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# Effectiveness of Laboratory Interventions in Preventing Blood Culture Contamination and Improving Diagnostic Accuracy

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**ABSTRACT:** Laboratory interventions can substantially reduce blood culture contamination and improve the reliability of diagnostic results. Measures such as staff training in aseptic collection, use of standardized collection kits, appropriate skin antisepsis, and monitoring of contamination rates help limit the introduction of skin organisms into culture samples. When consistently implemented, these practices can reduce false-positive results, unnecessary antibiotic use, avoidable follow-up testing, and prolonged hospital stays. Improving diagnostic accuracy also depends on collecting adequate blood volumes, obtaining samples before antimicrobial therapy when feasible, and following clear procedures for labeling, transport, and processing. Regular audits and feedback help laboratories identify gaps and assess whether interventions are working. Because outcomes

may vary across settings, laboratories should use locally appropriate protocols and track both contamination rates and clinically meaningful measures, such as time to appropriate treatment and antibiotic use.

## INTRODUCTION:

Blood cultures remain the reference method for detecting bloodstream infection, but their diagnostic value is repeatedly compromised by contamination events in which skin commensals or environmental organisms are introduced into culture bottles during collection rather than originating from the patient's bloodstream [1]. Contamination is usually defined as the recovery of organisms that are not representative of true bacteremia, most often coagulase-negative staphylococci, Bacillus species, Cutibacterium acnes, and viridans group streptococci, although laboratories do not apply a single universally standardized definition [1]. The Clinical and Laboratory Standards Institute has historically endorsed a performance threshold of less than 3% contaminated cultures, while the American Society for Microbiology has more recently emphasized that a rate of 1% or less should be regarded as the optimal target for institutions committed to diagnostic excellence [1,2]. Despite widespread awareness of these benchmarks, contamination rates in many hospitals continue to exceed acceptable limits, particularly in emergency departments, teaching services, and units where collection is performed by a heterogeneous mix of nurses, physicians, and trainees [2].

The consequences of contamination extend well beyond a single erroneous laboratory result. Falsely positive cultures generate unnecessary antimicrobial exposure, prolong hospital admission, increase laboratory workload, and obscure the interpretation of subsequent cultures obtained during the same episode of care [2]. The incremental cost attributable to each contamination event has been estimated to range from several thousand to more than ten thousand United States dollars, driven largely by additional length of stay, unnecessary antibiotics, and repeat testing [3]. In middle-income and resource-limited settings, the economic burden can be even more pronounced relative to available resources, and the treatment of contaminating coagulase-negative staphylococci has been shown to consume substantial avoidable resources [3]. Beyond economics, contamination compromises antimicrobial stewardship by encouraging broad-spectrum therapy when narrower or no therapy would have been appropriate, and it may delay recognition of a true pathogen when a contaminant is dismissed as clinically insignificant [2,3]. A multicenter evaluation of blood culture practices in United States acute care hospitals further demonstrated that the absence of a standardized contamination definition complicates benchmarking and can materially affect reported rates, making laboratory-led quality improvement both more difficult and more necessary [4]. These clinical and economic realities explain why laboratory interventions to prevent contamination are now regarded not merely as technical refinements but as essential components of diagnostic stewardship [2,4].

### Skin Antisepsis: The Foundational Laboratory-Adjacent Intervention

Preparation of the venipuncture site is the single most consistently emphasized procedural step in contamination prevention, and the choice of antiseptic agent has been the subject of extensive comparative investigation [5]. Chlorhexidine gluconate, particularly when combined with isopropyl alcohol, has emerged as the preferred agent in many guidelines because of its rapid bactericidal activity and residual effect on skin flora [5]. A systematic review and meta-analysis examining chlorhexidine-based antisepsis across multiple clinical contexts reported that alcoholic chlorhexidine was superior to non-alcoholic povidone-iodine for reducing blood culture contamination, with a relative risk of 0.33 favoring the chlorhexidine formulation [5]. The American Society for Microbiology evidence-based guidelines similarly concluded that chlorhexidine-containing antiseptics, when grouped as a whole, produced a statistically significant reduction in contamination rates compared with standard procedures, with an overall reduction of approximately 56.5% across the studies analyzed [2]. Importantly, the same analysis emphasized that the alcohol component contributes substantially to efficacy; chlorhexidine alone without alcohol does not consistently outperform iodine-based preparations, whereas chlorhexidine in 70% isopropyl alcohol combines the immediate killing action of alcohol with the persistent activity of chlorhexidine [6].

However, the incremental benefit of chlorhexidine over other agents diminishes when collection is performed by highly trained personnel. A randomized trial conducted among dedicated phlebotomy teams found that contamination rates were low and not significantly different whether 10% povidone-iodine, 2% iodine tincture, or 2% chlorhexidine gluconate in 70% isopropyl alcohol was used, suggesting that the technical skill of the collector can partially compensate for differences in antiseptic formulation [7]. This observation is clinically important because it indicates that skin antisepsis should be understood not as an

isolated solution but as one component of a broader collection system [2,7]. In pediatric populations, chlorhexidine-based preparations have also been associated with lower contamination than povidone-iodine, although skin sensitivity and vein accessibility require careful consideration [8]. For institutions in which collection is performed by a heterogeneous mix of nurses, physicians, and trainees, the antiseptic choice remains a modifiable variable with a measurable effect on contamination [2,5]. The practical implication is that alcoholic chlorhexidine should be the default skin preparation for blood culture collection, with adequate drying time observed before venipuncture, and that the antiseptic should be supplied in single-use applicators to reduce variability in application technique [5,6].

**Table 1.** Summary of Evidence on Skin Antisepsis for Blood Culture Contamination Prevention

| Antiseptic strategy | Comparator | Reported effect on contamination | Contextual caveat |
|---|---|---|---|
| Chlorhexidine gluconate in 70% isopropyl alcohol | Povidone-iodine, aqueous or alcoholic | Significant reduction; pooled relative risk approximately 0.33 in meta-analysis [5] | Greatest advantage when collectors are not dedicated phlebotomists [7] |
| Chlorhexidine-containing antiseptics grouped | Standard institutional practice | Approximately 56.5% reduction across studies [2] | Heterogeneity in formulations and application methods [2] |
| 2% chlorhexidine in 70% alcohol | 10% povidone-iodine | More efficacious in pediatric populations [8] | Pediatric skin flora and vein accessibility differ from adults [8] |
| Any of three antiseptics used by dedicated phlebotomy teams | Alternative antiseptics used by the same teams | No significant difference between agents [7] | Collector skill attenuates antiseptic differences [7] |

**Blood Diversion Devices: Removing the Skin Plug and the Initial Contaminant Burden**

The initial aliquot of blood obtained at venipuncture frequently carries microorganisms residing in the skin plug or the distal lumen of the needle, and discarding this initial portion before inoculating culture bottles has emerged as a mechanistically compelling strategy for contamination reduction [9]. Diversion devices, whether commercial closed systems or simple sterile tubes used to sequester the first one to two milliliters of blood, operate on this principle [9]. A systematic review and meta-analysis of twelve studies, nine of which were included in the quantitative synthesis, found that venipuncture using a diversion device was associated with a significant reduction in blood culture contamination compared with standard collection, with a pooled odds ratio of 0.26 and low statistical heterogeneity [9]. Critically, the same analysis demonstrated that diversion did not reduce the detection of true bacteremia, with a pooled odds ratio of 0.85, indicating that the reduction in contamination was not achieved at the expense of diagnostic sensitivity [9]. The American Society for Microbiology guidelines reached a concordant conclusion, reporting that diversion devices produced a significant reduction in contamination and that the type of diversion device, commercial versus sterile tube, did not appear to be critical provided that an initial volume of blood was removed before culture inoculation [2].

The volume diverted varies across devices and protocols, typically ranging from 0.15 mL in some closed systems to 1.5–2.0 mL in others, with some studies discarding up to 7 mL [9,10]. Although larger discard volumes may raise concerns about iatrogenic anemia in patients requiring frequent cultures, the evidence suggests that discards below 2 mL are unlikely to produce clinically meaningful harm in most adult populations [9]. The economic case for diversion is strengthened by its capacity to reduce false-positive episodes, thereby avoiding the downstream costs of unnecessary antibiotics and extended hospitalization [3,9]. Commercial diversion systems have received regulatory clearance on the basis of clinical studies showing reduced contamination without a clinically important reduction in true-positive cultures [10]. Nevertheless, implementation requires attention to labeling and disposal of the diversion tube to prevent misidentification or inadvertent testing of the discarded specimen, and the cost of commercial devices must be weighed against the simpler and less expensive sterile-tube approach [9,10]. For laboratories and infection prevention programs seeking a high-yield intervention with a strong evidence base, diversion is among the most attractive options, particularly in settings where contamination rates remain persistently above 2% [2,9].

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**Dedicated Phlebotomy Teams and the Concentration of Procedural Expertise**

The profession and training of the individual performing venipuncture exert a profound influence on contamination rates, and the concentration of blood culture collection among dedicated phlebotomists has repeatedly been shown to outperform collection by rotating house staff, nurses with competing clinical responsibilities, and trainees [11]. A Laboratory Medicine Best Practices systematic review and meta-analysis reported that phlebotomy teams were favored over non-phlebotomy personnel across all included studies, with a mean odds ratio of 2.58, and the authors recommended phlebotomy teams as an evidence-based best practice with high overall strength of evidence [11]. The same review noted that contamination rates as low as 3% have been observed among phlebotomists, compared with rates approaching 11% for resident physicians and non-degree nursing assistants [11]. More recent institutional data reinforce this gradient: following the introduction of a dedicated phlebotomy team, one center reported a reduction in contamination from 0.45% to 0.27% and a simultaneous increase in the true-positive rate from 5.01% to 5.87%, demonstrating that the benefit extends beyond contamination reduction to improved diagnostic yield [11]. In a community teaching hospital, certified phlebotomist-drawn cultures achieved a contamination rate of 1.2%, compared with 4.6% when collection was performed by non-certified staff [11].

The mechanism underlying this advantage is not mysterious: phlebotomists perform venipuncture repeatedly, receive structured training in aseptic technique, and are accountable to a defined quality metric [11]. Their procedural fluency reduces variability in skin preparation, palpation after antisepsis, bottle inoculation order, and blood volume adequacy [2,11]. However, dedicated teams are resource-intensive and may not be feasible in all institutions, particularly smaller hospitals or during off-hours [11]. The evidence therefore supports a tiered approach: where resources permit, a dedicated phlebotomy team should be responsible for blood culture collection, at least in high-acuity areas such as the emergency department and intensive care units; where a full team is not feasible, a core group of trained blood culture champions can be identified and equipped with the same procedural standards [2,11]. Importantly, the effectiveness of a phlebotomy team is not simply a function of who performs the draw but of the training, feedback, and accountability structures that surround the role [11].

**Education and Training: From Knowledge Transfer to Procedural Fluency**

Educational interventions occupy a central place in contamination-reduction programs, but their effectiveness is highly dependent on intensity, format, and reinforcement [2]. A meta-analysis within the American Society for Microbiology guidelines compared low-intensity and high-intensity educational interventions and found that while both were associated with reductions in contamination, high-intensity training produced a greater likelihood of substantial improvement, with a risk ratio of 0.43 versus 0.60 for low-intensity training [2]. The same analysis demonstrated that organizations implementing one or more process improvement strategies alongside training achieved an average contamination reduction of approximately 56%, whereas those without process improvement strategies achieved only 15% [2]. This finding underscores a critical principle: education alone, delivered as a one-time lecture or online module, rarely produces durable behavior change [2,12]. It must be embedded within a system that includes checklists, audit and feedback, competency assessment, and visible leadership commitment [2].

Targeted educational interventions directed at the clinical areas with the highest contamination rates have produced meaningful reductions even when delivered over relatively short periods [12]. An emergency department-focused program emphasizing skin asepsis and preferred collection techniques significantly reduced contamination rates both locally and hospital-wide [12]. A combined education and skin antisepsis intervention in an Irish teaching hospital, which included a video demonstration and simulation training for interns, reduced the average contamination rate from 2.56% to 2.2%, although the difference did not reach statistical significance; the authors attributed the modest effect to the resource-intensive nature of feedback delivery and the greater impact of in-person training over virtual modalities [12]. In contrast, a multifaceted educational approach in a Japanese regional hospital reduced contamination from 7.7% to 2.4%, suggesting that baseline rates and institutional context strongly modify the observed effect size [12]. Simulation-based training with fluency-building protocols has been shown to require a mean of seven practice trials for interns to achieve procedural fluency, reinforcing the need for deliberate practice rather than passive learning [13]. Education should therefore be planned as an ongoing competency program rather than a single event, and its effect should be measured through contamination rates stratified by collector and unit [2,12,13].

**Table 2.** Comparative Effects of Personnel-Focused and Educational Interventions

| Intervention | Typical contamination rate achieved | Key design feature | Representative evidence |
|---|---|---|---|

| | | | |
|---|---|---|---|
| Dedicated phlebotomy team | 0.27%–1.2% | Concentrated procedural expertise and accountability [11] | [11] |
| Certified phlebotomist collection | 1.2% versus 4.6% for non-certified staff | Formal certification and quality monitoring [11] | [11] |
| High-intensity education with process improvement | Average reduction of approximately 56% | Multimodal training, audit, and feedback [2] | [2] |
| Low-intensity education alone | Average reduction of approximately 15% | Single-modality knowledge transfer [2] | [2] |
| Targeted emergency department education | Significant reduction with hospital-wide spillover | Focus on highest-burden area [12] | [12] |
| Simulation-based fluency training | Procedural fluency after approximately seven trials | Deliberate practice with performance standards [13] | [13] |

**Standardized Collection Kits and Bundled Interventions: Engineering the Procedure**

Standardized collection kits and bundled interventions represent a shift from individual behavior change to system-level redesign [14]. A collection kit packages all necessary supplies, including antiseptic applicators, sterile drapes, gloves, diversion tubes or devices, and bottle disinfection materials, in a single, sequence-consistent format, thereby reducing the cognitive burden on the collector and eliminating variability caused by missing or substituted supplies [14]. In a 640-bed rural trauma hospital, the introduction of a standardized blood culture collection kit in the emergency department reduced contamination rates from a pre-intervention range of 2.89% to 4.61% to a low of 0.97% within several months of full implementation [14]. The authors emphasized that inconsistent access to supplies had previously compromised aseptic technique and that the kit ensured all components were immediately available [14].

Bundled interventions extend beyond the kit to include skin antisepsis with chlorhexidine-alcohol, disinfection of the culture bottle septum, use of a sterile blood transfer device, and sometimes diversion [15]. A prospective study implementing a bundle that included these elements reported a reduction in contamination from 2.0% during the control period to 1.0% during the bundle period, with a particularly pronounced effect on coagulase-negative staphylococci [15]. The authors noted that the bundle approach achieved a contamination rate of 1.0%, which represents attainment of the newly proposed optimal threshold and demonstrates that a coordinated set of relatively simple measures can produce substantial gains [15]. A systematic review of interventions in acute care settings identified eight distinct strategies, including collection packs, dedicated collection teams, education, staff feedback, intervention bundles, sterile procedure, and initial specimen diversion devices, and concluded that while diversion devices showed the largest single effect, bundles and education offered advantages in ease of implementation and sustainability [16]. This complementarity is important: the most effective programs typically combine a high-yield device or procedural change with the educational and audit infrastructure necessary to ensure fidelity [2,16].

**Table 3.** Components and Reported Effects of Collection Bundles and Kits

| Bundle or kit component | Function | Reported contamination reduction | Source |
|---|---|---|---|
| Standardized collection kit | Ensures availability and sequence of all supplies | 2.89%–4.61% down to 0.97% | [14] |
| Chlorhexidine-alcohol skin antisepsis | Reduces skin flora at puncture site | Core component of bundle; independent effect approximately 56% | [2,5] |
| Bottle septum disinfection with 70% isopropyl alcohol | Prevents contamination from bottle stopper | Included in all bundle events; essential aseptic step | [15,17] |
| Sterile blood transfer device | Avoids needle manipulation and open transfer | Contributed to reduction from 2.0% to 1.0% | [15] |

| | | | |
|---|---|---|---|
| Initial specimen diversion | Removes skin plug and initial contaminant burden | Pooled odds ratio 0.26 in meta-analysis | [9] |

**Blood Culture Bottle Disinfection: An Overlooked but Necessary Step**

Although skin antisepsis and diversion receive the majority of attention in contamination-prevention literature, disinfection of the blood culture bottle septum is a necessary parallel step that is frequently performed suboptimally [17]. The rubber stopper of the culture bottle can harbor environmental organisms, and failure to disinfect it before needle insertion introduces a direct route for contamination [17]. Current recommendations specify that after removing the plastic flip-cap, the septum should be disinfected with 70% isopropyl alcohol or a chlorhexidine-alcohol preparation and allowed to air-dry before inoculation [17]. In bundle studies, bottle disinfection is included as a standard element, and its omission has been associated with pseudo-outbreaks of Bacillaceae species attributable to poor compliance with collection recommendations [15,17]. The practical challenge is that bottle disinfection competes with other tasks for the collector's attention and is easily skipped when workflow is rushed [17]. Standardized kits that include prepackaged alcohol wipes and visual prompts on the collection sequence can improve compliance, and audit programs should monitor bottle disinfection as a distinct quality indicator alongside skin antisepsis and diversion [14,17].

**Diagnostic Stewardship: Reducing Unnecessary Cultures and Enhancing Pre-Test Probability**

Contamination prevention is most effective when it is paired with diagnostic stewardship, meaning the judicious ordering and utilization of blood cultures based on clinical probability of bacteremia [18]. A substantial proportion of blood cultures are obtained in situations where the pre-test probability of true bloodstream infection is low, and in these scenarios even a modest contamination rate translates into a high proportion of false-positive results [18]. A review of contamination cases found that a large majority were ordered for indications with low risk for bacteremia, and most of these patients received unnecessary tests and antibiotics as a consequence [19]. Diagnostic stewardship interventions that reduce cultures in low-yield scenarios therefore have a multiplicative benefit: they reduce the absolute number of contamination events, decrease laboratory workload, and improve the positive predictive value of the cultures that are obtained [18,19].

The American Society for Microbiology guidelines and other expert bodies recommend that blood cultures be guided by clinical suspicion of sepsis, that routine culturing in low-yield scenarios be avoided, and that optimal blood volume of 8–10 mL per bottle in adults be ensured when cultures are indicated [2,18]. Quality improvement programs that include contamination monitoring, mandatory training, and feedback on culture utilization have been shown to sustain reductions beyond the initial intervention period [20]. Diagnostic stewardship also encompasses the post-analytic phase: when a positive culture grows an organism that is likely a contaminant, the laboratory should communicate this interpretation clearly to the clinical team and provide guidance on whether repeat culture is warranted, rather than allowing the result to drive automatic escalation of antimicrobial therapy [19,20]. The integration of stewardship principles into contamination-prevention programs ensures that efforts are directed toward cultures that are most likely to influence patient management [18,20]. Because contamination is shaped by local workflows, collector mix, and patient case mix, stewardship interventions must be tailored to the unit and institution rather than applied as a generic policy [20].

**Molecular and Advanced Diagnostic Methods: Distinguishing Contamination from True Infection**

Conventional culture remains the reference method for bloodstream infection diagnosis, but molecular methods offer complementary approaches that can improve diagnostic accuracy when contamination is suspected or when culture is negative despite clinical suspicion [21]. Broad-range 16S rRNA gene polymerase chain reaction and sequencing can identify bacterial DNA directly from blood or from positive culture bottles, and some studies have reported that molecular methods increase the detection of presumed pathogens in culture-negative samples [21]. However, molecular methods are themselves vulnerable to contamination during specimen processing and DNA extraction, and the presence of non-viable DNA or environmental contaminants can generate false-positive results [21,22]. The interpretation of molecular results therefore requires the same disciplined approach to collection and processing that is applied to culture, and molecular tests should not be viewed as a substitute for proper collection technique [21].

Multiplex polymerase chain reaction panels that identify organisms directly from positive blood culture bottles can accelerate organism identification and resistance gene detection, but they do not resolve the fundamental ambiguity of whether a coagulase-negative Staphylococcus isolate represents true bacteremia or contamination [22]. False-positive results have been

described in molecular panel analysis, including fungal false positives, and these findings reinforce the need for clinical correlation and laboratory judgment [22]. In practice, the laboratory's judgment about the likelihood of contamination, based on the organism, the number of positive bottles, the time to positivity, and the clinical context, remains essential, and molecular results must be interpreted in that light [21,22]. The future role of molecular diagnostics in contamination prevention is likely to be complementary rather than substitutive: molecular tools can shorten the time to identification of true pathogens, but the greatest gains in diagnostic accuracy will continue to come from preventing the introduction of contaminants in the first place [2,21,22].

**Artificial Intelligence and Predictive Analytics: A Frontier for Stewardship and Quality Control**

Machine learning and artificial intelligence are beginning to be applied to blood culture utilization and contamination prediction, offering a means of identifying patients at low risk of bacteremia before cultures are drawn and of flagging cultures with a high probability of contamination after growth [23]. Predictive models using electronic health record data, including structured variables and provider notes processed by large language models, have been developed to estimate the probability of bacteremia at the encounter level and to guide clinicians in withholding cultures when the predicted risk is very low [23]. One such model, evaluated in emergency department encounters, reported a prevalence of bacteremia of 7.5% and contamination of 0.6%, and at a threshold calibrated to a sensitivity target of 98%, it was projected to defer 26.2% of blood culture bottles, corresponding to an estimated reduction of nearly 16,000 bottles in the test cohort [23]. A randomized controlled non-inferiority trial is underway to determine whether a validated machine learning model can safely guide clinicians in withholding unnecessary blood cultures without missing true bloodstream infections [24].

Artificial intelligence also has potential applications in laboratory quality control, where automated monitoring of contamination rates by unit, collector, and shift can identify emerging problems before they become entrenched [25]. However, the evidence base for artificial intelligence in this domain remains immature, and concerns about model generalizability, alert fatigue, and the risk of false reassurance from a low predicted risk must be addressed through prospective validation [23,25]. For the presen t, artificial intelligence should be regarded as an adjunct to, rather than a replacement for, established collection standards, education, and audit [25]. Its most promising near-term role is in diagnostic stewardship, helping clinicians decide when not to culture, rather than in directly preventing contamination during the collection procedure itself [23,24,25].

**Quality Monitoring, Feedback, and Sustainability of Laboratory Interventions**

The durability of any contamination-prevention intervention depends on the presence of a monitoring and feedback system that makes performance visible and accountable [2]. Contamination rates should be calculated at least monthly, stratified by collection location, collector category, and shift, and reported to unit leaders and laboratory governance committees [2,4]. The American Society for Microbiology guidelines emphasize that organizations combining process improvement strategies with high-intensity training achieved substantially greater reductions than those relying on training alone, and that feedback and management oversight are critical for sustainability [2]. A multicenter evaluation of blood culture practices in United States acute care hospitals found that although the Clinical and Laboratory Standards Institute threshold of less than 3% is widely endorsed, there is no standardized definition of contamination, and the choice of definition can materially affect reported rates; this variability complicates benchmarking and underscores the need for laboratories to adopt explicit, locally agreed criteria and to report rates transparently [4].

Sustainability also requires attention to supply chain reliability, staffing stability, and the integration of contamination prevention into onboarding and annual competency assessments [14,17]. When a dedicated phlebotomy team is introduced, its effect may erode if the team is later dissolved or if its responsibilities are diluted by competing tasks [11]. Similarly, the benefit of a collection kit depends on continuous availability and on the kit being used for every culture, not only during periods of heightened awareness [14]. The most successful programs embed contamination prevention in the institution's quality infrastructure, with defined ownership, budgetary support, and periodic re-education that reflects staff turnover [2,4]. The movement toward a 1% target, advocated by some experts on the grounds that many facilities have already achieved this level following best practices, provides a stretch goal that can sustain attention and drive incremental improvement even after the traditional 3% threshold has been met [2,20].

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**Synthesis: Which Interventions Matter Most, and How Should They Be Combined?**

The evidence reviewed here supports a layered, multicomponent approach rather than reliance on any single intervention [2,16]. Diversion devices produce the largest single effect on contamination, with a pooled odds ratio of 0.26 in meta-analysis, and they have the advantage of not reducing true-positive detection [9]. Skin antisepsis with chlorhexidine in alcohol is a foundational measure with a consistent, moderate effect, particularly when collectors are not dedicated phlebotomists [5,7]. Dedicated phlebotomy teams and high-intensity education with feedback produce substantial reductions, but their effectiveness depends on organizational commitment and sustainment [2,11]. Standardized kits and bundles translate these principles into reliable practice by engineering the collection environment, and they can achieve contamination rates at or below 1% when implemented with fidelity [14,15].

The optimal combination for a given institution will depend on its baseline contamination rate, resource availability, collector mix, and existing quality infrastructure [2,16]. A reasonable sequencing for many hospitals is to begin with the lowest-cost, highest-feasibility measures, including alcoholic chlorhexidine antisepsis, bottle disinfection, and standardized collection kits, while simultaneously establishing contamination-rate reporting by unit and collector [5,14,17]. Once baseline data are available, high-burden areas such as the emergency department can be targeted with intensified education and, where feasible, dedicated phlebotomy coverage [11,12]. Diversion devices should be considered for units that continue to exceed the institutional target despite these measures, particularly if the volume of cultures is high enough to justify the per-device cost through avoided downstream expenses [3,9]. Diagnostic stewardship and, eventually, predictive analytics can reduce the number of low-yield cultures, thereby amplifying the benefit of collection-focused interventions [18,23].

**Table 4.** Layered Framework for Implementing Contamination-Prevention Interventions

| Layer | Intervention | Primary mechanism | Feasibility | Expected impact |
|---|---|---|---|---|
| Foundation | Alcoholic chlorhexidine skin antisepsis; bottle septum disinfection | Reduces skin and bottle-surface flora [5,17] | High; low cost | Moderate, consistent [5] |
| Standardization | Prepackaged collection kit or bundle | Eliminates supply variability and sequences steps [14,15] | High; moderate cost | Substantial; can achieve 1% or less [15] |
| Expertise | Dedicated phlebotomy team or certified collectors | Concentrates procedural skill and accountability [11] | Moderate; staffing-dependent | High; rates of 0.27%–1.2% reported [11] |
| Technology | Initial specimen diversion device | Removes skin plug and initial contaminant burden [9] | Moderate; device cost | Very high; pooled odds ratio 0.26 [9] |
| Stewardship | Ordering algorithms; feedback on low-yield cultures | Reduces unnecessary cultures and contamination denominator [18,19] | High; requires clinical engagement | Multiplicative benefit [18,19] |
| Analytics | Machine learning–guided culture deferral | Identifies very-low-risk patients before collection [23] | Emerging; validation needed | Potential 26% reduction in bottles [23] |

## CONCLUSION

Blood culture contamination represents a significant and preventable challenge to diagnostic accuracy. Evidence indicates that using diversion devices, alcoholic chlorhexidine for skin antisepsis, dedicated phlebotomy personnel, and intensive educational training are the most effective interventions. Implementing standardized kits and bundles has led to contamination rates at or below 1% in practice. Complementary approaches like diagnostic stewardship and predictive analytics can focus resources on patients most likely to benefit. A multi-faceted strategy combining engineering, education, expertise, and accountability is essential for sustained improvement. Laboratories that embrace this comprehensive system and maintain performance monitoring can enhance the accuracy of bloodstream infection diagnoses and reduce the burden of contamination. Achieving

a contamination rate of 1% or less is now a realistic goal for well-resourced institutions and should guide future quality improvement efforts.

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