White Paper: Bridging the gap between human and animal surveillance data, antibiotic policy and stewardship in the hospital sector—practical guidance from the JPIAMR ARCH and COMBACTE-MAGNET EPI-Net networks

Maria Diletta Pezzani1†, Elena Carrara1†, Marcella Sibani1*, Elisabeth Presterl2,3,4, Petra Gastmeier5,6, Hanna Renk7, Souha S. Kanj8, Thirumalaisamy P. Velavan9,10,11, Le Huu Song10,12, Leonard Leibovici13, Didem Torumkuney14, Tomislav Kostyanov15, Marc Mendelson16‡ and Evelina Tacconelli1,17,18‡ on behalf of the ARCH working group§

1Infectious Diseases Section, Department of Diagnostics and Public Health, University of Verona, Verona, Italy; 2European Committee on Infection Control, Basel, Switzerland; 3ESCMID Study group for nosocomial infections, Basel, Switzerland; 4Department of Infection Control and Hospital Epidemiology, Medical University of Vienna, Vienna, Austria; 5German Centre for Infection Research Association (DZIF), Braunschweig, Germany; 6Institute for Hygiene and Environmental Medicine, Charité - Universitätsmedizin Berlin, Germany, corporate member of Freie Universität Berlin, Humboldt-Universität zu Berlin, and Berlin Institute of Health, Berlin, Germany; 7University Children’s Hospital Tübingen, Department of Paediatric Cardiology, Pulmology and Intensive Care Medicine, Tübingen, Germany; 8Division of Infectious Diseases, Department of Internal Medicine, and Infection Control and Prevention Program, and Antimicrobial Stewardship Program, American University of Beirut Medical Center, Beirut, Lebanon; 9Institute of Tropical Medicine, Universität zu Köln, Köln, Germany; 10Vietnamese German Center for Medical Research, 108 Military Central Hospital, Hanoi, Vietnam; 11Division of Infectious Diseases and HIV Medicine, Department of Medicine, University of Cape Town, Cape Town, South Africa; 12Infectious Diseases, Department of Internal Medicine I, Tübingen University Hospital, Tübingen, Germany; 13Division of Infectious Diseases and HIV Medicine, Department of Medicine, University of Cape Town, Cape Town, South Africa; 14International Federation of Pharmaceuticals and Manufacturers & Associations (IFPMA), Geneva, Switzerland; 15Department of Medical Microbiology, Vaccine & Infectious Disease Institute, University of Antwerp, Antwerp, Belgium; 16Division of Infectious Diseases and HIV Medicine, Department of Medicine, University of Cape Town, Cape Town, South Africa; 17Infectious Diseases, Department of Internal Medicine I, Tübingen University Hospital, Tübingen, Germany; 18German Centre for Infection Research (DZIF), Clinical Research Unit for Healthcare Associated Infections, Tübingen, Germany

*Corresponding author. E-mail: marcella.sibani@univr.it
†Equally contributing first authors.
‡Equally contributing last authors.
§Members are listed in the Acknowledgements section.

Background: Antimicrobial surveillance and antimicrobial stewardship (AMS) are essential pillars in the fight against antimicrobial resistance (AMR), but practical guidance on how surveillance data should be linked to AMS activities is lacking. This issue is particularly complex in the hospital setting due to structural heterogeneity of hospital facilities and services. The JPIAMR ARCH and COMBACTE-MAGNET EPI-Net networks have joined efforts to formulate a set of target actions for linking surveillance data with AMS activities.

Methods: A scoping review of the literature was carried out addressing research questions on three areas: (i) AMS leadership and accountability; (ii) antimicrobial usage and AMS; (iii) AMR and AMS. Consensus on the target actions was reached through a RAND-modified Delphi process involving over 40 experts in different fields from 18 countries.

Results: Evidence was retrieved from 51 documents. Initially 38 targets were proposed, differentiated as essential or desirable according to clinical relevance, feasibility and applicability to settings and resources. In the first consultation round, preliminary agreement was reached for 32 targets. Following a second consultation, 27 targets were approved, 11 were deleted and 4 were suggested for rephrasing, leading to a final approved list of 34 target actions in the form of a practical checklist.
Conclusions: This White Paper provides a pragmatic and flexible tool to guide the development of calibrated hospital-surveillance-based AMS interventions. The strength of this tool is that it is a comprehensive perspective that takes into account the hospital patient case-mix and the related epidemiology, which ultimately drives antimicrobial usage, and the feasibility in low-resource settings.

Introduction

Recommendations from major international public health institutions unanimously consider surveillance and antimicrobial stewardship (AMS) as fundamental pillars in the fight against antimicrobial resistance. However, the different structures of healthcare systems around the globe and the non-homogeneous availability of surveillance data and resources make these activities difficult to standardize. Therefore, guidance on practical aspects is lacking for many of these activities. Promotion regarding the safe use of antibiotics, for example, is becoming a strictly regulated issue in a growing number of countries with mandatory implementation of AMS programmes within the ‘quality and safety improvement’ framework. However, national recommendations in high-resource settings have difficulties in precisely indicating which types of professional figures and the amount of time necessary to carry out these activities.

Similarly, many practical guidelines for the implementation of stewardship policies in acute care hospitals recommend tailoring AMS interventions to local epidemiology and needs, but rarely provide details on how surveillance data should intertwine with stewardship activities. Only fragmentary indications are available concerning the type and frequency of data reporting, modalities for data aggregation and, more importantly, to what extent these data should inform AMS strategies, especially in terms of optimizing empirical prescribing. Additionally, even if most of the available literature focuses on acute care hospitals, the complexity of the ‘acute care’ structure means that the few available recommendations are not always generalizable, especially when considering special settings, such as ICUs, emergency departments and paediatric and onco-haematology wards.

Another key issue that is relevant to practical implementation of AMS programmes is the importance of having appropriate measures of antimicrobial consumption. While a vast body of literature is available on the topic, more practical guidance on what should be implemented in various settings would be of use to stakeholders who want to establish AMS interventions.

The JPIAMR ARCH and COMBACTE-MAGNET EPI-Net networks have joined forces to design a framework that provides a set of actions to facilitate antibiotic policy interventions and drive the link between surveillance data on antimicrobial resistance (AMR) and consumption and implementation of AMS activities.

The ARCH and COMBACTE MAGNET EPI-Net international expert panel has produced a series of four White Papers—Bridge the Gap: Survey to Treat—which are specifically focused on four settings: hospital; outpatient; long-term care facilities (LTCFs); and veterinary. The four White Papers, developed in the form of practical checklists, summarize the epidemiological, microbiological and antimicrobial data that are essential for antibiotic prescribing and policy. Three research questions were developed that constitute the evidence base for the recommendations focused on three main areas: (i) AMS leadership and accountability; (ii) antimicrobial usage (AMU) and AMS; and (iii) AMR and AMS. The practical framework is intended to guide a process to combine surveillance reports of AMU and resistance rates with AMS policy interventions in hospital, outpatient, LTCF and veterinary settings.

The process of the elaboration of these papers was underpinned by the One Health approach and had a strong focus on the feasibility of the recommended actions and their practical applicability in heterogeneous economic settings that include low- and medium-income countries (LMICs) as well as in contexts with limited expertise in surveillance and AMS. The hospital setting is discussed in the present White Paper. The intended audience of this White Paper is health professionals, including those with limited experience with AMS interventions, operating in the hospital setting and planning to start an AMS programme at their facility. Dissemination to the intended audience will be ensured by the networks involved in the JPIAMR ARCH project as listed in Table 1. Checklist formats of the target actions for the four settings are available for download on the ARCH website. These checklists can be used by health professionals and policymakers to establish and/or monitor stewardship activities.

Methods

Using a One Health approach, the process was underpinned by the development of expert consensus based on evaluation of the available literature and guidance documents on AMS and surveillance. This was followed by the development of a first draft of targets and a RAND-modified Delphi process for the definitive validation of targets (protocol available at the ARCH website).

Over 40 experts from 18 countries and 30 networks in infectious diseases (IDs), clinical microbiology, AMS, veterinary medicine and public health developed the protocol, contributed to all phases of the consensus and approved the final recommendations. Tables 1 and 2, respectively, detail the networks and stakeholders involved. A conflict of interest form was signed by each participant before starting the consensus process. During development of the project, the experts were divided into four distinct working groups, each one focusing on a separate setting. Each group was led by two senior researchers with the task of evaluating the body of evidence retrieved and who participated in the process of drafting the first set of recommendations for each specific setting. Details of the process are outlined below.

1. Development of research questions

The protocol and an initial set of research questions were drafted by the entire group based on personal expertise and the results of the EPI-Net COACH systematic review of AMR surveillance. The EPI-Net COACH project was launched in 2018 and targeted modalities of AMR surveillance linked to AMS in order to provide guidance to tailor stewardship interventions.

The general set of research questions is reported in Table 3. Slight modifications of the original set of questions were made, as necessary, to adapt the review process to the four different settings.
2. Narrative review of the evidence

A comprehensive literature search was carried out by seven reviewers (M.D.P., F.M., F.A., M.S., E.C., M.C. and L.G.) with the aim of identifying the existing evidence (clinical studies, guidelines and recommendations) relative to the use of data from microbiological surveillance and antibiotic consumption to inform AMS policies. For the literature search relevant articles in English, published in the last 10 years, were screened with a step-wise approach: first guidance (from scientific societies, international and national authorities) and documents included in the repository created by the EU-JAMRAI.14 Secondly, a search using MEDLINE (National Library of Medicine, Bethesda, MD, USA) was carried out with a combination of the following terms: antimicrobial consumption, antimicrobial drug resistance and surveillance.

All potentially relevant publications were screened by a single reviewer and evaluated against protocol eligibility criteria based on title and abstract. Any uncertainties were resolved by a second reviewer after evaluation of the full-text article. The publications included were summarized qualitatively into three evidence tables where information on the year, author/organization issuing the publication and part of the text relevant to each research topic was reported.

A first draft of targets was formulated by the reviewers and leaders of each working group after evaluation of evidence extracted that addressed the initial set of research questions. Key questions for which poor-quality evidence or no evidence was retrieved were suggested as a topic for further research. Recommendations, state of the art and original approaches were evaluated by focusing on feasibility and adaptability to different economic and healthcare contexts to compile a list of ‘essential’ and ‘desirable’ targets. Targets were recognized as ‘essential’ when widely practicable if not already broadly accomplished, and ‘desirable’ in case of limited feasibility or if they had a resource-intensive nature.

3. Consensus process

Consensus on essential and desirable targets was reached by using a RAND-modified Delphi approach based on a web-based survey followed by discussion during a face-to-face meeting. In October 2019, prior to the face-to-face meeting, the expert panel received the summary of the

Table 1. Networks involved

| No. | Acronym | Network |
|-----|---------|---------|
| 1   | ANISS   | Austrian Network for Nosocomial Infection Surveillance System |
| 2   | AMCLI   | Associazione Microbiologi Clinici Italiani |
| 3   | CAESAR  | Central Asian and Eastern European Surveillance of Antimicrobial Resistance network |
| 4   | CERMEL  | Centre de Recherches Médicales de Lambaréné |
| 5   | CDDEP   | Center For Disease Dynamics, Economics & Policy |
| 6   | JPJAMR-CONNECT | inCreasing cOmunicationN, awareNEss and data sharing in a global approaCh against resisTance |
| 7   | DZIF CRU | German Centre for Infection Research (DZIF), Clinical Research Unit for healthcare associated infections |
| 8   | EUCIC   | European Committee on Infection Control |
| 9   | EARS-NET | European Antimicrobial Resistance Surveillance Network |
| 10  | EARS-Vet | European Antimicrobial Resistance Surveillance network in Veterinary medicine |
| 11  | EUCAST  | European Committee on Antimicrobial Susceptibility Testing |
| 12  | FIDSSA  | Federation of Infectious Diseases Societies of Southern Africa |
| 13  | FASTEN  | Fighting Antimicrobial Resistance with STewardship Education Network |
| 14  | GAP-ONE | Global Antimicrobial resistance Platform for ONE Burden Estimates |
| 15  | VGCARE: HANNET | Vietnamese German Center for Medical Research: Hanoi Network |
| 16  | HighMed | Heidelberg-Goettingen-Hannover Medical Informatics |
| 17  | IFPMA   | International Federation of Pharmaceutical Manufacturers and Associations |
| 18  | APLA    | Alliance for the Prudent Use of Antibiotics |
| 19  | ISID    | International Society for Infectious Diseases |
| 20  | ISAC    | International Society of Antimicrobial Chemotherapy |
| 21  | IZSve   | Istituto Zooprofilattico Sperimentale delle Venezie |
| 22  | KISS    | Krankenhaus-Infektions-Surveillance-System (German National Reference Center for Surveillance of Nosocomial Infections) |
| 23  | COMBACTE LAB-Net | Combatting Bacterial Resistance in Europe (COMBACTE), Laboratory Network |
| 24  | LOTTA NETWORK | Long-Term care facility TriAls Network |
| 25  | PENTA-ID | Paediatric European Network for the Treatment of AIDS and Infectious Diseases |
| 26  | REIPI   | Red Española de Investigación en Patología Infectiosa (Spanish Network for Research in infectious diseases) |
| 27  | SAASP   | South African Antibiotic Stewardship Programme |
| 28  | SIM     | Società Italiana di Microbiologia |
| 29  | SIMPIOS | Società Italiana Multidisciplinare per la Prevenzione delle Infezioni nelle Organizzazioni Sanitarie |
| 30  | VetEffecT | Global specialists in Circular Animal Production, veterinary and public health |
evidence and a first proposal of the targets addressing each of the pre-
selected key questions. Using a SurveyMonkey questionnaire, participants
were asked to express their agreement with the content of the targets and
the level of recommendation on a nine-point Likert scale. Consensus on sin-
gle targets was reached if the median score was higher than 8 with at least
70% of the experts scoring in the highest tertile (i.e. scores of 7, 8 or 9).

A 2 day face-to-face meeting was held at the end of October 2019 dur-
ning which the experts were presented with a summary of the evidence rela-
tive to each setting and the results of the web-based survey. The entire set
of recommendations was reviewed and discussed, and a final decision was
made on whether to keep or retain recommendations that did not meet
the predefined threshold for agreement. The content of the remaining tar-
gets could also be rephrased following the suggestions of the panel.

After the face-to-face meeting, a final list of targets was drafted and
approved by the entire expert panel. Targets on which agreement was not
reached because of unconvincing evidence were added as priority topics for
further research.

Results

A total of 51 documents for evidence appraisal were evaluated.1,4–8,10,15–57 The majority (n = 39, 76%) were from high-
income countries. An initial set of 38 targets was proposed based
on the available evidence. Twenty experts rated the targets via the
online survey. Agreement was reached for 32 targets, of which 17
were labelled for editing due to new comments provided during
the survey. The remaining six targets were kept for discussion. The
majority of the comments were related to: the participants of
the AMS team and staffing personnel; antibiotics to monitor and
definition of prescription appropriateness; time interval for reporting;
resistant pathogens to target in different hospital wards; MIC report-
ing; and report stratification criteria and report delivery.

During the face-to-face meeting (October 2019), 27 targets
were approved, 11 were deleted and 4 suggested for rephrasing.
Following another round, the whole panel then approved a final list of 34 targets. Tables 4–6, respectively, list the recommended targets for the AMS team, AMU and AMS, and AMR and AMS.

For four research questions (‘Which criteria should be used to drive selective reporting of antibiograms?’; ‘Should specific thresholds be established for driving AMS recommendations for medical and surgical prophylaxis?’; ‘Should specific thresholds be set for driving AMS recommendations for empirical therapy?’; and ‘Which criteria should be used to drive selective reporting of antibiograms?’), the summary of evidence did not allow formulation of specific targets, and thus these topics were addressed as future research areas (Table 7).

### Discussion

Based on review of the available evidence, followed by expert consensus, a list of essential and desirable actions was provided that cover the three main core components of the stewardship framework: structural organization (participants, legal framework and staffing personnel), surveillance (monitoring of both AMU and AMR to identify potential targets for interventions) and reporting. With regard to structural organization, the AMS team should be multidisciplinary and work with the full support of hospital administration. The composition of teams should depend on the size of the hospital and availability of resources. Considering that in most LMICs having an ID specialist or a clinical microbiologist to head the team is not possible, it is essential to have GPs who are properly trained in infection management and antimicrobial use or who are already sufficiently experienced to lead AMS activities.8,10,18,20,34 Where resources allow it, core members should belong to the ID/microbiology areas with the essential contribution of a senior pharmacist with a specific expertise in antimicrobials; additional members can include an infection control practitioner, nurse, member of the IT department and/or a programme manager and specialists from other departments for programmes aimed at covering areas of particular complexity or different prescribing patterns (i.e. ICUs, haemato-oncology wards, emergency departments and paediatrics).

Within the AMS committee, the hospital Chief Executive Officer (CEO) or a member of the executive and the leader of the AMS programme team should work together with several other professionals to promote AMS interventions and link them with surveillance and infection prevention and control activities. Feedback on these activities should always be presented and discussed among hospital leadership. Planning dedicated time for AMS activities is essential. Because many determinants influence the need for human resources (i.e. the institutional structure and size, setting where the intervention is carried out and stages of the intervention itself), it is difficult to standardize the total amount of full-time equivalents (FTEs) per number of hospital beds. FTEs should be divided among the essential core elements of the team and allocated according to national requirements.10,15,16,19,49

Only a limited number of guidance documents have clearly stated which antibiotics should be routinely monitored. It is essential to monitor high-volume or top-ranking (i.e. most used) agents to capture significant variations and shifts in use and to relate data to local antimicrobial resistance trends. When possible, total consumption for antibiotics for systemic use (ATC J01 class) should be reported and further stratified by antibiotic classes (J01 subgroup) or individual agents.15,21,22,40,48 Data stratification according to the new AWARE index, introduced by the WHO in the Essential Medicines List,37 is an alternative to promote benchmarking.45,53

### Table 4. Leadership commitment, accountability and antimicrobial stewardship team

| Participants in the antimicrobial stewardship team |
|-----------------------------------------------------|
| 1.1. Essential                                      |
| All hospitals should establish a multidisciplinary  |
| antimicrobial stewardship team. The core members    |
| should always include an antibiotic prescriber and  |
| a pharmacist trained in infection management,       |
| antimicrobial usage and antimicrobial resistance     |
| or another professional with a similar role.        |
|                                                     |
| 1.2. Desirable                                      |
| The antimicrobial stewardship team should have core |
| members comprising an infectious disease specialist |
| and/or a clinical microbiologist, and an infection  |
| control professional trained in antimicrobial usage |
| and resistance.                                    |
|                                                     |
| 1.3. Desirable                                      |
| Include additional figures in the core group        |
| according to the setting, resources and type of     |
| intervention (i.e. other specialists from target     |
| wards, infection control nurses, clinical          |
| psychologists and IT experts).                     |

### Institutional support for organization and management of antimicrobial stewardship programmes: legal framework

| 1.4. Essential                                      |
| Regulate and promote antimicrobial stewardship     |
| activities at every level of the healthcare        |
| organization with well-defined roles and           |
| responsibilities and a clear governance structure. |

### Institutional support for the organization and management of antimicrobial stewardship programmes: staffing personnel

| 1.5. Essential                                      |
| Include dedicated time and specific salary         |
| support for antimicrobial stewardship activities    |
| as part of antimicrobial stewardship programmes.    |

| 1.6. Essential                                      |
| Allocate full-time equivalents according to national |
| requirements for the different settings and level of |
| intervention, where available.                      |
Table 5. Antimicrobial usage and antimicrobial stewardship

Which antibiotics should be monitored?

2.1. Essential
Monitor:
- overall consumption of antibiotics
- IV and oral antibiotics used in high volumes or according to the local ranking (5–10 most-used agents)
- antimicrobials included in the Watch and Reserve categories (WHO Essential Drug List AWARE index)
- antibiotics used for treating infections caused by local clinically relevant resistant pathogens as defined by the antimicrobial stewardship team

2.2. Essential
Monitor agents or antimicrobial classes included in the antimicrobial use surveillance programme or antimicrobial stewardship plan in countries or regions that developed specific plans for antimicrobial stewardship and antibiotic use surveillance.

2.3. Essential
Monitor the antibiotics that are targets of stewardship interventions in your setting and their plausible alternatives.

2.4. Desirable
Monitor the total consumption of systemic antimicrobials (ATC J01 class), both intravenous and oral formulations, as overall aggregated data and as subclasses (J01A, J01B, J01D, J01E, J01F, J01G, J01M, J01X) or individual agents.

2.5. Desirable
Monitor all antibiotics used in the hospital.

2.6. Desirable
Monitor antibiotics used for medical and surgical prophylaxis.

2.7. Desirable
Monitor systemic antifungal agents (agents included in the ATC J02 group) if the antimicrobial stewardship intervention is targeting institutions/wards with high rates of invasive fungal infections (i.e. haematology, transplant centre, ward with high consumption of broad-spectrum antibiotics).

Which metrics should be employed?

2.8. Essential
In high-resource settings, monitor DDD and/or DOT in the adult population and DOT in the paediatric population by defined denominators. Define denominators and source of data in the report.

2.9. Essential
When DDD/DOT monitoring is not feasible, perform at least an annual point prevalence survey, providing data on prevalence of antimicrobial use in each hospital ward, along with main indications for prescription and eventually appropriateness evaluation, for regular surveillance and for baseline assessment informing ASP design and implementation.

2.10. Desirable
Stratify antimicrobial usage data according to WHO AWaRe index categories to evaluate usage shift and reduction of usage of reserve and watch antibiotics.

2.11. Desirable
Supplement antimicrobial usage data with assessments of appropriateness of therapy (e.g. documentation of antimicrobial indication, compliance with local formulary and guidelines, duration and timing of surgical prophylaxis).

Report delivery

2.12. Essential
Deliver performance reports to prescribers, nurses, hospital executives/medical leadership and services cooperating with the antimicrobial stewardship team (microbiology, Infection Prevention and Control team, drugs therapeutic committee and other relevant staff).

2.13. Desirable
When a web platform for antimicrobial usage reporting is in place, set up a section dedicated to the role of surveillance and stewardship for the general public.

Which time interval for reporting?

2.14. Essential
Provide antimicrobial consumption data on a regular basis, at least annually, depending on the size of the institution and quantity of prescribed antibiotics.

2.15. Desirable
Where resources allow, provide antimicrobial usage reporting more frequently than yearly (e.g. quarterly/twice yearly).
Approaches that are more specific can be considered in the case of predefined outcome measures addressing specific syndromes and/or settings (i.e. anti-MRSA drugs or antibiotics that carry a high risk of precipitating *Clostridioides difficile* infection).

Adoption of DDD and/or days of therapy (DOT) divided by a standardized denominator is recommended. In the paediatric setting, due to high variability in body weight, DOT is preferred. It was considered probable that two metrics would need to be used simultaneously as per previous guidance, but this option has limited applicability in LMICs as it represents an extra workload. Types of denominators (100(0) patient days (PD)/day present (DP)/occupied bed days (OBD)), data sources (purchased/dispensed/
Table 7. Research priorities

- **Define thresholds to direct therapy decisions**
  
  **Rationale**
  There is no evidence to guide precise assessment of thresholds at which empirical therapy suggested in the hospital formulary and/or by the antimicrobial stewardship team should be changed. In addition to local resistance rates, important aspects to consider when deciding on antimicrobial therapy are the patient’s risk factors, severity of infection, access to antibiotics (which depends on the country and setting [not only hospital versus community, but also different hospital wards]). Considering that there is no solid evidence for a real threshold to adopt, the use of risk factors, severity of infection, setting and a patient-centred approach is the most reasonable strategy to direct therapy decisions and should be further explored.

- **Establish criteria for ranking antibiotics**
  
  **Rationale**
  A ‘ranking of antibiotics’ based on their ecological impact, PK/PD properties and toxicity can be a valuable tool to inform restrictive AMS intervention or to guide de-escalation. Selective reporting is a useful tool to drive the appropriate use of antimicrobial agents, but no criteria on which antibiotics should be concealed have been clearly defined. Studies on innovative strategies to identify standards for antibiotic classification and ranking for antimicrobial stewardship should be performed.

- **Develop stewardship guidelines for specific sub-settings**
  
  **Rationale**
  The available evidence in this field is not sufficient to provide recommendations by settings. Further research is needed to develop stewardship interventions adapted and validated for high-risk patients, specifically paediatrics and the immunocompromised.

administered data) and providers need to be clearly specified as they can generate relevant variations in metrics. Point prevalence surveys on antibiotic use, in both adult and paediatric inpatients, can provide useful information to detect problematic areas needing prompt AMS interventions or in the case of unavailability of AMU density data. As for the frequency of reporting, reporting of data yearly is recommended, although more frequent intervals can be considered.\(^{10,15,22}\) The panel agreed that it is essential to share AMU data with all prescribers, hospital medical leadership/executives and other disciplines involved in AMS activities.\(^{1,6,15,20,26}\)

One of the major goals of AMS is to improve prescription appropriateness. Different criteria have been used to assess appropriateness: definitions based on in vitro susceptibility (which are limited to cases with positive cultures); expert opinion based (which are subjective); compliance with local guidelines; or a combination of these criteria.\(^{59}\) The expert panel held that assessment of appropriateness of prescriptions is essential. However, objective criteria to measure it have yet to be determined in terms of individual prescriptions and facility-level consumption.

Selection of target bacteria should be based on local/national epidemiology and on the major clinical impact attributable to a specific pattern of bacterial resistance. In special settings (i.e. immunocompromised patients or ICUs), opportunistic resistant pathogens responsible for major clinical syndromes should also be monitored. Monitoring of C. difficile was considered to be an essential indicator of AMU at the patient level. An essential requirement of reporting is to allow distinction between clinical and screening/colonization samples. Therefore, blood cultures should be preferred instead of other specimen types due to their high level of sensitivity. In settings where other clinical samples might play a role (i.e. broncho-alveolar lavage in the ICU as a proxy for ventilator-associated pneumonia aetiology), they can also be reported as distinct numbers. Reporting of screening samples was more debated; the panel recommends careful interpretation of these data and suggests reporting to the AMS team if specific antibiotic policies are in place (i.e. surgical prophylaxis in MRSA-positive patients).

Resistance data should be displayed using cumulative stratified antibiograms, making sure to adopt adequate de-duplication strategies and to separate clinical from screening samples.\(^{13}\) Either qualitative interpretative categories or MICs can be used to express susceptibility/resistance results; the choice between them needs to account for the final recipients and the purpose of the report. Nevertheless, monitoring of MIC distributions is important to identify WT phenotypes, aid clinical decisions on treatment and compare testing of new agents. Among the antimicrobial susceptibility testing (AST) methods, broth dilution tests are considered the gold standard for MIC determination; they are standardized by different organizations.\(^{60-62}\) and should be used whenever possible. However, they are time-consuming to perform, require certain knowledge (are influenced by the reader, incubation time, temperature and inoculum size) and do not provide insights on resistance mechanisms.

If broth dilution tests are not available, well-standardized alternatives include gradient methods (i.e. Etest) and disc diffusion tests, with the shortcoming of potential biases towards higher or lower MICs determined by the Etest and of qualitative results provided by the diffusion techniques.\(^{63,64}\) Automated systems and genotypic test methods are relevant for epidemiological analysis as they can detect resistance genes or their products, thus helping to guide treatment protocols, but they are not technically feasible for all laboratories. In such circumstances, it is suggested that a reference laboratory be identified for technical support (Table 8).
There was general agreement on the need for at least annual reporting of antimicrobial resistance data, and twice-yearly reporting can also be considered. There was general agreement on the need for at least annual reporting of antimicrobial resistance data, and twice-yearly reporting can also be considered.8,15,18,27,29,30 Stratification of the results needs to be performed by unit, since hospital-wide antibiograms can mask trends in specific units.8,10,15,27,30,56 In reporting the prevalence of resistance, a denominator of <30 isolates of a particular species is discouraged.18,60,65 Where local antibiograms are not available, use of regional resistance data28 should be considered. Similar to the AMU report, AMR results should be delivered to the facility’s prescribers with comments to promote understanding and engagement.1,28 Of note, the report should also integrate infection and prevention control measures, if in place. It was also suggested that an English language version of the report be formulated to promote dissemination of data between countries.

At present, there are insufficient data to recommend thresholds for establishing empirical therapy and prophylaxis. However, indications are available for management of hospital-acquired pneumonia, ventilator-associated pneumonia and urinary tract infections.42,44,46,55 Other relevant areas identified among the priorities for future research are the development of specific criteria to guide decision-making regarding promotion and/or restriction of certain agents and the development of stewardship guidelines for the ‘high-risk patient’ category.

### Table 8. Main advantages and limitations of molecular (DMM) and conventional (CA) diagnostic techniques in antibiotic-resistance

| Core element                                | Molecular methodology                                                                 | Conventional antibiogram   | DMM   | CA   |
|---------------------------------------------|---------------------------------------------------------------------------------------|----------------------------|-------|------|
| Time frame                                  | • 3 h maximum (5–6 h longer from blood culture)                                       | • 16–24 h                 | ▲      | ▼    |
|                                             | • Appropriateness of antibiotic prescribing (except in critical patients)              |                            |       |      |
|                                             | • Immediate change from empirical therapy to targeted therapy                         |                            |       |      |
| Sample                                      | • Directly from clinical sample or blood culture positive                               | • From bacterial culture   | ▲      | ▼    |
| Microbiology characteristic                 | • Only some molecular methods distinguish homogeneous and heterogeneous bacterial populations | • Homogeneous and heterogeneous bacterial population | ■     | ▲    |
|                                             | • No bacterial load                                                                   | • Load and living bacteria |       |      |
|                                             | • No morphology from bacteria colonies                                                | • Morphology of bacterial colonies |       |      |
|                                             | • VBNC identification (viable bacteria but not culturable)                           |                            |       |      |
|                                             | • Useful for microorganisms that are difficult to cultivate or that have long growth times (mycobacteria, clostridia, Helicobacter) |                            |       |      |
| Gene expression                              | • Identification of resistance genes that are not expressed owing to silencers or repressors | • Yes                      | ■     | ▼    |
|                                             | • No identification of gene expression                                                |                            |       |      |
| Breakpoint indicator                         | • No                                                                                    | • Yes, MICs and ECOFF value | ▼      | ▲    |
| Species-specific identification and antibiotic resistance | • Simultaneous species-specific identification, multidrug resistance and genotyping | • Yes                      | ▲      | ▲    |
| Target resistance                            | • Intrinsically unable to detect unknown resistance mechanisms                         | • Multiple targets (coverage of all unknown and known resistance mechanisms) | ▼      | ▲    |
|                                             | • Narrow repertoire of detectable resistance mechanisms covered by the available systems |                            |       |      |
| Genotyping                                   | • To know molecular local epidemiology of community and healthcare-associated infections. | • NA                       | ▲      | ▼    |
|                                             | • Genomic comparison between humans/human and animal/human infection or colonization (livestock-associated infection). |                            |       |      |
|                                             | • Additional information for AMS                                                       |                            |       |      |
| Costs                                        | • Expensive                                                                            | • Less expensive than molecular methodology | ▼      | ▲    |

▲, advantage; ▼, limitation; ■, support technique; NA, not applicable.
Intrinsic limitations of our work include the subjective nature of the experts’ opinions, the narrative nature of the review and the main focus on bacterial infections. Finally, the experts discussed the need to extend or draft similar consensus targets for tuberculosis and other pathogens (fungi and viruses) in the future.

Conclusions
Many of the current guidance documents purposely include generic recommendations to allow greater flexibility by the end user according to the characteristics of individual sites. A major strength of this work is, in fact, the categorization of recommendations, where essential targets refer to what are considered the minimum requirements that need to be in place. Furthermore, the requirements were prioritized and developed taking into account settings with budgetary constraints, which often lack adequate capacity and support (in terms of qualified personnel and laboratory infrastructure). Another value of this White Paper is the attempt to differentiate the actions between different hospital wards (i.e. paediatric versus ICU versus haematologic-oncology) considering differences in local epidemiology and patient characteristics.

This consensus provides a checklist of what should be considered the cornerstones of a hospital AMS programme that can be easily implemented at every level of healthcare and be modelled according to the heterogeneous economic settings. It also highlights specific areas lacking specific guidance, which should be the targets for future research and investment.

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Members of the ARCH working group
Ayola Akim Adegnya, Centre de Recherches Médicales de Lambéré (CERME), Lambéré, Gabon, and Institut für Tropenmedizin and German Center for Infection Research, partner site Tübingen, Universitätsklinikum, Wilhelmsstraße, Tübingen, Germany; Fabiana Arieti, Infectious Diseases Section, Department of Diagnostics and Public Health, University of Verona, Verona, Italy; Nithya Babu Rajendran, Infectious Diseases, Department of Internal Medicine I, Tübingen University Hospital, Tübingen, Germany, and German Centre for Infection Research (DZIF), Clinical Research Unit for healthcare associated infections, Tübingen, Germany; Herman Goossens, Department of Medical Microbiology, Vaccine & Infectious Disease Institute, University of Antwerp, Antwerp, Belgium; Gunnar Kahlmeter, Department of Clinical Microbiology, Vaxjö Central Hospital, Vaxjö, Sweden; Souha S. Kanj, Division of Infectious Diseases, Department of Internal medicine, and Infection Control and Prevention Program, and Antimicrobial Stewardship Program, American University of Beirut Medical Center, Beirut, Lebanon; Tomáš Kostyaynev, Department of Medical Microbiology, Vaccine & Infectious Disease Institute, University of Antwerp, Antwerp, Belgium; Leonard Leibovich, Medicine E, Robin Medical Center, Belinson Hospital, Petah Tiqwa, Israel, and Faculty of Medicine, Tel-Aviv University, Tel-Aviv, Israel; Jean-Christophe Lucef, Infection Control Unit, Bichat-Claude Bernard Hospital, AP-HP, Paris, France, and IAM, UMR 1137, DeSCID team, Université Paris Diderot, Sorbonne Paris Cité, Paris, France; Lorena López-Cerero, Microbiology and Infectious Diseases Unit, University Hospital Virgen Macarena, Sevilla, Spain; Rodolphe Mader, University of Lyon, French Agency for Food, Environmental and Occupational Health and Safety (ANSES), Laboratory of Lyon, Antimicrobial Resistance and Bacterial Virulence Unit, Lyon, France; Fulvia Mazzaferrri, Infectious Diseases Section, Department of Diagnostics and Public Health, University of Verona, Verona, Italy; Elena Mazzolini, Department of Epidemiology, Istituto Zooprofilattico Sperimentale delle Venezie, Legnaro, Padua, Italy; Marc Mendelson, Division of Infectious Diseases and HIV Medicine, Department of Medicine, University of Cape Town, Cape Town, South Africa; Rita Muri, Institute of Infectious Diseases, Fondazione Policlinico Universitario A. Gemelli IRCCS, Università Cattolica del Sacro Cuore, Rome, Italy; Nico T. Mutters, Institute for Hygiene and Public Health, Bonn University Hospital, Bonn, Germany; Micol Pauli, Diseases Institute, Rambam Health Care Campus, Ruth and Bruce Rappaport Faculty of Medicine, Technion - Israel Institute of Technology, Haifa, Israel; Maria Diletta Pezzani, Infectious Diseases Section, Department of Diagnostics and Public Health, University of Verona, Verona, Italy; Elisabeth Presterl, European Committee on Infection Control, Basel, Switzerland, and Department of Infection Control and Hospital Epidemiology, Medical University of Vienna, Vienna, Austria; Hanna Renk, University Children’s Hospital Tübingen, Department of Paediatric Cardiology, Pulmology and Intensive Care Medicine, Tübingen, Germany; Oana Sandulescu, Department of Infectious Diseases I, Faculty of Medicine, Carol Davila University of Medicine and Pharmacy, Bucharest, National Institute for Infectious Diseases ‘Prof. Dr Matei Balș’, Bucharest, Romania; Le Huy Song, Vietnamese German Center for Medical Research, Hanoi, Vietnam, and 108 Military Central Hospital, Hanoi, Vietnam; Maurizio Sanguinetti,
Dipartimento di Scienze Biologiche di base, Cliniche Intensivologiche e Perioperatorie, Università Cattolica del Sacro Cuore, Rome, Italy, and Dipartimento di Scienze di Laboratorio e Infettivologiche, Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy; Remco Schrijver, VetEffect, Bilthoven, The Netherlands; Luigia Scudeller, Scientific Direction of IRCCS Ca’ Granda Ospedale Maggiore Policlinico di Milano, Milano, Italy; Mike Sharland, Paediatric Infectious Diseases Research Group, Department of Paediatrics and Public Health, University of Verona, Verona, Italy; Evelina Tacconelli, Infectious Diseases Section, Department of Diagnostics and Public Health, University of Verona, Verona, Italy, and Infectious Diseases, Department of Internal Medicine I, Tübingen University Hospital, Tübingen, Germany, and German Centre for Infection Research (DZIF), Clinical Research Unit for Healthcare Associated infections, Tübingen, Germany; Didem Torumkuney, International Federation of Pharmaceutical Manufacturers and Associations (IFPMA), Geneva Switzerland; Thirumalaisamy P. Velavan, Institute of Tropical Medicine, Universitätsklinikum Tübingen, Germany, and Vietnamese German Center for Medical Research, Hanoi, Vietnam, and Faculty of Medicine, Duy Tan University, Da Nang, Vietnam; Andreas Voss, Department of Medical Microbiology, Radboud University Medical Centre, Nijmegen, The Netherlands.

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