4-2021

Blood cultures central versus venipuncture: Summary

Children's Mercy Kansas City

Office of Evidence Based Practice (EBP) – Critically Appraised Topic (CAT): Central Line Versus Venipuncture Blood Cultures

Specific Care Question In pediatric patients, should blood culture samples be obtained/collected through venipuncture versus central line draw to ensure true bacteremia?

Recommendations Based on Current Literature (Best Evidence) Only

A strong recommendation is made for collecting blood cultures samples from venipuncture versus central line draws, based on the the Summary of Findings Table[a]. The overall certainty in the evidence is very low[a].

Twelve studies were identified that answered the question and found that blood draws through venipuncture will result in 33 to 39 fewer contaminations per 1,000 blood draws. (see Summary by Outcome for substantiation of recommendations).

Literature Summary

Background. For directing appropriate antibiotic therapy, blood cultures are the primary laboratory test for diagnosing serious blood stream infections, (Snyder et al., 2012). Accurate blood cultures are essential for providing safe, judicious, and efficient care for patients with these infections. However, accurate blood cultures are problematic as 25-50% of all positive blood cultures are considered to be contaminated (Doern et al., 2019). The cost of a false positive blood culture equates to approximately $8,000 per contaminant (Gander et al., 2009).

In a meta-analysis that compared venipunctures to both central and peripheral catheters, the odds of a contaminated sample were 2.7 times less likely with a venipuncture (Snyder et al., 2012). It is important to note that for the diagnosis of central line associated blood stream infections (CLABSI), the Infectious Disease Society of America (IDSA) (Baron et al., 2013) and the Center for Disease Control and Prevention (CDC) (Septimus, 2021), recommends simultaneous blood draws from the suspected catheter(s) and a venipuncture.

This review will summarize identified literature to answer the specific care question.

Study characteristics. The search for suitable studies was completed on January 5, 2021. Y, Ballam, BS, CIC and C. Duru, DNP, MSN, BSN, RN, CIC reviewed the 39 titles and/or abstracts found in the search and identified[b] 17 studies believed to answer the question. After an in-depth review of the 17 studies[d], 12 answered the question. Four cohort studies (Berger et al., 2018; Doganis et al., 2013; Handrup et al., 2015; Santos et al., 2018) and four systematic reviews (Dawson, 2014; Falagas et al., 2008; Garcia et al., 2015; Snyder et al., 2012) which included eight cohorts (Beutz et al., 2003; Boyce et al., 2013; Bryant & Strand, 1987; DesJardin et al., 1999; Martinez et al., 2002; McBryde et al., 2005; Stohl et al., 2011; Tafuro et al., 1986) answered the question.

Summary by Outcome

Contamination Rate. 12 studies (Berger et al., 2018; Beutz et al., 2003; Boyce et al., 2013; Bryant & Strand, 1987; DesJardin et al., 1999; Doganis et al., 2013; Handrup et al., 2015; Martinez et al., 2002; McBryde et al., 2005; Santos et al., 2018; Stohl et al., 2011; Tafuro et al., 1986) measured contamination rates, (n = 37,638). *OR* indicated results as contamination rates of blood draws comparing venipunctures versus central line draws and they are included in the meta-analysis (see Figure 2 & *Table 2*). The *OR* indicated the intervention of venipunctures was favorable to the comparator of central line draws, *OR* = 0.41 95% CI [0.36, 0.46], p-value <0.00001. Blood draws through venipuncture will result in 33 to 39 fewer contaminations per 1,000 blood draws.

Certainty of the evidence for Contamination Rate. The certainty of the body of evidence was very low based on four factors[a]: *within-study risk of bias*, *consistency among studies, directness of evidence*, and *precision of effect estimates*. The body of evidence was assessed to have serious risk of bias and serious inconsistency. *Risk of bias was serious as there is no gold standard for determining true blood stream infections. There was serious inconsistency as there was* considerable heterogeneity based on an I^2 of 83%.

Identification of Studies

Search Strategy and Results (see Figure 1)

Librarin K. Swaggart, MLIS, AHIP performed an informal hand search of Pubmed.
Records identified through database searching n = 31
Additional records identified through other sources n = 8

Studies Included in this Review

Citation	Study Type
Berger et al. (2018)	Cohort
Dawson (2014)	SR
*Boyce et al. (2013)	Cohort
*Stohl et al. (2011)	Cohort
Doganis et al. (2013)	Cohort
Falagas et al. (2008)	SR
*Bryant and Strand (1987)	Cohort
*Tafuro et al. (1986)	Cohort
Snyder et al. (2012)	SR
*Beutz et al. (2003)	Cohort
*DesJardin et al. (1999)	Cohort
*Martinez et al. (2002)	Cohort
*McBryde et al. (2005)	Cohort
Handrup et al., 2015	Cohort
Santos et al. (2018)	Cohort

References marked with an asterisk indicate studies included the meta-analysis

Studies Not Included in this Review with Exclusion Rationale

Citation	Reason for exclusion
Coventry et al. (2019)	No central lines
Doern et al. (2019)	Review article
Halstead et al. (2020)	No central lines
Mermel (2019)	No central lines
Garcia et al. (2015)	Duplicate studies

Methods Used for Appraisal and Synthesis

[a]The GRADEpro Guideline Development Tool (GDT) is the tool used to create the Summary of Findings table(s) for this analysis.

[b]Rayyan is a web-based software used for the initial screening of titles and / or abstracts for this analysis (Ouzzani, Hammady, Fedorowicz & Elmagarmid, 2017).

[c]Review Manager (Higgins & Green, 2011) is a Cochrane Collaborative computer program used to assess the study characteristics as well as the risk of bias and create the forest plots found in this analysis.

[d]The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram depicts the process in which literature is searched, screened, and eligibility criteria is applied (Moher, Liberati, Tetzlaff, & Altman, 2009).

[a]GRADEpro GDT: GRADEpro Guideline Development Tool (2015). McMaster University, (developed by Evidence Prime, Inc.). [Software]. Available from gradepro.org.

[b]Ouzzani, M., Hammady, H., Fedorowicz, Z., & Elmagarmid, A. (2016). Rayyan-a web and mobile app for systematic reviews. *Systematic Reviews, 5*(1), 210. doi:10.1186/s13643-016-0384-4

[c]Higgins, J. P. T., & Green, S. e. (2011). *Cochrane Handbook for Systematic Reviews of Interventions [updated March 2011]* (Version 5.1.0 ed.): The Cochrane Collaboration, 2011.

[d]Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). *P*referred *R*eporting *I*tems for *S*ystematic Reviews and *M*eta-*A*nalyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097 **For more information, visit www.prisma-statement.org.**

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Acronyms Used in this Document

Acronym	Explanation
AGREE II	Appraisal of Guidelines Research and Evaluation II
BC	Blood culture
BCC	Blood culture contamination
BSI	Blood stream infections
CAT	Critically Appraised Topic
CDC	Center for Disease Control and Prevention
CLABSI	Central line associated blood stream infections
CVL	Central venous line
EBP	Evidence Based Practice
IDSA	Infectious Disease Society of America
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PV	Peripheral vein

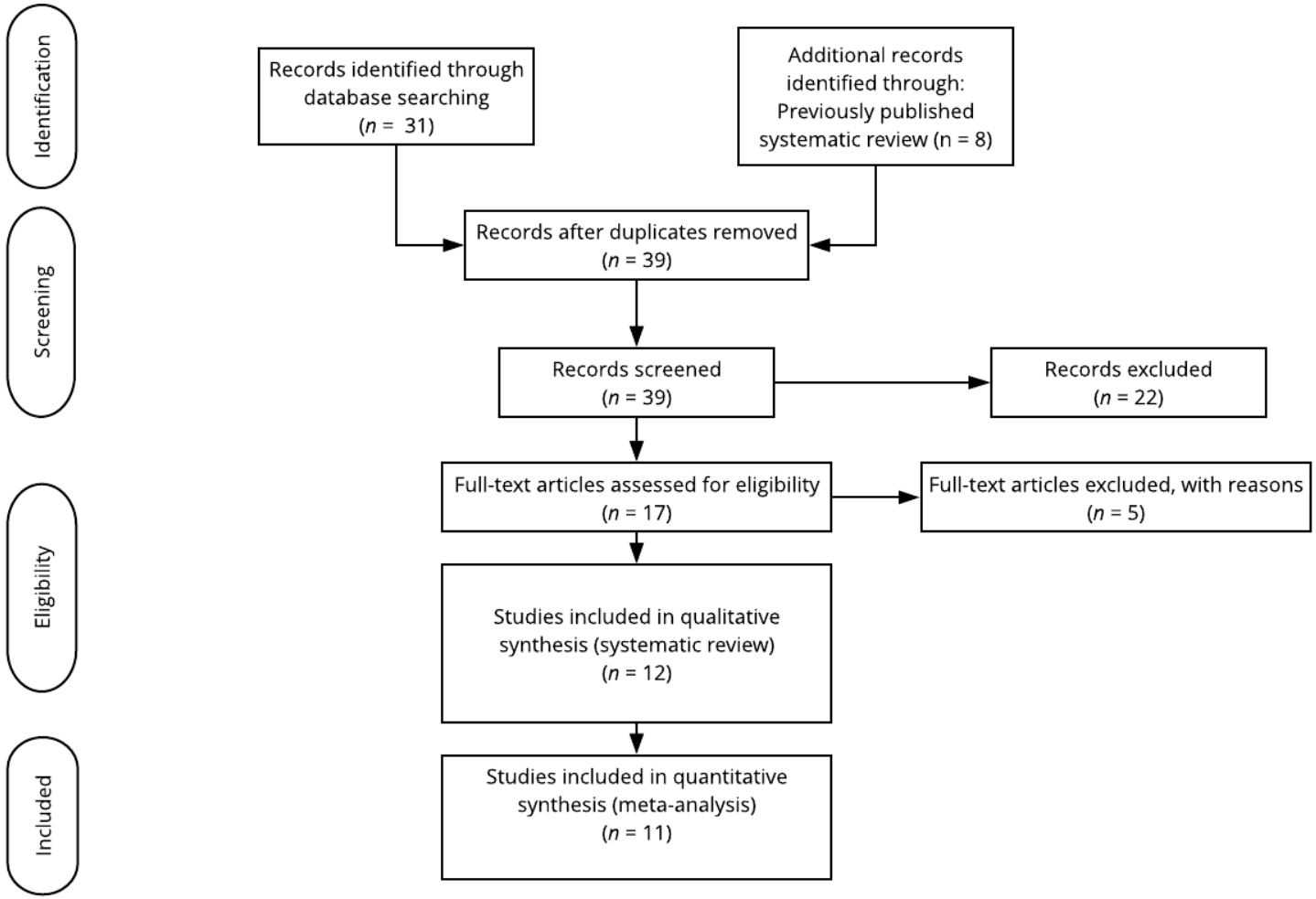

Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRIMSA)[d]

Table 1

Study Characteristics Table

Study	Study Type	Population/Sample	Comparison	Patients	Sample
Berger 2018	Retrospective Cohort	Pediatric ICU	Venipuncture versus central vascular catheter	138	276 paired
*Beutz 2003	Prospective Cohort	Adult Medical ICU	Venipuncture versus central vascular catheter	119	300 paired
*Boyce 2013	Retrospective Cohort	Adult ICU	Venipuncture versus central vascular catheter	not reported	14,479
*Bryant 1987	Prospective Cohort	Adult ICU	Venipuncture versus central vascular catheter	53	130 paired
*DesJardin 1999	Retrospective Cohort	Adult Hematology Oncology	Venipuncture versus central vascular catheter	185	551 paired
Doganis 2013	Retrospective Cohort	Pediatric Oncology	Venipuncture versus central vascular catheter	211	633 paired
Handrup 2014	Prospective Cohort	Pediatric Oncology	Venipuncture versus central vascular catheter	not reported	654 paired
*Martinez 2002	Retrospective Cohort	Adult Surgical and cardiothoracic ICU	Venipuncture versus central vascular catheter	271	499 paired
*Mcbryde 2005	Retrospective Cohort	Adult hospital - All units	Venipuncture versus central vascular catheter	not reported	962 paired
Santos 2018	Retrospective Cohort	Adult hospital - All units	Avoidance of central line or peripheral lines	not reported	234 per 1000 patient day post intervention
*Stohl 2011	Retrospective Cohort	Adult ICU	Venipuncture versus central vascular catheter	not reported	14,589
*Tafuro 1986	Prospective Cohort	Adult Surgical ICU	Venipuncture versus central vascular catheter	79	234 paired

*References marked with an asterisk (*) indicate studies included the meta-analysis (*Dawson, 2014; Falagas et al., 2008; Snyder et al., 2012)

Table 2

Summary of Findings Table: Contamination

Certainty assessment							Summary of findings				
							Study event rates (%)			Anticipated absolute effects	
Participants (studies) Follow up	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Publication bias**	**Overall certainty of evidence**	**With Central BC**	**With Venipuncture BC**	**Relative effect (95% CI)**	**Risk with Central BC**	**Risk difference with Venipuncture BC**
Contamination											
37638 (11 observational studies)	serious [a]	serious [b]	not serious	not serious	strong association	⨁◯◯◯ VERY LOW	608/9767 (6.2%)	560/27871 (2.0%)	**OR 0.41** (0.36 to 0.46)	62 per 1,000	**36 fewer per 1,000** (from 39 fewer to 33 fewer)

Explanations

a. No gold standard for determining true infection rate

b. Considerable heterogeneity based on I^2 of 83%

Study or Subgroup	Venipuncture Events	Venipuncture Total	Central Line Events	Central Line Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Berger 2018	4	276	11	276	1.5%	0.35 [0.11, 1.13]
Beutz 2003	11	300	20	300	2.6%	0.53 [0.25, 1.13]
Boyce 2013	100	13292	47	1187	11.6%	0.18 [0.13, 0.26]
Bryant 1987	3	130	23	130	3.0%	0.11 [0.03, 0.38]
Desjardin 1999	13	551	24	551	3.2%	0.53 [0.27, 1.05]
Doganis 2013	5	633	26	633	3.5%	0.19 [0.07, 0.49]
Handrup 2015	9	654	31	654	4.1%	0.28 [0.13, 0.59]
Martinez 2002	8	499	20	499	2.7%	0.39 [0.17, 0.89]
Mcbryde 2005	25	962	124	962	16.4%	0.18 [0.12, 0.28]
Stohl 2011	378	10340	273	4341	50.2%	0.57 [0.48, 0.66]
Tafuro 1986	4	234	9	234	1.2%	0.43 [0.13, 1.43]
Total (95% CI)		**27871**		**9767**	**100.0%**	**0.41 [0.36, 0.46]**
Total events	560		608			

Heterogeneity: $Chi^2 = 57.97$, df = 10 ($P < 0.00001$); $I^2 = 83\%$

Test for overall effect: $Z = 14.12$ ($P < 0.00001$)

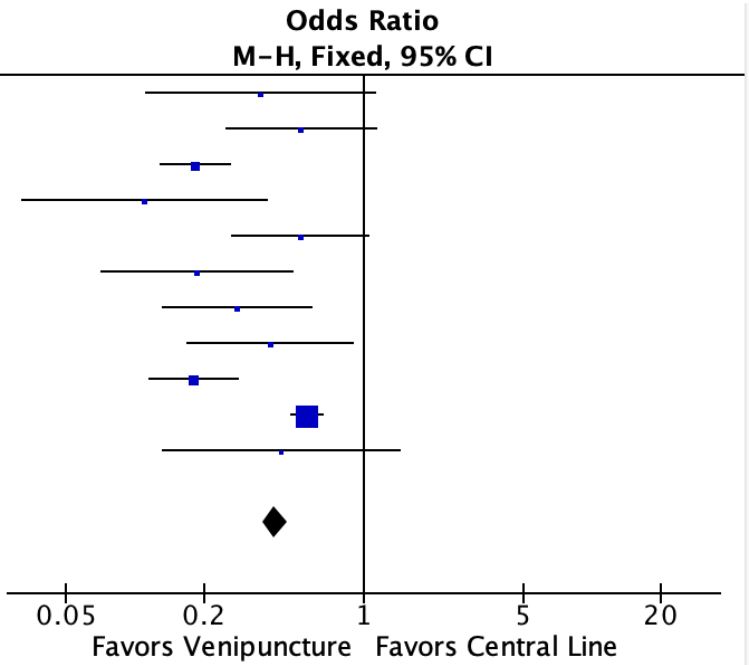

Figure 2. **Comparison: Venipuncture versus Central Line, Outcome: Contamination**

Characteristics of Intervention Studies

Berger et al. (2018)

Methods	Cohort
Participants	**Participants:** Blood culture samples from patients in two pediatric intensive care units between September 2014 and September 2015 **Setting:** Schneider Children's Medical Center of Israel **Number enrolled into study:** *N* = 138 • Blood culture obtained from peripheral site and arterial catheter**:** *n = 276* **Gender, males (as defined by researchers):** • *n* =78 (56.5%) **Race / ethnicity or nationality (as defined by researchers):** • Not given **Age, mean in months (SD)** • 45.5 months (71.4) **Inclusion Criteria:** • Patients in the pediatric intensive care unit (PICU) or pediatric cardiac intensive care unit (PCICU) • Presence of an indwelling arterial catheter • Indication for blood culture (fever, elevated inflammation indices, known BSI, suspected sepsis, or septic shock) **Exclusion Criteria:** • Inability to obtain peripheral site blood culture
Interventions	**Both:** Blood volume in accordance with departmental recommendations by patient weight obtained ○ Peripheral venipuncture performed by physician under sterile conditions to obtain blood ○ Blood drawn from stopcock of arterial catheter
Outcomes	**Primary outcome(s):** • True pathogen rate* **Secondary outcome(s):** • Contaminated samples* • Effect of arterial catheter duration *Outcomes of interest to the CMH CPG /CAT development team
Results	**Results:** • A total of 56 (20%) culture pairs were positive with either bacterial or fungal pathogen, 41 (75%) were diagnostic for true BSI (true positive): ○ Twenty-eight (66%) of positive cultures for true BSI had same pathogen in both groups ○ Eight true BSI positives were in only group 2 ○ Five true BSI positives were only in group 1 • Fifteen cultures were contaminated (false positive) with 11 contaminations occurring in the arterial line ○ Coagulase-negative *Staphylococcus* in 13 cases (4 in group 1 only, 9 in group 2 only) ○ One group 2 culture showed *Micrococcus* ○ One group 2 culture showed *Enterococcus* • No arterial catheter colonization occurred • BSI occurrence increases with duration of arterial catheter greater than 30 days; 10.1% positive for up to 10 days and 50-75% for 40-60 days • For diagnostic accuracy testing: Group 2 had higher sensitivity but lower positive predictive value than Group 1

	Group 1 [95% CI]	Group 2 [95% CI]
Sensitivity	80.5 [65, 91]	85.4 [71, 94]
Specificity	98.3 [96, 99]	95.3 [92, 98]
Positive predictive value	89.2 [75, 97]	76.1 [61, 87]
Negative predictive value	96.7 [93, 98]	97.4 [94, 99]
Positive likelihood ratio	47.3	18.2
False-negative rate	19.5	14.6
Accuracy	95.7	93.8

Limitations:

- Observational design, sterile technique and blood volumes recommendations may not have been followed
- Manner of determination of true BSI
- Time of blood culture positivity is not reported

Dawson et al., 2014

Design	Quantitative Synthesis
Objective	To review the literature for factors that influence the rate of blood culture (BC) contamination.
Methods	**Protocol and registration.** No mention of protocol or registration **Eligibility Criteria.** • Not specified **Information sources.** Medline and CINAHL, 1990 to December 2013 **Search Strategy (Search terms)** • Blood culture contaminant • Blood culture contamination • English language only **Study Selection.** Not specified **Data collection process.** Not specified **Risk of bias (RoB) across studies.** Not specified **Summary measures.** Not specified **Synthesis of results.** A table is included
Results	**Study Selection.** **Number of articles identified:** *N* = Not specified **Full-text articles assessed for eligibility:** *n* = Not specified **Studies included in qualitative synthesis** (Number of studies counted from table 1, some of the studies were included multiple times in the table with different interventions) • **Intervention: BC taken at insertion of IV catheter:** *n* = 3 • **Intervention: Insertion of IV catheter samples in pediatric population** *n* = 5 • **Intervention: Antisepsis of bottle tops** *n* = 1 • **Intervention: Type of gloves** *n* = 2 • **Intervention: Needle changes** *n* = 1 • **Intervention: Use of prepacked kits** *n* = 6 • **Intervention: Which type of healthcare worker takes BC sample** *n* = 8 • **Intervention: Surveillance** *n* = 6 • **Intervention: Education** *n* = 1 **Synthesis of results.** Not specified, some results are mentioned in discussion **Risk of bias across studies.** Not specified
Discussion	**Summary of evidence.** **Positive BC Rates:** Not really specified. A few of the studies reported BC rates, most reported BC contamination rates. **Contaminated Sample:** Factors influencing contamination rates include • Methods of obtaining sample (venipuncture vs IV, correct use of various antiseptic skin preps) • Glove use (sterile vs non-sterile) • Needle changed during procedure • Cross contamination from other collections tubes

	• Use of prepacked kits • Staff competency • Monitoring of rates **Limitations.** The authors did not provide any methodological data needed to determine if an unbiased systematic review (such as study selection, data collection, or risk of bias across studies) occurred. Contaminants are defined as a growth of bacteria in the blood culture bottle that were not present in the patient's bloodstream and that were introduced during sample collection. A meta-analysis was not performed between the included studies. There is no 'gold standard' used to classify contaminants: • Some studies opted for clinical opinion of the significance of the isolate • Some studies classified contaminates depending on the species of organism isolated.
Funding	**None**

Doganis et al., 2013

Methods	**Retrospective chart review**
Participants	**Participants:** Pediatric oncology patients who were diagnosed with malignancy **Setting:** Hematology & Oncology Division of Children's Hospital of Michigan January 1, 2005 to December 31, 2009 **Number enrolled into study: *N*** = 211 **Gender, males (as defined by researchers): *n*** = 123 (58%) **Race / ethnicity or nationality (as defined by researchers):** • Caucasian: *n* = 115 (55%) • African American: *n* = 63 (29.9%) • Asian: *n* = 7 (3.3%) • Arabic: *n* = 11 (5.2%) • Hispanic: *n* = 14 (6.6%) **Age, median in years:** 5 and 5/12 (range 2/12 to 20 and 2/12) **Inclusion Criteria:** • Patients who had received chemotherapy or radiation treatment before the collection of a blood culture **Exclusion Criteria:** • Any infection episode in which samples from all sources were not obtained from all sources as defined in the methodology
Interventions	**Both:** • Infection episode was defined as ○ Any case of a patient with a single axillary temperature ≥ 38.3℃ ○ Or a temperature of 38.0℃ or higher for at least one hour ○ Or any case of a patient with a temperature of less than 38.3℃ and chills and/or hypotension and/or altered mental status and/or focal findings • Cases of infection were considered as new, separate episodes provided that more than seven days had elapsed since the start of the previous episode and no symptoms or signs of infection remained • A blood culture (BC) set was defined as BC samples taken within two hours of each other from a peripheral vein and from all lumens of all central venous catheters (CVC) in place. • BC samples were collected from all lumens from all catheters
Outcomes	**Outcome(s):** • Infection episodes • Blood culture (BC) set results
Results	**Results:** • Detected 597 sets of BCs from 597 separate infection episodes in 211 patients • 25 cases of polymicrobial infections were considered as separate episodes (*n* = 61) for each one of isolated organisms. Therefore, the final number of BC sets was 633. • True blood stream infection (BSI): *n* = 602 ○ Peripheral negative-CVC negative: *n* = 468 ○ Peripheral negative-CVC positive: *n* = 57 ○ Peripheral positive-CVC negative: *n* = 7 ○ Peripheral positive-CVC positive: *n* = 70 **Limitations:**

	• Table 2 reports results in two categories, True BSI and False-positive BSI. The True BSI result would likely be more accurately labeled as Infection Episodes, thereafter, described by the BC set results. In the discussion section, the authors state "Seven out of 134 true BSIs…"

Flagas et al., 2008

Design	Quantitative Systematic Review
Objective	Objective: Determine best practices (diagnostic testing) for identifying true bacteremia either through central venous or peripheral atrial blood draws Outcomes of interest: diagnostic performance characteristics of the compared test (sensitivity, specificity and positive and negative predictive value (PPV and NPV).
Methods	**Protocol and registration:** n/a **Eligibility Criteria:** **Inclusion Criteria:** • Studies were included in the analysis if they provided data regarding the diagnostic utility of blood cultures drawn from • central venous • peripheral arterial • Swan-Ganz catheters in patients with suspected bacteremia. • Studies included reported clear definitions of true bacteremia to determine diagnostic performance characteristics of tests (sensitivity, specificity and positive and negative value. • Studies with prospective and retrospective design were evaluated for possible inclusion in further analysis. • Only studies reported in English. **Exclusion Criteria:** • Studies that did not report relevant results or the raw data that permitted the calculation of results for these characteristics (listed in inclusion criteria). • Case-control studies, case series, case reports, review articles and letters to the editor. **Information sources:** PubMed (January 1970-October 2005) and the Cochrane Central Register of Controlled Trials, including references of the initially found articles **Search Strategy.** • Two reviewers independently performed the literature search to identify relevant studies to be included in the analysis and extracted the data. • Search terms used included: intravascular device, vascular catheter, peripheral vein, venipuncture, blood culture, bacteremia, bacteremia, bloodstream infection, performance characteristics, sensitivity, specificity and predictive value. **Study Selection.** • 301 studies pulled initially that meant search terms. • 222 studies were excluded due to irrelevance to main research question • 66 studies excluded as they did not report comparative data • 6 studies included in analysis- 3 prospective and 3 retrospective providing data for 2677 pairs of blood cultures obtained from an intravascular catheter and a peripheral venipuncture. **Data collection process.** • Year of publication • Design of the study • Setting • Patient population • Details regarding the type of catheters used • Techniques of blood culture acquisition

	• Time allowed to elapse between obtaining the blood specimen from the intravascular catheter • Peripheral venipuncture for cultures • Definition used for true bacteremia • Outcomes of interest achieved with each type of blood culture regarding sensitivity, specificity, PPV and NPV and any other report of increase in catheter colonization or catheter-related infections attributed to the use of intravascular catheters for obtaining blood cultures. **Risk of bias (RoB) across studies:** not reported **Summary measures.** • Bacteremia prevalence obtained through central vascular catheter (CVC) or peripheral venipuncture (PV) • Diagnostic performance characteristics of blood cultures obtained through a central vascular catheter or peripheral venipuncture **Synthesis of results.** • Sensitivity • Specificity • PPV • NPV
Results	**Study Selection.** **Number of articles identified:** *N* = 301 **Full-text articles assessed for eligibility:** *n* = 66 ○ **Studies included in qualitative synthesis:** *n* = 6 **Synthesis of results.** • A culture obtained from an intravascular catheter is a test with better sensitivity and better negative predictive values in diagnosing bacteremia compared to a culture taken by peripheral venipuncture. • It is a diagnostic test with less specificity and lower positive predictive value compared to a culture obtained by peripheral venipuncture. • The use of intravascular catheters for obtaining at least one blood culture may be the preferred method. • The comparative characteristics of blood cultures obtained from an intravascular catheter and a peripheral vein suggested that the first test has a higher sensitivity in diagnosing true bacteremia than the second. • When cultures obtained from arterial lines and peripheral venipuncture are compared, the results of cultures form both sources are in most cases equivalent. • Sensitivity of cultures taken through intravascular catheters ranged from 78% to 95% • Sensitivity of cultures taken through peripheral venipuncture ranged from 64% to 95% • Highest observed positive predictive value of catheter-drawn cultures was 63.9% (range 17.2-63.9% with a weighted mean of 55.1)- Lowest PPV for catheter/central line drawn • Lowest PPV of cultures drawn via peripheral vein (66.7-85.4% with weighted mean of 79.3%). **Risk of bias across studies:** not reported
Discussion	**Summary of evidence.** • Culture obtained from an intravascular catheter showed better sensitivity, 1.85, 95% CI [1.14, 2.99] and better NPV, 1.55, 95% CI, [0.999, 2.39] for diagnosing bacteremia compared to a culture taken by peripheral venipuncture. • Testing blood culture from intravascular catheter shows less specificity 0.33, 95% CI [0.18, 0.59] and lower PPV 0.41, 95% CI [0.23, 0.76] compared to culture obtained by peripheral venipuncture. **Limitations.** • Performed analyses by polling the data from the individual studies noting that the unit of analysis in the reviewed studies was the pair of blood cultures obtained from central catheter and a peripheral vein

	• Some variability regarding the setting of the studies, the patient population, the year of the study, and the types of central venous catheters examined. • Comparative analysis of the diagnostic performance characteristics of two sets of blood cultures was not performed. • The results of the analysis were influenced by the prevalence of bacteremia • Antibiotic therapy may be a cause of difference regarding isolation of microorganisms from flood cultures taken from peripheral veins and central venous catheters. • No independent gold standard test to evaluate blood culture results.
Funding	**Funding.** Did not report any funding.

Garcia et al., 2015

Design	Diagnostic Quantitative Synthesis
Objective	To optimize best blood culture (BC) practices: • For the clinical determination of bacteremia, severe sepsis, and systemic inflammatory response syndrome caused by infection • To avoid contamination of BC sample • To increase surveillance accuracy of central line associated bloodstream infections (CLABSI) events
Methods	**Protocol and registration.** The protocol was not registered. **Types of studies.** Among the included articles were reviews and four meta-analyses on BC best practices. **Participants.** Not specified, 6 studies were either pediatric (4 studies) or neonatal (2 studies) specific **Index tests.** Not specified **Target Condition (s).** To minimize blood culture contamination (BCC) rates **Reference Standards.** Not specified **Information sources.** Medline, PubMed, and Ovid between January 1990-March 2015, English only **Search.** Keywords used: blood culture, blood culture collection, blood culture contamination, true pathogen, central line-associated bloodstream infection, bacteremia, and venipuncture References of retrieved articles were checked for additional articles. **Study Selection.** Process not specified. **Data collection process.** Not specified **Methodological quality (Risk of Bias)**. Not specified **Synthesis of results.** SR contains several tables; one is specific to use of various antiseptics for venipuncture as it relates to BCC
Results	**Study Selection.** **Number of articles identified:** *N* = 6809 (screening = 6719 articles, reference lists of articles = 18 articles) Additional information came from reference materials including laboratory standards and textbook chapters **Full-text articles assessed for eligibility:** *n* = 101 were considered **Studies included in qualitative synthesis** (these numbers were determined by counting the number of studies listed in tables): • Rates in BCC using various antiseptics for venipuncture *n* = 18 • Rates of BCC using pre-packaged kits (it is unclear if this is obtaining BC from venipuncture) *n* = 11 • ED studies on reducing Emergency Department (ED) BCC *n* = 11

	Synthesis of results. Some tables included, no specific synthesis of results **Methodological quality of included studies**. • Not specified

Discussion	The following have been shown as best practices for venous blood draws of BC:
	• Blood for BC testing should be drawn via peripheral venipuncture unless clearly necessary
	• Proper hand hygiene using soap and water or alcohol-based hand sanitizer prior to BC collection
	• Use of prepackaged kits specifically for BC collection
	• Appropriate skin antisepsis
	  ○ Appropriate size/method of skin prep relative to product
	  ○ Appropriate time of antisepsis prep
	  ○ Appropriate drying time
	• Universal decolonization of patients
	• Use of sterile gloves
	• Disuse of needleless connectors
	• Disinfection of BC bottles prior to inoculation
	• Drawing the correct volume of blood into BC bottles
	• Changing the order of draw so that the BC bottles are first
	• Increasing the number of sets of blood draws (2 draws leads to maximum organism recovery vs 1 draw, etc.)
	• Transport of BC specimen to lab within 2 hours
	• Obtain BC prior to starting empirical antibiotic therapy if possible
	• The use of dedicated phlebotomy teams who are specially trained
	• Monitor contamination rates and compliance
	• Educate and provide continuous feedback to clinicians
	• Bundle preventive practices
	• Utilize a BC checklist
	
	There is a table on pages 1230 and 1231 of the SR that compares interventions to pre and post intervention BCC contamination rates.
	
	Table 4 lists which non study references (those from textbooks, CDC, etc.) recommend which interventions.

Funding	Funding not addressed

Handrup et al., 2015

Methods	**Cohort - Prospective**
Participants	**Participants:** Blood cultures taken concomitantly from central venous line (CVL) and a peripheral vein (PV) in children with cancer admitted to the hospital with fever from April 2008 to December 2012 Setting: The Department of Pediatrics at Aarhus University Hospital Skejby, Denmark **Number enrolled into study (paired blood cultures):** *N* = 654 **Gender, males (as defined by researchers):** Not given **Age:** Not given **Inclusion Criteria:** • Children with cancer admitted to the hospital with fever • Fever requiring intravenous antibiotic therapy ○ ≥ 38.5° C axillary or 38-34.4° C axillary over 3-4 hours ○ Blood cultures drawn from CVL and PV **Exclusion Criteria:** • None noted **Covariates Identified:** • None noted
Interventions	**Both:** • Blood cultures were obtained before antibiotic therapy from CVL and PV by trained staff ○ Cultures obtained from CVL and PV within 2 hours were considered a pair ○ If cultures were discordant it was regarded as true positive when ▪ The patient had symptoms of sepsis and/or localized site of infection and a known pathogen was found. • Catheter-related bloodstream infection (CRBSI) was defined as growth detected in blood from the CVL more than 2 hours before growth of the same organism was detected in concomitant culture from PV or the blood culture from the CVL was defined as true positive and the corresponding blood culture from PV was negative ○ True negative refers to both cultures were negative ○ True positive refers to the same organism found in both cultures • An automated blood culture system was used for detection of bacterial growth • Differential time to positivity (DTP)was calculated
Outcomes	**Primary outcome(s):** • Proportion of catheter-related bloodstream infections (CRBSI) using differential time to positivity (DTP) • Frequency of blood stream infection only detected from a PV culture **Secondary outcome(s):** • CVL removed due to suspected infection ***Safety outcome(s):** • Adverse outcomes *Outcomes of interest to the CMH CPG /CAT development team
Results	**Results:** • **Pairs:** *N* = 654 ○ True negative: *n* = 502 ○ Positive blood culture: *n* = 52 ▪ PV only positive: *n* = 29 • Contaminants: *n* = 9

	▪ CVL only positive: *n* = 71 • Contaminants: *n* = 31 ▪ True positive PV: *n* = 20 ▪ True positive CVL: *n* = 40 • **CVL removed:** *N* = 30 ($p \leq .02$) ○ CRBSI (positive CVL, negative PV): *n* = 10 (25%) ○ CRSBI (true positive, DTP > 2 hours): *n* = 13 (54%) ○ Non-CRSBI (true positive DTP ≤ 2 hours): *n* = 4 (14%) ○ Non-CRSBI (positive PV, negative CVL): *n* = 3 (15%) • **Adverse Outcome (transferred to intensive care unit):** *N* = 4 ($p < .31$) ○ CRBSI true positive n = 3 (6%) ○ CRBSI (positive CVL, negative PV) n = 1 **Limitations:** • Potential bias in calculating DTP may be caused by variable amounts of blood drawn for pairs or a greater time between obtaining blood from CVL and PV. • No data on differences in blood volume in pairs

Santos et al., 2018

Methods	Cohort
Participants	**Participants:** This study examined the number of bloodstream infections and provided no demographic information. **Setting:** 700 -bed tertiary-care university hospital in Chicago **Pre-implementation**: January 2012 to June 2013 • Blood culture per 1000 inpatient days (Mean and range): 329 (302-353) **Post-implementation:** January 2014 to September 2015. • Blood cultures per 1000 inpatient day (Mean and range): 234 (196-256)

Interventions	Blood culture characteristics were collected and labeled indicating the site of sampling: central line or non-central line
	• **Pre-implementation:**
	  ○ Blood draws completed by phlebotomist, nursing or physicians from central line or peripheral lines
	• **Post-implementation:**
	  ○ Phlebotomist-only blood draws and central line avoidance for blood culture.

Outcomes	**Primary outcome(s):** • Blood cultures from central lines **Secondary outcome(s):** • Positive blood cultures • Contaminated blood cultures • Number of CLABSIs

Results	• **Number of blood cultures from central lines per 1000 inpatient days (mean and range),** *p*-value < .001
	  ○ **Pre-implementation:** *n = 43 (34-54)*
	  ○ **Post-implementation**: *n* = 6 (3-9)
	
	• **Positive blood cultures per 1000 inpatient days pre (mean and range),** *p*-value < .001
	  ○ **Pre-implementation:** *n = 19 (15-21)*
	  ○ **Post-implementation:** *n = 13 (10-18)*
	
	• **Contaminated blood cultures per 1000 inpatient days pre (mean and range)**, *p*-value = .030
	  ○ **Pre-implementation:** *n = 1.3 (0.4-2.7)*
	  ○ **Post-implementation:** *n = 0.8 (0.1-1.8)*
	
	• **Number of CLABSIs per 1000 central line days pre (mean and range),** *p*-value < .001
	  ○ **Pre-implementation:** *n = 2.9 (1.4-5.2)*
	  ○ **Post-implementation:** *n = 1.0 (0-2.9)*
	
	• Blood cultures from central lines decreased by 86% per 1000 inpatient days between pre and post implementation.
	• The mean number of positive blood cultures per month decreased by 31%
	• The mean number of contaminated blood cultures decreased by 38%
	• The mean number of CLABSIs decreased by 66%
	
	Limitations:
	• Ecological study with a historical control design which means that changes in outcome measurements may not relate to policy implementation

	• Study based in a single center which limits generalizability • Identification of patients with kidney disease, liver disease, cancer, stem cell transplants and abdominal organ transplants was based on ICD-9-CM coding, which is not perfectly accurate. • Safety indicators were assessed at the population level and not the individual level. • This change did not occur in a vacuum. Other efforts to decrease CLABSIs were also implemented both in the pre- period and post period.

Snyder et al., 2012

Design	Quantitative Synthesis (meta-analysis).
Objective	Review the effectiveness of three practices for reducing blood culture contamination rates: venipuncture, phlebotomy teams and prepackaged preparation/collection (prep) kits. P- all patients in healthcare settings who have a blood culture specimen collected I - Intervention (practice) vs. Comparison: • venipuncture versus intravenous catheter collection • phlebotomy team versus non-phlebotomist staff collection • prepackaged prep kit versus no prep kit for venipuncture collection O – Outcomes: blood culture contamination rate is the direct outcome of interest
Methods	**Protocol and registration:** CDC-funded Laboratory Medicine Best Practices Initiative "A-6 Cycle" systematic review methods for evaluating quality improvement practices were used. **Eligibility Criteria.** • Studies considered to provide valid and useful information addressing the review questions. • Studies with findings for at least one blood culture contamination rate outcome measure. **Information sources.** PubMed, Embase and CINAHL (1995 to 2012) **Search Strategy:** • The literature search strategy and terms were developed with the assistance of a research librarian • Included a systematic search in September 2011 of three electronic databases • English language articles from 1995 to 2012 about human subjects • Hand searching of bibliographies from relevant information sources • Solicitation of unpublished quality improvement studies resulting in direct submissions to the Laboratory Medicine Best Practices Initiative **Study Selection.** • A review team conducted the systematic review including a review coordinator and staff specifically trained to apply the LMBP methods. • Guidance on the conduct of the systematic review and draft recommendations was provided by an expert panel including individuals selected for their diverse perspectives and expertise in the review topic, laboratory management and evidence review methods. • All screening, abstraction and evaluation was conducted by at least two independent reviewers • All differences were resolved through consensus **Data collection process.** • Utilized two independent reviewers and all differences were resolved through consensus.

Risk of bias (RoB) across studies.

- Not reported

Summary measures.

- Practice effectiveness body of evidence ratings for venipuncture (versus catheter)- fair to good.
- Qualitative analysis calculated using odds ratio and confidence interval.

Synthesis of results:

- The odds ratios for all nine studies (venipuncture versus catheter) included in the body of evidence favor venipuncture over catheter blood draws with a mean odds ratio
- Quality and effect size ratings
- Meta-analysis using Forest Plots

Results

Study Selection: studies included as evidence were venipuncture (vs. intravenous catheter), phlebotomy team, or use of a prep kit

Number of articles identified: *N* = 456

Full-text articles assessed for eligibility: *n* = 21

- **Studies included in qualitative synthesis:** *n* = 17

Synthesis of results: All studies for venipuncture and phlebotomy teams favored these practices-venipuncture, phlebotomy team or prep kit- with metanalysis mean odds ratios for venipuncture of 2.69 and phlebotomy teams of 2.58. For prep kits 6 studies' effect sizes were not statistically significantly different from no effect (meta-analysis mean odds ratio 1.12). Table below includes results for the venipuncture vs. catheter collection for blood samples.

Study (Quality and Effect Size Ratings)	Population/Sample	Setting	Time period	Results (blood culture contamination rates)
Beutz et al., 2003 - Good - Moderate	300 paired blood cultures from 119 patients - medical ICU	Barnes - Jewish Hospital, St. Louis, MO: 1,000 bed university - affiliated teaching hospital	9 months (02/2001 – 10/2001)	Venipuncture: 3.7% Catheter: 6.7% OR = 1.88 (CI: 0.88 – 3.99)
DesJardin et al., 1999 - Good - Moderate	551 paired blood cultures from 185 patients – oncology ward	New England Medical Cente, Boston, MA; 300 - bed tertiary care university - affiliated hospital	22 months (08/1994 – 06/1996)	Venipuncture: 2.4% Catheter: 4.4% OR = 1.88 (CI: 0.95 – 3.74)
Martinez et al., 2002 - Good - Substantial	499 paired blood cultures from 271 patients - surgical and cardiothoracic ICUs	New England Medical Center, Boston, MA; 300 - bed tertiary care university - affiliated hospital	34 months (11/1994 – 08/1997)	Venipuncture: 1.6% Catheter: 4.0% OR = 2.57 (CI: 1.13 – 5.89)
Mcbryde et al., (2005) - Good - Substantial	962 paired venipuncture and catheter - drawn blood cultures from same patient – multiple wards	Mater Misericordiae Hospital, Brisbane, Queensland Australia; 280 beds; Teaching hospital	44 months (01/1998 - 08/2002)	Venipuncture: 2.6% Catheter: 13% OR = 5.60 (CI: 3.61 – 8.69)

	Risk of bias across studies. This was not reported.
Discussion	**Summary of evidence.** • Two practices identified as effective at reducing blood culture contamination rates includes venipuncture and phlebotomy teams • Venipuncture more effective at reducing blood culture collection however, venipuncture is not necessarily equally applicable in all hospital settings and populations (e.g., pediatric units, hematology-oncology patients and other settings where patients are critically ill and may have in-dwelling catheters in place). • Increased benefit (reported in outcomes of this review) when venipuncture performed by phlebotomists in reducing blood culture contamination rates. • Evidence supports venipuncture approach as feasible in all settings and patient populations apart from special cases as noted above. **Limitations.** • The LMBP systematic review methods are consistent with practice standards for systematic reviews but all similar methods are imperfect and include subjective assessments at multiple points that produce bias. • Publication bias must be considered although this review contains unpublished studies which may help mitigate that bias. • Restricted articles to English language studies to allow for multiple reviewers which may have introduce bias. • Most evidence in this review was from quality improvement studies lending itself to limitations with primary data. This also includes single institution site-specific differences which could affect study results. • Many studies were missing information including actual study sample sizes, dates for relevant time periods, and practice implementation and setting characteristics. • Individual study comparison group settings were not always identical. • Study periods more than ten years old. • Non-paired design may have yielded less valid findings when blood culture contamination was affected by patient or settings characteristics. • Several studies noted study design limitations in terms of phlebotomy teams and non-phlebotomist staff introducing confounding results on reported blood culture contamination rates and effect sizes due to differences in skill level of staff.
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