NHS National Services Scotland

Review of NHSGG&C paediatric haemato-oncology data

Health Protection Scotland

Report date
October 2019

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Introduction

Health Protection Scotland (HPS) supported NHS Greater Glasgow and Clyde (NHSGG&C) with a recent water related incident (March 2018 – September 2018) investigating and managing a contaminated water system across the Queen Elizabeth University Hospital (QEUH) and Royal Hospital for Children (RHC) with probable linked cases of bloodstream infections associated with wards 2A/2B RHC. Yorkhill Hospital (YH) relocated into the RHC in June 2015. Wards 2A/2B within RHC houses the haemato-oncology unit, also known as Schiehallion, the National Bone Marrow Transplant (BMT) Unit and the Teenage Cancer Trust (TCT). In September 2018, to allow remediation works to be undertaken in 2A/2B, patients were transferred to QEUH ward 6A and three rooms were allocated within the adult BMT of ward 4B for the paediatric BMT unit. To accommodate this move, adults from 6A were transferred to Gartnavel General. A **summary report** of the initial incident (Jan –Sept 2018) is available from Scottish Government web page.

Whilst a suspected increase in environmental Gram-negative blood cultures within ward 6A is investigated, admissions have been restricted since 1st August 2019.

The aim of this report is to review NHSGG&C paediatric haemato-oncology data and investigate the suspected increase in environmental Gram-negative blood cultures in the paediatric haemato-oncology population.

The objectives of this review are to:

- To describe the differences in the datasets currently being used to investigate cases of bacteraemia in patients cared for the in paediatric haemato-oncology wards in NHSGG&C.
- To review the environmental Gram-negative blood cultures in the paediatric haemato-oncology population.
- To identify whether there is a change in the type of reported environmental Gram-negative blood cultures in the paediatric haemato-oncology population.

Methods

The following data sets were provided for the review by NHSGG&C, further details can be found in Appendix 1 – Background information.

NHSGG&C data sets:

NHSGG&C CLABSI surveillance data

An extract was provided from the central line associated bloodstream infection (CLABSI) surveillance system for date range January 2015 –September 2019. CLABSI uses Centers for Disease Control (CDC) classification

> *'A CLABSI is a primary BSI in a patient that had a central line within the 48-hour period before the development of the BSI and is not bloodstream related to an infection at another site. However, since some BSIs are secondary to other sources other than the central line (e.g., pancreatitis, mucositis) that may not be easily recognized, the CLABSI surveillance definition may overestimate the true incidence of CRBSI'*

Paediatric haematology oncology patients were identified using theatre management system 'Opera' to obtain information on all patients who received a new central venous device at NHSGG&C and combining haematology oncology diagnosis via the Clinical Portal. This data was de-duplicated on a 7 day case definition per organism. Exclusion criteria include patients who have their central venous device inserted at another hospital even if the majority of their care was at RHC or if the patient was transferred to RHC with a CLABSI.

NHSGG&C ECOSS extract

Gram-negative extract was provided for data obtained locally from Electronic Communication of Surveillance in Scotland (ECOSS) for date range July 2013 – September 2019.

NHSGG&C Microbiology laboratory information management system (LIMS) Surveillance data

Microbiology laboratory information management system (LIMS) extract for date range June 2014 – September 2019. The dataset had been de-duplicated at species level by NHSGG&C. This is a dataset obtained through 'Telepath' the LIMS using a named consultant therefore linking cases from other hospitals/outpatients/previous admission/or coded elsewhere in the hospital which are linked to the unit through the consultant in charge of their care.

HPS dataset - ECOSS extract

A data extract from ECOSS system of all blood samples in children less than 18 years of age from 2013 to present was obtained the 7th October 2019. The following fields were used to assign the location of the samples. NHS Health Boards are coded by the location of the submitting laboratory. Additional hospital/ward data was derived from the ECOSS Unit Location field, or where incomplete free text within the medical specialty and requesting location fields were used to generate a final hospital list to be mapped against the total occupied bed days to generate hospital level rates.

For NHSGG&C hospitals, the free text within the unit location, medical specialty and requesting location fields are used to derive a location and ward within the hospital where the positive blood culture aspirated was associated, to find any specimens with a connection to wards 6A and 4B in the QEUH, ward 2A or 2B within RHC, or the equivalent within Schiehallion ward in Yorkhill hospital. In ECOSS the reporting laboratory codes for wards 6A and 4B were coded to RHC following the move to QEUH.

Positive blood cultures of the following micro-organisms were grouped. A full breakdown of the grouping is detailed in the Appendix 1:

- **Gram-negative bacteria**
- **Gram-positive bacteria**
- **Environmental bacteria group** all species of the following: *Achromobacter; Acinetobacter; Aeromonas; Brevibacillus species; Brevundimonas; Burkholderia; Cedecea; Chryseobacterium; Chryseomonas; Clavibacter; Comamonas; Cupriavidus; Delftia acidovorans; Elizabethkingia; Flavimonas; Gordonia; Pseudomonas; Pseudoxanthomonas; Psychrobacter; Ralstonia; Rhizobium; Rhodococcus; Roseomonas; Sphingomonas; Stenotrophomonas and atypical mycobacteria).*
- **Environmental including Enteric (ENT) group** - Environmental bacteria including following enteric organisms which as well as the environmental list above includes species of the following *Citrobacter; Enterobacter; Klebsiella; Pantoea; Serratia.*

Fungi (all species of the following: Candida; Rhodotorula) were excluded as it could not be established if all positive fungi blood cultures were being processed through ECOSS.

The following organisms grouped by genus, were previously isolated in water samples from ward 2A/2B: *Acinetobacter; Burkholderia; Chryseobacterium; Cupriavidus; Delftia acidovorans; Elizabethkingia; Pantoea; Pseudomonas; Rhizobium; Stenotrophomonas*.

The following organisms grouped by genus, were previously isolated in drain samples from ward 2A/2B: *Citrobacter; Cupriavidus; Delftia acidovorans; Enterobacter; Klebsiella; Pantoea; Pseudomonas; Serratia; Stenotrophomonas.*

Case definition

The trends in bacteraemia in this patient population were assessed using the HPS ECOSS data extract of positive blood cultures.

The study population includes patients less than 18 years of age cared for in the paediatric haematology oncology specialty in NHSGG&C (including new and existing patients).

A species level case definition was used in previous investigations and this was repeated for this review in order to make comparisons with the NHS GG&C datasets.

In order to account for the diversity of organisms likely to be identified if there is an environmental source and to account for polymicrobial episodes, case definitions were developed at group level. These groups are defined as an environmental bacteria group, environmental including enteric bacteria group and Gram-negative group. These groups are not mutually exclusive; therefore the trends analysis should be interpreted as such. A case definition for Gram-positive bacteraemia was also developed to provide context to the trends in the other groups.

From this population the proposed case definition of a case is defined as a patient with:

1) A positive blood culture of a single organism that has not been previously isolated from the patient's blood within the same 14 day period (i.e. 14 days from date last positive sample obtained).
2) A positive blood culture for any organism defined as environmental bacteria group (detailed above) that has not been previously isolated with same or other environmental bacteria group organism in the patient's blood within the same 14 day period.
3) A positive blood culture for an environmental including enteric bacteria group (detailed above) that has not been previously isolated with same or other environmental including enteric bacteria group organism in the patient's blood within the same 14 day period.
4) A positive blood culture where Gram-negative bacteria has been isolated in 14 day period that has not been previously isolated with same or other Gram-negative organism within the same 14 day period.
5) A positive blood culture where Gram-positive bacteria has been isolated in 14 day period that has not been previously isolated with same or other Gram-positive organism within the same 14 day period.

As per the case definition and to align with other national bacteraemia surveillance, a standard 14 day rolling deduplication was applied to the HPS ECOSS dataset. All positive blood cultures were included with the exception of post mortem blood, any quality test samples, foetal samples or non-human samples.

Denominator data

HPS use extracted data from ISD(1) provided by Information Services Division (ISD) for routine published reports. Due to unavailability of data for September 2019 data from August 2019 were used as a proxy.

Full details of ISD data collection can be obtained from http://www.isdscotland.org/Products-and-Services/Data-Support-and-Monitoring/ISDS1/

The activity data extract provided information on occupied bed days and bed occupancy of haematology and oncology from July 2013 to August 2019. In addition, it provided data on combined haemato-oncology day cases and outpatient appointments. The outpatient figures included patents who did not attend (DNA).

Incidence Rate

Rate per 1,000 total occupied bed days (TOBDs) = (Number of cases of positive blood culture of given case definition in hospital(s) or speciality /TOBDs in hospital(s) or speciality x 100,000). Incidence rates for the whole of RHC (including positive blood cultures and bed days of wards 6A and 4B following the move to QEUH) were compared with combined rates from the Royal Hospital for Sick Children in Lothian and the Royal Aberdeen Children's Hospital in Grampian. R was used to calculate rate ratios (RR) with corresponding exact 95% Confidence Intervals (95%CI).

SPC Charts

Hospital and specialty data were analysed using Byars method for statistical process control (SPC) U-charts using the rules detailed in Table 1. The mean, trigger/warning (+2 standard deviations) and upper control limits (+3 standard deviations) are presented. These control lines vary by month due to variations in the TOBD denominator. The mean was calculated from the data prior to the move to RHC when available (HPS and NHSGG&C Gram-negative data). Further information on SPC charts can be found at : http://www.isdscotland.org/Health-Topics/Quality-Indicators/Statistical-Process-Control/

Table 1: Statistical Process Control (SPC) rules.

Rule	Description	Marker
Outlier	Data point(s) exceeding the upper or lower control limit (as 3 standard deviations)	Red diamond
Trigger point	Data point(s) exceeding the upper or lower warning limit (as 2 standard deviations)	Yellow triangle
Shift	A run of 8 or more consecutive data points above the centreline	Circle drawn round points
	A run of 6 or more consecutive data points either increasing or decreasing.	N/A

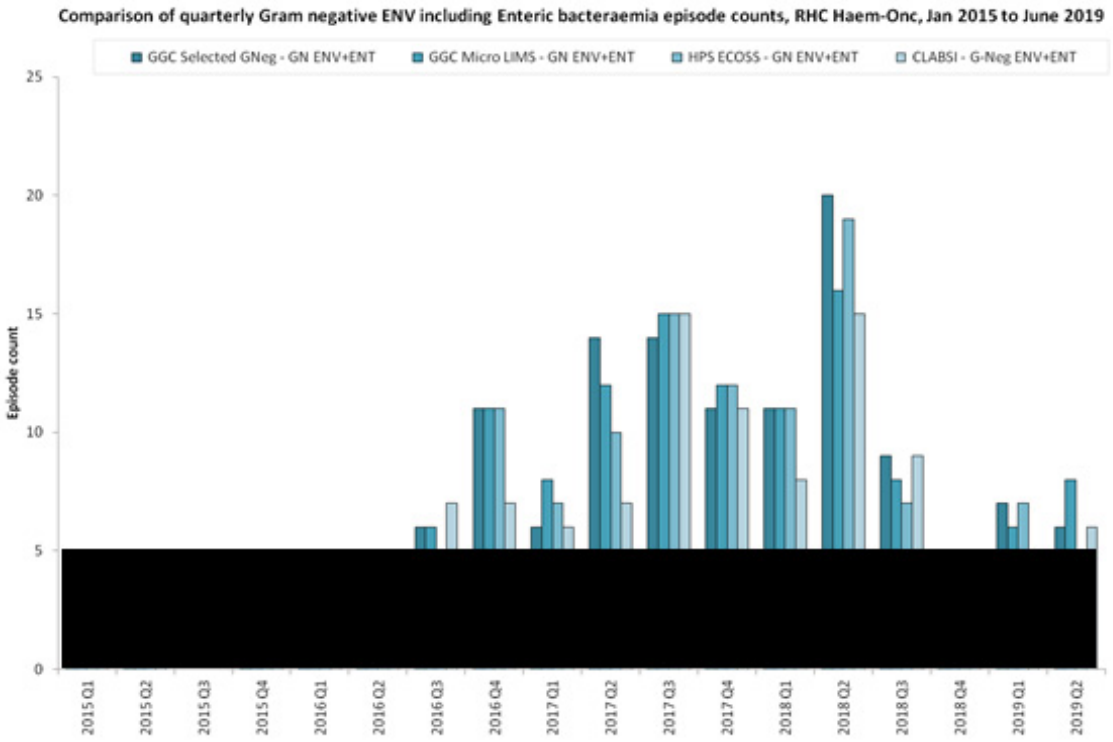
Results and Commentary

Comparison of datasets (species level)

In order to validate the datasets provided by NHSGG&C they were compared with an extract taken by HPS (ECOSS extract) a single organism at species level case definition (**1**) was used so all isolates could be compared. The datasets that were provided all contained data covering the period from January 2015 to June 2019. Figure 1 shows the differences between the datasets when selected environmental Gram-negative organism were compared. The main difference found between the datasets are detailed in Table 2 and Table 3.

It is important to note that each dataset used different case definitions and methods to identify patients who had samples taken or treatment in RHC haemato-oncology unit which accounts for most of the discrepancies identified between datasets.

Figure 1: Comparison of NHSGG&C selected Gram-negative quarterly counts of species level case definition (1) for NHSGG&C and HPS datasets from 2015 Quarter 1 to 2019 Quarter 2.



1. Source of data is Electronic Communication of Surveillance in Scotland (ECOSS), NHSGG&C central line associated bloodstream infection (CLABSI) surviellance system, and NHSGG&C laboratory information management system (LIMS).

Table 2: NHSGG&C CLABSI surveillance data and possible reasons for dataset not matching for the time period January 2015 and September 2019.

HPS episodes without corresponding NHSGG&C episode (n=118, 20.8%)	NHSGG&C episodes without corresponding HPS episode (n=56, 12.4%)
Possible contaminants (n=48, 40.7%) (only one result available for common skin contaminants coagulase-negative staphylococci, *Micrococcus spp., Propionibacterium acnes, Bacillus spp., Corynebacterium spp*.)	Location mapping 53.6% (n=30) could not be identified as belonging to the RHC haematology oncology cohort based on the details of their ECOSS result.
Differences in inclusion and exclusion criteria in CLABSI data - 48.3% (n=57) were either known pathogens or had more than one positive and were included in the other NHSGG&C datasets.	Using de-duplication of 7 rather than 14 days - 23.2% (n=13)
Using de-duplication of 7 rather than 14 days - [redacted]).	Missing in ECOSS [redacted]) of results were not in ECOSS but were included in the NHSGG&C Micro LIMS dataset.
Location errors [redacted]) were not included in any of the NHSGG&C datasets therefore it is likely that they were not part of the true RHC Haem-On cohort.	18 years of age or above excluded by HPS – [redacted])

1. Source of data is Electronic Communication of Surveillance in Scotland (ECOSS) and NHSGG&C central line associated bloodstream infection (CLABSI) surviellance system.

Table 3 NHSGG&C Microbiology LIMS surveillance data and possible reasons for dataset not matching for the time period June 2014 and September 2019.

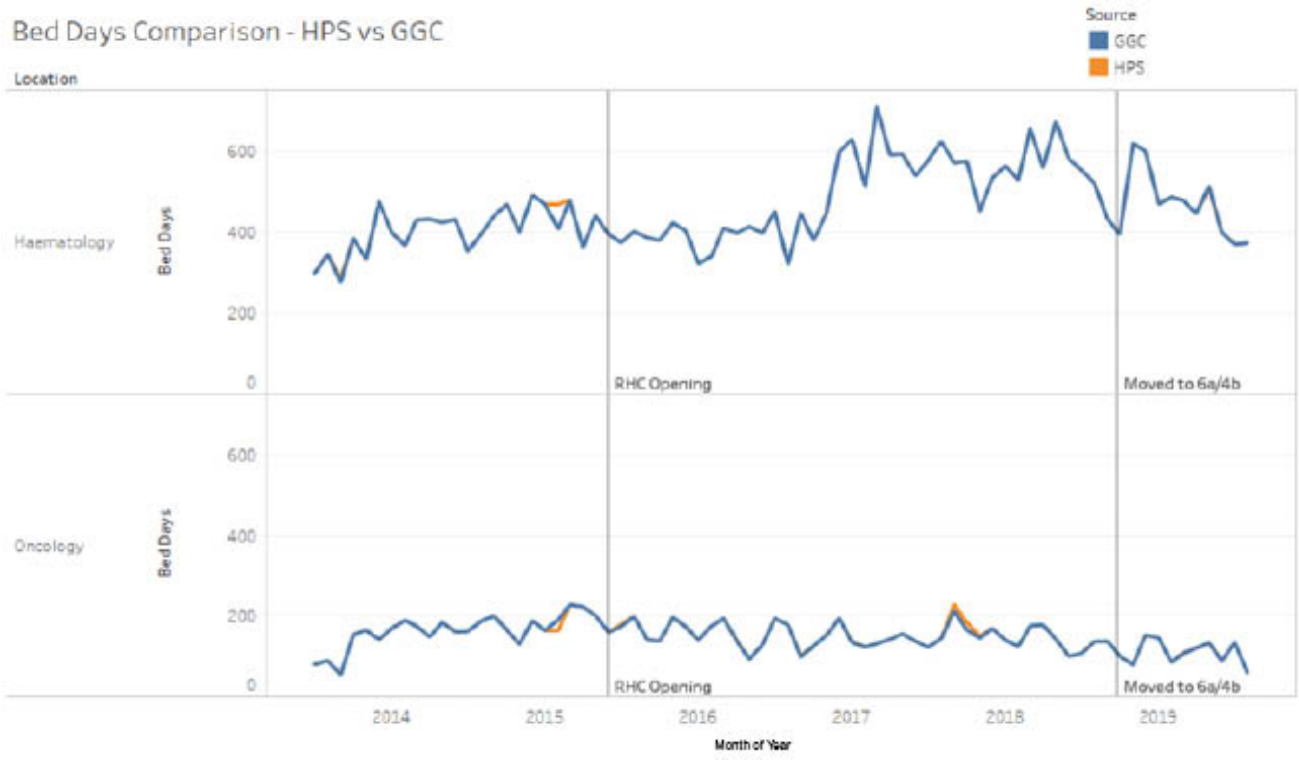
HPS episodes without corresponding NHSGG&C episode (n=42, 6.8%)	NHSGG&C episodes without corresponding HPS episode (n=85, 12.9%)
HPS episodes with corresponding results listed in NHS GGC CLABSI dataset but missing in Micro LIMS data (n=25, 59.5%)	Micro LIMS data included 24 (28.2%) episodes that should have been excluded using the 14 day species de-duplication rule.
Episodes missing from both the NHSGGC Micro LIMS and CLABSI datasets (n=15, 35.7%). [redacted] of these specimens were not collected from haem-oncology wards so were unlikely to be part of the true RHC Haem-Onc cohort and can be excluded from surveillance. [redacted] were possible contaminants with only one result available in ECOSS and can be excluded from surveillance. [redacted] were known enteric pathogens and aspirated in haem-oncology wards. [redacted] was an environmental organism which was also included in the NHSGGC selected Gram-neg dataset.	Location mapping 29.4% (n=25) could not be identified as belonging to the RHC haematology oncology cohort based on the details of their ECOSS result. Ten of these patients had their start of episode specimens taken in different hospitals across six health boards.
ECOSS result not updated with species name, these should be excluded as episodes during deduplication [redacted]	18 years of age or above excluded by HPS – [redacted]
	Non-blood culture specimens excluded by HPS – [redacted] This included four bone marrow specimens and one pus.
	Missing in ECOSS -30.6% (n=26) of results were not in ECOSS. Of these 10 were included in the NHSGG&C CLABSI dataset.

1. Source of data is Electronic Communication of Surveillance in Scotland (ECOSS) and and NHSGG&C laboratory information management system (LIMS).

Review of denominator data

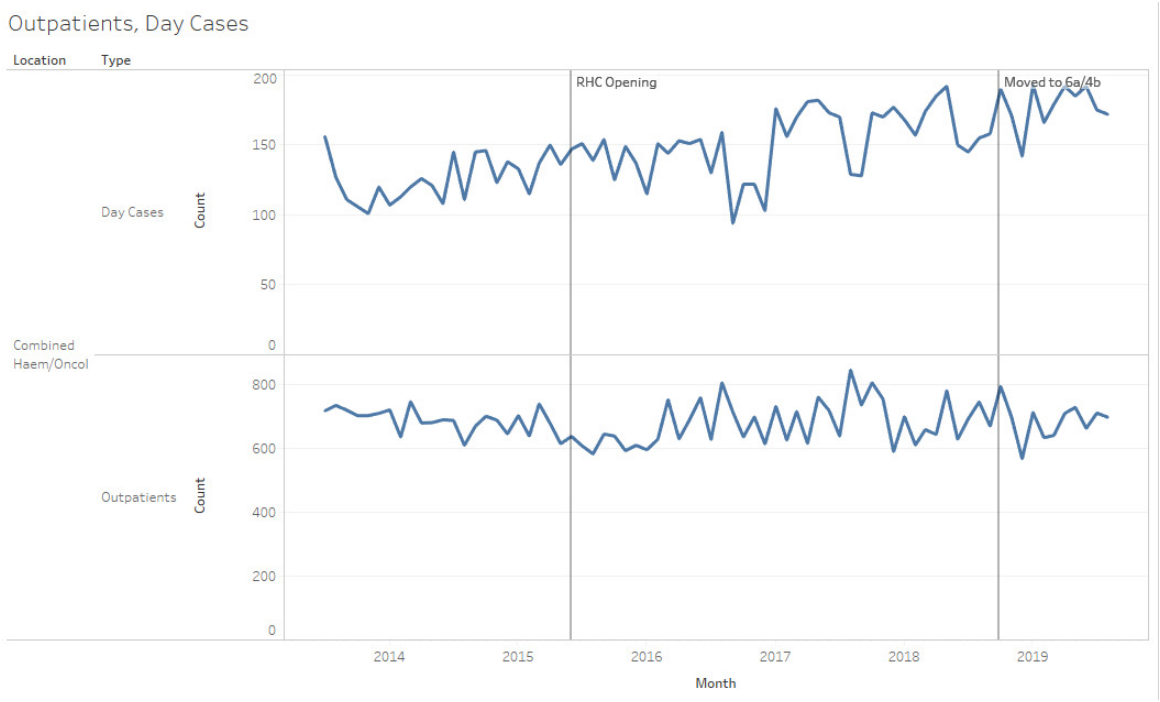
The NHSGG&C activity data was also validated by comparing it to data held by HPS provided by Information Services Division (ISD) and only minor differences were shown (Figure 2). An increase in occupied bed days' activity occurs in haematology in December 2016 which was not mirrored in the oncology figures. Activity data for day cases and outpatients including patients that did not attend (DNA) is shown in Figure 3 showing a gradual increase in day cases following the move to RHC.

Figure 2: Review of total occupied bed days by haematology and oncology specialities for the time period July 2013 to August 2019.



1. Total occupied bed days: Activity data (provided by NHSGG&C) & Information Services Division ISD(S)1 (HPS).

Figure 3: Day cases and outpatient appointments (including did not attend) of combined haematology and oncology activity from July 2013 to August 2019.



1. Activity data provided by NHSGG&C.

Case level data

From the data obtained by HPS from ECOSS there were 688 positive blood culture episodes at species level (case definition 1) for under 18 paediatric haematology oncology population in NHSGG&C linked to RHC between July 2013 and September 2019. From the 688 species level cases, 167 episodes were classed as environmental including enteric group from 97 different patients. Approximately one third (33.5%, n=56) of the species episodes reported formed part of polymicrobial environmental gram negative bacteraemia episodes.

For case definition 2, there were 70 cases of environmental organisms, and when expanding this group to include enteric organisms (case definition 3), there were 132 cases.

When deduplicating at Gram-stain level (case definitions 4 and 5), there were 390 cases of Gram-positive group organisms and 176 cases of Gram-negative group organisms.

Using the Gram-negative case definition an upward shift with a run of ten data points above the mean was observed from March to December 2017, with the upper warning limit (UWL) breached in August 2017, March 2018, May 2018 and again in September 2019 (Figure 4).

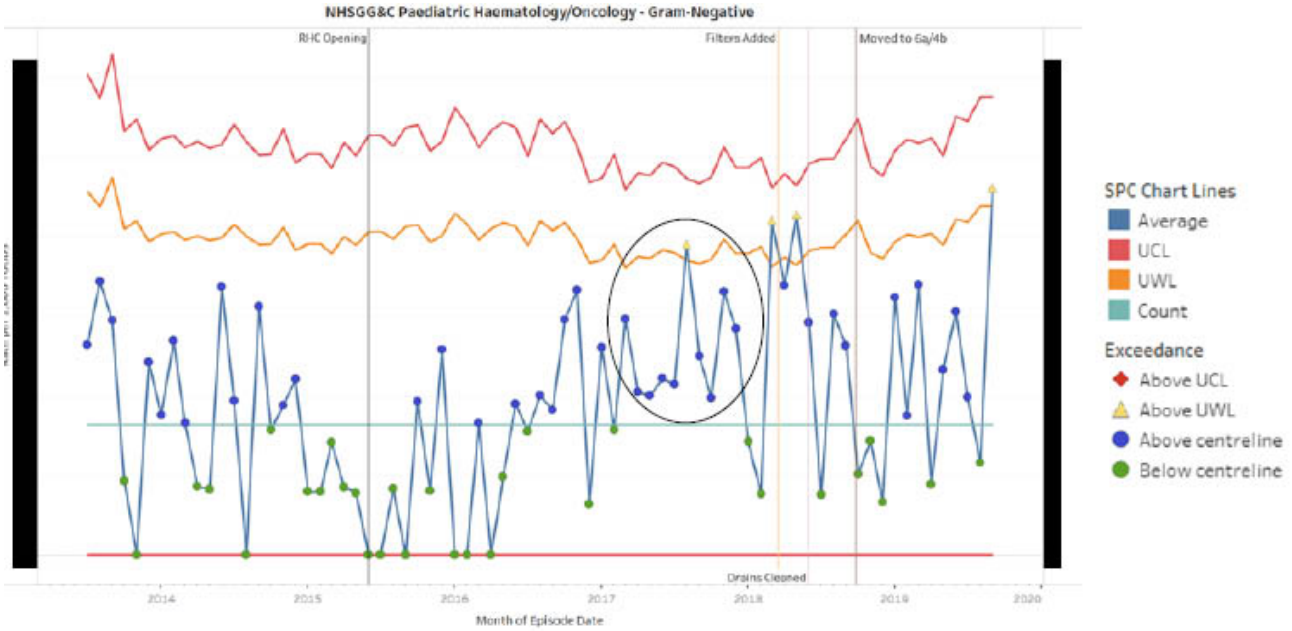
Figure 5 shows the SPC chart for the environmental group case definition. The UWL was breached in June 2018. The environmental group was extended to include selected enteric organisms such as species of *Enterobacter; Klebsiella* that were linked with drain contamination. The environmental including enteric group is described in Figure 6, showing the UWL was breached in March 2018 and March 2019.

Figure 7 describes the incidence of Gram-positive blood cultures in paediatric haematology oncology population. There was no upward shift in rates following the move to RHC however the upper control limit (UCL) was breached in January 2016, January 2017, April 2017 and June 2017. With rates above the UWL July 2016, May 2017, November 2017 and December 2017. Following the increase in activity at the RHC shown in Figure 7 with six out of twelve data points in 2017 breached a trigger limit (UWL or UCL). The rate now appears to be similar to that observed prior to the move to RHC with seven out twelve data points having a rate below the mean rate in the last year.

A summary of the SPC shifts and triggers shown in Figure 4 to Figure 7 is provided in Table 4.

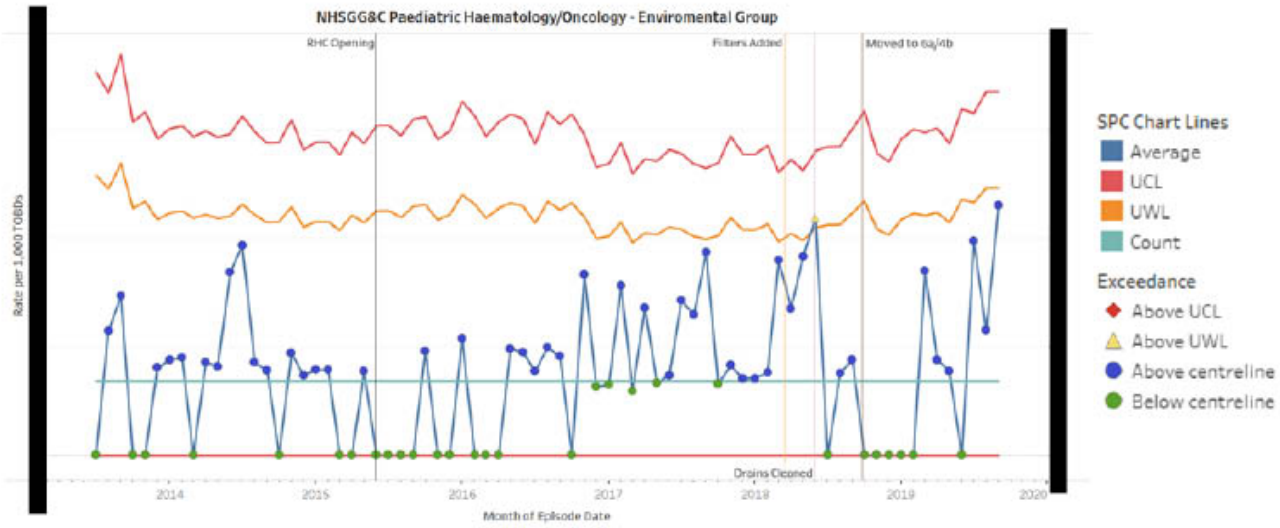
No change was observed when crude comparisons were made between the rates with the exception of the Gram-positive group (p=0.04) which significantly decreased when comparing the overall incidence before and after the move to RHC.

Figure 4: SPC chart using the Gram-negative case definition for HPS data from the July 2013 to September 2019.[1]



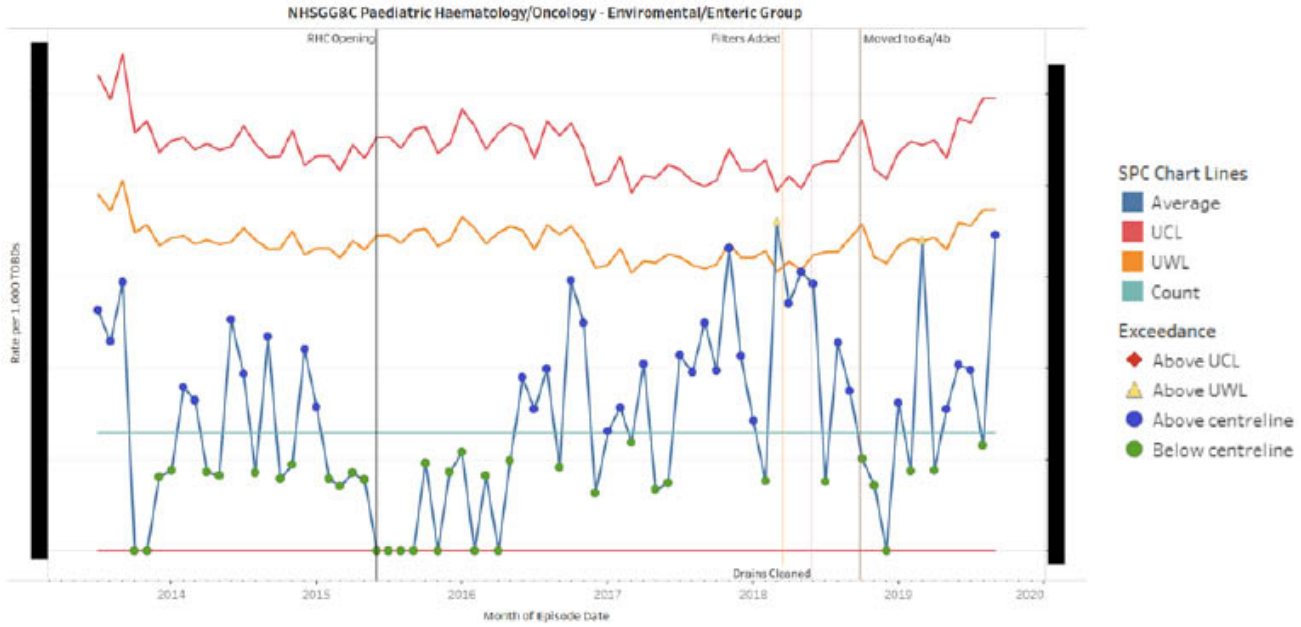
1. Source of data is Electronic Communication of Surveillance in Scotland (ECOSS) & Total occupied bed days: from activity data provided by NHSGG&C.

Figure 5: SPC chart using the environmental group case definition for HPS data from the July 2013 to September 2019.[1]



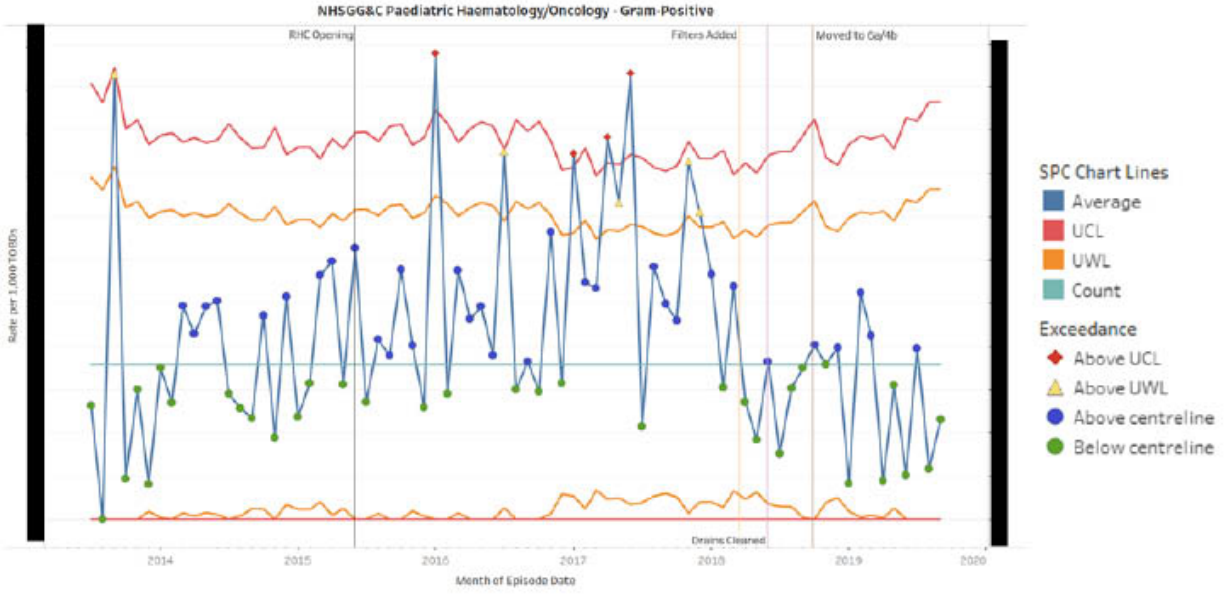
1. Source of data is Electronic Communication of Surveillance in Scotland (ECOSS) & Total occupied bed days: from activity data provided by NHSGG&C.

Figure 6: SPC chart using the environmental including enteric group case definition for HPS data from the July 2013 to September 2019.[1]



1. Source of data is Electronic Communication of Surveillance in Scotland (ECOSS) & Total occupied bed days: from activity data provided by NHSGG&C.

Figure 7: SPC chart using the Gram-positive case definition for HPS data from the July 2013 to September 2019.[1]



1. Source of data is Electronic Communication of Surveillance in Scotland (ECOSS) & Total occupied bed days: from activity data provided by NHSGG&C.

Table 4: Summary table listing SPC shifts, trigger points (UWL breach) and outliers(UCL breach) following the move to RHC using HPS data from July 2013 to September 2019.[1]

Year	Gram-positive	Gram-negative	Environmental	Enviro/Enteric
2015				
2016	Jan 2016 (UCL)			
	July 2016 (UWL)			
2017	Jan 2017 (UCL)	Upward shift (Mar 2017 – Dec 2017)		
	April 2017 (UCL)	Aug 2017 (UWL)		
	May 2017 (UWL)			
	June 2017 (UCL)			
	Nov 2017 (UWL)			
	Dec 2017 (UWL)			
2018		March 2018 (UWL)	June 2018 (UWL)	March 2018 (UWL)
		May 2018 (UWL)		
2019		Sept 2019 (UWL)		March 2019 (UWL)

1. Source of data is Electronic Communication of Surveillance in Scotland (ECOSS) & Total occupied bed days: from activity data provided by NHSGG&C.

Comparison with other health boards

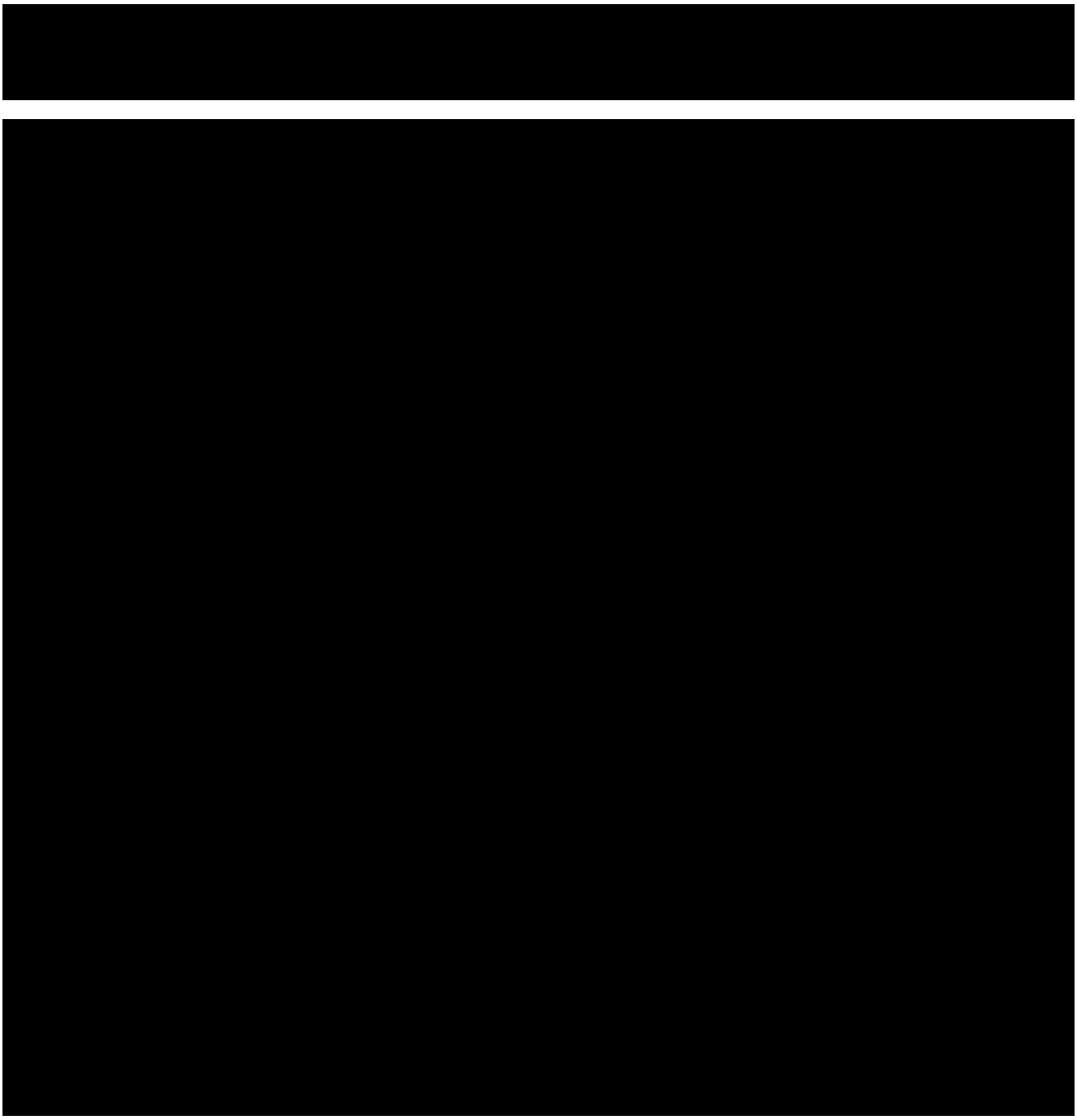
When comparing the overall hospital rate of positive blood cultures since the move to RHC (June 2015 to September 2019) to the combined rate of the other two Scottish children's hospitals (Royal Aberdeen Children's Hospital (NHS Grampian) and Royal Hospital for Sick Children (NHS Lothian)), the incidence of positive blood cultures, using the case definitions 2 to 5, was higher in RHC for environmental including enteric group (RR= 1.86 95%CI 1.42-2.47, p<0.001), but lower for Gram-positive group (RR=0.76, 95%CI 0.70-0.83, p<0.001). There was no difference in the rates of Gram-negative group (RR=1.18, 95%CI 0.96-1.42, p=0.07) or environmental group (RR=1.42, 95%CI 0.94-2.16, p=0.11).

When compared over two years (October 2017 to September 2019), the rate of positive blood cultures was higher in RHC for environmental including the enteric group (RR=1.70, 95%CI 1.17-2.53, p<0.005) and Gram-negative group (RR=1.31, 95%CI 1.00-1.73, p=0.05) but lower for the Gram-positive group (RR=0.74, 95%CI 0.66-0.84, p<0.001). There was no difference in the rates of the environmental group (RR=1.36, 95%CI 0.77-2.52, p=0.39).

In the last year following the move to QEUH (October 2018 to September 2019) there was no difference in the rate for Gram-negative group (RR=1.23, 95%CI 0.85-1.80, p=0.30), environmental including the enteric group (RR=1.26, 95%CI 0.74-2.18, p=0.44) or environmental group (RR=0.93, 95%CI 0.41-2.23, p=1) however the rate was lower for the Gram-positive group (RR=0.77, 95%CI 0.64-0.93, p=0.005).

Diversity of Environmental Organisms

The diversity of organisms isolated in the haemato-oncology unit prior and post move to RHC for the environmental group and the environmental including enteric group are shown in Figure 8 and Figure 9.



Caveats

There are a number of limitations associated with the use of ECOSS blood culture data. Blood samples are non-validated records. The cases may include interim results, contaminants, and may include non-blood cases which are incorrectly mapped to a blood sample within either the laboratory system or within ECOSS. Location mappings within ECOSS records may also be prone to error and it may be difficult to capture all haemato-oncology patients admitted to other RHC or YH wards who subsequently had a positive blood culture. Gram-negative blood culture data may be incomplete for September 2019 and non tuberculous mycobacteria data may be incomplete from July 2019 onward as samples are still to be reported. Due to uncertainty over positive fungal blood samples coming into ECOSS they were excluded from this review.

Improvements in speciation, for example using MALDI-TOF technologies, may change the identification over time. Species level case definitions may result in a patient having more than one episode of positive blood culture in a 14 day period.

Environmental bacteria grouping include bacteria commonly found in the environment however they may also be associated with normal human microbiome and laboratory surveillance is unable to distinguish.

It is not possible to determine whether changes in episodes are confounded by changes in the patient population and their underlying medical conditions.

The rates used to compare the overall rate at RHC following the move to QEUH to the combined rate of the other two Scottish children's hospitals used an estimated denominator (Total Occupied Bed Days) for September 2018 by taking the proportion of days following the move.

In the monthly analysis of environmental bacteria positive blood cultures, the numbers are small and should be treated with caution.

The main reasons documented about discrepancies in the review of datasets were only the most likely reason and due to time constraints were not further investigated.

Summary and Recommendations

This report provides a review of datasets currently being used in NHSGG&C and HPS to support the investigation of this incident; an updated description of trends in positive blood cultures; and a description of the diversity of organisms.

One of the key objectives of this review was to assess the NHSGG&C datasets and provide assurance that the data provides an accurate reflection of the current epidemiological situation in this patient population and where differences exist, to understand reasons and assist with the interpretation. The results from this exercise suggest that the datasets currently used by NHSGG&C provide important intelligence that is aligned with the microbiological data held nationally in ECOSS. There are pros and cons to each of the datasets. The ECOSS and LIMS microbiology datasets do not provide clinical information relating to the cases, without this it is difficult to ensure that the blood cultures are true cases of clinical bacteraemia and there is limited epidemiological and clinical information to support investigation. The CLABSI dataset includes clinical information but has strict case definitions that may exclude cases of bacteraemia associated with the haemato-oncology specialty including those presenting in the first 48 hours of admission and those where the line was inserted in another unit.

Reviewing monthly SPC charts has been shown to be an appropriate method in identifying triggers and outliers when a stable period can be used to set the mean. In this review, the crude incidence rates before and after the move did not reflect the variation in incidence over time within this population. The changes in activity, in particular the occupied bed days, have highlighted the importance of considering activity when interpreting charts and where possible to use incidence rates in SPC charts. The use of grouped case definitions have allowed the data to be reviewed without reporting bias of selecting significant organisms or over reporting when multiple organisms are isolated from the one patient.

The SPC charts included in this report describe that there has been instances of variation outside what would normally be expected in this patient population, the latest was a breach of an upper warning limit for Gram-negative blood culture episodes in September 2019. The characterisation of these cases alongside understanding in the context of environmental microbiology is critical to understanding and managing risk.

The purpose of developing triggers that identify areas where the number of cases is out with what would normally be expected due to random variation, is to identify when it is appropriate to instigate a local investigation into the possible increase in cases. In order to ensure that appropriate action is taken, high sensitivity where there is a high degree of suspicion for increased number of cases is important, particularly in such a vulnerable population. For this reason, the use of microbiological laboratory data rather than the CLABSI data would provide a more sensitive measure for identifying areas for local investigation.

Triggers for areas where there is a need to monitor infectious agents with a possible environmental source that are based on groups of organisms rather than single species triggers likely provides a better measure. This is due to the complex microbiology of

environmental sources. The data presented in this report provide a starting point for supporting the development of appropriate triggers for environmental pathogens. The organisms included in the environmental category can be reviewed following the comprehensive literature reviews being undertaken by HPS for Chapter 4 of the National IPC Manual.

These analyses also indicate that approximately a third of cases of positive blood culture of environmental organisms had a polymicrobial episode. This observation provides an indication of the complexity of the interpretation of microbiology data in the absence of clinical data for this patient population. In addition, there were patients who had multiple episodes of positive blood cultures with different organisms over extended periods of time. Again, the interpretation of the data requires clinical data collected systematically to support interpretation of both unusual clinical pictures and breaches in the limits in SPC charts. The microbiological and clinical data should also be set in the environmental context including the environmental microbiology results such as water and ventilation sampling.

The data presented in this report do not provide evidence of single point of exposure and there is a need to continually monitor the risk in this patient population. There is no immunity to the organisms under investigation, therefore all patients within this cohort are at risk from developing gram negative bacterium due to their co morbidities and treatment plan. The control measure of restricting clinical services for newly diagnosed patients over existing patients should now be reconsidered.

The following recommendations should be considered:

- NHS GG&C should systematically collect clinical data on cases to describe risk in this patient population and ensure ongoing monitoring is in place.
- NHS GG&C should further characterise of cases in terms of “person” and “place” to support understanding when there are more cases than normally expected.
- NHS GG&C should consider the epidemiological characterisation of cases in the context of environmental risks and incidents e.g. water testing results, ventilation testing results.
- NHS GG&C should consider the data provided in the context of the findings from the action plan
- NHS GG&C should consider current control measures around restriction on services for newly diagnosed patients as there is no evidence from the HPS review of the data that supports the continued restriction of services.
- HPS will review the categorisation of environmental organisms following the literature reviews for Chapter 4 of the **National Infection Prevention and Control Manual**.
- HPS will further support the development of an appropriate trigger for ongoing monitoring.
- HPS should consider these findings when developing methods to support other boards in monitoring infection risk associated with environmental organisms.

Glossary

BMT	Bone Marrow Transplant
CDC	Centers for Disease Control
CLABSI	Central line associated bloodstream infection
CI	Confidence intervals
DNA	Did not attend
ECOSS	Electronic Communication of Surveillance in Scotland
ENT	Enteric
HPS	Health Protection Scotland
ISD	Information Services Division
LIMS	Laboratory information management system
NHSGG&C	NHS Greater Glasgow and Clyde
QEUH	Queen Elizabeth University Hospital
RR	Rate ratios
RHC	Royal Hospital for Children
SPC	Statistical Process Control
TOBD	Total occupied bed days
UCL	Upper control limit
UWL	Upper warning limit
YH	Yorkhill Hospital

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Further Information

Further Information can be found on the HPS website.

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Appendices

Appendix 1 – Background information

NHS GG&C supplied methods statement for Royal Hospital for Children Blood Stream infections for HPS review.

CLABSI

CLABSI data is prepared according to the following protocol, agreed by the RHC CLABSI Quality Improvement Group:

The QI group refer to CLABSI as defined according to the CDC classification as:

> *'A CLABSI is a primary BSI in a patient that had a central line within the 48-hour period before the development of the BSI and is not bloodstream related to an infection at another site. However, since some BSIs are secondary to other sources other than the central line (e.g., pancreatitis, mucositis) that may not be easily recognized, the CLABSI surveillance definition may overestimate the true incidence of CRBSI'*

The data includes all patients within the haemato-oncology cohort, so inclusive of those cared for at home by the outreach nurses, those attending day care and those who are inpatients in ward 2A including Bone Marrow Transplant, and teenage cancer patients.

CLABSI Data Collection Process:

1) ALL patients receiving a new central venous device at Yorkhill/Glasgow Royal Hospital for Children between January 2015 and July 2019 were collated (using Opera data to look at every operation done in every theatre every day in the Children's Hospital)

2) Out of this group, only the haematology/oncology patients were kept (searching for and confirming a diagnosis via Clinical Portal)

3) The total line day data was obtained by counting the number of days each line was in situ

4) Each patient was analysed monthly or twice monthly looking at positive microbiology culture results from either a central line or a peripheral venous sample whilst a central line was in situ (via Clinical Portal)

5) Any positive microbiology result with a concurrent illness (IE chest infection or urinary tract infection) was excluded (again via Clinical Portal and the electronic notes)

6) If a culture positive result occurred repeatedly in the 7 days following the first positive culture and the organism was the same, this was excluded (IE a patient with a Staph Aureus infection on 5/9/18 and a subsequent culture positive Staph Aureus on 7/9/18 was only counted as ONE infection); a second Staph Aureus infection on 13/9/18 would be counted as TWO infections in total as one would presume that a week of treatment should have effectively treated the first organism.

7) If, however, a second culture positive result occurred in the 7 days following the first positive culture and the organism was different, this was included (IE a patient with a Staph Aureus infection on 5/9/18 and a subsequent culture positive pseudomonas infection on 7/9/18 was counted as TWO infections in total).

8) Patients receiving their Hickman/Broviac Line, Port, or Haemodialysis line in a unit other than the Royal Hospital for Children in Glasgow were excluded. This point was discussed at the first CLABSI QI meeting and it was felt that these (few) patients that had lines inserted elsewhere but were treated in Glasgow could not be analyzed in the same fashion as those receiving the majority of their care (from line insertion to treatment to line removal) here in Glasgow.

9) Patients shared care in local district general hospitals who presented locally initially with a CLABSI and were subsequently transferred to Glasgow did not have that single line infection counted for similar reasons (we would be looking at the management of care in the district general hospital and thus would not be able to analyze them in the same methodology).

To produce the total CLABSI/Gram negative CLABSI chart as shown in the presentation, each line was checked to assign he organism to either gram positive, gram negative or fungus. The same denominator (line days) was used.

Where there were multiple organisms in a single line, the first named organism was used for classification. One organism was not classified, as it can exist as gram positive, gram negative or gram neutral.

CLABSI funnel plot

The funnel plot was produced using the PHE fingertips funnel plot for rates tool. The data used was the gram negative counts, and line day denominator used in the other CLABSI charts. The plot was produced using the instructions included in the tool. As there is no long term stable average, and in recognition of the quality improvement project, the central line was set to the aim of 1 per 1000 line days.

Epicurves

The ECOSS system was queried to obtain data on positive blood cultures for selected gram negative organisms reported from the GLA:SGH or GLA:GRI laboratories, age <16. The initial extract (during the water/drains incident 2018) was for date of report from July 2013 to June 2018. Further extracts were made periodically. The list of gram negatives was provided by the NHS GGC lead Infection Control Doctor, and is contained in the appendix to this document. This list is based on organisms identified during the water/drains incident. Following further discussion since the initial extract, *Citrobacter* and Aeromonas were added

to that list. To increase sensitivity, data were pulled from ECOSS on basis of genus, rather than species.

Following extraction, the following exclusions were applied:

- Results from neonatal, maternity and pathology removed
- Results from areas not part of RHSC/RHC

During initial screening, laboratory GLA:RAH was also included, however as no relevant results noted, this parameter was removed from the query.

CHI numbers were replaced with new unique ID, and patient identifiers deleted. It is therefore not possible to directly link more recent cases to those form previous extracts. To ensure that the rules below could be applied, and to capture any late inclusions in the ECOSS data base, the 3 months data prior to the new months was also extracted and cases cross checked. One additional late inclusion was detected in this way.

Each case was assigned to a specialty based on the following data points included in the ECOSS reports –

1. Ward sample was taken
2. Diagnosis/clinical history recorded on lab request
3. Requesting consultant.

If it was not possible to identify a specialty from information contained in the ECOSS report, then speciality was confirmed using electronic patient records.

Two separate counts were calculated, based on methodologies described by PHE and CDC:

- Organism count: Number of positive blood cultures per calendar month. Results within 14 days of a previous positive for the **same** organism in the same patient excluded.
- Case count: Number of positive blood cultures per calendar month results within 14 days of previous positive for **any** organism in the same patient excluded (ie only one positive per patient per 14 days)

In both cases the date of result was counted as day one.

Rates were then calculated using activity data produced by NHS GGC acute service information team.

Division of organisms between “environmental” and “non-environmental” was based on advice from GGC mcirobiologists.

Non-environmental: *Citrobacter*, *Enterobacter, Klebsiella, Pantoea, Serratia.*

Environmental: All other organisms.

All gram negative positive blood cultures chart

An extraction from ICNet of blood cultures from RHSC Schiehallion, RHSC Schiehallion DCU, RHC 2A, RHC 2B & QEUH 6A, for patients under 18 years at time of BC aspiration for dates 01/11/2014 – 19/09/2019 (date of data extraction) was carried out by GGC IPCT surveillance team. Blood cultures were de-duplicated by 14 days i.e. new case on day 15 from previous isolate of the same organism in the same patient. More than one organism may have been isolated in the same blood culture specimen.

The counts were converted to rates using the occupied bed day data from NHS GGC acute services information team.

NHSGG&C Appendix: list of selected gram negative organisms

Achromobacter xylosoxidans	Morganella morganii
Acinetobacter lwofii	Pantoea agglomerans
Acinetobacter ursingii	Paracoccus sp
Brevundimonas versicularis	Pseudomonas chlororaphis
Burkholderia cepacia	Pseudomonas fluorescens
Cedecea lapagei	Pseudomonas oryzihabitans
Chryseobacterium indologenes	Pseudomonas putida
Commamonas testosterone	Pseudoxanthomonas mexicana
Cupriavidus gilardii	Ralstonia picketii
Cupriavidus pauculus	Rhizobium radiobacter
Delftia acidovorans	Serratia fonticola
Elizabehtkingia meningospetica	Shewanella puterfaciens
Enterobacter cloacae	Sphingomonas species
Klebsiella pnuemoniae	Stenotrophomonas maltophilia

Organism comparison list

Table 5 and Table 6 detail the organisms isolated in the positive blood cultures and the groupings used in this report.

Table 5: Organisms isolated from positive blood samples included in environmental groupings during the time period reviewed.[1]

NHSGGC CLABSI surveillance	NHSGGC ECOSS selected Gram-negative organisms (GGC Selected GNeg)	NHSGGC Microbiology LIMS Surveillance	HPS ECOSS Under18 bloods RHC HaemOnc
Gram Negative Environmental (GN ENV)	**Gram Negative Environmental (GN ENV)**	**Gram Negative Environmental (GN ENV)**	**Gram Negative Environmental (GN ENV)**
Achromobacter spp.	*Acinetobacter baumannii*	*Achromobacter sp*	*Achromobacter spp.*
Acinetobacter baumannii	*Acinetobacter ursingii*	*Acinetobacter baumannii*	*Acinetobacter spp.*
Acinetobacter ursingii	*Aeromonas hydrophila*	*Acinetobacter ursingii*	*Aeromonas hydrophila*
Aeromonas hydrophila	*Brevundimonas spp.*	*Aeromonas spp*	*Brevundimonas spp.*
Burkhold cepacia	*Burkholderia cepacia*	*Brev. spp.*	*Burkholderia cepacia*
Chryseomonas indologenes	*Chryseobacterium indologenes*	*Burk. cepacia group*	*Chryseobacterium indologenes*
Chryseob. spp	*Chryseobacterium spp.*	*Chryseob. spp.*	*Chryseobacterium spp.*
Cupriavidis pauculus	*Cupriavidus pauculus*	*Chryseobacterium indologenes*	*Cupriavidus pauculus*
Eliz. meningoseptica	*Delftia acidovorans*	*Chryseomonas spp.*	*Delftia acidovorans*
Elizabethkingia spp.	*Elizabethkingia meningoseptica*	*Cup. pauculus*	*Elizabethkingia meningoseptica*
Delftia acidovorans	*Elizabethkingia spp.*	*Del. acidovorans*	*Elizabethkingia miricola*
Pseudomonas spp.	*Pseudomonas spp.*	*Delftia spp.*	*Elizabethkingia spp.*
Rhiz. radiobacter	*Rhizobium radiobacter*	*Elizabethkingia. spp.*	*Pseudomonas spp.*
Roseomonas mucosa	*Sphingomonas paucimobilis*	*Herbaspirillum sp*	*Raoultella planticola*
Sphingomonas spp.	*Steno. maltophilia*	*Pseudomonas spp.*	*Rhizobium radiobacter*
Steno. maltophilia		*R. planticola*	*Roseomonas mucosa*
		R. radiobacter	*Sphingomonas paucimobilis*
		R. mucosa	*Steno. maltophilia*
		Sph. paucimobil	

		Steno. maltophilia	
Gram Negative Enteric /Environmental (GN ENT/ENV)	**Gram Negative Enteric /Environmental (GN ENT/ENV)**	**Gram Negative Enteric /Environmental (GN ENT/ENV)**	**Gram Negative Enteric /Environmental (GN ENT/ENV)**
Citrobacter spp. *Enterobacter cloacae* *Klebsiella spp.* *Pantoea spp.* *Serratia liquefaciens* *Serratia marcesens*	*Citrobacter spp.* *Enterobacter spp.* *Klebsiella spp.* *Pantoea spp.* *Serratia liquefaciens* *Serratia marcescens*	*Citrobacter spp.* *Enterobacter spp.* *Klebsiella spp.* *Pantoea spp.* *Ser. liquefac.* *Ser. marcescens*	*Citrobacter spp.* *Enterobacter spp.* *Klebsiella spp.* *Pantoea spp.* *Serratia liquefaciens* *Serratia marcescens*
Gram Positive Environmental (GP ENV)	**Gram Positive Environmental (GP ENV)**	**Gram Positive Environmental (GP ENV)**	**Gram Positive Environmental (GP ENV)**
Gordonia polyisoprenivorans	N/A	*Gordonia polyisoprenivorans*	*Gordonia bronchialis*
Acid Fast Environmental (AF ENV)	**Acid Fast Environmental (AF ENV)**	**Acid Fast Environmental (AF ENV)**	**Acid Fast Environmental (AF ENV)**
Mycobacterium chelonae	N/A	*Myc. chelonae group* *Myco fortuitum* *Mycobacterium chelonae*	*Mycobacterium chelonae* *Mycobacterium spp.*
Fungi Environmental (Fungi ENV)	**Fungi Environmental (Fungi ENV)**	**Fungi Environmental (Fungi ENV)**	**Fungi Environmental (Fungi ENV)**

1. May not include every organism of interest if no cases were found during the time period.

Table 6: Organisms isolated from positive blood samples included in non-environmental groupings during the time period reviewed.[1]

NHSGGC CLABSI surveillance	NHSGGC ECOSS selected Gram-negative organisms (GGC Selected GNeg)	NHSGGC Microbiology LIMS Surveillance	HPS ECOSS Under18 bloods RHC HaemOnc
Gram Negative Non-environmental (GN NON-ENV)	**Gram Negative Non-environmental (GN NON-ENV)**	**Gram Negative Non-environmental (GN NON-ENV)**	**Gram Negative Non-environmental (GN NON-ENV)**
Escherichia coli *Fusobacterium nucleatum* *Proteus mirabilis*	N/A	*Bact. uniformis* *Cap. sputigena* *Escherichia coli* *Fuso. nucleatum* *Haemophilus influenzae* *Mor. catarrhalis* *Moraxella nonliquefaciens* *Moraxella osloensis* *Neis. subflava* *Proteus mirabilis*	*Bacteroides uniformis* *Capnocytophaga sputigena* *Escherichia coli* *Escherichia fergusonii* *Fusobacterium nucleatum* *Haemophilus influenzae* *Moraxella spp.* *Neisseria spp.* *Ochrobactrum anthropi* *Proteus mirabilis*
Gram Positive Non-environmental (GP NON-ENV)	**Gram Positive Non-environmental (GP NON-ENV)**	**Gram Positive Non-environmental (GP NON-ENV)**	**Gram Positive Non-environmental (GP NON-ENV)**
Aerococcus viridans *Clostridium spp.* *Corynebacterium spp.* *Dermacoccus nishinomiyaens* *Diphtheroids* *Enterococcus spp.* *Gemella Sanguinis* *Gordonia polyisoprenivorans*	N/A	*Aerococcus viridans* *Alpha strep* *Bacillus spp.* *C. perfiringens* *Coag Neg Staph.* *Corynebacterium spp* *Derm. nishinomiyaens* *Diphtheroids* *Enterococcus spp.*	*Abiotrophia defectiva* *Aerococcus viridans* *Bacillus spp.* *Clostridium perfringens* *Clostridium septicum* *Corynebacterium spp.* *Dermacoccus spp.* *Enterococcus spp.* *Gemella sanguinis*

Gram +ve bacilli *Gram Pos B* *Gram Pos C* *Gran Adiac* *Granulicatella adiacens* *Kocuria rhizophilia* *Lactobacilus* *Micrococcus spp.* *Paenibacillus durus* *Propionibacterium acnes* *Rothia mucilaginosa* *Staphylococcus spp.* *STCNS* *Streptococcus spp.*		*Gemella.sanguinis* *GPC-Strep* *Gram +ve bacilli* *Gram positive cocci* *Gran. adiacens* *Kocuria rhizophilia* *Lactobacillus spp* *Micrococcus spp.* *Paenibacillus spp.* *Propionibacterium acnes* *Rothia mucilaginosa* *Staphylococcus spp.* *Streptococcus spp.*	*Granulicatella adiacens* *Kocuria spp.* *Lactobacillus spp.* *Lactococcus lactis* *Leuconostoc lactis* *Micrococcus spp.* *Paenibacillus spp.* *Propionibacterium spp.* *Rothia spp.* *Staphylococcus spp.* *Streptococcus spp.*
Acid Fast Non-environmental (AF NON-ENV)	**Acid Fast Non-environmental (AF NON-ENV)**	**Acid Fast Non-environmental (AF NON-ENV)**	**Acid Fast Non-environmental (AF NON-ENV)**
Nil	N/A	Nil	Nil
Fungi Non-environmental (Fungi NON-ENV)	**Fungi Non-environmental (Fungi NON-ENV)**	**Fungi Non-environmental (Fungi NON-ENV)**	**Fungi Non-environmental (Fungi NON-ENV)**
Candida spp. *Yeasts*	N/A	*Candida spp.*	*Candida spp.*

1. May not include every organism of interest if no cases were found during the time period.

Appendix 2 – Publication Metadata

Metadata Indicator	Description
Publication title	**Review of NHSGG&C paediatric haemato- oncology data**
Description	This management report provides information on paediatric haematology oncology related in NHS Greater Glasgow &Clyde (NHSGG&C)
Theme	Infections
Topic	Paediatric haematology oncology
Format	Management report and supplementary excel document
Data source(s)	Electronic Communication of Surveillance in Scotland (ECOSS) Total occupied bed days: Information Services Division ISD(S)1 Data provided by NHSGG&C
Date that data are acquired	ECOSS extract 07/10/2019
Release date	25 October 2019
Frequency	Ad hoc
Timeframe of data and timeliness	NA
Continuity of data	NA
Revisions statement	Case definitions have changed since previous reports (refer to methods section)
Revisions relevant to this publication	NA
Concepts and definitions	Covered in methods section.
Relevance and key uses of the statistics	NA
Accuracy	Laboratory data that has not been validation so treated with caution.
Completeness	Data not been validated
Comparability	Comparisons have been made to other Children's hospitals in Scotland however there may be differences in patient population so comparisons should be treated with caution.
Accessibility	It is the policy of HPS to make its web sites and products accessible according to **published guidelines**.
Coherence and clarity	NA
Value type and unit of measurement	Rate per 100,000 total occupied bed days (TOBDs) = (Number of cases of positive blood culture of given case definition in hospital(s) or speciality /TOBDs in hospital(s) or speciality x 100,000).
Disclosure	NA
Official Statistics designation	NA
UK Statistics Authority Assessment	NA
Last published	NA
Next published	NA
Date of first publication	NA
Help email	**mailto:NSS.HPSHAIIC@nhs.net**
Date form completed	25/10/2019

Appendix 3 – HPS and Official Statistics

About HPS

HPS is a division of NHS National Services Scotland which works at the very heart of the health service across Scotland, delivering services critical to frontline patient care and supporting the efficient and effective operation of NHS Scotland.

HPS was established by the Scottish Government in 2005 to strengthen and coordinate health protection in Scotland. It is organised into three specialist groups with expertise provided by a multi-disciplinary workforce which includes doctors, nurses, scientists and information staff, all of whom are supported by core business and IM&T teams. The specialist groups are:

- Healthcare Associated Infections and Infection Control;
- Blood Borne Viruses and Sexually Transmitted Infections, Immunisation, and Respiratory and Vaccine Preventable Diseases;
- Gastrointestinal and Zoonoses Travel, and Environmental Public Health.

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Our official statistics publications are produced to a high professional standard and comply with the Code of Practice for Official Statistics. The Code of Practice is produced and monitored by the UK Statistics Authority which is independent of Government. Under the Code of Practice, the format, content and timing of statistics publications are the responsibility of professional staff working within NHS National Services Scotland.

Our statistical publications are currently classified as one of the following:

- National Statistics (ie assessed by the UK Statistics Authority as complying with the Code of Practice)
- National Statistics (ie legacy, still to be assessed by the UK Statistics Authority)
- Official Statistics (ie still to be assessed by the UK Statistics Authority)
- other (not Official Statistics)

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