The Specialist Advisory Committee on Antimicrobial Resistance Surveillance Subgroup has reviewed national surveillance systems for antimicrobial resistance (AMR). The review has included literature searches and web searches to identify published and unpublished data relevant to surveillance systems, semi-structured interviews with 25 key informants (including representatives of the Health Protection Agency at national, regional and local level, consultant microbiologists, those involved in novel surveillance initiatives, those involved in the National Health Service information strategy, representatives of GP networks and representatives of academic primary care) and a stakeholder workshop with over 40 participants. The report also draws on recent Department of Health funded work on surveillance of AMR, antimicrobial prescribing and complications of infection. This report presents a summary of current and planned surveillance activities related to AMR, identifies gaps and makes recommendations for enhancements in surveillance of resistance in primary care and the community.

Keywords: UK, resistance surveillance, surveillance systems

Overview of current surveillance of antimicrobial resistance in the UK

Most antimicrobial resistance (AMR) surveillance is undertaken by the Health Protection Agency (HPA) or involves projects sponsored by the British Society for Antimicrobial Chemotherapy (BSAC). The main AMR surveillance schemes of the HPA and the data arising from them have recently been summarized.1

**CoSurv and Lab-Link**

CoSurv is the main system used for communicating results from microbiology laboratories around the country to the HPA. It is a set of database modules installed in microbiology laboratories, Health Protection Units (HPU) and Regional Units. Results are fed electronically (or occasionally on paper forms) to Regional HPUs and then to the Centre for Infections (CfI) in London.2 Lablink+ is the software that links local laboratory information management systems (LIMS) and the CoSurv module. CoSurv reports contain demographic and some clinical data. For bacteraemias, data on antibiotic susceptibility results are also routinely collected.

**Bacteraemia surveillance**

The majority of AMR surveillance in the UK is based on collation of data from bacteraemias. CoSurv is the main system for the voluntary reporting of bacteraemia data to LabBase 2, the database maintained by the HPA. CoSurv is also being developed to allow collection of data needed for mandatory reporting of *Staphylococcus aureus* and glycopeptide-resistant enterococci (GRE).

The mandatory *S. aureus* bacteraemia surveillance scheme began in April 2001.3 The methicillin-resistant *S. aureus* (MRSA) bacteraemia Enhanced Surveillance Scheme (MESS) has been mandatory for all NHS acute trusts in England since 1 October 2005. Trusts have access to a website that they can use to enter details about each MRSA bacteraemia episode that is detected in their Trust. Enhanced surveillance involves collecting patient details for each MRSA bacteraemia episode.
including NHS number, hospital number, date of birth and sex, as well as information concerning the patient’s location, date of admission, consultant specialty and care details at the time the blood sample was taken. Mandatory GRE bacteraemia surveillance monitoring vancomycin resistance in clinically significant isolates began in 2003.3

A potential weakness of surveillance based on bacteraemias is that these specimens represent the severe end of the disease spectrum and are primarily from hospitalised patients. The extent to which this matters is likely to vary depending on the organism under study. For example, resistance levels reported in Streptococcus pneumoniae bacteraemias through the HPA surveillance scheme are broadly similar to those identified from the BSAC respiratory surveillance scheme which focuses on community-acquired infections (see below). Conversely, for E. coli infections, resistance levels from bacteraemic patients are higher than from community-derived isolates from urinary tract infection.5 For staphylococci, the resistance levels are clearly not representative of community resistance levels. Despite these concerns, the bacteraemia surveillance schemes provide a very valuable way of monitoring trends in the development of resistance and guiding prescribing policy, particularly in hospital settings.

Data from HPA reference laboratories

Data from HPA reference laboratories are also used to monitor resistance trends in Mycobacterium tuberculosis, Neisseria meningitidis and Haemophilus influenzae. These surveillance systems are largely independent of the CoSurv system and rely on isolates being forwarded to the reference laboratories. For these infections, the reference laboratories aim to capture information on all clinically relevant culture-confirmed cases. Where resistance testing is the main reason for referral (e.g. M. tuberculosis) then this form of surveillance is likely to be highly complete. Monitoring of resistance in Campylobacter spp., Salmonella spp., Helicobacter pylori and fungi is based on analysis of isolates referred to reference laboratories. For these organisms, the systems do not attempt to include all isolates. For Salmonella, most are likely to be referred but for H. pylori and Campylobacter relatively few are referred and they are therefore unlikely to be representative.

The Gonococcal Resistance to Antimicrobials Surveillance Programme

Gonococcal Resistance to Antimicrobials Surveillance Programme (GRASP) was created in 2000 to monitor resistance in gonococci in England and Wales. GRASP collects and centrally tests isolates from 24 sentinel surveillance laboratories between June and August each year.6 Clinical and epidemiological data is collected from genitourinary medicine clinics, including site of infection, gender, sexual orientation, country of birth, ethnicity and geographical location.

HIV resistance surveillance

UK surveillance of HIV antiviral resistance is based on the submission of resistance test data to a national database held at the MRC Clinical Trials Unit and includes the HPA as a major partner. All major clinical centres and/or virology laboratories providing resistance testing for UK patients (England, Scotland, Wales and Northern Ireland) are represented, and it is estimated that more than 85% of resistance tests undertaken within the UK are submitted.

Other viruses

There are currently no routine systems for monitoring resistance to antivirals for hepatitis B or C viruses, influenza virus, cytomegalovirus or herpes simplex virus although the European surveillance network for vigilance against viral resistance (VIRGIL) is seeking to develop methodology for surveillance of resistance in hepatitis B and C and influenza viruses.

Parasites

Data on malarial resistance are collated by the HPA Malaria Reference Unit.7

BSAC Respiratory and Bacteraemia Resistance Surveillance Programmes

BSAC surveillance covers community-acquired lower respiratory and hospital- and community-acquired bacteraemia isolates gathered by a network of laboratories in England and Wales (as well as Scotland, Northern Ireland and the Republic of Ireland). Isolates are tested in a central laboratory; bacteraemia isolates are tested by the Antibiotic Resistance Monitoring and Reference Laboratory of the HPA in London and respiratory isolates are tested by GR Micro Ltd, London.8 The respiratory surveillance programme asks laboratories to send in S. pneumoniae, H. influenzae and Moraxella catarrhalis isolates from lower respiratory tract samples from patients with presumed community-acquired lower respiratory tract infections during the winter season (isolates from patients in hospital more than 48 h, with cystic fibrosis and repeat isolates within 2 weeks are excluded).9 During the winter collection period each centre collects: 50 consecutive isolates of S. pneumoniae (total 1000), 50 consecutive isolates of H. influenzae (total 1000) and 25 consecutive isolates of M. catarrhalis (total 500). MICs are determined using the BSAC agar dilution method. Organisms monitored in the bacteraemia programme are shown in Table 1.

The UK also participates in a number of European surveillance schemes for AMR.

Table 1. Organisms monitored in BSAC bacteraemia surveillance

<table>
<thead>
<tr>
<th>Gram-negative</th>
<th>Gram-positive</th>
</tr>
</thead>
<tbody>
<tr>
<td>E. coli</td>
<td>S. aureus</td>
</tr>
<tr>
<td>Klebsiella spp.</td>
<td>Coagulase-negative staphylococci</td>
</tr>
<tr>
<td>Proteus spp.</td>
<td>S. pneumoniae</td>
</tr>
<tr>
<td>Pseudomonas spp.</td>
<td>β-haemolytic streptococci</td>
</tr>
<tr>
<td>Enterobacter spp.</td>
<td>Non-haemolytic streptococci</td>
</tr>
<tr>
<td>Other Gram-negative bacteria (pooled group)</td>
<td>Enterococcus spp.</td>
</tr>
</tbody>
</table>
European Antimicrobial Resistance Surveillance System

European Antimicrobial Resistance Surveillance System (EARSS) collects resistance information on invasive isolates of *S. aureus*, *S. pneumoniae*, *Enterococcus faecium*, *Enterococcus faecalis*, *E. coli*, Klebsiella spp. and *Pseudomonas aeruginosa*.

Invasive isolates were chosen as these are relatively completely sampled and tested, avoiding the sampling bias associated with isolates causing less severe disease. As of December 2003, there were ~791 participating laboratories in 28 countries. EARSS gathers basic clinical and demographic data and distinguishes between ambulatory and hospitalized patients.

Information on laboratory methodology, hospital type and size (number of bed days and catchment population) are collected. The system also includes EARSS-IBIS, an internet-based information system allowing sharing of information and tracking of unusual resistances.

External quality assurance is a collaborative effort carried out by UK National External Quality Assessment Service, Centre Nationale de Reference des Antibiotiques and the EARSS External Quality Assessment Committee.

European Committee on Antimicrobial Susceptibility Testing and European Society for Clinical Microbiology and Infectious Diseases

European Committee on Antimicrobial Susceptibility Testing (EUCAST) was formed by the European Society for Clinical Microbiology and Infectious Diseases and National Breakpoint Committees in Europe in 1997. EUCAST is working towards the harmonization of breakpoints across Europe and standardized susceptibility testing methods.

European Network for Antimicrobial Resistance

European Network for Antimicrobial Resistance was established at the end of 1995 and is funded by the European Union. The network has built a European strain bank of relevant organisms from ongoing surveillance studies. It uses these organisms to study the epidemiology and molecular mechanisms of AMR and how these interact with infection control policies and antibiotic consumption in Europe.

Enteric surveillance in Europe

Enteric surveillance in Europe (Enter-Net) performs surveillance across the European Union and Australia, Canada, Japan, South Africa, Switzerland and Norway of *Salmonella/AMR in Salmonella* and verotoxin-producing *E. coli* that are reported to national reference laboratories. Resistance in selected *Salmonella* strains is monitored.

European surveillance network for vigilance against viral resistance

VIRGIL is seeking to develop methodology for surveillance of resistance in hepatitis B and C and influenza viruses.

Other international AMR surveillance systems

There are a range of international surveillance systems including: International Network for the Study and Prevention of Emerging Antimicrobial Resistance (INSPEAR—surveillance of nosocomial resistance—led by the Centers for Disease Control), Meropenem Yearly Susceptibility Test Information Collection (MYSTIC—resistance to carbapenems in hospitals), SENTRY—pathogens of interest are: bloodstream infections, community-acquired respiratory tract infections, pneumonias in hospitalized patients, skin and soft tissue infections, and urinary tract isolates from hospitalized patients, gastroenteritis pathogens and β-haemolytic streptococci. Prospective Resistant Organism Tracking and Epidemiology (PROTEKT) monitoring susceptibility of *S. pneumoniae*; the Surveillance Network Database (TSN—routine data automatically extracted from microbiology laboratories updated daily and available over the internet) and the Global Advisory on Antibiotic Resistance Data (GAARD—which brings together data from a number of surveillance systems and is organized by the Alliance for the Prudent Use of Antibiotics).

Surveillance of antimicrobial prescribing

National monitoring of antimicrobial prescribing in the community uses the Prescription Pricing Authority’s Prescribing Analysis and Cost (PACT) data. This is able to monitor trends in prescribing of specific drugs and has enabled major decreases in prescribing of antibiotics to be identified but has important limitations. There is no record as to the indication for which each drug was prescribed. There is no information on age or gender. It is not possible to estimate from these data what proportion of patients with infection receive prescriptions.

With the exception of HIV, there is no systematic attempt to link previous prescribing history with resistance in any of the resistance surveillance systems. Within hospitals, there is no overarching system to monitor antimicrobial prescribing.

The UK is part of the European Surveillance of Antibiotic Consumption (ESAC) project. ESAC was launched in 2001 to monitor antibiotic consumption in ambulatory and hospital care using standardized data. The data will be used to monitor consumption, identify problems and assess the effectiveness of interventions designed to decrease or change the use of different antibiotics. It is expected that ESAC and EARSS data will eventually be linked.

Surveillance of outcomes of infection

There is concern that adverse sequelae of minor infections such as rheumatic fever, quinsy, mastoiditis and pneumonia might become more common as antibiotic use is restricted. Although data on hospitalizations for these conditions is routinely collected via hospital episode statistics (HES) there is no system for time trends to be routinely monitored or to assess prior antibiotic exposure in those affected. There is also no system to routinely monitor and compare clinical outcomes in resistant and sensitive strains and for many organisms there is a paucity of evidence of the extent to which resistance affects clinical outcomes.
Planned future developments of AMR surveillance in England

The AmSurv Project

AmSurv was piloted as the surveillance of antibiotic resistance using Routinely Generated Susceptibility Data (RGSD) project. The pilot system gathered all RGSD from selected microbiology laboratories in the Trent region and allowed for analysis of the results. The project focused on the provision of results at the local level. All susceptibility results were gathered and a facility to remove repeat results within up to 90 days was included.25

Once deployed, the AmSurv system will gather susceptibility results for all tested isolates, including those from urinary tract infections, meaning it will gather more results than CoSurv. Anticipated outputs from AmSurv are expected to include information to allow the laboratories to compare themselves with others in their region. AmSurv should provide the ability to look at resistance at the Primary Care Trust, Strategic Health Authority, regional and laboratory levels. The field for the centre where the specimen was taken should allow community and hospital samples to be analysed separately.26

A piece of software called LabLink+ is used to take files from laboratory systems and translate the codes and format to those required by AmSurv and CoSurv. Two major suppliers of LIMS systems were commissioned to produce suitable file outputs for Lab Link+ in order to allow transfer of data into AmSurv, and this project was completed at the end of March 2007.27

The Microbiology Datastore Project

The Welsh Assembly funded a project called Microbiology Datastore which included the installation of Phoenix automated microbiology testing systems in 13 laboratories across Wales and the creation of a system to automatically download and collate laboratory results in all laboratories in Wales. Automated testing systems were installed to allow testing of a larger set of antibiotics and to standardize testing methods and antibiotics tested. The data downloading system that was developed (Microbiology Datastore) automatically collects data directly from the LIMS in laboratories. An important aspect of Microbiology Datastore is to feed information back to laboratories and the system can differentiate between GP and hospital samples.

Automated microbiology testing systems have a daily throughput of ~100 isolates per machine. Testing for important resistance mechanisms such as extended-spectrum β-lactamase (ESBL; not tested routinely by all laboratories) and species identification of some organisms are undertaken by the automated microbiology testing systems. The system was used initially for the Wales Community Antibiotic Surveillance project to obtain several years of historical data and will now continue to collect data prospectively that will be used for surveillance of AMR.

Gaps in current surveillance in England

In comparison to most countries the UK has relatively robust systems in place for monitoring resistance levels in organisms causing bacteraemias (through mandatory reporting and voluntary reporting via CoSurv), respiratory tract infections (particularly through the BSAC respiratory resistance surveillance programme), Neisseria gonorrhoea, Neisseria meningitidis, M. tuberculosis and HIV and malaria. However, a number of important gaps remain. These were identified as follows.

Urinary tract infection

A lack of nationally collated data on resistance levels in organisms identified among urine specimens in primary care. This is particularly concerning given the marked rise in cefotaxime and ceftazidime resistance in E. coli bacteraemias which is associated with the emergence of ESBL-producing strains. There has also been a dramatic rise in quinolone resistance in E. coli and other Enterobacteriaceae from bacteraemia.

Community-onset S. aureus infection

There is increasing international concern about the emergence of community-acquired MRSA (CA-MRSA). At present the HPA Staphylococcal Reference Laboratory is able to monitor the occurrence of CA-MRSA among suspicious isolates that are referred to the laboratory. However, these may represent the tip of the iceberg. Members of the Subgroup have collected HES and General Practice Research Database (GPRD) data showing a dramatic rise in hospitalizations for community-onset staphylococcal infections (likely to be mainly methicillin sensitive) over the last decade and a large increase in GP prescribing of fluclouxacillin.28 Fusidic acid resistance is also common in strains causing impetigo, but the clinical significance of this is unclear.29 There has been a particularly marked increase in consultations and admissions for impetigo over the last decade.

Antiviral resistance

With the exception of HIV, monitoring of resistance to antivirals is poorly developed. The main viruses of concern are hepatitis B and C, influenza, herpes simplex and cytomegalovirus.

Antimicrobial prescribing

The lack of routine systems to monitor prescribing behaviour for different conditions in primary care, the virtually complete lack of information on antibiotic prescribing in secondary care and the dislocation between antibiotic prescribing and antibiotic resistance hinders our understanding of resistance and of how to target interventions to reduce prescribing. There is also a paucity of data on how antibiotics are used in food production and whether this affects resistance in humans.

Outcomes of infection

The relative lack of routine information on the extent to which resistance affects outcomes of infection prevents us from understanding the full public health impact of resistance. Failure to monitor trends in sequelae of minor infections could undermine messages to decrease prescribing.
Options for surveillance in primary care

The discussion that follows outlines possible options for AMR surveillance in primary care. These would build on existing systems.

Three main strategies for surveillance of AMR in primary care are considered.

(i) Use of routine laboratory data with distinction between GP and hospital samples with or without linkage of microbiology and prescribing data.
(ii) Use of GP sampling protocols to reduce sampling bias.
(iii) Community sampling of asymptomatic individuals.

We also consider options for routine monitoring of antimicrobial prescribing in primary care and for surveillance of severe complications of infection.

Use of routine laboratory data with distinction between GP and hospital samples

The report assumes that any AMR surveillance system in England will utilize AmSurv as implementation plans are well advanced. Surveillance systems based upon AmSurv could be based upon AmSurv alone, based upon AmSurv with automated testing or based upon AmSurv linked with GP prescribing data (this option could be with or without automated testing). Surveillance systems that rely on routinely generated susceptibility data have the potential to be highly sustainable over time as they should minimize the additional work needed by laboratories to provide data. AmSurv has the potential of providing detailed information on resistance profiles and allowing separate analysis of samples submitted from primary care. Although the distinction between primary care and secondary care specimens is important, it should be noted that some specimens from primary care may represent nosocomial resistance (e.g., nursing home specimens or post-discharge infections).

Standardization of laboratory methodology will be important to ensure comparability of results. The level of standardization can be greatly increased by the use of automated identification and susceptibility systems. A few laboratories are still using the Stokes method, for example, which is reliable in general but has an unacceptable major error rate and differing levels of performance for different antibiotic/species combinations. In addition, results from BSAC disc testing can vary between laboratories. Many laboratories do not routinely identify coliform isolates to species level which has important implications for surveillance.

Which resistances are routinely tested for has an important impact on surveillance. Laboratories commonly undertake secondary testing based on the results of an initial battery of tests. The smaller the percentage of isolates that are tested for a specific resistance, the more biased the results are likely to be. Different protocols for this can potentially lead to spurious differences between laboratories. Other potentially important variations include site-specific testing of antibiotics on specimens from certain body sites, direct susceptibility testing without identification of the species (especially in urinary coliforms) and rule-based reporting of isolates as resistant or sensitive based on intrinsic qualities of bacteria rather than actual test results. The availability of MICs would be a valuable addition to surveillance although these are not routinely measured in many laboratories. There has been some discussion of the need for different MIC breakpoints for clinical purposes and for resistance mechanisms/development (epidemiological cutoffs). Such epidemiological cutoffs are being defined by EUCAST while they are working on the European harmonization of breakpoints, so these might need to be taken into consideration.

Automated testing systems are a potential route to standardizing laboratory testing methodology. The systems have good accuracy for most tests. The systems include expert rule systems, which use the MIC distributions expected with different resistance mechanisms to interpret the likely mechanism causing resistance. They also test many antibiotics as opposed to the relatively few antibiotics tested by most UK laboratories in routine disc tests. The systems are therefore easily able to detect ESBL, for example. Species identification of coliforms can readily be performed routinely.

In sentinel laboratories, the AmSurv data collection system could be supplemented with the use of automated sensitivity testing. This would provide the additional benefit of standardization of laboratory methods and capture of MICs, routine speciation of organisms, ready identification of ESBL producers and testing against a standard panel of antibiotics. There are costs to using automated testing systems although many laboratories already use such systems so it might be possible to focus surveillance activities on these centres. Costs are likely to be tempered by decreases in staff costs. The results from the systems would need to be incorporated into LIMS systems although there may be loss of MIC data as most LIMS systems only handle sensitive/intermediate/resistant (S/I/R) data fields.

The two automated susceptibility testing systems currently most widely used in the UK are the Phoenix and Vitek. Vitek has wider coverage in England than does Phoenix. Both systems can be purchased in full or can be acquired through leasing agreements. Service plans are available which cover servicing and the cost of some consumables in some cases. Custom panels can be designed in both cases, but this would likely incur costs and can impair interpretive reading.

In addition to standardized testing protocols, rules are needed about the removal of screening and duplicate isolates as inclusion of these can affect estimated resistance levels. In most cases, use of the first isolate from patients has also been shown to give similar results to using the average result per patient or the most resistant results. There is some evidence that although duplicate isolates in community samples including urines have a relatively minor effect on resistance estimates for non-hospital samples, using the first isolate per episode only from each person can decrease the effect.

Linkage with primary care prescribing data could greatly enhance the value of AMR surveillance. The ability to stratify resistances by prior antibiotic exposure would provide valuable insight into the extent to which prescribing drives resistance as well as providing clinically useful output to guide prescribing decisions based on knowledge of previous treatment. Such linkage would also be very valuable in secondary care. When systems are developed to monitor secondary care prescribing the ability to link with resistance data should be a prime concern.
There are three potential methods for linkage:

(i) Export of encrypted data from local GPs and linkage to encrypted data from local laboratories. Willing GPs could be selected around a sentinel laboratory.

(ii) Reliance on data exported with the pathology message into the GP record.

(iii) Use of ‘Connecting for Health’ (previously the National Programme for IT).

Strategy (i) has been piloted as part of a DH-funded study undertaken by members of the group and has been shown to be feasible allowing individual pseudonymized linkage of GP prescribing data with microbiology laboratory data. Resistance rates in UTIs were found to be very high in those who had recently received antibiotics but to drop off rapidly over time. Thus, resistance rates in those without recent antibiotic exposure remain low (e.g. the overall trimethoprim resistance rate in coliforms was 26%, resistance in those who had received a trimethoprim prescription in the previous 1 month was 56%). Such data linkage can be performed intermittently at relatively low cost using the methodology developed.

In recent years, the pathology messaging service has allowed automated transfer of laboratory results into the GP record. This provides the potential to use existing large GP data sets such as the GPRD, THIN or Q research to monitor resistance in primary care, analyse the effect of prior exposure to antibiotics and even examine the clinical implications of resistance. Unfortunately, the information sent with the laboratory message is a highly unstructured block of text. Laboratories also commonly censor which resistance results they report in order to discourage inappropriate prescribing. A standardized coded format for the microbiology data transferred to the GP database needs to be agreed and implemented across a range of LIMS systems for the potential to use GP databases for surveillance of resistance to be realized.

Connecting for Health is working towards a universal Electronic Patient Record for all residents of the UK linking hospital and GP data. There will also be a Secondary Uses Service (SUS) data warehouse that will contain a wider range of pseudonymized information. The SUS’s initial functionality will be financial, but this data repository could potentially be used for surveillance and other public health activities. If both GP antibiotic prescribing information and microbiology laboratory data are included then this could provide a valuable resource for surveillance.

A Connecting for Health Pathology Review Group has been formed and is working towards the inclusion of newly structured pathology messages that may be sent between laboratories and GPs and possibly included in the Electronic Patient Record. The group is trying to affect the pathology message such that it is in a more structured data format with fields for each type of data, such as organism, susceptibility results and so on. Any new pathology message would be likely to use Systematized Nomenclature of Medicine Clinical Terms codes. There may need to be additional messages sent from the laboratories and others in addition to the primary pathology message, for example, to include suppressed susceptibility results. There remain many uncertainties regarding the roll out of ‘Connecting for Health’ and whether or not laboratory IT systems will be able to comply with recommendations for a standardized pathology message.

**Surveillance using sampling protocols in General Practice**

Sampling bias is a frequently mentioned issue with the estimation of resistance levels. GPs often treat patients with infections such as respiratory infections, UTI or skin infections without taking microbiological specimens. Specimens may be more likely to be taken from patients with complex problems, such as those with recurrent disease, previous antibiotic treatment or treatment failure. These specimens may give an erroneously high estimate of resistance. Studies supporting the idea that routine samples are biased have shown that primary care requests for microbiology testing (including urines and wounds) differ within trust catchment areas and between trusts and that children submitting urines were found to be more likely to be socioeconomically deprived, to have been exposed to antibiotics and to have been hospitalized. A number of studies have shown significant differences in resistance levels between routine samples and those taken during a sampling protocol, but other studies have been inconclusive or did not show significant differences. These studies are summarized in Table 2.

The Welsh Community Antibiotic Study found no relationship between per capita sampling and trimethoprim and ampicillin resistance in urinary isolates and noted that while sampling varies between GPs, indices of sampling were not strongly correlated with antibiotic usage or resistance. Donnan et al found that the urine submission rate among practices was not significantly associated with trimethoprim resistance after controlling for prescription and other variables.

Sampling bias may have some effect on the level of resistance measured in routinely submitted isolates. However, overcoming this bias by asking some GPs to submit all specimens routinely may be difficult to sustain in the long term. Projects undertaken by members of the group have found it difficult to get GPs to increase sampling rates, even with financial incentives and in the context of relatively short-term research initiatives. The process is likely to be complicated by the need to obtain consent if the specimens would not normally have been collected for clinical purposes. This can be a time-consuming process which is difficult to incorporate into routine practice. If this strategy were used, it would need to be streamlined and standardized, with form filling to be minimal and ideally incorporated into the GP data management system. Financial incentives could help but may need to be quite large to be of greater utility. Asking a large number of practices to do a small amount of work on a short-term basis could be a good approach. For example, all patients in one clinic or all patients for a week/month with symptoms could be sampled. Sampling protocols may be most useful for conditions for which microbiology samples are relatively rarely submitted (e.g. skin infections).

Utilization of existing GP networks such as the Royal College of General Practitioners Weekly Returns Service or the MRC GP Research Framework could facilitate such studies.

**Community sampling of asymptomatic individuals**

The potential surveillance systems described above focus on measuring resistance levels in those with clinical infections. There is also potential value in measuring resistance levels in
bacteria from asymptomatic individuals as a way of monitoring the pool of resistant organisms and trends over time. This could be achieved by surveillance in convenience samples (such as those from individuals attending their GP for non-infection reasons, people presenting for non-acute services such as colon cancer screening, which relies on submission of stool samples, immunizations, dental checkups, etc., or people who are part of existing large-scale surveys such as the DH-funded Health Survey for England which already collect blood and urine for other purposes.63 Research conducted by members of the group has shown that community surveillance by postal surveys is feasible for coliforms from urine samples and S. aureus from nasal swabs.64 Such surveys would be most valuable if information is collected on antimicrobial prescribing and contact with hospitals. There remains uncertainty about the clinical implications of carriage of resistant organisms. Such surveys provide a potential mechanism for monitoring the emergence of rare resistances such as CA-MRSA or ESBL-producing coliforms as they have the potential to recruit large numbers efficiently. While such studies could be considered as one of the research initiatives, their main value may be if incorporated into a rolling programme allowing longer-term monitoring of trends in carriage of resistance.

### Monitoring of antibiotic prescribing

There are major limitations to PACT data as described above. Members of the group have undertaken a DH-funded study to examine the feasibility of using primary care databases such as the GPRD to monitor GP prescribing behaviour. Outputs from this work are available on http://www.idrn.org/antimicrobial_prescribing.php. The work found that although there was considerable work involved in such analyses, they can produce valuable insight into GP prescribing trends for different infections. Such analyses could be incorporated into routine surveillance systems although there would be data and analysis costs associated with this approach.

Selected outputs showing the leading indications for antibacterial prescribing and the management of these infections are shown in the article on antibacterial prescribing in Primary Care in this Supplement.

Limitations to analysis of such primary care data are that not all consultations for minor infections may be recorded, prescribing data represent those issued by the GP rather than those dispensed (some patients may not redeem or consume prescriptions), GPs are prone to code infections differently and the practices involved in the GPRD may not be fully representative of all GPs (e.g. they may be lower prescribers than others). Despite these potential limitations, the trends in antibiotic prescribing identified through the GPRD closely mirror those in PACT data.

### Monitoring of outcomes of infection

HES data are freely available online65 and can be used to monitor trends in potential complications of minor infections such as mastoiditis, quinsy and rheumatic fever. While such analyses are straightforward, no group currently has specific responsibility for undertaking them. Increases in the occurrence of such complications would be of concern but need to be interpreted in light of the absolute risk of complications as this is likely to remain very low. Members of the group have analysed data from the GPRD, showing that for sore throat, otitis media and upper respiratory tract infection over 4000 patients need to be treated to prevent a single case of quinsy, mastoiditis or pneumonia. The number of patients with chest infections who need to be treated to prevent a case of pneumonia, however, is much smaller at around 40 in those aged over 65 years.66

Analysis of linked GP prescribing, consultation and resistance data has the potential to allow monitoring of the effect of resistance on indicators of clinical outcome such as reconsultation rates. This would be an additional benefit of systems linking such data. In the secondary care sector, linkage of data on outcomes such as mortality and duration of hospital stay with resistance data could provide important insights into the clinical impact of resistance.

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**Table 2. Effect of GP sampling bias**

<table>
<thead>
<tr>
<th>Study</th>
<th>Samples</th>
<th>Organism: drug</th>
<th>Routine samples (%)</th>
<th>Sampling protocola (%)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>MacGowan et al.55</td>
<td>Sputa</td>
<td><em>H. influenzae</em>: Amp</td>
<td>20.0</td>
<td>11.0</td>
<td>NR</td>
</tr>
<tr>
<td>Batchelor et al.56</td>
<td>Urine</td>
<td><em>E. coli</em>: Trim</td>
<td>28.4</td>
<td>62.5</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Richards et al.57</td>
<td>Urine</td>
<td><em>E. coli</em>: Trim</td>
<td>22.6</td>
<td>18.0</td>
<td>0.016</td>
</tr>
<tr>
<td>Baerheim et al.58</td>
<td>Urine</td>
<td><em>E. coli</em>: Trim</td>
<td>36.3</td>
<td>32.5</td>
<td>0.08</td>
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<tr>
<td>Burman et al.59</td>
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<td><em>E. coli</em>: Trim</td>
<td>20.0</td>
<td>15.5</td>
<td>0.72</td>
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<tr>
<td>Hayward et al.45</td>
<td>Urine</td>
<td><em>E. coli</em>: Trim</td>
<td>18.5</td>
<td>12.9</td>
<td>0.21</td>
</tr>
<tr>
<td>McNulty et al.60</td>
<td>Urine</td>
<td><em>E. coli</em>: Trim</td>
<td>9.7</td>
<td>3.0</td>
<td>0.03</td>
</tr>
</tbody>
</table>

Amp, Ampicillin; Trim, Trimethoprim; Nitro, Nitrofurantoin; NR, not reported.

Bold font indicates statistically significant difference.

"In all studies except that by Batchelor et al., the sampling protocol aimed to increase the number of samples submitted. In the study by Batchelor et al., the protocol restricted sample submission."
Recommendations of the Surveillance Subgroup

The aims of a surveillance system for AMR should be to inform clinical decision making about treatment of important pathogens and to inform policy for control of resistance. In order to achieve these aims an ideal surveillance system should: use standardized methods for measuring resistance in an agreed range of pathogens against an agreed panel of antimicrobials; have broad geographical coverage; include relevant information on the source of samples (e.g. hospital or primary care); be linked with relevant clinical data, particularly data on antimicrobial prescribing and data on outcomes of infection; allow monitoring of prescribing behaviour and severe sequelae of infections; be based primarily on routinely submitted samples but with additional sampling and testing for clinically important problems where it is not common practice to submit samples, and should allow clinicians, public health authorities and policy makers timely access to relevant data to inform decision making.

The following specific recommendations are made.

(i) There should be a standardized system for electronically transferring data for surveillance.

(a) Given that plans for implementation of AmSurv are well advanced, any AMR surveillance system for England should be based on this. The system will need ongoing development to ensure standardization and compliance with Connecting for Health (CfH) and to enable linkage of microbiological and clinical data including risk factors and outcome data resulting in a fully integrated data system.

(ii) Laboratory methods for surveillance need to be standardized.

(a) Laboratory methods for surveillance need to be standardized and quality assured. Given the great variations in methodology and systems between laboratories in England, there should be a focus on identifying sentinel laboratories that can participate in surveillance using standardized approaches.

(b) Standardization for surveillance across multiple and diverse laboratories can be achieved much more easily if automated testing is used. It is therefore recommended that sentinel laboratories should already be using automated susceptibility testing, or be equipped to do so. Sentinel laboratories must agree to a standard antibiotic panel.

(c) Sentinel laboratories must perform consistently well in external quality assurance.

(iii) Resistance data need to be interpreted in light of information on geographical area, source of sample, antibiotic prescribing, other risk factors and outcomes.

(a) AMR surveillance needs to have a broad geographical coverage with adequate representation of samples from all regions.

(b) Sentinel laboratories must be able to distinguish between hospital and GP submitted specimens when reporting surveillance results.

(c) We recommend that surveillance of resistance levels in community-acquired pneumonia based on samples from recently hospitalized patients continues.

(d) Surveillance should mainly be based on routinely submitted samples. Given that GP sampling bias may not make a major difference to results and can be difficult to overcome, institution of GP protocols involving additional systematic sampling should not be a part of routine continuous surveillance.

(e) Interpretation of resistance data is greatly enhanced by linkage to clinical and antibiotic prescribing data. We recommend that Connecting for Health ensures that the format of information sent from laboratories to GPs in the pathology message is standardized. This would allow monitoring of linked data through large GP databases. Connecting for Health should also ensure that laboratory resistance data and clinical data from general practices and hospitals are linkable. These should include data on resistance, antimicrobial prescribing, clinical conditions and outcomes.

(f) We recognize that such comprehensive linkage may not be achieved in the short-to-medium term and therefore recommend that in some areas individual linkage of data from specified general practices and sentinel laboratories be performed.

(g) We recommend that periodic analyses of large-scale GP databases are conducted to monitor changes in GP prescribing behaviour for different infections. Care must be taken to restrict such analyses to practices meeting quality criteria.

(h) We recommend that Hospital Episodes Statistics Data are routinely examined to monitor the occurrence of severe adverse sequelae to infections. Results need to be interpreted in light of inherent limitations in the data.

(i) Studies of the effect of resistance on clinical outcomes need to be commissioned.

(iv) Additional sampling and testing is required to strengthen surveillance for some specific problems.

(a) Relatively few respiratory specimens are submitted from General Practice. Interpretation of bacterial resistance data from community-acquired pneumonia requires understanding of the range of pathogens (including viruses) causing acute respiratory infection. We recommend that this understanding is underpinned by primary care surveillance of acute respiratory infection.

(b) GPs also submit relatively few samples that grow staphylococci. In view of concerns about community staphylococcal infection including CA-MRSA and PVL-associated disease, we recommend specific studies to estimate community carriage and disease rates due to CA-MRSA prior to developing routine surveillance.

(c) We recommend that work be initiated to develop systems to monitor resistance to antivirals. This is currently restricted to antivirals for HIV but should also include other clinically important viruses where antivirals are used, e.g. hepatitis B and C, influenza and herpes simplex viruses.

(d) Consideration should be given to commissioning a rolling programme of surveillance based on samples from asymptomatic individuals in the community, with
different organisms in different years and/or specific clinical syndromes. This could be achieved through primary care networks.

(v) Reporting of surveillance needs to be timely and relevant to clinicians and policy makers.

(a) Surveillance data should be reported contemporaneously through an open-access web-based interface enabling timely reporting at national and local levels.

(b) There should also be an annual report summarizing key data from across the different surveillance systems.

(c) Local and national treatment guidelines need to be informed by surveillance data.

Transparency declarations

None to declare.

References


31. Heginbothom ML, Magee JT, Bell JL et al. Welsh Antibiotic Study Group. Laboratory testing policies and their effects on routine


