

# Scottish Antimicrobial Prescribing Group (SAPG)

## Report on Antimicrobial Resistance and Use in Humans in 2008

## Acknowledgement

This report could not have been compiled without antimicrobial resistance data provided by diagnostic and reference laboratories within Scotland and the prescribing team at ISD who assisted with analysis of consumption data. We also extend thanks to the Scottish Microbiology forum for advice on the development of this programme and their ongoing input into national surveillance of antimicrobial resistance.

© Health Protection Scotland and Information Services Division 2010

Published by Health Protection Scotland and Information Services Division

First Published January 2010

ISBN: 978-1-873772-36-2

Brief extracts from this publication may be reproduced provided the source is fully acknowledged. Proposals for reproduction of large extracts should be addressed to:

Health Protection Scotland  
Clifton House  
Clifton Place  
Glasgow G3 7LN  
Tel: +44 (0) 141 300 1100  
Email: NSS.HPSAMR@nhs.net

HAI & IC Group  
Health Protection Scotland  
1 Cadogan Square  
Cadogan Street  
Glasgow G2 7HF  
Tel: 0141 300 1100  
Email: NSS.HPSAMR@nhs.net  
[www.hps.scot.nhs.uk](http://www.hps.scot.nhs.uk)

Healthcare Information Group  
Information Services Division  
Gyle Square  
1 South Gyle Crescent  
Edinburgh EH12 9EB  
Tel: 0131 275 7777  
Email: tracey.cromwell@nhs.net  
[www.isdscotland.org](http://www.isdscotland.org)

## Citation for this document

Health Protection Scotland, Information Services Division. Scottish Antimicrobial Prescribing Group (SAPG), Report on Antimicrobial Resistance and Use in Humans in 2008. Health Protection Scotland and Information Services Division.

# Tables of contents

---

<b>Acknowledgements</b>	ii
<b>Tables of contents</b>	iii
<b>List of Abbreviations</b>	1
<b>Executive summary</b>	3
<b>Use of antimicrobials</b>	3
<b>Antimicrobial resistance</b>	3
<b>Introduction</b>	5
<b>Chapter 1 – Antimicrobial use</b>	6
<b>Background</b>	6
<b>Methods</b>	6
Data source – primary care	6
Data presentation	6
<b>Results</b>	<b>7</b>
Primary Care	7
Overall use of antibacterials	7
Choice of antibacterial	7
Seasonal variation of antibacterials	9
Use of antibacterials in dentistry	10
International comparison	10
<b>Future developments</b>	11
<b>Chapter 2 – Antimicrobial resistance</b>	13
<b>Background</b>	13
<b>Methods</b>	13
Susceptibility data	13
Data	14
<i>Clostridium difficile</i> Infection (CDI)	14
<b>Results</b>	14
Gram-negative bacteraemia	14
<i>Escherichia coli</i>	15
<i>Klebsiella pneumoniae</i>	17
<i>Pseudomonas aeruginosa</i>	19
Emerging resistance - Carbapenemase-producing Enterobacteriaceae	20
Gram-positive bacteraemia	21
<i>Staphylococcus aureus</i>	21
Meticillin sensitive <i>S. aureus</i> (MSSA)	22
Meticillin resistant <i>S. aureus</i> (MRSA)	22
<i>Streptococcus pneumoniae</i>	22
<i>Enterococcus species</i>	23
Emerging resistance - Glycopeptide resistant enterococci	24
<i>Clostridium difficile</i> Infection (CDI)	24
<b>Future developments</b>	25
<b>References</b>	26
<b>Figures</b>	27
<b>Tables</b>	28

## List of Abbreviations

---

<b>AmpC</b>	AmpC-type beta-lactamase
<b>AMR</b>	Antimicrobial resistance
<b>AMT</b>	Antimicrobial management team
<b>ARMRL</b>	Antibiotic Resistance Monitoring and Reference Laboratory
<b>AST</b>	Antimicrobial susceptibility testing
<b>ATC</b>	Anatomical Therapeutic Chemical
<b>CDAD</b>	<i>Clostridium difficile</i> Associated Disease
<b>CDI</b>	<i>Clostridium difficile</i> infection
<b>CHI</b>	Community Health Index
<b>CLSI</b>	Clinical and Laboratory Standards Institute
<b>DDD</b>	Defined daily dose
<b>EARSS</b>	European Antimicrobial Resistance Surveillance System
<b>ECDC</b>	European Centre for Disease Prevention and Control
<b>ECOSS</b>	Electronic Communication of Surveillance in Scotland
<b>EMRSA-15/16</b>	Epidemic meticillin resistant <i>Staphylococcus aureus</i> type 15/16
<b>ESAC</b>	European Surveillance of Antimicrobial Consumption
<b>ESBL</b>	Extended spectrum beta-lactamase
<b>GRE</b>	Glycopeptide resistant enterococci
<b>HMUD</b>	Hospital Medicines Utilisation Database
<b>HPA</b>	Health Protection Agency
<b>HPS</b>	Health Protection Scotland (NHS National Services Scotland)
<b>ISD</b>	Information Services Division (NHS National Services Scotland)
<b>KPC</b>	<i>Klebsiella pneumoniae</i> carbapenemase
<b>LIMS</b>	Laboratory information management system
<b>MIC</b>	Minimum inhibitory concentration
<b>MLS</b>	Macrolide-lincosamide-streptogramin
<b>MRSA</b>	Meticillin resistant <i>Staphylococcus aureus</i>
<b>MSSA</b>	Meticillin sensitive <i>Staphylococcus aureus</i>
<b>NDM-1</b>	New Delhi beta-lactamase (type 1)
<b>NHS</b>	National Health Service
<b>NPHS</b>	National Public Health Service (Wales)
<b>OCBD</b>	Occupied bed days
<b>OXA-48</b>	OXA-type beta-lactamase
<b>PCR</b>	Polymerase chain reaction
<b>PCV7</b>	7-valent pneumococcal conjugate vaccine
<b>PRISMS</b>	Prescribing Information System for Scotland

<b>SAPG</b>	Scottish Antimicrobial Prescribing Group
<b>ScotMARAP</b>	Scottish Management of Antimicrobial Resistance Action Plan
<b>SGHD</b>	Scottish Government Health Department
<b>SMC</b>	Scottish Medicines Consortium
<b>SMPRL</b>	Scottish Meningococcus and Pneumococcus Reference Laboratory
<b>SMRSARL</b>	Scottish MRSA Reference Laboratory
<b>SSSCDRL</b>	Scottish Salmonella, Shigella and Clostridium difficile Reference Laboratory
<b>STRAMA</b>	Swedish Strategic Programme Against Antibiotic Resistance
<b>SWEDRES</b>	Swedish report on antimicrobial resistance
<b>UK</b>	United Kingdom
<b>VRE</b>	Vancomycin resistant enterococci
<b>WHO</b>	World Health Organisation

## Executive summary

This is the first joint annual report from the Scottish Antimicrobial Prescribing Group (SAPG), published by Health Protection Scotland (HPS) in collaboration with Information Services Division (ISD) that combines information from the monitoring of antimicrobial use and resistance in humans in Scotland.

Antimicrobial resistance is recognised as a major threat to public health and patient safety. It reduces the available treatment options for infection and is associated with increased morbidity and mortality due to a failure of the initial choice of empirical antimicrobial therapy. It is accepted that the way in which antimicrobials are used, sometimes inappropriately, will increase the risk of antimicrobial resistance developing.

The information presented covers the period up to the end of 2008 and sets the baseline against which the emerging trends in antimicrobial use and resistance can be monitored. The report is intended to support NHS Boards, hospitals and primary care in their long-term planning of antimicrobial prescribing. In particular this report should be of use to Antimicrobial Management Teams (AMTs), Infection Control Teams (ICTs) and Microbiologists.

### Use of antimicrobials

The report presents information on the use of systemic antimicrobials within primary care in Scotland. It shows that between 2004 and 2008 there has been an increase of 18.3% in overall use of antimicrobials when expressed as the number of defined daily doses per 1000 population per day (DDD/1000/day). In 2008 the three most commonly used groups of antimicrobials were tetracyclines, penicillins with extended spectrum and macrolides which made up 25%, 24% and 17% of total use respectively.

SAPG published guidance in 2009 on management of commonly encountered infections that aims to restrict the use of fluoroquinolones, cephalosporins and co-amoxiclav that are known to increase the risk of *Clostridium difficile* infection (CDI). Whilst the information in this report predates this guidance, in 2008 eight of the ten most commonly used antimicrobials are those recommended by SAPG. Looking more specifically at the use of antimicrobials that increase the risk of CDI, ciprofloxacin, the most commonly used fluoroquinolone has increased by 30% between 2004 and 2008, co-amoxiclav use has increased by 22% and cephalosporin use has decreased by 4%.

In 2010 the Hospital Medicines Utilisation Database (HMUD) will become available in Scotland. HMUD will present standardised information on hospital use of antimicrobials, complementing the information on use in primary care. This will support an enhanced understanding of antimicrobial usage across all healthcare sectors in Scotland.

### Antimicrobial resistance

The report presents information on patterns of antimicrobial resistance for key organisms causing bacteraemias, including *Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Streptococcus pneumoniae*, *Staphylococcus aureus* and *Enterococcus* spp. in line with data collected by the European antimicrobial resistance surveillance system (EARSS).

For the Gram-negative organisms resistance was observed towards a number of important antibiotic groups, including aminopenicillins, second and third generation cephalosporins, fluoroquinolones and aminoglycosides. Resistance proportions for the Scottish isolates were in most cases within the same range as reported in previous United Kingdom (UK) reports, but for third generation cephalosporins and fluoroquinolones resistance proportions in the Scottish isolates were above the latest UK figures reported to EARSS for 2008.

It has been suggested that the rise in third generation cephalosporin resistance in many countries is caused by dissemination of ESBL-producers (extended spectrum beta-lactamase producers) in hospitals and the community. Substantial proportions of the Scottish *E. coli* (7.2%) and *K. pneumoniae* (8.4%) isolates were ESBL-producers. Furthermore, combined resistance to third generation cephalosporins and fluoroquinolones or aminoglycosides was observed in proportions of *E. coli* and *K. pneumoniae* isolates.

This development of combined resistance limits the treatment options for Gram-negative infections, and poses the threat of further evolution of multi-drug resistance. Although rare in Scotland emergence of carbapenem resistance in Gram-negatives has been detected by the UK Reference Laboratory for Antimicrobial Resistance (ARMRL). The emergence of combined resistance needs to be carefully monitored particularly in the context of a shift in prescribing towards *C. difficile* sparing antibiotics.

Based on the data in this report resistance among the Gram-positives is currently less of a concern in Scotland. All but one isolate of *S. pneumoniae* was sensitive to penicillin and no resistance to glycopeptides (vancomycin) was detected among MRSA isolates. However, 16.7% resistance to vancomycin was observed among the *E. faecium* isolates from bacteraemias (also referred to as VRE). This is of particular concern as these resistance mechanisms can be transferred to other pathogens (including MRSA) via plasmids.

In looking forward, the ongoing implementation of national standardisation and automation of testing and reporting of antimicrobial susceptibility data will greatly enhance the quality of national data. Alongside developments in antimicrobial use and resistance surveillance, systems to monitor unintended consequences that arise from changes in antimicrobial use will be developed.

In conclusion this report presents the baseline data for antimicrobial use and resistance in Scotland. It provides information on which national programmes, commissioned by the Healthcare Associated Infection (HAI) Taskforce and overseen by SAPG and the HPS (HAI) programme board, can be based. The publication of future annual reports from HPS/ISD will help assess the effectiveness of these national programmes in minimising antimicrobial resistance in Scotland and continue to monitor this in the context of the changing international situation.

## Introduction

---

Emerging antimicrobial resistance (AMR) is recognised as a worldwide public health threat. It reduces the available treatment options for infections and is associated with increased morbidity and mortality and increases in costs due to failure of empirical antimicrobial therapy. The World Health Organisation (WHO) produced the global strategy for containment of antimicrobial resistance in 2001. The European Centre for Disease Prevention and Control (ECDC) has also identified antimicrobial resistance as a key area under Target 1 (disease specific work) of its annual work programme. It is estimated that approximately 4 million patients acquire healthcare associated infection (HAI) each year in the 27 European member states, and that approximately 37,000 deaths are a direct result of these infections, of which about one half are due to the most common multi-drug resistant bacteria. The European programme aims to support the improvement and co-ordination of methods for surveillance of AMR in Europe. Increasing awareness among the European public and clinical staff about both AMR and prudent use of antibiotics is an important first step. This is further supported by co-ordination of activities and effective exchange of experiences among member states.

Within this context the Scottish Government produced The Scottish Management of Antimicrobial Resistance Action plan (ScotMARAP) in 2008. This is a national antimicrobial stewardship programme that brings together key activities in antimicrobial prescribing, surveillance and infection management and which links with other national programmes on infection control to contain the emergence of antimicrobial resistance.

Rational use of antimicrobials also plays a key role in preventing and controlling *Clostridium difficile* infection (CDI). The Scottish surveillance programme for antimicrobial resistance and use is a key component of the ‘Scottish Management of Antimicrobial Resistance Action Plan’ (ScotMARAP) aimed at containing antimicrobial resistance and preserving the effectiveness of antimicrobial drugs, and preventing and controlling CDI. It complements the national mandatory surveillance of CDI and the CDI reduction programme coordinated by Health Protection Scotland (HPS).

The Scottish surveillance programme for antimicrobial resistance is modelled on the European Antimicrobial Resistance Surveillance System (EARSS) and the European surveillance of antimicrobial consumption (ESAC). However, as these systems are not sufficient

to monitor emerging resistances and new issues with prescribing, the Scottish programme will be expanded as it develops, with surveys and other short studies that address specific clinical issues.

Furthermore, when new antimicrobial prescribing policies are implemented to contain antimicrobial resistance harmful effects may occur in other areas e.g. under-prescribing and selection for new resistances. The Scottish surveillance programme will therefore in the future be expanded with studies on ‘unintended consequences’.

This is the first national annual report that brings together antimicrobial resistance and use data. The collection and reporting of Scottish data on antimicrobial resistance and use is intended to support National Health Service (NHS) boards in their long-term strategic planning, implementation and evaluation of antimicrobial prescribing in order to prevent and control infections.

Whilst the datasets currently available are limited (partially due to complexities in implementing certain key components for the data collection, including automated transfer of susceptibility data, and hospital data on antimicrobial use), the intention of this report is to give an indication of the type of information currently available and indicate what will be produced in future.

# Chapter 1 - Antimicrobial use

---

## Background

Resistance to antimicrobials is recognised nationally and internationally as a major threat to public health and patient safety. It is accepted that a major driver for the development of antimicrobial resistance is the way in which antimicrobials are used, and misused.

Antibacterials, a type of antimicrobial, are synthetic or naturally occurring compounds that destroy or suppress bacterial growth. Exposure to antibacterials will kill bacteria that are susceptible but any that have developed resistance will not be affected and will therefore survive. Thus the potential beneficial impact from the use of an antibacterial in an individual may be offset by increasing the population of naturally occurring resistant bacteria that can go on to cause clinical problems.

It is also recognised that use of all antibacterials and in particular certain prescribing patterns will impact on the population of naturally occurring bacteria and create the opportunity for other bacteria that can cause infection. One example is the use of antibacterials as important risk factors for CDI.

SAPG aims to co-ordinate a national antimicrobial stewardship programme to enhance the quality of prescribing and treatment of infection in Scotland. An initial priority for SAPG has been the development of prescribing policies that support NHS boards to reduce the use of antibacterials that are associated with a greatly increased risk of CDI. SAPG has produced and issued guidance on both hospital and primary care use of antibacterials that aim to ensure that the use of fluoroquinolones, cephalosporins and co-amoxiclav are restricted.

The surveillance of use of antibacterials is important to understand the developing patterns of antimicrobial resistance and to monitor the impact of strategies that aim to improve antimicrobial stewardship in Scotland.

In this chapter information is presented on use in humans of systemic antibacterials in primary care at a national level. National information developments for secondary care (hospital) use of antibacterials are outlined in the future developments section.

## Methods

### *Data source - primary care*

In Scotland all antibacterials for systemic use are Prescription Only Medicines. This means that they can only be supplied in accordance with a prescription given by a doctor, dentist or other authorised prescriber.

The information on the use of antibacterials in primary care has been obtained from a database of all NHS prescriptions dispensed in the community in Scotland. ISD collate and present this information through a system known as the Prescribing Information System for Scotland (PRISMS). PRISMS is a web based system which is updated monthly and contains the last five years of use of all medicines dispensed in primary care.

### *Data presentation*

The data on antibacterial usage is based on the Anatomical Therapeutic Chemical (ATC) classification. This is the internationally recognised classification system to identify the therapeutic ingredient of all medicines for human use. Antibacterials for systemic use fall into ATC group J01. For further details on the ATC system please see the WHO Collaborating Centre for drug statistics methodology website at [www.whocc.no/atcddd/](http://www.whocc.no/atcddd/)

The Defined Daily Dose (DDD) is the internationally recognised technical unit of measurement of medicine consumption. DDDs are recommended by WHO as the standard to allow comparative use of medicines over time and between locations. The DDD is the assumed average maintenance dose per day for a medicine used in its main indication in adults.

In general, the DDDs for antibacterials are based on their use in moderately severe infections. However, some antibacterials are only used in severe infections and their DDDs are assigned accordingly. For further details on the DDD please see the WHO Collaborating Centre for drug statistics methodology website at [www.whocc.no/atcddd/](http://www.whocc.no/atcddd/)

The use of number of items to depict activity refers to the number of times an antibacterial appears on prescription.

The normal convention is to present information on use of antibacterials expressed as total DDD per 1000 population in Scotland per day (DDD/1000/day) and number of items per 1000 population per day

(items/1000/day). This allows comparison of usage over time.

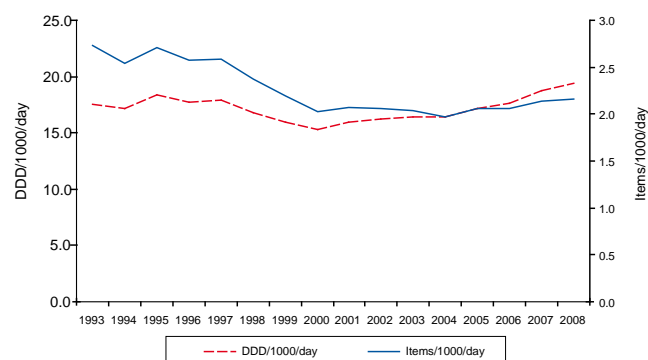
## Results

### Primary Care

#### Overall use of antibacterials

In 2008 the overall use of systemic antibacterials in the primary care setting in Scotland was 19.4 DDD/1000/day. Figure 1 shows the overall use of antibacterials over a 15 year period since 1993. Between 1993 and 2000 there was a downward trend in overall use but between 2000 and 2008 the pattern changed and there have been year on year increases in use. The rate of increase has accelerated in more recent years. From 2004 to 2008 there has been an increase in use of 18.3%.

**Figure 1:** NHS Scotland: use of antibacterials in primary care 1993-2008.



When use of antibacterials is expressed as number of items/1000/day a slightly different pattern emerges. The overall use in 2008 was 2.2 antibacterial items/1000/day. Figure 1 shows a clear downward trend between

1993 and 2000, followed by a period of little change between 2000 and 2004. From 2004 to 2008 there has been a small annual increase in number of items/1000/day resulting in growth of 10.1% over this period.

#### Choice of antibacterial

##### Ten most commonly used antibacterials

In 2009, SAPG published national guidance on the management of commonly encountered infections in primary care to support the AMTs. This guidance includes the recommended antibacterial, dose and length of course for the common infections that are seen in primary care. It aims to minimise the emergence of bacterial resistance in primary care and the use of antibacterials that are known to increase the risk of CDI.

Table 1 shows usage of the ten most commonly used antibacterials that account for 84% of all antibacterial use in 2008.

Eight of the antibacterials in the top ten most commonly used in 2008 are those recommended in the SAPG guidance as first line agents for the management of commonly encountered infections in primary care in Scotland.

##### Use of antibacterials by group

Antibacterials are divided into a number of different groups (e.g. penicillins) on the basis of their chemical structure and spectrum of activity against different organisms. The distribution of the different groups of antibacterials used in 2008 is shown in Figure 2. The two most frequently prescribed are tetracyclines which

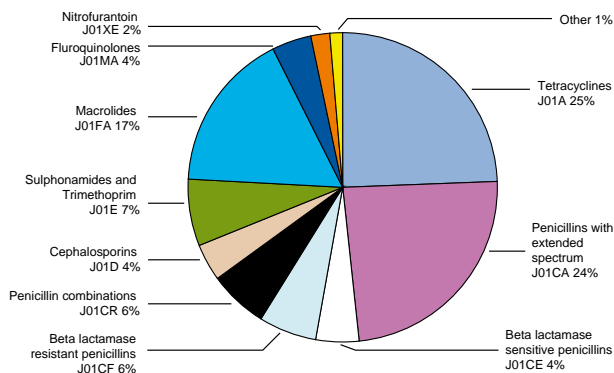
**Table 1:** NHS Scotland: Use of antibacterials in primary care - top 10 in 2008.

Antibacterial	Anatomical Therapeutic Classification Group	Number of Defined Daily Doses	% total (DDDs)
Amoxicillin*	Penicillins with extended spectrum	8,746,853	24
Erythromycin*	Macrolides	3,313,899	9
Oxytetracycline*	Tetracyclines	3,262,427	9
Lymecycline	Tetracyclines	2,636,114	7
Clarithromycin*	Macrolides	2,525,922	7
Trimethoprim*	Trimethoprim and derivatives	2,466,154	7
Flucloxacillin*	Beta-lactamase resistant penicillins	2,203,700	6
Co-amoxiclav	Penicillin combinations	2,169,644	6
Doxycycline*	Tetracyclines	2,011,638	5
Phenoxymethylpenicillin*	Beta-lactamase sensitive penicillins	1,623,444	4
<b>All antibacterials</b>		<b>36,612,779</b>	<b>100</b>

\* recommended in SAPG guidance as first line agents.

represent 25% of total use in primary care and penicillins with extended spectrum which account for 24%.

**Figure 2.** NHS Scotland: use of antibacterials in primary care, percent of total DDD/1000/day 2008.

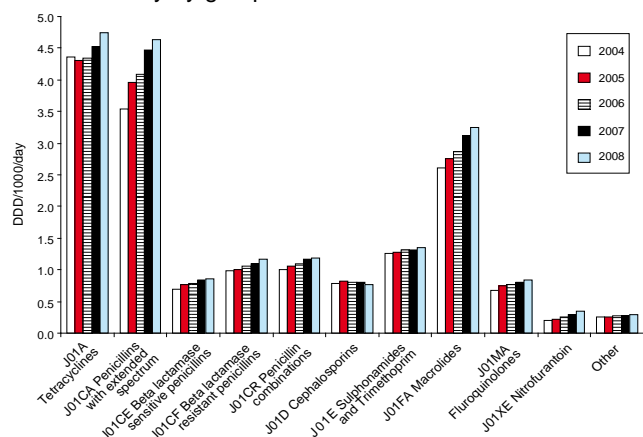


Tetracyclines are long established antibacterials with a narrow spectrum of activity that have a broad range of indications in primary care. They are often used in the management of long term infections including acne. The SAPG national guidance on primary use of antibacterials recommends doxycycline as a treatment for exacerbations of chronic bronchitis, chronic obstructive pulmonary disease or acute sinusitis. From 2004 to 2008 there has been an increase of 22.4% in use of doxycycline.

Other frequently used antibacterial groups were macrolides (17%), sulphonamides and trimethoprim (7%), beta lactamase resistant penicillins, mainly flucloxacillin (6%) and penicillin combinations including co-amoxiclav (6%). Overall, penicillins (J01C) accounted for 40% of total antibacterial use in 2008.

Figure 3 shows the pattern of use of antibacterials for each of these groups over the five year period from 2004-2008. This shows that there is an upward trend in the majority of antibacterial groups.

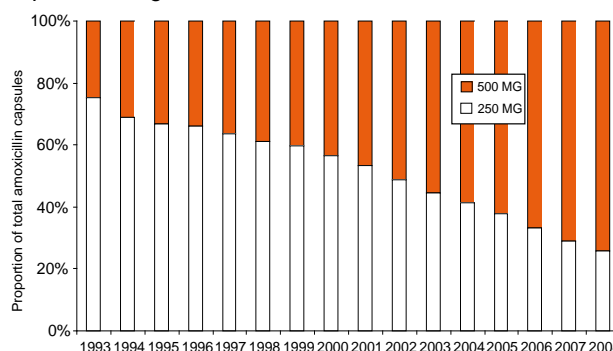
**Figure 3.** NHS Scotland: use of antibacterials in primary care, DDD/1000/day by group 2004 - 2008.



### Penicillins with extended spectrum (amoxicillin)

Between 2004 and 2008 there has been an increase of 31% in use of penicillins with extended spectrum. This is due to an increase in the use of amoxicillin, the most commonly used antibacterial in Scotland. SAPG recommend amoxicillin for a range of respiratory tract infections, which are the most commonly encountered types of infection in primary care. Since 1993 there has been a considerable change in the way in which amoxicillin has been used as illustrated in Figure 4.

**Figure 4.** NHS Scotland: use of amoxicillin in primary care, % capsule strength, 1993-2008.



This shows that in 1993 only 25% of all amoxicillin capsules used were 500mg strength. Since 1993 there have been annual increases in the proportionate use of 500mg capsules and by 2008 they account for 74% of all amoxicillin used.

Over the 15 year period there is no evidence that course length has changed. This means that in 2008 it is much more likely that when amoxicillin is used the strength will be 500mg. This move to increased use of the 500mg strength of amoxicillin is in line with SAPG prescribing guidance. Consequently, the move to use of higher strength amoxicillin is increasing the total number of DDD and helps to explain the increase in overall DDD for antibacterials in Scotland.

### Penicillin combinations (co-amoxiclav)

Between 2004 and 2008 there has been an increase in use of penicillin combinations. This change is predominantly due to greater use of co-amoxiclav, which has increased by 21.6% as illustrated in Figure 5. Co-amoxiclav is a combination of amoxicillin and a beta lactamase inhibitor which extends the spectrum of activity. This broader spectrum is counterbalanced by resistance and increased risk of CDI. Co-amoxiclav is not a first line choice for empirical treatment of most commonly encountered infections in primary care and SAPG guidance aims to limit its use.

**Figure 5.** NHS Scotland: combination penicillins in primary care, DDD/1000/day, 1993-2008.

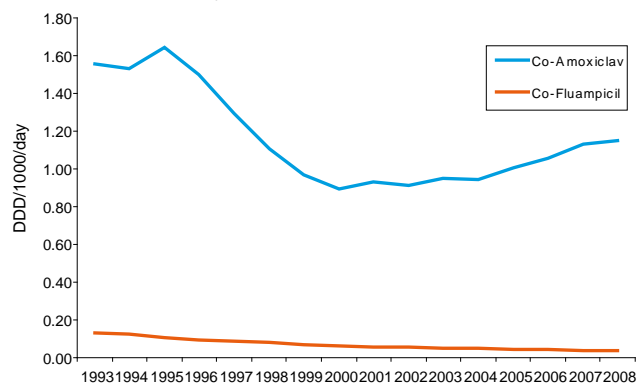


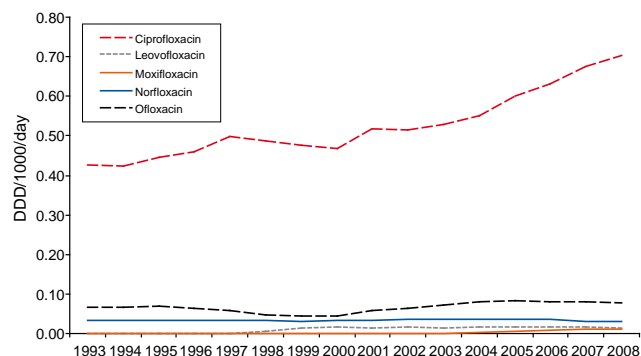
Figure 5 shows a considerable reduction in the use of co-amoxiclav from 1993 to 2000. Since 2004, however, there have been repeated annual increases and in 2008 the use of co-amoxiclav is higher than at any point in the previous ten years.

### Fluoroquinolones

Fluoroquinolone antibacterials are not recommended in the SAPG guidance as a first line agent for empirical treatment of most commonly encountered infections in primary care. It is recognised that use of fluoroquinolones is associated with a significantly increased risk of CDI. In particular, outbreaks with the hypervirulent strain PCR ribotype 027 that cause CDI with high morbidity and mortality have been linked to use of fluoroquinolones.

The use of fluoroquinolones is presented in figure 6. This illustrates that there has been little change over time in the use of levofloxacin, moxifloxacin, norfloxacin and ofloxacin. However, since 1993 there has been increased use of ciprofloxacin and since 2004 the upward trend has accelerated with a 30% increase between 2004 and 2008. The continued upward trend is unexplained and predates guidance from SAPG that aims to limit use of fluoroquinolones.

**Figure 6.** NHS Scotland: fluoroquinolone in primary care, DDD/1000/day, 1993-2008.



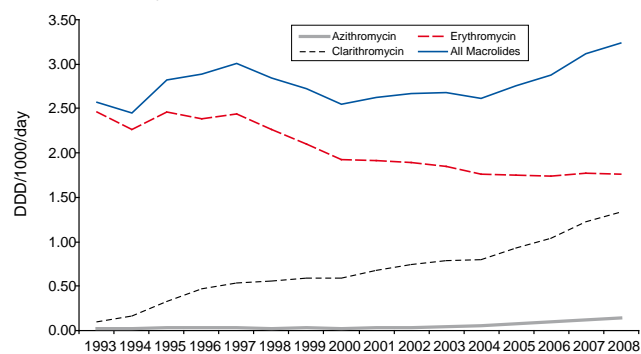
### Cephalosporins

Cephalosporins are not routinely recommended as first line agents for empirical treatment of commonly encountered infections in primary care. Their use is associated with an increased risk of CDI and SAPG guidance aims to limit their use. From 2004 to 2008 there has been an overall decrease of 4% in use of cephalosporins.

### Macrolides

Between 2004 and 2008 there has been an increase of 24% in the use of macrolides. Macrolides are recommended as a treatment choice in the SAPG guidance for management of commonly encountered infections in a number of types of infection and they are often used as the preferred treatment in individuals that are allergic to penicillin. Figure 7 shows the use of all macrolides from 1993-2008. The major change since 2004 has been a 71% increase in the use of clarithromycin with little reduction in the use of erythromycin thereby driving the total increase in macrolide use. The increased use of clarithromycin may in part be due to differences in frequency of dosing; erythromycin taken four times daily compared to clarithromycin taken twice daily and a possible different side effect profile.

**Figure 7.** NHS Scotland: macrolides in primary care, DDD/1000/day, 1993-2008.



### Seasonal variation of antibacterials

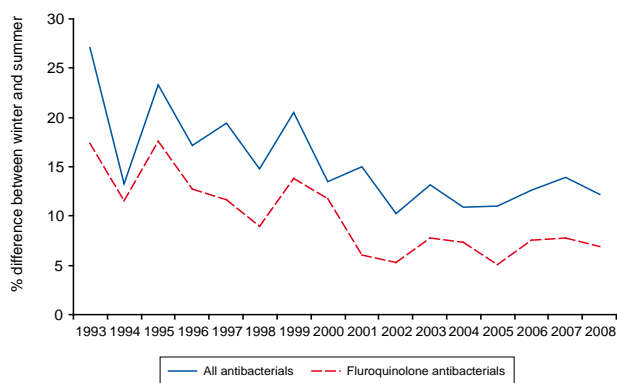
Seasonal variation is defined as the increase in use of antibacterials during the two winter quarters (October to March) relative to use in the preceding two summer quarters (April to September). In the winter quarters more respiratory tract infections are seen but many are caused by viruses, are self limiting and do not require treatment with an antibacterial. Any significant excess of use of antibacterials in the winter months may indicate an element of inappropriate use in viral infections.

A priority area for SAPG and Scottish Government is reduction in CDI incidence. The HEAT target for CDI

was defined in a letter to NHS Board Chief Executives (CEL 11 (2009)) issued by the Scottish Government in April 2009. The target is to reduce the rate of CDI among people aged 65 years and above by at least 30% by 31 March 2011. The Scottish Government and SAPG have agreed three supporting antimicrobial prescribing indicators. One of these indicators is that seasonal variation in use of fluoroquinolones (which are not recommended by SAPG for treatment of respiratory tract infections) should be no more than 5% greater in the winter quarters compared to the preceding summer quarters. This will be measured using prescribing data up to 31 March 2011.

Figure 8 shows annual seasonal increase in overall use of all antibacterials and use of fluoroquinolones expressed as DDD in the winter quarters relative to the preceding summer quarters

**Figure 8.** NHS Scotland use of antibacterials in primary care, % seasonal variation 1993-2008.



From 2004 to 2008 the seasonal variation for overall use of antibacterials has been between 11% and 14%. There has been a considerable reduction in annual seasonal variation from the levels in 1993 which may indicate less use of antibacterials for viral infections in the winter months.

Figure 8 also illustrates that from 2004 to 2008 the seasonal variation for fluoroquinolones has been between 5% and 8%, with a steady reduction since 1993. This may indicate that there is less use of fluoroquinolones for viral infections in the winter months. The level in 2008 remains above the Scottish Government target of 5% to be reached by 2011.

### Use of antibacterials in dentistry

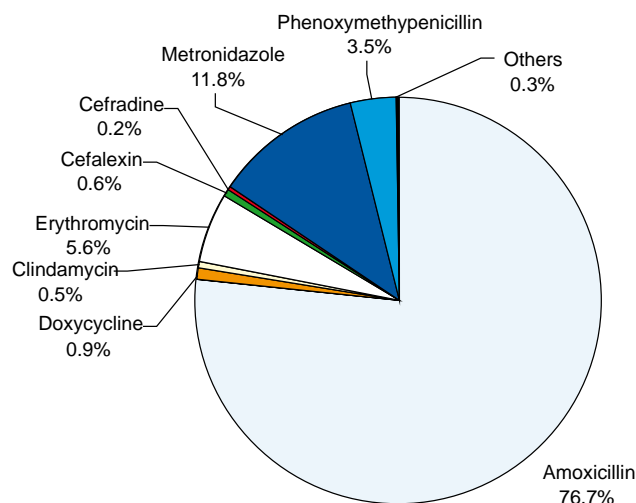
Dental practitioners in Scotland may only prescribe on NHS prescriptions from a limited list of medicines. This includes a range of 13 antibacterials; amoxicillin, ampicillin, azithromycin, cefalexin, cefradine, clindamycin, co-amoxiclav, doxycycline,

erythromycin, metronidazole, oxytetracycline, phenoxymethylpenicillin and tetracycline.

In 2008, the overall use of antibacterials in dentistry was 0.84 DDD/1000/day which accounts for 4.1% of total use in primary care. Over the last five years there has been a 1.8% increase in use.

Around 77% of all dental use of antibacterials in 2008 was amoxicillin. The breakdown of antibacterials in dentistry in 2008 is shown in Figure 9. This shows that in addition to amoxicillin the other main antibacterials used were metronidazole (11.8%), erythromycin (5.6%) and phenoxymethylpenicillin (3.5%). These four most commonly prescribed agents make up around 98% of all antibacterial use in dentistry.

**Figure 9.** NHS Scotland: use of antibacterials in dentistry, percent of total DDD/1000/day 2008.



Over the last five years there has been a fall in the use of the two cephalosporins that dentists can prescribe on NHS prescription in Scotland. In 2004, cefalexin and cefradine together accounted for 1.1% of all dental use of antibacterials and by 2008 this had fallen to 0.8%.

An area of note is that the use of clindamycin, known to increase the risk of CDI has increased. The overall level of use is low, but increasing, although clindamycin is no longer recommended for prevention of endocarditis.

### International comparison

It is accepted that the threat from resistance to antibacterials is an international issue. Surveillance of use of antibacterials is undertaken in many other countries. A number of these countries including Sweden, Denmark and the Netherlands have established programmes that aim to improve the stewardship of antibacterials and the work of SAPG has been influenced by the models adopted in these countries.

This section presents how the pattern of use in Scotland compares to other parts of the UK and Europe.

Within a UK context the most recently published data is from 2007 and shows use of antibacterials expressed as items/1000/day. The information for the UK is presented in Table 2. This illustrates that in 2007 Scotland used 14% more items/1000/day than England but use was lower than in Wales or Northern Ireland.

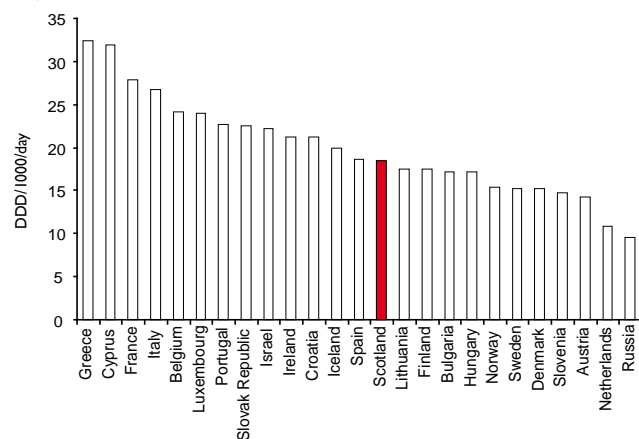
**Table 2:** Antibacterial use (ATC J01 exclude antituberculous and antileprotic medicines).

Country	Items/1000/day
England	1.88
Scotland	2.14
Wales	2.46
Northern Ireland	2.93

Source Health Protection Agency (HPA) Antimicrobial Resistance and Prescribing in England, Wales and Northern Ireland, 2008

In a European context the ESAC project is funded by ECDC to undertake surveillance of antimicrobial agents in Europe. Figure 10 presents the use of antibacterials expressed as DDD/1000/day in 2006 for Scotland compared to a number of European countries for which data is available. Scotland sits in the centre for use of antibacterials in 2006 when compared to the range of European countries.

**Figure 10.** Use of antibacterials in primary care (DDD/1000/day) 2006.

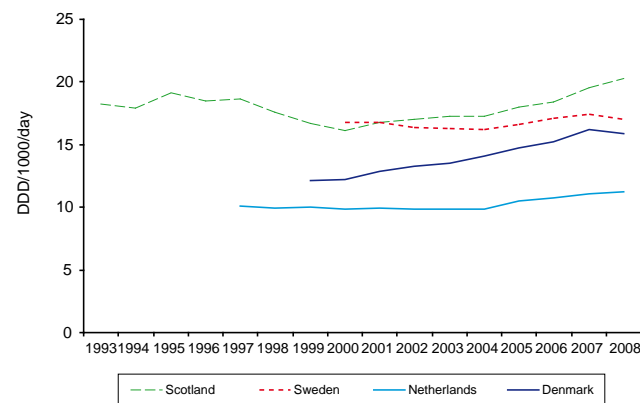


Source: European Surveillance of Antimicrobial Consumption (ESAC)

The experience and models of practice in a number of other countries were considered when SAPG was being formed. More extensive data is available for some European countries with well established surveillance programs. In particular the work of Swedish Strategic Programme Against Antimicrobial

Resistance (STRAMA) was considered in detail. Figure 11 presents longer term data on antimicrobial use expressed as DDD/1000/day for Scotland compared to Sweden, Denmark and Netherlands where there are well established programmes for surveillance of antimicrobial use in place.

**Figure 11.** Use of antibacterials in primary care (DDD/1000/day) in Denmark, Netherlands, Scotland and Sweden. Source: Danmap 2008, Nethmap 2008 and Swedres 2008.



This demonstrates that in 2008 antibacterial use is higher in Scotland. In 2000 the use of antibacterials in Sweden was marginally higher than in Scotland. Since then there have been annual increases in use in Scotland but in Sweden, over the period of implementation of STRAMA, usage of antibacterials has stabilised.

From 2000 to 2008 the rate of growth in Scotland is similar to that in Denmark. Use of antibacterials in the Netherlands is amongst the lowest in Europe.

### Future developments

In 2009/10 the SAPG information workstream is focussing on a number of other key prescribing initiatives:

- Publication of national prescribing indicators for primary care use of antibacterials. These are available as standard reports on PRISMS.
- Development of an audit tool for GPs to provide qualitative local and national information on the management of commonly encountered infections and use of antibacterials in primary care in Scotland.
- Publication of a national report showing qualitative information about use of antimicrobials in hospitals following the participation by a number of Scottish hospitals in a European wide study of antimicrobial use.

The impact of these developments will be monitored through the annual publication of this report. This will add to the quantitative surveillance and will support AMT and front line health care professionals to improve the way in which antibacterials are used.

In 2010 the national database of use of medicines in hospital will become available for the first time in Scotland. HMUD (Hospital Medicines Utilisation Database) will collect information from individual hospital pharmacy systems and present standardised information of the use of medicines at hospital and national level. HMUD is a major national development and the first main clinical area to benefit from this new national information will be the surveillance of use of antibacterials in a hospital setting.

It is anticipated that the second annual report on antimicrobial use and resistance in Scotland will contain information on the hospital use of antibacterials. This will complement the information on use in primary care allowing for an enhanced understanding of the use of antibacterials across all healthcare sectors in Scotland and will support the work of SAPG and AMTs across Scotland to improve antimicrobial stewardship.

The second major information advancement on the horizon is from the Scottish Government's e-Pharmacy programme roll out which enables capture of an individual's Community Health Index (CHI) number on all NHS prescriptions issued in primary care in Scotland. This enriched information will enable analysis of use of antibacterials among different age groups, genders and by deprivation category. This will provide a platform for SAPG and the wider NHS in Scotland to gain a better understanding of the use of antimicrobials.

## Chapter 2 - Antimicrobial resistance

### Background

Resistance to antimicrobials is a recognised threat to public health. It reduces the available treatment options and causes increased morbidity and mortality and increases costs due to failure of empirical antimicrobial therapy. Collection and feedback of standardised surveillance data on antimicrobial usage and resistance is intended to support NHS Boards (and AMTs) in their long-term strategic planning, implementation and evaluation of antimicrobial prescribing in order to prevent and control infections.

In this first annual report, we present data on antimicrobial susceptibility testing (AST) in isolates obtained from blood cultures of the clinically important key organisms reported under EARSS. The decision to focus on these organisms in the first instance is supported by the evidence from the HPS national reporting scheme for blood culture isolates. Table 3 lists the most common pathogens which were isolated from blood cultures in Scotland in 2007-2008.

Blood cultures are the single most reliably collected and reported type of patient specimen, and also represent markers for clinical and epidemiological developments in antimicrobial resistance. A short summary of epidemiological and susceptibility data on *C. difficile* is also presented. The epidemiology of resistant pathogens and *C. difficile* are both affected by antimicrobial prescribing strategies.

**Table 3.** Most common pathogens causing bacteraemia recorded in Scotland in 2007-2008.

Pathogen in blood culture	Reports received by HPS
<i>Escherichia coli</i>	> 2500
<i>Staphylococcus aureus</i>	1000-2000
<i>Enterococcus</i> species	500-1000
<i>Klebsiella</i> species	500-1000
<i>Streptococcus pneumoniae</i>	500-1000
<i>Enterobacter</i> species	200-400
<i>Pseudomonas aeruginosa</i>	200-400
<i>Proteus mirabilis</i>	100-200
Group B <i>Streptococcus</i>	100-200
Group A <i>Streptococcus</i>	100-200
<i>Serratia</i> species	100-200
<i>Acinetobacter</i> species	100-200

### Methods

#### Susceptibility data

Antimicrobial susceptibility data were extracted from ECOSS (Electronic Communication of Surveillance in Scotland) an electronic data link for microbiology laboratories to HPS. Data were obtained from all diagnostic laboratories in Scotland and relevant reference laboratories (see 'Data' section below). The susceptibility data (originating from VITEK 2 systems and disc diffusion tests) were interpreted locally before they were submitted to ECOSS. It is assumed that the laboratories used Clinical and Laboratory Standards Institute (CLSI) breakpoints for categorising the data into Sensitive (S), Intermediate (I) and Resistant (R) (also referred to as the SIR data).

The data from ECOSS were imported into a Microsoft Access® database and numerical analyses were made on the interpreted susceptibility SIR data on key organisms from blood cultures.

#### Case definition (adapted from EARSS):

A case of bacteraemia is a patient from whom an organism has been isolated from the patient's blood, and who has not previously had the same organism isolated within the same quarter.

Deduplication was done in Microsoft Access® according to the EARSS criterion; only the first blood isolate (of one specific organism) per patient per quarter is reported as a case (equivalent of one episode) of bacteraemia.

Resistance proportions in this report refer to the percentages of isolates reported as resistant ("R") to the antimicrobial.

Proportions of combined cephalosporin and fluoroquinolone resistance, and combined cephalosporin and aminoglycoside resistance for *E. coli* and *K. pneumoniae* were also calculated. These were calculated as the number of isolates resistant to ceftriaxone and ciprofloxacin, or to ceftriaxone and gentamicin, divided by the number of reports containing susceptibility data on both of these antimicrobials (ceftriaxone was chosen because it was most frequently reported).

ESBL-producing organisms were reported for *E. coli* and *K. pneumoniae* to HPS based on local laboratory tests. The frequency of cases infected with ESBL producing organisms was calculated using the total number of cases as denominator.

Proportions of resistance were compared to previously published data from the UK (reported to EARSS), and

HPA (England, Wales and Northern Ireland), National Public Health Service Wales (NPHS) and Sweden (STRAMA) where available. A comparison to the STRAMA data was made because this is a European country that has put extensive efforts into promoting rational prescribing of antimicrobials over the past 15 years.

## Data

All susceptibility data (except for those on *C. difficile*) in this report were derived from cases of bacteraemia. Given that blood cultures are the single most reliably collected and reported type of sample, it is assumed that these data are representative of the actual numbers of bacteraemias.

Susceptibility testing was not standardised across Scotland during this data collection period (2008). A number of different laboratory methods have been used to determine the susceptibilities, including disc diffusion, agar dilution, Etest® and automated testing systems. Work is ongoing on standardising antimicrobial susceptibility testing across Scotland by the implementation of VITEK 2 automated susceptibility testing systems in all Scottish diagnostic microbiology laboratories. The exception to this is data pertaining to *S. aureus* and *S. pneumoniae*, which is provided by the Scottish Meticillin Resistant *S. aureus* Reference Laboratory (SMRSARL) and the Scottish Meningococcus and Pneumococcus Reference Laboratory (SMPRL) respectively, where a consistent laboratory method has been applied to all Scottish isolates. Likewise, susceptibility data on *C. difficile* was obtained from the Scottish Salmonella, Shigella and Clostridium difficile Reference Laboratory (SSCDRL).

Selective reporting may have occurred where laboratories have chosen only to test and/or report susceptibility results against certain agents for clinical

reasons. This will skew the resistance data available to HPS. The reporting frequency with which susceptibility data are provided varies for each drug-organism combination reported (see Table 5 and 10 for reporting frequencies of Gram-negatives and Gram-positives respectively). It is assumed that the higher the reporting frequency the more reliable the resistance rate.

## Clostridium difficile Infection (CDI)

Calculated rates of CDI per 1000 total occupied bed days (for those aged 65 years and above), previously published by HPS (on a quarterly basis since January 2007), are presented in this report. Susceptibility data for *C. difficile* on metronidazole and vancomycin and other antimicrobials provided by SSCDRL are also presented.

## Results

### Gram-negative bacteraemia

Quarterly numbers of Gram-negative bacteraemia cases are listed in Table 4 (only the first blood culture per patient per quarter was included). *E. coli*, with 2499 cases reported, is by far the most common Gram-negative organism associated with bacteraemia in Scotland.

Reporting of AST results varied by antimicrobial agent for each organism. Resistance proportions for the most frequently reported antimicrobials, the numbers of cases for which susceptibility testing result was reported and reporting frequencies for each antimicrobial are listed in Table 5 (for the Gram-negatives).

For comparison with the Scottish data presented in this report, proportions of resistance previously reported to EARSS (for the UK), The National Public Health Service for Wales, The Health Protection Agency and STRAMA are listed in Table 6, 7 and 8.

**Table 4.** Gram-negative bacteraemia in 2008.

Time period	Cases as per EARSS case definition (numbers, percentage of ESBL producers)		
	<i>E. coli</i>	<i>K. pneumoniae</i>	<i>P. aeruginosa</i>
Q1 – 2008	454 (34, 7.5%)	86 (7, 8.1%)	33
Q2 – 2008	552 (42, 7.6%)	107(10,9.3%)	44
Q3 – 2008	720 (46, 6.4%)	160 (15, 9.4%)	64
Q4 - 2008	773 (57, 7.4%)	159 (11, 6.9%)	55
<b>Total 2008</b>	<b>2499 (179, 7.2.%)</b>	<b>512 (43, 8.4%)</b>	<b>196</b>

**Table 5.** Reported resistance in Gram-negative blood cultures, 2008.

<b><i>E. coli</i>, <i>K. pneumoniae</i> and <i>P. aeruginosa</i> from blood cultures</b>														
Duplicate Cut Off: ≤ 90 days (only first case per quarter was included)														
Time period: 1st January 2008 – 31st December 2008														
Total number of cases: <i>E. coli</i> =2499, <i>K. pneumoniae</i> =512, <i>P. aeruginosa</i> =196														
	AMP	AMX	AMC	CXM	CRO	CTX	CAZ	GEN	CIP	MEM	PTZ	TMP	3GC/ FQ	3GC/ AG
<b><i>E. coli</i></b> (%resistance)	61.0	60.6	26.8	18.4	12.1	14.3	10.3	7.3	20.0	0	3.0	35.6	10.5	5.0
Susceptibility reported (cases)	464	1841	1935	1128	1658	753	1489	2305	2191	1459	1687	891	1550	1649
Reporting frequency (%)	18.6	73.7	77.4	45.1	66.3	30.1	59.6	92.2	87.7	58.4	67.5	35.7	62.0	66.0
<b><i>K. pneumoniae</i></b> (%resistance)	100	98.9	13.7	22.3	15.6	12.4	12.5	9.7	10.9	0	7.3	18.1	9.3	10.2
Susceptibility reported (cases)	73	365	437	229	327	170	304	465	440	316	328	171	301	323
Reporting frequency (%)	14.3	71.3	85.4	44.7	63.9	33.2	59.4	90.8	85.9	61.7	64.1	33.4	58.8	63.1
<b><i>P. aeruginosa</i></b> (%resistance)	100	93.7	96.2	96.0	94.3	97.5	8.3	2.3	11.8	5.3	8.3	95.1	-	-
Susceptibility reported (cases)	16	63	78	50	70	40	133	171	161	114	133	41	-	-
Reporting frequency (%)	8.2	32.1	39.8	25.5	35.7	20.4	67.9	87.2	82.1	58.2	67.9	20.9	-	-

Key: 3GC/FQ=ceftriaxone/ciprofloxacin, AMP = ampicillin, AMX = amoxicillin, AMC = amoxicillin-clavulanic acid, CXM = cefuroxime, CRO = ceftriaxone, CTX = cefotaxime, CAZ = ceftazidime, GEN = gentamicin, CIP = ciprofloxacin, MEM = meropenem, PTZ=piperacillin/tazobactam, TMP = trimethoprim. Combined resistance: 3GC/FQ = CRO/CIP, 3GC/AG= CRO/GEN. Susceptibility to imipenem was reported in ≤5% of the cases.

### *Escherichia coli*

*E. coli* is the most frequently reported cause of bacteraemia. A total of 2499 cases were reported in Scotland in 2008. Resistance among the *E. coli* isolates was observed towards a number of important antibiotic classes, including aminopenicillins, second and third generation cephalosporins, fluoroquinolones and aminoglycosides (for overview of susceptibility results see Table 5 and Figure 12).

Resistance to aminopenicillins among the Scottish isolates (61%) was similar to that reported throughout the rest of the UK in 2008, but higher than reported by Sweden (32%), (see Table 6 for details). Resistance to third generation cephalosporins among the Scottish

isolates (10.3-14.3%) was in the same range as previous UK reports, but higher than the most recent EARSS figures for the UK (6.9%) and Sweden (2.3%).

It has been suggested that the rise in third generation cephalosporin resistance in many countries is caused by the rapid dissemination of ESBL-producers in hospitals and the community. A substantial proportion (7.2%) of the Scottish *E. coli* isolates were ESBL-producers.

Resistance to fluoroquinolones (ciprofloxacin) among the Scottish isolates (20%) was in the same range as the resistance proportions reported by the Welsh and HPA, but 5% higher than the most recent UK proportions reported to EARSS. Resistance to aminoglycosides (here gentamicin) among the Scottish isolates (7.3%)

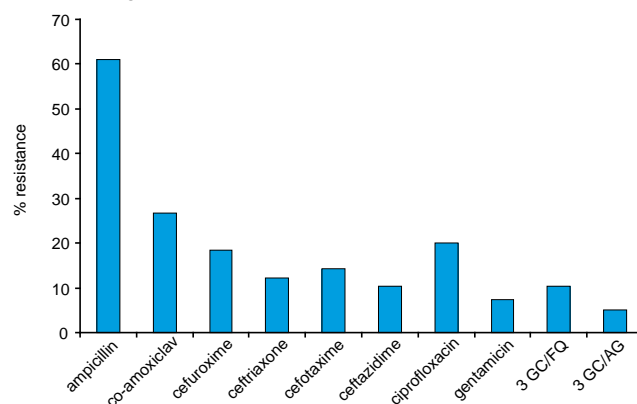
was in the same range as recently reported for the UK to EARSS (2.7-8.4%), but higher than in Sweden (2.2%).

Of particular concern is the combined resistance to third generation cephalosporins and fluoroquinolones observed in 10.5% of the Scottish isolates, and the combined resistance to third generation cephalosporins and aminoglycosides in 5.0% of the isolates.

No resistance to carbapenems (imipenem nor meropenem) was reported among the Scottish *E. coli* isolates. In comparison some carbapenem resistance was reported by HPA (0.2%) and Wales (0.1%) in 2007. Furthermore, the Antibiotic Resistance Monitoring and Reference Laboratory (ARMRL) identified increasing numbers of carbapenemase producers among Gram-

negative isolates in 2008/2009 (see text box on carbapenemases on page 20).

**Figure 12.** Antimicrobial resistance in *E. coli* isolated from blood cultures in 2008. In total 2499 cases were recorded. AST results were reported on subsets of these (see Table 5 for reporting frequencies for each antimicrobial).



**Table 6.** Resistance (%) in *E. coli* in Scotland and other countries.

	Scotland annual report 2008	EARSS 2007 (Summary data for the UK 2001-2007, not including Scotland)	EARSS 2008 (UK 2008 data, not including Scotland)	National Public Health Service for Wales 2006/2007 report (2007 data)	Health Protection Agency, 2008 (2007 data incl. England, Wales and Northern Ireland)	SWEDRES 2008 (2008 data)
	2499 cases (49 cases per 100,000)	1424-2393 reported isolates per year	2493 isolates	44 cases per 100,000 OCBD	21,933 reports (40 cases per 100,000)	4028 isolates
Aminopenicillins	60.6	50.8 - 56.8	60.6	59.0	61.0	*31.9
Co-amoxiclav	27.0	-	-	28.9	-	-
Sec gen cephs.	18.4	-	-	15.9	-	-
Third gen cephs.	12.1 (CRO) 14.3 (CTX) 10.3 (CAZ)	- 1.2 - 9.4 -	- 6.9 -	- 12.6 -	- 12.0 (CTX) 12.0 (CAZ)	- - 2.3
Fluoroquinolones	20.0	6.2 - 19.9	15.1	20.9	23.0	*14.3
Aminoglycosides	7.3	2.7 - 8.4	7.2	6.3	8.5	*2.2
Carbapenems	0	-	-	0.1	≤0.2	-
ESBL (proportion of third gen. cephs resistant isolates)	62 - 75%	-	-	-	78% (2002-2006)	83%

CRO = ceftriaxone, CTX = cefotaxime, CAZ = ceftazidime

\*55-60% of isolates tested

## *Klebsiella pneumoniae*

*K. pneumoniae* is with 512 cases in 2008 the second most frequent cause of Gram-negative bacteraemia. Resistance among *K. pneumoniae* isolates was observed for a number of important antibiotic classes, including second and third generation cephalosporins, fluoroquinolones and aminoglycosides (for overview of susceptibility results see Table 5 and Figure 13).

*K. pneumoniae* is intrinsically resistant to aminopenicillins (e.g. ampicillin) as it carries chromosomally encoded beta-lactamases. Resistance to third generation cephalosporins among the Scottish isolates (12.5-15.6%) was within the same range as previous UK reports, but higher than reported for the UK to EARSS (6.7%) in 2008, where resistance proportions have decreased remarkably since 2007 (see Table 7).

Resistance traits carried on plasmids are frequently acquired by *K. pneumoniae* and many novel ESBL variants are initially identified in *K. pneumoniae* before they emerge in *E. coli*. As for *E. coli* resistance it is assumed that cephalosporin resistance in *K. pneumoniae* is a consequence of dissemination of ESBL producers. In 2008 a total of 44 ESBL producing *K. pneumoniae* (8.4% of *K. pneumoniae* bacteraemias) were recorded in Scotland.

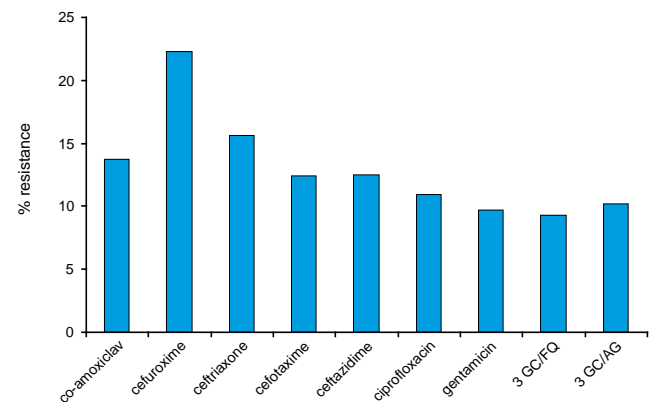
Furthermore, one isolate of *K. pneumoniae* submitted to ARMRL from a Scottish hospital was characterised as a carbapenemase producer. Although carbapenem resistance was not reported among routine submissions of *K. pneumoniae* in Scotland, resistance elsewhere in the UK (1.2% in 2008) and increasing numbers of reports coming from the ARMRL, suggest that carbapenem resistance is an emerging phenotype among *K. pneumoniae* (see text box on carbapenemases below on page 20).

Resistance to fluoroquinolones (10.9%) among the Scottish isolates was in the same range as previously reported for the UK (11.8-12.6%) and Sweden (12.9%), but higher than the most recent figure (7.0%) reported for the UK in 2008. Resistance to aminoglycosides (here gentamicin) was 9.7% among the Scottish isolates of *K. pneumoniae*, above previous (6.3-8.5% in 2005-2007) and latest reports for the UK to EARSS (5.6% in 2008).

Of particular concern is combined resistance in *K. pneumoniae*. Combined resistance to cephalosporins and fluoroquinolones was observed in 9.3% and to

cephalosporins and aminoglycosides in 10.2% of the isolates.

**Figure 13.** Antimicrobial resistance in *K. pneumoniae* isolated from blood cultures in 2008. In total 512 cases were recorded. AST results were reported on subsets of these (see Table 5 for reporting frequencies for each antimicrobial).



**Table 7.** Resistance (%) in *K. pneumoniae* in Scotland and other countries.

	Scotland annual report 2008	EARSS 2007 (Summary data for the UK 2005-2007, not including Scotland)	EARSS 2008 (UK 2008 data, not including Scotland)	National Public Health Service for Wales 2006/2007 report* (2007 data)	Health Protection Agency, 2008 (2007 data incl. England, Wales and Northern Ireland)**	SWEDRES 2008 (2008 data)
	512 cases (10.0 cases per 100,000)	394-425 reported isolates per year	356 isolates	10 cases per 100,000 OCBD	5,990 reports (10.8 per 100,000)	826
Co-amoxiclav	13.7	-	-	18.5	-	-
Sec gen cephs.	22.3	-	-	22.7	-	-
Third gen cephs.	15.6 (CRO) 12.4 (CTX) 12.5 (CAZ)	- 11.1 - 12.5 -	- 6.7 -	- 16.8 -	- 14.0 (CTX) 14.0 (CAZ)	- 2.3 -
Fluoroquinolones	10.9	11.8 - 12.6	7.0	17.8	15.0	12.9
Aminoglycosides	9.7	6.3 - 8.5	5.6	11.0	10.0	1.1
Carbapenems	0	0.0 - 0.3	1.2	0.0	≤0.5	-
ESBL (proportion of third gen. cephs resistant isolates)	50 - 76%	-	-	-	-	100%

\* *Klebsiella* spp.

\*\*70% of the reports on *Klebsiella* spp. were on *K. pneumoniae*, 23% on *K. oxytoca*

CRO = ceftriaxone, CTX = cefotaxime, CAZ = ceftazidime

## *Pseudomonas aeruginosa*

A total of 196 cases of *P. aeruginosa* bacteraemia were recorded in 2008. *P. aeruginosa* is intrinsically resistant to a broad range of antimicrobials due to outer membrane and efflux systems that efficiently exclude antimicrobials from the bacterial cells. Resistance to all available anti-pseudomonal agents, including piperacillin-tazobactam, ceftazidime, carbapenems, fluoroquinolones and aminoglycosides was observed among the Scottish isolates (for overview of susceptibility results see Table 5 and Figure 14).

Resistance to piperacillin-tazobactam (8.3%) in the Scottish isolates of *P. aeruginosa* was above what was reported for the UK (1.3-5.4% in 2005-2008) and Wales (3.9% in 2007) (see Table 8). Resistance to ceftazidime in *P. aeruginosa* was 8.3% among the Scottish isolates, while most recent figures reported from the UK and Wales were below 5%.

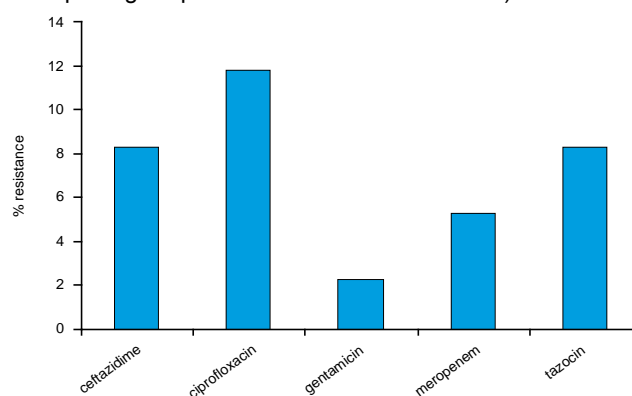
Resistance to carbapenems (here meropenem) was 5.3% among the Scottish isolates of *P. aeruginosa*, which is within the same range as reported for the rest of the UK (6.4%) and Sweden (4.0%) in 2008.

Resistance to fluoroquinolones (11.8%) among the Scottish isolates of *P. aeruginosa* was within the same range as reported by HPA (12%) and Wales (13.6%) in 2007, but above that of the UK resistance figure (7.6%) reported to EARSS in 2008.

Resistance to aminoglycosides (here gentamicin) among the Scottish isolates of *P. aeruginosa* (2.3%) was below of that reported throughout the UK in previous and recent publications.

As few antimicrobial agents are available to treat *P. aeruginosa* multiple resistance is a major concern. Multiple resistance (defined as  $\geq 3$  anti-pseudomonal agents/groups) was observed in 5 of the Scottish isolates (corresponding to 6% of isolates where results were available), all involving resistance to ceftazidime combined with resistance to 2 or 3 of the following agents: tazocin, meropenem, ciprofloxacin or gentamicin.

**Figure 14.** Antimicrobial resistance in *P. aeruginosa* isolated from blood cultures in 2008. In total 196 cases were recorded. AST results were reported on subsets of these (see Table 5 for reporting frequencies for each antimicrobial).



**Table 8.** Resistance (%) in *P. aeruginosa* in Scotland and other countries.

	Scotland annual report 2008	EARSS 2007 (Summary data for the UK 2005-2007, not including Scotland)	EARSS 2008 (UK 2008 data, not including Scotland)	National Public Health Service for Wales 2006/2007 report* (2007 data)	Health Protection Agency, 2008 (2007 data incl. England, Wales and Northern Ireland)**	SWEDRES 2008 (2008 data)
	196 cases (3.8 cases per 100,000)	353 - 438 reported isolates per year	345 isolates	5.0 cases per 100,000 OCBD	3871 reports (7.0 per 100,000)	315 isolates
Third gen cephs.	8.3	3.1 - 7.2	3.5	4.8	6.0	5.2
Fluoroquinolones	11.8	7.6 - 9.1	7.6	13.6	12.0	7.6
Aminoglycosides	2.3	3.3 - 5.1	2.9	8.4	5.0	0.3
Carbapenems	5.3	6.2 - 10.0	6.4	5.8	8.0	4.0
Piperacillin-tazobactam	8.3	1.3 - 5.4	1.8	3.9	4.0	-

\*\* *Pseudomonas* spp; 91.7% were *P. aeruginosa*.

### **Emerging resistance - Carbapenemase-producing Enterobacteriaceae**

Carbapenems are a group of potent broad-spectrum beta-lactams that are active against many multi-resistant Gram-negatives including cephalosporin resistant *E. coli* and *K. pneumoniae* that produce AmpC beta-lactamases or ESBLs. As cephalosporin resistance and ESBL production have become more prevalent among Gram-negatives the need for using carbapenems in hospitals has increased. Emergence of resistance mediated by carbapenem destroying enzymes (carbapenemases) is of major public health concern as few other antimicrobials are available to treat infections with multi-resistant Gram-negative organisms. One study has shown significantly increased rates of mortality in patients with bloodstream infections caused by carbapenem-resistant *Acinetobacter* spp (Kwon et al. 2007).

In the UK, carbapenemase resistance was until recently confined to *P. aeruginosa* and *Acinetobacter baumannii*. However, in 2008 a total of 21 carbapenemase producing Enterobacteriaceae were referred to ARMRL. This trend continued in 2009 where 17 further isolates were referred during the first 6 months of the year. This represents a steep

increase in carbapenem resistance as such frequent submissions were not observed previously.

Three major types of carbapenemases; metallo-beta-lactamases, KPC enzymes and OXA-48 have been identified among submissions to ARMRL. The predominating phenotype among the recent submissions in 2009 was identified as NDM-1 (New Delhi Metallo beta-lactamase). Of the UK NDM-1 producers 14 were *K. pneumoniae*, 4 *E. coli*, 1 *Enterobacter* spp and 2 *C. freundii*. The isolates were obtained from patients widely scattered across 16 hospitals in the UK, one of those in Scotland. Several of the patients had received medical treatment in India, where carbapenem resistance is a growing problem.

Most carbapenemase producers are resistant to all available antimicrobials except for polymyxins and tigecycline (in vitro), and are therefore posing a major potential risk to any medical procedure where infection with opportunist Gram-negative bacteria may occur.

An UK-wide resistance alert was issued by HPA in January 2009, advising hospital staff to be alert to NDM-1 producers and limit their spread by effective infection control measures.

## Gram-positive bacteraemia

Numbers of reported cases of Gram-positive bacteraemia are listed in Table 9. *S. aureus* with 1846 reports (meticillin sensitive *S. aureus* (MSSA) and (meticillin resistant *S. aureus* (MRSA)) was the most common cause of Gram-positive bacteraemia followed by *S. pneumoniae* with 607 cases and then *E. faecalis* and *E. faecium*.

## *Staphylococcus aureus*

The *S. aureus* bacteraemia data is supplied directly to HPS by SMRSARL and as such compliance with reporting of antibiotic susceptibility is 100%. The total number of recorded cases of *S. aureus* bacteraemia was 1846. A total of 605 of these cases can be attributed to meticillin resistant strains (33.0%).

Analysis was conducted on MRSA and MSSA due to significant differences in antimicrobial susceptibility patterns (for overview of susceptibility results see Table 10 and figures 15 and 16).

**Table 9.** Gram-positive bacteraemias in 2008.

Time period	Cases as per EARSS case definition				
	MSSA	MRSA	<i>S. pneumoniae</i>	<i>E. faecalis</i>	<i>E. faecium</i>
Q1 - 2008	336	189	172	68	72
Q2 - 2008	296	141	140	92	66
Q3 - 2008	302	129	114	114	59
Q4 - 2008	307	146	181	105	72
<b>Total</b>	<b>1241</b>	<b>605</b>	<b>607</b>	<b>379</b>	<b>269</b>

**Table 10.** Resistance (%) in MSSA, MRSA and *S. pneumoniae* from blood cultures, 2008.

<b>MSSA, MRSA and <i>S. pneumoniae</i> from blood cultures</b>																			
Duplicate Cut Off: ≤ 90 days (only first case per quarter was included)																			
Time period: 1st January 2008 – 31st December 2008																			
Total number of cases: MSSA = 1241, MRSA = 605, <i>S. pneumoniae</i> = 607.																			
	AMP	AMX	CHL	CIP	CLI	ERY	FUS	GEN	KAN	LNZ	MUP	OXA	PEN	RIF	TEC	TCY	TOB	TMP	VAN
MSSA	-	-	0.2	7.1	0.9	10.5	10.6	1.2	2.3	0	0.3	0	-	0.1	0	5.3	2.1	15.6	0
MRSA	-	-	0.5	96.0	32.1	76.8	6.9	7.3	15.9	0	5.3	100	-	2.5	0	9.8	20.7	27.8	0
<i>S. pneumoniae</i>	-	-	-	1.0		3.1	-	-	-	-	-	-	0.2	-	-	-	-		

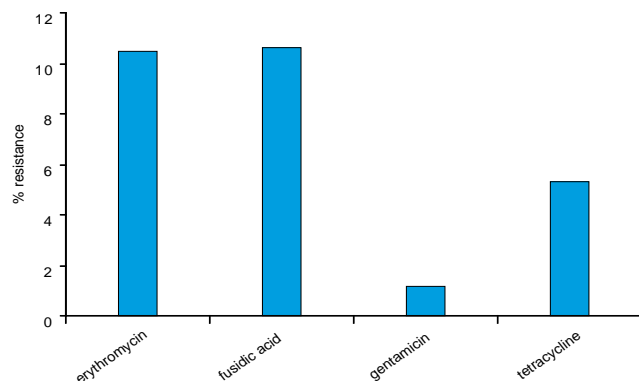
Key: AMP = ampicillin, AMX = amoxicillin, CHL = chloramphenicol, CIP = ciprofloxacin, CLI = clindamycin, ERY = erythromycin, FUS = fusidic acid, GEN = gentamicin, KAN = kanamycin, LNZ = linezolid, MUP = mupirocin, OXA = oxacillin, PEN = penicillin, RIF = rifampin, TEC = teicoplanin, TCY = tetracycline, TOB = tobramycin, TMP = trimethoprim, VAN = vancomycin.

The data in this table originates from the SMRSARL (*S. aureus*) and SMPRL (*S. pneumoniae*) and so all antibiotics are reported in all instances. Data pertaining to *Enterococcus* spp are not included due to the incompleteness of this dataset.

### Meticillin sensitive *S. aureus* (MSSA)

MSSA resistance to the macrolide erythromycin was 10.5%. Resistance to gentamicin, tetracycline and fusidic acid was 1.2%, 5.3% and 10.6% respectively. These figures are comparable to the rest of the UK.

**Figure 15.** Antimicrobial resistance in MSSA isolated from blood cultures in 2008. The total number of isolates reported was 1241.



### Meticillin resistant *S. aureus* (MRSA)

The majority of MRSA isolates were resistant to the quinolone ciprofloxacin (96.0%). Resistance to erythromycin, fusidic acid and gentamicin was 76.8%, 6.9% and 7.3% respectively (see figure 16). These percentages are very similar to the resistance figures published for the rest of the UK but higher than reported in Sweden (where 36.7% were resistant to ciprofloxacin and 39.6% to erythromycin). In contrast to this, resistance to fusidic acid and gentamicin in the Scottish isolates was lower than reported in Sweden (where 14.6% were resistant to fusidic acid and 19.0% to gentamicin).

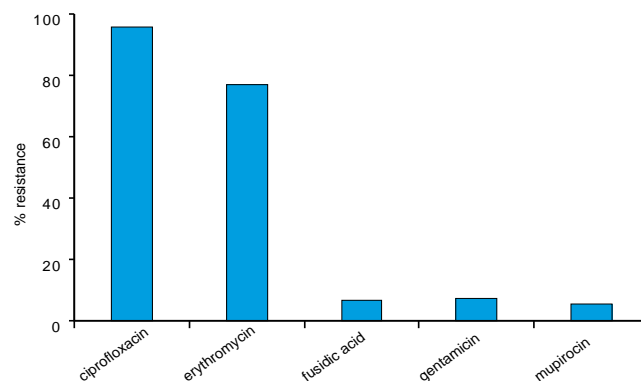
Mupirocin resistance proportions are presented in this report. Whilst mupirocin would not be used to treat a bloodstream infection it is used by HPS as a proxy indicator of overall mupirocin resistance in all MRSA isolates. Intelligence gathered from the MRSA Snapshot programme will be used to further inform our knowledge in this area. In 2010, the National MRSA Screening Programme will be rolled out in all hospitals in Scotland and so it is essential that we remain vigilant in our monitoring of mupirocin resistance. Mupirocin resistance in the Scottish bacteraemia isolates was 5.3%. There is currently no published data in the UK against which this can be compared. Sweden reported that 1.8% of all of their MRSA isolates were resistant to mupirocin.

*S. aureus* glycopeptide resistance (vancomycin and teicoplanin) was not reported in the Scottish bacteraemia

dataset in 2008. Glycopeptide resistance has remained relatively low throughout the world. HPS continues to work in close conjunction with SMRSARL to monitor this type of resistance.

It should be noted that erythromycin can induce MRSA clindamycin resistance (dissociation due to the shared macrolide-lincosamide-streptogramin (MLS) resistance mechanism). In Scotland the predominant strain of MRSA is the epidemic meticillin resistant *S. aureus* type 15 (EMRSA-15) followed by EMRSA-16. In 2008 73.4% of EMRSA-15 and 100% of EMRSA-16 were resistant to erythromycin. In instances where it is known that erythromycin resistance is of the MLS type, clindamycin cannot be used to treat.

**Figure 16.** Antimicrobial resistance in MRSA isolated from blood cultures in 2008. The total number of isolates reported was 605.



### *Streptococcus pneumoniae*

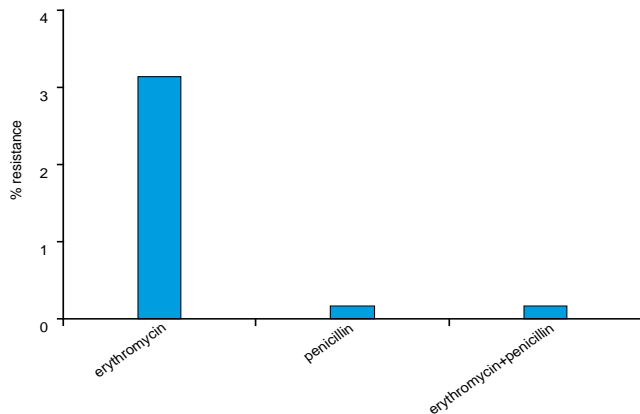
Resistance in *S. pneumoniae* was observed against macrolides and penicillins (an overview of susceptibility results can be found in Table 10 and Figure 17).

Resistance of *S. pneumoniae* to erythromycin and penicillin was 3.14% and 0.17% respectively with combined resistance to both antibiotics being 0.17%. This compares favourably to the rest of the UK with the HPA (2007) publishing resistance of 9.3% for erythromycin and 3.8% for penicillin. There is a wide range of resistance proportions throughout Europe. EARSS reported a range of 0.0-50.0% for erythromycin, 0.0-53.8% for penicillin and a combined resistance range of 0.0-33.0%. In Sweden resistance to erythromycin was higher than that reported in Scotland (5.2%) and resistance to penicillin was comparable at 0.1%.

In September 2006, the 7-valent pneumococcal conjugate vaccine (PCV7) was introduced into the Scottish Routine Childhood Immunisation Programme with a catch-up campaign for children up to two years

of age. Whilst resistance to penicillin and erythromycin remains low in Scotland it is essential that we continue to monitor the impact of routine PCV immunisation on drug resistance in pneumococci.

**Figure 17.** Antimicrobial resistance in *S. pneumoniae* isolated from blood cultures in 2008. The total number of isolates reported was 607.



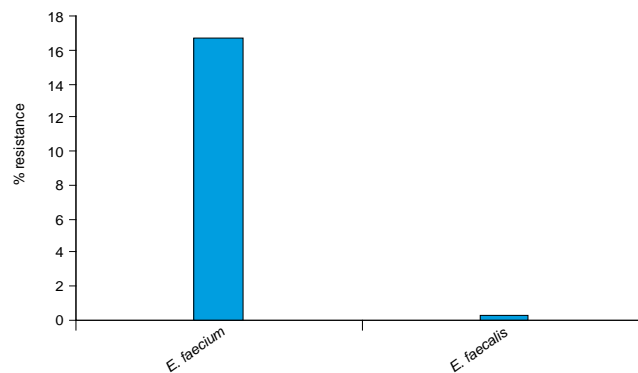
### Enterococcus species

Glycopeptide (e.g. vancomycin) resistance in *Enterococcus* species is of particular interest as the resistance mechanisms can be transferred to other pathogens (including MRSA) via plasmids.

Vancomycin resistance was 16.7% for *E. faecium* and 0.26% for *E. faecalis*. This is lower than that reported by HPA, 2007 (24% for *E. faecium*, 3% for *E. faecalis*) (see Figure 18). The EARSS interactive database reports vancomycin resistance ranges of 0% – 34.6% for *E. faecium* and 0% - 6.8% for *E. faecalis* for 2008.

Approximately 90% of Scottish diagnostic laboratories provided vancomycin susceptibility data. For most other antibiotics, including the aminopenicillins and aminoglycosides, data was generally only provided in instances of failed treatment options and so are not included in this report.

**Figure 18.** Vancomycin resistance in *E. faecium* and *E. faecalis* isolated from blood cultures in 2008. The total number of *E. faecium* and *E. faecalis* isolates reported was 269 and 379 respectively.



### Emerging resistance - Glycopeptide resistant enterococci

Glycopeptides such as vancomycin and teicoplanin are the antimicrobial agents of choice for enterococcal bacteraemia and endocarditis. In the last decade, enterococci with acquired resistance to these antibiotics have been emerging.

The first vancomycin resistant enterococci (VRE) were reported in the UK in 1987 and in 1988 the first articles on plasmid mediated, inducible high level resistance to glycopeptides were published. Subsequently, enterococci with inducible low level resistance to vancomycin, which remain teicoplanin susceptible, have emerged.

Strains with constitutive low-level vancomycin resistance have also been isolated.

Five phenotypes have been identified of which three have clinical relevance: VanA, VanB and VanC.

VanA phenotype confers inducible, high level resistance to vancomycin; VanB phenotype confers resistance to vancomycin, but isolates remain susceptible to teicoplanin. VanC phenotype is only associated with *E. gallinarum*, *E. casseliflavus* and *E. flavescens* and confers low level constitutive vancomycin resistance.

The VanA and VanB phenotypes, mostly found among *E. faecalis* and *E. faecium*, may be transferred by plasmids and conjugative transposition.

The number of vancomycin resistant *E. faecium* isolates reported to EARSS in 2008 was low with 6 out of 33 countries reporting fewer than 20 isolates. Three countries however reported that more than 25% of *E. faecium* isolates were vancomycin resistant (Ireland, Greece and the UK). There is currently an upward trend for the United Kingdom with percentage of resistant isolates increasing steadily since 2006.

It is essential that we continue to monitor antimicrobial prescribing as not only are enterococci a common cause of bacteraemia but they have the ability to transfer glycopeptide resistance to more pathogenic bacteria such as *S. aureus*.

This would considerably impact on the availability of treatment options for *S. aureus* bacteraemia.

Cephalosporins are the most cited antimicrobial risk factor for glycopeptide resistant enterococci (GRE) colonisation or infection. Fluoroquinolones have also been implicated, as has preceding therapy with agents active against anaerobes, especially in the context of *C. difficile* infection.

### *Clostridium difficile* Infection (CDI)

Data on CDI rates (per 1000 occupied bed days) have been collected, for those aged 65 years and above, from all NHS boards by HPS since October 2006. In 2007 full compliance with the national surveillance protocol was obtained. Seasonal variation was observed in this first year of the surveillance. However, in 2008 the overall rates of CDI for Scotland decreased throughout the year and eliminated the seasonal variation; a trend that has continued into the first 6 months of 2009. Overall rates of CDI for Scotland were 1.41, 1.33, 1.15 and 1.02 in quarter 1 to 4 in 2008, representing a drop in the overall rate for Scotland of 28% throughout 2008 (see figure 19).

By the end of 2008 a total of 823 isolates had been submitted to the *C. difficile* reference laboratory for genotyping and susceptibility testing. All these isolates were susceptible to metronidazole and vancomycin. The majority of these isolates were resistant to multiple

antimicrobials including levofloxacin, moxifloxacin, cefotaxime, clindamycin and erythromycin.

**Figure 19.** Rates of *Clostridium difficile* Infection (CDI) per 1000 OCBDs.



Previous and up to date figures by NHS boards are available at: <http://www.hps.scot.nhs.uk/haic/sshaip/clostridiumdifficile.aspx>

## Future developments

During 2008 standardisation of susceptibility testing was introduced across Scotland by installation of automated susceptibility testing systems (VITEK 2) in all diagnostic laboratories using CLSI testing criteria. All laboratories now use VITEK 2 for testing blood cultures, but for other sample types, including urine, sputum and others, not all laboratories have implemented VITEK 2. In addition, complexities in electronic data transfer to HPS have occurred and it has therefore not been possible to produce a national dataset for 2008 based on data derived directly from the VITEK 2 systems. The resistance data described in this report are interpreted susceptibility data (that were reported to HPS as S, I, R data) derived from the VITEK 2 systems and other susceptibility testing methods. As the data were filtered through local laboratory information management systems (LIMS) before transfer to HPS (via ECOSS) they were in many instances incomplete as selective reporting may have occurred for clinical reasons. Furthermore, antimicrobial testing panels varied between laboratories. The accuracy of reported resistance rates for each organism therefore vary considerably as the number of isolates reported ranged from 20-100% of the total numbers of invasive isolates. These limitations are compounded by variations in antimicrobial susceptibility testing methods which could affect interpretation of results. The most complete datasets of high quality were those on *S. aureus* and *S. pneumoniae* that were generated by the respective reference laboratories. For those organisms all invasive isolates were tested against a fixed panel of antimicrobials, using CLSI standards, and reported to HPS.

Development of the automatic transfer of susceptibility data from the VITEK 2 systems in all diagnostic laboratories is currently ongoing in order to complete the standardisation of antimicrobial susceptibility testing. The implementation of agreed antimicrobial testing panels (i.e. VITEK 2 AST-cards) for Gram-negative and Gram-positive organisms to be used by all laboratories in Scotland will be a part of this process. The electronic transfer of data directly from the VITEK 2 systems to ECOSS will give HPS access to the full datasets (including phenotypic data) on all antimicrobial-pathogen combinations without omitting susceptibility data suppressed in the reporting procedure for clinical reasons. These datasets will also contain MIC (minimum inhibitory concentration) values that will support the standardisation of data by applying the same breakpoints for all laboratories. This will enable

HPS to generate MIC distributions and detect shift in those over time that could have clinical implications.

The changes to local prescribing policies that have been introduced in many NHS boards to reduce the incidence rate of CDI may have a substantial impact on colonisation and susceptibility patterns of other pathogens, as new selective pressures are introduced as result of changes in antimicrobial prescribing.

The national surveillance programme will only show overall trends of antibacterial use and resistance. Therefore additional surveys and studies which address specific clinical problems will be designed to support the programme. These will include diagnosis-prescribing surveys that investigate the appropriateness of prescriptions for certain infections, and focussed resistance surveys that address specific clinical infections.

It is important to remain aware that changes in prescribing may have unintended consequences beyond the development of antimicrobial resistance. Prudent prescribing is a balance between avoiding the use of antimicrobials when they are not warranted and under-prescribing which may lead to an increase in certain types of bacterial infection. Preliminary work has been undertaken in 2009 to assess the feasibility of monitoring trends of certain infections as a means of monitoring unintended consequences. Based on this work a surveillance programme for unintended consequences will be developed.

## Conclusion

This report is the first SAPG joint annual report on antimicrobial use and resistance in Scotland. It sets the baseline from which the Scottish Surveillance Programme will develop.

The report highlights specific trends in antimicrobial use and patterns of antimicrobial resistance that potentially could lead to problems with preventing and treating infections. The report aims to support NHS Boards, hospitals and primary care in their long-term planning of antimicrobial prescribing. In particular this report should be of use to Antimicrobial Management Teams (AMTs), Infection Control Teams (ICTs) and microbiologists.

## References

---

DANMAP and The Danish Integrated Antimicrobial Resistance Monitoring and Research Programme. DANMAP 2008 - Use of antimicrobial agents and occurrence of antimicrobial resistance in bacteria from food animals, foods and humans in Denmark. (2009).

EARSS Management Team, members of the Advisory Board and national representatives of EARSS Bilthoven The Netherlands October 2008. EARSS Annual Report 2007. (2008).

EARSS Management Team, members of the Advisory Board and national representatives of EARSS Bilthoven The Netherlands October 2009. EARSS Annual Report 2008. (2009).

Health Protection Agency. Antimicrobial Resistance and Prescribing in England, Wales and Northern Ireland, 2008. (2008).

National Public Health Service for Wales. Heginbotham, M, Howe, R. Antimicrobial Resistance in Wales 2006/2007. (2007).

Kwon, K.T., and et.al. "Impact of imipenem resistance on mortality in patients with Acinetobacter bacteraemia." Journal of Antimicrobial Chemotherapy 59 (2007): 525-30.

NethMap and SWAB, the Dutch Foundation of the Working Party on Antibiotic Policy in collaboration with the RIVM the National Institute for Public Health and the Environment of the Netherlands. NETHMAP - Consumption of antimicrobial agents and antimicrobial resistance among medically important bacteria in the Netherlands 2008. (2009).

Strama, The Swedish Strategic Programme against Antibiotic Resistance and The Swedish Institute for Infectious Disease Control. SWEDRES 2008 - A report on Swedish Antimicrobial Utilisation and Resistance in Human Medicine. (2009).

## Figures

---

Figure 1: NHS Scotland: use of antibacterials in primary care 1993-2008	7
Figure 2. NHS Scotland: use of antibacterials in primary care, percent of total DDD/1000/day 2008	8
Figure 3. NHS Scotland: use of antibacterials in primary care, DDD/1000/day by group 2004 - 2008	8
Figure 4. NHS Scotland: use of amoxicillin in primary care, % capsule strength, 1993-2008	8
Figure 5. NHS Scotland: combination penicillins in primary care, DDD/1000/day, 1993-2008	9
Figure 6. NHS Scotland: fluoroquinolone in primary care, DDD/1000/day, 1993-2008	9
Figure 7. NHS Scotland: macrolides in primary care, DDD/1000/day, 1993-2008	9
Figure 8. NHS Scotland use of antibacterials in primary care, % seasonal variation 1993-2008	10
Figure 9. NHS Scotland: use of antibacterials in dentistry, percent of total DDD/1000/day 2008	10
Figure 10. Use of antibacterials in primary care (DDD/1000/day) 2006	11
Figure 11. Use of antibacterials in primary care (DDD/1000/day) in Denmark, Netherlands, Scotland and Sweden	11
Figure 12. Antimicrobial resistance in <i>E. coli</i> isolated from blood cultures in 2008.	16
Figure 13. Antimicrobial resistance in <i>K. pneumoniae</i> isolated from blood cultures in 2008.	17
Figure 14. Antimicrobial resistance in <i>P. aeruginosa</i> isolated from blood cultures in 2008.	19
Figure 15. Antimicrobial resistance in MSSA isolated from blood cultures in 2008.	22
Figure 16. Antimicrobial resistance MRSA isolated from blood cultures in 2008.	22
Figure 17. Antimicrobial resistance in <i>S. pneumoniae</i> isolated from blood cultures in 2008.	23
Figure 18. Vancomycin resistance in <i>E. faecium</i> and <i>E. faecalis</i> isolated from blood cultures in 2008.	23
Figure 19. Rates of <i>Clostridium difficile</i> Infection (CDI) per 1000 OCBD.	24

## Tables

---

Table 1: NHS Scotland: Use of antibacterials in primary care - top 10 in 2008	7
Table 2: Antibacterial use (ATC J01 exclude antituberculous and antileprotic medicines)	11
Table 3. Most common pathogens causing bacteraemia recorded in Scotland in 2007-2008	13
Table 4. Gram-negative bacteraemia in 2008.	14
Table 5. Reported resistance in Gram-negative blood cultures, 2008	15
Table 6. Resistance (%) in <i>E. coli</i> in Scotland and other countries	16
Table 7. Resistance (%) in <i>K. pneumoniae</i> in Scotland and other countries	18
Table 8. Resistance (%) in <i>P. aeruginosa</i> in Scotland and other countries	19
Table 9. Gram-positive bacteraemias in 2008	21
Table 10. Resistance (%) in MSSA, MRSA and <i>S. pneumoniae</i> from blood cultures, 2008	21