Journal of Hospital Infection 101 (2019) 93–99

Available online at www.sciencedirect.com

Journal of Hospital Infection

journal homepage: www.elsevier.com/locate/jhin

Sepsis programme successes are responsible for the increased detection of bacteraemia

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ARTICLE INFO

Article history:
Received 1 February 2018
Accepted 5 April 2018
Available online 11 April 2018

Keywords:
Escherichia coli
Bacteraemia
Sepsis
Change point methodology

SUMMARY

Background: *Escherichia coli* bacteraemia reduction targets are challenging but, in West Wales, this was the key infection surrogate measure set by the local health board in 2013, prior to the introduction of a Welsh Government target. The initial plateau of cases was not maintained and prompted this review.

Aim: To review all blood cultures submitted between 2002 and 2016, both positive and negative.

Methods: With access to a microbiology data warehouse in Wales, all blood culture results were collected, extracted to Excel tables and analysed using change point analysis.

Findings: Just under 200,000 blood culture results were examined. This study found an increase in blood culture submissions, but the positivity rate remained constant throughout the period and the increased number of *E. coli* reflected the increased number of blood cultures taken. This demonstrated the success of sepsis awareness and the use of sepsis bundles for rapid diagnosis and management.

Conclusion: Success in one area (sepsis management) conflicts with 'failure' in reducing *E. coli* bacteraemia. It is argued that targets need to be considered carefully in the light of all available information, which have currently set the National Health Service up to fail.

Introduction

Escherichia coli bacteraemia is recognized by microbiologists and infection prevention and control teams as a challenge. Underwood *et al.* [1] suggested that achieving a significant reduction in the number of *E. coli* bacteraemia cases would be extremely challenging. Melzer and Welch [2], while welcoming the attention that the new *E. coli* mandatory reporting would engender around infection prevention and control, stated that the Department of Health should have been more explicit and should make the aim to reduce bacteraemia episodes associated with medical devices.

The Hywel Dda University Health Board (HDUHB) provides acute and community health care to the population of Carmarthenshire, Ceredigion and Pembrokeshire in west Wales. In December 2013, HDUHB set a target to reduce *E. coli* bacteraemia by 20%, and this was formally adopted in June 2014 [3].

This paper presents a retrospective review of all bacteraemia episodes reported in the HDUHB area between 2002 and 2016. The review was prompted following the continued increase of the *E. coli* bacteraemia rate (Figure 1), which was identified by HDUHB as a concern [3].

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https://doi.org/10.1016/j.jhin.2018.04.009
0195-6701/

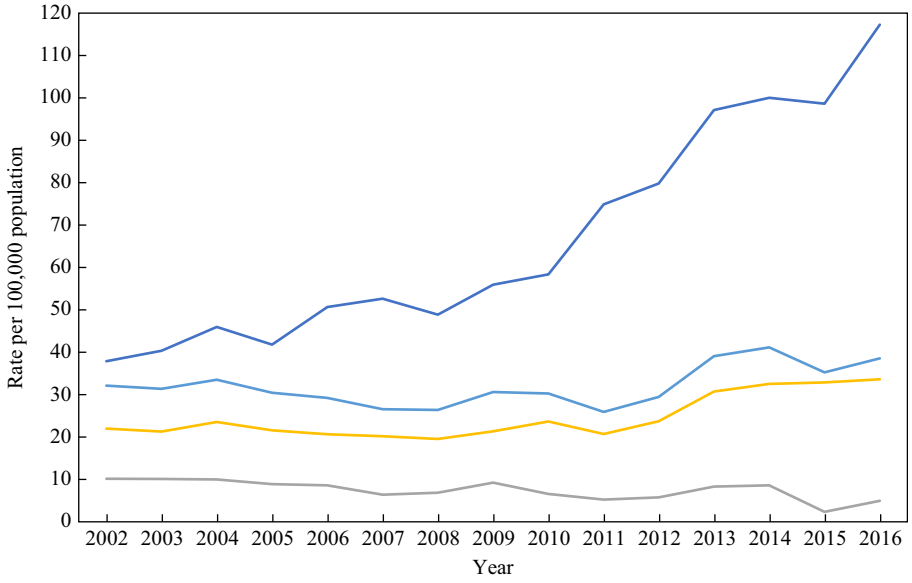

Figure 1. Annual change in organism rates. *Escherichia coli* (dark blue line), total *Staphylococcus aureus* (light blue line), meticillin-susceptible *S. aureus* (yellow line) and meticillin-resistant *S. aureus* (grey line) bacteraemia rates for 2002–2016.

While the HDUHB area continues to have the highest *E. coli* bacteraemia rate in Wales, other health board rates are also increasing, with some now approaching the HDUHB level. For the previous three years, and ongoing, the local infection prevention and control programme has targeted the three principle healthcare-associated infections: urinary, respiratory and skin/soft tissue infections. Against this background, the increase in *E. coli* bacteraemia rate in 2016 was surprising, and prompted a full review of all blood cultures (positive and negative) for the previous 15 years in an effort to understand what might be behind this unexpected increase.

Methods

Pathology laboratories in Wales use the all-Wales Laboratory Information Management System (LIMS) (TrakCare Lab, InterSystems Corporation, Cambridge, USA). Local microbiology services moved to this system from June 2012. Previously, the three local laboratories used separate LIMS provided by Telepath (Computer Sciences Corporation). However, in Wales, all microbiology results, positive and negative, are uploaded to DataStore; this is a data warehouse/repository of microbiology results that provides long-term data storage and is LIMS independent, storing results in a standardized consistent way regardless of historical idiosyncratic LIMS configurations (Mark Thomas, lead developer, personal communication.)

Using DataStore, separate downloads for all blood cultures from 2002 to 2016 were obtained for each laboratory and exported to Excel spreadsheets (Microsoft Corp., Redmond, WA, USA). The totals for all organisms and the total number of blood cultures for each month were calculated, subtracting positive cultures from total cultures to give the negative cultures.

The positive numbers include all potential blood culture contaminants. From laboratory data such as these, it is impossible to determine whether a particular isolate has clinical significance. For the purpose of this exercise, blood culture isolates reported as coagulase-negative staphylococci (CNS), proprionobacteria, corynebacteria, micrococcus or mixed CNS were deemed to be contaminants. However, CNS that were speciated were not included in the 'contaminant' count; pragmatically, it was considered that identification to species level had been prompted by an opinion that the isolate was clinically significant. Subtracting the number of contaminants from the total number of positive cultures resulted in an 'adjusted positive' result, and this was added to the number of negative cultures to produce an 'adjusted negative' result. The ratios of positive to negative cultures and adjusted positive to negative cultures were calculated.

Data for the three laboratories were summed for each month to arrive at HDUHB level figures prior to export for analysis.

Analysis was undertaken by Change Point Analysis [4] using Change Point Analyzer from Taylor Enterprises Inc. (www.variation.com/cpa), using the developer's recommended method [5]. Default confidence levels for identifying candidate changes at 50%, confidence level for inclusion in the table of changes at 95%, and confidence interval around change at 95% were used. The system was set to use 10,000 bootstrap iterations. For all figures, data were aggregated into three-month blocks (quarters) to smooth the peaks and troughs in monthly data. For each parameter inspected, there were 45 quarters to plot.

Results

Just under 200,000 blood culture sets were taken during the study period. The outputs from the change point analysis are presented as a series of figures. The x-axis is the timeline, while the y-axis is the count or ratio of blood culture numbers. Each data point is the mean for the quarter. Upper and lower control limits for the whole data set appear as solid lines, while the shaded area shows the limits of the 'expected variation' of the fitted model. Thus, change points of both mean and

Table I
Numerical output from change point analysis software

Figure	Change points	Confidence interval	Confidence level	From	To	Level
2: Total blood cultures	Oct-03	Oct-03, Oct-04	98%	857.52	979.49	2
	Apl-11	Apl-11, Apl-11	100%	979.49	1294.7	1
3: Positive blood cultures	Jul-03	Oct-02, Apl-04	100%	139.44	161.97	4
	Oct-11	Oct-11, Apl-12	100%	161.97	201.98	1
4: Negative blood cultures	Oct-03	Jul-03, Jan-05	96%	713.95	818.57	2
	Apl-11	Jan-11, Apl-11	100%	818.57	1043.3	1
	Oct-14	Apl-14, Jan-16	95%	1043.3	1175.6	3
5: *Escherichia coli*	Apl-06	Oct-05, Oct-07	100%	14.02	20.64	2
	Jul-12	Apl-12, Jul-12	100%	20.64	36.796	1
6: Meticillin-susceptible *Staphylococcus aureus*	Jul-12	Jul-11, Oct-13	100%	8.9683	13.352	1
7: Meticillin-resistant *Staphylococcus aureus*	Oct-06	Oct-05, Oct-08	100%	4.807	2.7398	2
8: Positive:negative culture ratio	Jul-10	Jul-05, Apl-13	99%	0.19979	0.18396	2
9: Adjusted positive:negative culture ratio	None noted	N/A	N/A	N/A	N/A	N/A
10: Contaminants	Jan-04	Jul-02, Jan-06	97%	0.079167	0.070815	1
	Apl-15	Oct-13, Jul-15	100%	0.070815	0.060476	2

variation (if any) are readily visualized in the graph, with detailed summaries in Table I.

Figure 2 shows total blood cultures grouped by three-monthly periods. Change point analysis notes changes at October 2003 and April 2011. Figures 3 and 4 show the total unadjusted positive and negative cultures. Both note the same early change in 2003, similar to the total cultures, and the later change in 2011, albeit with variation in the confidence intervals

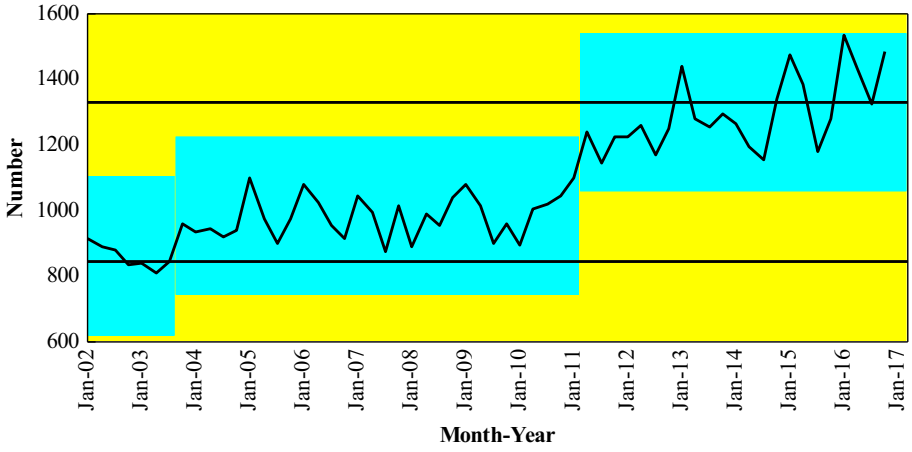

Figure 2. Change in total blood cultures submitted.

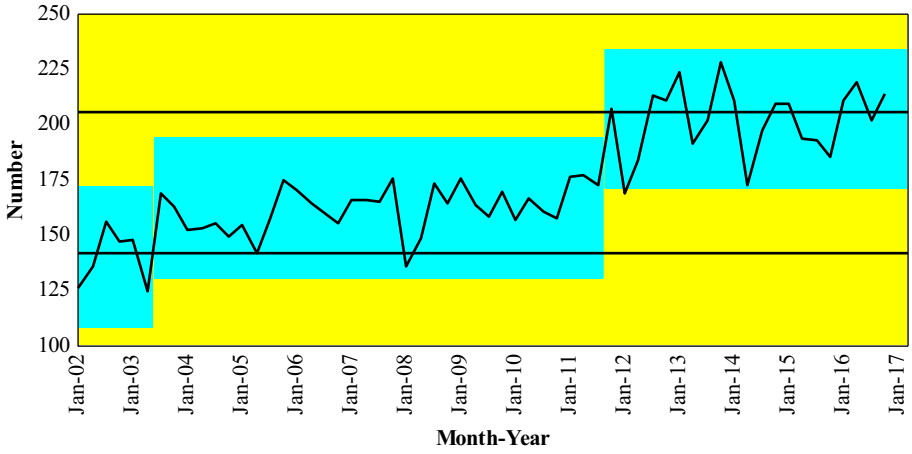

Figure 3. Change in positive blood cultures.

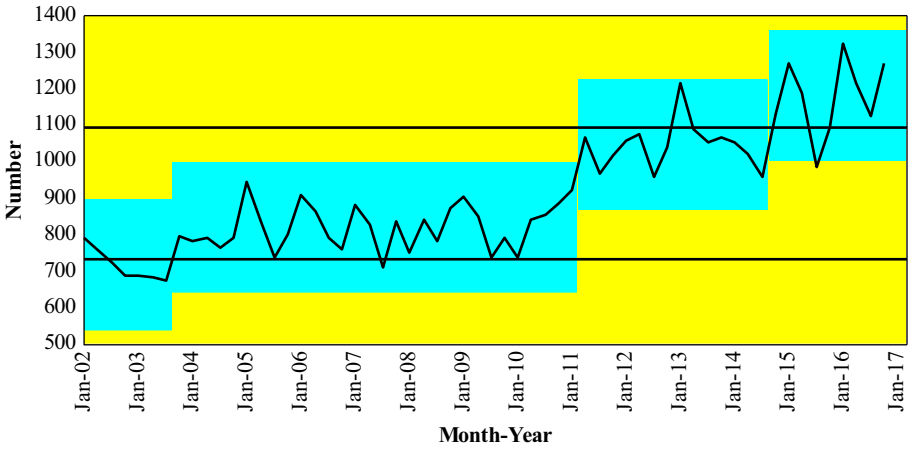

Figure 4. Change in negative blood cultures.

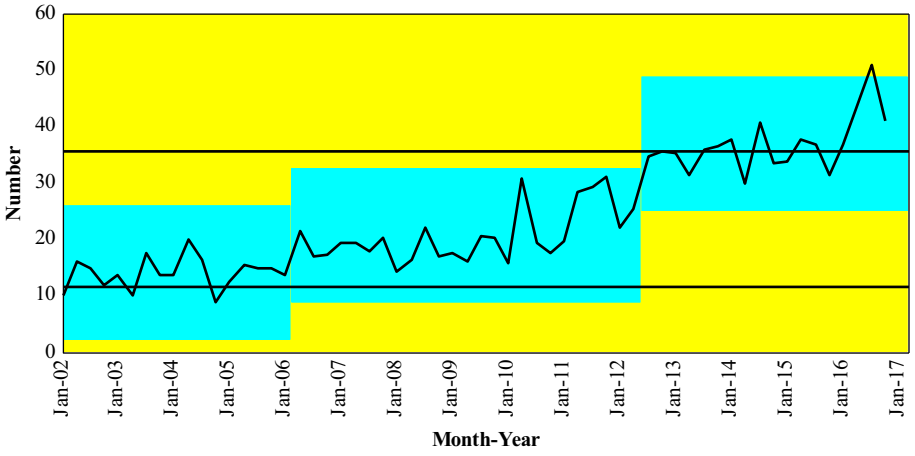

Figure 5. Change in *Escherichia coli* bacteraemia numbers.

(Table I). The negative cultures have a further change in October 2014. Figure 5 illustrates the change in *E. coli* over the 15 years. Two change points are identified: an earlier change in April 2006 with wide confidence intervals, and a later change in 2012.

Similar patterns of change were noted for the second most common organism, meticillin-susceptible *Staphylococcus aureus* (MSSA) (Figure 6), which had a parallel increase more recently with *E. coli*; this was not noted for meticillin-resistant *S. aureus* (MRSA) (Figure 7). Figure 8 shows the ratio of positive

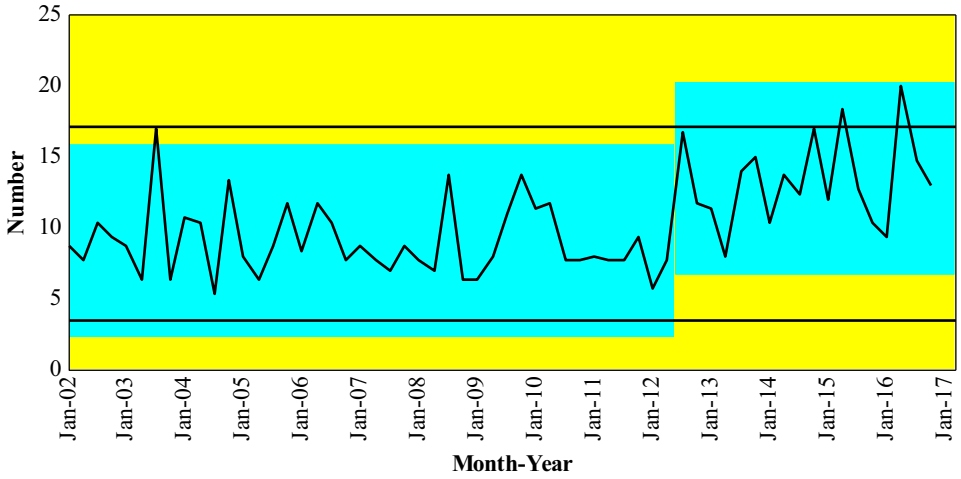

Figure 6. Change in meticillin-susceptible *Staphylococcus aureus* bacteramia numbers.

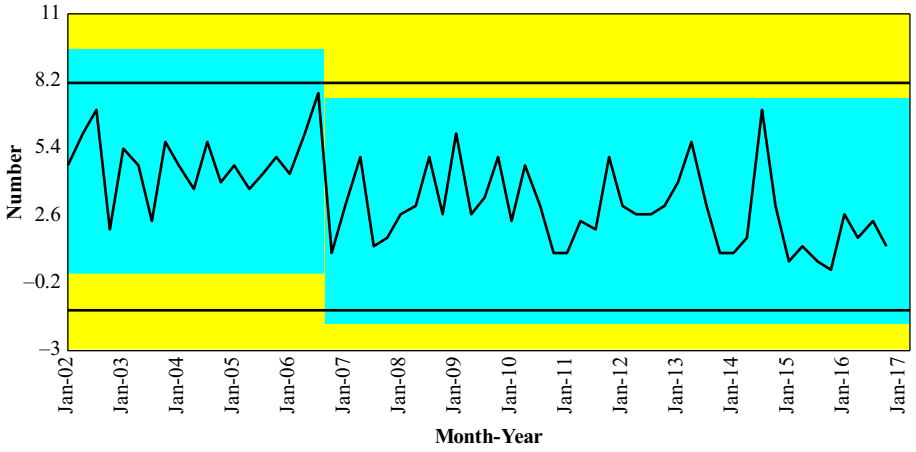

Figure 7. Change in meticillin-resistant *Staphylococcus aureus* bacteramia numbers.

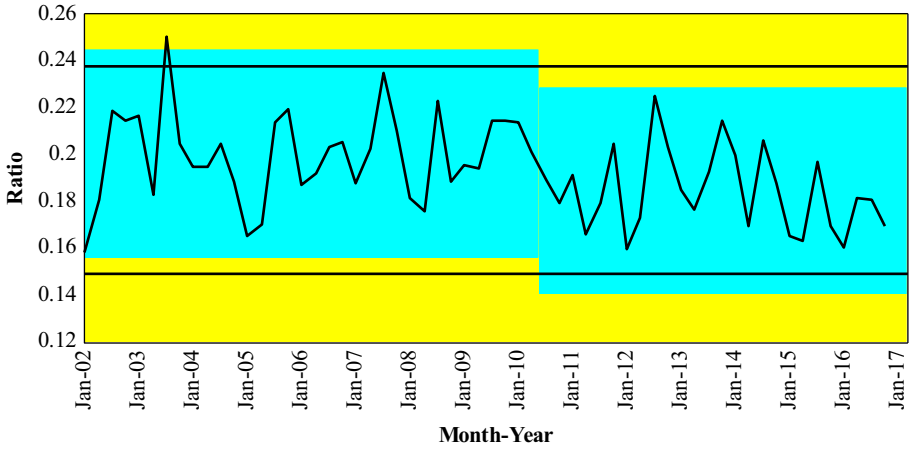

Figure 8. Change in ratio of positive to negative cultures.

to negative cultures, Figure 9 shows the adjusted positive to negative cultures, and Figure 10 shows the change in rate of contaminants over the 15 years.

Discussion

From 2014, with additional resources provided by HDUHB for infection prevention, an extensive programme of clinical engagement commenced, using a complexity science approach to healthcare-associated infection [3]. This identified significant changes. However, the expected decline in *E. coli* bacteraemia was not observed.

This bacteraemia investigation demonstrated unexpected results, and provides an explanation of why the anticipated reduction in *E. coli* bacteraemia has not occurred despite increased infection prevention activities. Looking at all blood culture results over 15 years, rather than concentrating on individual organisms, demonstrated a set of consistent results.

There were two principal change points over the past 15 years. An early change occurred sometime around 2005/06. Corporate memory failed to identify any clinical or laboratory reason for the increase. By 2005, the laboratories were all using automated blood culture detection systems, so this change is not considered to be a result of increased sensitivity of the testing.

The more marked change, however, occurred over the past six years and is demonstrated in both negative and positive results. Since 2010 in HDUHB, there has been considerable interest in increasing morbidity and mortality in local hospitals associated with sepsis presentations. As such, the project lead for the sepsis programme in Wales was approached and asked about the timings for the all-Wales programme. He advised that sepsis screening tools were introduced across Wales in April 2012, and embedded in all acute hospitals by April 2013. The screening and documentation was standardized in HDUHB in 2014, with improved compliance from 2015 onwards (Chris Hancock, personal communication).

Increases have been seen in two of the Welsh Government's target organisms — *E. coli* and MSSA — which coincides with the increased attention given to sepsis. These results appear to demonstrate increased sensitivity of sepsis screening. Since 2011, increased awareness of sepsis and the all-Wales sepsis programme have led to significantly more blood cultures being taken, as the selection criteria for triggering the sepsis bundle in Wales represents a low hurdle. While more blood cultures are being taken, an increase has been seen in all positive blood cultures, as well as those that are targeted: *E. coli* and

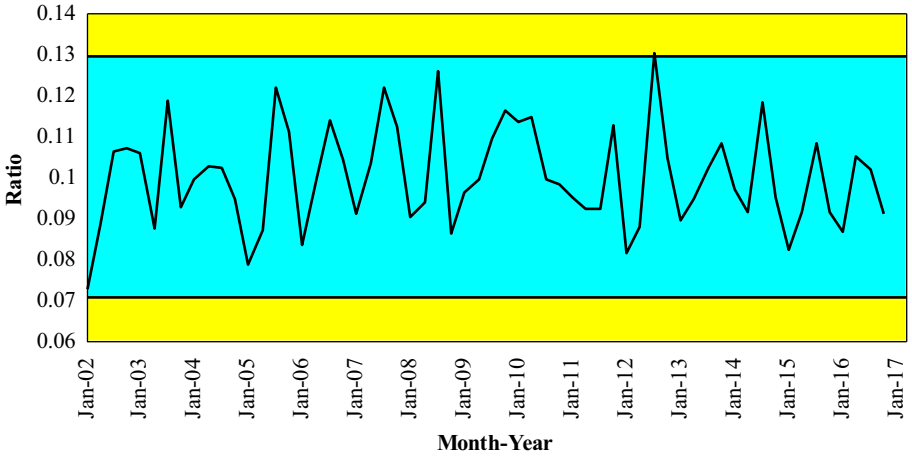

Figure 9. Change in ratio of adjusted positive to negative cultures.

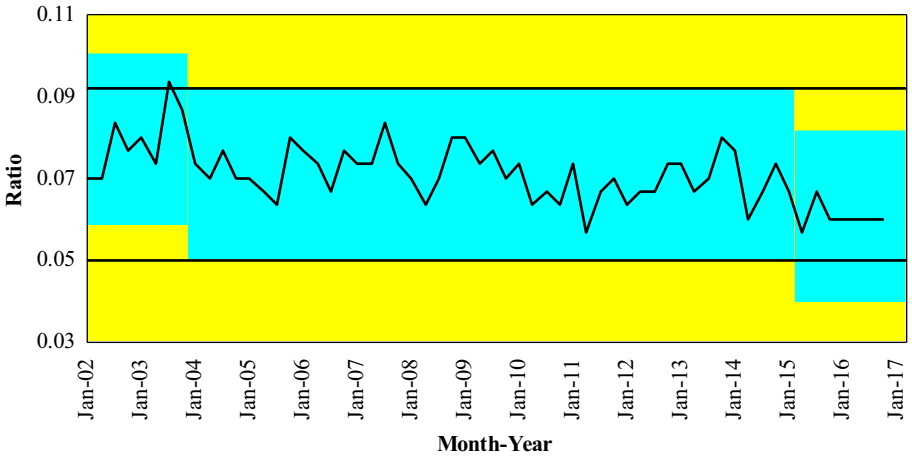

Figure 10. Change in number of contaminated blood cultures.

S. aureus. However, when looking at the ratio of positive to negative cultures, while there is an apparent reduction in the proportion of positive cultures from around May 2010, this disappears when using the adjusted positive and negative results; this may be due to a reduction in contaminants. While the confidence intervals for the change point for contamination are broad (Table I: October 2013–July 2015), the likely change point is noted as April 2015. This corresponds with the introduction of blood culture sampling packs across the four local hospitals from January 2015.

In conclusion, these results show the success of the sepsis programme, with additional improvement in quality by the reduction in contaminants following the introduction of blood culture sampling packs. The downside of a sensitive sepsis programme is the effect it has when looking at specific organisms. With the increase in *E. coli* and MSSA per 100,000 population, the Welsh Government has set challenging reduction targets. Similar targets have been set in England, but may be ill placed when viewed in the light of these findings. Requiring the National Health Service (NHS) to detect sepsis is leading to increased detection of *E. coli* and *S. aureus* bacteraemia. The *E. coli* target is therefore not being met simply as a result of increased sampling and increased detection, while the positivity rate remains unchanged. This is setting the NHS up to fail when seeking to reduce the *E. coli* and *S. aureus* rates.

These results also demonstrate that there is little benefit in maintaining an MRSA reduction target that has been achieved. The HDUHB area has been active since 2014 in having a community infection reduction programme. If any board area is to achieve the reductions required by the Welsh Government, this should occur first in the HDUHB area. Other Welsh health boards may see their levels exceed those of HDUHB as they begin their sepsis reduction journeys. With inter- and intra-country discussions around the best screening tools for sepsis, choice may influence the number of bacteraemia detections. Alternative metrics such as the ratio of positive to negative cultures may be a better measure of real change.

Conflict of interest statement
None declared.

Funding sources
None.

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