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State of the Science Review

Economic health care costs of blood culture contamination: A systematic review

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Background: Blood culture contamination with gram-positive organisms is a common occurrence in patients suspected of bloodstream infections, especially in emergency departments. Although numerous research studies have investigated the cost implications of blood culture contamination, a contemporary systematic review of the literature has not been performed. The aim of this project was to perform a systematic review of the published literature on the economic costs of blood culture contamination.

Methods: PubMed was searched (January 1, 1978, to July 15, 2018) using the search terms "blood culture contamination" or "false-positive blood cultures." Articles were title searched and abstracts were reviewed for eligible articles that reported immediate or downstream economic costs of blood culture contamination.

Results and Discussion: The PubMed search identified 151 relevant articles by title search, with 49 articles included after abstract review. From the studies included, overall blood culture contamination rates ranged from 0.9%-41%. Up to 59% of patients received unnecessary treatment with parenteral vancomycin as a result of blood culture contamination, resulting in increased pharmacy charges between $210 and $12,611 per patient. Increases in total laboratory charges between $2,397 and $11,152 per patient were reported. Attributable hospital length of stay increases due to blood culture contamination ranged from 1-22 days.

Conclusions: This systematic review of the literature identified several areas of health care expenditure associated with blood culture contamination. Interventions to reduce the risk of blood culture contamination would avoid downstream economic costs.

Blood cultures are commonly used to provide important diagnostic information to determine the presence of bacteremia. However, it is often challenging to determine whether certain organisms are pathogenic or contaminants. Treatment of a contaminant can result in unnecessary antibiotic usage and increased health care costs. The Clinical and Laboratory Standards Institute recommend that hospitals achieve an overall blood culture contamination rate of <3%, although contamination rates at many institutions remain higher than this recommendation.[1] Contamination rates reported in the literature have ranged from 0.9%-7.9%.[2-6] Organisms commonly identified as blood culture contaminants include coagulase-negative staphylococci, diphtheroids, *Bacillus* sp, micrococci, *Propionibacterium acnes*, and *Corynebacterium* sp; of these, the coagulase-negative staphylococci are the most common blood culture contaminants isolated.[2,7]

Rates of blood culture contamination or false positives are often highest in emergency departments. Robertson et al[8] observed contamination rates of 11.7% in the emergency department versus 2.5% in other areas of the hospital. Likely causes of higher contamination rates in emergency departments include a fast-paced environment, frequent changes in staffing, increasing pressure for rapid culture collection prior to antimicrobial administration, lack of adequate training, and lack of accountability for adherence to the correct procedure to draw cultures.[9] Culture collection via pre-existing lines and peripheral lines can further perpetuate rates of contamination, as these lines are often quickly colonized with bacteria. False-positive blood cultures have

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extensive negative downstream effects. Increases in length of stay, inappropriate antimicrobial administration, and overuse of laboratory resources have been observed as a result of blood culture contamination. Although research studies have investigated the cost implications of blood culture contamination, a contemporary systematic review of the literature has not been performed. The purpose of this study was to perform a systematic literature review of published literature on the economic costs of blood culture contamination.

METHODS

Search strategy

PubMed was searched (January 1, 1978, to July 1, 2018) using the search terms "blood culture contamination" or "false-positive blood cultures." Additional articles were searched by hand from bibliography review. Articles were title searched and abstracts reviewed for relevant articles by 2 authors (C.D. and E.S.).

Inclusion criteria

Articles that reported immediate or downstream economic costs of blood culture contamination from a societal, hospital, or patient perspective were eligible for inclusion. Studies were sought that reported outcome data in terms of increased costs within the microbiology department, pharmacy department, and overall hospital owing to contaminated blood cultures. Observational and experimental data were included.

Data extraction

Incidences and economic costs were recorded for the following variables associated with blood culture contamination: hospital length of stay, expenditure of laboratory devices and labor, the use of diagnostic procedures, medication use, therapeutic drug monitoring, and the development of secondary nosocomial infections. Costs were collected preferentially over hospital charges that were collected only if hospital costs were not available. All costs extracted from the literature were adjusted to 2017 US dollars based on the Consumer Price Index.

RESULTS

The PubMed search identified 151 relevant articles by title search and 45 articles were reviewed by a manual bibliography search, with 49 articles included after abstract review. Of the 49 articles, 12 articles were highlighted as they specifically examined the impact of either contaminated cultures on antimicrobial therapy, pharmacy charges, length of stay, laboratory and microbiology costs, or total patient charges (Fig 1).[3-6,10-16] Ten studies were conducted in the United States, with the remaining 2 studies performed in Northern Ireland and Taiwan. Publication dates ranged from 1991-2014 (Table 1).

Antimicrobial therapy

Three studies discussed duration of therapy in patients with false-positive blood cultures. In 1 study, the total duration of therapy for any antimicrobial agent administered among patients with contaminated blood cultures was a median of 7 days (range, 1-15 days).[7] Two studies specifically investigated the duration of vancomycin therapy in patients with false-positive cultures. Total durations of vancomycin therapy were 5 ± 4 days (range, 1-17) and 6.5 days.[4,5] Two studies examined the percentage of patients who received antimicrobial therapy after a false-positive blood culture. Both studies found that treatment courses of antimicrobials were administered in 41% of

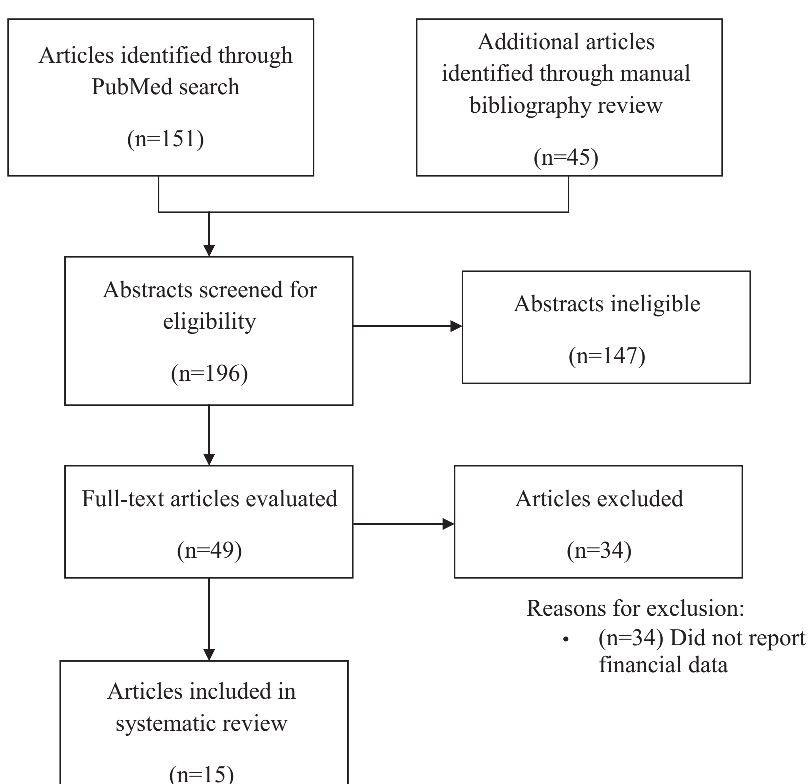

Fig 1. Search process and study selection.

Table 1
Clinical studies that have investigated economic effects of blood culture contamination

First author, year of study	Study design, period, country	Setting	Population	Sample collection	Number of blood cultures	False-positive blood cultures; n (%)
Gander, 2009[3]	Quasi-experimental, 2006-2007, USA	Emergency department	Adult	Routine blood cultures	5,432	Phlebotomist-drawn: 62 (3.1)
Nursing/technicians-drawn: 122 (7.4)						
Segal, 2000[15]	Retrospective descriptive study, 1994-1996, USA	Emergency department	Pediatric	Specific evaluation of blood culture contaminants	209	86 (41)
Little, 1999[4]	Randomized trial, 1995-1996, USA	Inpatient	Adult	Routine blood cultures	3,851	120 (3.1)
Souvenir, 1998[5]	Prospective cohort study, 1995, USA	Inpatient	Adult	Routine blood cultures	3,276	59a (1.8)
Alahmadi, 2011[13]	Retrospective case control, 2007-2008, UK	Inpatient	Adult	Routine blood cultures	284	254 (4.7)
Bates, 1991[2]	Prospective cohort study, 1988-1989, USA	Inpatient	Adult	Routine blood cultures	1,191	94 (7.9)
Little, 1997[4]	Prospective descriptive study, 1994, USA	Inpatient	Adult	Routine blood cultures	5,732	134 (2.3)
Zwang, 2006[16]	Retrospective descriptive study, 2002, USA	Inpatient	Adult	Routine blood cultures	939	56 (6)
Lee, 2007[17]	Randomized trial, 2003-2004, Taiwan	Inpatient	Adult	Specific evaluation of blood culture contaminants	212	178 (84)
Beekman, 2005[11]	Retrospective descriptive study; 1999-2000; USA	Inpatient	Mixed	Specific evaluation of blood culture contaminants	405	316 (78)
Waltzman, 2001[6]	Retrospective descriptive study, 1993-1996, USA	Inpatient	Pediatric	Routine blood cultures	9,465	87 (0.9)
Juthani-Mehta, 2014[12]	Retrospective descriptive study, 2001, USA	Inpatient (cancer specialty)	Adult	Specific evaluation of blood culture contaminants	43	12 (27.9)

patients with a false-positive blood culture.[4,5] Additionally, the percentage of patients with contaminated cultures who received vancomycin therapy was assessed in 4 studies, with rates of administration reported as 20%, 34%, 55%, and 59%.[4,5,11,17]

The administration of vancomycin therapy often necessitates pharmacokinetic monitoring, further increasing pharmacy costs. Two studies evaluated the costs of pharmacokinetic vancomycin monitoring, with 1 study reporting costs of $96 per level and the second study reporting costs of $1,073 per patient with contaminated blood cultures.[5,12] Beekmann et al[11] found the mean total number of antibiotics administered to patients with false-positive cultures was not significantly different to those with bacteremia, with a mean of 4.8 antibiotic agents versus 6.3 antibiotic agents, respectively. Total pharmacy costs per patient varied among the 4 studies, ranging from $210 to as high as $12,611 per patient.[4,5,11,13] Pharmacy costs for patients with true-negative blood cultures were drastically lower, ranging between $18.71 and $8,407.[4,13]

Length of stay

Six studies assessed total length of stay in patients with false-positive blood cultures, of which 5 were compared versus negative cultures.[2-4,10,13,16] Lengths of stay ranged from 1-22 days for patients with contaminated cultures and 1-17 days for negative cultures.

Laboratory and microbiology

The costs associated with blood culture collection per patient ranged from $96-$423 among 6 studies (Table 2).[2,6,12,18,19] Bates et al[2] found that blood culture charges per patient with false-positive blood cultures were significantly higher than true negatives, with median costs of $242 and $128, respectively ($P$ = .0001). Two studies identified that 70.6% and 27.5% of patients with false-positive blood cultures had repeat blood cultures collected, further enhancing the downstream costs of blood culture contamination.[7,17] Microbiology costs associated with contaminated blood cultures were specifically assessed in 4 studies, ranging from $182-$1,426.[4,11,13,16] Little et al observed statistically significant differences in mean microbiology costs between false- positive and true-negative blood cultures, at $900 and $571, respectively ($P$ =.001). Two studies addressed the costs associated with sensitivity testing for contaminated blood cultures, ranging from $89.75-$111 per instance, using conventional techniques.[15,16] Laboratory costs in 2 studies ranged from $2,397-$11,152 per patient with contaminated cultures.[11,20] Bates et al[2] identified a statistically significant difference between total laboratory charges in patients with false-positive and true-negative cultures with median costs of $3,770 and $2,613, respectively ($P$ = .0003).

Total patient charges

Seven studies highlighted the total hospital-wide patient charges associated with contaminated blood cultures (Table 2). Potential contributions to total hospital cost charges included catheter-related and noncatheter-related procedures, consultation costs, microbiology costs, and length of stay. Total patient charges ranged from $6,715-$111,627 per patient admission with false-positive cultures.[2,3,6,11,16,21] Three studies found statistically significant differences in charges for false-positive and true-negative blood cultures.[2,16,22]

DISCUSSION

This systematic review identified significant costs associated with blood culture contamination, including increased antimicrobial costs, laboratory and microbiology costs, and wider indirect costs, including those due to extended lengths of hospital stay and increased patient charges. This review also underscores the potential for negative patient outcomes due to unnecessary antimicrobial therapy after false-positive blood cultures, including increased risks of antimicrobial resistance and adverse drug events. Extended hospital stays may further increase the risk of hospital-acquired infections and adverse events. In fact, a 6% incremental daily risk of experiencing an adverse event has been previously reported for each day of hospital admission.[23]

Table 2
Pharmacy, microbiologic, and total hospital costs associated with blood culture contamination

First author, year of study	Cost versus charge evaluated	Variable evaluated	False positive	No growth
Pharmacy costs per patient (CPI-adjusted USD)				
Little, 1999[4]	Costs	Total pharmacy costs	$4,504 ± $8,107*	$3,453 ± $4,954
Souvenir, 1998[5]	Costs	Vancomycin monitoring	$1,073	—
Alahmadi, 2011[13]	Costs	Antimicrobials	$210 ($23-$543)	19 ($3-$135)
Laboratory costs associated with false positives (CPI-adjusted USD)				
Bates, 1991	Charge	Blood culture collection costs	$242 ($128-$423)	$128 ($110-$242)
Waltzman, 2001[6]	Charge	Blood culture collection costs	$107	—
Juthani-Mehta, 2014[12]	Costs	Blood culture collection costs	$208	—
Bates, 1991	Charge	Laboratory costs	$3,770 ($2,394-$8,036)	$2,613 ($1,253-$5,965)
Beekman, 2005[11]	Charge	Microbiology costs	$1,426	—
Zwang, 2006[16]	Charge	Microbiology costs	$183	—
Alahmadi, 2011[13]	Costs	Microbiology costs	$182 ($35-$434)	—
Little, 1997[10]	Costs	Microbiology costs	$900 ± $1,232	$571 ± $571
Segal, 2000[15]	Charge	Susceptibility testing	$111	—
Total patient costs (CPI-adjusted USD)				
Zwang, 2006[16]	Charges	Total hospital costs	$34,138 ($20,109-$74,296)	$21,644 ($10,005-$57,502)
Bates, 1991	Charges	Total hospital costs	24,642 ($12.616-$47,148)	$16,403 ($8,332-$42,133)
Gander, 2009[3]	Charges	Total hospital costs	$27,471 ($21,063-37,841)	$18,752 ($17,046-$20,315)
Beekman, 2005[11]	Charges	Total hospital costs	$111,627	—
Waltzman, 2001[6]	Charges	Total hospital costs	$16,200	—
Little, 1999[4]	Costs	Total hospital costs	$34,000 ± $66,000	$26,000 ± $33,000

CPI, Consumer Price Index; *USD*, US dollar.

The data compiled in this review provides evidence to support the potential economic benefit of interventions designed to reduce the rate of false-positive blood cultures. Using a 1.5:1 charge-to-cost ratio, our review identifies total additional hospital costs attributable to a false-positive blood culture between $2,923 and $5,812. When considering direct-only costs, additional pharmacy and microbiology costs attributable to a false-positive blood culture result ranges from $305-$1,389. These findings highlight significant potential costs, which may be avoided by interventions designed to reduce the rate of false-positive blood cultures.

Specific strategies have been highlighted to decrease contamination rates within hospitals. Gander et al[3] found statistically significant differences in blood culture contamination rates when collection was performed by trained phlebotomists versus non-phlebotomy staff in the emergency department, 3.1% versus 7.4%, respectively. The use of a diversion device to collect blood cultures has also been observed to further decrease the contamination rate in a population of trained phlebotomists from 1.78%-0.22% ($P = .001$).[24] Use of these techniques may benefit institutions with high blood culture contamination rates.[25]

This systematic review also revealed data gaps in the literature and methodological inconsistencies between studies that should be noted. There are a variety of formats for reporting costs due to false-positive blood cultures, including patient charges or hospital costs, which may complicate meaningful comparisons, although standard conversion ratios between these metrics exist. Furthermore, the type of data reported in studies (ie, patient charges vs hospital costs) is not always clearly stated or distinguishable. Additionally, not all studies reported costs in sufficient granularity (eg, specific costs associated with blood culture collection vs those associated with pathogen identification and characterization), which may account for a wide range of reported costs for seemingly similar services. Finally, the adoption of rapid diagnostic instruments for pathogen identification and characterization jeopardizes the generalizability of older cost data, reflective of more conventional microbiology techniques.

Limitations to our study should be considered, including the potential for incomplete retrieval of relevant articles using our search parameters. However, the potential for relevant data loss was minimized by our strategy that included manual searching of article bibliographies for additional references. The risk of bias from data heterogeneity was also minimized by delineating clear, objective outcome variables to extract from data sources. More formal measures of disease burden studies that include measures such as quality adjusted life years has not been performed in this population and may provide more objective or alternative measures of poor outcomes.

CONCLUSIONS

This systematic review of the literature identified several areas of health care expenditure associated with blood culture contamination. Interventions to reduce the risk of blood culture contamination have a wide-reaching potential to avoid downstream economic costs while improving the quality of care to patients.

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