The University of the Witwatersrand

Faculty of Health Sciences

Optimising Blood Culture Collection Techniques to Minimise Contamination Rates in a Busy Public Sector Paediatric Department in South Africa: A Quality Improvement Project

By

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A Research Report submitted to the Faculty of Health Sciences,
University of the Witwatersrand, Johannesburg,
in partial fulfillment of the requirements for the degree of
Masters of Medicine in Paediatrics

May 2025

Declaration

I Lucy Nicola Wilson declare that this Research Report is my own, unaided work. It is being submitted for the Degree of Masters of Medicine in Paediatrics at the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at any other University.

(Signature of the candidate)

4th day of June 2025 in Johannesburg

Dedication

This work is dedicated to every child and their families who come through the doors of Chris Hani Baragwanath Academic Hospital. Your resilience inspires us to strive for clinical excellence and uphold the highest standards of care. May these findings contribute to better practices and brighter futures for all.

Presentations and Publications

The findings of this study were presented at the University of the Witwatersrand Paediatric Research Day on 7 December 2023. The presentation "Optimising Blood Culture Collection Techniques to Minimize Contamination Rates in a Public Sector Paediatric Department" was awarded a prize for best research project by a paediatric registrar at the Research Day.

Abstract

Background

Blood culture (BC) is the gold standard in diagnosing sepsis in hospitalised children. A limitation of BC is contamination with skin commensals, which gives rise to false positive results and may impact on health care expenses related to laboratory costs and increased hospital length of stay. We undertook a Quality Improvement Project (QIP) to evaluate BC contamination rates, laboratory costs and length of hospital stay in children admitted in the general paediatric wards at Chris Hani Baragwanath Hospital in Soweto, South Africa.

Methods

The QIP was implemented in three successive time periods each lasting two months (01 December 2022 to 31 May 2023). The study population included all children aged 0-14 years from whom a BC was collected as part of routine clinical care on the day of admission. Period 1 was a pre-intervention period. During Period 2 (intervention), a Standard Operating Procedure (SOP) was implemented and admitting clinicians were taught how to adhere to the SOP. During unobserved BCs in Period 2, clinicians were expected to obtain BCs according to the SOP. All BCs obtained during Period 3 (post-intervention) were unobserved. Contamination rates, length of hospital stay and laboratory costs were compared between study periods.

Results

During Period 1 the contamination rate was 9.0% (66 of 732 BCs), compared to 5.5% (54 of 974 BCs) during Period 2; P=0.007. In Period 2, observed BCs (n=250) had a lower contamination rate compared to unobserved BCs (n=720) (3.9% versus 6.1%; P=0.253). In Period 3 BC contamination rebounded to 9.7% (71 of 732 BCs). In Period 1, the average cost of BC processing was R483.20 (IQR R483.20-R649.16), compared to R361.16 (IQR R361.16-R361.16) in Period 2 ($p < 0.001$). Cost increased to R480.56 (IQR R480.56-R480.56) in

Period 3. Children with contaminated BCs had longer hospital stay (median 5.0 (IQR 3.0 to 8.0) days) compared to those with negative BCs (4.0 (IQR 3.0 to 6.0) days; $P < 0.001$).

Conclusions

Implementation of a SOP significantly decreased the BC contamination rate. However, without reinforcement of correct technique, lower contamination rates were not sustained. Patients with negative BCs had reduced hospital length of stay and laboratory costs compared to those with contaminated cultures, which demonstrates the economic burden of contaminated BCs.

Acknowledgements

I would like to express my deepest gratitude to my supervisors for their invaluable support and guidance throughout this study. My main supervisor, Professor David Moore, played a crucial role in helping me formulate the protocol and finalise this dissertation. His expertise in statistics and his encouragement, dedication, and investment in the study were instrumental to its success. I am also appreciative of my co-supervisor, Dr Jeanette Wadula from the NHLS, for her insightful guidance and support during this process.

I would like to thank Professor Velaphi, whose assistance with ethics and methodology was critical to this project. His leadership in enabling the departmental-wide implementation of the standard operating procedure (SOP) for blood culture collection that was used in this study, ensured the success of this project.

This study would not have been possible without the dedicated efforts of the clinicians - interns, registrars, medical officers, and consultants — who played a major role in the implementation of the SOP. Their commitment to improving the quality of blood culture collection was truly inspiring and integral to the progress we achieved.

On a personal note, I would like to extend my heartfelt thanks to my family for their unwavering support. In particular, my husband, Paul, has always stood by me and encouraged me in all my endeavours. His belief in me has been a constant source of strength throughout this journey.

To all who contributed to this work, directly or indirectly, I am deeply grateful.

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Nomenclature

AMR	antimicrobial resistance
BC	blood culture
CAP	community-acquired pneumonia
CDC	Centers for Disease Control and Prevention
CHBAH	Chris Hani Baragwanath Academic Hospital
CLSI	Clinical and Laboratory Standards Institute
CNS	coagulase negative staphylococcus
CO_2	carbon dioxide
IEIP	International Emerging Infections Program
HREC	Human Research Ethics Committee
LED	light-emitting diode
MAC	Medical Advisory Committee
NHLS	National Health Laboratory Service
PERCH	Pneumonia Etiology Research for Child Health
SOP	standard operating procedure
UTI	urinary tract infection

1 LITERATURE REVIEW

1.1 Introduction

Although blood culture (BC) has low yield of bacterial pathogens in children hospitalised with meningitis, pneumonia, septicaemia, urinary tract infections and other infections, it is widely used to inform empiric antibiotic choice [1]. Pathogenic bacteria or fungi isolated from BC are tested for their antimicrobial susceptibility patterns, thus adding to the evidence on changes in antimicrobial resistance (AMR) patterns over time, as well as changes in the prevalence of certain organisms in response to interventions which have been adopted to prevent infection, such as vaccination [2,3]. A major challenge of BC is their low sensitivity, coupled with the fact that a positive BC does not always represent detection of the causative infecting agent. Skin commensals commonly contaminate BC obtained from children hospitalised with presumed severe bacterial or fungal infection, giving rise to false positive BC results.

Not only are contaminated BC troublesome because they obscure the true underlying cause of infection in children with severe presumed bacterial or fungal infection, but they also contribute to wastage of funds allocated to healthcare. BC specimens that flag positive are channelled down standard workflow pathways in the laboratory, in which additional costs are incurred in the process of identifying the organism that was cultured in the specimen. High rates of BC contamination thus incur unnecessary expenditure.

1.2 Laboratory processing of blood cultures

Chris Hani Baragwanath Academic Hospital (CHBAH), the site for this study, uses the BacT/ALERT system for BC testing. BacT/ALERT is an automated colorimetric microbial detection system. Each BC bottle contains culture media and an internal sensor which indicates the presence of microbes by detection of carbon dioxide (CO_2). Once blood has been inoculated into the BC bottle, it should be promptly transported to the laboratory and loaded into the instrument, where it is incubated for up to five days or until the specimen flags positive. If a micro-organism is present, it metabolises substrate in the culture medium and

produces CO_2, which then changes the sensor at the bottom of the bottle from dark to light in colour, increasing the amount of reflected light-emitting diode (LED) in the system [4]. The sensor is gas-permeable and is separated from the broth medium by a semi-permeable membrane. Once the sensor changes colour, the specimen is designated positive. Once the bottle has flagged positive, it should be removed from the system for Gram-stain and subculture [4].

Despite its limitations, BC remains the gold standard in the diagnosis of sepsis. In a cross-sectional study performed over 5 years with 7,509 children admitted with community acquired pneumonia (CAP), only 2.5% of children who had BCs performed on admission had a positive result [5]. Urinary tract infections (UTIs) also have a low BC positivity rate, where in one retrospective cohort study, only 5.6% of patients with febrile illness in the setting of a UTI had a true bacteraemia (after excluding false positives due to contaminated specimens) [6]. The BC contamination rate in that study was 3.8%. Meningitis tends to have a higher BC positivity rate. In a retrospective study of 128 children with proven meningitis, BCs were positive in 78% in the group that had not received pre-treatment antibiotics [7].

Various factors can negatively influence the sensitivity of blood cultures, the most important being inadequate volume of blood in the blood culture bottle, and contamination of the sample with skin commensals. Inadequate volume of blood inoculated into the blood culture bottle can result in a false negative blood culture. The ideal volume of blood in the paediatric clinical practice has not yet been well established and varies between 1 and 5 mL, depending on the patient's age. During the neonatal period, 1 to 2 mL of blood is usually sufficient to allow positivity [8]. In a study of almost 20,000 children in rural Kenya, the BC yield in children of at least 60 days old increased with each mL of blood used as a sample, with a positivity rate of 5.6% at 1 mL, 6.8% at 2mL and 7.9% at 3mL of blood used [9].

Pre-treatment with antibiotics (prior to BC collection) significantly reduces the microbial detection rate. In the Pneumonia Etiology Research for Child Health (PERCH) study, a multi-country case-control study which determined the aetiology and risk factors for severe

pneumonia in children under-5 years of age in sub-Saharan Africa and South-east Asia, pre-treatment with antibiotics reduced the BC positivity rate by 40% [10].

Blood culture contamination, resulting in a false positive blood culture, is another important factor in determining the significance of a blood culture result. Commonly occurring BC contaminants, representing the normal skin flora, include coagulase negative staphylococcus (CNS), Micrococcus spp, Bacillus spp, Corynebacterium spp and Cutibacterium spp (previously known as Pripionobacterium spp) [8].

1.3 The problem of bacterial contamination of blood cultures

Contamination of BCs by skin commensals occurs due to inadequate disinfection of the skin and poor technique utilized by the person obtaining the specimen for culture [11]. Another important cause of contamination is collection of the blood sample through an existing indwelling venous or arterial catheter [11]. The broth medium in the BC bottle can also have an impact on contamination rates, where those that contain antibiotic binding resins give rise to an increased yield of causative pathogens and contaminants [11].

There are clinical and laboratory consequences of having a high BC contamination rate, which incur an economic impact and increased cost per contaminated BC. Contaminated BCs are difficult for a clinician to interpret, and could result in additional tests being ordered, e.g. additional BCs, laboratory tests to assess infective markers, and echocardiography to exclude subacute bacterial endocarditis, in order to assist in determining the significance of the result. This leads to an increase in length of hospital stay and an increase in risk of the patient acquiring a nosocomial infection, increased clinician workloads, and additional healthcare expenditure. Unnecessary antibiotics may be ordered, some of which require close monitoring of drug levels (such as amikacin and vancomycin), further increasing laboratory costs [12]. A retrospective study of 142 BC contaminants showed an increase in hospital length of stay of 5.4 days in patients who had contaminated BCs compared to the control group (which were deemed as true negative results) [13]. A systematic review assessed six studies which

showed a hospital length of stay of 1 to 22 days in patients with contaminated cultures (false positive), compared to 1 to 17 days in patients with negative BCs and substantially higher pharmacy and laboratory costs in those with BC contamination [12].

1.4 Strategies to limit blood cultures contamination rates

The Clinical and Laboratory Standards Institute (CLSI) targets an ideal BC contamination rate of no more than 3% [14]. In various settings, standard operating procedures (SOPs) have been implemented in order to guide the collection of BC specimens, so as to minimise contamination. An adaptation of one such SOP, which has been successfully implemented in national laboratory surveillance studies of pneumococcus in Thailand [15], was used in this study.

The method of skin anti-sepsis is the single most important factor in limiting BC contamination rates. The most commonly used antiseptics are iodine tincture, 10% povidone iodine aqueous solution and 2% chlorhexidine gluconate/70% isopropyl alcohol. There is no clear evidence in the difference between chlorhexidine and iodine based solutions, but the efficacy of both solutions is enhanced with the addition of alcohol in skin antisepsis [16]. A back and forth motion is more effective in disinfecting the skin compared to a concentric motion, because the technique of the back and forth motion is more likely to be applied with friction to disinfect the first five dermal layers of the skin, and is more likely to use the same pathway around the site of venepuncture [16]. Adequate drying time, which varies according to the reagent used for skin decontamination, is required prior to venepuncture. It is essential that the clinician does not re-palpate the area to be venepunctured after it has been disinfected [13]. The use of sterile gloves compared to non-sterile gloves showed a significant reduction in BC contamination rates from 4.3% to 1.7% in one study of over 10,000 BCs [13]. In addition to disinfection of the skin, the rubber top of the culture bottle (not sterile) should also be disinfected with a 70% alcohol wipe or solution prior to inoculation with blood [16].

1.4.1 The Thailand SOP

The Thailand Ministry of Public Health (MOPH), together with the U.S. Centers for Disease Control and Prevention (CDC) has undergone a pneumonia surveillance network in 20 hospitals within Thailand. This is supported by the International Emerging Infections Program (IEIP). This collaboration has formulated SOPs to ensure quality control and assurance in all stages of the project [15]. Children in the intervention arm in this study underwent BC collections using this SOP.

The BC supply kit for children consists of:

1. Specimen collection form
2. 1 sterile 10 mL syringe
3. 1 sterile 23-gauge wing (butterfly) set
4. 1 sterile 24-gauge wing (butterfly set)
5. 70% isopropyl alcohol packaged swabs $\times 3$
6. 2% tincture of iodine swab stick $\times 1$
7. Adhesive bandage
8. BacT/Alert®PF (bioMérieux, Marcy l'Etoile, France) BC bottle (yellow lid) $\times 1$

The BC collection occurs as follows:

1. Gather the required equipment – BC supply kit, tourniquet, non-sterile gloves and sterile cotton balls;
2. Explanation of the procedure to the child (as appropriate) and the caregiver;
3. Wash off any visible dirt at the chosen collection site with soap and water;
4. Select the blood collection site, usually an arm, and apply a tourniquet. Use the most visible or prominent vein on the hand, forearm, or cubital fossa;
5. Skin disinfection:
    a. Scrub the collection site with a 70% alcohol wipe for 30 seconds;
    b. Apply the iodine swab to an area 5 centimetres in diameter around the venepuncture site. Allow one minute of drying time;

c. If the area is re-palpated, re-disinfection needs to be repeated;

d. In patients with iodine sensitivity, use 70% alcohol instead of iodine.

6. Remove the flip-top cover off the BC bottle and disinfect the top of the BC bottle with a 70% alcohol wipe;
7. Wipe gloves with 70% alcohol;
8. Insert the needle with the bevel facing upwards into the vein, and withdraw the required amount of blood;
9. Release the tourniquet and remove the needle;
10. Place a sterile cotton ball over the puncture site. The cotton ball should be held firmly in place until bleeding stops;
11. The blood sample should be immediately injected in the BC bottle, without changing needles;
12. Wipe the top of the BC bottle once more with a 70% alcohol wipe;
13. Dispose needles safely into a sharps bin.

1.5 Justification for this study

The BC contamination rates in the general paediatric wards at CHBAH, a busy secondary/tertiary level public sector hospital in Soweto, South Africa, exceed 20% [personal communication, Prof Moore], which is far above the recommended rate of 3%. These high contamination rates incur unnecessary expenditure to the hospital and compromise patient care through obscuring or inhibiting the growth of the bacterial and fungal pathogens which may be causative of the infection episode. In this quality improvement project, we evaluated the impact of the Thailand BC SOP on BC contamination rates and laboratory expenditure in the general paediatric wards at CHBAH. Currently, there is no SOP in place for the collection of BC in the general paediatric wards at CHBAH, and very little training to the junior staff (medical students and intern doctors), who are usually responsible for the collection of all laboratory specimens, in how to collect these specimens. There is also a

high turnover of staff in this area, due to the nature of rotations at teaching hospitals such as CHBAH in South Africa.

At the time of writing, the cost of processing a BC at the NHLS is R 120.82 for a negative BC, compared to R 351.77 for a positive blood culture with one organism identified. The cost of the positive culture includes Gram staining, bacterial identification and antibiotic susceptibility testing per organism. A positive BC therefore will cost three times more than a negative BC. The cost will be higher if two organisms are isolated from the specimen, which can be the case especially in contaminated cultures [personal communication with Dr Wadula].

1.6 Aim and objectives

The aim of the study was to compare BC contamination rates, hospitalisation duration and laboratory expenditure in children hospitalised in the general paediatric wards at CHBAH in a pre-intervention, intervention, and post-intervention period of a Quality Improvement Project.

The aims of the study were to:

1. Compare BC contamination rates in children hospitalised from 01 December 2022 to 31 January 2023 (pre-intervention cohort), to contamination rates in children hospitalised from 1 February to 31 March 2023 (intervention cohort), and a post-intervention cohort (01 April to 31 May 2023). The intervention cohort BCs were collected during ongoing on-site reinforcement of correct BC specimen collection using the Thailand SOP as a Departmental wide effort to optimise clinical practice as standard of care in the collection of paediatric BC specimens.
2. Compare the laboratory costs processing BCs collected in the pre-, during- and post-intervention phases of the Quality Improvement Project.
3. Compare the hospitalisation costs (length of stay) of children in the pre-intervention, intervention and post-intervention cohorts.

4. To compare the contamination rates, laboratory costs and hospitalisation costs (length of stay) of paediatric patients hospitalised in the intervention period who had BC collections observed by the principal investigator (Dr Wilson) to contamination rates, laboratory costs and hospitalisation costs (length of stay) of paediatric patients whose BC collections were not observed directly by the principal investigator.

1.7 Hypothesis

The working hypothesis of the study was that BC contamination rates would be significantly lower in children whose specimens were collected using the Thailand SOP, compared to those whose blood cultures were collected in the period prior to implementation of the SOP. Furthermore, we hypothesised that contamination rates and costs would be significantly lower in children whose BC collections were directly observed, compared to those whose BC specimens were not directly observed by the principal investigator. We estimated that the BC contamination rates would be 5% on average in children during the intervention phase of the study, as a result of implementation of the SOP, 12-20% in the pre-intervention cohort, and 5-12% in unobserved BC collections in the intervention period. We estimated that in the post-intervention group, BC contamination rates would be 5-12%, higher than the directly observed BC specimens in the intervention group, but lower than the contamination rates in the pre-intervention group.

We also hypothesised that it would be cost-effective to adhere to the SOP-guided approach of BC collection, through reductions in the rates of contaminant cultures translating into significantly lower laboratory costs in the prospective group.

2 ARTICLE IN SUBMISSIBLE FORMAT

Abstract

Background

Blood culture (BC) is the gold standard in diagnosing sepsis in hospitalised children. A limitation of BC is contamination with skin commensals, which gives rise to false positive results and may impact on health care expenses related to laboratory costs and increased hospital length of stay. We undertook a Quality Improvement Project (QIP) to evaluate BC contamination rates, laboratory costs and length of hospital stay in children admitted in the general paediatric wards at Chris Hani Baragwanath Hospital in Soweto, South Africa.

Methods

The QIP was implemented in three successive time periods each lasting two months (01 December 2022 to 31 May 2023). The study population included all children aged 0-14 years from whom a BC was collected as part of routine clinical care on the day of admission. Period 1 was a pre-intervention period. During Period 2 (intervention), a Standard Operating Procedure (SOP) was implemented and admitting clinicians were taught how to adhere to the SOP. During unobserved BCs in Period 2, clinicians were expected to obtain BCs according to the SOP. All BCs obtained during Period 3 (post-intervention) were unobserved. Contamination rates, length of hospital stay and laboratory costs were compared between study periods.

Results

During Period 1 the contamination rate was 9.0% (66 of 732 BCs), compared to 5.5% (54 of 974 BCs) during Period 2; P=0.007. In Period 2, observed BCs (n=250) had a lower contamination rate compared to unobserved BCs (n=720) (3.9% versus 6.1%; P=0.253). In Period 3 BC contamination rebounded to 9.7% (71 of 732 BCs). In Period 1, the average cost of BC processing was R483.20 (IQR R483.20-R649.16), compared to R361.16 (IQR R361.16-

R361.16) in Period 2 ($p < 0.001$). Cost increased to R480.56 (IQR R480.56-R480.56) in Period 3. Children with contaminated BCs had longer hospital stay (median 5.0 (IQR 3.0 to 8.0) days) compared to those with negative BCs (4.0 (IQR 3.0 to 6.0) days; $P < 0.001$).

Conclusions

Implementation of a SOP significantly decreased the BC contamination rate. However, without reinforcement of correct technique, lower contamination rates were not sustained. Patients with negative BCs had reduced hospital length of stay and laboratory costs compared to those with contaminated cultures, which demonstrates the economic burden of contaminated BCs.

Introduction

Although blood culture (BC) has low yield of bacterial pathogens in children hospitalised with meningitis, pneumonia, septicaemia, urinary tract infections and other infections, it is widely used to inform empiric antibiotic choice [1]. A major challenge of BC is their low sensitivity, coupled with the fact that a positive BC does not always represent the causative infecting agent. Skin commensals commonly contaminate BC obtained from children hospitalised with presumed severe bacterial or fungal infection, giving rise to false positive BC results. Inadequate specimen volume and antimicrobial pre-treatment prior to specimen collection also impact on BC sensitivity [8–10].

Contamination of blood cultures with skin commensals occurs due to inadequate disinfection of the skin and poor technique utilized by the person obtaining the specimen, or by collection of the specimen through an existing indwelling venous or arterial catheter [11]. Clinicians treating patients from whom skin commensals have been isolated on BC specimens may submit additional BCs, laboratory tests to assess infective markers, and to request echocardiography to exclude subacute bacterial endocarditis. This leads to an increase in length of hospital stay, increases the risk of hospital-associated infection, and compounds healthcare expenditure [12,13].

The method of skin anti-sepsis is the single most important factor in limiting BC contamination rates. The most commonly used antiseptics are iodine tincture, 10% povidone iodine aqueous solution and 2% chlorhexidine gluconate/70% isopropyl alcohol. There is no clear evidence in the difference between chlorhexidine and iodine based solutions, but the efficacy of both solutions in skin antisepsis is enhanced with the addition of alcohol [16]. Adequate drying time, avoidance of re-palpation of the area to be venepunctured, and use of sterile gloves have been shown to reduce BC contamination rates [13,16].

The Clinical and Laboratory Standards Institute (CLSI) targets an ideal BC contamination rate of 3% [14]. Contamination rates in paediatric BCs may range from 6% to 75% [1]. We evaluated the impact of adoption of a standard operating procedure (SOP) on BC contamination rates, laboratory expenditure and hospital length of stay, in the general paediatric wards at a public sector hospital in South Africa.

Methods

We evaluated BC contamination rates over a six month period, from 01 December 2022 through 31 May 2023, in children aged 0 to 14 years hospitalised at the general paediatric wards at Chris Hani Baragwanath Academic Hospital (CHBAH), Johannesburg, South Africa. In Period 1 (01 December 2022 through 31 January 2023), all admission BC results were retrospectively assessed for contamination, with the following organisms considered as contaminants: Coagulase negative staphylococcus (CNS), Micrococcus spp, Bacillus spp, Corynebacterium spp and Cutibacterium spp [8]. In Period 2 (01 February through 31 March 2023), the primary investigator (LW) instructed admitting clinicians how to collect BCs according to a standardised SOP. Correct BC collection technique was evaluated against a check list. Teaching and observation of BC collections occurred from 08:00 to 18:00 during weekdays, and on weekends as required. Weekend cover by the principal investigator was resorted to if weekly quotas of observed blood cultures were lagging behind the expected number of cases needed to meet the target sample size of 250 observed cultures (see below). Admitting clinicians were requested to adhere to the SOP even when the primary investigator was not on site.

In Period 3 (01 April 2023 through 31 May 2023), sustainability of BC contamination rates was evaluated and all BC collections were unsupervised by the primary investigator. For all study Periods, patient diagnoses and date of discharge were obtained from an electronic database maintained by the CHBAH Department of Paediatrics and Child Health.

Costings provided by the NHLS were used to assign the cost of laboratory processing of blood cultures. For the analysis of blood culture expenditure, a weighted cost of blood cultures was derived by dividing individual patient blood culture costs by the total number of children that underwent blood culture collections in each time period and multiplying by 1000. Hospitalisation costs were estimated by multiplying the length of hospitalisation (in days) by the daily cost of hospitalisation in a general paediatric ward at the facility (R 3500.00).

A sample size of 250 observed BCs was calculated to be sufficient to appreciate a difference of 7% in BC contamination rates (with the assumption of 12% BC contamination in the Period 1 BCs and 5% in BCs collected during Period 2), with 80% power at a significance level of 5%.

The study was approved by the Human Research Ethics Committee (HREC) at the University of the Witwatersrand (M220621), and the NHLS through the Academic Affairs and Research Management System (PR2222632).

Results

There were a total of 3267 admissions across the three study periods, most of which (1299, 39.8%) occurred in period 2. Blood cultures at baseline were performed in 2434 (73.5%) admissions. Blood culture contamination rates decreased significantly from 9.1% in period 1 to 5.5% in period 2 ($p = 0.007$). However, in period 3, the contamination rate rebounded to 9.7% (Table 1).

In period 2, observed cultures had a contamination rate of 3.9% (10 of 254 cultures), whereas unobserved cultures had a higher rate of contamination (6.1%, 44 of 720 cultures); however,

the difference was not statistically significant ($p = 0.253$).

The proportion of positive blood cultures that signified true bacteraemia was 4.1% in period 1 (30 of 728), 2.6% in period 2 (25 of 742), and 3.4% in period 3 (25 of 596) (Table 1). Recovery of significant isolates from blood cultures was not significantly lower in period 2 compared to period 1 or period 3 ($p = 0.098$ and $p = 0.377$, respectively).

Of the children who underwent blood culture collection, a significantly greater proportion in periods 1 and 3 had more than on blood culture submitted for processing through the course of their hospitalisation compared to those admitted in period 2 ($p < 0.001$; Table 1).

The weighted cost of processing blood cultures decreased significantly during period 2 compared to the other periods. In period 1, the average cost of processing was R483.20 (IQR R483.20-R649.16). This dropped to R361.16 (IQR 361.16-R361.16) in period 2 ($p < 0.001$). However, in period 3, the cost increased again to R480.56 (IQR R480.56-R480.56), reflecting the cost of laboratory processing of contaminated cultures, and the need for repeat cultures (Table 1).

The average length of hospital stay in period 1 was 4 days (IQR 2.00–6.00), with a median hospitalization cost per patient of R14,000.00 (IQR R7000.00–R21,000.00). In periods 2 and 3, the average length of stay decreased to 3.00 days (IQR 2.00–6.00) and the average cost declined to R10,500.00 (IQR R7000.00–R21,000.00).

Patients with negative blood cultures had a median hospital stay of 4.0 (IQR 3.0 to 6.0) days, whereas those who did not have a blood culture had a shorter stay (median 2.0 (IQR 2.0 to 4.0) days). Children with contaminated blood cultures had significantly longer hospital stay (median 5.0 (IQR 3.0 to 8.0) days) compared to those with negative blood cultured ($p < 0.001$). Patients with a significant blood culture isolate (true bacteraemia) experienced the longest stays, with a median of 7.0 (IQR 3.0 to 14.0) days.

Table 2.1: Characteristics of study cohort, stratified by time period

	Overall	Period 1	Period 2	Period 3	P-value
n	3267	941	1299	1027	
Median age (months, IQR)	7.81 [1.26, 36.01]	8.23 [1.23, 38.32]	6.38 [1.26, 29.09]	9.68 [1.33, 39.64]	0.101
Male (%)	1885 (57.8)	547 (58.1)	742 (57.2)	596 (58.1)	0.878
BC done (%)	2434 (74.5)	728 (77.4)	974 (75.0)	732 (71.3)	0.007
Specimen volume (mL, IQR)	-	-	2.00 [1.20, 2.50]	-	-
TTP (hours, IQR)	17.00 [10.70, 26.10]	18.00 [12.00, 34.50]	14.00 [7.00, 20.00]	18.80 [14.20, 30.00]	<0.001
TTP contaminated (hours, IQR)	17.75 [14.00, 22.15]	18.00 [15.00, 26.50]	16.00 [10.00, 18.00]	18.00 [15.20, 23.10]	0.001
TTP significant (hours, IQR)	11.00 [6.00, 17.00]	9.00 [5.00, 13.25]	9.00 [6.00, 15.00]	15.25 [7.72, 24.05]	0.063
Group (%)					0.009
BC negative	2108 (86.6)	615 (84.5)	876 (89.9)	617 (84.3)	
Contaminated BC	191 (7.8)	66 (9.1)	54 (5.5)	71 (9.7)	
Flag positive, culture negative	55 (2.3)	17 (2.3)	19 (2.0)	19 (2.6)	
Significant BC isolate	80 (3.3)	30 (4.1)	25 (2.6)	25 (3.4)	
BCs submitted (n, IQR)	1.00 [1.00, 1.00]	1.00 [1.00, 1.00]	1.00 [1.00, 1.00]	1.00 [1.00, 1.00]	<0.001
BCs submitted in those with >1 BC (n, IQR)	2.00 [2.00, 3.00]	2.00 [2.00, 2.25]	2.00 [2.00, 2.00]	2.00 [2.00, 3.00]	0.243
More than one BC sent (%)	211 (6.5)	92 (9.8)	55 (4.2)	64 (6.2)	<0.001
Cost of BCs (ZAR, IQR)	351.77 [351.77, 351.77]	351.77 [351.77, 472.59]	351.77 [351.77, 351.77]	351.77 [351.77, 351.77]	<0.001
Weighted cost of BC (ZAR, IQR)	361.16 [361.16, 480.56]	483.20 [483.20, 649.16]	361.16 [361.16, 361.16]	480.56 [480.56, 480.56]	<0.001
Length of stay (days, IQR)	3.00 [2.00, 6.00]	4.00 [2.00, 6.00]	3.00 [2.00, 6.00]	3.00 [2.00, 6.00]	0.449
Cost of hospital stay (ZAR, IQR)	10500.00 [7000.00, 21000.00]	14000.00 [7000.00, 21000.00]	10500.00 [7000.00, 21000.00]	10500.00 [7000.00, 21000.00]	0.449
Outcome (%)					0.320
Died	96 (2.9)	28 (3.0)	37 (2.8)	31 (3.0)	
Discharged	2607 (79.8)	742 (78.9)	1045 (80.4)	820 (79.8)	
Refused treatment	1 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	
Transferred out	30 (0.9)	4 (0.4)	11 (0.8)	15 (1.5)	
Unknown	533 (16.3)	167 (17.7)	205 (15.8)	161 (15.7)	

Note:
BC = blood culture; IQR = interquartile range; TTP = time to positivity; ZAR = South African Rand. Period 1 = 01 December 2022 to 31 January 2023; Period 2 = 01 February to 31 March 2023; Period 3 = 01 April to 31 May 2023. P-values for comparison between time periods.

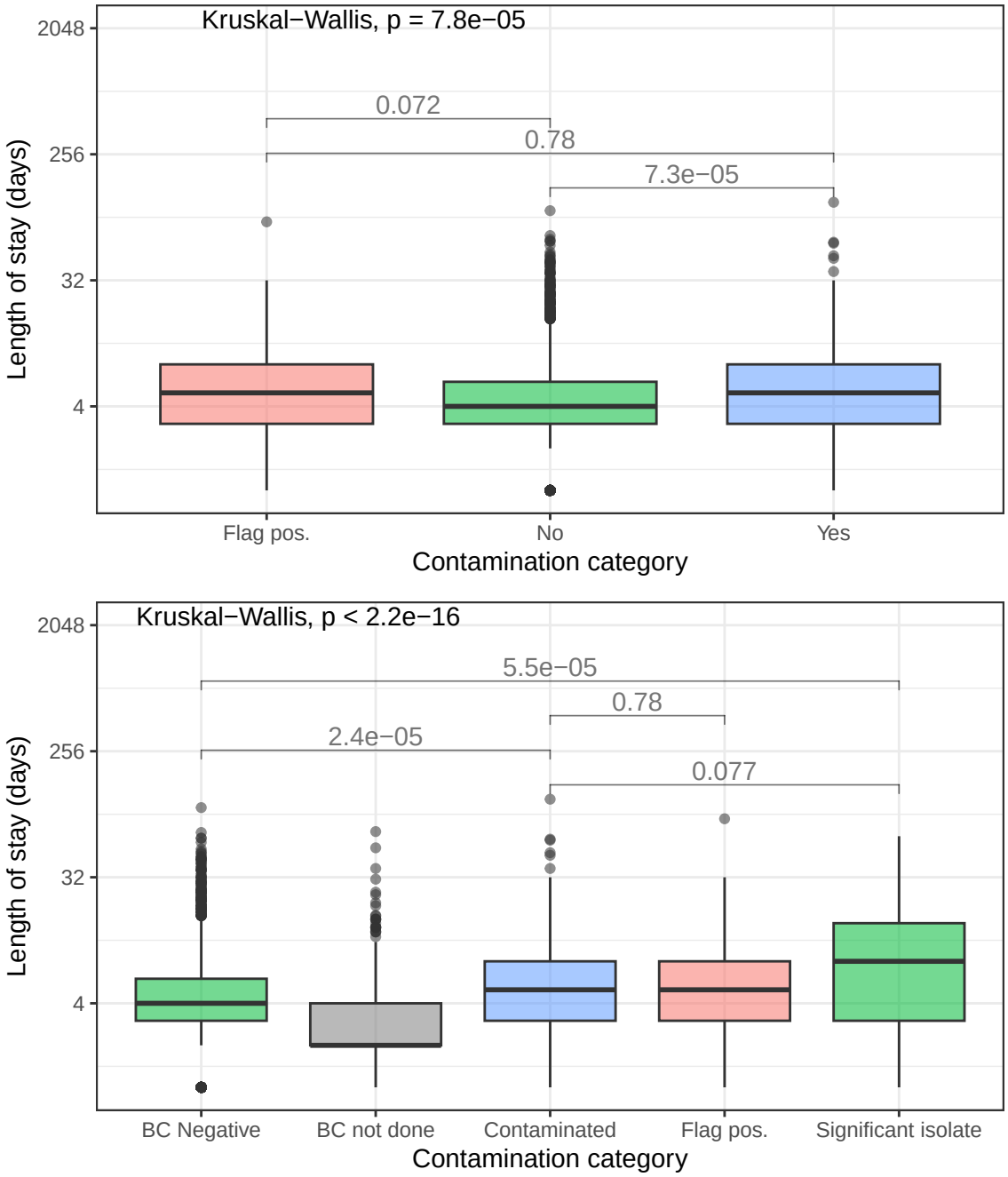

Figure 2.1: Length of hospital stay, stratified by blood culture contamination results

Checklists

Two hundred and fifty blood cultures were directly observed for adherence to a checklist of activities by the principal investigator. Although blood culture contamination rates were highest among specimens collected by interns (7/137, 5.1%) there was no statistically significant difference in contamination rates when stratifying by category of staff member (p-vale = 0.472).

Table 2.2: Characteristics of observed blood cultures, stratified by blood culture result

Parameter	Overall	BC Negative	Contaminated	Flag pos.	Significant isolate	p
n	250	232	10	6	2	
Staff (%)						0.472
Consultant	9 (3.6)	8 (3.4)	0 (0.0)	1 (16.7)	0 (0.0)	
Intern	137 (54.8)	126 (54.3)	7 (70.0)	3 (50.0)	1 (50.0)	
Medical Officer	33 (13.2)	31 (13.4)	1 (10.0)	1 (16.7)	0 (0.0)	
Registrar	55 (22.0)	52 (22.4)	2 (20.0)	1 (16.7)	0 (0.0)	
Student	16 (6.4)	15 (6.5)	0 (0.0)	0 (0.0)	1 (50.0)	
BC volume (%)						0.696
0-0.9 mL	1 (0.4)	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	
1-1.9 mL	208 (83.5)	196 (84.8)	8 (80.0)	3 (50.0)	1 (50.0)	
2-2.9 mL	36 (14.5)	30 (13.0)	2 (20.0)	3 (50.0)	1 (50.0)	
3-3.9 mL	2 (0.8)	2 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)	
4-4.9 mL	2 (0.8)	2 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)	
Proportion of specimen used for blood culture bottle innoculation (mL, IQR)	0.60 [0.50, 1.00]	0.60 [0.50, 1.00]	0.65 [0.50, 0.92]	0.54 [0.43, 0.89]	0.70 [0.55, 0.85]	0.965
Checklist score (IQR)	27.00 [27.00, 27.00]	27.00 [27.00, 27.00]	27.00 [27.00, 27.00]	27.00 [27.00, 27.00]	27.00 [27.00, 27.00]	0.905

Discussion

This study demonstrated that adherence to a standard operating procedure (SOP) significantly reduced blood culture contamination rates in paediatric patients. The contamination rate decreased from 9.1% in the pre-intervention period to 5.5% during the intervention phase. However, this was not sustained in period 3, during which use of the SOP was not enforced and the contamination rate rebounded to 9.7%. These findings suggest that while the SOP was initially effective, continuous training and supervision are critical to maintain acceptable rates of blood culture contamination.

Blood culture contamination rates vary across the world and institutions. In an observational study performed over a four-month period in two tertiary hospitals in the Free State, South Africa in 2019, the contamination rate was 15.2% (37 out of a total 244 BCs) [17]. A Multicentre Retrospective Observational study in Public hospitals in Malaysia revealed that the contamination rate for paediatric patients over a 9 month period in 2018 was 2.6%, which was lower than 7.7% achieved at a single-site study in Malaysia in 2016 [18]. A year long, multi-disciplinary interventional study with implementation of an SOP in Guangzhou, China in 2023 demonstrated that blood culture contamination rates declined from 1.4% to 0.9% ($p = 0.002$) [19].

The significant reduction in contamination rates in period 2 highlights the positive effect of structured interventions, such as the implementation of an SOP. The observed versus unobserved blood culture analysis in period 2 also reinforces the importance of direct observation in maintaining the quality of blood culture collection, with observed cultures showing a lower contamination rate (3.9% vs. 6.1%). However, the lack of a statistically significant difference between observed and unobserved cultures suggests that while observation may help, it is likely not the sole factor contributing to the improvement in contamination rates. This finding points to the complexity of ensuring procedural adherence and the need for a multifaceted approach to reduce blood culture contamination rates.

The increase in contamination rates during period 3, despite no changes to the SOP, is con-

cerning and implies that initial improvements may wane without sustained reinforcement. Factors such as poor procedural adherence, rapid staff turnover, and complacency may contribute to this decline in performance. Furthermore, lack of basic resources, including cleaning materials, soap, hand towels and water outages, may contribute to unacceptably high blood culture contamination. This underscores the importance of ongoing training, regular audits, continuous quality improvement initiatives and a commitment from hospital administrators to provide a working environment conducive to optimisation of hygiene practice to maintain and sustain lower contamination rates over time.

Hospital Stay and Costs

Blood culture contamination appears to impact on hospital length of stay and costs. We observed that patients with contaminated blood cultures had a median hospital stay of 5 days, compared to 4 days for those with negative cultures, and 2 days for those who did not have a blood culture. Children with contaminated blood cultures stayed in hospital for a significantly longer period than did those whose blood cultures were negative. This finding is consistent with previous research indicating that contaminated cultures often lead to unnecessary antibiotic treatments, additional diagnostic procedures, and longer hospital stays due to concerns about potential sepsis or other infections. A 2014 retrospective study by Dawson, et al [13] of 142 patients showed an increase in hospital length of stay of 5.4 days in patients who had contaminated BCs compared to the control group (which were deemed as true negative results). A systematic review assessed six studies which showed a hospital length of stay of 1 to 22 days in patients with contaminated cultures (false positive), compared to 1 to 17 days in patients with negative blood cultures, which was associated with substantially higher pharmacy and laboratory costs in those with BC contamination [12]. Extended hospitalizations contribute to an increased burden on healthcare systems, both in terms of resource use and financial costs, and a greater risk to patients for developing hospital-associated infections.

An interventional study in Houston, Texas compared the costs of contaminated versus uncon-

taminated blood cultures, including laboratory, pharmacy, hospital stay and other indirect costs. The laboratory cost alone (for standard laboratory procedure) per episode of contaminated blood cultures was $275, compared to $118 per episode of negative blood cultures. A systematic review showed that false positive blood cultures had a median laboratory cost of $242, compared to $128 for true negative BCs ($p = 0.0001$) [20].

Challenges and Future Directions

While our intervention successfully reduced contamination rates in the short term, the return to higher rates of blood culture contamination in period 3 emphasizes the difficulty of achieving sustained improvements. The SOP alone may not be sufficient to maintain lower contamination rates without continued oversight and training. Most institutions that have implemented an SOP to improve blood culture contamination rates have ongoing efforts and training to sustain more acceptable contamination rates. A study performed in Qatif Central Hospital, Saudi Arabia, implemented a series of workshops with monthly report back, with the aim of improving blood culture contamination rates. The baseline contamination rate was 9.4% at study start, and reduced to 2.4% 10 months later [21]. Interruptions to the downward trend in blood culture contamination rates during the mid-phase of the study were attributed to staff shortages and lack of ongoing training during vacation and holiday periods [21].

Future efforts should focus on reinforcing best practices, ensuring staff adherence to protocols, and possibly incorporating regular feedback mechanisms to identify and address areas of non-compliance. Additionally, future research could explore the role of periodic refresher training, real-time performance feedback and incentives in maintaining procedural standards over time. Institutional commitment to providing sustainable supplies of equipment and uninterrupted water sources are essential, particularly in resource limited settings.

3 Recommendations

To ensure sustained improvements in blood culture contamination rates and associated outcomes, several key strategies should be implemented in the context of a tertiary hospital in a developing country.

A structured and ongoing training programme for healthcare personnel involved in blood culture collection should be established, including periodic refresher sessions to reinforce best practices and address any procedural drift that may occur over time. Special attention should be given to ensuring that staff rotating into the department, or newly hired staff, receive comprehensive training upon commencement of their clinical duties.

Regular feedback to staff on blood culture contamination rates should be prioritised. A systematic approach to monitoring and reporting contamination rates can be established through regular feedback. Sharing this data in an actionable and constructive manner will help staff identify areas for improvement and foster accountability. Feedback sessions can also serve as a platform to discuss challenges encountered during blood culture collection and to collaboratively develop solutions.

The role of the Infection Prevention and Control (IPC) department is pivotal in supporting these efforts. Hospital administrators and the IPC team should ensure the availability of essential equipment, such as gloves, sterile gauze or cotton, disinfectants, and appropriate collection bottles, to facilitate proper blood culture collection. Adequate stock levels must be maintained to avoid disruptions in the adherence to standard protocols.

Supervision and oversight are also essential components of maintaining quality. Trained supervisors or champions should be designated within clinical teams to observe and guide staff during blood culture collection procedures. Real-time feedback during these observed sessions will help correct deviations from protocol immediately and reinforce correct techniques.

References

1. Iroh Tam PY, Bernstein E, Ma X, Ferrieri P. Blood Culture in Evaluation of Pediatric Community-Acquired Pneumonia: A Systematic Review and Meta-analysis. Hosp Pediatr **2015**; 5:324–336.

2. Iroh Tam PY, Musicha P, Kawaza K, et al. Emerging resistance to empiric antimicrobial regimens for pediatric bloodstream infections in Malawi (1998-2017). Clin Infect Dis **2019**; 69:61–68.

3. von Gottberg A, de Gouveia L, Tempia S, et al. Effects of Vaccination on Invasive Pneumococcal Disease in South Africa. N Engl J Med **2014**; 371:1889–1899.

4. bioMérieux Inc. BacT / ALERT ® BPA IVD. 2010: 1–10. Available at: https://www.mycts.org/Portals/0/Assay_PI/CQC/BacT ALERT.pdf. Accessed 10 May 2022.

5. Neuman MI, Hall M, Lipsett SC, et al. Utility of Blood Culture Among Children Hospitalized With Community-Acquired Pneumonia. Pediatrics **2017**; 140:e20171013.

6. Pitetti RD, Choi S. Utility of blood cultures in febrile children with UTI. Am J Emerg Med **2002**; 20:271–4.

7. Kanegaye JT, Soliemanzadeh P, Bradley JS. Lumbar Puncture in Pediatric Bacterial Meningitis: Defining the Time Interval for Recovery of Cerebrospinal Fluid Pathogens After Parenteral Antibiotic Pretreatment. Pediatrics **2001**; 108.

8. Ntusi N, Aubin L, Oliver S, Whitelaw A, Mendelson M. Guideline for the optimal use of blood cultures. S Afr Med J **2010**; 100:839–43.

9. Berkley JA, Lowe BS, Mwangi I, et al. Bacteremia among Children Admitted to a Rural Hospital in Kenya. N Engl J Med **2005**; 352:39–47.

10. Driscoll AJ, Knoll MD, Hammitt LL, et al. The effect of antibiotic exposure and specimen volume on the detection of bacterial pathogens in children with pneumonia. Clin Infect Dis **2017**; 64:S368–S377.

11. Doern GV, Carroll KC, Diekema DJ, et al. A comprehensive update on the problem of blood culture contamination and a discussion of methods for addressing the problem. Clin Microbiol Rev **2020**; 33:1–21.

12. Dempsey C, Skoglund E, Muldrew KL, Garey KW. Economic health care costs of blood culture contamination: A systematic review. Am J Infect Control **2019**; 47:963–67.

13. Dawson S. Blood culture contaminants. J Hosp Infect **2014**; 87:1–10.

14. Gander RM, Byrd L, DeCrescenzo M, Hirany S, Bowen M, Baughman J. Impact of blood cultures drawn by phlebotomy on contamination rates and health care costs in a hospital emergency department. J Clin Microbiol **2009**; 47:1021–4.

15. Thailand Ministry of Public Health and U.S. Centers for Disease Control and Prevention. Population-based surveillance for microbial agents of pneumonia and sepsis with detection of *Streptococcus pneumoniae*. 2005;

16. Snyder JW. Blood Cultures: the Importance of Meeting Pre-Analytical Requirements in Reducing Contamination, Optimizing Sensitivity of Detection, and Clinical Relevance. Clin Microbiol Newsl **2015**; 37:53–7.

17. Krause RC. Blood culture contamination in the departments of paediatrics and child health at two tertiary training hospitals in central South Africa. S Afr Med J **2022**; 112:13503.

18. Mokhtar NA, Ting SY, Zainol Abidin NZ, et al. The rate of blood culture contamination and common organisms isolated in Malaysian public hospitals. Malays J Pathol **2024**; 46:307–314.

19. Li Z, Hu K, Wang T, et al. Effectiveness of multidisciplinary interventions to improve blood culture efficiency and optimize antimicrobial utilization. Front Public Health **2024**; 12:1432433.

20. Skoglund E, Dempsey CJ, Chen H, Garey KW. Estimated Clinical and Economic Impact through Use of a Novel Blood Collection Device To Reduce Blood Culture Contamination in the Emergency Department: a Cost-Benefit Analysis. J Clin Microbiol **2019**; 57.

21. Al-Hamad AM. Successful Reduction of Blood Culture Contamination in an Emergency Department by Monitoring and Feedback. Open Mibcrobiol J **2019**; 13:297–285.

Supplementary Materials

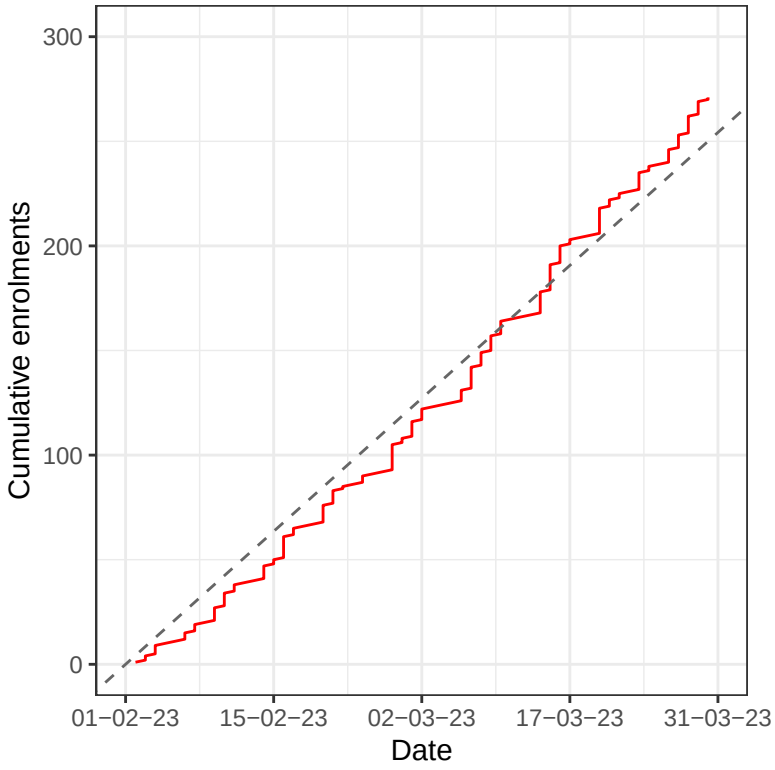

Figure 3.1: Cumulative enrollments of observed blood cultures in Period B of the study

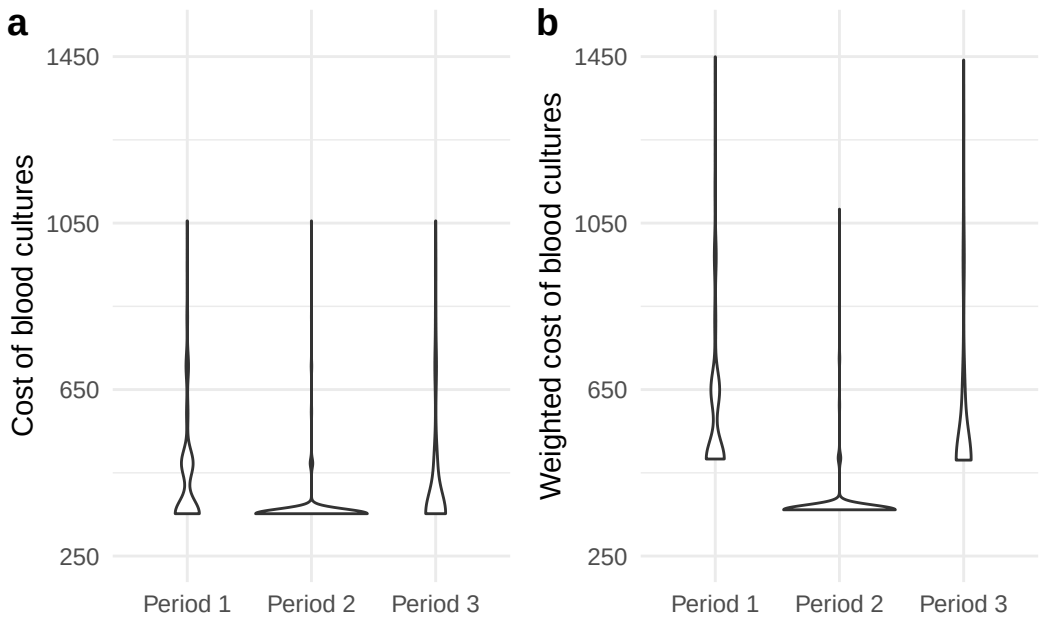

Figure 3.2: Cost of blood culture processing in each of the study periods

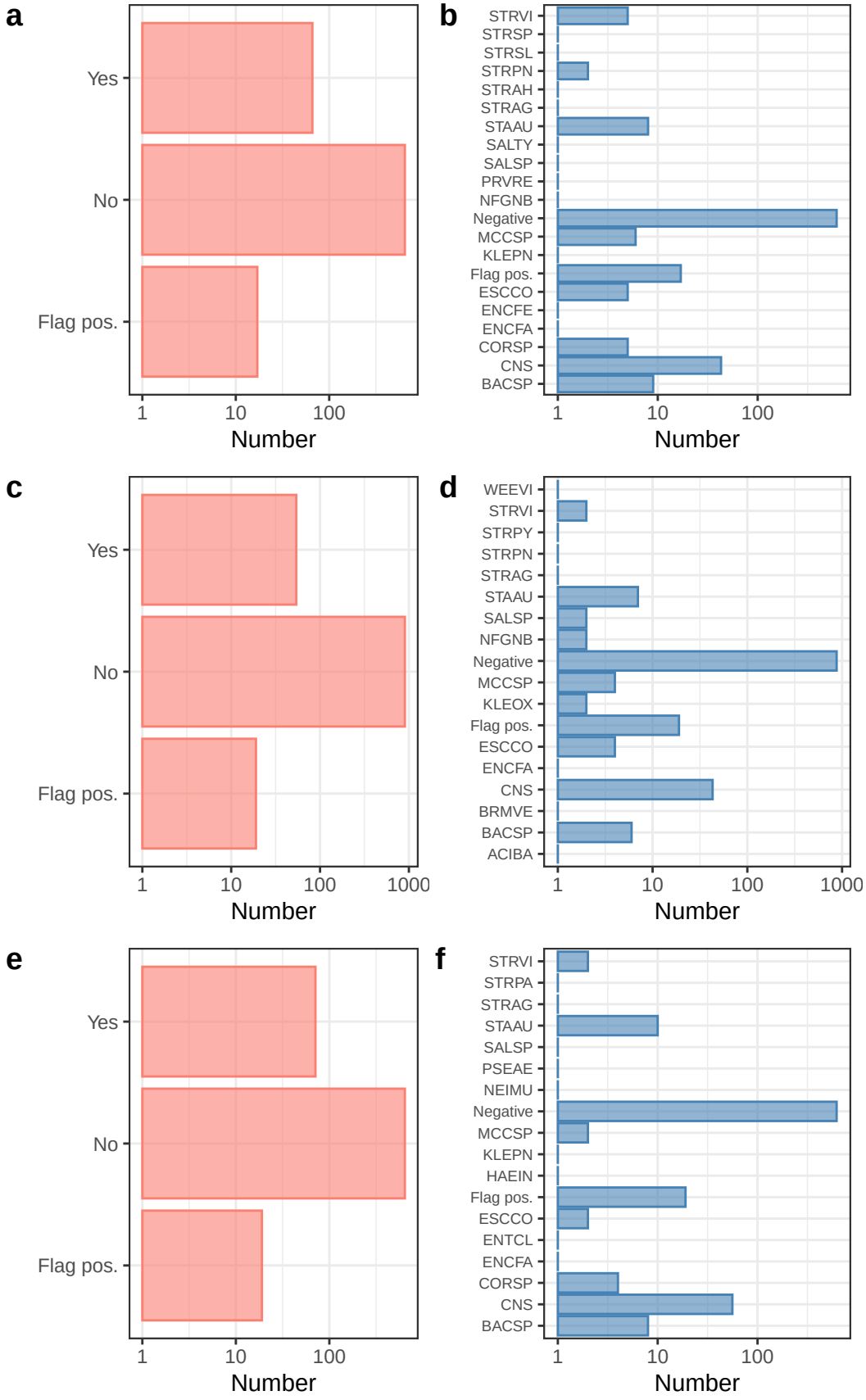

Figure 3.3: Blood culture results

Organism codes: ACIBA = *Acinetobacter baumannii*; BACSP = Bacillus spp; BRMVE = *Brucella melitensis*; CNS = Coagulase negative staphylococcus; CORSP = Corynebacterium spp; ENCFA = *Enterococcus faecalis*; ENCFE = *Enterococcus faecium*; ENTCL = *Enterobacter cloacae*; ESCCO = *Escherichia coli*; Flag pos. = Flag positive, culture negative; HAEIN = *Haemophilus influenzae*; KLEOX = *Klebsiella oxytoca*; KLENPN = *Klebsiella pneumoniae*; MCCSP = Micrococcus spp; NEIMU = *Neisseria mucosa*; NFGNB = Non-fermenting Gram-negative bacilli; PRVRE = Presumptive Vancomycin-Resistant Enterococcus; PSEAE = *Pseudomonas aeruginosa*; SALSP = Salmonella spp; SALTY = Salmonella enterica serovar Typhi; STAAU = *Staphylococcus aureus*; STRAG = *Streptococcus agalactiae*; STRAH = Alpha-haemolythic streptococcus spp; STRPN = *Streptococcus pneumoniae*; STRPA and STRPY = *Streptococcus pyogenes*; STRSL = *Streptococcus salivarius*; STRSP = Streptococcus spp; STRVI = Viridans streptococcus; WEEVI = *Weissella viridescens*.

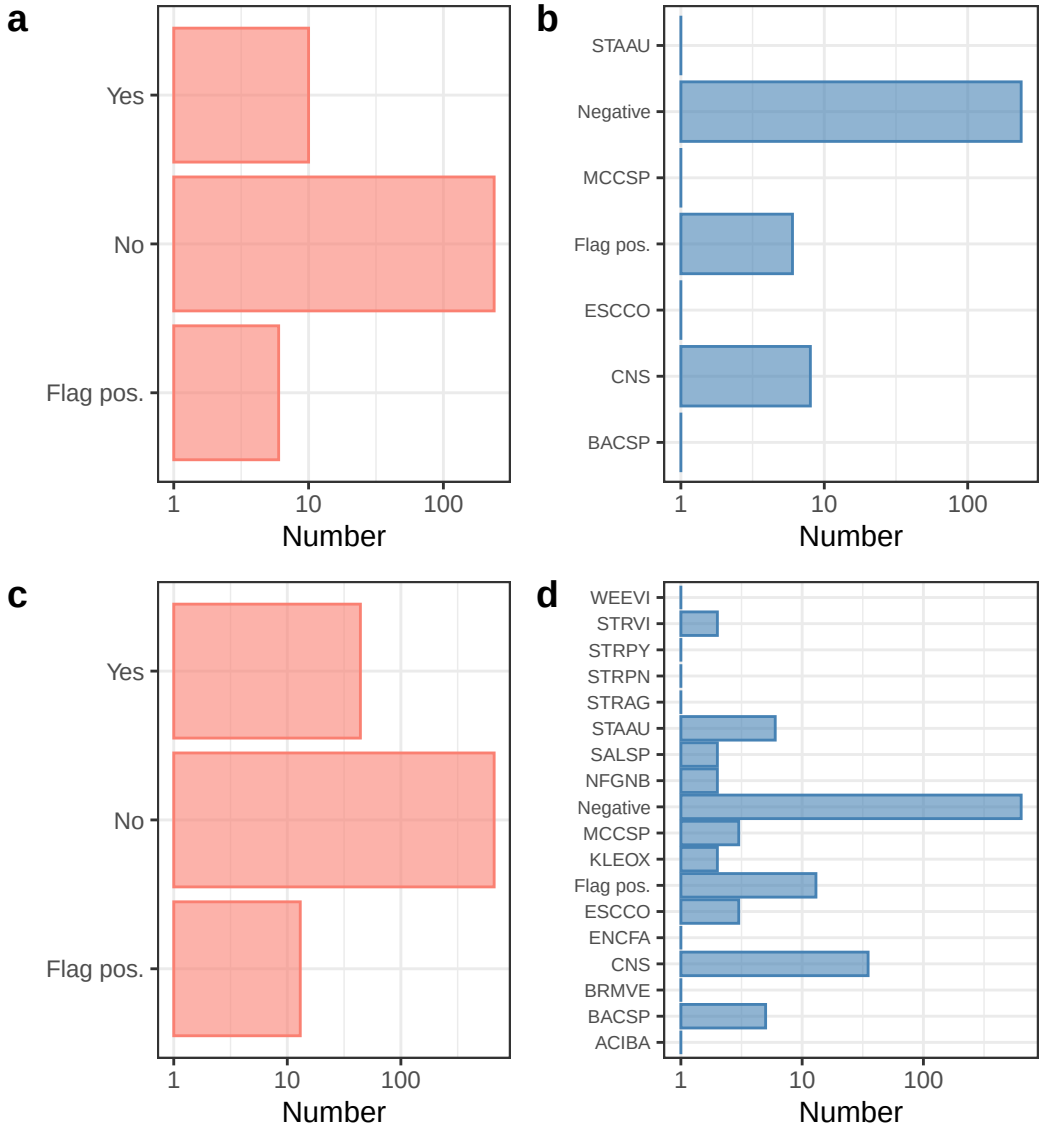

Figure 3.4: Blood culture results - Period 2

Organism codes: ACIBA = *Acinetobacter baumannii*; BACSP = Bacillus spp; BRMVE = *Brucella melitensis*; CNS = Coagulase negative staphylococcus; ENCFA = *Enterococcus faecalis*; ESCCO = *Escherichia coli*; Flag pos. = Flag positive, culture negative; KLEOX = *Klebsiella oxytoca*; MCCSP = Micrococcus spp; NFGNB = Non-fermenting Gram-negative bacilli; SALSP = Salmonella spp; STAAU = *Staphylococcus aureus*; STRAG = *Streptococcus agalactiae*; STRPN = *Streptococcus pneumoniae*; STRPY = *Streptococcus pyogenes*; STRVI = Viridans streptococcus; WEEVI = *Weissella viridescens*.

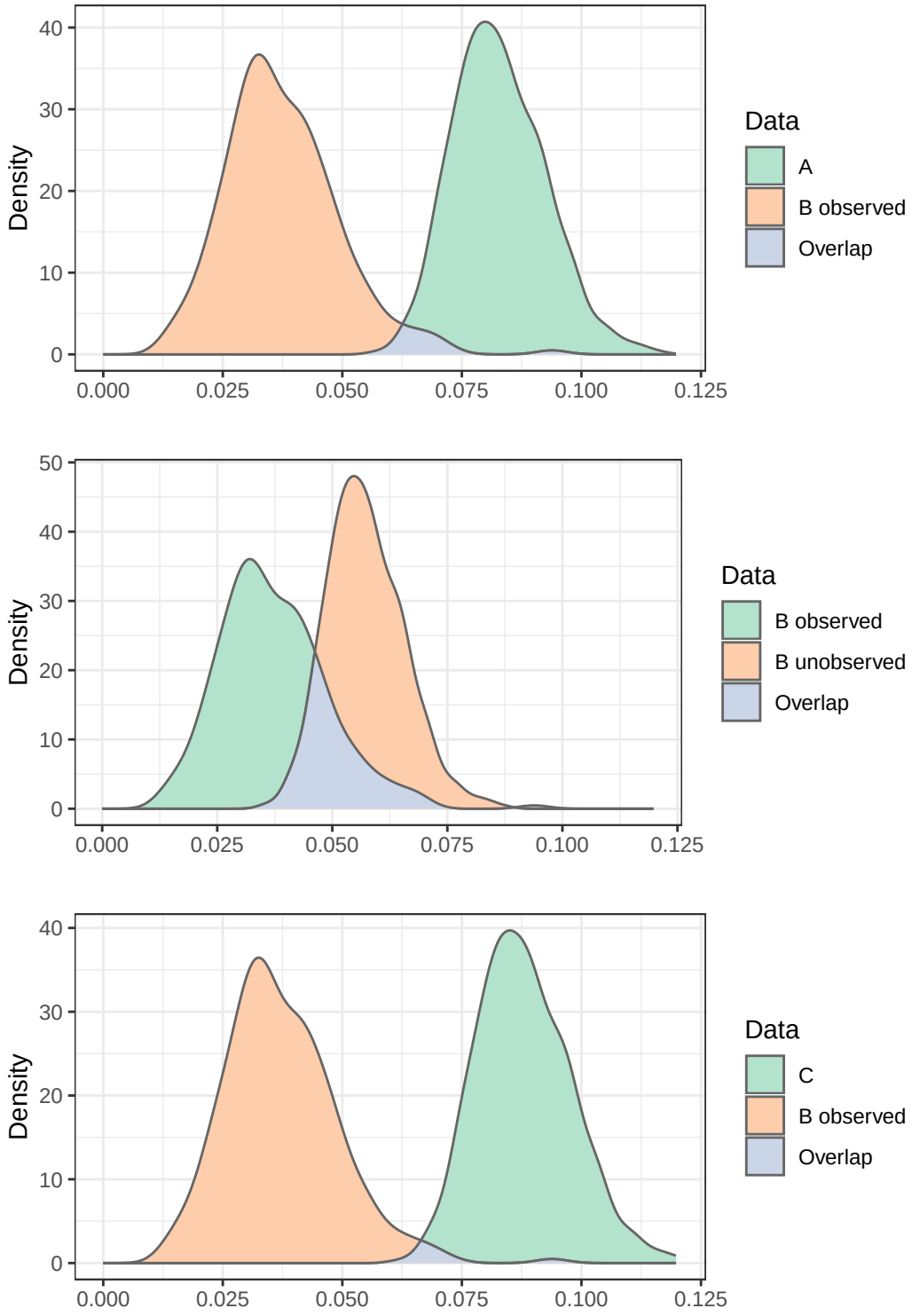

Figure 3.5: Density distributions for overlap between contamination rates

Table 3.1: Summary statistics of length of stay, stratified by group

Group	n	Minimum	Mean	Median	IQR	Maximum
BC Negative	1831	0	5.8	4	3.0 - 6.0	101
BC not done	624	0	3.6	2	2.0 - 4.0	68
Contaminated	166	0	8.3	5	3.0 - 8.0	116
Flag pos.	46	1	8.1	5	3.0 - 8.0	84
Significant isolate	67	0	9.8	7	3.0 - 14.0	63

APPENDIX 1: Study Protocol

Optimising Blood Culture Collection Techniques to Minimise Contamination Rates in a Busy Public Sector Paediatric Department in South Africa: A Quality Improvement Project

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Degree: Master of Medicine (Paediatrics)

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CONTENTS

NOMENCLATURE

AMR	antimicrobial resistance
BC	blood culture
CAP	community acquired pneumonia
CHBAH	Chris Hani Baragwanath Academic Hospital
CLSI	Clinical and Laboratory Standards Institute
CNS	coagulase negative staphylococcus
CO_2	carbon dioxide
IEIP	International Emerging Infections Program
HREC	Human Research Ethics Committee
MAC	Medical Advisory Committee
NHLS	National Health Laboratory Service
PERCH	Pneumonia Etiology Research for Child Health
SOP	standard operating procedure
UTI	urinary tract infection

INTRODUCTION

Although blood culture (BC) has low yield of bacterial pathogens in children hospitalised with meningitis, pneumonia, septicaemia, urinary tract infections and other infections, it is widely used to inform empiric antibiotic choice (1). Pathogenic bacteria or fungi isolated from BC are tested for their antimicrobial susceptibility patterns, thus adding to the evidence on changes in antimicrobial resistance (AMR) patterns over time, as well as changes in the prevalence of certain organisms in response to interventions which have been adopted to prevent infection, such as vaccination (2)(3). A major challenge of BC is their low sensitivity, coupled with the fact that a positive BC does not always represent detection of the causative infecting agent. Skin commensals commonly contaminate BC obtained from children hospitalised with presumed severe bacterial or fungal infection, giving rise to false positive BC results.

Not only are contaminated BC troublesome because they obscure the true underlying cause of infection in children with severe presumed bacterial or fungal infection, but they also contribute to wastage of funds allocated to healthcare. BC specimens that flag positive are channelled down standard workflow pathways in the laboratory, in which additional costs are incurred in the process of identifying the organism that was cultured in the specimen. High rates of BC contamination thus incur unnecessary expenditure.

LABORATORY PROCESSING OF BLOOD CULTURES

Chris Hani Baragwanath Academic Hospital (CHBAH), the site for this study, uses the BacT/ALERT system for BC testing. BacT/ALERT is an automated colorimetric microbial detection system. Each BC bottle contains culture media and an internal sensor which indicates the presence of microbes by detection of carbon dioxide

(CO_2). Once blood has been inoculated into the BC bottle, it should be promptly transported to the laboratory and loaded into the instrument, where it is incubated for up to five days or until the specimen flags positive. If a microorganism is present, it metabolises substrate in the culture medium and produces CO_2, which then changes the sensor at the bottom of the bottle from dark to light in colour, increasing the amount of reflected LED light in the system (4). The sensor is gas-permeable and is separated from the broth medium by a semi-permeable membrane. Once the sensor changes colour, the specimen is designated positive. Once the bottle has flagged positive, it should be removed from the system for Gram-stain and subculture (4).

Despite its limitations, BC remains the gold standard in the diagnosis of sepsis. In a cross-sectional study performed over 5 years with 7509 children admitted with community acquired pneumonia (CAP), only 2.5% of children who had BCs performed on admission had a positive result (5). Urinary tract infections (UTIs) also have a low BC positivity rate, where in one retrospective cohort study, only 5.6% of patients with febrile illness in the setting of a UTI had a true bacteraemia (after excluding false positives due to contaminated specimens) (6). The BC contamination rate in that study was 3.8%. Meningitis tends to have a higher BC positivity rate. In a retrospective study of 128 children with proven meningitis, BCs were positive in 78% in the group that had not received pre-treatment antibiotics (7).

Various factors can negatively influence the sensitivity of blood cultures, the most important being inadequate volume of blood in the blood culture bottle, and contamination of the sample with skin commensals. Inadequate volume of blood inoculated into the blood culture bottle can result in a false negative blood culture. The ideal volume of blood in the paediatric clinical practice has not yet been well established and varies between 1 and 5 mL, depending on the patient's age. During

the neonatal period, 1 to 2 mL of blood is usually sufficient to allow positivity (8). In a study of almost 20,000 children in rural Kenya, the BC yield in children of at least 60 days old increased with each mL of blood used as a sample, with a positivity rate of 5.6% at 1 mL, 6.8% at 2mL and 7.9% at 3mL of blood used (9).

Pre-treatment with antibiotics (prior to BC collection) significantly reduces the microbial detection rate. In the Pneumonia Etiology Research for Child Health (PERCH) study, a multi-country case-control study which determined the aetiology and risk factors for severe pneumonia in children under-5 years of age in sub-Saharan Africa and South-east Asia, pre-treatment with antibiotics reduced the BC positivity rate by 40% (10).

Blood culture contamination, resulting in a false positive blood culture, is another important factor in determining the significance of a blood culture result. Commonly occurring BC contaminants, representing the normal skin flora, include coagulase negative staphylococcus (CNS), *Micrococcus* spp, *Bacillus* spp, C*orynebacterium* spp and *Cutibacterium* spp (previously known as *Pripionobacterium* spp) (8).

THE PROBLEM OF BACTERIAL CONTAMINATION OF BLOOD CULTURES

Contamination of BCs by skin commensals occurs due to inadequate disinfection of the skin and poor technique utilized by the person obtaining the specimen for culture (11). Another important cause of contamination is collection of the blood sample through an existing indwelling venous or arterial catheter (11). The broth medium in the BC bottle can also have an impact on contamination rates, where those that contain antibiotic binding resins give rise to an increased yield of causative pathogens and contaminants (11).

There are clinical and laboratory consequences of having a high BC contamination rate, which incur an economic impact and increased cost per contaminated BC.

Contaminated BCs are difficult for a clinician to interpret, and could result in additional tests being ordered, e.g. additional BCs, laboratory tests to assess infective markers, and echocardiography to exclude subacute bacterial endocarditis, in order to assist in determining the significance of the result. This leads to an increase in length of hospital stay and an increase in risk of the patient acquiring a nosocomial infection, increased clinician workloads, and additional healthcare expenditure. Unnecessary antibiotics may be ordered, some of which require close monitoring of drug levels (such as amikacin and vancomycin), further increasing laboratory costs (12). A retrospective study of 142 BC contaminants showed an increase in hospital length of stay of 5.4 days in patients who had contaminated BCs compared to the control group (which were deemed as true negative results) (13). A systematic review assessed six studies which showed a hospital length of stay of 1 to 22 days in patients with contaminated cultures (false positive), compared to 1 to 17 days in patients with negative BCs and substantially higher pharmacy and laboratory costs in those with BC contamination (12).

STRATEGIES TO LIMIT BLOOD CULTURE CONTAMINATION RATES

The Clinical and Laboratory Standards Institute (CLSI) targets an ideal BC contamination rate of ≤3% (14). In various settings, standard operating procedures (SOPs) have been implemented in order to guide the collection of BC specimens, so as to minimise contamination. An adaptation of one such SOP, which has been successfully implemented in national laboratory surveillance studies of pneumococcus in Thailand (15), will be used in this study.

The method of skin anti-sepsis is the single most important factor in limiting BC contamination rates. The most commonly used antiseptics are iodine tincture, 10% povidone iodine aqueous solution and 2% chlorhexidine gluconate/70% isopropyl

alcohol. There is no clear evidence in the difference between chlorhexidine and iodine based solutions, but the efficacy of both solutions is enhanced with the addition of alcohol in skin antisepsis (16). A back and forth motion is more effective in disinfecting the skin compared to a concentric motion, because the technique of the back and forth motion is more likely to be applied with friction to disinfect the first five dermal layers of the skin, and is more likely to use the same pathway around the site of venepuncture (16). Adequate drying time, which varies according to the reagent used for skin decontamination, is required prior to venepuncture. It is essential that the clinician does not re-palpate the area to be venepunctured after it has been disinfected (13). The use of sterile gloves compared to non-sterile gloves showed a significant reduction in BC contamination rates from 4.3% to 1.7% in one study of over 10,000 BCs (13). In addition to disinfection of the skin, the rubber top of the culture bottle (not sterile) should also be disinfected with a 70% alcohol wipe or solution prior to inoculation with blood (16).

JUSTIFICATION FOR THIS STUDY

The BC contamination rates in the general paediatric wards at CHBAH, a busy secondary/tertiary level public sector hospital in Soweto, South Africa, exceed 20% [personal communication, Prof Moore], which is far above the recommended rate of ≤3%. These high contamination rates incur unnecessary expenditure to the hospital and compromise patient care through obscuring or inhibiting the growth of the bacterial and fungal pathogens which may be causative of the infection episode. In this quality improvement project, we will evaluate the impact on adoption of the Thailand BC SOP on BC contamination rates and laboratory expenditure in the general paediatric wards at CHBAH. Currently, there is no SOP in place for the collection of BC in the general paediatric wards at CHBAH, and very little training to the junior staff (medical students and intern doctors), who are usually responsible for

the collection of all laboratory specimens, in how to collect these specimens. There is also a high turnover of staff in this area, due to the nature of rotations at teaching hospitals such as CHBAH in South Africa.

At the time of writing, the cost of processing a BC at the NHLS is R120.82 for a negative BC, compared to R351.77 for a positive blood culture with one organism identified. The cost of the positive culture includes Gram staining, bacterial identification and antibiotic susceptibility testing per organism. A positive BC therefore will cost three times more than a negative BC. The cost will be higher if two organisms are isolated from the specimen, which can be the case especially in contaminated cultures [personal communication with Dr Wadula].

AIM AND OBJECTIVES

The aim of the study is to compare BC contamination rates, hospitalisation duration and laboratory expenditure in children hospitalised in the general paediatric wards at CHBAH in a pre-intervention, intervention, and post-intervention period of a Quality Improvement Project.

The aims of the study will be to:

1. Compare BC contamination rates in children hospitalised from 01 December 2022 to 31 January 2023 (pre-intervention cohort), to contamination rates in children hospitalised from 1 February to 31 March 2023 (intervention cohort), and a post-intervention cohort (01 April to 31 May 2023). The intervention cohort BCs will be collected during ongoing on-site reinforcement of correct BC specimen collection using the Thailand SOP (see details of the SOP below) as a Departmental wide effort to optimise clinical practice as standard of care in the collection of paediatric BC specimens.

2. Compare the laboratory costs processing BCs collected in the pre-, during- and post-intervention phases of the Quality Improvement Project.
3. Compare the hospitalisation costs (length of stay) of children in the pre-intervention, intervention and post-intervention cohorts.
4. To compare the contamination rates, laboratory costs and hospitalisation costs (length of stay) of paediatric patients hospitalised in the intervention period who had BC collections observed by the principal investigator (Dr Wilson) to contamination rates, laboratory costs and hospitalisation costs (length of stay) of paediatric patients whose BC collections were not observed directly by the principal investigator.

The working hypothesis of the study is that BC contamination rates will be significantly lower in children whose specimens will be collected using the Thailand SOP, compared to those whose blood cultures are collected in the period prior to implementation of the SOP. We further hypothesise that contamination rates and costs will be significantly lower in children whose BC collections are directly observed, compared to those whose BC specimens are not directly observed by the principal investigator. We estimate that the BC contamination rates will be 5% on average in children during the intervention phase of the study, as a result of implementation of the SOP, 12-20% in the pre-intervention cohort, and 5-12% in unobserved BC collections in the intervention period. We predict that in the post-intervention group, BC contamination rate will be 5-12%, which is higher than the directly observed BC specimens in the intervention group, but lower than the contamination rate in the pre-intervention group.

We also hypothesise that it will be cost-effective to adhere to the SOP-guided approach of BC collection, through reductions in the rates of contaminant cultures translating into significantly lower laboratory costs in the prospective group.

METHODS

STUDY DESIGN

The study entails data collection using three time periods, as part of a pre-, during, and post-intervention Quality Improvement Project. Analysis of the BC contamination rates in all children admitted to the general paediatric wards at CHBAH from 01 December 2022 to 31 January 2023 will be undertaken (pre-intervention cohort).

Admission and discharge dates of all paediatric hospitalisations to Wards 36, 17, 18, 19 and 33 during the intervention period from 01 February 2023 to 31 March 2023 will be obtained from the CHBAH Paediatric Departmental electronic database, which is maintained by the Vaccines and Infectious Diseases Analytics (VIDA) Research Unit. All BCs obtained from children hospitalised to the above-mentioned wards during their hospitalisation episodes will be evaluated for contamination rates, laboratory costs of BC processing, and length of hospitalisation.

The Quality Improvement Project will be implemented during the intervention phase of the study (01 February to 31 March 2023), during which the principal investigator will teach ward clinicians the SOP-guided BC collection technique, and observe BC collections. BC contamination rates, laboratory costs of BC processing and hospitalisation costs (length of stay) in the intervention phase of the study will be compared to the contamination rates and costs in the pre-intervention period.

As not all BC collections will be observed by the principal investigator during the prospective phase of the study (as they may be done after hours), a comparison of

the rates of contamination and costs will be made between BCs whose collection technique were observed, and those that were unobserved. It is anticipated that contamination rates and costs will be marginally higher in the unobserved specimens, compared to observed BC collections. This is assumed, as clinicians may frequently revert to suboptimal practice if constant reinforcement of optimal technique is not emphasised.

The post-intervention group will be those patients admitted to the general paediatric wards in the time period 01 April 2023 to 31 May 2023. BC collection in this group will not be observed by the principal investigator but clinicians will be expected to adhere to the SOP as taught and reinforced during the intervention period of the Quality Improvement Project. BC contamination rates in this group will be compared to the contamination rate in the pre-intervention and intervention groups.

STUDY SITE

The study will be undertaken at CHBAH, in the paediatric admission ward (Ward 36), which runs a 24 hour service. CHBAH is a secondary/tertiary hospital, affiliated with the University of the Witwatersrand, and serves a large population of Soweto within the Johannesburg Metro.

STUDY POPULATION

Inclusion criteria

1. Age: birth to 14 years;
2. Hospitalised with suspected pneumonia, meningitis, urinary tract infection or septicaemia, requiring collection of a BC specimen on the day of hospital admission as part of standard of care.

In the intervention phase of the study, only the admission BC will be observed by the principal investigator, as it is not feasible to be deployed to all general paediatric

wards to observe specimen collections in children with suspected nosocomial sepsis events who may undergo a further BC collection during the course of the hospitalisation.

SAMPLE SIZE

In this study, we aim to observe BC collections on admission in at least 250 children over a 2-month period during the intervention phase of the study. There are on average 528 children admitted to the general paediatric wards per month in December through March (see Table 1), of which approximately 50% require a BC specimen collection on the day of hospitalisation. We anticipate that from 01 December 2022 to 31 January 2023, there will be 500 BCs submitted in the pre-intervention phase of the study, 500 BCs in the intervention phase, and 500 BCs in the post-intervention phase.

Table 1: Number of admissions to the general paediatric wards at CHBAH in December through March

Year and Month	Number of children admitted to the CHBAH general paediatric wards
December 2020	510
January 2021	457
February 2021	444
March 2021	525
December 2021	461
January 2022	475
February 2022	602
March 2022	748
Average number of admissions, December through March	528

A sample size of 250 observed BCs will be sufficient to appreciate a difference of 7% in contamination rates (12% in the pre-intervention collected BCs compared to 5% in BCs collected using the SOP) with 80% power at a significance level of 5% (Table 2). Should baseline contamination rates be higher, a smaller sample size of observed BCs will be required to demonstrate statistical significance, if SOP guided BC collections are able to achieve and maintain a contamination rate of 5% or lower (Table 2).

Table 2: Sample size calculation of the number of observed BC specimens required during the intervention phase of the study

BC Contamination rates (%; routine sampling)	Target contamination rates (%; BC SOP)	Effect size	Number of children in each arm of the study (80% Power)	Number of children in each arm of the study (90% Power)
12	5	0.26	239	320
13	5	0.29	191	256
14	5	0.32	157	210
15	5	0.34	132	177
16	5	0.37	113	152
17	5	0.40	99	132
18	5	0.43	87	116
19	5	0.45	77	103
20	5	0.48	69	93

IMPLEMENTATION OF THE QUALITY IMPROVEMENT PROJECT

The study principal investigator (Dr Wilson) will teach admitting doctors (which include interns, medical officers and registrars) how to perform BC collection using the Thailand SOP during the intervention phase of the study (01 February to 31 March 2023). During this two month period, the primary investigator will liaise with admission ward nursing managers to ensure that all equipment necessary for correct implementation of SOP-guided BC collections are available in the ward. There will be

ongoing teaching and observation of the BC collections during this period. The primary investigator will teach and observe BC collections in children admitted between 08:30 and 16:00 on weekdays. In children admitted after hours, on weekends and public holidays, the admitting clinicians will be instructed to adhere to the SOP in the absence of the primary investigator.

DESCRIPTION OF THE THAILAND SOP

The Thailand Ministry of Public Health (MOPH), together with the U.S Centers for Disease Control and Prevention (CDC) has undergone a pneumonia surveillance network in 20 hospitals within Thailand. This is supported by the International Emerging Infections Program (IEIP). This collaboration has formulated SOPs to ensure quality control and assurance in all stages of the project (15). Children in the intervention arm in this study will undergo BC collections using this SOP.

The BC supply kit for children consists of:

1. Specimen collection form
2. 1 sterile 10 mL syringe
3. 1 sterile 23-gauge wing (butterfly) set
4. 1 sterile 24-gauge wing (butterfly set)
5. 3 × 70% isopropyl alcohol packaged swabs
6. 1 × 2% tincture of iodine swab stick
7. Adhesive bandage
8. 1 paediatric fan (PF) BC bottle (yellow lid)

The BC collection occurs as follows:

1. Gather the required equipment – BC supply kit, tourniquet, non-sterile gloves and sterile cotton balls;

2. Explanation of the procedure to the child (as appropriate) and the caregiver;
3. Wash off any visible dirt at the chosen collection site with soap and water;
4. Select the blood collection site, usually an arm, and apply a tourniquet. Use the most visible or prominent vein on the hand, forearm, or cubital fossa;
5. Skin disinfection:
    a. Scrub the collection site with a 70% alcohol wipe for 30 seconds;
    b. Apply the iodine swab to an area 5 centimetres in diameter around the venepuncture site. Allow one minute of drying time;
    c. If the area is re-palpated, re-disinfection needs to be repeated;
    d. In patients with iodine sensitivity, use 70% alcohol instead of iodine.
6. Remove the flip-top cover off the BC bottle and disinfect the top of the BC bottle with a 70% alcohol wipe;
7. Wipe gloves with 70% alcohol;
8. Insert the needle with the bevel facing upwards into the vein, and withdraw the required amount of blood;
9. Release the tourniquet and remove the needle;
10. Place a sterile cotton ball over the puncture site. The cotton ball should be held firmly in place until bleeding stops;
11. The blood sample should be immediately injected in the BC bottle, without changing needles;
12. Wipe the top of the BC bottle once more with a 70% alcohol wipe;
13. Dispose needles safely into a sharps bin.

A check list will be maintained for all observed BC collections during the intervention phase of the study, and a line list of observed BC collections will be maintained by the principal investigator.

DATA COLLECTION

Each study participant will have their information captured in a data collection sheet (see Appendix). The investigator will trace each participant's blood results, including BC result, over a 5 day period from the time of admission. Laboratory costs incurred through specimen processing of significant and contaminant BC isolates will be obtained from the National Health Laboratory Service (NHLS) Clinical Microbiology Department at CHBAH.

ANALYSIS PLAN

The outcome of interest in this study is the difference in admission BC contamination rates between children admitted in the pre-intervention phase (01 December 2022 to 31 January 2023), the intervention phase (01 February to 31 March 2023), and the post-intervention phase (01 April to 31 May 2023)of the study. A secondary outcome of interest will be the BC contamination rates of observed compared to unobserved BCs collected in the intervention phase of the study. The overall BC contamination rate between the three groups will be compared. Results will be obtained from admission sheets which are filled out by the admitting unit on a daily basis, and from the NHLS LABTRAK database.

Proportions will be compared using the Chi square test (or Fisher's exact test, as appropriate). Participant characteristics, including sex, age (in months), length of hospital stay, time to BC positivity and outcome, will be compared. Continuous variables (age, time to blood culture positivity, and length of hospital stay) will be compared using the Student t test (for means) or the Wilcoxon sign rank test (for medians), as appropriate.

Differences in laboratory costs will be compared between the groups, through liaison with the NHLS Clinical Microbiology Department. Line lists of all BCs conducted on

children admitted to wards 36, 17, 18, 19 and 33 at CHBAH during the pre-intervention phase (01 December 2022 through 31 January 2023), intervention phase (01 February through 31 March 2023), and post-intervention phase (01 April to 31 May 2023) of the study will be obtained from the laboratory and reviewed for positivity and characterisation of organisms cultured, as well as time to culture positivity. It is anticipated that laboratory costs of BC processing will be significantly lower in children who undergo SOP-guided BC collections.

Analyses will be conducted using R version 4.0.4 or higher (18). Two sided p-values of 0.05 will be considered to be statistically significant.

ETHICS

The study requires approval by the University of the Witwatersrand Human Research Ethics Committee (HREC) prior to enrolment of study participants. Additionally, approvals will be required from the Head of Department of Paediatrics and Child Health at CHBAH, and the Medical Advisory Committee (MAC) at CHBAH. The Central Data Warehouse (CDW) of the NHLS will also be approached in order to access laboratory results, and costings for blood culture processing per participant.

For the purposes of this Quality Improvement Project, we request a waiver of informed consent and assent on study participants. The Quality Improvement Project will be part of a Departmental-wide agreement to improve BC collection techniques by admitting clinicians. The aim of the study is to demonstrate significant reductions in cultures contamination rates, laboratory processing costs and hospital length of stay in children enrolled in the prospective phase of the study. We hypothesise that SOP-guided BC collections will assist in achieving lower contamination rates, and will therefore impact on all of the study outcomes of interest. We view the study intervention as being an important aspect of routine care which has not been

adequately adhered to, and anticipate that optimisation of specimen collection will assist clinicians in making informed decisions regarding length of hospitalisation in children hospitalised with suspected infection.

STUDY TIMELINE

	05/2021 - 06/2021	06/2021 – 07/2021	08/2021 - 09/2022	09/2021 – 10/2021	05/2022 - 09/2023	12/2022 - 05/2023	06/2023 - 09/2023
Literature Review							
Preparing Protocol							
Protocol Assessment							
Protocol Revisions							
Ethics Application							
Data Collection							
Analysis							
Writing up							

Data Collection will occur between 01 December 2022 and 31 May 2023, with the three phases of the study, as follows:

1. Pre-intervention phase: 01 December 2022 to 31 January 2023
2. Intervention phase and Implementation of the Quality Improvement Project (01 February to 31 March 2023)
3. Post-intervention phase (01 April to 31 May 2023).

BUDGET

Equipment required for SOP-directed BC collections in the intervention and post intervention phase of the study is available on site at CHABH, and is supplied routinely by the Gauteng Department of Health. Stationery and printing costs is estimated to be R2000-00. The Faculty will also be approached to assist with publication costs for any journal articles that emanate from this research.

REFERENCES

1. Blood Culture in Evaluation of Pediatric Community-Acquired Pneumonia: A Systematic Review and Meta-analysis - PubMed [Internet]. [cited 2021 Jun 24]. Available from: https://0-pubmed-ncbi-nlm-nih-gov.innopac.wits.ac.za/26034164/

2. Tam PYI, Musicha P, Kawaza K, Cornick J, Denis B, Freyne B, et al. Emerging resistance to empiric antimicrobial regimens for pediatric bloodstream infections in Malawi (1998-2017). Clin Infect Dis. 2019;69(1):61–8.

3. von Gottberg A, de Gouveia L, Tempia S, Quan V, Meiring S, von Mollendorf C, et al. Effects of Vaccination on Invasive Pneumococcal Disease in South Africa. Vol. 371, New England Journal of Medicine. 2014. p. 1889–99.

4. bioMérieux Inc. BacT / ALERT ® BPA IVD. 2010;1–10. Available from: https://www.mycts.org/Portals/0/Assay_PI/CQC/BacT ALERT.pdf

5. Neuman MI, Hall M, Lipsett SC, Hersh AL, Williams DJ, Gerber JS, et al. Utility of Blood Culture Among Children Hospitalized With Community-Acquired Pneumonia [Internet]. Available from: www.aappublications.org/news

6. Pitetti RD, Choi S. Utility of blood cultures in febrile children with UTI. Am J Emerg Med. 2002;20(4):271–4.

7. Kanegaye JT, Soliemanzadeh P, Bradley JS. Lumbar Puncture in Pediatric Bacterial Meningitis: Defining the Time Interval for Recovery of Cerebrospinal Fluid Pathogens After Parenteral Antibiotic Pretreatment [Internet]. 2001 [cited 2021 Jun 25]. Available from: www.aappublications.org/news

8. Ntusi N, Aubin L, Oliver S, Whitelaw A, Mendelson M. Guideline for the optimal use of blood cultures. South African Med J. 2010;100(12):839–43.

9. Berkley JA, Lowe BS, Mwangi I, Williams T, Bauni E, Mwarumba S, et al. Bacteremia among Children Admitted to a Rural Hospital in Kenya. N Engl J Med. 2005;352(1):39–47.

10. Driscoll AJ, Knoll MD, Hammitt LL, Baggett HC, Brooks WA, Feikin DR, et al. The effect of antibiotic exposure and specimen volume on the detection of bacterial pathogens in children with pneumonia. Clin Infect Dis. 2017;64(June):S368–77.

11. Doern G V., Carroll KC, Diekema DJ, Garey KW, Rupp ME, Weinstein MP, et al. A comprehensive update on the problem of blood culture contamination and a discussion of methods for addressing the problem. Clin Microbiol Rev. 2020;33(1):1–21.

12. Dempsey C, Skoglund E, Muldrew KL, Garey KW. Economic health care costs of blood culture contamination: A systematic review. Am J Infect Control. 2019;47(8):963–7.

13. Dawson S. Blood culture contaminants. J Hosp Infect [Internet]. 2014;87(1):1–10. Available from: http://dx.doi.org/10.1016/j.jhin.2014.02.009

14. Gander RM, Byrd L, DeCrescenzo M, Hirany S, Bowen M, Baughman J. Impact of blood cultures drawn by phlebotomy on contamination rates and health care costs in a hospital emergency department. J Clin Microbiol. 2009;47(4):1021–4.

15. Thailand Blood Culture Protocol.

16. Snyder JW. Blood Cultures: the Importance of Meeting Pre-Analytical Requirements in Reducing Contamination, Optimizing Sensitivity of Detection, and Clinical Relevance [Internet]. Vol. 37, Clinical Microbiology Newsletter.

2015 [cited 2021 Jun 25]. Available from: www.cmnewsletter.com

17. Uschner D, Schindler D, Hilgers R, Heussen N (2018). “randomizeR: An R Package for the Assessment and Implementation of Randomization in Clinical Trials.

18. R Core Team (2021). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. URL https://www.R-project.org/.

APPENDIX A: DATA COLLECTION SHEET

Variable	**Variable code**		**Variable**	**Variable code**	
Patient Hospital Number	Hosp_no		Unit number (I / II / III / IV)	unit	
Study number	patid		Admission diagnosis 1	Adm_Dx_1	
Date of admission (dd/mm/yyyy)	DOA		Admission diagnosis 2	Adm_Dx_2	
Patient date of birth (dd/yy/yyyy)	DOB		Admission diagnosis 3	Adm_Dx_3	
Sex (M, F)	Sex		Admission diagnosis 4	Adm_Dx_4	
Date of first blood culture (dd/mm/yyyy)	BC_date		Time of specimen arrival at NHLS (24 hour clock)	BC_delivery_time	
Blood culture observed? (Y, N)	Obs		Blood culture result (Pos, Neg)	BC_result	
Person doing BC (intern, MO, registrar, consultant)	BC_personnel		Time to positive BC (hours)	TTP	
Blood volume withdrawn (mL)	Spec_vol		Positive admission BC species 1	BC_sp_1	
BC inoculum volume (mL)	BC_spec_vol		Positive admission BC species 2	BC_sp_2	
Blood culture barcode	BC_code		Positive admission BC species 3	BC_sp_3	
Time of completion of BC blood draw (24 hour clock)	BC_time		Admission BC contaminant (Yes, No)	Contam	

Variable	Variable code		Variable	Variable code	
Admission BC processing cost	Adm_BC_cost				
Date of outcome (dd/mm/yyyy)	DOD		Length of stay (days)	lengthstay	
Total number of blood cultures during admission episode	BC_total_n		Total number of contaminated blood cultures	BC_contam_total	
Total laboratory BC processing cost (through course of admission)	BC_total_cost		Discharge diagnosis 1	DC_Dx_1	
Hospitalisation cost (for length of stay)	Hosp_cost		Discharge diagnosis 2	DC_Dx_2	
Outcome (1 = discharged, 2 = died, 3 = transferred out, 4 = refused hospital treatment)	Outcome		Discharge diagnosis 3	DC_Dx_3	
			Discharge diagnosis 4	DC_Dx_4	

APPENDIX B: CHECK LIST FOR OBSERVED BLOOD CULTURE COLLECTIONS

Step		Tick if step done
Record the date of the BC observation	___/___/_____ (dd/mm/yyyy)	
Record the admitting Unit (I / II / III / IV)	_____	
Record designation of person doing BC collection (intern / medical officer / registrar / consultant)	_____	
Gather the required equipment	BC supply kit	
	tourniquet	
	non-sterile gloves	
	sterile cotton balls	
Explain the procedure to caregiver and child		
Wash off any visible dirt with soap and water		
Apply a tourniquet		
Wash your hands		
Don non-sterile gloves		
Skin disinfection	Scrub the collection site with a 70% alcohol wipe for 30 seconds	
	Check whether the patient is known to have iodine sensitivity or not	
	If no iodine sensitivity: Apply the iodine swab to an area 5 centimetres in diameter around the venepuncture site	
	If the patient has iodine sensitivity: Use 70% alcohol instead	
	Allow one minute of drying time	
If the area is re-palpated, re-disinfection needs to be repeated		
Remove the flip-top cover off the BC bottle		
Disinfect the rubber top of the BC bottle with a 70% alcohol wipe		
Wipe gloves with 70% alcohol		

Insert the needle with the bevel facing upwards into the vein, and withdraw the required amount of blood		
Record the total volume of blood withdrawn (in mL)	_____ mL	
Release the tourniquet		
Remove the needle		
Place a sterile cotton ball over the puncture site		
Apply gentle pressure until bleeding stops		
Transfer blood sample immediately into the BC bottle, without changing needles		
Record the volume of blood inoculated into the BC bottle (in mL)	_____ mL	
Wipe the top of the BC bottle once more with a 70% alcohol wipe		
Dispose needles safely into a sharps bin		
Fill in the lab requisition form		
Record the specimen barcode in the patient's notes	_____	
Record the time of completion of the blood culture collection	_____:_____ (24 hour clock)	
Transport BC specimen to the laboratory		
Record the time of delivery of the specimen to the NHLS laboratory	_____:_____ (24 hour clock)	

APPENDIX 2: Ethics Approval Certificates

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG	HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

Office of the Deputy Vice-Chancellor (Research and Innovation)

TO: Dr L Wilson
School of Clinical Medicine
Department of Paediatrics and Child Health
Medical School
University

E-mail: lucynicolawilson@gmail.com

CC: Supervisor: Professor DP Moore and Dr J Wadula
<David.Moore@wits.ac.za>
and <HREC-Medical Research Office@wits.ac.za>

FROM: Mr Iain Burns
Human Research Ethics Committee (Medical)
Tel: 011 717 1252

E-mail: Iain.Burns@wits.ac.za

DATE: 2022/12/02

REF: R14/49

PROTOCOL NO: **M220621** (This is your ethics application reference number. Please quote it in all enquiries, oral or written, relating to this study.)

PROJECT TITLE: *Optimising blood culture collection techniques to minimise contamination rates in a busy public sector paediatric department in South Africa: a quality improvement project*

Please find attached the Clearance Certificate for the above project. I hope it goes well and that an article in a recognized publication comes out of it. This will reflect well on your professional standing and contribute to Government funding of the University.

MSWorks2000/Iain0007/Clearscan.wps

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

R49 Dr L Wilson

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)
CLEARANCE CERTIFICATE NO. M220621

NAME: (Principal Investigator) Dr L Wilson

DEPARTMENT: School of Clinical Medicine
Department of Paediatrics and Child Health
Medical School
University

PROJECT TITLE: *Optimising blood culture collection techniques to minimise contamination rates in a busy public sector paediatric department in South Africa: a quality improvement project*

DATE CONSIDERED: 2022/06/24

DECISION: Approved unconditionally

CONDITIONS:

NOTE: If contact information regarding student study participants is required, please contact the Registrar's office - <Nicoleen.Potgieter@wits.ac.za>

SUPERVISOR: Professor DP Moore and Dr J Wadula

APPROVED BY: CB Penny
Dr CB Penny, Chairperson, HREC (Medical)

DATE OF APPROVAL: 2022/12/02

This Clearance Certificate is valid for 5 years from the date of approval. An extension may be applied for.

DECLARATION OF INVESTIGATORS

To be completed in duplicate and **ONE COPY** returned to the Research Office secretariat on the 3rd floor, Phillip Tobias Building, Parktown, University of the Witwatersrand, Johannesburg.

I/we fully understand the conditions under which I am/we are authorized to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions. Should any departure be contemplated from the research protocol as approved, I/we undertake to submit details to the Committee. **I agree to submit a yearly progress report**. When a funder requires annual re-certification, the application date will be one year after the date when the study was initially reviewed. In this case, the study was initially reviewed in **June** and therefore reports and re-certification will be due in the month of **June** each year. Unreported changes to the study may invalidate the clearance given by the HREC (Medical).

Signature of Principal Investigator _____ Date _____

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19 August 2022

Applicant: Lucy Wilson
Institution: University of the Witwatersrand
E-mail Address: lucynicolawilson@gmail.com
Cell: 072 326 7888

CC: Jeanette Wadula, David Moore

Project Title: Optimising blood culture collection techniques to minimize contamination rates in a busy public sector paediatric department in South Africa: A pragmatic prospective randomised controlled trial
Reference Number: PR2222632

Research Application Type(s):
1. Request for Data

RE: APPROVAL LETTER: REQUEST TO ACCESS NHLS RESOURCES FOR RESEARCH PURPOSES

This letter serves to advise that the application requesting permission to conduct the above-mentioned research using the listed NHLS resources has been reviewed and **"Approved"**. Please note that the approval is granted on the condition that you comply with the NHLS Research Material and Data Access Policy and requirements stated below.

1. All material and data requested shall be used as per the research protocol submitted to the NHLS and as approved by the relevant Health Research Ethics Committee (HREC) in South Africa.
2. Access to the NHLS material and/or data shall be limited to the minimum required for successful completion of the approved study and shall be made available ***without patient names***.
3. Confidentiality shall be maintained at the participant and institutional level and there shall be no disclosure of personal information or confidential information.
4. The material and/or data obtained from the NHLS shall be anonymised and not, for any reason, be used to track or recruit patients as no pre-approval/consent is obtained from patients.
5. Processes shall be discussed with the relevant NHLS departments (i.e. Corporate Data Warehouse (CDW), NHLS Laboratory Management, Operations Office, etc.) and agreed upon.
6. Any amendments to the study requirements, including the use of the material and/or data for purposes not initially disclosed to the NHLS) shall be cleared by an approved HREC and submitted to the NHLS for approval via the AARMS system – https://aarms.nhls.ac.za.
7. The NHLS shall be acknowledged as a source of material and/or data in any output, such as abstracts and journal articles, emanating from the project.
8. A final report of the research study and any published output resulting from this study shall be submitted to the NHLS via AARMS

Please note that this letter constitutes approval by the NHLS Academic Affairs and Research Office. The NHLS entities tasked with providing the material and/data may have additional requirements for access. Data related queries may be directed to NHLS CDW, email: zarina.sabat@nhls.ac.za; contact number: 011 386 6074 and sample related queries (if applicable) shall be directed to the relevant business manager.

Dr Babatyi Malope-Kgokong
National Manager: Academic Affairs and Research