

EUROPEAN CONFERENCE REPORT

Report of the Consensus Conference on Antibiotic Resistance; Prevention and Control (ARPAC)

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ABSTRACT

Antimicrobial resistance is a key public health concern in Europe. It is known that there are significant variations in the prevalence of resistance across Europe, and methods to reduce the problem are also assumed to vary significantly. The 'Antibiotic Resistance; Prevention and Control (ARPAC)' Concerted Action project was funded by the European Commission and conducted by four study groups of the European Society of Clinical Microbiology and Infectious Diseases (ESCMID). The project established a network of European hospitals and collated data on antimicrobial resistance prevalence, antimicrobial susceptibility testing methods, typing methods employed, antimicrobial use, antibiotic policies and practices, and infection control policies and practices. The ARPAC Consensus Conference, entitled 'Control of antibiotic resistance in European hospitals—informing future evidence-based practice', was held in Amsterdam in November 2004. The conference was co-hosted by the European Commission, ESCMID and the Dutch Working Party on Antibiotic Policy (SWAB). Key ARPAC findings were presented and discussed in the context of the worldwide situation. The conference delivered a set of high-priority recommendations likely to have a significant impact on antimicrobial resistance. This report summarises these recommendations.

Keywords Antibiotic resistance, ARPAC, European hospitals, infection control, recommendations, review

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CONFERENCE FACULTY

Plenary lectures

Chairpersons: H. Verbrugh (Rotterdam, The Netherlands), J. Vila (Barcelona, Spain).

Presenters: J. Bruce (Aberdeen, UK), H. Goossens (Antwerp, Belgium), F. M. MacKenzie (Aberdeen,

UK), I. M. Gould (Aberdeen, UK), M. J. Struelens (Brussels, Belgium), K. J. Towner (Nottingham, UK), J. van der Meer (Nijmegen, The Netherlands).

Workshop 1

Rapporteur: G. Duckworth (London, UK).

Presenters: R. Canton (Madrid, Spain), H. Goossens (Antwerp, Belgium), H. Grundmann (Bilthoven, The Netherlands), V. Jarlier (Paris, France), G. Cornaglia (Verona, Italy).

Workshop 2

Chairperson: J. van der Meer (Nijmegen, The Netherlands).

Rapporteur: B. Cookson (London, UK).

Presenters: D. Nathwani (Dundee, UK), I. M. Gould (Aberdeen, UK), B. Cookson (London,

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UK), H. Kolmos (Odense, Denmark), I. Gyssens (Rotterdam, The Netherlands), J. van der Meer (Nijmegen, The Netherlands).

Workshop 3

Chairperson: V. Krcmery (Bratislava, Slovak Republic).

Rapporteur: D. Monnet (Copenhagen, Denmark).
Presenters: F. M. MacKenzie (Aberdeen, UK), R. Polk (Virginia, USA), C. Brandt (Copenhagen, Denmark), D. Monnet (Copenhagen, Denmark), V. Krcmery (Bratislava, Slovak Republic), G. Zanetti (Lausanne, Switzerland), I. M. Gould (Aberdeen, UK).

Workshop 4

Chairpersons: P. J. van den Broek (Leiden, The Netherlands), J. Vila (Barcelona, Spain).

Rapporteur: M. J. Struelens (Brussels, Belgium).
Presenters: A. Voss (Nijmegen, The Netherlands), C. Suetens (Brussels, Belgium), M. Struelens (Brussels, Belgium), S. Harbarth (Geneva, Switzerland), K. J. Towner (Nottingham, UK), L. Dijkshoorn (Leiden, The Netherlands), J. Green (London, UK), K. Levi (Nottingham, UK).

INTRODUCTION

Antimicrobial resistance is causing major concern worldwide. There is a fear that a return is being made to the situation 50 years ago, when there were few, if any, effective antibiotics, with the result that numerous infections serious enough to necessitate hospital admission were usually fatal. Many of the major resistance problems currently causing concern emanate from the hospital environment. It is difficult at the start of the 21st century to grasp what life must have been like before antibiotics were widely available. For example, staphylococcal septicaemia had a mortality rate of 80% [1], and infective endocarditis and meningitis had mortality rates approaching 100% [2].

The antibiotic era transformed the treatment and outcome of infectious diseases, but there is no doubt that the pendulum has now swung the other way, and intensive antibiotic use (often overuse) in hospitals has generated more resistance problems than could ever have been imagined. These problems are compounded by the ever-increasing immunosuppression that comes

with modern diagnostic and therapeutic modalities, and are magnified further by the opportunities for cross-infection that exist in modern, busy, often over-crowded, under-staffed hospitals.

It is in this setting that four study groups of the European Society of Clinical Microbiology and Infectious Diseases (ESCMID) sought to investigate what measures are being attempted to control antimicrobial resistance at a pan-European level. It was already well-known that methicillin-resistant *Staphylococcus aureus* (MRSA) is a major scourge of many European hospitals (<http://www.earss.rivm.nl>), but there was less information regarding the problems with other major antimicrobial-resistant pathogens. There had been no previous attempt to quantify these problems in the context of parallel infection control and antibiotic policy measures in European hospitals. Furthermore, there had been no previous efforts to relate the resistance problem at a hospital level to actual antibiotic use, which is responsible for the Darwinian evolution that selects so many antimicrobial-resistant bacteria.

Against this background, the 'ARPAC' project was conceived. This initiative was a Concerted Action project funded by the European Commission's Research Directorate General within the Fifth Framework Programme (project number QLK2-CT-2001-00915). The full title of the project was 'Development of Strategies for Control and Prevention of Antibiotic Resistance in European Hospitals'; the short title was 'Antibiotic Resistance; Prevention and Control (ARPAC)'. Hereafter, the project will be referred to as ARPAC.

The ARPAC project ran from 1 January 2002 to 30 June 2005, with the work being carried out under the auspices of four ESCMID study groups, namely the ESCMID Study Group on Antibiotic Policies (ESGAP), the ESCMID Study Group for Antimicrobial Resistance Surveillance (ESGARS), the ESCMID Study Group on Nosocomial Infections (ESGNI) and the ESCMID Study Group on Epidemiological Markers (ESGEM). The goals of the ARPAC project were to: (1) lay the foundations for a better understanding of the emergence and epidemiology of antibiotic resistance in human pathogens; and (2) evaluate and harmonise strategies for the prevention and control of antibiotic-resistant pathogens in European hospitals.

The ARPAC Consensus Conference was the culmination of this Concerted Action project. The conference was held in Amsterdam, The Netherlands, on 22–24 November 2004, and was co-hosted by the European Commission, ESCMID and the Dutch Working Party on Antibiotic Policy (SWAB). The goals of the Consensus Conference were:

- to deliver a plenary session giving all delegates an overview of the key ARPAC findings;
- to allow delegates to explore further the data gathered in their specific area of expertise and interest within workshops;
- to allow extensive discussion of the ARPAC findings in the context of the worldwide status quo;
- to deliver from each workshop a set of high-priority strategic goals likely to be broadly feasible and to have a significant impact on antibiotic resistance.

Workshop 1 was entitled 'Surveillance of antimicrobial resistance' and aimed to review current methods of surveillance, the choice of resistant Alert organisms and resistance prevalence. The stated topics covered in the workshop were:

1. Antibiotic threats among ARPAC Alert organisms.
2. Critical appraisal of antimicrobial surveillance studies.
3. Towards a consensus for standards for the surveillance of antimicrobial resistance.
4. Creation of a repository of information about resistance in Europe.
5. Future of antimicrobial resistance surveillance in Europe.

Workshop 2 was entitled 'Antibiotic policies in European hospitals' and aimed to address optimal antibiotic stewardship strategies. The stated topics covered in the workshop were:

1. The role of antibiotic control measures.
2. Antibiotic guidelines and implementation.
3. Education and audit.
4. The role of the laboratory.
5. The role of the pharmacy.

Workshop 3 was entitled 'Antibiotic prescribing and consumption in European hospitals' and aimed to explore the prospects for harmonisation of treatment guidelines and how/why antibiotic consumption should be measured. The stated topics covered in the workshop were:

1. Harmonisation of antibiotic prescribing.
2. Measurement of antibiotic consumption.
3. How does consumption relate to resistance?

Workshop 4 was entitled 'Infection control policies for containment of antimicrobial resistance, including the role of molecular typing' and aimed to address optimal infection control policies, outbreak investigations and possibilities for their harmonisation in European hospitals. The stated topics covered in the workshop were:

1. The organisation of infection control programmes in healthcare facilities.
2. Infection control guidelines development, implementation, audit and benchmarking.
3. The role of surveillance of Alert organisms.
4. The role of targeted control of Alert organisms.
5. The role of microbial typing.
6. The current impact of microbial typing.
7. Construction and operation of typing databases and the ARPAC demonstration databases.

The task of each workshop was to deliver a set of Consensus Recommendations, which would be high-priority strategic goals likely to be broadly feasible and to have a significant impact on antibiotic resistance. The guidelines and strategies were constructed in order that they could be incorporated into local quality improvement efforts and subjected to intervention trials. The Consensus Recommendations were categorised as either 'high-priority recommendations', which are minimum requirements for the control of antibiotic resistance, or as 'desirable recommendations', which were perceived to be necessary to control antibiotic resistance in the long-term, but which would not be achievable by all hospitals in Europe in the short-term because of limitations such as lack of resources.

Each of the workshops also categorised the recommendations into four groups:

1. Recommendations for individual hospitals in Europe.
2. Recommendations for national health authorities.
3. Recommendations for European health authorities.
4. Recommendations for future research.

The detailed scientific results of the ARPAC project will be published elsewhere. The purpose of this report is to present the Consensus Recommendations formulated by the participants of the four ARPAC workshops, which were presented on the final morning of the Consensus Conference.

The Recommendations are presented by the four main target groups as detailed above. Within these four headings, they are further split by conference workshop, workshop question, and finally by 'high-priority' vs. 'desirable' recommendations.

RECOMMENDATIONS FOR HOSPITALS

Workshop 1: Surveillance of antimicrobial resistance

The ARPAC project selected antibiotic-resistant Alert organisms of clinical and infection control significance in the hospital environment. These organisms were MRSA, vancomycin-resistant enterococci, *Klebsiella pneumoniae* resistant to third-generation cephalosporins, *Escherichia coli* resistant to quinolones, *Acinetobacter baumannii* resistant to carbapenems, and *Pseudomonas aeruginosa* resistant to carbapenems, quinolones, aminoglycosides, ceftazidime or cefepime. Data on the prevalence of *Clostridium difficile* were also collated.

Greater emphasis is being placed upon the ability of antibiotic susceptibility testing (AST) to generate resistance surveillance and antibiotic resistance data across different laboratories, countries, etc. This necessitates a reassessment of methods in common use. Data were collated for 2001 from 192 acute-care hospitals (73% of ARPAC participants) on AST methods, interpretative criteria, participation in quality assurance programmes, and the detection of specific resistance phenotypes. Of the 192 responding hospitals, 170 used a disk-diffusion method routinely for AST in 2001; the most commonly reported method involved the use of disks manufactured by Oxoid. There were significant variations in the use of disk-diffusion according to geographical region. MICs were determined routinely in 135 (70%) hospitals, of which 82% used the Etest method. In total, 173 (90%) hospitals reported using breakpoints to interpret AST results; Clinical Laboratory Standards Institute (CLSI; previously NCCLS) guidelines were used most widely (84% of hospitals), although other national guidelines were also employed. Most hospitals participated in an external quality assurance programme and conducted internal quality control, although the frequency with which controls

were included varied significantly according to geographical region.

High-priority recommendations

- Local hospitals should draw up a list of local Alert organisms that are relevant to the local situation.
- AST methods to detect new and emerging resistant phenotypes should be standardised; these methods should be used by other hospitals with which data will be compared.
- Each hospital should formalise its antibiotic resistance surveillance methods.
- It is essential that hospitals should participate in quality assurance schemes.
- Agreed Alert organisms should be referred to national reference laboratories as appropriate.
- Outbreak strains should be investigated for epidemiological purposes.
- Isolates with an unusual resistance phenotype should be routinely stored and investigated, either locally or by an expert in another laboratory.

Workshop 2: Antibiotic policies in European hospitals

The ARPAC project found significant associations between the presence of several antibiotic control measures and reduced antibiotic use, including the presence of an antibiotic formulary, a multidisciplinary drugs and therapeutics committee (DTC), and an active education programme on antibiotic use and resistance. Whilst the absolute reduction in antibiotic consumption might be perceived as small, this is in line with most of the evidence from the published literature, which confirms that it is extremely difficult (if not impossible) to achieve, and certainly to maintain, significant changes in the volume of prescribing [3]. The effects of interventions often erode over time, perhaps because of the high mobility of hospital doctors, and therefore require continual programme reinforcement in the case of restrictive measures, and repetition in the case of educational programmes. Within the hospitals that participated in the ARPAC project, perhaps the greatest shortcoming was an almost complete absence of audit activities. Clearly, this must change if the quality of prescribing is to be ascertained and improved. All the published evidence suggests that there is much scope for improvement in this area.

Effectiveness of antibiotic control measures

High-priority recommendations

- All hospitals should have an antibiotic stewardship programme with strategic goals, and a multidisciplinary DTC with expertise and authority regarding antimicrobial agents.
- All hospitals should have a written Antibiotic Formulary, which should be easily accessible to all prescribers (e.g., paper copy, intranet) and updated annually where feasible.

Desirable recommendations

- Multidisciplinary antibiotic committees, policies, restricted lists and computerised prescribing should be introduced where possible, followed by an assessment of their impact according to the Cochrane Effective Practice and Organization of Care Group (EPOC) guidelines (<http://www.epoc.uottawa.ca>).
- An Antibiotic Co-ordinator should be appointed to collect and feed back data, perform audits of compliance with guidelines, and inform the Antibiotic Committee regarding the quality of prescribing.

Successful guidelines

High-priority recommendations

- The DTC should maintain responsibility for antimicrobial policy management in response to national guidelines, local requirements and susceptibility data.
- All clinical practitioners should accept responsibility for following good antimicrobial prescribing and policy practice.
- The DTC should take responsibility for prudent antimicrobial prescribing by developing and implementing guidelines.

Laboratory recommendations

High-priority recommendations

- Annual antimicrobial susceptibility data should be analysed (with duplicates removed) and fed back to inform prescribers, policies and formularies in different areas of the hospital.
- Interpretative reporting should be employed to anticipate difficult-to-detect resistance mechanisms and treatment failures.

Desirable recommendations

- First-line agents should be listed first in reports of susceptibility test results.
- Awareness of cost-effectiveness among clinicians should be encouraged.

- There should be a limit to the number of agents reported (a figure of six is suggested).

Education and audit

High-priority recommendations

- Educational initiatives should be continuous and involve multimedia.
- Audit should be initiated and developed where there is poor performance, as revealed by antimicrobial resistance surveillance and antimicrobial usage data.

Workshop 3: Antibiotic prescribing and consumption in European hospitals

One of the major achievements of the ARPAC project was to enable many hospitals to calculate their antibiotic consumption for the first time. This not only allows benchmarking with other hospitals with a similar case-mix, but also allows a clearer understanding at a local level of what drives current resistance problems and, importantly, what might be done to control them. Whilst there are many technical issues to be solved concerning the best ways to study relationships between antibiotic consumption and resistance, and the best ways to benchmark, enough is known to allow ARPAC to make some basic recommendations which, it is believed, are achievable for most hospitals, particularly if they have computerised pharmacy stock orders. Most of this work will no doubt be carried out in the future by pharmacists, as it is clear from ARPAC data that there is huge potential in Europe for an increased role for pharmacists, not only in measuring and benchmarking consumption, but also in many other aspects of antibiotic stewardship, including being a key member of multidisciplinary DTCs and teams that visit hospital wards to guide and audit antibiotic therapy.

Antibiotic consumption

High-priority recommendations

- Whole-hospital, antimicrobial usage data, categorised by class, should be recorded quarterly (yearly, if based on pharmacy purchases) using the WHO-defined unit of defined daily dose (DDD)/100 patient-days and the Anatomical Therapeutic Chemical (ATC) classification system.

- Reasons for high/low levels and changes in consumption of antimicrobial agents should be investigated and documented.
- Pharmacy computer databases to store and retrieve antibiotic usage data should be implemented.

Desirable recommendations

- Participation in multicentre/multinational benchmarking surveillance networks/surveys should be encouraged.
- Antimicrobial usage data should be reviewed according to individual wards/units, diagnosis and the proportion of patients treated with an antimicrobial agent.
- Data should be recorded and reviewed monthly.
- In addition to DDD/100 patient-days, locally defined prescribed daily doses (PDD)/100 patient-days can be reported.
- Antimicrobial usage data should be combined with drug utilisation prevalence studies at the patient level (duration of therapy, treatment failure).
- Antimicrobial usage data should be fed back to prescribers.

Relationship between consumption and resistance

High-priority recommendations

- Choices of antibiotic–bacteria combinations should be based on local epidemiology.

Desirable recommendations

- Ongoing surveillance and analysis of antimicrobial resistance and consumption should be carried out, if possible using computerised prescribing data and at the individual patient level.

Pharmacy and antibiotic use

High-priority recommendations

- There should be provision of clinical pharmacy services to support antibiotic prescribing.
- Pharmacists should be part of the multidisciplinary DTC.
- Pharmacy departments should be involved in measuring and analysing antibiotic consumption as part of a multidisciplinary team.

Desirable recommendations

- Antibiotic pharmacists should be appointed with a hospital-wide brief to: review antibiotic orders, e.g., selected drugs, duration of therapy; design and promote clinical practice guidelines;

implement and run antibiotic ‘switch’ programmes;
document effectiveness of interventions.

Harmonisation of antibiotic prescribing

High-priority recommendations

- Guidelines must be evidence-based, taking account of local epidemiology.
- Glycopeptides should only be used for prophylaxis in high-risk surgery if there are clinical problems with MRSA infections.
- Key antibiotics should be reserved, e.g., carbapenems, glycopeptides, fourth-generation cephalosporins, oxazolidinones.

Desirable recommendations

- Participation in networks to share and increase expertise on antibiotic management programmes should be encouraged.
- Antibiotics used for prophylaxis should not be used for therapy.

Workshop 4: Infection control policies for containment of antimicrobial resistance, including the role of molecular typing

The ARPAC project identified major gaps in staff resources available to European hospitals for their infection control programmes, with significant regional differences. For instance, a majority of ARPAC hospitals did not meet recommendations based on the SENIC study [4] that an infection control programme should be operated with at least one infection control nurse per 250 acute-care beds and one infection control physician per 1000 beds. The ARPAC project also revealed that, while most hospitals had an ongoing programme to promote the use of standard infection control precautions, only about half conducted regular audit of healthcare compliance with these precautions. In addition, only two-thirds of the hospitals surveyed recommended the use of alcohol-based solutions for hand hygiene, although this method has been shown in the literature to be most efficacious for hand decontamination. Moreover, the ARPAC project found a significant association between the use of alcohol-based hand disinfection and lower rates of MRSA infection. Other significant predictors of lower resistance rates were a policy for placing MRSA-colonised patients in single rooms, and having no practical problem in implementing such a policy. The ARPAC project found that most

hospitals have developed a laboratory system for notification of patients colonised by selected Alert antibiotic-resistant organisms to the infection control team, most frequently, but not exclusively, targeted at MRSA. It was apparent, however, that most of these hospitals did not fully implement contact isolation and barrier precautions (single room placement and protection with gloves and gown for patient care procedures) for patients colonised by Alert organisms, nor did they perform active surveillance cultures for early detection of patient colonisation with MRSA.

At the laboratory level, rapid molecular typing techniques are becoming essential tools for monitoring the geographical spread of particular virulent, epidemic or antibiotic-resistant pathogens. Microbial typing can be performed for different reasons and at different levels, including the local hospital level, the regional level and the (supra)national level. Probably the most frequent reason at the local level is to rapidly identify cases of cross-infection caused by antibiotic-resistant strains. Thus, within a hospital, typing allows recognition and confirmation of outbreaks of infection caused by particular antibiotic-resistant bacteria (i.e., cross-infection between patients), leading to action by infection control teams. Many different methods are available for typing microorganisms, and the ARPAC project gathered data on the typing methods being used by participating hospital laboratories around Europe for typing Alert organisms. It became apparent that a wide range of typing methods was currently in use, but that there was very little uniformity or standardisation of the methods being used. In the past decade, several networks, including ARPAC, have attempted to standardise methodology and establish typing databases to monitor the spread of important pathogens. These pilot databases have demonstrated the feasibility of the database approach at a European level, but much more work, reflected in the following recommendations, is required to make the database approach a reality.

General infection control policies

High-priority recommendations

- Hospital management should ensure that its infection control programme is implemented by a sufficient staff resource, meeting at least the levels recommended by the SENIC study

(one infection control physician per hospital, and one infection control nurse per 250 acute-care beds).

- Hospital infection control programmes should ensure implementation of standard precautions, including the use of alcohol-based solutions for hand hygiene, as well as audit of the compliance of healthcare workers with these precautions.
- Hospital management should provide sufficient isolation facilities (single patient rooms) and staff reinforcement to cope with the workload incurred by placing patients in contact isolation.
- Control of healthcare-associated infection (HAI) should be part of the curriculum of medical and nursing undergraduate students.

Desirable recommendations

- Infection control personnel should use feedback of HAI and antimicrobial resistance surveillance data, together with the results of compliance studies, in educational sessions for healthcare workers.
- Control of HAI should be part of all induction training programmes for newly appointed healthcare workers, including medical doctors.
- Hospital infection control teams should consider implementing a link nurse system, link medical doctors, or link high-risk unit teams.
- There should be better retrieval of demographic data for surveillance of HAIs.

Surveillance and control policies for antibiotic-resistant Alert organisms

High-priority recommendations

- Hospitals should have a system to identify patients at high risk for carriage of Alert organisms.
- Rapid microbiological methods should be validated and implemented for screening and detection of Alert organism carriers among high-risk patients admitted to acute-care hospitals, particularly in intensive care units.
- Local surveillance, outbreak detection and ad-hoc control measures should be developed and evaluated for containment of emerging or importable Alert organisms.

Desirable recommendations

- The transmission capacity and attributable morbidity, cost and mortality of infection with specific Alert organisms should be estimated within the local and regional patient populations.

- Compliance of healthcare workers with internal guidelines for Alert organism surveillance and control measures should be audited regularly, with performance scores being fed back to healthcare workers.

Containment of MRSA

High-priority recommendations

- Every institution should establish an MRSA surveillance, alert and control programme that is adjusted to local and regional circumstances. The surveillance system should include the automated flagging of colonised patients upon readmission.
- Active MRSA surveillance cultures should be performed so that the MRSA reservoir among high-risk patients can be ascertained faster and more exhaustively.
- Screening of healthcare workers for MRSA carriage is indicated if associated with an MRSA outbreak, at least in settings where the incidence has not reached an endemic level.
- MRSA-colonised patients should be placed in single rooms or in an isolation ward; healthcare workers should wear gowns and gloves, at least before taking care of patients.
- Attempts should be made to decolonise patients who are MRSA carriers, in the absence of colonised chronic lesions or colonised indwelling devices such as endotracheal tubes.

Desirable recommendations

- Mortality and morbidity associated with MRSA infections should be monitored.

Establishment of electronic typing databases for key Alert organisms

High-priority recommendations

- Hospitals should have a policy to prospectively collect Alert organisms for typing.
- Direct access to rapid molecular typing facilities, preferably locally based, should be provided.

Desirable recommendations

- Individual hospitals should have electronic access to centralised typing databases for key Alert organisms.
- Hospital information technology systems should enable typing information to be recorded in patients' records.

- Individual hospitals should have access to robust typing methods to establish a local database.

RECOMMENDATIONS FOR NATIONAL HEALTH AUTHORITIES

Workshop 1: Surveillance of antimicrobial resistance

National bodies should be responsible for monitoring emerging resistance problems, which, although not widespread in local situations, may pose future threats. National surveillance of Alert organisms should be altered accordingly. It is at national level that decisions should be taken regarding laboratory methodology to ensure that local laboratories are producing comparable and standardised data. Inevitably, standardisation of methods and surveillance systems will not come without financial costs and a requirement for expert knowledge and advice—all of which should be provided at national level and made available to individual hospitals.

High-priority recommendations

- A list of nationally agreed and relevant Alert organisms should be defined.
- Alert organisms should be typed using molecular techniques.
- A network of reference laboratories should be established and consolidated.
- National bodies should facilitate standardisation of all methodologies in local laboratories.
- National bodies should establish and consolidate quality assurance programmes for use in local laboratories.
- National sampling programmes should be coordinated nationally.
- National surveillance and control of communicable disease programmes should be established, sustained and networked across countries to allow comparability.

Workshop 2: Antibiotic policies in European hospitals

This is clearly an area that would benefit from a degree of national coordination and input of resource. While guidelines should always be tailored to local situations, particularly in the context of local resistance issues, the resource for the assembly of the evidence base is not within

the capabilities of individual hospitals, and the same may be true for expert opinion in the absence of a robust evidence base. Whilst the ARPAC project did not uncover evidence on which to base guidelines influencing antibiotic consumption or resistance, they are clearly widely implemented. Formularies and educational programmes will be moulded by input at a national level. It is also likely that a national steer on educational issues is likely to be beneficial, at the level of both undergraduates and prescribers. Finally, a requirement for audit and demonstration of quality antibiotic prescribing (clearly not performed adequately at the moment) could become a hospital accreditation issue.

Effectiveness of antibiotic control measures

High-priority recommendations

- There should be national programmes to coordinate antibiotic stewardship, policy and practice. These should be integrated with programmes for monitoring antibiotic resistance and consumption.

Desirable recommendations

- National programmes should coordinate multicentre evaluations of control measures according to EPOC guidelines.

Successful guidelines

High-priority recommendations

- Strict methodology in accordance with 'The Consensus Council Inc.' (<http://www.agree.org>) should be used.

Desirable recommendations

- Interactions between national surveillance of antimicrobial consumption and resistance data should be reviewed annually.
- Local policies should be encouraged, e.g., performance indicators.

Laboratory recommendations

High-priority recommendations

- There should be a national accreditation system for laboratories.

Education and audit

High-priority recommendations

- National guidelines should be endorsed.
- Major national educational programmes should be coordinated.
- Audits on antibiotic prescribing should be promoted, particularly compliance with guidelines.

Workshop 3: Antibiotic prescribing and consumption in European hospitals

A national approach to benchmarking of hospital antibiotic consumption is likely to be helpful in gaining the extra resources necessary. Similarly, a national programme of education of pharmacists to create more clinical specialists with a particular expertise in antibiotic prescribing is essential. Such a programme has recently been initiated at the Hammersmith Hospital in London; although a distance-learning package is planned, it is essential that other countries also take similar initiatives.

Whilst harmonisation of prescribing of particular antimicrobial agents may not be desirable on a wide scale, there are issues, such as non-availability of individual agents, that can best be addressed at a national level, and this is certainly the case when assessing the need to restrict key antibiotics for fear of undue toxicity or resistance.

National programmes to coordinate surveillance of resistance and consumption, such as those already operating in The Netherlands and certain Scandinavian countries, are felt to be very valuable and should be expanded. Computerised antibiotic prescribing and analysis of emergence of resistance in individual patients are desirable, but remain a long-term goal for most hospitals. A national steer in this area would be helpful.

Antibiotic consumption

High-priority recommendations

- Resources to retrieve, collate and analyse antibiotic usage data, including computer support, software and personnel, should be provided.
- The WHO-recommended unit of DDD/100 patient-days should be endorsed as a standard unit of measurement for antibiotic consumption.

Desirable recommendations

- Participation in international collaboration and benchmarking should be the norm.
- National surveillance systems for collation, feedback and benchmarking of data should be established.

Pharmacy and antibiotic use

High-priority recommendations

- National antibiotic guidelines for clinical pharmacy services should be provided.

Desirable recommendations

- Nationwide education/training/accreditation for antibiotic pharmacists should be promoted.

*Harmonisation of antibiotic prescribing***High-priority recommendations**

- Inappropriate use of restricted agents should be monitored and action taken.

Workshop 4: Containment of antimicrobial resistance: role of infection control policies and molecular typing

The ARPAC Project revealed major gaps in the human resources available to European hospitals to conduct effective infection control programmes, in terms of both insufficient numbers of staff and a lack of nurses and physicians specially trained for these positions. This deficit showed marked regional variations, being more pronounced in less affluent countries. It is essential that national authorities review these situations urgently and redress deficits according to minimum standards. Likewise, a majority of hospitals, particularly in less affluent countries, reported frequent practical problems with isolation policies because of a lack of nursing staff or insufficient room capacity. Again, national health authorities should act urgently to remove these serious obstacles to effective isolation, which may otherwise allow for uncontrolled spread of epidemic resistant Alert organisms, leading to adverse patient outcomes and enormous additional costs for the healthcare system. Political leadership is key in making prevention and control of HAI and antimicrobial resistance a national health priority, with objectivity in the accreditation and quality assurance programme for healthcare facilities. Surveillance-derived quality indicators may be useful if designed and analysed carefully to stimulate and monitor progress of prevention programmes at an institutional level.

At the national level, typing allows recognition of the epidemic spread between hospitals of particular antibiotic-resistant bacteria, possibly requiring action by national health authorities. ARPAC identified a need for national health authorities to establish a network of typing expertise and availability, and to coordinate the common use of standardised operating proce-

dures to enable data to be shared among laboratories. Although typing is clearly of benefit in recognising outbreaks of cross-infection at the local hospital level, little is known about the overall impact of typing on controlling the spread of hospital-acquired infection in different types and sizes of hospitals. Such a programme should be coordinated and funded adequately at the national level, with national reference facilities being established for key antibiotic-resistant Alert organisms.

*General infection control policies***High-priority recommendations**

- National authorities should provide support and require acute-care hospitals to implement infection control staff levels that meet at least those recommended by the SENIC study (one infection control physician per hospital and one infection control nurse per 250 acute-care beds) [4].
- Infection control staff (physicians and nurses) should receive specialised training and certification of competence according to national standards.
- Provision of sufficient isolation room capacity in acute-care hospitals should be ensured.
- National infection control standards for the complete healthcare system should be developed and implemented; these should be considered standards of care.
- Development of educational material, e.g., for hand hygiene (alcohol-based hand rubs), should be supported and adapted for different professional groups.

Desirable recommendations

- A national nosocomial infection surveillance system that meets European criteria and case definitions should be developed and/or sustained.

*Surveillance and control policies for antibiotic-resistant Alert organisms***High-priority recommendations**

- Standardised Alert organism definitions, detection and reporting methods should be developed for use by infection control teams for local surveillance, and may also be applied to multicentre surveillance networks. Appropriate data protection guidelines should be enforced to prevent misuse of data.

- A national surveillance system should be established to monitor the institutional incidence of MRSA acquisition/infection and allow hospital benchmarking of MRSA rates.
- Financial and regulatory support should be provided to allow local deployment of adequate human and technical resources for effective Alert organism surveillance and control efforts (nursing staff, laboratory facilities, isolation room capacity).
- A national surveillance programme for Alert organisms in acute-care hospitals should be established and linked to an early outbreak detection and response system.

Desirable recommendations

- Regional care networks should be established to help hospitals and long-term care facilities conduct harmonised surveillance and management of MRSA and other epidemic Alert organisms.
- National guidelines and standards for control of MRSA (and other relevant Alert organisms) in healthcare facilities should be developed, updated and implemented.
- Prevention of community-based transmission of MRSA should be tested and implemented through regional infection control networks.

Establishment of electronic typing databases for key Alert organisms

High-priority recommendations

- National health authorities should establish an inventory of typing expertise and availability.
- Molecular typing methods should be standardised at the national level and standard operating procedures should be made available to local laboratories.
- A national network of laboratories capable of undertaking molecular typing at the local level should be established.
- There should be support and provision for training of laboratory staff in typing methods and the use of typing databases.
- External quality control/proficiency programmes should be established with panels of well-characterised strains.
- Funding should be provided for the necessary staff and equipment/consumables at the local level.
- National reference laboratory facilities should be established for key Alert organisms.

RECOMMENDATIONS FOR EUROPEAN HEALTH AUTHORITIES

Workshop 1: Surveillance of antimicrobial resistance

The ARPAC study identified a wide variation in AST methods among European hospitals. Of key significance, there was considerable variation in the breakpoints used to interpret AST results. The lack of harmonised breakpoints among methods in different countries, or even within the same country, often prevents meaningful comparison of resistance rates and monitoring of the development of resistance in international surveillance systems. The European Committee for Antimicrobial Susceptibility Testing (EUCAST) is a standing ESCMID committee, set up to standardise susceptibility testing in Europe so that comparable results and interpretations are produced. EUCAST has published documents proposing standardised methodologies and breakpoints [5–7].

High-priority recommendations

- There should be a European-wide body to coordinate and ensure the sustainability of surveillance efforts, including external quality assurance.
- Harmonisation of approaches across Europe should be encouraged.
- A list of Alert organisms (e.g., MRSA, vancomycin-resistant *S. aureus*, vancomycin-resistant enterococci, penicillin-resistant group A streptococci) should be established at a European level.
- The activities of EUCAST should be encouraged and extended.

Workshop 2: Antibiotic policies in European hospitals

One of the most intriguing ARPAC findings was the highly significant geographical variation in antibiotic formularies, coupled with the association between the existence of a formulary and lower antibiotic consumption. Whilst ARPAC project data cannot be used to attribute cause and effect, a consensus is widely held that there are regional and cultural issues regarding restrictive control measures that may best be addressed with Europe-wide input. Similarly, although perhaps in the longer term, hospitals may benefit from adherence to European guidelines or initi-

atives on other aspects of antibiotic stewardship, including education, audit and hospital accreditation programmes in antibiotic prescribing. A European centre for implementation of evidence-based guidelines would clearly be a major step forwards, as would a European core educational curriculum.

Effectiveness of antibiotic control measures

High-priority recommendations

- There should be a Europe-wide organisation to coordinate multicentre evaluations of control measures, and to oversee harmonisation of antibiotic stewardship, policy and practice.
- Such an organisation should coordinate its activities with national counterparts and Europe-wide bodies monitoring antibiotic resistance and consumption.
- Europe-wide minimum standards of antibiotic stewardship for hospitals should be established.

Successful guidelines

High-priority recommendations

- 'The Consensus Council Inc.' process for deriving the evidence base for guideline development should be utilised (<http://www.agree.org>).
- Performance indicators should be agreed.

Laboratory recommendations

High-priority recommendations

- There should be a national accreditation system for laboratories.

Education and audit

High-priority recommendations

- Educational programmes on antibiotic prescribing should be developed and exchanged.
- Multinational explorative and educational site visits to encourage mutual learning and reflection regarding antibiotic usage should be organised.
- A European standard for auditing should be formulated.

Workshop 3: Antibiotic prescribing and consumption in European hospitals

Within the hospitals that participated in the ARPAC project, there were issues regarding

benchmarking antibiotic consumption, marked differences in hospital antibiotic usage data within individual countries, and a widespread lack of clinical pharmacy input into antibiotic prescribing, all of which would benefit from a European initiative, including programmes for implementation and education. Similarly, the lack of consistency in availability of certain antibiotic classes causes problems at an individual hospital policy level. It may be possible to solve these problems at a European level. As recommended by Workshop 2, perhaps hospital or pharmacy accreditation at a European level is a goal worth working towards.

Antibiotic consumption

High-priority recommendations

- The WHO-recommended standard measurement of DDD/100 patient-days should be endorsed.
- A surveillance system for Europe-wide feedback and benchmarking of hospital antibiotic consumption should be implemented.
- Computerised tools for measuring antibiotic consumption (e.g., transfer of data, data/control checks, analysis, feedback) should be developed.
- Collaboration with multinational surveillance systems should be promoted.

Harmonisation of antibiotic prescribing

High-priority recommendations

- Proposals for a framework of common principles and quality standards for hospital diagnosis and treatment of infections should be developed.
- Use of evidence-based guidelines should be encouraged.
- Development of diagnostic tools for infections in hospitals should be encouraged.

Desirable recommendations

- Networks of hospital antibiotic management programmes should be implemented.
- Licensing of and registered indications for new antibiotics should reflect true clinical needs.

Workshop 4: Containment of antimicrobial resistance: role of infection control policies and molecular typing

Pooling of expertise at the European level would benefit the much-needed development of profes-

sional training of HAI control specialists at the national level. In addition, assessment of the public health impact of infections caused by resistant bacterial pathogens in healthcare settings at the European level would better define the costs/benefits of control programmes and the merits of different models of healthcare delivery, notably in the context of increasing patient mobility within the EU.

Similarly, pooling of typing expertise and an exchange of laboratory data at the European level should help to identify particular virulent and/or epidemic clones spreading in Europe, and will aid in the development of newer and better typing methods that exploit new proteomic and genomic approaches. A key component of such activity would be the establishment and use of validated typing databases by large European collaborative networks of laboratories. For this to occur, European health authorities should promote and fund the harmonisation of typing methods for key Alert organisms at the European level, including the provision of advanced training to facilitate the dissemination of methodology and best standards of laboratory practice.

General infection control policies

High-priority recommendations

- Concepts for a European core curriculum training programme for infection control nurses and physicians should be developed and approved by professional groups.

Surveillance and control policies for antibiotic-resistant Alert organisms

High-priority recommendations

- The public health impact of infections caused by antimicrobial-resistant bacterial pathogens should be determined. Findings on the human and financial costs should then be used to inform patient organisations, policy-makers and the media, and should be considered in perspective with other disease burdens.
- National surveillance of community-acquired and hospital-acquired MRSA infections should be harmonised, using Europe-wide standard definitions and denominators.
- The European Council should encourage national authorities to reduce the incidence of MRSA infections throughout Europe.
- International surveillance of MRSA infections should be strengthened.

- Cross-border patient transfer procedures should be harmonised, and regional cross-border care networks should be strengthened, to ensure proper exchange of health information and to limit international dissemination of Alert organisms of epidemiological significance, such as MRSA.

Establishment of electronic typing databases for key Alert organisms

High-priority recommendations

- Typing methods for key Alert organisms should be harmonised at the European level.
- Advanced training should be provided to disseminate best standards of laboratory practice.
- Data exchange methods (and their availability) should be coordinated for important clones of Alert organisms.
- New practical arrangements should be agreed to enable easier and more cost-effective international exchange of important strains of bacteria.

Desirable recommendations

- The establishment of typing databases at the European level should be supported and coordinated.

FUTURE RESEARCH

Workshop 1: Surveillance of antimicrobial resistance

The surveillance of antimicrobial resistance alone is likely to have a minimal effect on changing practices to try to reduce the problem of resistance in Europe. Robust surveillance data are crucial, however, when assessing the impact of a range of possible interventions to tackle the problem. Antimicrobial resistance rates are an obvious outcome measure to assess the effect of interventions, such as the role of antibiotic policies, antibiotic prescribing and infection control measures on reducing resistance.

High-priority recommendations

- There should be a European programme to establish how practices in clinical microbiology can be informed by epidemiology.
- The role of different denominators should be investigated.
- Any research carried out should be both qualitative and quantitative.

- The current situation regarding the prevalence of all Alert organisms across Europe should be established via representative surveys.
- European research should focus on resistance determinants and selection pressures, from bacterial populations down to genes.
- Research should also focus on the impact of antibiotic usage on normal flora, the environment and the community.
- There should be a focus on interventions to control the spread of resistance genes and resistant organisms.

Workshop 2: Antibiotic policies in European hospitals

Whilst some of the ARPAC findings corroborate previous findings, the published literature is of poor quality and much more research needs to be performed. In particular, there is a lack of good-quality studies showing an improved clinical outcome (or at least no harm to patients) or reduced resistance following interventions to decrease or improve the quality of antibiotic use. While modern techniques, such as time-series analysis, should make it possible for individual hospitals to generate their own good-quality data, there is also a need for pan-European multicentre randomised control studies to negate confounding issues and show the appropriateness of such interventions. There is a huge need for such activities at all levels, ranging from guideline implementation to education and audit, and the role of multidisciplinary teams, etc.

Effectiveness of antibiotic control measures

High-priority recommendations

- There should be a European programme to evaluate interventions for improving the quality of antibiotic use in European hospitals, reducing consumption and resistance, and improving patient outcomes.

Desirable recommendations

- There should be a European programme for development and evaluation of new antibiotics.

Successful guidelines

High-priority recommendations

- Research into compliance with guidelines should be undertaken, including behavioural aspects.
- There is a need to further mine/model the large ARPAC database.

Laboratory recommendations

High-priority recommendations

- The influence of laboratory results on patient outcomes, including cost-effectiveness and rapid methods, should be evaluated.
- The most relevant tests for advising on combination treatments should be assessed.

Education and audit

High-priority recommendations

- Independently funded studies should be performed to provide the evidence for efficacy of 'older' antibiotics.
- Successful methods for audit and education should be established.

Workshop 3: Antibiotic prescribing and consumption in European hospitals

Many 'older' antibiotics are used increasingly for the treatment of multiresistant infections because of a lack of new alternatives. Usually there is no proper evidence base, other than clinical experience, as these agents were developed and marketed before the advent of modern clinical trials. One such example is the use of agents such as the tetracyclines and co-trimoxazole for the treatment of MRSA infections. A European facility for scientific assessment of the efficacy of such treatment would be a major beneficial development. The assessment of combination therapies requires similar facilities.

Antibiotic consumption

High-priority recommendations

- A standard definition for patient-days, e.g., occupied bed-days, should be developed and tested.
- The best ways to benchmark antibiotic consumption and the effects of feedback (quantitative, qualitative) should be investigated.
- The consequences for patient outcomes of reducing hospital antibiotic usage should be investigated.

Relationship between consumption and resistance

High-priority recommendations

- The effects of changes in consumption on resistance rates (e.g., reversibility of resistance, including the influence of reduction of the use of key antibiotics on MRSA) should be studied.

Desirable recommendations

- The best ways to explore the relationship between antibiotic consumption and resistance should be established, e.g., DDD/100 patient-days, number of patients treated or duration of treatment.

Pharmacy and antibiotic use

High-priority recommendations

- The effect of antibiotic pharmacists on improving and reducing antibiotic prescribing should be investigated.

Desirable recommendations

- The most efficient pharmacy-based interventions should be established.

Harmonisation of antibiotic prescribing

High-priority recommendations

- Evidence-based stratification of patients for empirical therapy should be performed.
- The feasibility of harmonising existing national, evidence-based guidelines, e.g., on infective endocarditis, neurosurgical infections and surgical prophylaxis, to create Europe-wide policies should be studied.
- The potential dangers of harmonisation, with regard to the efficacy and selection of resistance, should be established.

Desirable recommendations

- The optimal use of combination therapies for the treatment of multiresistant microorganisms should be established.

Workshop 4: Containment of antimicrobial resistance: role of infection control policies and molecular typing

Some of the ARPAC findings corroborate previously published evidence that use of alcohol-based hand disinfection and full implementation of isolation policies for colonised patients can be effective in limiting the spread of resistant bacterial pathogens of global concern, such as MRSA. There is, however, a glaring lack of robust evidence from well-designed epidemiological studies to ascertain the burden of disease and the direct costs associated with infections caused by these pathogens in European hospitals, and to determine the effectiveness and cost-effectiveness of currently recommended or innovative control interventions.

In addition to its role in the immediate control of cross-infection, typing can also be performed to investigate diversity in the microbial population at the European level and to study the relationships between epidemiological markers, antibiotic resistance, epidemicity and pathogenicity mechanisms. Such studies would be particularly well-served by the establishment and use of validated typing databases by large European collaborative networks of laboratories, but further research on intra- and inter-laboratory reproducibility and standardisation of typing methods, including strategies for data analysis, is urgently needed.

General infection control policies

High-priority recommendations

- The burden of HAI and the effectiveness of infection control outside the acute-care setting should be assessed.
- Optimal staff levels for effective infection control should be critically assessed.

Desirable recommendations

- Epidemiological research is required to ascertain the risk factors for and transmission dynamics of community-based Alert organisms, e.g., community-acquired MRSA.

Surveillance and control policies for antibiotic-resistant Alert organisms

High-priority recommendations

- International studies should be established to measure the burden of disease (cost, morbidity, mortality, resource utilisation, hospital bed occupancy) resulting from healthcare-associated MRSA and Alert organism infections in Europe.
- Epidemiological investigations should be conducted across Europe to estimate the duration of carriage of MRSA/Alert organisms after hospital discharge, and to determine the size of the population reservoir of MRSA/Alert organisms in the extended-care sector and the community.
- Controlled intervention trials should be performed to confirm/compare the effectiveness of active control measures for MRSA/Alert organisms.
- Health economics studies should be undertaken to determine the cost-effectiveness and cost/benefit ratio of applying rapid microbiological methods for screening and detection of

MRSA/Alert organism carriage in high-risk patients admitted to healthcare settings such as intensive care units.

Desirable recommendations

- Intervention trials should be conducted to determine effective prevention methods against infection with community-acquired MRSA.

Establishment of electronic typing databases for key Alert organisms

High-priority recommendations

- Studies on intra- and inter-laboratory reproducibility and standardisation of typing methods, including bioinformatics data analysis, should be performed.
- New and better typing methods, exploiting new proteomic and genomic approaches, should be investigated and developed.
- The role and cost-effectiveness of typing in containing the increase in antibiotic resistance should be investigated.
- Research should be performed to identify particular virulent and/or epidemic clones for infection control purposes, and to find out why these particular clones are important.
- Epidemicity and virulence/pathogenicity mechanisms should be investigated in important epidemic clones.

COMMENTARY

For the first time, ARPAC has provided a pan-European picture, albeit a snapshot, of the attempts being made to control antimicrobial resistance. Of course, the ARPAC project did not attempt to answer all possible questions; indeed, it probably posed more questions than it answered. The project study design did not allow cause and effect to be attributed. Nevertheless, many fascinating associations were identified, which both confirmed previous work and pointed the way to further studies. Serious shortcomings were also documented in many aspects of European measures for the control of antimicrobial resistance. These shortcomings are likely to be underestimated by the project, as the hospitals that took part in ARPAC are likely to be among the most active in their attempts to control the problem, simply because of the self-selecting nature of a voluntary study.

The recommendations made at the Consensus Conference are, of necessity, not strictly evidence-based. They arose from a synthesis of findings from the ARPAC project and expert opinion, so ably presented at the Consensus Conference by many authorities in the field, and discussed exhaustively by the participants. After the conference, the recommendations were refined by the ARPAC project Steering Group, before their presentation in this report.

Several caveats regarding controversial issues that were discussed at the Conference are worth mentioning. Although priority is given to specific control of MRSA infections in many of the ARPAC recommendations, it was emphasised that many other emerging or regionally epidemic resistant Alert organisms may well deserve equal priority at local, national or regional levels. Therefore, focus on MRSA should be no reason for complacency about other epidemiologically relevant organisms. With regard to surveillance of Alert organisms, it was agreed that there is no easy access to 'quality indicators' for control efforts. Whereas calculation of the proportion of resistant strains in a species (e.g., % MRSA/*S. aureus* isolates) is often done for the sake of routine accessibility from laboratory data, this practice was recognised as being clearly insufficient as an indicator of effectiveness for control measures. Benchmarking of healthcare institutions based on such crude indicators is generally of limited value. Incidence data are far more relevant for this purpose, and should, ideally, be adjusted for colonisation pressure and case-mix as far as possible. Nevertheless, it should be remembered that risk-factor adjustment may divert substantial skilled resources from prevention and education efforts towards extensive data collection and analysis. A related issue is the increasing public and political demand for public reporting of Alert organism surveillance data at facility level. If required, this should be done with care, and data must be presented and interpreted in the context of local/regional epidemiology.

Those with knowledge of previous European Consensus Conferences on Antimicrobial Resistance, such as those held in Copenhagen in 1998 and in Rome in 2003 [8,9], will, inevitably, notice some repetition. However, if a recommendation is worthwhile and has not been implemented successfully, it is worth repeating. These recommendations must now be carried forward by all

stakeholders. In particular, the ESCMID Study Groups involved in the ARPAC Project are encouraged to mobilise ARPAC participants to join their activities and contribute further to the implementation of advanced professional training and sharing of best practice, harmonisation and validation of policies, as well as future research. ESCMID will support these follow-up efforts. Dissemination of these recommendations to hospital managers, and advocacy of their urgent implementation, are of primary importance to unlock solutions to logistic and personnel deficits by allocation of appropriate resources. It is hoped that national health authorities, as well as EU research and public health programmes, will cooperate to provide financial, regulatory and logistic support for implementation and refinement of the strategies outlined in these recommendations.

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SUPPLEMENTARY MATERIAL

The following supplementary material is available for this article online:

Appendix S1. ARPAC Consensus Conference Participants.

This material is available as part of the online article from <http://www.blackwell-synergy.com>

REFERENCES

1. Skinner D, Keefer CS. Significance of bacteraemia caused by *Staphylococcus aureus*. *Arch Intern Med* 1941; **68**: 851–875.
2. Anonymous. Medical Department of the US Army in the World War. Surgeon General Office, Washington DC. *Communic Other Dis* 1928; **9**: 203.
3. Brown EM. Guidelines for antibiotic usage in hospitals. *J Antimicrob Chemother* 2002; **49**: 587–592.
4. Haley RW, Culver DH, White JW *et al*. The efficacy of infection surveillance and control programs in preventing nosocomial infections in US hospitals. *Am J Epidemiol* 1985; **121**: 182–205.
5. European Committee for Antimicrobial Susceptibility Testing. EUCAST Definitive Document E.DEF 2.1, August 2000: Determination of antimicrobial susceptibility test breakpoints. *Clin Microbiol Infect* 2002; **8**: 570–572.
6. European Committee for Antimicrobial Susceptibility Testing. Determination of minimum inhibitory concentrations (MICs) of antibacterial agents by agar dilution. *Clin Microbiol Infect* 2000; **6**: 509–515.
7. European Committee for Antimicrobial Susceptibility Testing. Terminology relating to methods for the determination of susceptibility of bacteria to antimicrobial agents. *Clin Microbiol Infect* 2000; **6**: 503–508.
8. Anonymous. *Report from the Invitational EU Conference on the Microbial Threat*, Copenhagen, Denmark, 1998. Brussels: European Commission, 1998.
9. Cornaglia G, Lonroth A, Struelens M, Participants of the Conference. Report of the European Conference on the Role of Research in Combating Antibiotic Resistance, 2003. *Clin Microbiol Infect* 2004; **10**: 473–497.