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AmWeb: a novel interactive web tool for antimicrobial resistance surveillance, applicable to both community and hospital patients

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Background: Antimicrobial resistance (AMR) is recognized as one of the most significant threats to human health. Local and regional AMR surveillance enables the monitoring of temporal changes in susceptibility to antibiotics and can provide prescribing guidance to healthcare providers to improve patient management and help slow the spread of antibiotic resistance in the community. There is currently a paucity of routine community-level AMR surveillance information.

Methods: The HPA in England sponsored the development of an AMR surveillance system (AmSurv) to collate local laboratory reports. In the West Midlands region of England, routine reporting of AMR data has been established via the AmSurv system from all diagnostic microbiology laboratories. The HPA Regional Epidemiology Unit developed a web-enabled database application (AmWeb) to provide microbiologists, pharmacists and other stakeholders with timely access to AMR data using user-configurable reporting tools.

Results: AmWeb was launched in the West Midlands in January 2012 and is used by microbiologists and pharmacists to monitor resistance profiles, perform local benchmarking and compile data for infection control reports. AmWeb is now being rolled out to all English regions.

Conclusions: It is expected that AmWeb will become a valuable tool for monitoring the threat from newly emerging or currently circulating resistant organisms and helping antibiotic prescribers to select the best treatment options for their patients.

Keywords: microbiology, health informatics, antibiotics

Introduction

Antimicrobial resistance (AMR) is a serious and growing public health problem that has been recognized as one of the greatest threats to human health and its prevention and control is a global priority.[1] In Europe, a worrying increase in combined resistance to third-generation cephalosporins, fluoroquinolones and aminoglycosides in *Escherichia coli* and *Klebsiella pneumoniae* has been reported in one-third of countries reporting to EARS-Net in the period 2008–11.[2] In Europe, ~25 000 patients die annually from an infection with the most commonly isolated multidrug-resistant bacteria, with an annual estimated cost of ~€1.5 billion.[3] The estimated cost in the USA for patients with infections caused by antimicrobial-resistant bacteria is between US$6000 and US$30 000 more per patient than for those infected with susceptible bacteria.[4]

An important action in the global strategy to contain AMR is the establishment of effective surveillance systems at local, subnational and national levels.[1,5] Such surveillance systems should be designed to meet clearly defined objectives that address the requirements of key health partners. These objectives may include defining the extent of the problem and changes over time, detecting the emergence of new mechanisms of resistance and outbreaks, providing local information to inform the development of formularies and improve empirical prescribing, guiding the development of effective strategies and interventions, and evaluating the effectiveness of implemented control measures.[6–13] Surveillance information from these systems is only useful when it triggers an intervention. To this end, surveillance outputs from AMR surveillance systems must be timely, present data unambiguously and meet the needs of a range of users, including physicians, general practitioners, microbiologists, commissioners and providers of healthcare, and national and international health organizations.

Internationally, to support effective surveillance of AMR in member states, the WHO and European Union have separately sponsored technical initiatives aimed at enhancing the consistent collection, analysis and use of AMR data. The WHO provides

adaptable database software called 'WHONET' for collecting and analysing antimicrobial susceptibility data,[14] which is now used by many member states to support local and national AMR surveillance. The European Union sponsors the DebugIT project that aims to overcome the challenge of disparate data formats in different hospitals and countries by bringing together various routinely collected healthcare data, including microbiology results and prescribing data.[15]

A number of supranational AMR surveillance programmes have been launched, coordinated by the WHO or regional institutes.[16] The European Centre for Disease Prevention and Control sponsors EARS-Net, which brings together data from national surveillance systems to create a Europe-wide resource of AMR surveillance data for seven bacterial species isolated from blood or CSF cultures.[2] In the USA, the Emerging Infections Programs (EIP) were established in 1995, collating data from a network of 10 state health departments and other collaborators with the aim of forming a representative demographic population for national surveillance. A number of surveillance schemes operated within EIP collect data on AMR in specific disease areas, such as invasive bacterial infections, foodborne disease, healthcare-associated infections and enteric infections.[17]

In England, AMR surveillance has mostly been undertaken by the HPA, which became part of Public Health England in April 2013, and the British Society for Antimicrobial Chemotherapy (BSAC). These are targeted surveillance systems that monitor AMR trends in specific infections or isolates from respiratory and blood specimens sent to participating laboratories, including reference laboratories.[18] A further source of AMR data in England, Wales and Northern Ireland is an HPA-operated surveillance system known as CoSurv, which monitors laboratory notifications of infectious diseases of public health interest from individual diagnostic laboratories.[19] Together, the notification and targeted systems provide a mechanism for monitoring AMR in specific organisms and infections in the UK. However, there is a significant gap in monitoring the resistance of isolates acquired from routine diagnostic microbiology, particularly those from community specimens. Specifically, there has not been a system to collate resistance data from urinary tract infections (UTIs), from which plasmid-mediated multiresistance is increasingly being reported in community isolates.[8]

In order to complement existing UK systems and address the current gaps in AMR surveillance in England, the HPA developed antimicrobial surveillance software (AmSurv) to facilitate the collection of antimicrobial susceptibility reports for all bacterial isolates, including those from community samples, tested in participating laboratories against antibiotics. The implementation of this system across the nine English regions began in 2009. We have developed AmWeb, a novel web-enabled reporting tool, to allow laboratories in the region to analyse and review their own data, which are electronically submitted to the regional server. This produces both an incentive for their continued participation and a means for the local, timely monitoring of changes in AMR and the intervention of changing prescribing practice.

Methods

Population studied

The West Midlands is one of nine English regions, with a population of 5.6 million (2011 census) and contains the City of Birmingham, the second most populous city in the UK. At the time of writing, the region was divided into 17 Primary Care Trusts (PCTs), which acted as commissioners of health services for their local populations. However, due to a reorganization of the National Health Service (NHS) in England, PCTs were abolished on 31 March 2013, with newly established Clinical Commissioning Groups (CCGs) taking on their commissioning role.

AmSurv system and data sources

There are 15 diagnostic microbiology laboratories in the West Midlands region serving primary and secondary healthcare settings. Six different laboratory information systems (LIS) are operated across the region, with each individual laboratory using a range of bespoke codes for recording data items, including antibiotic susceptibility test results. LIS reporting tools are used in each laboratory to output routine AMR surveillance data in a predefined text format. These laboratory text files are then reformatted and local codes translated to NHS Organisation Data Service codes,[20] where available, or standard HPA codes by HPA-provided software called LabLink+. The resultant files are then encrypted and delivered weekly using semi-automated batch routines to the AmSurv database at the Regional Epidemiology Unit (REU) by e-mail.

In the West Midlands, all 15 microbiology laboratories report weekly to the REU. The reports include the organism isolated, antibiotic susceptibility interpretation (i.e. susceptible (S)/intermediate (I)/resistant (R)), MIC value (where available), patient identifier, date of birth, gender, patient postcode, requesting source (community or hospital), specimen type, specimen date and medical specialty of the doctor who submitted the specimen to the laboratory.

Data validation

Laboratory reports received by the REU are checked for completeness of data items and correct coding. Reports failing data validation are held in 'quarantine' until the sending laboratory is contacted to obtain the missing data items/codes translations. Following import of the laboratory data, de-duplication routines remove exact duplicates (i.e. same patient and same specimen number with matching results) and append any changes in results to existing records.

AmWeb

This is a web-based surveillance reporting application developed to host the regional AmSurv AMR data. Extraction, cleaning and secure transfer of AMR data from the AmSurv database to the AmWeb application are automated on a weekly schedule. The application includes management tools that control internet access via set user permissions and log-ins. The application has in-built reporting tools that enable users to define and run graphical and tabular reports.

Architecture and processes

The AmWeb application runs on Microsoft.Net Framework 2.0 and is database driven using SQL Server 2005. It was built using Microsoft Visual Studio 2008 in VB.NET and ASP.NET (Figure 1).

A copy of the regional AmSurv database is created using scheduled SQL Server routines that remove subsequent specimens from the same patient and specimen type, with matching results, within a 14 day episode length (based on specimen date) from the copied database. The fields used for matching and de-duplicating records are laboratory ID, patient ID, patient NHS number, patient date of birth, patient postcode, organism, antibiotic, antibiotic result, specimen, specimen date, specimen source location and medical speciality. Once duplicate episodes have been excluded, the records are anonymized by removing patient ID, NHS number, date of birth and postcode data from the

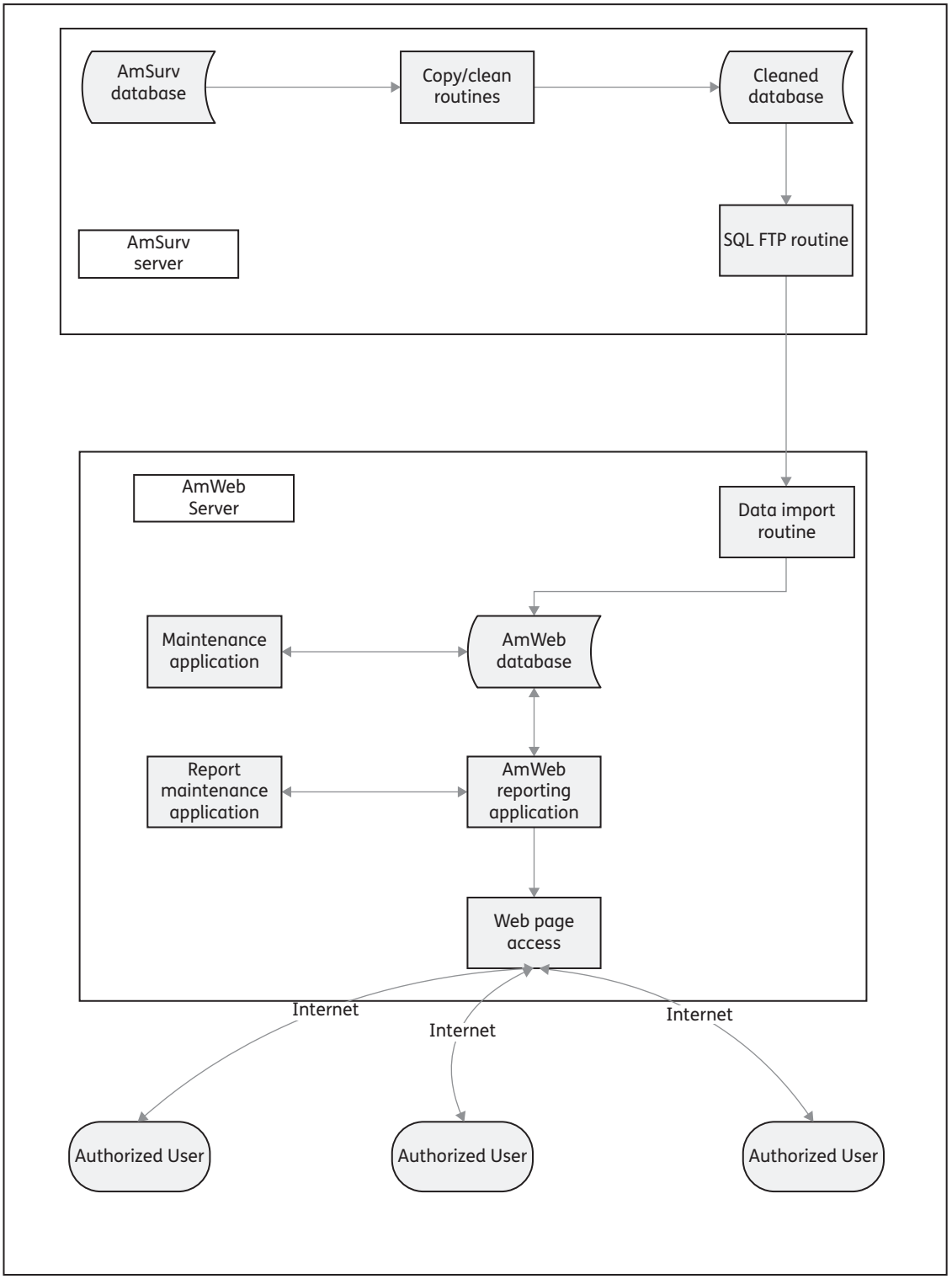

Figure 1. AmWeb process map.

copied database. A scheduled output file is created using Microsoft SQL Server Integration Services. The export application polls for a suitable file every 15 min and when found uses secure FTP to transmit the file to a designated directory on the AmWeb server. In the AmWeb application, an import routine built in VB.NET runs continually as a Windows service. The import directory is polled every 15 min for new files. When a new file is found, the application inserts the data into the AmWeb database using SQL database transaction routines.

User-defined reports

Microsoft SQL Server 2005 Reporting Services are used to extract data from the SQL Server database and provide graphical and tabular outputs. Reports are viewed using a report viewer control, which is embedded into the web application.

Two report types have been developed: drug/bug combinations and tabular reports. For drug/bug reports, a maintenance screen allows users to select antibiotic and organism combinations and save these to their log-in accounts (Figure 2). Users are provided with an option for the report to be included or excluded when reports are next run.

A maintenance screen also allows users to select antibiotics to be included in a tabular report, which can be used to review susceptibility against selected organisms or organism groups over a defined period of time. The antibiotic panels can be retrieved at any time for editing or deletion.

The reports menu enables users to select either a tabular or drug/bug report type and allows reports to be filtered by hospital trust, reporting laboratory, local government authority or PCT (to be replaced by CCG geographical boundaries in April 2013). Reports can be also be filtered by age group, gender and specimen type.

Results

Since the implementation of the AmSurv surveillance system in the West Midlands in September 2009, data volumes have increased significantly. Monthly reports of individual antimicrobial susceptibility tests rose from 120 000 per month in November 2009, with three laboratories reporting, to ~320 000 per month from 15 reporting laboratories in November 2012. As of January 2013, there are 10 million individual records of antimicrobial susceptibility tests captured in the database.

With all laboratories reporting in the region, an average of 40 000 bacterial isolate reports are received each month by the REU, ranging from 40 isolates/month from the smaller specialist laboratories to 4000 isolates/month from the larger laboratories.

Although the AmSurv database has been implemented across England, not all regions have yet achieved sufficient levels of reporting from their laboratories to allow valid and representative national comparison.

AmWeb Case Study A

Figures 3 and 4 are the AmWeb graphical representations of a time series of drug/bug combination reports at the local and regional setting. Figure 3(a) shows the trends in the proportion of *E. coli* isolates reported as susceptible, intermediate or resistant to co-amoxiclav by a local laboratory. Figure 3(b) shows the number of *E. coli* isolates tested against co-amoxiclav by the same laboratory over the same period. These graphs show that over a 14 month period, testing of *E. coli* isolates against co-amoxiclav remained relatively stable, but the proportion of isolates reported as resistant to co-amoxiclav increased steeply in July 2011 from ~15% to ~40% and remained at this level for 6 months before decreasing to the levels observed in the first half of 2011. On investigation, this observed pattern was found to be due to a change to BSAC breakpoint guidelines,[21] recommending an increase in the zone diameter for interpreting *E. coli* susceptibility to co-amoxiclav, which the laboratory instituted in July 2011. The breakpoint was subsequently reversed by the laboratory for isolates from patients with a UTI; consequently, resistance proportions returned to the previous level. Following concerns raised by laboratories regarding reporting increased resistance to co-amoxiclav for urine isolates following implementation of new guidelines, the BSAC has now introduced an increased MIC breakpoint specifically for UTIs.[22] Figure 4 shows the regional trends for the same drug/bug combination during this period for comparison and clearly shows a stable trend over time, suggesting that most laboratories ignored the change recommendation.

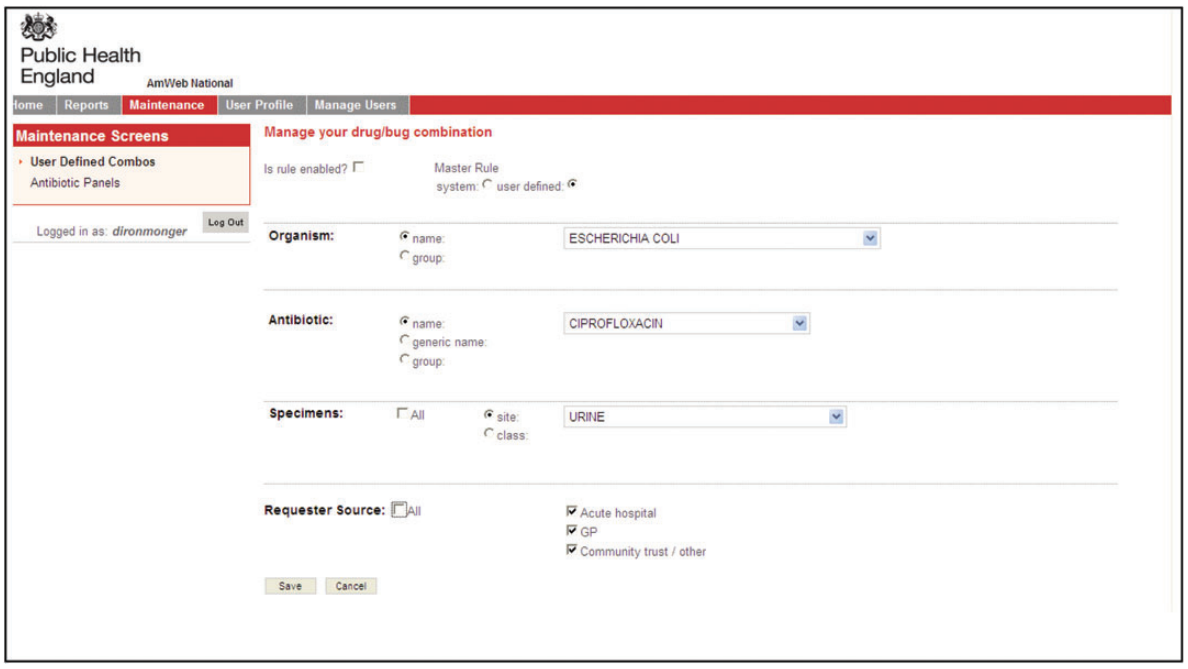

Figure 2. AmWeb drug/bug report maintenance screen.

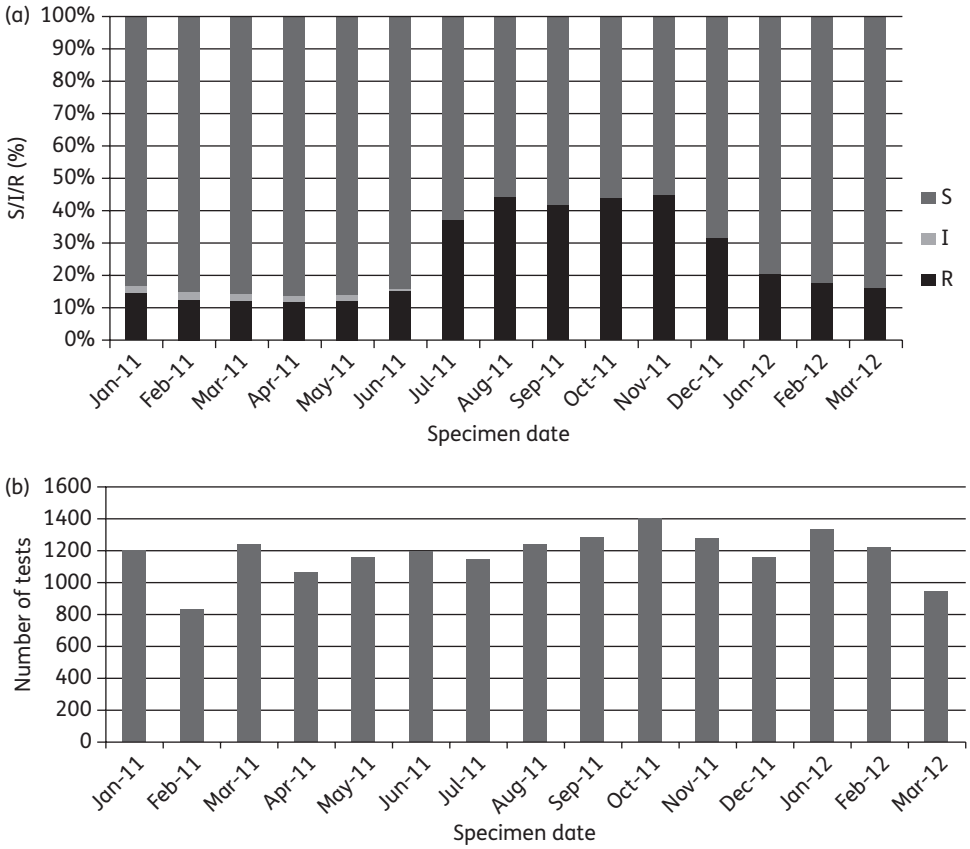

Figure 3. (a) Distribution of resistance profile of *E. coli* isolates from all specimens, tested against co-amoxiclav in Laboratory A between January 2011 and March 2012. (b) Number of *E. coli* isolates from all specimens, tested against co-amoxiclav in Laboratory A between January 2011 and March 2012.

AmWeb Case Study B

Table 1 shows an AmWeb tabular report for numbers of isolates and proportions of *E. coli* urinary isolates reported as resistant in selected PCTs in the West Midlands in 2011. The table shows wide variation in the reported resistance proportions between the PCT areas, with the proportion of *E. coli* isolates resistant to cefalexin ranging from 4% to 10% and co-amoxiclav resistance ranging from 9% to 24%. The number of tests performed for each antibiotic against the specific organism is also displayed. It can be observed that in some areas, local laboratories are performing selective testing for certain antibiotics by not testing all *E. coli* isolates against specific antibiotics, which may lead to higher apparent rates of resistance due to selection bias. This is particularly true for PCT 4, where the local laboratory only tests isolates against ciprofloxacin when resistance to first-line antibiotics is detected. The corresponding resistance proportion to ciprofloxacin in this area was 27%, compared with the regional average of 10%.

Regional epidemiology

In the first 6 months of operation, the AmWeb application has also been used by the West Midlands REU to detect and monitor unusual resistance profiles, such as outbreaks of multidrug-resistant Gram-negative bacteria in local hospitals. In recent small outbreaks of carbapenemase-producing organisms, AmWeb has been used to monitor the occurrence of new, potentially linked cases, through the use of distinctive AMR profiles set up as alerts on the system so as to detect potential local spread of these resistant organisms. As an example, Figure 5 shows a time-series chart marking the appearance of *K. pneumoniae* resistant to imipenem in a local hospital. The number of *K. pneumoniae* isolates tested against imipenem by the laboratory is also shown. Following investigation, this was found to be due to spread of a strain producing Verona integron-encoded metallo-β-lactamase (VIM).

Discussion

The development of surveillance systems to monitor trends in AMR at the local, subnational and national levels is an important element in controlling the emergence and spread of AMR. Advances in informatics reduce the burden on laboratories of reporting timely routine surveillance data and web-enabled database tools are now able to process large datasets in real time.[8,12] For example, in Germany, a sentinel laboratory-based antibiotic resistance surveillance system collects electronic reports of all clinically relevant bacterial pathogens from healthcare providers in 9 of the 16 federal states (as of 2011) with access to reports via a web portal.[23]

An ideal AMR surveillance system will receive susceptibility test data from laboratories using a standardized testing and reporting methodology with a consistent set of antibiotics tested. This is underscored by the observed shift in the resistance trend in Laboratory A following the adoption of different guidelines for the interpretation of susceptibility to co-amoxiclav (Figure 3).

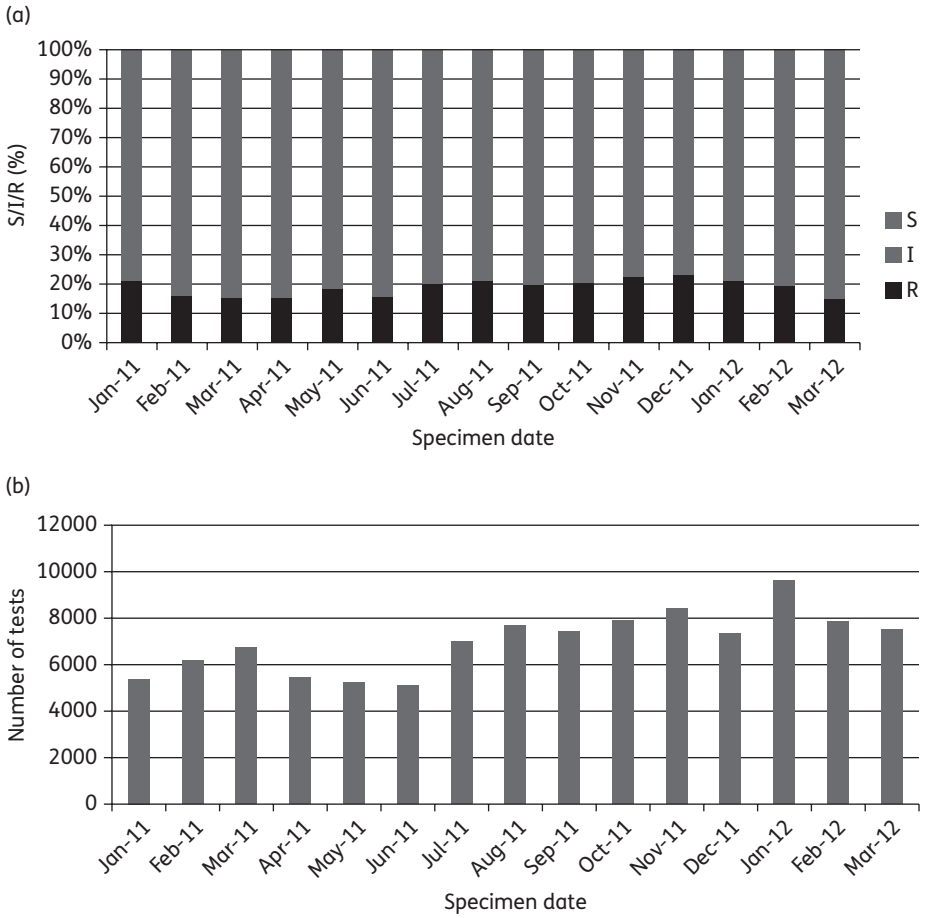

Figure 4. Drug/bug example regional reports for *E. coli* isolates from all specimens tested against co-amoxiclav by laboratories in the West Midlands region between January 2011 and March 2012. (a) *E. coli* susceptibility to co-amoxiclav for isolates from West Midlands laboratories. (b) Number of *E. coli* isolates tested against co-amoxiclav in West Midlands laboratories.

Table 1. Susceptibility of *Escherichia coli* isolates from urine samples to co-amoxiclav, ciprofloxacin and cefalexin in PCT areas showing the greatest between-area differences in 2011

		Co-amoxiclav		Ciprofloxacin		Cefalexin	
	No. of *E. coli* UTI isolates	no. isolates tested	% resistant	no. isolates tested	% resistant	no. isolates tested	% resistant
PCT 1	2523	2523	21	2519	7	2516	6
PCT 2	1685	1685	24	1681	15	1685	10
PCT 3	3165	3162	10	411	14	132	4
PCT 4	9830	9067	9	923	27	8557	5
Regional totals[a]	54287	50339	18	44493	10	48068	7

[a]Includes isolates from all 17 Primary Care Trusts areas within the region.

A recent survey of laboratories in the West Midlands by one of the authors (D. Ironmonger, unpublished data) showed variation in the laboratory methods and protocols for both the identification of bacterial isolates and the determination of antimicrobial susceptibility.

However, this survey also demonstrated a recent growing trend towards using automated susceptibility-testing systems, with 11 of the 15 diagnostic laboratories now using the bioMérieux Vitek 2 system for some or all of their antimicrobial susceptibility testing. This is likely to have a positive impact on the standardization of methods, the range of antibiotics tested and the consistency of regional AMR data, as well as enabling microbiologists to benchmark AMR rates across the region. There has also been a progressive move to greater international standardization

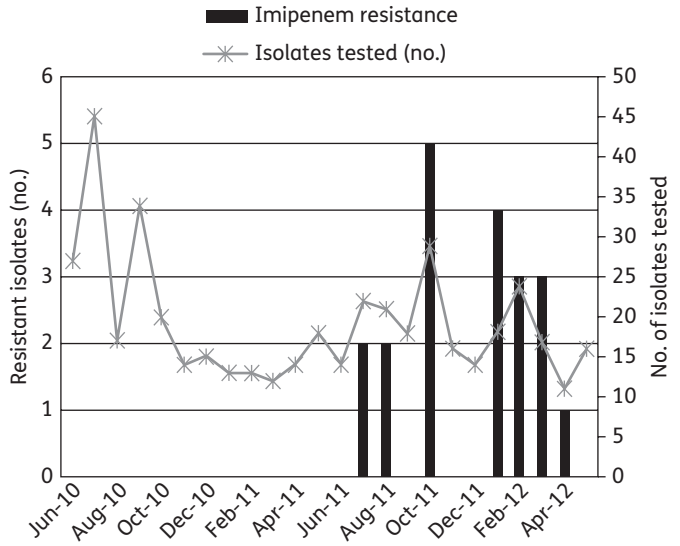

Figure 5. Results of susceptibility testing to imipenem for *K. pneumoniae* isolates from all specimens, reported by Laboratory B, together with totals of *K. pneumoniae* isolates tested against imipenem by Laboratory B.

with the adoption of much more similar breakpoints by the CLSI and EUCAST recently.[24]

AMR surveillance systems need to implement a process for identifying and handling duplicate entries. Inadequate clean-up processing risks affecting the validity of AMR surveillance information through the introduction of measurement bias. Guidelines from the CLSI (formerly NCCLS) recommended that results from only the first isolate of a species from a patient should be included in calculating the percentage susceptibility to an antibiotic.[25] However, selecting only the first isolate limits the ability to monitor and identify any changes in antimicrobial susceptibility at the individual level, perhaps as the result of antimicrobial therapy.[26] A study reviewing exact duplicates found that exclusion of duplicates did not make a significant difference in regional resistance estimates, with the exception of screening for methicillin-resistant *Staphylococcus aureus*.[27] We found that a 14 day repeat exclusion rule removes on average <5% of AmSurv reports and this did not increase significantly if the repeat exclusion episode length was extended beyond 14 days. To this end, we were confident in implementing a 14 day blanket repeat exclusion rule in AmWeb, which is also the period used to determine episodes of infection in the HPA CoSurv system.

The number and variety of LIS in use across England has always posed a problem for those designing laboratory-based surveillance systems. In parts of Europe, one laboratory can serve >60 hospitals; however, in the UK, each NHS laboratory usually provides services for a single or small group of hospitals and their local community healthcare providers. There are nearly 200 NHS diagnostic laboratories in England and 14 different varieties of LIS. Each of these laboratories has developed bespoke codes for pathology data items. This poses a real challenge in extracting and collating healthcare information from the disparate information systems and an even greater challenge in trying to impose new standard codes on historic patient-care data.[12] AmSurv has been designed to manage this diversity of LIS systems by simplifying the output requirements and translating local codes to nationally recognized formats.

As culture-based susceptibility testing information is not always available to the clinician at the time of therapeutic decision making, and there can be geographical differences in susceptibility to specific antimicrobials,[7,28,29] timely antibiotic susceptibility information, filtered by hospital or community samples and viewed by local geographies, has the potential to inform local prescribing. Initial feedback from hospital and community pharmacists suggests that AmWeb data are being used actively to review the validity of current local hospital and community antimicrobial formularies. A survey of local antibiotic prescribing by the West Midlands Strategic Health Authority (R. Seal, West Midlands Strategic Health Authority, unpublished data) demonstrated significant variation between PCTs for commonly prescribed antibiotics in the community. Variation in prescribing patterns and observed resistance through AmWeb have prompted the initiation of further work in the region, reviewing variables such as local prescribing formularies, local antibiotic susceptibility testing methods, microbiology sampling policies and local demography, in an attempt to identify and quantify potential confounders and bias that may impact on observed relationships between reported resistance and local prescribing habits.

In order to expand the availability of local AMR information to clinicians in primary care settings in the West Midlands, a regional AMR focus group of microbiologists, pharmacists and epidemiologists has been formed to guide the development of surveillance outputs that will meet the needs of the local community. The group also has responsibility for the ongoing assessment of the usefulness, acceptability and impact of the AmWeb application within the region. The group will provide an advisory role regarding the planned expansion of access to AmWeb and surveillance outputs to those responsible for commissioning community health services, and will be involved in investigating the potential for linkage with other systems, such as hospital and community prescribing datasets. Although individual reports of multidrug-resistant organisms are analysed by the REU using scheduled database queries, AmWeb reports are presently based on aggregate data. However, the group is also exploring the incorporation of real-time resistant phenotype profiling tools as used by WHONET to detect unusual individual resistance, clusters or potential outbreaks.[30] Following a successful pilot in three regions, the AmWeb web reporting tool is now being rolled out across England.

The AmSurv system collates routine reports of all positive bacterial isolates tested against antimicrobials, rather than the small proportion of positive isolates that laboratories have a statutory requirement to report under the Health Protection (Notification) Regulations 2010.[31] The development of AmWeb therefore provides a tool for health professionals to interrogate a complete range of AMR surveillance data, produce reports relevant to their geographic area and identify the first appearance of novel resistance markers. It also provides an opportunity, for the first time in England, to review variation in laboratory-to-laboratory antimicrobial susceptibility testing as a first step to identifying and understanding the reasons behind the observed differences.

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All other authors: none to declare.

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