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EVALUATION REPORT

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Abstract

Infections with resistant microorganisms have been associated with higher morbidity, mortality and health care costs, affecting both individuals and society. Reliable surveillance programmes are needed to tackle antimicrobial resistance (AMR) by creating awareness and supporting the development of clinical guidelines and AMR control policies. The Proof-of-Principle AMR routine diagnostics surveillance study (PoP study) is a protocol that supports the development of expertise within a country for clinicians in collecting blood samples from patients with a clinical suspicion for a bloodstream infection; for hospital laboratories for culturing and analysing these samples, including microbial species identification and antimicrobial susceptibility testing; and for a national reference laboratory to confirm results and collect data to support a surveillance system. The PoP study was started as a pilot project in Georgia in July 2015 and the final data for the study period plus recommendations for the future institution of an AMR detection and surveillance system are presented here.

Keywords

DRUG RESISTANCE, MICROBIAL
ANTI-INFECTIVE AGENTS
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DIAGNOSTIC TESTS, ROUTINE - METHODS
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Abbreviations

AMR	antimicrobial resistance
AST	antibiotic susceptibility testing
BSI	bloodstream infection
CAESAR	Central Asian and Eastern European Surveillance of Antimicrobial Resistance Network
EQA	external quality assessment
EUCAST	European Committee on Antimicrobial Susceptibility Testing
ID	identification (species)
IPC	infection prevention and control
MRSA	methicillin-resistant *Staphylococcus aureus*
NCDC	National Centre for Disease Control and Public Health (Georgia)
PoP study	Proof-of-Principle antimicrobial resistance routine diagnostics surveillance study
RIVM	National Institute for Public Health and the Environment, the Netherlands
SIRS	systemic inflammatory response syndrome
SOP	standard operating procedure

Introduction

Antimicrobial resistance (AMR) is a threat to effective treatment and prevention of infectious diseases in individual patients. Infections with resistant microorganisms have been associated with higher morbidity, mortality and health care costs; consequently, this has an effect on society as a whole over and above the negative effect on the individual patient and their family. Reliable surveillance programmes are needed to tackle the AMR threat by creating awareness and supporting the development of clinical guidelines and AMR control policies. This is also clearly stated in WHO's Global action plan on antimicrobial resistance *(1)*, where as part of Objective 2 Member States are urged to develop a national surveillance for AMR.

In parts of the WHO European Region, the implementation of a national AMR surveillance system based on routine antibiotic susceptibility testing (AST) is limited by the underutilization of microbiological diagnostics in routine clinical practice. The main reasons reported for this low utilization are the lack of funds for microbiological diagnostics and a perception by clinicians of a lack of clinical utility. The Proof-of-Principle antimicrobial resistance routine diagnostics surveillance study (PoP study) was set up with the aims of stimulating the collection of blood for culturing from patients with a clinical suspicion for bloodstream infection (BSI) by providing materials and technical support to facilitate bacteriological processing of these samples and starting the assessment of antibiotic susceptibility patterns in the main pathogens causing community-acquired and hospital-acquired (nosocomial) BSIs in the area, thus:

- demonstrating the value of clinical microbiological diagnostics in routine patient care by providing timely feedback of laboratory results to clinicians to guide antibiotic treatment of BSIs;
- establishing good clinical practice for routine clinical work-up in hospitals and strengthening the AMR reference and surveillance capacity at a national reference laboratory; and
- establishing and supporting a surveillance infrastructure as point of departure for a national sentinel laboratory-based surveillance system for AMR.

The PoP study was developed by the Central Asian and Eastern European Surveillance of Antimicrobial Resistance Network (CAESAR) *(2)* to provide Member States that had limited routines in taking blood for culturing and performing species identification (ID) and AST with the support they need to set up good clinical practice and local and national AMR surveillance. The PoP study was started as a pilot project in Georgia in July 2015 and the final data for the study period are presented here.

Georgian regulatory framework on AMR

In recent years, Georgia has increased efforts to address AMR in order to meet global guidelines and to improve national capacity for surveillance and response. A short overview of important regulations is provided below and Annex 1 provides a more detailed list of relevant legislation.

A regulation prohibiting the sale of antibiotics without prescription has been effective since September 2014. An e-prescribing system has been activated since 2016, enabling collection, monitoring and analysing data on all the prescriptions. Moreover, the Government of Georgia with Decree No. 82 in 2016 made it mandatory to send "alert" organisms and organisms with interesting AST results to the national reference laboratory (the Lugar Centre at the National Centre for Disease Control and Public Health (NCDC)).

On 11 January, 2017, the Government of Georgia issued a decree that approved the National Strategy for Combating Antimicrobial Resistance (Decree No. 29). The primary goals of the National Strategy are to

promote the rational use of antibiotics, introduce and maintain surveillance of AMR and improve infection prevention and control (IPC) practices in health care facilities. Eight specific objectives were formulated to reach these goals; in addition to surveillance, IPC and use of antibiotics, the objectives cover laboratory capacity, awareness, and food and feed safety. In accordance with the goals of the PoP study, the National Strategy obliges health care facilities to monitor hospital-acquired infections and antibiotic resistance by routine examination of patients, including blood sampling for culture and laboratory analyses.

Methods

Data were collected between 1 July 2015 and 31 December 2016 in four general regional hospitals: the Ghudushauri National Medical Centre (240 beds), the High Medical Technology Centre (250 beds), the Iashvili Children's Central Clinic (290 beds) and Telavi Referral Hospital (70 beds). The study was coordinated by the Lugar Centre, a facility of the NCDC of Georgia. The study team consisted of a project manager, a research coordinator, a microbiologist, an epidemiologist and support personnel. Weekly visits to the research sites were made by the study team to support implementation of the study. The study team was supported by WHO Regional Office for Europe, Unit for Control of AMR, and AMR surveillance experts from the National Institute for Public Health and the Environment (RIVM) in the Netherlands and clinical microbiology experts from the University Hospital of Infectious Disease in Zagreb, Croatia.

Prior to study start (June 2015), staff in participating laboratories were trained by the NCDC team in blood culturing procedures and techniques and AST, following methods set out by the European Committee on Antimicrobial Susceptibility Testing (EUCAST). This training was a refresher of prior laboratory trainings on EUCAST methodology organized by WHO Regional Office for Europe in July 2014. All blood culture materials and laboratory consumables for species ID and AST at hospital laboratories and confirmatory testing at the Lugar Centre for a maximum of 1800 patients were provided free of charge by the study.

At each study site, a local team consisting of a clinician, a hospital epidemiologist and a microbiologist were responsible for conducting the study. Clinicians were instructed to recruit patients through active case finding from hospital departments admitting patients with suspected BSI from the community (e.g. emergency department) and from wards where patients were at risk of developing hospital-acquired BSIs (e.g. intensive care unit, urology or surgical departments). Patients fulfilling criteria for the systemic inflammatory response syndrome (SIRS) *(3)* were eligible for the study. For paediatric patients, SIRS criteria were adapted by the local clinicians. The study team completed a clinical data form for each included patient and a laboratory data form for each positive blood culture. Data forms were collected at the weekly study meetings and entered into an electronic database at NCDC.

Blood cultures were processed at the hospital's bacteriology laboratory. One hospital (the High Medical Technology Centre) at the central level and one hospital (Telavi Referral Hospital) at the regional level did not have bacteriology laboratory capabilities. Therefore, blood cultures were transported to the national AMR reference laboratory at Lugar Centre and Telavi Laboratory of Sentinel Site, respectively, for full processing directly following the blood draw. Microbiologists were advised to actively report preliminary results (Gram stain of a positive blood culture) and final reports (species ID and AST) back to the clinician as soon as these were available to allow clinicians to adjust the (empiric) antibiotic therapy. All positive blood culture isolates were sent to the AMR reference laboratory for quality assurance and confirmatory AST testing. The results from testing at the AMR reference laboratory were used for the analyses presented in this report.

Blood culturing was carried out using a manual blood culture system according to standard operating procedures (SOP) *(4)*. Culture bottles were checked for growth daily. Blind subcultures were made at 24 hours, 48 hours, 72 hours and at 7 days if no growth was seen. AST was assessed using disc diffusion according to EUCAST standards. The tested "bug–drug" combinations were based on the recommendations in the CAESAR manual *(5)*, including indicator antibiotics for the main antibiotic groups, plus some empiric treatment options not described in the CAESAR manual.

At the end of the study, the NCDC organized an evaluation workshop for the hospital staff involved, together with WHO Regional Office for Europe, RIVM and the Croatian University Hospital of Infectious Disease. The aim of the workshop was to present findings from the study and to discuss the data obtained, the lessons learned during the study period and the next steps needed at the hospital and the national level

to ensure sustainable implementation. The informal focus group discussion included representation from all hospital teams involved in the study and was facilitated by the NCDC. The discussion was transcribed and analysed following Creswell's (2009) model for qualitative data analysis *(6)*. A summary of the findings are presented in the results.

Results

Blood culture results

Blood cultures were collected from 1559 patients with suspected BSI between 1 June 2015 and 31 December 2016. Table 1 shows the distribution of all patients with suspected BSI among the four hospitals and Table 2 shows the characteristics of these patients. The most common clinical diagnoses were respiratory distress syndrome in neonates (66.8%), fever in children (28.6%) and respiratory failure in adults (12.7%) (Table 3). The overall rate of taking blood for culturing was 5.9/1000 patient-days, which was a significant increase compared to the year prior to implementation of the PoP study (1.8/1000 patient-days). The majority of blood cultures were from patients admitted to an intensive care unit (69.2% of blood cultures; rate 29.3/1000 patient-days), in particular in neonatal intensive care (46.1% of blood cultures; rate 35.8/1000 patient-days). Relatively few blood samples for culture were taken in departments other than intensive care (30.8% of blood cultures; rate 2.1/1000 patient-days).

Table 1. Distribution of patients with BSIs by hospitals

Hospital	Patients
High Medical Technology Centre	226
Iashvili Children's Central Clinic	682
National Medical Centre	570
Telavi Referral Hospital	81
Total	1559

Note: Telavi Referral Hospital was enrolled in the study from 1 July, 2016.

Table 2. Demographic characteristics of all patients who had blood taken for culture

	No. (%)	Mean	No. positive cultures (%)
Sex			
Male	940 (60.3%)	–	127 (13.5%)
Female	619 (39.7%)	–	75 (12.1%)
Age (years)			
<31 days	730 (46.8%)	4.5 ± 6.7	81 (11.1%)
1–11 months	197 (12.6%)	3.4 ± 3.1	33 (16.8%)
1–5 years	112 (7.2%)	2.6 ± 1.3	14 (12.5%)
6–16 yearss	111 (7.1%)	10.8 ± 3.2	7 (6.3%)
17–35 years	108 (6.9%)	26.6 ± 5.5	15 (13.9%)
36–49 years	72 (4.6%)	43.5 ± 4.2	14 (19.4%)
50–64 years	129 (8.9%)	57.7 ± 4.2	23 (16.5%)
>64 years	90 (5.8%)	73.8 ± 6.1	14 (15.6%)

Table 3. Three most common clinical diagnosis in patients with suspected BSIs

Age group (No.)	Diagnosis	No. positive (%)
Neonates (730)[a]	Respiratory distress syndrome	488 (66.8%)
	Respiratory acute failure	69 (9.4%)
	Low birth weight	50 (6.8%)
Children (420)[b]	Fever	120 (28.6%)
	Respiratory acute failure	106 (25.2%)
	Respiratory distress syndrome	54 (12.8%)
Adult (409)	Respiratory failure	52 (12.7%)
	Pneumonia	49 (12.0%)
	Fever	44 (10.8%)
Total (1559)	Respiratory distress syndrome	550 (35.3%)
	Respiratory acute failure	195 (12.5%)
	Fever	177 (11.4%)

Notes: [a] Neonates include children ≤1 month and children admitted to neonatal ward; [b] Children >1 month to <17 years of age.

Table 4 gives the number and percentage of blood cultures taken in duplicate. The percentage of positive blood cultures was 13.3% (123/924) when taken in duplicate and 12.5% (79/635) when taken as a single sample. Of all blood cultures, 79.5% were taken in duplicate in children and 86.8% in adults. In neonates, only 32.2% of blood cultures were taken in duplicate. The yield of positive blood cultures in a single or duplicate blood cultures taken was similar; 12.5% vs. 13.3%.

Table 4. Number and percentage of blood samples taken in duplicate for culturing

Patient group	No. patients	No. blood samples taken in duplicate (%)
Neonates	731	236 (32.3%)
Child	419	333 (79.5%)
Adult	409	356 (87.0%)
Total	1559	924 (59.3%)

Of the 1559 blood cultures examined, 217 (13.91%) were positive (201 bacterial pathogens, 16 fungi). Table 5 shows the patient characteristics of those with positive bacterial isolates by pathogen. Antibiotic susceptibility for the pathogens is reported under CAESAR surveillance as well as for the most commonly isolated pathogens. With the exception of *Klebsiella pneumoniae*, a low number of isolates was available for each pathogen (30), and the percentage resistance should be interpreted with caution. In *Escherichia coli* and *K. pneumoniae*, 71% and 82% were resistant to aminoglycosides, respectively, and 53% and 96% were resistant to third-generation cephalosporins, respectively. None of the *E. coli* and 11% of the *K. pneumoniae* isolates was resistant to carbapenems, and multidrug resistance was found in 31% and 25% of *E. coli* and *K. pneumoniae*, respectively (Table 6). For both *Pseudomonas aeruginosa* and *Acinetobacter* spp., carbapenem resistance reached 67% (Table 7). Multidrug resistance was present in 26% of *P. aeruginosa* and 67% of *Acinetobacter* spp. (Table 7). In *Staphylococcus aureus*, 24% was characterized as methicillin-

resistant *S. aureus* (MRSA) (Table 8). Coagulase-negative staphylococci had 41% resistance to cefoxitin and rifampicin and 47% resistance to fluoroquinolones (Table 9). Carbapenem resistance reached 40% in *Serratia marcescens* (Table 10). In *Burkholderia cepacia*, fluoroquinolone resistance was 75% (Table 11). Too few isolates of *Enterococcus* spp. were available to draw conclusions about their antibiotic susceptibility, with no data for *E. faecium* and only a few isolates for *E. faecalis* (Table 12); similarly no conclusions could be drawn about the antibiotic susceptibility of *Streptococcus pneumoniae* (Table 13).

Table 6. Resistance levels for *Escherichia coli* and *Klebsiella pneumoniae*

Antibiotic class[a]	*E. coli*		*K. pneumoniae*	
	No.	Resistance (%)	No.	Resistance (%)
Aminopenicillins (R)	12	100	NA	NA
Beta-lactam–beta-lactamase inhibitor combinations (R)	17	41	54	93
Aminoglycosides (R)	17	71	54	82
Gentamycin	17	59	54	61
Amikacin	11	27	36	51
Fluoroquinolones (R)	16	38	49	27
Fluoroquinolones (I+R)	16	38	49	35
Third-generation cephalosporins (R)	17	53	54	96
Third-generation cephalosporins (I+R)	17	59	54	96
Cefotaxime/ceftriaxone (R)	17	53	54	96
Ceftazidime (R)	17	41	56	98
Carbapenems (R)	17	0	54	11
Carbapenems (I+R)	17	5	54	20
Ertapenem (R)	8	0	32	28
Colistin (R)	17	0	53	4
Multidrug resistance (R)[b]	17	31	49	25

Notes: NA: Not applicable; [a] Aminopenicillins comprise amoxicillin and ampicillin; aminoglycosides comprise amikacin, gentamicin and tobramycin; fluoroquinolones comprise ciprofloxacin, ofloxacin and levofloxacin; third-generation cephalosporins comprise cefotaxime, ceftriaxone and ceftazidime; carbapenems comprise imipenem and meropenem; [b] Multidrug resistance is defined as resistance to fluoroquinolones, third-generation cephalosporins and aminoglycosides.

Table 5. Patient characteristics by pathogen

Pathogen	No. isolates	Sex (%)		Age category (%)					Hospital department (%)		Source of infection (%)	
		Male	Female	1–30 days	1–11 months	1–16 years	17–35 years	>35 years	ICU	Non-ICU	Nosocomial[a]	Community[b]
Escherichia coli	17	58.8	41.2	47.1	5.9	11.8	0	35.3	52.9	47.1	17.6	82.4
Klebsiella pneumoniae	57	64.9	35.1	45.6	26.3	10.55	1,8	15.8	82.4	17.6	86.0	14.0
Pseudomonas aeruginosa	18	55.6	44.4	44.4	22.2	11.1	5.6	16.7	94.4	5.6	88.9	11.1
Acinetobacter baumannii	9	66.7	33.3	11.1	11.1	0	11.1	66.7	100	0	100	0
Staphylococcus aureus	21	61.9	38.1	61.8	4.8	4.8	0	28.6	71.4	28.6	71.4	28.6
Streptococcus pneumoniae	3	100	0	0	0	100	0	0	66.7	33.3	33.3	66.7
Enterococcus faecalis	3	33.3	66.7	100	0	0	0	0	100	0	100	0
Enterococcus faecium	-											
Coagulase-negative staphylococci[c]	19	68.4	31.6	21.0	15.8	0	31.6	31.6	78.9	21.1	63.2	36.8
Enterococcus spp.	5	80	20	40	40	20	0	0	80	20	100	0
Enterococcus gallinarum	4	50	50	25	25	0	0	50	100	0	100	0
Burkholderia cepacia	5	60	40	60	0	0	0	40	100	0	100	0
Enterobacter cloacae	6	66.7	33.3	66.7	0	16.7	0	16.7	66.7	33.3	83.3	16.7
Providencia stuartii	2	0	100	0	50	0	0	50	50	50	100	0
Klebsiella oxytoca	2	100	0	0	50	0	0	50	100	0	50	50
Serratia liquefaciens	3	100	0	0	33.3	33.3	0	33.3	100	0	100	0
Serratia marcescens	4	50	50	0	25	75	0	0	100	0	75	25
Pseudomonas oryzihabitans	2	50	50	0	0	0	50	50	100	0	100	0
Staphylococcus epidermidis	2	50	50	0	0	0	50	100	50	50	100	0
Klebsiella terrigena	2	100	0	0	0	0	50	50	50	50	50	50
Other[d]	17	64.7	35.3	41.2	5.9	5.9	17.6	29.4	94.1	5.9	82.4	17.6

Note: ICU: Intensive care unit; [a] Patients admitted to hospital at least 48 hours previously (including patients transferred from other hospitals) and children born in the hospital; [b] Patients developing signs of infection within 48 hours of admission to hospital; [c] All isolates were obtained from two or more blood cultures and were judged clinically relevant; [d] *Pseudomonas luteolla*, *Pseudomonas .fluo/putida*, *Pseudomonas vulgaris*, *Chryseobacterium meningosepticum*, *Citrobacter braakii*, *Flavimonas ozyhabitans*.

Table 7. Resistance levels for *Pseudomonas aeruginosa* and *Acinetobacter* spp.

Antibiotic class[a]	*P. aeruginosa*		*Acinetobacter* spp.	
	No.	Resistance (%)	No.	Resistance (%)
Aminoglycosides (R)	18	44	8	63
Fluoroquinolones (R)	16	31	2	50
Piperacillin/piperacillin–tazobactam (R)	18	26	NA	NA
Ceftazidime (R)	18	39	NA	NA
Carbapenems (R)	17	59	8	75
Carbapenems (I+R)	17	59	8	75
Colistin (R)	18	11	9	0
Multidrug resistance (R)[b]	17	35	2	0

Notes: NA: Not applicable; [a] Aminoglycosides comprise gentamicin and tobramycin; fluoroquinolones comprise ciprofloxacin and levofloxacin; carbapenems comprise imipenem and meropenem; [b] Multidrug resistance is defined for *P. aeruginosa* as resistance to ≥3 antimicrobial groups among piperacillin + tazobactam, ceftazidime, fluoroquinolones, aminoglycosides and carbapenems and for *Acinetobacter* spp. as resistance to fluoroquinolones, aminoglycosides and carbapenems.

Table 8. Resistance levels for *Staphylococcus aureus*

Antibiotic class[a]	*S. aureus*	
	No.	Resistance (%)
MRSA[b]	20	15
Fluoroquinolones (R)	16	19
Vancomycin (R)	21	0
Rifampicin (R)	21	10
Linezolid (R)	21	0

Notes: [a] Fluoroquinolones comprise ciprofloxacin, ofloxacin, levofloxacin and norfloxacin; [b] MRSA is calculated as resistance against cefoxitin, or, if not available, to one or more of oxacillin, flucloxacillin, methicillin, cloxacillin and dicloxacillin.

Table 9. Resistance levels for coagulase-negative staphylococci

Antibiotic class[a]	Coagulase-negative staphylococci	
	No.	Resistance (%)
Cefoxitin	17	41
Fluoroquinolones (R)	17	47
Vancomycin (R)	17	0
Rifampicin (R)	17	41
Linezolid (R)	17	0

Note: [a] Fluoroquinolones comprise ciprofloxacin, ofloxacin, levofloxacin and norfloxacin.

Table 10. Resistance levels for *Serratia marcescens* and *Enterobacter cloacae*

Antibiotic class[a]	*S. marcescens*		*E. cloacae*	
	No.	Resistance (%)	No.	Resistance (%)
Aminopenicillins (R)	1	100	1	100
Beta-lactam–beta-lactamase inhibitor combinations (R)	4	50	3	0
Aminoglycosides (R)	4	50	3	0
Gentamycin	4	50	3	0
Amikacin	2	0	3	0
Fluoroquinolones (R)	4	25	3	0
Fluoroquinolones (I+R)	4	25	3	0
Third-generation cephalosporins (R)	4	50	3	0
Third-generation cephalosporins (I+R)	4	50	3	0
Cefotaxime/ceftriaxone (R)	4	50	3	0
Ceftazidime (R)	4	50	3	0
Carbapenems (R)	4	25	3	0
Carbapenems (I+R)	4	50	3	0
Ertapenem (R)	–	–	–	–
Colistin (R)	2	0	3	0

Notes: [a] Aminopenicillins comprise amoxicillin and ampicillin; aminoglycosides comprise amikacin, gentamicin and tobramycin; fluoroquinolones comprise ciprofloxacin, ofloxacin and levofloxacin; third-generation cephalosporins comprise cefotaxime, ceftriaxone and ceftazidime; carbapenems comprise imipenem and meropenem.

Table 11. Resistance levels for *Burkholderia cepacia*

Antibiotic class[a]	*B. cepacia*	
	No.	Resistance (%)
Aminoglycosides (R)	5	80
Fluoroquinolones (R)	5	80
Piperacillin/piperacillin–tazobactam (R)	5	60
Ceftazidime (R)	5	60
Carbapenems (R)	5	0
Carbapenems (I+R)	5	0
Colistin (R)	5	20

Notes: [a] Aminoglycosides comprise gentamicin and tobramycin; fluoroquinolones comprise ciprofloxacin and levofloxacin; carbapenems comprise imipenem and meropenem.

Table 12. Resistance levels for *Enterococcus faecalis*

Antibiotic class[a]	*E. faecalis*	
	No.	Resistance (%)
Aminopenicillins (R)	3	0
High level gentamicin (R)	3	100
Vancomycin (R)	3	0
Linezolid (I+R)	3	67

Notes: No data for *E. faecalis*; [a] Aminopenicillins comprise amoxicillin and ampicillin.

Table 13. Resistance levels for *Streptococcus pneumoniae*

Antibiotic class[a]	*S. pneumoniae*	
	No.	Resistance (%)
Penicillins (R)[b]	3	33
Penicillins (I+R)	3	33
Macrolides (R)	3	0
Macrolides (I+R)	3	0
Fluoroquinolones (R)	3	0
Third-generation cephalosporins (R)	3	0
Third-generation cephalosporins (I+R)	3	0
Multidrug resistance (I+R)[c]	3	0

Notes: [a] Macrolides comprise erythromycin, clarithromycin and azithromycin; fluoroquinolones comprise moxifloxacin and levofloxacin; third-generation cephalosporins comprise cefotaxime and ceftriaxone; [b] Penicillin resistance is based on penicillin or, if not available, on oxacillin; [c] Multidrug resistance is defined as resistance to penicillins and macrolides.

All samples, except those from High Medical Technology Centre, were tested in the hospital laboratory as well as at the Lugar Centre. For species ID, results matched in 78%. The hospital results did not match the reference laboratory results in 13% of the samples. In addition, in 9% only the Gram stain or the species level was identified by the hospital laboratory. For AST, results matched in 76% of the pathogen–drug combinations that were tested in both the hospital laboratory and the reference laboratory.

At the time of taking a blood sample for culture, antibiotics were already being administered in 457 (29.3%) of the patients suspected of BSI (Table 14). Of these patients, 84.9% were characterized as having a suspected nosocomial infection (i.e. having been admitted for at least 48 hours, including transfer from another hospital, and children born in the hospital). In the patient group with a suspected community-acquired infection, 17.5% had taken antibiotics in the seven days before the blood culture. The most common combination of antibiotics administered in that period was a carbapenem and a glycopeptide. The top three most frequently given antibiotics is presented per age category in Table 15.

Table 14. Number and percentage of patients with positive blood culture by antibiotic treatment condition at moment of blood culture

	No. suspected BSIs	No. positive blood cultures (%)
Nosocomial	1164 (75%)	
On antibiotic treatment	388 (33.3%)	85 (21.9%)
Not on antibiotic treatment	776 (66.7%)	83 (10.7%)
Community	353 (25%)	
On antibiotic treatment	69 (17.5%)	7 (10.1%)
Not on antibiotic treatment	326 (82.5%)	27 (8.3%)
Total	1559	202 (13.0%)

Note: Nosocomial was defined as a suspected BSI in a patient admitted at least 48 hours before (including transfer from another hospital) or in a child born in the hospital.

Table 15. Three most common given antibiotics before blood culture

Age group (No.)	Diagnosis	No. positive (%)
Neonates (730)[a]	Ampicillin/sulbactam	64 (8.8%)
	Gentamicin	61 (8.4%)
	Vancomycin	24 (3.3%)
Children (420)[b]	Vancomycin	58 (13.8%)
	Meropenem	45 (10.7%)
	Ceftriaxone	33 (7.9%)
Adult (409)	Vancomycin	148 (36.2%)
	Meropenem	111 (27.1%)
	Cefepime	90 (22.2%)
Total (1559)	Vancomycin	220 (14.1%)
	Meropenem	168 (10.8%)
	Ampicillin/sulbactam	114 (7.3%)

Notes: [a] Neonates include children ≤1 month and children admitted to neonatal ward; [b] Children includes >1 month to <17 years of age.

In 75% of the patients, the infection was defined as nosocomial. Overall, 14.4% of the patients with a suspected nosocomial BSI had a positive blood sample. *K. pneumoniae* (4.3% vs. 2.0%) and *P. aeruginosa* (1.4% vs. 0.5%) were slightly more often isolated in nosocomial BSI. One third of the patients suspected of having a BSI were transferred from another hospital. The largest group of transferred patients comprised neonates transferred to Iashvili Childrens Central Clinic (48%). Referred patients significantly more often had a positive culture than patients who had not been transferred (17.1% vs. 11.0%).

Laboratory results were communicated to the clinicians twice: first as preliminary results (Gram stain) and second as final results (final species ID and AST results). Data on the duration between taking the blood sample for culture and preliminary and final result feedback are shown in Table 16. The time before the preliminary report was communicated to the clinician became shorter during the study but this was not the case for the time until the final result was reported back to the clinician.

Table 16. Feedback reporting time for the total period and for six-month intervals

	Reporting time to clinicians (median days and interquartile range)			
	Total period	1 June 2015 to 31 December 2016	1 January 2016 to 30 June 2016	1 July 2016 to 31 December 2016
Time until first (preliminary) report to clinician	3 (1–5)	4 (2–5)	3 (1–5)	2 (1–3)
Time until final report to clinician	7 (5–9)	6 (5–7)	7 (5–9)	7 (5–9)

In half of the patients with a positive blood sample, data were available about treatment that changed in response to the preliminary results and/or AST result. In 80% of these cases, the antibiotic therapy guidelines were followed. Antibiotic therapy was adjusted based on species ID and AST results (de-escalation) in 65% of these patients.

Occasionally, several pathogens with similar resistance pattern were identified from the same intensive care unit within a week. For example, an *Acinetobacter baumannii* with an identical phenotypic carbapenem resistance pattern was isolated from three different patients within a one week period, which might be an indication of nosocomial source of infection.

Qualitative findings from the evaluation meeting

At the end of the PoP study, the NCDC team organized a meeting (6–7 May 2017) with the participating hospitals to discuss the data obtained, the lessons learned during the study period and the next steps needed at the hospital and the national level to ensure sustainable implementation. The findings from this evaluation meeting are presented here.

The administrative representatives of all the participating hospitals supported the project and recognized that standardization of blood culturing (both in clinic and laboratory) helped to de-escalate BSI treatment. All hospitals expressed the intention to keep following the PoP approach and to make taking blood for culturing standard practice for all patients with suspected BSIs. Some hospitals had already changed their internal regulation and increased the budget for laboratory materials. However, some participants expressed concern that there was still a lack of support from top management and this affected implementation. Without this support, it was a challenge to form and run multidisciplinary teams, develop and implement SOPs and address barriers in the diagnostic pathway. Some participants, therefore, suggested that future efforts should include engaging top management more through stakeholder meetings and workshops.

It was recognized that involving hospital personnel directly was very important and contributed to the success of the project. In many hospitals, the multidisciplinary team met regularly and this helped to facilitate communication between the hospital personnel involved in the study, generate interest in and support for the study and improve collaboration between the clinicians, epidemiologists and microbiologists. However, some hospitals reported poor communication practices between these groups. Participants explained that lack of accountability can be an issue; that it is not always clear who is responsible for what and how each actor is expected to behave. This creates distrust and makes groups blame one

another when things go wrong. Participants explained that such dynamics can influence the clinician to take fewer samples. The microbiologists, in turn, may not share preliminary results because they do not want to mislead the clinician and so lead to development of tension. All administrative representatives, including those from research sites with good transparent communication, stressed the need to address communication barriers in future efforts. It was recommended that it was necessary to actively work on building trust between groups and to highlight the benefit of sharing information. A focus on this is expected to improve reporting and turnaround time.

Many clinics incorporate continuous training into their work, and work actively towards improving practices. Yet, several participants explained that further training is still required at all levels of organization: it is necessary to train the top managers on the importance of proper reporting and quality-assured laboratory capacity as a basis for improving patient safety through active IPC and antibiotic stewardship programmes; to train nurses on how to collect and store samples; and to train laboratory staff on SOPs. Participants also expressed a need for training to include methods of improved communication between the various actors in the process, and in ways to motivate people to change behaviours. Several participants also highlighted the need to provide additional support for epidemiologists to help them to facilitate dialogue between microbiologists and clinicians.

Discussion and recommendations

The PoP study was set up with the aim of stimulating collection of blood samples for culture from patients with suspected BSIs. In Georgia it was run as a pilot in clinical settings to assess the antibiotic susceptibility patterns in the main pathogens causing community-acquired and hospital-acquired BSIs.

The specific project goals were to:

- demonstrate the value of clinical microbiological diagnostics in routine patient care by providing timely feedback of laboratory results to clinicians to guide antibiotic treatment of BSI;
- establish good clinical practice for routine clinical work-up in hospitals and strengthen the AMR reference and surveillance capacity at the Lugar Centre, the national reference laboratory; and
- establish and support a surveillance infrastructure as point of departure for a national laboratory-based surveillance system for AMR.

Project goals

The value of clinical microbiological diagnostics in routine patient care

The first goal, demonstrating the value of clinical microbiological diagnostics in routine patient care by providing timely feedback of laboratory results to clinicians to guide antibiotic treatment of BSI, was reached in all four hospitals, as most of the participating clinicians indicated that they received the blood culture results more timely and could, therefore, use the preliminary results in their treatment decisions. During the PoP study, the working relation and trust between clinicians and the laboratory staff improved, which was mainly due to better communication of preliminary blood culture results – in particular the Gram stain result giving an indication about the most likely (group of) organism(s) – but communicating also when the blood culture was negative after 48 hours. From the clinicians' perspective, the PoP study helped to decrease the usage of antibiotics by allowing de-escalation of antibiotic therapy, and it shortened the therapy period, which was beneficial for the patients' health and made treatment more cost-effective. The median time until preliminary feedback decreased to two days as the study progressed. However, there is still room for improvement in the time that elapses before feedback of the final result. The median time for final feedback of the results was seven days (maximum 15), and it even increased slightly during the study. After such a long period, the antibiotic treatment may already be completed and the feedback is not useful for the clinician.

In intensive care units, some situations continue to occur where guidelines are not followed and clinicians keep prescribing broad-spectrum antibiotics without following laboratory investigation and AST results. For example, when a patient was very ill, clinicians as a precautionary option still chose to maintain initial antibiotic treatment covering a broad spectrum of pathogens even after Gram-stain excluded a group of pathogens. This indicates the need to further improve trust in laboratory results and the acceptance and adherence to clinical guidelines, especially for reserved antibiotics.

In addition to improving informed decision-making by clinicians, a surveillance system based on routine blood culturing has several other purposes. First, it enables hospitals to follow trends and emergence of new AMR. Timely identification by appropriate laboratory analysis and prompt feedback of results will help in achieving a faster response to newly emerging resistant strains, preventing their spread in health care facilities. For example, during the study period, carbapenem-resistant *K. pneumoniae* was discovered

several times in the same hospital during a short period and urgent feedback was given to the hospital's epidemiologists and infectious disease specialist to take specific preventive measurements. Second, the surveillance data can help to prioritize the actions that need to be taken. The data from the PoP study indicated that there is a need for IPC because carbapenem resistance, multidrug resistance and typical nosocomial infections as *B. cepacia* and *S. marcescens* were detected. Third, under certain conditions, the collected data can be used to develop or change existing guidelines on antibiotic administration and empirical therapy, countrywide as well as locally. For example, in the hospitals of the PoP study, a low proportion of MRSA (15%) was seen, suggesting that coverage of MRSA with vancomycin could be omitted from empiric therapy. However, because only a low number of *S. aureus* isolates were found in this survey (N=20), there was a large margin of statistical error (95% confidence interval, 5–36%), and decisions about changing antibiotic policy may need to be postponed until larger numbers of *S. aureus* isolates have been tested or policies should be implemented under strict monitoring of changing trends and readjusted if needed. In addition, care should be taken when extrapolating local data to national level and vice versa, because local spread/outbreaks of MRSA or other nosocomial bacteria may occur.

Good clinical practice for clinical work-up in hospitals and AMR reference and surveillance

The second goal was to improve the clinical work-up of patients with suspected BSI in the hospital and to strengthen laboratory skills and capacity at the national reference laboratory. In all four participating clinics, the use of blood culture diagnostics significantly improved during the project. This improvement was most apparent in intensive care units. Not only was the number of blood samples taken for culture higher but also the SOP for blood sampling was clearly followed in most cases and two blood culture sets were used. This is a very positive result because a higher blood volume improves the chance of identifying a pathogen and also gives more certainty when declaring a blood culture negative. The increase in samples taken for blood culture was achieved by training clinicians in identifying patients with suspected BSI, by encouraging them to take blood for culturing and by providing blood culturing materials free of charge. Although an important improvement was seen, the overall average rate of blood samples taken for culture (5.9/1000 patient-days) was lower than that seen in hospitals in most countries in the European Union, where the median rate is 30/1000 patient-days (range, 6.6–66.2) *(7)*. This observation, together with the facts that the rate of blood culturing in patients who were not in intensive care units remained low (2.1/1000 patient-days) and that the majority of blood samples were taken in patients already admitted to hospital for more than 48 hours, suggests that patients may have been missed, in particular those with community-acquired infections. In addition, nearly half of the samples were taken from patients who were younger than 1 month of age. This may have been due to a difficulty of changing current clinical practice throughout the hospital (i.e. active case finding was not effectively introduced in all wards) and that establishing trust and a working relationship between clinicians and the laboratory may have needed more time.

Regarding the second part of the goal, strengthening laboratory skills and capacity, the increased number of isolates for the PoP study allowed laboratories to gain experience using state-of-the-art AST methods. The processing of blood culturing was made more reliable by improving local laboratory procedures in the two hospitals with an in-house bacteriology laboratory, and by setting up a service-level agreement between the third and fourth hospital and the AMR reference laboratory and Telavi Laboratory of Sentinel Site to allow blood culture processing. The PoP study also prompted the implementation of EUCAST standards in the clinics as well as at the Lugar Centre. An important finding of the project was that hospital results agreed with central laboratory results in 78% of the isolates tested in duplicate. The discrepancies in laboratory results between the Lugar Centre and hospital laboratories show that it is important to keep working on quality improvement. A national reference laboratory can play a leading role to accomplish this by providing continued training to microbiologists, supporting the implementation of a harmonized approach to species ID and supporting the implementation of a laboratory quality management system, including daily quality assurance using strains from the American Type Culture Collection. For the last action to be successful, it is essential that laboratories participate in an external quality assessment (EQA) programme and implement internal quality control practices. Already since 2014, all laboratories participating in the PoP study have been enrolled in the WHO-CAESAR EQA programme for AMR. Under this programme, another 10 laboratories in the country have been receiving strains for proficiency testing

once per year to identify the bacterial species and to perform the AST. This was a big step in becoming part of CAESAR.

To expand the EQA practice to other laboratories in the country, important steps have been taken in the legislative process with the publishing of the Government of Georgia Decree No. 29, which approved the National Strategy 2016–2020 for Combating Antimicrobial Resistance. One of the objectives of the Decree is microbiological laboratory capacity-building, for which two specific activities were indicated:

5.1. Improvement of the quality of diagnostic testing in the microbiology laboratories; and

5.2. Preparing documents, standards, protocols and standard operating procedures (SOPs), regulating the process of provision of microbiological diagnostic service in health-care facilities.

A mandatory process for licensing of microbiological laboratories will be executed, and both external and internal quality control will be required. The indicated period to achieve this objective is 2017–2019.

Following the Decree, a national EQA programme was developed in early 2017 with support of the Ministry of Health, Labour and Social Affairs and is currently in the process of being implemented. The NCDC will be a leading agency to implement EQA in the country and is currently working to get the ISO 15189 licence that is needed to provide EQA. All microbiology laboratories that are registered in the country will become part of the national EQA programme, for which the legislation will be finished in June 2017. In addition, the NCDC is working on achieving the standards needed for ISO 17043, as Proficiency Testing Provider. As for the internal quality control, the NCDC Lugar Centre is already providing the reference strains to the PoP clinics to make sure the test performed at the local laboratories are reliable and match the control results. When the national EQA programme starts, it will include a laboratory quality management system and internal quality control and the Lugar Centre will provide training for laboratory personnel, standardization of laboratory methods and feedback and corrective actions for laboratories providing poor quality.

One additional and very important issue to take into account regarding laboratory quality is the procurement process for materials. The reliability and reproducibility of the laboratory results depend on the quality of the materials used. Therefore, it is strongly recommended that price should not be the only consideration in the procurement process but that there would also be minimal requirements set for the quality of materials. Preferably, minimum quality requirements will be formulated by a regulatory agency for a list of essential laboratory materials.

Surveillance infrastructure for a national sentinel laboratory-based surveillance system for AMR

The third goal for this study was also reached. A solid basis for a multicentre collaborative surveillance network was laid down by the study and a routine for standardized collection of AST results from the network laboratories has been developed. In its role as AMR reference centre, the Lugar Centre provides technical support and receives isolates for confirmatory testing and further characterization from clinics throughout Georgia. Fig. 1 (page 19) has an overview of the collaboration between hospitals, laboratories and the reference laboratory.

Recommendations

A number of recommendations can be made based on the PoP study for sustainable implementation of the routine practices instituted during the study and for further actions.

Strengthening the role of the Lugar Centre as the national reference laboratory

The Lugar Centre is acting as the national reference laboratory for AMR and provides technical and human resource support across the country. Following the end of the PoP study, the Lugar Centre will continue to support clinics with confirmatory species ID and AST and will do blood culture processing, species ID

and AST for clinics in the state programme that do not have laboratory capacity in-house. In addition, the NCDC will play a role in implementing the National AMR Strategy. The NCDC is named as (shared) responsible entity for objectives 1 to 7 of Decree 422 and will take the lead in the following:

- improving the quality of diagnostic testing in the microbiology laboratories, as described above for national EQA and internal quality controls;
- preparing documents, standards, protocols and SOPs, and regulating the process of provision of microbiological diagnostic service in health care facilities;
- training microbiologists and laboratory workers;
- defining clear surveillance objectives for national and local levels; and
- collecting at the Lugar Centre alert organisms as well as interesting AMR strains for additional investigation and storage.

The NCDC will provide training on standardization of laboratory investigations and AST, based on EUCAST standards, depending on the needs of newly enrolled laboratories. It also welcomes collaboration with any laboratory specialists who are willing to be part of the network or would like test confirmation at the central level.

It needs to be determined exactly what the collected data on alert organisms and AMR strains will be used for and this, in turn, will affect the decision on what data to collect and how. National surveillance objectives could be for monitoring quality and benchmarking, while local objectives could include developing antibiotic stewardship and IPC guidelines. It is also important to define how data will be presented publically and shared with third parties (Ministry of Health, Labour and Social Affairs, WHO, scientists, commercial parties), and how confidentiality of patients and business-sensitive information will be respected.

The Lugar Centre will collect alert organisms as well as interesting AMR strains for additional investigation and storage. It is mandatory for laboratories to send such organisms to the Lugar Centre under Decree 82, and the NCDC will start to actively monitor compliance. A complete list of alert organisms and interesting AMR strains needs to be created and shared.

At the NCDC, an AMR surveillance team was formed, including laboratory specialists, epidemiologists, representatives of the Ministry of Health, Labour and Social Affairs, hospital management representatives and the AMR focal point. Since 2016, the AMR surveillance team has held meetings to discuss new guidelines and the national strategy. In future, the role and responsibilities of the AMR surveillance team should be defined more clearly to include expected roles, responsibilities, format and so on.

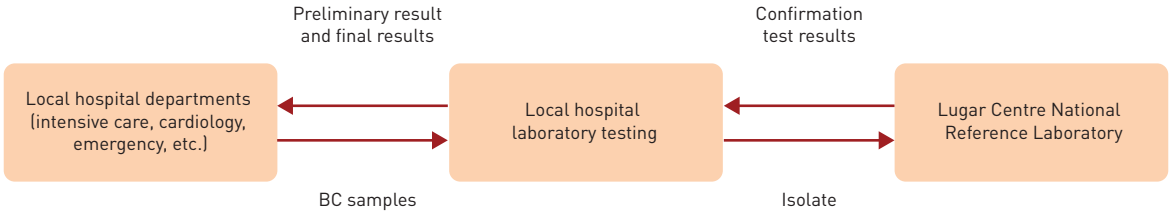
Expanding the national AMR surveillance network

The continuation and expansion of the surveillance network is of utmost importance, and the national AMR surveillance team can play an important role in leading the transition from the PoP study to routine AMR surveillance. This transition process has already started, as strong collaboration has been established and the network has grown since the start of the study. Currently, there are more than 15 laboratories involved in the network, which covers now more than 100 hospitals. The first data have been exchanged with CAESAR for the 2017 report, and the NCDC, with support of WHO and RIVM, will continue to collect and submit resistance data based on CAESAR requirements.

To facilitate the expansion of the national surveillance network, the AMR surveillance team should:

- complete the list of all registered laboratories in Georgia by May 2017, including the hospitals served by these laboratories;

Fig. 1. Overview of the collaboration between hospitals, laboratories and the reference laboratory for blood culture (BC) samples



- organize a meeting with laboratory and hospital managements to explain the importance of the network and encourage the hospitals and laboratories to join the surveillance network and work together (led by the NCDC); and

- organize periodic workshops, including multidisciplinary representation from participating hospitals, to foster collaboration by jointly discussing surveillance results, their consequences and future perspectives for AMR surveillance and control.

The mandatory registration of laboratories will be coordinated by the Ministry of Health, Labour and Social Affairs to provide an insight into the number of microbiology laboratories and their specifications.

In addition, the AMR surveillance team should take a lead in standardizing procedures in the surveillance process, in particular within these three stages:

- pre-analytical stage (blood culturing) to continue to spread and monitor use of SOPs;

- analytical stage (laboratory, sample processing and testing) to continue to develop and use SOPs, as stated in the National AMR Strategy activity 5.2 and enforceable through a governmental decree; and

- post-analytical stage (data entry, feedback report) to continue to support PoP laboratories and to start supporting newly connected laboratories with data collection by visits and direct meetings.

First steps should be for the NCDC to visit hospitals to help to standardize data collection, to organize a workshop on data management and data collection and to prepare AMR/health care-associated infection surveillance reports on a yearly basis.

These objectives will be closely monitored as described in the National AMR Strategy chapter 5, where 22 indicators for monitoring are listed. Every year, each indicator will be assessed within the evaluation frame and described in the Annual Report.

Strengthening diagnostic stewardship in hospitals

Diagnostic stewardship is defined as the "coordinated guidance and interventions to improve appropriate use of microbiological diagnostics to guide therapeutic decisions. It should promote appropriate timely diagnostic testing, including specimen collection, and pathogen identification and accurate, timely reporting of results to guide treatment" *(8)*.

While significant progress has been made as a result of the PoP study, there is still a need to continue working on implementation of practices to improve diagnostic stewardship. Hospitals administration should prioritize focus on the following activities:

- continuing to stimulate taking blood cultures and improve the rate of samples taken in patients with a suspected BSI by:
    - improving identification of patients with potential BSI in all departments by raising awareness, training nurses and physicians to improve active case finding of patients with suspected BSI and sepsis and disseminating widely information posters or leaflets that explain the SIRS criteria,
    - stimulating blood sample taking on all wards to attain full coverage of patients with BSI or sepsis, including community-acquired BSI, and
    - reducing the price for hospitalized patients (if paid out of pocket) to get bacteriological investigations of blood samples based on internal regulation, thus giving clinicians the opportunity to investigate all possible cases;
- continuing to improve turnaround time by improving communications and understanding between microbiologists and the clinician by emphasizing the connectedness between the different stages in the diagnostic pathway and drawing attention to the importance for the patient and patient safety;
- improving the quality of sampling and the laboratory processing of samples by:
    - continually stressing the need for clinicians to collect blood for culture before administering antibiotic therapy whenever possible,
    - training those taking blood for culture on best practice for blood sampling, to decrease the risks of contamination of the culture, and in other pre-analytical procedures such as sample handling (storage of the blood sample) and comprehensive collection of patient information,
    - training laboratory personnel to improve their knowledge of basic bacteriology, susceptibility testing and interpretation, as well as for SOPs for laboratory practice in accordance with internationally agreed standards and EUCAST methodology,
    - implementing laboratory quality management systems in all hospitals, including quality assurance using strains from the American Type Culture Collection;
- expanding the microbiology laboratory diagnostic arsenal to include quality-assured diagnostic capacities beyond blood cultures, by:
    - emphasizing that, although blood cultures are among the most important cultures taken to guide antimicrobial therapy and provide input for AMR surveillance, laboratory capacity should not be limited to blood cultures, and
    - including evidence-based recommendations about microbiological diagnostics that allow the guidance of antimicrobial therapy and inform IPC (e.g. active surveillance cultures or skin and soft tissue cultures).

The Lugar Centre will be in charge of coordinating and overseeing the education and training for laboratory personnel in the network (16 microbiological laboratories across the country) as well as for establishing the national EQA programme.

Improving IPC

This study has shown that nosocomial BSIs with multidrug resistant organisms occur in clinical settings in Georgia. Action needs to be taken to improve IPC in the coming years as it plays a significant role in the control of nosocomial infections and AMR; local surveillance data can be used to support IPC. The National Strategy 2016–2020 for Combating Antimicrobial Resistance suggests two main activities for improving IPC:

- establishing infection control committees at hospitals and strengthening surveillance of their performance; and
- updating documents and preparing protocols, guidelines and other information material; regulating IPC at health care facilities; and ensuring their communication.

In September 2016, the Ministry of Health, Labour and Social Affairs started monitoring IPC systems in hospitals. The regulatory agency and NCDC developed a checklist for hospital evaluation and monitoring of IPC, which will give a good overview of the state of IPC in Georgian hospitals and help to define steps to take in future. After the evaluation, hospitals receive a timeline for IPC improvement and will be re-evaluated after a defined time period. When hospitals are not able or willing to improve IPC, fines will be imposed and ultimately hospitals may even be closed.

With support of the Ministry of Health, Labour and Social Affairs, the NCDC has started to develop and translate IPC guidelines and help hospitals to implement them in each clinic. Specialists from the United States Centers for Disease Control and Prevention are supporting these activities. In addition, training will be given for WHO-recommended hand hygiene methods, sterilization and so on. It should be mentioned that hospital managements are open to strengthening their IPC and training specialists as well as to establishing local IPC committees.

Further improvement of IPC can be reached through the following activities:

- elaborating on national IPC regulations (Order No. 01-148/O in 2009; Order No. 01-38/N and Decree No. 165 in 2015) in by-laws to make them more tangible and practical, in particular stating clear indicators that hospitals and government can use to monitor the hospital's progress and setting minimal requirements for IPC (e.g. the establishment of an IPC committee in each hospital, a date by which it should be formed and specific indicators to monitor whether it performs adequately) (NCDC);
- strengthening measures for active and passive surveillance, improving sterilization, proper waste management, case definition and so on (hospital administration);
- using the national and local surveillance results to make and adapt IPC guidelines and to monitor the effectiveness of the IPC programme (NCDC); and
- training hospital staff in IPC, including active and passive surveillance, sterilization, waste management and case definition. (hospital administration/NCDC).

The NCDC provides a course certified and accredited by the Ministry of Health, Labour and Social Affairs that provides training for hospital staff in IPC and further efforts to include this programme in the curriculum of medical university schools is required.

Financing blood culturing and laboratory diagnostics in hospitals

The costs of materials and personnel for the blood analyses varied from hospital to hospital. The costs depended on whether the hospital had an in-house laboratory or had to make use of an external laboratory. In addition, costs depended on the testing method the laboratory used: performing testing manually or by machine. To give an indication of the price, in one of the hospitals the commercial price of a negative blood culture was $13, while a positive blood culture cost $17.

During the PoP study, the hospitals and NCDC were financially supported to partly cover for the needed human resources and to procure the needed materials for blood sampling and laboratory diagnostics. During the duration of the study (17 months), the financial support was decreased to gradually work towards a situation where NCDC and the hospitals were able to support their own costs. This has been partly achieved but more investment is needed for financing routine blood culturing and laboratory diagnostics to make this practice sustainable.

In Georgia, the costs of patient care at the hospital are paid by governmental insurance up to a certain amount. When the costs of care get above that limit, it should be covered by the patient or private insurance (if any). However, the governmental budget is mainly used by the hospitals to cover other expenses, leaving no budget for laboratory investigation unless the situation for the patient is very critical, for example when empiric therapy is not effective.

In order to make the process of taking blood for culture in patients with suspected BSI sustainable, hospital administrations need to see the benefits of using the laboratory results. These benefits include cost-saving, for example by reduced the length of stay in the hospital as a result of more efficient treatment and by reduced the number and amount of antibiotics prescribed because of better targeting of treatment. Although there are no figures for cost-saving calculated in the PoP study, hospitals indicated that they noticed a reduction in costs for antibiotic use. This may give room in the budget to cover the expenses of laboratory testing.

Conclusions

This PoP study has been beneficial for Georgia as laboratory capacity was strengthened for blood culture processing, species ID and AST at the local laboratories as well as at the national AMR reference laboratory. The laboratories are now capable of processing samples according to standard protocols and providing microbiological diagnostic information to guide appropriate treatment decisions. In addition, clinicians de-escalated empiric treatment for BSIs more often based on the blood culturing results according to international guidelines. Hospital epidemiologists also started IPC measures (e.g. waste management). All these can improve patient safety and quality of care in line with current international standards.

The PoP study provided baseline AMR data for the main pathogens causing BSIs in the country and formed a basis for a national AMR surveillance network and participation in CAESAR. The project gave a first systematic insight into the pathogens causing BSIs and their antibiotic susceptibility in Georgia. Even though the number of blood cultures initiated and processed significantly improved over the study period, the absolute number of isolates per species was low. As a consequence, the results should be interpreted with care and cannot be used to inform empiric antibiotic therapy guidelines. The majority of isolates was from paediatric patients with a suspected BSI of nosocomial origin, precluding generalization of results to (adult) patients with community-acquired infections. A further increase in the number of blood cultures taken from different patient populations is needed to allow the data to be used to inform empiric antibiotic treatment guidelines.Notwithstanding, resistance levels were high in general and suggest nosocomial spread of (multi-)drug-resistant pathogens and supports the plans to improve IPC policies.

The NCDC is currently working on expanding the number of hospitals in the surveillance network, including in all regions of Georgia. The new AMR strategy will be of great importance to make the surveillance network in Georgia sustainable. Expansion of the AMR surveillance network will contribute to collection of comprehensive and clinically well characterized local AMR surveillance data. Based on such data, local guidelines regarding empirical antimicrobial treatment choices may be composed.

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ANNEX 1

Laws and regulations

The Constitution of Georgia

The Law of Georgia "on Health Care"

The Law of Georgia "on Medical Practice"

The Law of Georgia "on Public Health"

The Law of Georgia "on the Rights of Patients"

Government of Georgia Decree No. 359, 22 November 2010 "On Adoption of Technical Regulations for the High-risk Medical Activities

Government of Georgia Decree No. 385, 17 December 17 2010 "On Adoption of the Provisions Concerning Rules and Conditions for Licensing of Medical Practice and Issuing Permits for Inpatient Health-care Facilities"

Government of Georgia Decree No. 422, 7 May 2013

Government of Georgia Decree No. 64, 15January 2014 "On Technical Regulations for Approval of Sanitary Rules for Waste Collection, Storage and Treatment in Healthcare and Preventive Healthcare Facilities"

Government of Georgia Decree No. 165, 24 April 2015 "On Approval of Technical Regulations for Disinfection and Sterilization in Healthcare, Public Health and Public Facilities"

Government of Georgia Decree No. 82, 19 February 19 2016 "On Sanitary Norms for Work on Biological Agents"

Government of Georgia Decree No. 29, 11 January 2017 "National Strategy 2016–2020 for Combating Antimicrobial Resistance"

Minister of Health, Labour and Social Affairs of Georgia Order No. 01-148/O, 14 April 2009 National Clinical Practice Guideline "Infection Control in Health Care Facilities"

Minister of Health, Labour and Social Affairs of Georgia Order No. 01-63/N, 12 September 2012 "On Ensuring Functioning of Internal System for Improving Quality of Medical Services and Safety for In-Patients at Inpatient Health-care Facilities"

Minister of Health, Labour and Social Affairs of Georgia Order No. 01-38/N, 7 September 2015 "On Approval of Rules for Epidemiological Surveillance, Prevention and Control of Nosocomial Infections"

ANNEX 2

List of protocols/SOPs

API 20E kit for Enterobacteriaceae No. SOP-BSL2-II-044-13

AST by disc diffusion No. SOP-BSL2-II-059-13

AST by Etest No. SOP-BSL2-II-059-13

Bacitracin test No. SOP-BSL2-II-047-13

Bacterial culture packaging and transportation No. SOP-NCDC/LC;LSS;ZDL-I-005-13

Beta-lactamase No. SOP-BSL2-II-007-13

Biosafety and biosecurity during visiting and handling patient No. SOP- NCDC/LC;LSS;ZDL-I-038-13

Catalase No. SOP-BSL2-II-004-13

Clinical sample transportation No. SOP-NCDC/LC;LSS;ZDL-I-004-13

Coagulase test No. SOP-BSL2-II-048-13

Collection of whole blood from patient for processing and transportation No. SOP- NCDC/LC;LSS;ZDL-I-036-13

Desoxilate test No. SOP-BSL2-II-049-13

E. coli identification No. SOP-BSL2-II-055-13

Gram stain No. SOP-BSL2-II-003-13

Indole No. SOP-BSL2-II-008-13

Motility No. SOP-BSL2-II-010-13

Optochine test No. SOP-BSL2-II-046-13

Oxidase No. SOP-BSL2-II-005-13

Risk assessment No. SOP-NCDC/LC-I-009-13 (SOP_CPHR_I-012-00_GEO)

Sample labelling No. SOP-NCDC/LC;LSS;ZDL-I-003-13

Sample receiving No. SOP-NCDC/LC-I-008-13 (SOP_CPHR_I-011-00_GEO)

Sample rejection No. SOP-NCDC/LC;LSS;ZDL-I-009-13

Shipping of biological agent No. SOP-NCDC/LC-I-010-13 (SOP_CPHR_I-013-02_GEO) (SOP_CPHR_I-015-02_GEO)

Smear fixation No. SOP-BSL2-II-002-13

Subculturing from blood culture bottles, microscopy and macroscopy investigation No. SOP-BSL2-II-038-13

Triple sugar iron/hydrogen sulphide No. SOP-BSL2-II-009-13

Urease No. SOP-BSL2-II-006-13

Using personal protective equipment No. SOP-NCDC/LC-I-022-13 (SOP_CPHR_I-032-00_GEO)

Waste management No. SOP-NCDC/LC-I-006-13 (SOP_CPHR_I-008-00_GEO)

The WHO Regional Office for Europe

The World Health Organization (WHO) is a specialized agency of the United Nations created in 1948 with the primary responsibility for international health matters and public health. The WHO Regional Office for Europe is one of six regional offices throughout the world, each with its own programme geared to the particular health conditions of the countries it serves.

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