lumen-associated culture had been eliminated for both double-lumen and triple-lumen catheters, 27.2% and 15.8% of episodes of CRBSI would have missed. | N/A |

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| the conservative diagnosis of catheter-related bloodstream infections? <i>Clinical Infectious Diseases</i> , 50(12), 1575-1579. PMID: 20455693 | | | clots) were used to draw blood culture samples. | If 2 cultures were eliminated for triple-lumen catheters, 37.3% of episodes would have been missed. | |
| Koc, O., Peynircioglu, B., & Cil, B. E. (2008). Role of culturing from the tip and the tunneled segment of the catheters in tunneled catheter infection. <i>Diagnostic & Interventional Radiology</i> , 14(4), 228-232. PMID: 19061170 | C | 22 tunneled jugular catheters | 22 tunneled jugular catheters were removed due to infection. Clinical indications for catheter removal secondary to infection were repetitive positive catheter cultures, persistent fever with no other known etiology, tunnel infections, and sepsis most likely attributed to the catheter. | Mean duration of catheter placement was 110.7 days; 13 patients (59%) whose catheters were removed had negative catheter cultures. Cultures from 9 catheters were positive from the tip and/or tunneled segment. Among those, 7 patients had catheter-related bloodstream infections and 2 had local tunnel infections. | N/A |
| Mermel, L. A., Allon, M., Bouza, E., Craven, D. E., Flynn, P., O'Grady, N. P., Warren, D. K. (2009). Clinical practice guidelines for the diagnosis and management of intravascular catheter-related infection: 2009 update by the infectious diseases society of america. <i>Clinical Infectious Diseases</i> , 49(1), 1-45. PMID: 19489710 | Guideline | N/A | N/A | N/A | Guideline Document. Relevant evidence cited from original source material. See evidence tables in source. |
| Raad, I., Hanna, H. A., Alakech, B., Chatzinikolaou, I., Johnson, M. M., & Tarrand, J. (2004). Differential time to positivity: A useful method for diagnosing catheter-related bloodstream infections. <i>Annals of Internal Medicine</i> , 140(1), 18-25. doi:140/1/18 [pii]. PMID: 14706968 | B | 191 patients with bloodstream infections | Patients who had the same organism isolated from blood cultures drawn simultaneously through the central venous catheter and the peripheral vein. | Catheter-related bacteremias were more frequently caused by staphylococci and less likely to be associated with underlying hematologic malignant conditions, neutropenia, and longer duration of hospitalization. As a diagnostic tool for catheter-related bacteremia (using a composite definition reference standard according to the Infectious Diseases Society of America guidelines), differential time to positivity of 120 minutes or more was associated with 81% sensitivity and 92% specificity for short-term catheters and 93% sensitivity and 75% specificity for long-term catheters. | N/A |
| Safdar, N., Fine, J. P., & Maki, D. G. (2005). Meta-analysis: Methods for diagnosing intravascular device-related bloodstream infection. <i>Annals of Internal Medicine</i> , 142(6), 451-466. doi:142/6/451 [pii]. PMID: 15767623 | A | 51 studies of IVD-related bloodstream infection | Pooled sensitivity and specificity were calculated for 8 diagnostic methods. | Paired quantitative blood culture is the most accurate test for diagnosis of IVD-related bloodstream infection. However, most other methods studied showed acceptable sensitivity and specificity (both >0.75) and negative predictive value (>99%). The positive predictive value of all tests increased greatly with high pretest clinical probability. Catheters should not be cultured | Meta-analysis |

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| | | | | routinely but rather only if IVD-related bloodstream infection is suspected clinically. | |
| Scheinemann, K., Ethier, M. C., Dupuis, L. L., Richardson, S. E., Doyle, J., Allen, U., & Sung, L. (2010). Utility of peripheral blood cultures in bacteremic pediatric cancer patients with a central line. <i>Supportive Care in Cancer</i> , 18(8), 913-919. PMID: 19727845 | C | 318 episodes of positive CVC cultures in children with cancer | Children with cancer who had peripheral and CVC cultures obtained on the same day in which at least one culture was positive. Only cultures obtained prior to the initiation of broad-spectrum antibiotics were included. | 228/318 (71.7%) were classified as true bloodstream infections while 90/318 (28.3%) were classified as contaminants. 28/228 (12.3%) true bloodstream infections were detected only in peripheral culture while 85/228 (37.3%) true bloodstream infections were detected only by CVC cultures. Contaminants were identified in peripheral culture in 45/318 (14.2%) of episodes and in CVC culture in 45/318 (14.2%) episodes. | N/A |
| Ruhe, J., Menon, A., Mushatt, D., Dejace, P., & Hasbun, R. (2004). Non-epidermidis coagulase-negative staphylococcal bacteremia: Clinical predictors of true bacteremia. <i>European Journal of Clinical Microbiology & Infectious Diseases: Official Publication of the European Society of Clinical Microbiology</i> , 23(6), 495-498. doi:10.1007/s10096-004-1134-4 [doi]. PMID: 15141334 | C | 160 patients with positive blood cultures for non-epidermidis, coagulase-negative staphylococci (NECNS) | Blood cultures positive for non-epidermidis, coagulase-negative staphylococci (NECNS). | 28 of the 32 significant isolates were resistant to methicillin, compared to only 50 of the 128 contaminants. This could be explained by the highly preserved methicillin sensitivity found among the common contaminants <i>S. capitis</i> and <i>S. auricularis</i> (i.e., among 45 isolates only 4 were resistant to methicillin). Another remarkable finding in our study was the high rate (38%) of true bloodstream infections with only one positive blood culture. This finding is consistent with results of previous studies suggesting that a single positive blood culture should not always be considered a contaminant. | N/A |

* For study design notation, see legend on first page of appendix

Topic D. Removal vs Salvage

| Reference Citation | Study Design * | Patient Population <ul style="list-style-type: none"> • Description • Total N of patients • If systematic review, N of studies | Description of <ul style="list-style-type: none"> • Study group (n) • Comparison group (n) | Summary of Results for Relevant Main Outcome(s) <ul style="list-style-type: none"> • Effect size • Statistical significance) | Reviewer notes <ul style="list-style-type: none"> • Methodological issues, • Noteworthy harms • Other |
|--|----------------|--|--|--|--|
| <p>Lai, C. H., Kan, C. D., Wu, H. Y., Luo, C. Y., Chao, C. M., & Wen, J. S. (2009). Modified exchange technique for management of dysfunctional tunneled hemodialysis catheters in the presence of exit-site infection: A quality improvement report. <i>American Journal of Kidney Diseases: The Official Journal of the National Kidney Foundation</i>, 53(1), 112-120. doi:10.1053/j.ajkd.2008.08.024. PMID: 18976847</p> | C | <p>Consecutive case series (Quality improvement report) n=28 catheters (23 patients)</p> | <p>Study of introduction of a new tunneled hemodialysis catheters (THC) through a remote exit site and preexisting subcutaneous tunnel. 28 consecutive dysfunctional THCs with exit-site infection (ESI) in 23 patients who did not have tunnel infection or bacteremia before the procedures.</p> | <p>There was only 1 failure, giving an overall technical success rate of 96%. The other 27 exchanged THCs achieved satisfactory flow during subsequent hemodialysis, and the ESI gradually resolved within 2 weeks. Although 8 episodes of new ESI occurred, no subcutaneous tunnel infection or bacteremia occurred within 120 days.</p> | NA |
| <p>Martinez, E., Mensa, J., Rovira, M., Martinez, J. A., Marcos, A., Almela, M., & Carreras, E. (1999). Central venous catheter exchange by guidewire for treatment of catheter-related bacteraemia in patients undergoing BMT or intensive chemotherapy. <i>Bone Marrow Transplantation</i>, 23(1), 41-44. doi:10.1038/sj.bmt.1701538. PMID: 10037049</p> | C | <p>Evaluated prospectively the usefulness of CVC exchange by guidewire for the treatment of CRB in patients undergoing BMT or intensive chemotherapy n=19 episodes of bacteraemia during a 1-year period</p> | <p>CVC exchange was considered when fever and positive blood cultures persisted after 2 days of adequate antimicrobial therapy and no potential source of bacteraemia other than CVC could be identified. Bacteraemia was confirmed as catheter-related by demonstrating concordance between isolates from the tip and blood cultures.</p> | <p>14 episodes (74%) were catheter-related and 71% of these were due to coagulase-negative staphylococci. Guidewire replacement was accomplished uneventfully 4 days after development of sepsis (range 3-6). In all cases, clinical signs of sepsis disappeared less than 24 h after replacement. Definitive catheter withdrawal was carried out a median of 16 days (range 3-42) after guidewire exchange; in all cases, the tip culture was negative. CVC replacement by guidewire under adequate antimicrobial therapy may be a reasonable option for the treatment of CRB when antimicrobial therapy alone has been unsuccessful.</p> | <p>Small case sample. Limited quality of data.</p> |

* For study design notation, see legend on first page of appendix

Topic E. Additional Considerations

| Reference Citation | Study Design * | Patient Population | Description of | Summary of Results for Relevant Main Outcome(s) | Reviewer notes |
|--|----------------|--|---|---|--|
| | | <ul style="list-style-type: none"> Description Total N of patients If systematic review, N of studies | <ul style="list-style-type: none"> Study group (n) Comparison group (n) | <ul style="list-style-type: none"> Effect size Statistical significance) | <ul style="list-style-type: none"> Methodological issues, Noteworthy harms Other |
| Daneman, N., Downing, M., & Zagorski, B. M. (2012). How long should peripherally inserted central catheterization be delayed in the context of recently documented bloodstream infection? <i>Journal of Vascular & Interventional Radiology</i> , 23(1), 123-125. PMID: 22221476 | C | Patients q/ PICC placed within 6 weeks after documented bacteremia n=348 | One retrospective cohort of patients receiving PICC post bacteremia, to characterize risk of re-infection. | The overall risk of relapsing bacteremia was low (three of 348; 0.9%) when PICC insertion was performed in the context of a recent bloodstream infection. The relapse risk was higher when PICCs were inserted within 2 days (two of 31; 6.5%) versus at least 3 days (one of 317; 0.3%) after documentation of bacteremia (P = .02). | N/A |
| Fowler, V. G. Jr, Sanders, L. L., Sexton, D. J., Kong, L., Marr, K. A., Gopal, A. K., . . . Corey, G. R. (1998). Outcome of staphylococcus aureus bacteremia according to compliance with recommendations of infectious diseases specialists: Experience with 244 patients. <i>Clinical Infectious Diseases: An Official Publication of the Infectious Diseases Society of America</i> , 27(3), 478-486. PMID: 9770144 | C | Hospitalized patients with Staphylococcus aureus bacteremia Followed for 12 weeks from first positive culture n=244 | ID management advice was followed 112 patients (45.9%). ID management advice partially or completely ignored for 132 patients (54.1%). | Pts following ID advice more likely to be cured of their S. aureus infection and less likely to relapse (P < .01). Failure to remove an infected CVC biggest risk for treatment failure. Patients whose intravascular device was not removed were 6.5 times more likely to relapse or die. | Patient-specific management advice by infectious diseases consultants can improve the clinical outcome for patients with S. aureus bacteremia. |
| Honda, H., Krauss, M. J., Jones, J. C., Olsen, M. A., & Warren, D. K. (2010). The value of infectious diseases consultation in staphylococcus aureus bacteremia. <i>The American Journal of Medicine</i> , 123(7), 631-637. doi:10.1016/j.amjmed.2010.01.015 [doi]. PMID: 20493464 | C | A 2-year prospective cohort study of patients with S. aureus bacteremia at a large tertiary care hospital n=341 | Independent risk factors for 28-day mortality were determined: 185 (54%) had methicillin-resistant S. aureus. 108 (32%) had nosocomial bacteremia. 231 (68%) had a central venous catheter at the time of diagnosis. | Factors associated with mortality were: <ul style="list-style-type: none"> Intensive care unit admission 48 hours or less after the first positive blood culture (adjusted hazard ratio, 4.65; 95% confidence interval [CI], 2.65-8.18). Cirrhosis (adjusted hazard ratio, 4.44; 95% CI, 2.40-8.20). Advanced age (adjusted hazard ratio, 1.27 per every 10 years of age; 95% CI, 1.08-1.50). Infectious diseases consultation was associated with a 56% reduction in 28-day mortality (adjusted hazard ratio, 0.44; 95% CI, 0.22-0.89). | Infectious diseases consultation was independently associated with a reduction in 28-day mortality. |

* For study design notation, see legend on first page of appendix