Clinical Audits/Service Improvements

Increasing the volume of blood received in adult paired blood culture bottles at a regional public health laboratory: results of a quality improvement project to optimise the diagnosis of bacteraemia

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ABSTRACT

Background: Optimising the diagnosis of bacteraemia has clinical, infection control and antimicrobial stewardship benefits. It’s well documented that volume of blood received in blood culture bottles affects test sensitivity. The ability of blood cultures to detect bacteraemia is proportional to the volume of blood cultured. We undertook a period of baseline measurement and established that mean blood culture fill volume was inadequate.

Aim: The primary aim was to increase the percentage of adequately filled blood cultures (>5ml) by 20% and increase the percentage of optimally filled bottles (8–10ml) by 10% in six months (by 1st August 2018). Our secondary aim was to increase the mean volume in blood culture bottles to 8ml (by 1st August 2018). We measured the clinical impact of this on test sensitivity by comparing blood culture positivity rate between adequately and inadequately filled bottles.

Methods: Following a period of baseline measurement we implemented three phases of plan/do/study/act (PDSA) intervention cycles (including a small test pilot cycle). Interventions were focused around user education/engagement, real time user feedback and laboratory reporting. User questionnaires were administered to investigate knowledge and practice; further informing the interventions.

Results & Conclusion: Between 1st March - 1st August 2018 the mean volume of blood inoculated into culture bottles rose from 5ml (95% CI 4.1–6.0ml) to 7.5ml (95% CI 6.4–8.5ml). The percentage of adequately-filled (>5ml) blood culture bottles increased from 47% to 61% (absolute increase of 14%) and the percentage of optimally-filled (8–10ml) bottles increased from 16% to 29% (absolute increase of 13%). Although our project didn’t fully meet its aims, we observed a significant and sustained improvement in filling of blood culture bottles.

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Introduction

Background

Blood cultures remain the gold standard for diagnosis of blood stream infection. Positive blood cultures ensure an improved standard of care including; appropriate antibiotic choice, prompt of further investigations (e.g. imaging, echocardiography, fundoscopy) and often alludes to the source of infection. *Staphylococcus aureus* bacteraemia, for example, is associated with risk of metastatic infection (34% of cases), requires prolonged courses of intravenous antibiotics and carries 22% mortality rate. [1] A proportion of undetected bacteraemic patients will not be on effective empirical antimicrobial treatment. The UK Sepsis Trust recommends that blood cultures be taken within one hour of a diagnosis of suspected sepsis. This recommendation forms part of the "Sepsis Six" bundle, that has been proven to significantly reduce the mortality associated with sepsis. [2] Locally, within the hospital, it’s advised that at least one blood culture set is taken in adults with suspected sepsis. Each hour of delay in initiation of appropriate antibiotics leads to a 7.6% increase in patient mortality rates. [3]

The benefits of detecting bacteraemia go beyond the individual patient. Diagnosis of certain organisms allows for prompt infection control precautions, reduces the risk to patient contacts and potential nosocomial outbreaks. For example, diagnosis of invasive Group A streptococcus may prompt a patient to be nursed in isolation facilities.

Furthermore, diagnosing bacteraemia has institutional benefits. Prompt identification of the aetiological pathogen in a septic patient allows rapid rationalisation of antibiotics. It facilitates antimicrobial stewardship practice by ensuring clinicians use the right antibiotic at the right time. National toolkits advocating "Start smart — then focus" advise "reviewing the clinical diagnosis and the continuing need for antibiotics at 48—72 hours". [4] Blood culture results can enable this process, allowing organisations to use fewer broad spectrum antibiotics. In England, acute hospital trusts are financially incentivised to ensure clinical antibiotic review 24—72 hours following initiation in patients with sepsis as part of NHS England’s Commissioning for Quality and Innovation. [5]

Furthermore, hospitals are expected to reduce overall antibiotic consumption, and increase the proportion of narrow spectrum agents (e.g. flucloxacillin, amoxicillin) prescribed. Optimising the use of blood cultures to diagnose blood stream infection remains pivotal to such diagnostic stewardship.

It is well documented that volume of blood received in blood culture bottles affects test sensitivity. The ability of blood cultures to detect bacteraemia is directly proportional to the volume of blood cultured. Kim et al [6] compared blood culture yield between cultures containing 5ml and 10ml (per bottle) and found that increasing the volume of blood produced a significantly higher pathogen detection rate (14.7% improvement in the isolation of microorganisms, P = 0.023). Yin et al [7] also reported that blood volume was in direct proportion to recovery rate for the detection of bacteraemia and fungaemia; authors report recovery rates for filling of <3 mL, 3—7 mL, 8—10 mL and >10 mL as 13.31%, 15.02%, 17.68%, and 14.96%, respectively. Bouza et al [8] investigated the impact of clinical variables too, but also found the volume of blood cultured correlated with yield of detection of bloodstream infection.

Local problem

Birmingham Public Health laboratory (PHL) provides regional specialist public health testing and routine clinical diagnostic work to a large acute trust. Birmingham PHL performs >700,000 tests annually and received >31,000 blood cultures in 2017/2018.

In January 2018 the laboratory acquired a BD BACTECTM FX blood culture system. This system measures virtual blood volume by measuring glucose consumption within the anaerobic bottle of each adult blood culture pair. Blood cultures that remain negative are removed from the machine after 5 days and blood volume is measured at this time in batches of 25 bottles. Independent investigators have reported that estimated virtual volumes are reliable substitutes (compared to actual volumes) to monitor overall blood volumes and provide feedback to the individual departments or locations. [9]

During a period of baseline measurement (1st February - 11th March 2018) the mean blood culture volume was only 5ml (95% C.I. 4.6-6.0ml). Based on existing literature, we proposed that many bacteraemic patients were going undiagnosed in our hospital. This prompted a quality improvement project to increase the volume of blood inoculated into blood culture bottles and improve test sensitivity.

Aim

The primary aim was to increase the percentage of adequately filled blood cultures (≥5ml) by 20% and increase the percentage of optimally filled bottles (8—10ml) by 10% in six months (by 1st August 2018). Our secondary aim was to increase the mean volume in blood culture bottles to 8ml (by 1st August 2018). We measured the clinical impact of this on test sensitivity by comparing blood culture positivity rate between adequately and inadequately filled bottles.

Methods

Following recognition of the problem, a driver diagram (Table I) was drafted to investigate primary and secondary drivers to change. Change ideas were generated in order to meet the quality improvement objectives. A series of plan/do/study/act (PDSA) intervention cycles (including a small test pilot cycle) were then planned and implemented.

**Intervention (PDSA) cycles**

**Phase One — engaging users and raising awareness**

Following a period of baseline measurement, phase one of the quality improvement initiative ran from March to May 2018, and involved a focused period of education and user engagement to raise awareness. The intervention team consisted of a Microbiology Consultant and Specialist Registrar. High-volume service users were identified using laboratory data (Emergency Departments and Acute Medical Units across all sites and the Haematology Unit).

Following a successful pilot PDSA cycle within the Haematology unit we completed a programme of engagement sessions to all high volume service users. Presentations were also delivered to Foundation Year 1 and 2 doctors across the trust at weekly education sessions (as a high proportion of blood
Teaching sessions highlighted a simple message, that increasing blood volume in blood culture bottles maximises sensitivity and advised on optimal filling of blood culture bottles (8–10ml). Questionnaires (Appendix 1) were administered alongside the teaching sessions to gather qualitative and quantitative data regarding knowledge and practice of blood culture collection. During phase one posters were also disseminated to high-volume areas (emphasising the same message).

**Phase two - report comment**

Following phase one (May–July), feedback was provided to clinicians through the implementation of an automated comment on electronic reports for all inadequately filled blood culture bottles (<5ml). Questionnaires (Appendix 1) were administered alongside the teaching sessions to gather qualitative and quantitative data regarding knowledge and practice of blood culture collection. During phase one posters were also disseminated to high-volume areas (emphasising the same message).

**Phase three – user feedback**

Phase three (June and July 2018) focused on monitoring of blood culture volume and feedback of data to clinical teams. The BD BACTECTM FX blood culture system enables collation of data for volumes of blood in culture bottles on a weekly basis, stratified by the ward or department sending the sample. The intervention team fed back this information on a regular basis to service users through departmental meetings and by email. The engagement of individual clinicians to act as “champions” within key areas (in particular Haematology and the Emergency Department) was crucial to enable further dissemination of monitoring data to their departments. During this period, smaller departments (intensive care units, Obstetrics) were also contacted, given information on the quality improvement initiative and provided with real-time feedback.

**Outcome measures**

1. Blood culture volume - Trends in blood culture volume were tracked through mean, median and interquartile range for the three hospital sites and for individual departments and clinical areas. Averages were collated on a weekly basis, and also before and after intervention periods. These were plotted on a run chart over time to assess sustainability of results. Descriptive statistics were performed using Excel.

2. Blood culture positivity rate - At the end of phase two, the blood culture positivity rate was calculated. A comparison of adequately (>5ml) and inadequately (<5ml) filled bottles was performed. A Chi² test was employed to compare the proportion of positive cultures in the two groups and calculate statistical significance. Questionnaires administered during phase one were analysed with quantitative and qualitative...
methods to describe variations in knowledge and practice regarding blood culture collection by junior doctors. These identified barriers to optimal filling of blood cultures, but did not identify an alternative cause for the observed changes to blood culture filling volume.

Balancing measures

The total number of blood cultures received by the laboratory was also monitored to ensure this wasn’t negatively impacted by the initiative.

Ethical considerations

There were no ethical implications.

Results

Blood culture volume

During a period of baseline measurement (1st February - 11th March 2018) the mean blood culture volume was 5ml (95% C.I. 4.1–6.0ml) the median was 4ml (n = 4,694). During this period, 47% of bottles were adequately filled; only 16% were optimally filled. Clinical areas of particular concern included our Haematology/Oncology ward (mean 2.7ml, n = 334) and Emergency departments (means of 5.1ml and 5.3ml). Between 1st March and 1st August 2018 13,148 blood culture bottles were received and analysed for blood volume. During the five month intervention period the mean volume of blood inoculated into culture bottles rose from 5ml (95% CI 4.1–6.0ml) to 7.5ml (95% CI 6.4–8.5ml); an absolute increase of 50%.

The percentage of adequately-filled (≥5ml) blood culture bottles increased from 47% to 61% during this period (absolute increase of 14%, relative increase of 30%). The percentage of optimally-filled (≥8ml) bottles increased from 16% to 29% (absolute increase of 13%, relative increase of 80%).

The percentage of adequately-filled (≥5ml) blood culture bottles increased from 47% to 61% during this period (absolute increase of 14%, relative increase of 30%). The percentage of optimally-filled (≥8ml) bottles increased from 16% to 29% (absolute increase of 13%, relative increase of 80%). Figure 1 demonstrates the trend in mean blood volumes received over the time period of this project.

Knowledge and practice

During phase one 60 junior doctors were surveyed anonymously. 47% admitted to regularly under filling blood cultures bottles and overall 53% of respondents were unaware of the importance of blood volume. Evidence of correlation between knowledge and practice was observed, as of the doctors who regularly under filled blood culture bottles, a greater proportion (75%) were unaware of the relevance of blood volume. Qualitative analysis of survey responses identified recurrent themes: (a) lack of awareness: "I do not think blood volume matters for the test" (b) lack of understanding of laboratory methodology: "If there is a single bacterium it will be detected" (c) time constraints and job pressures: "I'm in a rush and it takes a long time" (d) misconceptions about potential risk (particularly regarding Haematology and Oncology patients): "I take as little as possible to avoid anaemia". Notably, difficulty with blood culture equipment was not identified as a significant barrier by the junior doctor cohort. The primary drivers identified through these questionnaires, as well as discussion with key service users, were lack of knowledge and awareness. This was used as evidence to support our quality improvement methodology and generate our change ideas (Table I).

Key service users

Phase one of the project involved focused interventions aimed at key service users (Emergency departments, Acute Medicine departments, Haematology unit). Table II demonstrates the change in mean blood volume received from these areas over the course of the study. The Haematology unit was of particular focus, given the low baseline mean volume of 2.7ml per blood culture bottle. Over the course of phase one the mean volume increased to 4.7ml, and further to 5.8ml by the end of phase two (July 2018), with the percentage of adequately-filled (≥5ml) bottles rising from 18% to 54%. These results emphasised the efficacy and success of the user engagement interventions.

Test sensitivity

During phase two, an automated laboratory comment was applied to all inadequately filled bottles (≤5ml). This enabled comparison of blood culture positivity rate between inadequately and adequately filled bottles. Positivity rate in bottles with >5ml blood was 12.2%, compared to 8.2% in those with ≤5ml. This difference was statistically significant as demonstrated by a Chi² test (p = 0.02417). We fed back this data to clinical teams, highlighting that positivity rate was increased by 49% in adequately-filled blood culture bottles, in order to motivate continued improvement during phase two.

The number of blood cultures received within the laboratory during the quality improvement project remained constant and was not negatively affected by any of the interventions.

Discussion

Summary

During a period of baseline observation we identified that only 16% of adult blood culture bottles were optimally filled (8–10ml per bottle). We aimed to increase the percentage of adequately filled blood cultures (≥5ml) by 20% and increase the percentage of optimally filled bottles (8–10ml) by 10%.
Following a quality improvement project the percentage of adequately-filled blood culture bottles increased from 47% to 61% (absolute increase of 14%) and the percentage of optimally-filled bottles increased from 16% to 29% (absolute increase of 13%). Overall fill volume increased from 5ml (95% CI 4.1–6.0ml) to 7.5ml (95% CI 6.4–8.5ml). During phase two blood culture positivity rate was measured and was significantly higher (8.2% vs 12.2%; p=0.024) in blood cultures containing >5ml of blood compared to those containing <5ml.

This quality improvement project was designed and implemented in a large, busy laboratory that provides both clinical diagnostics and specialised Public Health testing. The laboratory serves a wide range of primary, secondary and tertiary care services. The methodology could be readily generalised to other clinical diagnostic Microbiology laboratories.

**Interpretation**

Although our quality improvement project did not fully meet our aims, we observed a significant and sustained improvement in filling of blood culture bottles. This was observed for all of our key service users and resulted in the direct clinical benefit of increased blood culture positivity. This has provided improved diagnosis of bacteraemia and new opportunities for our infection specialist colleagues to optimise management of septic patients and rationalise antibiotic use.

Prior to the initiative, there was little fluctuation in the baseline measurement of mean volume of blood received. Furthermore, there was no change in the methodology of outcome measurement during the initiative. Hence, we conclude that changes in volume of blood received can be attributed to the interventions implemented.

There was no additional financial funding involved in the project. The largest resource was the time given by those involved. This includes:

- gathering data from the BD BACTECTM FX blood culture system on a regular basis (minimal)
- preparation and delivery of user engagement/education presentations to key service users
- medical laboratory assistant time for measurement of blood culture volume upon specimen receipt within the laboratory and application of the automated code where appropriate

In the era of national performance management to monitor and prevent healthcare associated Gram-negative bloodstream infections, quality improvement projects that increase bacteraemia detection rates may seem to contradict efforts to reduce it. However, it is the responsibility of Infection Specialists to educate management teams and policy makers about factors impacting on bacteraemia rates and the importance of rapidly diagnosing Gram negative blood stream infections.

**Limitations**

Due to limitations of the blood culture analyser, only anaerobic bottles from adult blood culture pairs have their blood volume estimated and recorded. Based on previous studies these were used as a proxy for paired blood culture sets during our project. [9] This outcome measure was consistent throughout the project allowing clinical areas to be compared and trends to be monitored throughout time. For this reason, we also excluded paediatric blood culture bottles. These bottles also contain different media designed to allow for small volume samples.

Finally, volume estimates are only made and recorded for negative blood culture bottles. Therefore the fill volume of positive blood cultures are not included in our data. However, we have mitigated for this by analysing data on all bottles (positive and negative) using the comment code applied to inadequately filled bottle reports during phase two of our intervention. Therefore, overall the results of this initiative are generalizable to most clinical diagnostic laboratories, with the exception of those providing specialised paediatric services.

**Conclusions**

This quality improvement project has demonstrated considerable benefit to the diagnosis of bacteraemia within our trust with no additional financial funding. It was enabled through utilisation of an existing function within the laboratory’s BD BACTECTM FX blood culture system and dedicated time of a handful of Microbiology staff.

Going forward, plans to sustain the improvement in blood culture bottle filling include:

- Education regarding the impact of blood volume on blood culture test sensitivity are embedded during staff induction and mandatory training.
- Ongoing use of the automated report comment for blood culture bottles received containing <5ml.
- Ongoing feedback to key service users with real time data regarding blood culture bottle filling volumes.
- There are plans to include mean blood culture fill volume as a parameter within a key performance indicator blood culture dashboard for the laboratory and its’ users.

| Location          | Mean volume in blood culture bottles (ml) (95% confidence intervals) |
|-------------------|---------------------------------------------------------------------|
|                   | Baseline (1st Feb – 1st March)                                      | Phase 1 end (May 2018) | Phase 2 end (July 2018) |
| A&E Site 1        | 5.3 (5.1–5.4)                                                      | 6.5 (6.2–6.8)          | 7.2 (6.9–7.4)          |
| A&E Site 2        | 5.1 (4.9–5.4)                                                      | 5.3 (5.0–5.6)          | 5.9 (5.6–6.2)          |
| AMU Site 1        | 6.2 (5.0–7.3)                                                      | 8.1 (7.0–9.1)          | 8.1 (7.0–9.1)          |
| AMU Site 2        | 5.4 (5.0–5.8)                                                      | 6.2 (5.7–6.7)          | 7.3 (6.9–7.7)          |
| Haematology Unit  | 2.7 (2.5–3.0)                                                      | 4.7 (4.4–5.0)          | 5.8 (5.4–6.1)          |
The next steps include an analysis of the clinical impact of this work, including impact on clinical outcomes, infection control and antimicrobial stewardship. Comparison of the time to positivity between adequately and inadequately filled blood culture bottles is also planned.

**Contributorship statement**

Edmund Birkhamshaw; collected and analysed the data, designed and delivered of quality improvement PDSA cycles, writing of final report. Gemma Winzor; planned the project, designed and delivered the quality improvement PDSA cycles, writing of final report.

**Funding**

No external funding was received.

**Conflicts of interest**

Nil declared.

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**Appendix 1. Questionnaire**

**Blood culture survey**

1) Do you take blood cultures in your job?
2) If so, how often on average?

- 1 blood culture daily
- Daily
- Weekly
- Monthly
- Less than monthly

3) What is the purpose of blood cultures?
   (a)
   (b)

4) How much blood should be put in each bottle?

   - I’m not sure
   - It doesn’t matter
   - < 2ml
   - 2–5ml
   - 5–10ml
   - > 10ml

5) Why is this amount needed?

6) In every day practice how much blood do you estimate you actually put into each bottle? (Totally anonymous answers!)

   - I’m not sure
   - It doesn’t matter
   - < 2ml
   - 2–5ml
   - 5–10ml
   - > 10ml

7) What are the factors that affect how much blood you put into blood culture bottles?

   - Difficult venous access
   - Time pressures
   - Difficult to use BC bottle-butterfly system
   - Other (please state below)

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