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Effectiveness of practices to reduce blood culture contamination: A Laboratory Medicine Best Practices systematic review and meta-analysis☆

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Abstract

Objectives—This article is a systematic review of the effectiveness of three practices for reducing blood culture contamination rates: venipuncture, phlebotomy teams, and prepackaged preparation/collection (prep) kits.

Design and methods—The CDC-funded Laboratory Medicine Best Practices Initiative systematic review methods for quality improvement practices were used.

Results—Studies included as evidence were: 9 venipuncture (vs. versus intravenous catheter), 5 phlebotomy team; and 7 prep kit. All studies for venipuncture and phlebotomy teams favored these practices, with meta-analysis 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).

Conclusions—Venipuncture and the use of phlebotomy teams are effective practices for reducing blood culture contamination rates in diverse hospital settings and are recommended as evidence-based "best practices" with high overall strength of evidence and substantial effect size ratings. No recommendation is made for or against prep kits based on uncertain improvement.

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The findings and conclusions in this article are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention/the Agency for Toxic Substances and Disease Registry (CDC/ATSDR).

Keywords

Bacterial infections/diagnosis; Blood culture; Blood specimen collection/methods/standards; Comparative effectiveness research; Contamination; False positive reactions; Healthcare quality improvement; Laboratory medicine; Phlebotomy; Practice guideline

Introduction

A blood culture is the primary laboratory test for diagnosing serious blood stream infections, including septicemia or sepsis, and in directing appropriate antibiotic therapy [1–3]. Septicemia among hospitalized patients is widely prevalent and was the single most expensive condition treated in U.S. hospitals affecting nearly one of every 23 patients (4.2%) at an aggregate cost of nearly $15.4 billion (4.3% of all hospital costs) in 2009 [4]. The number of hospital stays for septicemia more than doubled between 2000 and 2009 [5], and it had an in-hospital mortality rate of about 16% in 2009, more than 8 times higher than other stays [4]. Accurate blood culture results are essential for providing safe, timely, effective and efficient care for patients with serious infections. These procedures also affect healthcare expenses as well as public health tracking and reporting of healthcare acquired infections and bloodstream infection rates for infection control activities [3].

Quality gap: blood culture contamination[a]

False positive blood culture test results are common and are caused by contamination that occurs from the introduction of organisms outside the bloodstream (e.g., skin or environmental contaminants) into the sample of blood obtained for culture [6] that cannot be completely eliminated [7–9]. While a relatively small percentage of all blood cultures are contaminated, it represents a large proportion of all positive results and therefore has been recognized as an important quality problem for decades [3]. Although no definitive estimate is available, of all positive cultures, 20% to 50% are likely false positives [10–12]. According to the American Society for Microbiology (ASM) and the Clinical Laboratory Standards Institute (CLSI) overall blood culture contamination rates should not exceed 3% [1,2], however reported contamination rates in hospitals vary widely ranging from 0.6% to 12.5%, with the highest rates associated with emergency department settings [3,6–9,11,13–20]. One study reported a 26% contamination rate in pediatric outpatients [21]. False positive results can lead to inappropriate patient diagnosis, follow-up, and unnecessary treatment [3,9,11], creating substantial adverse consequences for patients and cost burdens for the healthcare system. This includes re-collection of blood cultures, other laboratory tests for reevaluation, incorrect or delayed diagnosis due to errors in clinical interpretation, inappropriate antibiotic treatment as well as unnecessary and longer hospital stays and costs associated with these outcomes [3,12,14,22,23].

To reduce this important quality gap and its consequences, it is essential to identify effective practices for reducing blood culture contamination rates. Other than the use of skin antiseptics [24] and changing needles prior to inoculation of blood culture bottles [25], no

[a]See Glossary for more information on the definition of blood culture contamination and other terms.

systematic reviews of quality improvement practice evidence of effectiveness have been conducted. The use of strict aseptic techniques by healthcare workers when obtaining blood culture specimens is an important factor in reducing contamination [9], and there is sufficient evidence to evaluate the effectiveness of three practices used to obtain blood culture specimens: venipuncture, phlebotomy teams and prepackaged prep kits. The purpose of this article is to evaluate evidence of these practices' effectiveness at reducing blood culture contamination (false positive) rates by applying the CDC Laboratory Medicine Best Practices Initiative's (LMBP) systematic review methods for quality improvement practices and translating the results into evidence-based guidance [26].

Methods

This evidence review followed the CDC's Laboratory Medicine Best Practices Initiative's (LMBP) "A-6 Cycle" systematic review methods for evaluating quality improvement practices and reported in detail elsewhere [26]. This approach is derived from previously validated methods, and is designed to transparently evaluate the results of studies of practice effectiveness to support evidence-based best practice recommendations. A review team conducts 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 is provided by an expert panel including individuals selected for their diverse perspectives and expertise in the review topic, laboratory management and evidence review methods.[b] The results of the evidence review are translated into an evidence-based best practice recommendation by the expert panel for approval by the LMBP Work-group, an independent, multi-disciplinary group composed of 15 members with expertise in laboratory medicine, clinical practice, health services research and health policy.

The question answered by this evidence review is: *What practices are effective for reducing blood culture contamination?* This review question is addressed in the context of an analytic framework for the quality issue of blood culture contamination depicted in Fig. 1. The relevant PICO elements are:

- *P*opulation: all patients in healthcare settings who have a blood culture specimens collected
- *I*ntervention (practice) versus *C*omparison:
  - venipuncture versus intravenous catheter collection
  - phlebotomy team versus non-phlebotomist staff collection
  - prepackaged prep kit versus no prep kit for venipuncture collection
- *O*utcome: blood culture contamination rate is the direct outcome of interest

The three practices being evaluated in this review are *venipuncture*, puncture of a vein through the skin to withdraw blood as opposed to an indwelling catheter in the vein to withdraw blood (or other purposes such as delivery of antibiotics, pain medication, and

[b]See Appendix A for the LMBP Blood Culture Contamination Expert Panel Members and LMBP Workgroup members. See Appendix Edits/Notes.

saline solution); use of a *phlebotomy team* of certified or trained phlebotomists for specimen collection using venipuncture instead of other healthcare personnel (e.g., physicians, interns, nurses); and *prepackaged prep kits* of aseptic supplies for collection of blood specimens by venipuncture that are commercially purchased versus using usual disinfectant supplies that are not prepackaged.

The search for studies of practice effectiveness included a systematic search of multiple electronic databases, hand searching of bibliographies from relevant information sources, consultation with and references from experts in the field including members of the expert panel (Appendix A), and by solicitation of unpublished quality improvement studies resulting in direct submissions to the Laboratory Medicine Best Practices Initiative.[c] The literature search strategy and terms were developed with the assistance of a research librarian and included a systematic search in September 2011 of three electronic databases (PubMed, Embase and CINAHL) for English language articles from 1995 to 2012 about human subjects. The search contained the following Medical Subject Headings: allied health personnel, blood, blood specimen collection, catheterization, disinfectants, health personnel, laboratory personnel, phlebotomy as well as these keywords: anti-infective agent, local; antisepsis; blood sampling; blood culture; catheter; contaminants; contamination; costs; disinfection; health care cost(s); healthcare personnel; intravenous catheter; microbiology; paramedical personnel; phlebotomists; phlebotomy team; skin; skin decontamination; quality; and venipuncture.

Included studies were considered to provide valid and useful information addressing the review question, with findings for at least one blood culture contamination rate outcome measure. To reduce subjectivity and the potential for bias, all screening, abstraction and evaluation was conducted by at least two independent reviewers, and all differences were resolved through consensus. The effect size for each study was standardized using its reported data and results to calculate an odds ratio (OR)[d] since the outcome of interest is dichotomous (i.e., blood culture is contaminated or is not contaminated) and the findings for these practices are typically expressed in terms of rates or percentages. The OR compares the intervention practice to the comparison practice, or comparator, in terms of the relative odds of a successful outcome (i.e., no contamination versus contamination). Each study is assigned one of three quality ratings (Good, Fair, Poor) and one of three effect size ratings (Substantial, Moderate or Minimal/None).[e]

The results from the individual effectiveness studies are aggregated into a practice body of evidence that is analyzed to produce the systematic review results for translation into an evidence-based recommendation (Recommend, No recommendation for or against, Recommend against). Both qualitative and quantitative analyses are used to assess the effect size consistency and patterns of results across studies [27], and to rate the overall strength of the body of evidence for practice effectiveness (High, Moderate, Suggestive, Insufficient).

[c]More information on submission of unpublished studies to the Laboratory Medicine Best Practices Initiative is available at www.futurelabmedicine.org.
[d]See Glossary for more information on odds ratios.
[e]The criteria for a substantial effect size rating: OR>2.0 and significantly different from OR=1.0 at p=0.05 (i.e., the lower limit of the 95% confidence interval is>1.0).

Criteria for these ratings are described in greater detail elsewhere [26,28]. The qualitative analysis synthesizes the individual studies to convey key study characteristics, results and evaluation findings summarized in a body of evidence table. The quantitative analysis is provided using meta-analysis of results from similar individual studies to provide a weighted average effect size and 95% confidence interval (CI) estimated using a random-effects model[f] and presented in a forest plot [29,30] with the individual studies' and overall mean odds ratios along with their respective 95% confidence interval upper and lower limits. The I^2 statistic is used to estimate the percent of variability associated with between-study differences [31,32].

Evidence review synthesis and results

The search identified 456 separate bibliographic records that were screened for eligibility to contribute evidence of effectiveness for the three practices (venipuncture, phlebotomy teams, and prepackaged prep kits) with respect to blood culture contamination rate outcomes. After initial screening, 348 of these records were excluded as off-topic, and 87 were excluded for not meeting effectiveness study inclusion criteria (i.e., a study using data evaluating a practice of interest with at least one finding for a relevant blood culture contamination rate outcome measure). A total of 21 full-text studies met the review inclusion criteria. A systematic review flow diagram in Fig. 2 provides a breakdown of the search results. The full-text review and evaluation of the 21 eligible studies (10 venipuncture; 6 phlebotomy team; 6 prep kits), with one evaluating two practices, resulted in excluding 4 studies (1 venipuncture; 1 phlebotomy team; 2 prep kit) for not meeting the minimum required LMBP study quality inclusion criteria. Appendix C provides a Body of Evidence table for each practice, as well as abstracted and standardized information and study quality ratings in evidence summary tables for each of the 21 eligible studies. Appendix B provides bibliographic reference information for these studies. A total of 17 studies are included in this review as evidence of practice effectiveness (9 venipuncture; 5 phlebotomy team; 4 prep kits). One published study contained data evaluating 2 practices (Weinbaum [19]) and another published study (Wilson et al., 2000, Appendix B) contains 4 studies at separate sites resulting in a total of 7 prep kit studies.

Venipuncture practice effectiveness evidence

Information on the nine published studies that comprise the practice effectiveness body of evidence comparing venipuncture to catheter blood sample collection with respect to blood culture contamination rates is summarized in Table 1. The publication dates for these studies range from 1999 (DesJardin [34]) to 2011 (Weddle [18]), with the earliest study time periods beginning in 1994 (DesJardin [34]; Martinez [39]). Of the nine studies, seven were rated "Good" study quality and two were rated "Fair." Paired blood cultures from the same patient (one collected by venipuncture and one by catheter) were used as the study samples in five studies (Beutz [35], DesJardin [34], Everts [40], Martinez [39], Mcbryde et al., 2005, Appendix B), ranging from 300 (Beutz [35]) to 1408 pairs (Everts [40]). The four non-

[f]Random-effects model assumes there is no common population effect size for the included studies and the studies' effect size variation follows a distribution with the studies representing a random sample. This is in contrast to the fixed-effects model which assumes a single population effect size for all studies and that observed differences reflect random variation.

paired study samples (Norberg [38], Qamruddin et al., 2007, Appendix B, Ramsook et al., 2000, Appendix B, Weddle [18]) ranged in size from 1138 (Qamruddin et al., 2007, Appendix B) to 4108 total blood cultures (Norberg [38]). These studies all involve hospital patients and include a range of settings as follows: all patients (adult and pediatric), (Everts [40]), all adult patients, (Qamruddin et al., 2007, Appendix B) intensive care units (Beutz [35], Martinez [39]), an oncology ward (DesJardin [34]), and pediatric emergency departments (Norberg [38], Ramsook et al., 2000, Appendix B, Weddle [18]). Seven studies were conducted in U.S. hospitals, two in the same hospital (DesJardin [34] and Martinez [39]), one in the UK (Qamruddin et al., 2007, Appendix B), and one in Australia (Mcbryde et al., 2005, Appendix B).

Body of evidence qualitative analysis

Evidence of practice effectiveness for reducing blood culture contamination rates by using venipuncture indicates consistent and substantially lower rates compared to catheter collection with a high strength of evidence in hospital settings (Table 1). The venipuncture odds ratios for all nine studies included in the body of evidence (with >1.0 favoring venipuncture over catheter blood draws) ranged from 1.53 (95% CI: 0.88–2.68) to 5.60 (95% CI: 3.61–8.69). The odds ratio for six of the nine studies exceeded 2.0 for a "Substantial" effect size rating. For the remaining three studies, the lower limit of their odds ratios' 95% confidence interval is less than 1.0, with the lowest at 0.88. The odds ratio results of the five studies using paired blood cultures provide more reliable evidence and ranged from 1.88 (95% CI: 0.88–3.99) to 5.60 (95% CI: 3.61–8.69), offering greater support overall for the effectiveness of venipuncture compared to those of the four less suitable study designs ranging from 1.53 (95% CI: 0.88–2.68) to 3.46 (95% CI: 2.55–4.69). All three studies in the pediatric emergency department setting have similar high odds ratios ranging from 2.96 (95% CI: 1.96–4.47) to 3.46 (95% CI: 2.55–4.69).

Meta-analysis

The forest plot in Fig. 3 presents the meta-analysis effect size results for venipuncture compared to catheter blood culture contamination rates for the body of evidence estimated using a random effects model. The odds ratios for all nine studies included in the body of evidence favor venipuncture over catheter blood draws with a mean odds ratio of 2.69 (95% CI: 2.03–3.57), strongly favoring venipuncture over catheter blood collection for reducing blood culture contamination rates. The meta-analysis results show moderate statistical heterogeneity (Q=19.5, p=0.012), with approximately 60% of the variability in results attributable to between-study differences. (I^2=59.0) [33].

Phlebotomy team practice effectiveness evidence

Of the five studies included in the body of evidence for phlebotomy team practice effectiveness (Table 2), all were conducted in large U.S. hospitals, two in emergency departments only (Gander [41], Sheppard [13]). One of the studies is unpublished (Geisinger Wyoming Valley, 2009, Appendix B) and four are rated "Good" study quality and one is rated "Fair." Of the included studies, three had phlebotomy team comparison groups using only venipuncture for blood draws (Gander [41], Surdulescu [16], Weinbaum [19]) which provide more reliable evidence for estimating phlebotomy team practice effectiveness than

the two studies which include both venipuncture and catheter draws in their comparison groups. The earliest reported study time period began in 1993 (Surdulescu [16]) and the most recent began in 2009 (Geisinger Wyoming Valley, 2009, Appendix B). All of the studies had large sample sizes exceeding 1000 blood cultures, and overall appear to represent a broad and diverse hospital patient population.

Body of evidence qualitative analysis

The evidence of practice effectiveness for phlebotomy teams at reducing blood culture contamination rates indicates consistent and substantial improvement compared to collections by non-phlebotomist staff with a high strength of evidence in hospital settings (Table 2). For all five studies in the practice body of evidence, the phlebotomy team odds ratio exceeded 2.0 (favoring phlebotomy teams over non-phlebotomist staff), ranging from 2.09 (95% CI: 1.68–2.61) to 4.83 (95% CI: 1.53–15.28), and were all statistically significantly different from 1.0, exceeding the threshold criteria for a “Substantial” effect size rating. The phlebotomy practice odds ratio effective size for the three studies with a venipuncture only comparison group ranged from 2.09 (95% CI: 1.68–2.61) to 4.34 (95% CI: 1.82–10.36), which is slightly lower and potentially more representative of the true effect than the range for the two other studies that included catheter draws with odds ratios of 2.93 (95% CI: 2.13–4.02) and 4.83 (95% CI: 1.53–15.28). There is not a notable difference in the effect sizes of the two studies conducted in emergency departments with odds ratios 2.51 (95% CI: 1.84–3.43) and 4.83 (95% CI: 1.53–15.28) compared to the three studies conducted hospital-wide.

Meta-analysis

The forest plot in Fig. 4 presents the meta-analysis effect size results for the phlebotomy team compared to non-phlebotomist collection blood culture contamination rates for the body of evidence estimated using a random effects model. The odds ratios for all five included studies favor phlebotomy teams over non-phlebotomists, with a mean odds ratio of 2.58 (95% CI: 2.07–3.20) strongly favoring phlebotomy teams for reducing blood culture contamination rates. The meta-analysis results are homogeneous (Q=6.2, p=0.182) with moderate variability attributed to between study differences (I^2=35.8%) [33].

Prepackaged prep kit practice effectiveness evidence

Of the four published studies included in the prepackaged prep kit practice effectiveness body of evidence (Table 3), one (Wilson et al., 2000, Appendix B) contains four separate trials, each at a different hospital, yielding a total of seven studies. All seven studies were conducted in hospitals, six in the U.S. and one in the UK (McLellan [6]), and involved venipuncture blood collections in a broad range of hospital settings by multiple types of staff (i.e., phlebotomists, healthcare technicians, staff physicians and interns). One of the studies was rated “Good” study quality and six were rated “Fair.” The study time periods for five of the seven studies began prior to 2000 (Wilson et al., 2000, Appendix B, Weinbaum [19]), with only one study period occurring in the last five years (McLellan [6]). The study sample sizes ranged from 495 (Weinbaum [19]) to 6,460 total blood cultures (Wilson et al., 2000, Appendix B).

Body of evidence qualitative analysis

The evidence of practice effectiveness for prepackaged prep kits at reducing blood culture contamination rates often indicated either minimal or no improvement compared to venipuncture collections without prep kits in hospital settings (Table 3). For six of the seven studies in the practice body of evidence, the prep kit odds ratio was not statistically significantly different from 1.0. (i.e., no difference between blood culture contamination rates for prep kits versus no prep kits) with one study showing substantial improvement. The odds ratios for the seven individual studies ranged from 0.91 (95% CI: 0.62–1.34) to 3.68 (95% CI: 1.27–10.73). Five of the studies received a “Minimal/None” effect size rating with odds ratios ranging from 0.91 (95% CI: 0.62–1.34) to 1.22 (95% CI: 0.79–1.87), one was rated “Moderate,” and only one study exceeded the threshold criteria for a “Substantial” effect size rating.

Meta-analysis

The forest plot in Fig. 5 presents the meta-analysis blood culture contamination rate effect size results for venipuncture collections with prepackaged prep kits compared to without prep kits for the practice body of evidence estimated using a random effects model. The mean odds ratio of 1.12 (95% CI: 0.94–1.35) is homogeneous (Q=7.9, p=0.242) and does not favor prepackaged prep kits for reducing blood culture contamination rates. The meta-analysis results show low between-study variability with an I^2 statistic of 24.4% [33].

Discussion

Additional considerations

This section addresses additional considerations for evaluating venipuncture and phlebotomy teams, the two practices identified as effective at reducing blood culture contamination rates.

Applicability

While venipuncture is demonstrated to be more effective at reducing blood culture contamination than intravenous catheter for blood culture collection, venipuncture and its effect size results are 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) [18,34–38]. Catheter blood collection may remain a secondary source of blood specimens for blood culture or other laboratory tests when there are problems with venipuncture due to poor peripheral access, since it is convenient and prevents trauma to the veins when blood is needed frequently [34] (e.g., for ruling out infection in critically ill patients in surgical intensive care units [39]). In addition, catheter blood collections are required to identify or rule out catheter colonization with bacteria, in which case catheters may need to be removed and replaced. As indicated by the higher contamination rates from this systematic review, interpretation of positive blood culture results from catheter drawn samples must be exercised with care [3,40].

Phlebotomy teams are applicable to a variety of hospital environments such as tertiary care, community and academic medical centers, emergency departments, adult general medical and surgical care settings [13,16,19,41]. Based on the included studies, phlebotomy team results are highly applicable across several patient groups in hospital settings, but less so in special cases where venipuncture may be less applicable such as neonatal intensive care units and critically ill patients in long term care. It is important to note that well-trained and experienced non-phlebotomist staff can potentially achieve comparable blood culture contamination rates when using the same collection techniques as phlebotomists.

Harms

Venipuncture procedures should be performed using universal precautions [1], as there are needle stick injuries [42] and pathogen exposure risks for the phlebotomists or other healthcare staff drawing patient blood samples [1]. Patients are at risk for needle insertion site injury from multiple attempts to obtain blood specimens [42].

Additional benefits

Studies reviewed report beneficial outcomes associated with venipuncture performed by phlebotomists in addition to reducing blood culture contamination rates. These benefits include decreased turnaround time for laboratory test results on specimens other than blood cultures [13]; reduced frequency of misidentified and mislabeled specimens [43,44]; decrease in patient needle-stick bruises; improved quality of specimens; improved working relationships between phlebotomists and nurses; and higher levels of patient satisfaction [42,45].

Economic evaluation

Venipuncture, like catheter collection, is a primary means of blood sample collection for blood cultures; however the cost of this practice has not been evaluated. Four studies of phlebotomy teams included estimated and projected labor costs and healthcare savings (e.g., reduced hospital length of stay, pharmacy and laboratory services) associated with reduced blood culture contamination rates or false positives [13,16,19,41]. Some studies' estimated savings were associated with either a general reduction in blood culture contamination rates or relied on other sources for key cost-related assumptions [13,16,19]. All four studies concluded that the healthcare cost savings from reduced contaminated blood cultures exceeded total phlebotomist labor costs, however they did not compare phlebotomist to non-phlebotomist costs (i.e., implies $0 cost for non-phlebotomist labor). Nonetheless, these studies all support a conclusion that phlebotomy teams are not only cost-effective but cost-saving solely based on reduction in blood culture contamination.

Feasibility of implementation

Venipuncture is feasible in all settings and patient populations with some special patient case exceptions as noted in the applicability section. The evidence reviewed clearly demonstrates the feasibility of adopting phlebotomy teams in a variety of hospital settings [13,16,41]. Implementing phlebotomy teams for blood culture collection may require assessment of the availability of currently trained phlebotomist staff in various areas of the

hospital settings and possible reorganization of resources. In settings where phlebotomy has been decentralized or eliminated, changes may be instituted to achieve workforce goals. Selected environments where high volumes of blood cultures are initiated at specific hours of the workday may be an excellent starting point for implementation [41]. Phlebotomist salaries and training costs may be perceived as initial barriers to adoption of phlebotomy teams, therefore an assessment of blood culture contamination rates and associated costs within an institution may be helpful to support perceived additional costs for implementing phlebotomy teams compared to using non-phlebotomist staff. Involvement from multiple, relevant departments and leaders within an organization to support implementation will likely be required [13,19,41].

Future research needs

Research is needed to identify and better clarify the impact of blood culture contamination on patient care and health outcomes and their associated costs. This can be accomplished in conjunction with new economic evaluation research to more rigorously and transparently demonstrate blood culture contamination clinical and economic outcomes as well as those associated with phlebotomy teams due to the limited cost-savings information in available studies. Given the evidence on higher blood culture contamination rates from catheter blood collections, more investigation is needed regarding practices to effectively reduce catheter use by non-phlebotomists (e.g., through educational interventions), and by clarifying the specific circumstances for its use (e.g., based on patient characteristics, only newly inserted catheters) to reduce contamination. More research is also needed, however, to determine blood culture contamination rates in patient subgroups, particularly pediatric patient subgroups, to refine guidance on catheter use. Research on the rate of blood culture contamination and quality improvement practices in relatively high volume non-hospital settings, such as in nursing homes and rehabilitation centers, is needed to evaluate and improve quality gaps in other important care settings.

Limitations

The LMBP systematic review methods are consistent with practice standards for systematic reviews [27], but all similar methods are imperfect and include subjective assessments at multiple points that may produce bias. Rating study quality depends on consensus assessments that may be affected by rater experience and the criteria used. Publication bias must be considered although this review contains unpublished studies which may help mitigate that bias. The restriction to English language studies to satisfy the requirement of multiple reviewers for each study may also introduce bias. Most of the evidence for this review is from quality improvement studies, thus the primary data have many limitations, including single institution site-specific differences which may affect study results. Many studies were missing information including actual study sample sizes, dates for relevant time periods, and practice implementation and setting characteristics. Several studies were conducted in specific settings within a hospital such as emergency departments, medical intensive care units and academic settings which may not be generalizable to other settings. Individual study comparison group settings were not always identical, therefore potential differences in practice patterns and patient clinical status could influence results.

As noted in the Results section, several studies included in this review have study periods that are more than ten years old, with three dating to the early 1990s; two for venipuncture (DesJardin [34] and Martinez [30]); one for phlebotomy teams (Surdulescu [16]); and six of the seven prep kit study periods began prior to or in 2000. As indicated in the venipuncture results section, five of the nine studies used a paired blood culture sample study design comparing venipuncture and catheter blood samples from the same patient within a pre-defined time limit, while the other four studies used group-wise comparisons. Although systematic differences are not observed and all nine included studies favored venipuncture, the non-paired design may yield less valid findings when blood culture contamination is affected by patient or setting characteristics. Three of the five phlebotomy team studies used comparison groups of non-phlebotomists performing only venipuncture collections, thereby controlling for the possibility of catheter contamination. Although systematic differences were not observed, it is likely that the results from these three studies were more representative of the practice's true effect size. All five studies favored phlebotomy teams, but the two studies with non-phlebotomist catheter collections in the comparison group may have had a slight upward bias on the meta-analysis mean effect size estimate. Several studies in this review noted study design limitations in terms of phlebotomy teams and non-phlebotomist staff which may have introduced confounding results on reported blood culture contamination rates and effect sizes due to differences in the skill level and training of staff performing venipuncture.

Conclusions and recommendations

On the basis of a high overall strength of evidence of effectiveness, venipuncture is recommended as a best practice to reduce blood culture contamination (false positive) rates in all hospital settings. The high overall strength of evidence rating is due to sufficient evidence of practice effectiveness from nine individual studies, all favoring venipuncture over catheter blood collection and demonstrating consistent and substantial reductions in blood culture contamination rates (mean odds ratio of 2.69; 95% CI: 2.03–3.57).

On the basis of a high overall strength of evidence of effectiveness, phlebotomy teams are recommended as a best practice to reduce blood culture contamination (false positive) rates in all hospital settings. The high overall strength of evidence rating is due to sufficient evidence of practice effectiveness from five individual studies, all favoring phlebotomy team over non-phlebotomist staff collection and demonstrating consistent and substantial reductions in blood culture contamination rates (mean odds ratio of 2.58; 95% CI: 2.07–3.20).

On the basis of an insufficient overall strength of evidence of effectiveness, no recommendation is made for or against prepackaged prep kits. The overall insufficient strength of evidence rating is based on evidence that indicates inconsistent and unlikely improvement in blood culture (false positive) contamination rates compared to venipuncture collections without prep kits in hospital settings from the results of seven trials in a broad range of hospital settings by multiple types of staff. For six of the seven studies, the prep kit failed to significantly reduce blood culture contamination relative to a standard practice, and

the overall effect size was homogeneous and not statistically significantly different from collections without prep kits (mean odds ratio of 1.12; 95% CI: 0.94–1.35).

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Abbreviations

CDC	U.S. Centers for Disease Control and Prevention
CI	Confidence interval
IV	Intravenous
LMBP	Laboratory Medicine Best Practices Initiative
QI	Quality improvement

Glossary

Antiseptic	a substance that inhibits the growth and development of microorganisms without necessarily killing them.
Bacteremia	the presence of bacteria in the bloodstream.
Bias	systematic error; threats to validity; tendency to produce results that depart systematically from the ‘true’ results. Unbiased results are internally valid. Four types of bias are selection/allocation, performance, measurement/detection and attrition/exclusion.
Blood culture	a specimen of blood that is submitted for bacterial or fungal culture [1].
Blood culture contamination rate	the number of contaminated cultures per number of blood cultures received by the laboratory per month or per year. Contamination rates vary based on laboratory-specific definitions due to variation in the definition of contaminant (see Contaminant definition).
Bloodstream infection	an infection associated with bacteremia or fungemia.
Catheter	an indwelling device inserted into the vein for injection of medication or as an access for collection of blood samples using a thin flexible tube [35,36].
Consistency	the degree to which estimates of effect for specific outcomes are similar across included studies.
Contaminant	a microorganism isolated from a blood culture that was introduced into the culture during specimen collection or processing and that was not pathogenic for the patient from whom blood was collected

	(i.e., not present in the patient's blood when the blood was sampled for culture). Organisms are most commonly coagulase-negative *Staphylococci* but also include other skin flora species such as viridans streptococci, *Corynebacterium* species other than *C. jekieum; Bacillus* species, *Propioonibacterium acnes* [1,2,11].
Disinfectant	a substance used to reduce the concentration of bacteria, fungi, or viruses on a surface.
External validity	generalizability, applicability — extent to which the effects observed in the study are applicable outside of the study to other populations and settings.
Effect size	a value which reflects the magnitude of the difference in a study's outcome measure between the group with the intervention/practice being evaluated and its control or comparison group.
False positive blood culture	a culture with one or more contaminants producing a positive test result for a patient without a bloodstream infection. False positive rates are the percent of cultures contaminated relative to the total number of cultures positive.
Fungemia	the presence of fungi (yeasts or molds) in the bloodstream.
Internal validity	extent to which the design and conduct of the study are likely to prevent systematic error. Internal validity is a prerequisite for external validity.
Meta-analysis	the process of using statistical methods to combine quantitatively the results of similar studies in an attempt to allow inferences to be made from the sample of studies and be applied to the population of interest.
Non-phlebotomist staffs	hospital staff whose primary work responsibilities consist of duties other than collection of patient blood samples for laboratory tests by venipuncture [19,41].
Odds ratio	the ratio of two odds of an event from two groups - a treatment or intervention group (*a/c*) versus a control group (*b/d*) where *a* and *c* represent the number of times the event occurs for the intervention and control group, respectively, using the formula below and the barcoding and comparison practice example table. An OR=1 means the two practices are equally successful (no difference in reducing risk with respect to the outcome evaluated); OR>1 means the barcoding practice is more successful; and OR<1 means the barcoding practice is less successful. Odds ratio estimate formula: $OR=\frac{ad}{bc}=\frac{p_a p_d}{p_b p_c}=\frac{p_a/p_b}{p_c/p_d}=\frac{p_a(1-p_c)}{p_c(1-p_a)}$; Where $p_a = a/(a + b)$, $p_c = c/(c+d)$ and *a*, *b*, *c*, and *d* are proportions in the table below.

	Frequencies		Proportions	
	Success	**Failure**	**Success**	**Failure**
Barcoding practice	*A*	*B*	$p_a = a/(a + b)$	$p_b = b/(a + b)$
Comparison Practice	*C*	*D*	$p_c = c/(c + d)$	$p_d = d/(c + d)$

Phlebotomy team	a team of trained persons with primary responsibility for collecting blood for laboratory evaluation using sterile technique by puncture of a vein [19,41].
Septicemia (also Bacteremia, Sepsis, Systemic inflammatory response syndrome (SIRS))	a serious systemic illness caused by bacteria and bacterial toxins circulating in the bloodstream.
Systematic review	a scientific investigation that focuses on a specific question and that uses explicit, planned scientific methods to identify, select, assess, and summarize the findings of similar but separate studies. It may or may not include a quantitative synthesis of the results from separate studies (meta-analysis).
Transparency	methods are explicitly defined, consistently applied, and available for public review so that observers can readily link judgments, decisions, or actions to the data on which they are based. Allows users to assess the strengths and weaknesses of the systematic review of the associated guidance and recommendations.
Venipuncture	puncture of a vein. A method used to collect blood specimens for culture removed through a sterile needle inserted into a vein [1].

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Appendix A. LMBP blood culture contamination expert panel members and LMBP Workgroup members

LMBP Blood Culture Contamination Expert Panel

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Ann Vannier, MD[a] (Kaiser-Permanente)

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Laboratory Medicine Best Practices Work Group, 2008 – 2011

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Ann Watt, MBA, RHIA (The Joint Commission)

Ex-officio Members:

Sousan S. Altaie, PhD (Food and Drug Administration)

[a]Laboratory Medicine Best Practices Workgroup member.

James Cometa (Centers for Medicaid and Medicare Services)

Appendix B. LMBP blood culture contamination systematic review eligible studies

Venipuncture vs. intravenous catheter collection

Included studies

Published

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Excluded studies

Published

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Phlebotomy teams

Included studies

Published

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Unpublished

References

60. Geisinger Wyoming Valley Hospital; 2009.

Excluded

Unpublished

References

61. Providence Regional Medical Center Everett, WA 2009

Prepackaged prep kit

Included studies

Published

References

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Excluded studies

Published

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Appendix C. Supplementary data

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.clinbiochem.2012.06.007.

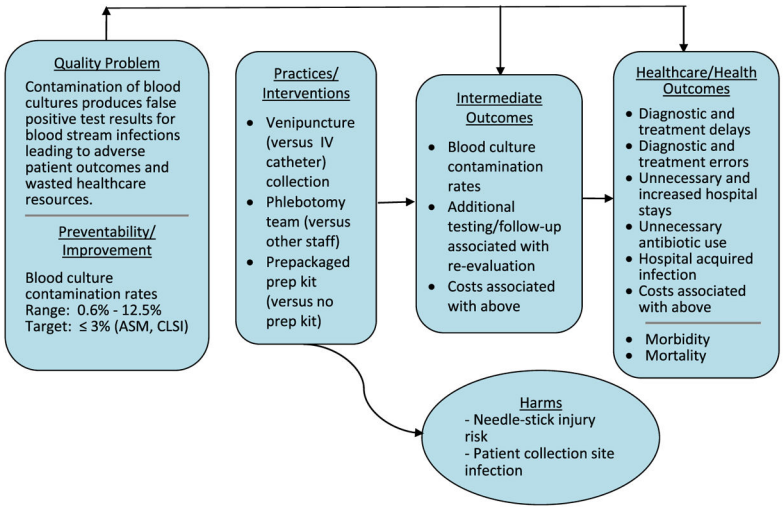

Fig. 1.
LMBP QI analytic framework: blood culture contamination.

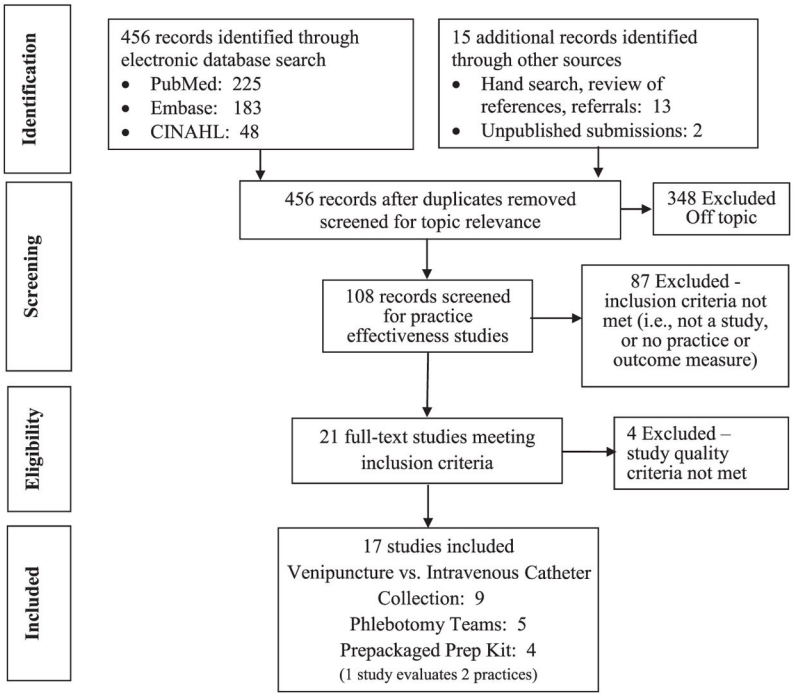

Fig. 2.
Systematic review flow diagram.

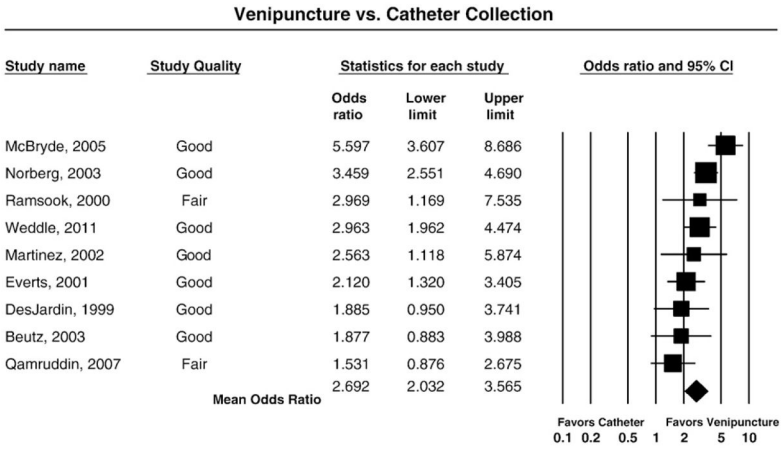

Fig. 3.

Meta-analysis forest plot: venipuncture versus catheter collection.

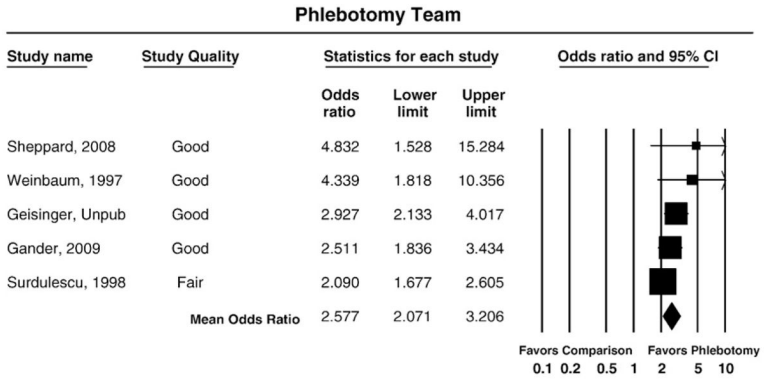

Fig. 4.

Meta-analysis forest plot: phlebotomy teams.

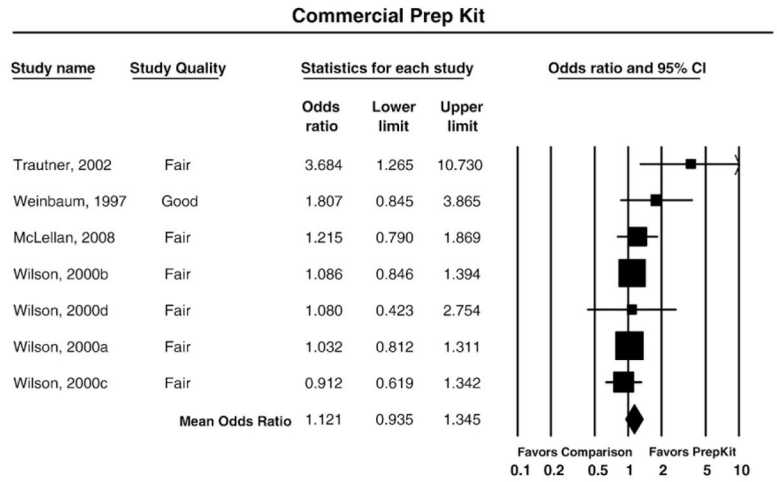

Fig. 5.
Meta-analysis forest plot: prepackaged prep kits.

Table 1

Body of evidence summary table: venipuncture (versus catheter).

Study (Quality and Effect Size Ratings)	Population/Sample	Setting	Time period	Results (Blood Culture Contamination Rates)
Beutz 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 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)
Everts 2001 - Good - Substantial	1,408 pairs of concurrent catheter-drawn and venipuncture samples	Tertiary - care medical setting; Duke University School of Medicine, Durham, NC	24 months (01/1997 – 12/1998)	Venipuncture: 1.8% Catheter: 3.8% OR = 2.12 (CI: 1.32 – 3.41)
Martinez 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)
Norberg 2003 - Good - Substantial	4,108 total blood cultures – pediatric emergency department Catheter: 2108 Venipuncture: 2000	Children's Hospital Medical Center of Akron, Akron, OH	12 months (01/1999 - 12/1999)	Venipuncture: 2.8% Catheter: 9.1% OR = 3.46 (CI: 2.55 – 4.69)
Qamruddin et al. (2007) - Fair - Moderate	1,138 total blood culture samples – adult patients from multiple wards Venipuncture: 979 Catheter: 159	Manchester Royal Infirmary, Manchester, UK.	2 months (02/2006 - 04/2006)	Peripheral vein: 7.3% Catheter: 10.7% OR = 1.53 (CI: 0.88 – 2.68)
Ramsook et al. (2000) - Fair - Substantial	1,722 total blood cultures – pediatric emergency room Venipuncture: 427 Catheter: 1295	Texas Children's Hospital; Houston University - affiliated Houston, Texas	6 months (02/1999 - 07/1999)	Venipuncture: 1.2% Catheter: 3.4% OR = 2.97 (CI: 1.17 – 7.54)
Weddle 2011 - Good - Substantial	3,025 total blood cultures - pediatric emergency department Venipuncture: 1229 Catheter: 1796	Children's Mercy Hospitals and Clinics, Kansas City, MO. 263-bed tertiary children's hospital.	12 months (9/2008 - 8/2009)	Venipuncture: 2.4 (29/1229) Catheter: 6.7% (120/1796) OR = 2.96 (CI 1.96 – 4.47)
BODY OF EVIDENCE RATINGS		# Studies by Quality and Effect Size Ratings 5 Good/Substantial 1 Fair/Substantial 2 Good/Moderate 1 Fair/Moderate		
Consistency		YES		
Overall Strength		HIGH		

Bibliographic information for all studies is provided in Appendix C.

Table 2

Body of evidence summary table: phlebotomy teams.

Study (Quality and Effect Size Ratings)	Population/Sample	Setting	Time period	Results (Blood Culture Contamination Rates)
Gander 2009 - Good - Substantial	3,662 total venipuncture blood cultaaures - Emergency Dept (West): Phlebotomists: 2,012 Non -phlebotomists: 1,650	Parkland Memorial Hospital, Dallas, TX; 968 bed tertiary care teaching hospital	12/2006–12/2007; 5mos. of a 13-mo. period	Phlebotomists: 3.1% Non-phlebotomists: 7.4% OR = 2.51 (CI: 1.84 – 3.43)
Sheppard 2008 - Good - Substantial	2,854 total blood cultures-Emergency Dept.: Phlebotomists: 278 Non-phlebotomists: 2,576 (include venipuncture and catheter)	Emory Crawford Long Hospita, Atlanta, GA; Academic Medical Center	3 months– no dates reported	Phlebotomists: 1.1% Non-phlebotomists: 5.0% OR = 4.83 (CI: 1.53 – 15.28)
Surdulescu 1998 - Fair - Substantial	Venipuncture blood draws with prep kits; Sample size not reported;~6,900 total for 1995; from 1/93–10/93 approx. ½ phlebotomy team draws	St. Luke's Medical Center, Case Western Reserve University, Cleveland, OH; teaching hospital.	10 months 01/1993–10/1993	Phlebotomists: 2.6% Non-phlebotomists: 5.6% (p= 0.003) OR = 2.09 (CI: 1.68 –2.61)
Weinbaum 1997 -Good - Substantial	1,164 total blood culture venipuncture draws with prep kits; adult general medical and surgical care Phlebotomists: 956 Non-phlebotomists: 208	New York Medical Center Hospital of Queens, Flushing, NY; 487-bed community hospital	No dates reported. Baseline: 3mos.; Intervention: 6 mos.	Phlebotomists: 1.2% Non-phlebotomists: 4.8%, OR = 4.34 (CI: 1.82 – 10.36)
Unpublished				
Geisinger Wyoming Valley Hospital 2009 - Good - Substantial	~7020 total blood cultures; 73% by phlebotomists; non-phlebotomist blood collections include venipuncture and catheter	Geisinger Wyoming Valley Hospital; Wilkes-Barre PA	9 months (01/2009–09/2009)	Phlebotomists: 1.5% Non-phlebotomists: 4.3% OR = 2.93 (CI: 2.13 – 4.02)
BODY OF EVIDENCE RATINGS		# Studies by Quality and Effect Size Ratings 4 Good/Substantial 1 Fair/Substantial		
Consistency		YES		
Overall Strength		HIGH		

Bibliographic information for all studies is provided in Appendix C.

Table 3

Body of evidence summary table: prepackaged prep kits.

Study (Quality and Effect Size Ratings)	Population/Sample	Setting	Time period	Results (Blood Culture Contamination Rates)
McLellan 2008 -Fair -Minimal/None	1,115 total blood cultures collected by Doctor Support Workers (DSWs), junior and on call doctors No prep kit (Pre): 563 Prep kit (Post): 552 (2% chlorhexidine gluconate in 70% isopropyl alcohol)	Northern General Hospital, Sheffield Teaching Hospitals NHS Foundation Trust, Sheffield, South Yorkshire, UK Academic Medical Center; 2 units; accident/emergency and general practice	Pre: 5/2007- 7/2007 Post: 8/2007–10/2007	Overall: No prep kit (Pre): 8.88% Prep kit (Post): 7.43 % OR= 1.22 (CI: 0.79 –1.87)
Trautner 2002 -Fair -Substantial	813 total blood cultures collected by phlebotomists, house staff (medical students/residents) and healthcare technicians No prep kit:383 Prep kits: 430 paired sets from 215 patients-2 separate sites (chlorhexidine and tincture of iodine)	VA Medical Center, Houston, TX; Tertiary-care teaching hospital, inpatient service wards (telemetry, oncology, geriatric), medical and cardiac ICU.	11/2000–5/2001	No prep kit: 6.5% Prep kits: 0.9% OR = 3.68 (CI: 1.27 –10.73)
Weinbaum 1997 -Good -Moderate	495 total blood culture specimens collected by house staff (interns & residents No prep kit: 287 Prep kits: 208 (isopropanol and tincture of iodine)	New York Medica Center Hospital of Queens Flushing, NY.; 487-bed community hospital); general medical unit	3 months (1995); dates not reported	No prep kit: 6.5% Prep kits: 0.9% OR = 1.81 (CI: 0.85 –3.87)
Wilson et al. (2000) -Fair -Minimal/None (4 studies)	12,367 total blood samples; 6,362 with alcohol pledgets; 6005 with prep kits (70% isopropyl alcohol & 2% iodine tincture on separate sterile applicators). By site: Site a: No kit: 3536; Prep kit 2924; Site b: No kit: 1632; Prep kit 1801; Site c: No kit: 1007; Prep kit 906; Site d: No Kit: 187; Prep kit 374; collected by house staff physicians/ medical students except phlebotomy teams at Site c.	4 Academic medical centers: Duke Univ. Med. Ctr., Durham, NC (Site a), Robert Wood Johnson Univ. Hosp., New Brunswick, NJ (Site b), Denver Health Med. Ctr., Denver, CO (Site c), and Salt Lake Veterans Affairs Med. Ctr., Salt Lake City, UT (Site d)	Dates not reported; prior to 2000	Overall: No prep kit: 5.5% Prep kits:* 5.5% By site: Conventional; Prep kit Site a: 4.4%; 4.3% OR = 1.03 (CI: 0.81–1.31) Site b: 8.1%; 7.5% OR = 1.09 (CI: 0.85–1.39) Site c: 5.5%; 6.0% OR = 0.91 (CI: 0.62–1.34) Site d: 3.7%; 3.5% OR = 1.08 (CI: 0.42 –2.75)
BODY OF EVIDENCE RATINGS		# Studies by Quality and Effect Size Ratings 1 Fair/Substantial 1 Good/Moderate 5 Fair/Minimal/None		
Consistency		NO		
Overall Strength		INSUFFICIENT		

Bibliographic information for all studies is provided in Appendix C.