

# Improving Blood Culture Quality with a Medical Staff Educational Program: A Prospective Cohort Study

Yunbo Chen<sup>1,2</sup>, Yuanyuan Dai<sup>3</sup>, Yizheng Zhou<sup>4</sup>, Ying Huang<sup>5</sup>, Yan Jin<sup>6</sup>, Yan Geng<sup>7</sup>, Bing Ji<sup>8</sup>, Rong Xu<sup>9</sup>, Wencheng Zhu<sup>10</sup>, Shuyan Hu<sup>11</sup>, Zhuo Li<sup>12</sup>, Jinhua Liang<sup>13</sup>, Yonghong Xiao<sup>1,2</sup>

<sup>1</sup>State Key Laboratory for Diagnosis and Treatment of Infectious Diseases, The First Affiliated Hospital, Zhejiang University School of Medicine, Hangzhou, People's Republic of China; <sup>2</sup>Collaborative Innovation Center for Diagnosis and Treatment of Infectious Diseases, Hangzhou, People's Republic of China; <sup>3</sup>Clinical Laboratory, The First Affiliated Hospital of USTC, Division of Life Sciences and Medicine, University of Science and Technology of China, Hefei, People's Republic of China; <sup>4</sup>Clinical Laboratory, Jingzhou Central Hospital, Jingzhou, People's Republic of China; <sup>5</sup>Clinical Laboratory, First Affiliated Hospital of Anhui Medical University, Hefei, People's Republic of China; <sup>6</sup>Clinical Laboratory, Shandong Provincial Hospital, Jinan, People's Republic of China; <sup>7</sup>Clinical Laboratory, The Second Affiliated Hospital of Xi'an Jiaotong University, Xi'an, People's Republic of China; <sup>8</sup>Clinical Laboratory, Affiliated Hospital of Binzhou Medical College, Binzhou, People's Republic of China; <sup>9</sup>Clinical Laboratory, People's Hospital of Yichun City, Yichun, People's Republic of China; <sup>10</sup>Clinical Laboratory, Lu'an Civil Hospital, Lu'an, People's Republic of China; <sup>11</sup>Clinical Laboratory, People's Hospital of Qingyang, Qingyang, People's Republic of China; <sup>12</sup>Clinical Laboratory, The First Affiliated Hospital of Xi'an Medical University, Xi'an, People's Republic of China; <sup>13</sup>Clinical Laboratory, The Affiliated Hongqi Hospital of Mudanjiang Medicine College, Mudanjiang, People's Republic of China

Correspondence: Yonghong Xiao, The First Affiliated Hospital, School of Medicine, Zhejiang University, 79 Qingchun Road, Hangzhou, Zhejiang, 310003, People's Republic of China, Tel/Fax +86 571 87236421, Email xiao-yonghong@163.com

**Purpose:** Blood cultures (BCs) are essential laboratory tests for diagnosing blood stream infections. BC diagnostic improvement depends on several factors during the preanalytical phase outside of innovative technologies. In order to evaluate the impact of an educational program on BC quality improvement, a total of 11 hospitals across China were included from June 1st 2020 to January 31st 2021.

**Methods:** Each hospital recruited 3 to 4 wards to participate. The project was divided into three different periods, pre-implementation (baseline), implementation (educational activities administered to the medical staff) and post-implementation (experimental group). The educational program was led by hospital microbiologists and included professional presentations, morning meetings, academic salons, seminars, posters and procedural feedback.

**Results:** The total number of valid BC case report forms was 6299, including 2739 sets during the pre-implementation period and 3560 sets during the post-implementation period. Compared with the pre-implementation period, some indicators, such as the proportion of patients who had 2 sets or more, volume of blood cultured, and BC sets per 1000 patient days, were improved in the post-implementation period (61.2% vs 49.8%, 18.56 vs 16.09 sets, and 8.0 vs 9.0mL). While BC positivity and contamination rates did not change following the educational intervention (10.44% vs 11.97%, 1.86% vs 1.94%, respectively), the proportion of coagulase negative staphylococci-positive samples decreased in BSI patients (6.87% vs 4.28%).

**Conclusion:** Therefore, medical staff education can improve BC quality, especially increasing volume of blood cultured as the most important variable to determine BC positivity, which may lead to improved BSI diagnosis.

**Keywords:** blood culture, bloodstream infection, medical education, medical staff, quality improvement

## Introduction

A bloodstream infection (BSI) is defined as positive blood cultures in a patient with systemic signs of infection that may be primary or secondary to a documented source. A recent scientific publication estimated that there were approximately 48.9 million sepsis episodes and 11 million sepsis-related deaths each year worldwide, which accounts for almost 20% of all global deaths.<sup>1</sup> Early adequate antimicrobial therapy is key to improving patient outcomes.<sup>2</sup> A retrospective study showed that patient survival drops an average of 7.6% for every additional hour before antibiotic administration.<sup>3</sup> Identifying the causative pathogen and assessing its antimicrobial susceptibility allows for better targeted treatments and optimization of antibiotic therapy. Blood cultures (BCs) remain the first-line tool for the diagnosis and successful

management of patients with BSIs. BCs are also essential to antimicrobial resistance (AMR) countermeasures, which can potentially decrease patient exposure to inadequate antibiotics or inappropriate antibiotic use, avoiding the consequences of multidrug-resistant organisms and decreasing hospital length of stay and costs.<sup>4,5</sup>

Although major improvements have been made in recent years to increase the sensitivity and specificity of BCs and reduce the time to microorganism identification,<sup>6</sup> improved quality management of BC diagnostics is increasingly recommended.<sup>7</sup> The framework for BC described by the international standard ISO 15189 established quality indicators across critical points of BC pre-analytics, examination and post-analytics processes, which can serve as fundamental tools for accuracy and patient safety.<sup>8,9</sup> Many factors influence BC quality and the likelihood of detecting a pathogen, including antibiotic pretreatment prior to the blood draw, suboptimal sample volume, an inadequate number of BC bottles cultured and delayed incubation times and processing methods.<sup>10,11</sup> BC approved guidelines (CLSI2007) recommend 103–188 BC sets per 1000 patient days, with goal positivity rates of 5–15% and contamination rates of 2%–3%.<sup>12</sup> Many prior works have focused on improving the quality management of BC diagnostics.<sup>13–15</sup> Increased awareness of the importance of pre-analytics to BSI diagnostic quality has been evidenced through a number of improvement initiatives, recognition of the low achievement of the recommended targets for contamination and blood volume, and recognition of the need for extra tools to visualize and promote improvements.<sup>7,16</sup> Educational interventions have been among the most economical and effective measures of the above strategies.<sup>17,18</sup>

Current BC practices remain inefficient in China, with low yields and inconsistent adequacy,<sup>19</sup> especially in the context of an increasing rate of multidrug-resistant organisms. The main shortfalls of current practice include delayed BC orders, inadequate skin antisepsis and collection via intravenous catheters. This limits the type and number of BC sets and blood volumes, time to bottle incubation, the rapid processing of positive bottles and the close involvement of antimicrobial stewardship teams. In this study, we selected 11 hospitals from different provinces in China to conduct BC education actions for 4 months in order to 1) strengthen clinician and nurse understanding of the pre-analytical phase of BC; 2) evaluate the influence of educational interventions on BC quality, such as positivity, contamination rate and reporting time; and 3) identify challenges and solutions associated with education that may be broadly applicable to other hospitals.

## Materials and Methods

### Participating Hospitals

A total of 11 hospitals from different provinces in China that were members of the Blood Bacterial Resistant Investigation Collaborative System (BRICS) were included in this study. All sites used BacT/Alert blood culture system (bioMérieux, USA) for routine blood cultures. Matrix-assisted laser desorption ionization–time of flight mass spectrometry (MALDI-TOF MS) identification was carried out in 5 hospitals while the remains used traditional biochemical identification methods. His project was registered in the “Chinese Clinical Trial Registry” (Registration Number: ChiCTR2000034404).

### Design

This was a prospective study that consisted of three phases (between June 1st 2020 and January 31st 2021), each lasting eight weeks. During the first phase, or the pre-implementation period, each hospital collected routine blood culture data (the quality indicators as described below) as a basic group. In this stage, medical staff were not trained and blood culture data in participating departments were collected. The second phase, or training period, was the implementation of educational activities for healthcare staffs, including clinicians, nurses and microbiologists. Medical education provided medical training to medical staff in the form of presentations, printed materials, videos, distance learning, etc. Records of each relevant training were kept, including the date of training, the method of training (eg round-table discussions, seminars, lectures, etc.), and the duration of training. During the third phase, or the post-implementation period, each hospital collected routine blood culture data as an experimental group. In this stage, educational activities continued to be implemented but at a reduced frequency, and blood culture data was collected.

Each hospital recruited 3 to 4 different wards where blood culture is usually sent for examination relatively frequent to participate. The wards covered different professional departments and comprised the different wards, such as emergency ward, intensive care unit (ICU), infectious disease ward, respiratory medicine ward and hematology ward.

## Inclusion and Exclusion Criteria

Inclusion criteria were: 1) patients suspected of a BSI or sepsis who had blood cultures collected according to clinical guidelines;<sup>12</sup> 2) hospitalized patients aged 18 years or older; and 3) blood samples collected during the study period by nurses based on relevant indications and guidelines. Exclusion criteria were: 1) children younger than 18 years old; 2) patients who do not meet the clinical diagnostic criteria for a BSI or sepsis; 3) patients who had positive blood cultures but deemed to be a contaminant; and 4) patients who had repeated blood cultures within a week with the same pathogen or negative results.

## Definition

A set of blood culture was defined as the bottles (1 or 2 bottles) obtained from one doctor's order, which represented one submission with a single accession number. Blood culture submission rate was calculated as the total number of blood culture submissions per 1000 patient days. BSI incidence was calculated as the number of positive blood culture sets excluding contaminated specimens per 1000 patient days.

Blood volume of each bottle were determined by weighing bottle by using an electronic precision scale and recorded at receiving bottles.

Negative bottles were removed and discarded after 5 days of incubation. A blood culture was considered contaminated if one of the following organisms was present in only one bottle: coagulase-negative *staphylococci* (CNS), alpha-hemolytic *streptococci*, *Micrococcus* species, *Cutibacterium* species, *Corynebacterium* species and *Bacillus* species. If two different contaminants were separately present in only one bottle, only one contaminated set was recorded. The contamination rate was calculated by dividing the total number of contaminated sets by the total number of obtained BC sets.

Positivity rate was calculated as the number of positive blood culture sets divided by the total number of BC sets. A positive set was defined as a set that contained positive BC that did not meet contamination criteria.

## Educational Program

The educational program was led by hospital microbiologists and was composed of professional presentations, morning meetings, academic salons, seminars, posters and procedural feedback. An educational seminar was set up for all nursing team members who were involved in obtaining blood samples for culture. At least two educational sessions on blood culture processing were held at each participating ward during the second phase to ensure that all staff would be able to attend. Different professional presentations were held weekly at staff meetings during the training phase, then every two weeks during the post-implementation period. During the training period and the post-implementation period, microbiologists gave feedback on BC set results, blood volumes, positivity rates and contamination rates every week to participating wards.

Where available, microbiologists invited clinicians and nurses to visit the laboratory to see how bottles were processed after arriving at the lab. Some hospitals used mini-programs to answer questions about blood cultures. Two hospitals set up WeChat groups to communicate.

At the start of the educational intervention, mouse pads and posters related to blood culture were distributed and posted in participating wards. The contents of the posters and mouse pads included: the clinical significance of blood cultures, blood culture collection requirements (such as the number of BC sets and the amount of blood to collect) and recommended guidelines for BC collection.

## The Case Report Forms

Case Report Forms (CRFs) were used to collect individual patient data on paper forms, including patient gender, department, the number of bottles per capita, collection type, number of bottles per BC set and prescription purpose

and the times of different points, such as the positive time, the first Gram stain, the final report). The data were collected according to electronic medical record systems, laboratory information systems, the blood culture instruments.

## Quality Indicators

The following quality indicators were chosen for monitoring: 1) the number of BC bottles received per 1000 patient days, 2) the proportion of patients who had 2 sets (4 bottles) of BCs or more per order, 3) the average volume of blood collected per bottle, 4) delay from sampling to registering and loading the bottles into the incubation system, 5) turnaround time for bacterial isolates (the time from blood bottles loaded to the positive time, the first Gram stain, the first report), 6) BC set positivity rate and 7) the rate of BC sample contamination.

## Statistics

Epidata 3.2 was used to input data and establish the database. Logic proofreading was performed through the file which was established in advance to ensure appropriate data input.

R4.0.2 was used for statistical analysis. Measurement data conforming to a normal distribution were expressed as mean  $\pm$  standard deviation or median (Q1, Q3) interval [Median (Q1, Q3)]; categorical data were expressed as frequency and percentage [N (%)]. An independent sample *t*-test was used to compare differences between measurement data with a normal distribution, such as the number of bottles/sets per capita and the number of bottles sent for blood culture before and after education. Nonparametric tests were used to compare differences in measurement data that did not conform to a normal distribution before and after education, such as the patient's age, change of time nodes in each bottle of blood culture in the clinical stage and the change of time nodes in the clinical microbiology laboratory stage. The chi-squared test was used to compare differences in the distribution of categorical variables before and after education, such as patient gender, department, the number of bottles per capita, collection type, number of bottles per BC set and prescription purpose. In addition, stratified analysis was used to compare differences in the number of BC test sets per capita and the number of test bottles per capita during the pre-implementation and assessment periods in different departments, and to compare differences in BC set positivity before and after the educational intervention. All tests were two-sided, and  $P < 0.05$  was considered statistically significant.

## Results

### Participating Hospitals

Eleven participating hospitals, 10 tertiary hospitals and 1 secondary hospital, representing 7 provinces across China participated in this study ([Supplementary Table 1](#)). A total of 42 wards were included in this survey. The ICU was the most selected ward in this study (23.8%, 10/42), followed by the respiratory medicine and hematology wards (14.3%, 6 wards each). The total number of beds in this survey was 2573, of which 18.2% (469/2573) were in respiratory medicine wards, 17.2% (442/2573) were in hematology wards and 12.3% (316/2573) were in the ICU. Compared with other reports that most BC are obtained in the ED rather than on inpatient wards,<sup>20</sup> it is surprising that the emergency department (ED) was not the most surveyed area. This may be due to the differences in the admission processes in China as outpatients with fever of unknown origin were admitted to different wards according to their underlying medical conditions.

A total of 204 actions of different forms were implemented during the training period to train clinicians, nurses and other medical staff. Presentations were the most frequent, accounting for 49.0% (100/204). Other forms included consultation during morning meetings (8.3%, 17/204), academic salons (10.8%, 22/204) and professional topics (1.0%, 2/204) ([Supplementary Table 1](#)).

### General Data Collection

A total of 7321 CRF were collected. A total of 1022 CRFs provided by 8 hospitals included data from outside the pre-implementation or post-implementation periods were excluded, leaving 6299 valid CRFs. This included 2739 sets

(43.48%, 2739/6299) during the pre-implementation period and 3560 sets (56.52%, 3560/6299) during the post-implementation period ([Supplementary Table 1](#)).

BCs were collected from a total of 4716 patients, of which 2203 were during pre-implementation period while 2513 were during the post-implementation period. Most of these patients were male (60.38%), with a median age of 58 years (IQR: 46–71) ([Table 1](#)). The ICU, internal medicine ward and infectious disease ward most frequently ordered BCs, representing 27.93%, 19.34% and 13.14% of orders, respectively ([Table 2](#)). No significant differences were found in gender, age and ward distribution between the two collection periods.

A total of 18,388 bottles were collected during the study period, including 7792 (42.38%, 7792/18333) during the pre-implementation period and 10,596 (57.62%, 10,596/18,388) during the post-implementation period ([Table 1](#)). This translates to 54.46 bottles per 1000 patient days during the pre-implementation period and 64.02 bottles per 1000 patient days during the post-implementation period. Bottle submission per 100 patients was 39.14 during pre-implementation period and 46.30 during the post-implementation period. After education, the proportion of patients who had 2 sets (4 bottles) or more of BCs drawn increased significantly, from 49.80% during pre-implementation period to 61.20% during the post-implementation period ( $P < 0.01$ ). However, less than 3.00% of patients among patients who had BCs collected had a single bottle collected (2.00% during the pre-implementation period and 2.23% during the post-implementation period) ([Figure 1](#)). The median number of BC sets or bottles collected per patient significantly increased in the emergency department, ICU and the infectious disease ward after education ([Table 2](#)).

Of the 6299 CRFs included in this work, 5374 were blood cultures recorded with diagnosis purpose. BC positivity increased from 10.44% (286/2740) to 11.97% (426/3559) during the post-implementation period compared with the pre-implementation period ( $P = 0.062$ ). The BC contamination rate was 1.91% (120/6299) overall, and did not reach statistical significance between the pre-implementation and post-implementation periods (1.86%, 51/2740 and 1.94%, 69/3559,  $P = 0.586$ ), respectively. This may be due to the fact that the pre-implementation rates were already reasonably low, within an acceptable range.

**Table 1** Comparisons of Data from Pre-Implementation versus Post-Implementation Period

	Total	Pre-Implementation Period	Post-Implementation Period	P*
Number of CRF	6299	2740	3559	-
Number of patients with BC	4716	2203	2513	-
Total number of hospitalized patients	42,794	19,908	22,886	-
Total days of hospitalized patients	362,269.8	170,338.3	191,931.5	-
Age, Median (Q1, Q3)	58 (46, 71)	58 (46, 71)	59 (46, 70)	0.367
Gender, n (%)				0.299
Male	2845 (60.38)	1311 (59.56)	1534 (61.09)	
Female	1867 (39.62)	890 (40.44)	977 (38.91)	
Total number of sets	6299	2739	3560	-
Proportion of 2 set collects	2635 (55.87%)	1097 (49.805)	1538 (61.20%)	< 0.001
Total number of bottles	18,388	7792	10,596	-
Sets per 1000 patient day	17.40	16.09	18.56	-
Bottles per 1000 patient day	59.53	54.46	64.02	-
Bottles per 100 patients	42.97	39.14	46.30	-
Number of patients with positive BC	712 (11.30)	286 (10.44)	426 (11.97)	0.062
Contamination rates	120 (1.91)	51 (1.86)	69 (1.94)	0.586
Incidence of BSI	1.66	1.44	1.86	< 0.001
Purpose of BC order, n (%)				< 0.001
Diagnosis of BSI	3918 (98.12)	1847 (98.88)	2071 (97.46)	
Evaluation of treatment	54 (1.35)	19 (1.02)	35 (1.65)	
Follow-up	3 (0.08)	1 (0.05)	2 (0.09)	
Others	18 (0.45)	1 (0.05)	17 (0.8)	

**Notes:** \*The used tests described in Method.

**Abbreviations:** CRF, Case Report Form; ICU, Intensive Care Unit; BC, Blood Culture; BSI, blood Stream Infection.

**Table 2** Comparisons of Data on Different Wards from Pre-Implementation versus Post-Implementation Period

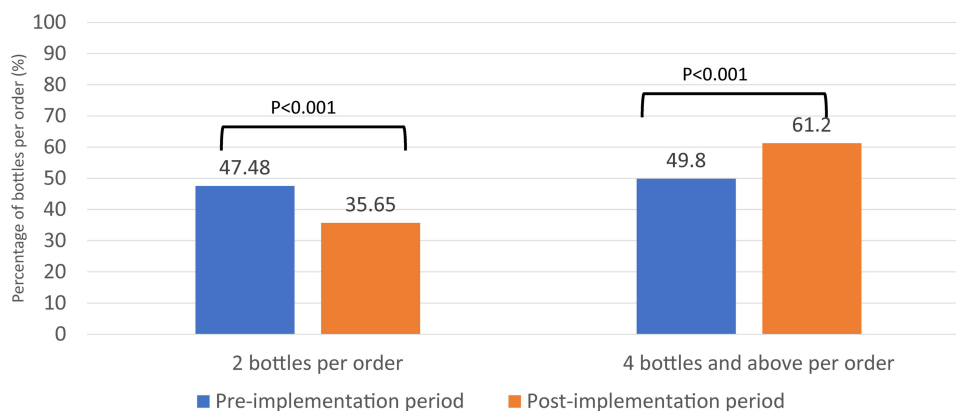
	Total	Pre-Implementation Period	Post-Implementation Period	P*
Wards distribution, n (%)				< 0.001
Emergency department	427 (9.33)	185 (8.77)	242 (9.82)	
ICU	1278 (27.93)	541 (25.64)	737 (29.9)	
Infectious disease ward	601 (13.14)	292 (13.84)	309 (12.54)	
Internal medicine ward	885 (19.34)	383 (18.15)	502 (20.37)	
Others	1384 (30.25)	709 (33.6)	675 (27.38)	
Number of sets per patients with BC in different ward, mean (SD)				
Emergency department	1.29 (0.67)	1.17 (0.48)	1.37 (0.78)	0.002
ICU	1.55 (1.16)	1.41 (0.96)	1.65 (1.28)	<0.001
Infectious disease ward	1.15 (0.42)	1.11 (0.33)	1.19 (0.49)	0.021
Internal medicine ward	1.29 (0.64)	1.27 (0.65)	1.31 (0.63)	0.457
Others	1.27 (0.71)	1.18 (0.54)	1.37 (0.86)	<0.001
Number of bottles per patients with BC in different ward, mean (SD)				
Emergency department	3.21 (2.11)	2.83 (1.63)	3.50 (2.37)	0.001
ICU	5.46 (4.61)	4.78 (3.94)	5.96 (4.99)	<0.001
Infectious disease ward	3.65 (1.75)	3.69 (1.54)	3.61 (1.94)	0.585
Internal medicine ward	3.27 (1.94)	2.91 (1.61)	3.54 (2.12)	<0.001
Others	3.23 (1.98)	3.10 (1.90)	3.39 (2.06)	0.005

Note: \*The used tests described in Method.

## Pre-Analytic Procedures

While the decision to order a BC is typically made by the physician, blood samples are obtained by nurses. Using data collected from CFR, the average blood bottle volume during the pre-implementation period was 8.0 mL. Over the course of education, bottle volume increased to 9.0 mL ( $P < 0.01$ ) (Table 3).

Pre-analytic delay, or the time from the doctor's order to registering and loading the BC sample bottle, was divided into three parts: the time from the doctor's order to nurse's performance (order delay), the time from the nurse's performance to registration at the microbiology laboratory (routing delay) and the time from registration at the microbiology laboratory to loading (loading delay). Nurses carried out the doctor's orders in an average of 40 minutes (Table 3). All three times were improved after education (Table 3) ( $P < 0.05$ ).



**Figure 1** Percentage of bottles per patient during the two periods. Comparison of bottles per set between the pre-implementation and post-implementation periods. Bottles per set were binned into the following categories: 2 bottles per order, and 4 or more bottles per order. The pre-and post-implementation groups were significantly different ( $P < 0.01$ , the chi-squared test).

**Table 3** The Average Volume and the Turnaround Times During the Two Periods

	Total (n = 18,388 Bottles)	Pre-Implementation (n = 7792 Bottles)	Post-Implementation (n = 10,596 Bottles)	P*
The average volume per blood bottle (mL)	8 (7, 10)	8 (7, 9)	9 (7, 10)	< 0.001
The turnaround times before loading bottles to instruments, Median (Q1, Q3)				
Order delay (minute)	38 (13, 128)	39 (14, 129)	37 (12, 126)	0.037
Routing delay (hour)	2 (0, 3)	2 (0, 4)	1 (0, 2)	< 0.001
Loading delay (hour)	2 (1, 4)	2 (1, 6)	1 (1, 3)	< 0.001
The turnaround times, Median (Q1, Q3)				
From blood bottles loaded to the positive time (hour)	22 (15, 37)	22 (15, 37)	22 (15, 38)	0.360
From blood bottles loaded to the first Gram stain (hour)	24 (18, 40)	24 (17, 39)	24 (18.25, 40)	0.033
From blood bottles loaded to the first report (hour)	31 (21, 45)	32 (21, 45)	31 (22, 45.25)	0.688
From blood bottles loaded to the first organism ID (hour)	46 (39, 64)	47 (40, 65)	45 (33, 63)	< 0.001
From blood bottles loaded to the second report (hour)	49 (40, 66)	50.5 (41, 66)	47 (38.75, 67)	0.110
From blood bottles loaded to the first AST (hour)	46 (40, 62)	47 (40, 63)	45 (35, 61)	0.005
From blood bottles loaded to the final report (hour)	71 (64, 90)	72 (64, 91)	71 (63, 88)	0.046

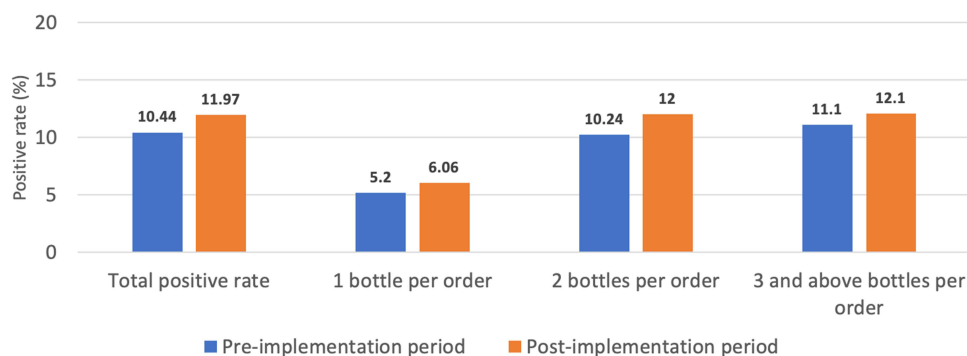
**Notes:** \*The used tests described in Method.

**Abbreviations:** ID, Identification; AST, Antimicrobial susceptibility test.

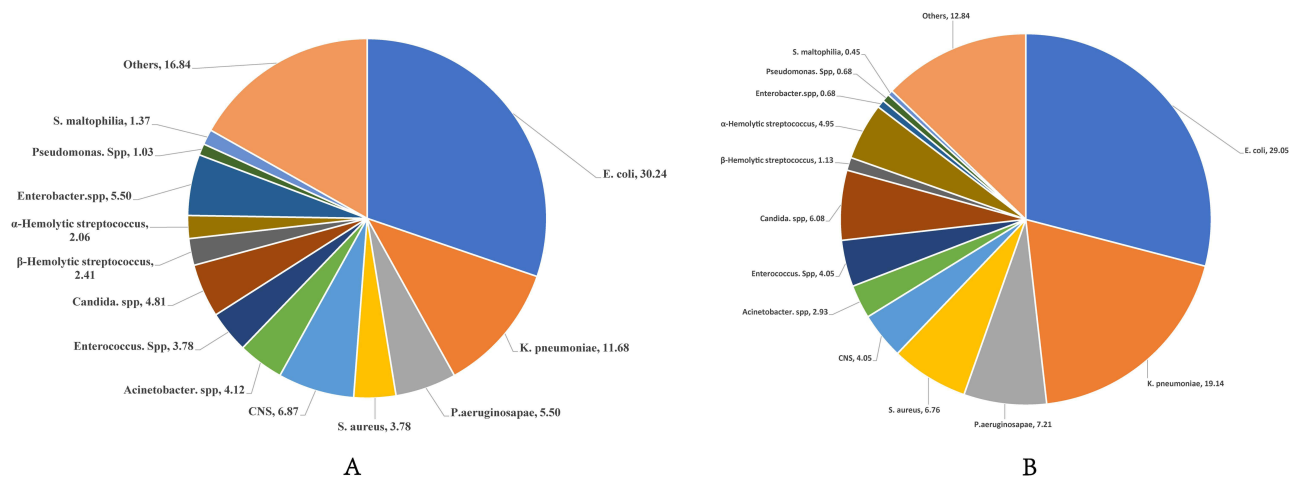
## Microbiology Procedures and Results

The median turnaround times for bacterial isolates from blood bottles loaded were 24, 46 and 71 hours for gram stains, organism identification and antimicrobial susceptibility testing (AST), respectively. Compared with the pre-implementation period, all these indicators in the post-implementation period were improved significantly (all  $p < 0.05$ ) (Table 3). The post-implementation period had a slightly shorter AST turnaround time compared with the pre-implementation period ( $p = 0.005$ ).

There was no significant difference of the average positivity rates between the pre-implementation and post-implementation periods (Figure 2). *Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, and *Staphylococcus aureus* were the main pathogenic bacteria of BSI in this study, accounting for 29.52%, 16.19%, 6.53%, and 5.58% of the total isolated pathogenic bacteria, respectively. Pathogen distribution was the same between the two time periods (Figure 3). Coagulase-negative staphylococci (CNS) fell from the top three common pathogens during the pre-implementation period to the fifth most common pathogen during the post-implementation period (6.87% to 4.28%, respectively). The isolation rate of CNS was also different between departments, and was highest in internal medicine department (more than 3%) in particular during the pre-implementation period (4.52%) (Supplementary Table 2). After education, the isolation rate of CNS in the medical department decreased to 1.96%.



**Figure 2** Blood culture positive rates among different bottles per order of blood culture.



**Figure 3** Composition of pathogens in pre-implementation and post-implementation periods. **(A)** Construction of pathogens in pre-implementation period. **(B)** Construction of pathogens in post-implementation period.

## Discussion

To our knowledge, this is the first multisite study that utilized continuous monitoring and tracking of BC quality improvement, describes the impact of educational strategies on medical staff and demonstrates improvement in blood culture quality in China. Through this medical staff educational program, we found that the education for clinicians and nurses can effectively improve the volume of BCs, including the sets and the volume of blood collection, which is the most important variable to determine BC positivity.<sup>21</sup> Furthermore, the educational program including professional presentations, morning meetings, academic salons, seminars, posters and procedural feedback is easily implemented in most institutions.

The results of the present work showed that overall blood culture delivery speed and the proportion of patients who had two sets of blood cultures (2 bottles per set) drawn increased after education. However, some patients still only had a single BC bottle collected. Previous studies have shown that the positivity rate of one set of BCs is 73.1%, two sets of BCs is 89.7% and three sets of BCs reaches 98.3%.<sup>22</sup> The positivity rate of BCs increased from 10.44% to 11.97% following education, which was similar to the 8.3–13.0% positivity reported in foreign countries.<sup>23</sup>

The accuracy and quality of blood culture specimen collection directly affects its accuracy, impacting clinical diagnosis and patient treatment. According to the M47 guidelines by the Clinical and Laboratory Standards Institute (CLSI), increasing the sample blood volume and selecting the right collection site are key to improving BC positivity and avoiding contamination. The guidelines recommend that 20 mL of blood per BC set should be collected from different veins at the same time.<sup>12</sup> In our survey, nurses were the main executors of the medical order for BCs. In clinical practice, nurses often collect BC specimens from a single unilateral vein, predisposing to contamination and reduced positivity rates.<sup>24</sup> Education therefore focused on the timely execution of medical instructions, skin disinfection with appropriate disinfectants and bilateral venous specimen collection. Our survey found that nurses carried out blood culture orders earlier after education. There was no difference in the rate of blood samples collected from unilateral veins, which may partly explain why the culture positivity rate did not significantly increase despite increased blood volume. However, recent evidence suggesting benefit of one site vs multi-site sampling techniques.<sup>25</sup> Further and more experiments are needed to confirm this. It has been reported that if a set of BCs contains 1 mL less blood volume, the sensitivity of those cultures decreases by 3%.<sup>26</sup> Ingen et al also found that increasing the volume of blood in BC bottles increased the culture positivity rate.<sup>27</sup> The mean blood volume per bottle increased from 8 mL to 9 mL after education. Although there was no significant difference in BC positivity between the two periods, there was an absolute increase in this value (10.44% to 11.97%). Compared with the emergency department, it is interesting to note that the infectious disease ward had more BC bottles per order of patients during the two periods. This may be due to infectious disease physicians are trained to take responsibility for treating infectious diseases in China.



After the collection of blood cultures, blood bottles should be sent to the microbiology laboratory and loaded into the analysis device within 2 hours.<sup>12</sup> Delayed loading may reduce the detection rate or prolong the detection time, introducing the potential risk of a missed detection.<sup>28</sup> The reasons for the sample delay include increased specimen transport time due to a shortage of nurses, the need for further specimen registration after specimen collection or limited laboratory operating time on weekends.<sup>29</sup> Prior studies have shown that although there is no significant change in the rate of culture positivity in delayed samples, the positivity rate of specific pathogens will decrease.<sup>14</sup> In this study, the average time required to perform the doctor's BC order was very satisfactory (within 40 minutes) independently of the duty period. The original guidelines recommended BCs if a patient develops fever or chills. Recent work suggests that blood should be obtained as soon as possible. As most clinical microbiology labs are closed overnight, other on-duty lab staff were also trained to load bottles, which may explain improvements in the loading delay during the post-implementation period. However, compared with the guidelines,<sup>12</sup> BC transportation times still need to be further improved.<sup>30</sup>

As the most reliable method for diagnosing BSIs, blood cultures provide a reliable basis for clinical treatment and can significantly reduce mortality from BSIs. Kumar et al found that each 1-hour delay in antibiotic administration was associated with a 7.6% reduction in BSI survival.<sup>31</sup> Most microbiology laboratories report blood culture results as "critical values". In this study, the laboratory process was optimized to accelerate the reporting time of positive blood culture gram stains, organism identifications and AST by 2–3 hours. Tabak et al studied BCs in the clinical microbiology rooms of 13 hospitals in the United States and found that gram stains, organism identification and AST were reported within 24, 48 and 72 hours of bottle loading.<sup>32</sup> This result is similar to what was found in the post-implementation period of this study. We found that the average turnaround times differed between different hospitals (data not shown). Hospitals that used MALDI-TOF MS had slightly shorter organism ID times than those that did not (data not shown). However, improved turn-around-time could also be achieved by modifying the workflow practices using existing laboratory technologies.<sup>32</sup>

*E. coli*, *K. pneumoniae*, *Pseudomonas aeruginosa*, *Staphylococcus aureus* and CNS were the main pathogenic bacteria identified in patients with BSIs in this study, which was similar to what was noted by a national surveillance report on bacterial resistance to BSIs.<sup>33</sup> CNS, determined as pathogen, dropped from third to fifth place after education. As mentioned above, CNS is the most common bacterial contaminant in BCs, accounting for 93.33% of all bacterial contaminants in this study, and is primarily the result of substandard skin disinfection. Specialized skin disinfection training for blood collection nurses, including disinfectant use and disinfection time, may be one of the main reasons for reduced CNS detection after education.

There are some limitations to this work. First, one of the major limitations of this study is a short follow up period of 8 weeks and the majority of hospitals in this study were tertiary hospitals. Compared with secondary hospitals in China, medical staff at tertiary hospitals have better BC knowledge, which may explain why some of our indicators did not significantly improve. Second, another limitation is lack of facility specific data on the outcomes, such as length of stay, duration of antibiotic therapy, appropriateness of antibiotic therapy, mortality. Combining all the data and increasing the sample size would make it easier to demonstrate statistical significance, but this may not necessarily correlate with clinical significance. Furthermore, we have to acknowledge that the effectiveness of the interventions could have been different among the participating hospitals and some facilities may have had significant improvement while others had no improvement after the interventions. Third, we have not designed training materials for specific departments, which may lead to reduced training effects in specific wards. Fourth, we labeled bacteria as contaminants based on the number of positive bottles rather than the patient's medical history. Such judgments are crude and may lead to undercounting the actual infection rate.

## Conclusion

This was the first study that sought to improve BCs by emphasizing the importance of pre-analysis to be led by clinical microbiologists in China. By comparing BC indicators before and after educational intervention, such as professional presentations, morning meetings, academic salons, we found that medical staff education can improve BC quality by reducing order delay and routing delay and increasing the amount of blood drawn and the number of BC bottles used. We hope to preserve BC hospital policy in the future by carrying out regular educational activities, publicizing the contamination rates of different departments and optimizing bottle delivery time.

## Data Sharing Statement

The datasets used and/or analysed during the current study available from the corresponding author on reasonable request.

## Ethics Approval and Consent to Participate

There was no additional collection of blood samples nor data other than what is usually collected in the clinical routine. Only laboratory data was used, and no information from patient records was collected. Data on gender and age was anonymized in the data file and analyzed only at group level. This project was registered in the “Chinese Clinical Trial Registry” (Registration Number: ChiCTR2000034404). The study protocols were approved by the Ethical Committee of The First Affiliated Hospital, Zhejiang University School of Medicine (2022-106). All methods were carried out in accordance with relevant guidelines and regulations. This study complies with the Declaration of Helsinki.

## Funding

This study was supported by Key Research and Development Program of Zhejiang province (2021C03068) and National Nature Science Foundation of China (No. 81971984).

## Disclosure

The authors have no relevant financial or non-financial interests to disclose for this work.

## References

- Rudd KE, Johnson SC, Agesa KM, et al. Global, regional, and national sepsis incidence and mortality, 1990–2017: analysis for the global burden of disease study. *Lancet*. 2020;395(10219):200–211. doi:10.1016/S0140-6736(19)32989-7
- Timsit JF, Ruppé E, Barbier F, Tabah A, Bassetti M. Bloodstream infections in critically ill patients: an expert statement. *Intensive Care Med*. 2020;46(2):266–284. doi:10.1007/s00134-020-05950-6
- Kumar A, Roberts D, Wood KE, et al. Duration of hypotension before initiation of effective antimicrobial therapy is the critical determinant of survival in human septic shock. *Crit Care Med*. 2006;34(6):1589–1596. doi:10.1097/01.CCM.0000217961.75225.E9
- Pliakos EE, Andreatos N, Shehadeh F, Ziakas PD, Mylonakis E. The cost-effectiveness of rapid diagnostic testing for the diagnosis of bloodstream infections with or without antimicrobial stewardship. *Clin Microbiol Rev*. 2018;31(3). doi:10.1128/CMR.00095-17
- Evans L, Rhodes A, Alhazzani W, et al. Surviving sepsis campaign: international guidelines for management of sepsis and septic shock 2021. *Crit Care Med*. 2021;49(11):e1063–e1143. doi:10.1097/CCM.0000000000005337
- Dubourg G, Lamy B, Ruimy R. Rapid phenotypic methods to improve the diagnosis of bacterial bloodstream infections: meeting the challenge to reduce the time to result. *Clin Microbiol Infect*. 2018;24(9):935–943. doi:10.1016/j.cmi.2018.03.031
- Lamy B, Ferroni A, Henning C, Cattoen C, Laudat P. How to: accreditation of blood cultures’ proceedings. A clinical microbiology approach for adding value to patient care. *Clin Microbiol Infect*. 2018;24(9):956–963. doi:10.1016/j.cmi.2018.01.011
- Cockerill FR 3rd, Wilson JW, Vetter EA, et al. Optimal testing parameters for blood cultures. *Clin Infect Dis*. 2004;38(12):1724–1730. doi:10.1086/421087
- McElvania SK. *Manual of Clinical Microbiology*. 12th ed. Washington, DC: ASM Press; 2019.
- Lamy B, Dargère S, Arendrup MC, Parienti JJ, Tattevin P. How to optimize the use of blood cultures for the diagnosis of bloodstream infections? A state-of-the-art. *Front Microbiol*. 2016;7:697. doi:10.3389/fmicb.2016.00697
- Dargère S, Cormier H, Verdon R. Contaminants in blood cultures: importance, implications, interpretation and prevention. *Clin Microbiol Infect*. 2018;24(9):964–969. doi:10.1016/j.cmi.2018.03.030
- Institute CaLS. Principles and procedures for blood cultures: approved guidelines. In: *CLSI Document M47-A*. Wayne, PA: Clinical and Laboratory Standards Institute; 2007.
- Tajima T, Asai Y, Endo M, et al. Rate of blood culture submissions in Japan as an indicator of bloodstream infections. *J Infect Chemother*. 2021;27(8):1270–1272. doi:10.1016/j.jiac.2021.04.019
- Adamik M, Hutchins A, Mangilit J, Katzin B, Totty H, Deol P. Effect of delayed entry on performance of the BACT/ALERT FAN PLUS bottles in the BACT/ALERT VIRTUO blood culture system. *Eur J Clin Microbiol Infect Dis*. 2021;40(4):699–705. doi:10.1007/s10096-020-04042-z
- Dien Bard J, Chang TP, Yee R, et al. The addition of anaerobic blood cultures for pediatric patients with concerns for bloodstream infections: prevalence and time to positive cultures. *J Clin Microbiol*. 2020;58(9). doi:10.1128/JCM.01844-19
- Willems E, Smismans A, Cartuyvels R, et al. The preanalytical optimization of blood cultures: a review and the clinical importance of benchmarking in 5 Belgian hospitals. *Diagn Microbiol Infect Dis*. 2012;73(1):1–8. doi:10.1016/j.diagmicrobio.2012.01.009
- McLeod CG. Reducing blood culture contamination in the emergency department. *J Nurs Care Qual*. 2020;35(3):245–251. doi:10.1097/NCQ.0000000000000441
- Steiner K, Baron-Stefaniak J, Hirschl AM, Barousch W, Willinger B, Baron DM. Education of medical personnel optimizes filling volume of blood culture bottles without negatively affecting microbiology testing. *BMC Health Serv Res*. 2020;20(1):1105. doi:10.1186/s12913-020-05959-z
- Haiyan Cao YL. Investigation of blood culture specimen inspection situation in a general hospital. *Int J Lab Med*. 2012;33(17):2.
- Wang HE, Jones AR, Donnelly JP. Revised national estimates of emergency department visits for sepsis in the United States. *Crit Care Med*. 2017;45(9):1443–1449. doi:10.1097/CCM.00000000000002538

21. Miller JM, Binnicker MJ, Campbell S, et al. A guide to utilization of the microbiology laboratory for diagnosis of infectious diseases: 2018 update by the Infectious Diseases Society of America and the American Society for microbiology. *Clin Infect Dis*. 2018;67(6):e1–e94. doi:10.1093/cid/ciy381
22. Lee A, Mirrett S, Reller LB, Weinstein MP. Detection of bloodstream infections in adults: how many blood cultures are needed? *J Clin Microbiol*. 2007;45(11):3546–3548. doi:10.1128/JCM.01555-07
23. Ehrenstein BP, Ehrenstein V, Henke C, et al. Risk factors for negative blood cultures in adult medical inpatients--a retrospective analysis. *BMC Infect Dis*. 2008;8:148. doi:10.1186/1471-2334-8-148
24. Alahmadi YM, McElnay JC, Kearney MP, et al. Tackling the problem of blood culture contamination in the intensive care unit using an educational intervention. *Epidemiol Infect*. 2015;143(9):1964–1971. doi:10.1017/S0950268814003008
25. Ekwall-Larson A, Yu D, Dinnézt P, Nordqvist H, Özenci V. Single-site sampling versus multisite sampling for blood cultures: a retrospective clinical study. *J Clin Microbiol*. 2022;60(2):e0193521. doi:10.1128/JCM.01935-21
26. Mermel LA, Maki DG. Detection of bacteremia in adults: consequences of culturing an inadequate volume of blood. *Ann Intern Med*. 1993;119(4):270–272. doi:10.7326/0003-4819-119-4-199308150-00003
27. van Ingen J, Hilt N, Bosboom R. Education of phlebotomy teams improves blood volume in blood culture bottles. *J Clin Microbiol*. 2013;51(3):1020–1021.
28. Saito T, Iinuma Y, Takakura S, et al. Delayed insertion of blood culture bottles into automated continuously monitoring blood culture systems increases the time from blood sample collection to the detection of microorganisms in bacteremic patients. *J Infect Chemother*. 2009;15(1):49–53. doi:10.1007/s10156-008-0664-6
29. Venturelli C, Righi E, Borsari L, et al. Impact of pre-analytical time on the recovery of pathogens from blood cultures: results from a large retrospective survey. *PLoS One*. 2017;12(1):e0169466. doi:10.1371/journal.pone.0169466
30. Elvy J, Walker D, Haremza E, Ryan K, Morris AJ. Blood culture quality assurance: what Australasian laboratories are measuring and opportunities for improvement. *Pathology*. 2021;53(4):520–529. doi:10.1016/j.pathol.2020.09.020
31. Rivers E, Nguyen B, Havstad S, et al. Early goal-directed therapy in the treatment of severe sepsis and septic shock. *N Engl J Med*. 2001;345(19):1368–1377. doi:10.1056/NEJMoa010307
32. Tabak YP, Vankeepuram L, Ye G, Jeffers K, Gupta V, Murray PR. Blood culture turnaround time in U.S. acute care hospitals and implications for laboratory process optimization. *J Clin Microbiol*. 2018;56(12). doi:10.1128/JCM.00500-18
33. Chen Y, Ji J, Ying C, et al. Blood bacterial resistant investigation collaborative system (BRICS) report: a national surveillance in China from 2014 to 2019. *Antimicrob Resist Infect Control*. 2022;11(1):17. doi:10.1186/s13756-022-01055-5

## Infection and Drug Resistance

Dovepress

### Publish your work in this journal

Infection and Drug Resistance is an international, peer-reviewed open-access journal that focuses on the optimal treatment of infection (bacterial, fungal and viral) and the development and institution of preventive strategies to minimize the development and spread of resistance. The journal is specifically concerned with the epidemiology of antibiotic resistance and the mechanisms of resistance development and diffusion in both hospitals and the community. The manuscript management system is completely online and includes a very quick and fair peer-review system, which is all easy to use. Visit <http://www.dovepress.com/testimonials.php> to read real quotes from published authors.

Submit your manuscript here: <https://www.dovepress.com/infection-and-drug-resistance-journal>