**Supplementary data**

**File S1. Data extraction form**

|  |  |
| --- | --- |
| Reference:  |  |
| Author: |  |
| Year published: |  |
| Study location: |  |
| Area of AMS applicable to: |  |
| Study design/ methodology to develop the QIs: |  |
| Number of QI’s developed |  |
| Types of QI’s developed (i.e. Process, structure or outcome) |  |
| The QIs developed |  |
| Methodological assessment with AIRE criteria completed |  |

**File S2. AIRE instrument description and scoring**

The AIRE instrument is divided into four quality domains of a QI and consists of 20 criteria which are applied to each completed set of QIs. Three domains address the methodological quality of QIs and were used in this review: ‘Stakeholder involvement’, ‘Scientific evidence’ and ‘Additional evidence, formulation and usage’. The fourth domain: ‘purpose, relevance and organisational context’ reflect the relevance of the QIs within a particular context rather than methodological quality so was not used.

Scoring of the AIRE instrument items

Each of the included domains consisted of several item statements and were assigned a score by each reviewer according to a 4-point Likert scale

1-‘strongly disagree’ (confident that the criterion has not been fulfilled or no information is available);

2- ‘disagree’ (disagree or unsure whether the criterion has been fulfilled)

3-‘agree’ (fairly confident the criterion has been fulfilled)

4-‘strongly agree’ (confident that the criterion has been fulfilled).

The scores from each reviewer were summed to provide a ‘total score’ per quality domains.

A standardised domain score was then calculated according to the instrument’s guidelines with the following formula: (total score—minimum possible score) / (maximum score—minimum possible score) x 100%.

A higher standardized score indicates a higher methodological level of quality (range 0–100%). QI sets were considered to have a high methodological quality for a domain if they scored 50% or higher, which correlates with an overall “agree” or “strongly agree”. Domain scores are independent and should not be combined into a single quality score

|  |  |
| --- | --- |
| AIRE domain | AIRE items |
| Stakeholder involvement | 1. The group developing the indicator includes individuals from relevant professional groups
 |
| 1. Considering the purpose of the indicator, all relevant stakeholders have been involved at some stage of the development process
 |
| 1. The indicator has been formally endorsed
 |
| Scientific evidence | 1. Systematic methods were used to search for scientific evidence
 |
| 1. The indicator is based on recommendations from an evidence-based guideline or studies published in peer-reviewed scientific journals
 |
| 1. The supporting evidence has been critically appraised
 |
| Additional evidence, formulation, usage | 1. The numerator and denominator are described in detail
 |
| 1. The target patient population of the indicator is defined clearly
 |
| 1. A strategy for risk adjustment has been considered and described (‘case-mix adjustment’)
 |
| 1. The indicator measures what it is intended to measure (validity)
 |
| 1. The indicator measures accurately and consistently (reliability)
 |
| 1. The indicator has sufficient discriminative power
 |
| 1. The indicator has been piloted in practice
 |
| 1. The efforts needed for data collection have been considered
 |
| 1. Specific instructions for presenting and interpreting the indicator results are provided
 |

**File S3. Inter rater reliability AIRE instrument**

Weighted Cohens Kappa (FOR &AF)= 0.69

|  |  |
| --- | --- |
| Article Berenholtz Reviewer: | AIRE domains and items |
| Stakeholder involvement | Scientific evidence | Additional evidence, formulation, usage |
| 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 |
| FOR | 4 | 4 | 1 | 3 | 4 | 3 | 4 | 4 | 3 | 1 | 1 | 3 | 1 | 3 | 1 |
| AF | 4 | 4 | 1 | 2 | 4 | 3 | 4 | 4 | 3 | 1 | 1 | 3 | 1 | 3 | 1 |

|  |  |
| --- | --- |
| Article Thern Reviewer: | AIRE domains and items |
| Stakeholder involvement | Scientific evidence | Additional evidence, formulation, usage |
| 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 |
| FOR | 4 | 4 | 1 | 3 | 4 | 1 | 1 | 4 | 1 | 3 | 3 | 1 | 4 | 4 | 1 |
| AF | 3 | 3 | 1 | 3 | 3 | 1 | 1 | 3 | 2 | 3 | 3 | 2 | 4 | 4 | 1 |

Weighted Cohens Kappa (FOR & FS)= 0.73

|  |  |
| --- | --- |
| Schouten 2005Reviewer: | AIRE domains and items |
| Stakeholder involvement | Scientific evidence | Additional evidence, formulation, usage |
| 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 |
| FOR | 2 | 3 | 1 | 4 | 4 | 4 | 2 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 1 |
| FS | 2 | 3 | 1 | 4 | 4 | 3 | 2 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 1 |

|  |  |
| --- | --- |
| Van den Bosch 2015Reviewer: | AIRE domains and items |
| Stakeholder involvement | Scientific evidence | Additional evidence, formulation, usage |
| 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 |
| FOR | 4 | 4 | 1 | 3 | 4 | 4 | 4 | 4 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| AF | 3 | 4 | 1 | 4 | 4 | 4 | 4 | 4 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |

**File S4.** **Quality indicators extracted**

**Berenholtz 2007** (Sepsis-refers to severe sepsis or septic shock)

1. The percentage of patients with sepsis and an unidentified organism received vancomycin within 24 hours of identification
2. Median time to vancomycin initiation following sepsis diagnosis
3. The percentage of patients with sepsis and an unidentified organism who received a recommended broad spectrum antibiotic within 24 hours of sepsis identification
4. Median time to broad spectrum antibiotic initiation following sepsis diagnosis
5. The percentage of patients with sepsis who had 2 sets of blood cultures collected within 24 hours following sepsis identification
6. The percentage of patients with sepsis and an organism other than MRSA or MRSE (metacillin-resistant staphyloccus epidermis) who had vancomycin discontinued within 96 hours of diagnosis.

**Buyle 2013**

1. (Services) Bedside expert consultant advice regarding antibiotics by microbiologist/infectious disease specialist/antibiotic officer on request available on the same day
2. (Services) Regular ward rounds by members of the AMT (multi-disciplinary antibiotic management team) performed (at least weekly)
3. (Services) Clinical audit of prescribers’ compliance with local clinical guidelines/guide performed by AMT/AB officer
4. (Tools) Antimicrobial formulary list biannually updated
5. (Tools) Local clinical practice guidelines for microbiologically documented therapy updated biannually
6. (Tools) Local clinical practice guidelines for empirical therapy available
7. (Tools) Local clinical practice guidelines for surgical antimicrobial prophylaxis available
8. (Human resources and mandate) Formal mandate for hospital multi-disciplinary antibiotic management team (AMT) existing
9. (Human resources and mandate) AB officer or AMT member is member of the drugs and therapeutics committee
10. (Personnel development) Prescriber education by personalised interactive methods (like daily ward rounds) performed

**Coll 2012**

Bacterial specimens

1. Bacterial specimens are taken before initiation of antimicrobial treatment and there is evidence of analysis at the laboratory

Allergy status

1. Patients allergy status is documented at the time antimicrobial(s) to be prescribed
2. The nature and severity of the past allergic reaction is documented
3. Patients with a history of anaphylaxis (wheezing, collapse or an itchy rapid onset, urticarial rash) immediately after penicillin therapy should not receive antimicrobial treatment with a beta lactam antimicrobial is prescribed alternative drug class
4. Patients with a history of minor rash (non-confluent, non-pruritic, restricted to a small area of the body, or occurring more than 72 h after penicillin administration) is prescribed a cephalosporin or carbapenem if indicated

Guideline compliance

1. Choice of antimicrobial treatment is compliant with local policy
2. The route of administration of antimicrobial is compliant with local policy
3. The dosage regimen of prescribed antimicrobial is compliant with local policy

Renal impairment

1. Review and adjustment of dosage regimen as recommended in the guidelines is documented in mild renal impairment (CrCl = 20–50 ml/min)
2. Review and adjustment of dosage regimen as recommended in the guidelines is documented in moderate renal impairment (CrCl = 10–20 ml/min)
3. Review and adjustment of dosage regimen as recommended in the guidelines is documented in severe renal impairment (CrCl <10 ml/min)

Interaction management plan

1. Identified interactions between antimicrobial regimen and concurrent medications are documented with a recommended management plan of the interaction

Documentation

1. The indication for prescribing of antimicrobial treatment is documented
2. The intended duration of antimicrobial treatment is documented

Therapeutic drug monitoring

1. The gentamicin level is taken at the correct time recommended by the antimicrobial guidelines
2. The measured gentamicin level is documented
3. The gentamicin dosage regimen is managed according to the guideline and a management plan is documented
4. The vancomycin level is taken at the correct time
5. The measured vancomycin level is documented
6. The vancomycin dosage regimen is managed according to the guideline and a management plan is documented

Improvement in renal impairment

1. Due to an improvement in mild renal impairment review and adjustment of dosage regimen is documented
2. Due to an improvement in moderate renal impairment) review and adjustment of dosage regimen is documented
3. Due to an improvement in severe renal impairment review and adjustment of dosage regimen is documented

Interactions

1. Documented interaction management plan (criteria 12) is followed

De-escalation

1. The results of bacteriological sensitivity(s) is documented
2. The choice of antimicrobial treatment is reviewed according to clinical response and/or sensitivities
3. The intravenous route of administration is switched to the oral route at an appropriate time (48 h after initiation and if not clinically indicated, requirement for intravenous route is reviewed every 24 h)
4. The indication for prescribing an oral antimicrobial as a result of an intravenous to oral switch is documented in the case notes or the inpatient medication administration chart
5. The intended duration of oral antimicrobial treatment as a result of an intravenous to oral switch is documented
6. Antimicrobial treatment is discontinued on completion of the documented course

**Farida 2014**

1. Take two sets of blood samples for culture
2. Obtain sputum samples for Gram stain and culture
3. Obtain sputum sample and start antibiotic therapy in the emergency department
4. Timely initiation of antibiotic therapy within four hours after presentation
5. Switching from iv to oral therapy when clinically stable
6. Length of therapy is five days for uncomplicated CAP (CURB score ≤ 2)

**Thern 2014**

Structural indicators

1. (Prerequisites) MDT AMS team authorised by hospital management , headed by ID physician (or trained abx expert) plus a pharmacist
2. AMS team represented in the drugs and therapeutic committee
3. Minimum of 2 AMS team meetings annually (minuted)
4. ABS strategic report to D&T and hospital management includes quantitative objectives with selected performance indicators
5. Written in-house preanalytical requirements for microbiologic samples (including rejection criteria)
6. Antimicrobial drug use data (as DDD/RDD or PDD per 100 occupied bed [patient] days and/or admission) available for several clinical divisions or departments (division-specific or aggregated for surgical and nonsurgical services and/or for general wards vs intensive care units) at least annually (in total and detailing the most important antibiotic classes)
7. Rate of oral vs. parenteral dispensed or prescribed daily doses of the most important and relevant drugs or drug classes available at least once per year for several clinical services
8. Other resistance rates and corresponding incidence figures (for clinical isolates) available at least once per year for several clinical services (divisions/departments)
9. Incidence figures for *C. difficile* associated diarrhoea available for several clinical services (division-specific and/or general wards vs. intensive care units) at least once per year
10. Hospital-wide incidence figures for nosocomial sepsis/bacteraemia available at least once per year
11. In-house list of anti-infectives (formulary, see above) which is up to date (not older than 2 years) available
12. Prescriptions concerning restricted / alert anti-infectives from a defined list are approved for specific patients, not generically
13. Written, locally consented practice guidelines (see above) available and updated (not older than 2 years)
14. Written, locally consented practice guidelines for surgical prophylaxis available and updated (not older than 2 years) available
15. Written recommendation for parenteral-to-oral switch antimicrobial therapy (prerequisites / criteria and drugs) available and updated (not older than 2 years)
16. Regular ward rounds of members of ABS team together with the attending physicians (at least 3 clinical services/departments, at least 3 times each in the previous 12 months)
17. Educational sessions by the ABS team and/or ABS representatives about locally consented guidelines (tailored to division or at least differentiating conservative vs. surgical specialities) at least every other year
18. In-house and/or extramural ABS-relevant continuing medical education about antimicrobial therapy and prophylaxis for at least 10% of medical staff who are not ABS representatives (at least 4 documented CME credits relevant for ABS per year)
19. ABS-relevant continuing medical education for ABS team members and ABS representatives from clinical services (at least 8 documented CME credits relevant for ABS per year)
20. Use of selected antibiograms (adapted according to local guidelines)
21. Locally consented guidelines / decision-making aids electronically available (e.g. via physician's computer, PDA or smartphone)

Process indicators CAP

1. Initial therapy (drugs and dosing) according to local / national guideline
2. Obtain blood cultures (2 sets) on the day of initialization of antibiotic therapy
3. Combination therapy, if any, no longer than three days (patients on general ward)
4. Duration of therapy no longer than 7 days (patients on general ward)

Process indicators HAP

1. Initial therapy (drugs) according to local / national guideline
2. Obtain blood cultures (2 sets) on the day of start of therapy
3. Duration of therapy no longer than 10 days

Process indicators BSI

1. Heart ultrasound (TEE) within 10 days of collection of first blood culture that became positive (etiologies of bacteremia/sepsis: *Staphylococcus aureus*, streptococci, enterococci (non-nosocomial), HACEK)
2. Collection of follow-up blood cultures 4-7 days after collection of first blood culture that became positive (etiology of bacteremia/sepsis: *Staphylococcus aureus* or patients with fungemia)

Process indicators UTI

1. Documented positive urine culture (significant bacteriuria, no mixed flora)
2. Initial therapy (drugs and dosing) according to local / national guideline
3. Duration of pyelonephritis therapy not longer than 10 days (patients on general ward)
4. Oral antimicrobial drugs initiated not later than day 5 (pyelonephritis, patients on normal wards only)
5. No antimicrobials for asymptomatic, catheter- associated bacteruria

Process indicators (Other empiric therapy, iv/po switching, renal adjustment)

1. Initial empiric therapy (drugs, before/without knowledge of etiology) according to local guideline
2. Oral administration of drugs with high bioavailability (fluoroquinolones [exept norfloxacin], clindamycin, doxycycline, linezolid, metronidazole, rifampin, fluconazole, voriconazole) (not for patients with resorption disorders, short bowel syndrome, emesis, severe sepsis / septic shock)
3. Dosing adjustments for patients with reduced renal function within 2 days

Process indicators (Surgical antimicrobial prophylaxis)

1. Antibiotic prophylaxis (drugs, dosage) administered according to local guideline
2. Antibiotic prophylaxis administered within 1h before incision
3. Antibiotic prophylaxis stopped within 1 day (<24 h)

Process indicators (MDR management)

1. Infection and/or colonization by multidrug- resistant (MDR) organisms explicitly listed in discharge summary

**Hermanides 2008**

1. Performance of urine culture
2. Prescription of treatment in accordance with empiric guidelines
3. Tailoring of treatment on the basis of culture results
4. Switch to oral treatment when possible (after 48-72 hours based on clinical condition)
5. Selective use of fluoroquinolones (only as oral or in beta-lactam allergy/anaphylaxis)
6. Duration of treatment for at least 10 days (in accordance with national guideline)
7. Initiation of treatment within 4 hours after clinical presentation
8. Prescription of treatment for men in accordance with national guidelines
9. Start iv antibiotics in pregnant women with pyelonephritis
10. Do not prescribe antibiotic prophylaxis to patients with a urinary catheter in place
11. Change urinary catheter within 24 hours of initiation of antibiotic treatment
12. Consider all diabetic patients with cystitis as having a complicated UTI and treat with empiric treatment according to national guidelines
13. Adaptation of the dosage on the basis of renal function

**Kallen 2018**

1. Perform at least two sets of blood cultures before start of empirical systemic therapy

2. Perform therapeutic drug monitoring in patients treated with vancomycin or aminoglycosides

3. Perform surveillance cultures if selective digestive or oropharyngeal decontamination is applied at the ICU

4. Biannual face-to-face meetings between ICU and microbiology staff in which local resistance rates are discussed

Quantity metric

5. Quantitative antibiotic use at the ICU expressed in days of therapy (DOT).

**Monnier 2018**

Antibiotic Prescribing

1. Antibiotics should be prescribed according to local practice guidelines.
2. Antibiotics should be prescribed according to national guidelines when no local guidelines are available.
3. Antibiotic prescriptions that deviate from guidelines should be justified.

Antibiotic Stewardship

1. Surveillance of antibiotic use and resistance should be performed at least once per year at the health care facility.
2. An antibiotic formulary should be available and updated continuously at the health care facility.
3. An approval system should be in place for prescriptions of restricted antibiotics at the health care facility.
4. An antibiotic stewardship programme (antibiotic prescribing control programme and/or antibiotic prescribing policy) should be in place at the health care facility.
5. Antibiotic prescribing should be compliant with recommendations from infectious disease and/or microbiology specialist(s).
6. Audits of antibiotic use by the antibiotic stewardship team should be performed regularly at the health care facility.
7. A multidisciplinary antibiotic stewardship team appointed by the health care facility management should have meetings at least twice a year and make a report with objectives and selected performance indicators.

Availability

1. Antibiotics from the antibiotic formulary should not be out of stock at the health care facility.

Diagnostics

1. Two sets of blood culture should be taken before antibiotic administration when bacteraemia is suspected.
2. Specimens for culture from suspected sites of infection should be collected before antibiotic administration.
3. Microbiological investigations should be performed according to guidelines.

Documentation

1. An antibiotic plan should be documented in the medical record at the start of the antibiotic treatment. Antibiotic plan includes: indication, name, doses, duration, route, and interval of administration.
2. Clinical and laboratory sepsis parameters should be documented in the medical records when prescribing antibiotics.
3. The results of bacteriological sensitivities should be documented in the medical records.

Dosing

1. Dosing and dosing interval of antibiotics should be prescribed according to guidelines.
2. Dosing and dosing interval of renally eliminated antibiotics should be adapted to the patient’s renal function.
3. The dosage regimen of antibiotics with an increased risk of toxicity (such as vancomycin or gentamicin) should be managed according to guidelines.

Duration-Discontinuation

1. Duration of antibiotic therapy should be compliant with guidelines.
2. Antibiotic therapy should be discontinued based on the lack of clinical evidence of infection.
3. Antibiotic therapy should be discontinued on completion of the documented antibiotic course.

Education

1. Educational sessions about practical guidelines should be organized for medical staff and should have a predetermined attendance target.

Guidelines

1. A local antibiotic guideline should be present at the health care facility.
2. An evaluation whether an update should be considered for the local antibiotic guideline should be done once a year.
3. The local guidelines should correspond to the national guideline but should be adapted based on local resistance patterns.

Outcome

1. Clinical outcomes of patients receiving antibiotics should be monitored at the health care facility.
2. Rates of nosocomial Clostridium difficile should be monitored at the health care facility.

Prescribing-Administration

1. Prescribed antibiotics should actually be administered to the patients.

Route

1. The route of administration of antibiotics should be compliant with guidelines.
2. Antibiotic therapy in adult patients with sepsis should be started intravenously.
3. Switching from intravenous to oral antibiotic(s) should be performed according to guidelines.
4. Switching from intravenous to oral antibiotic(s) should be done within 48–72 hours based on the clinical condition and when oral treatment is adequate.

Safety/General

1. Contraindications should be taken into account when prescribing antibiotics.

Safety/Allergy

1. Allergy status should be taken into account when antibiotics are prescribed.
2. Allergy status (including nature and severity) of the patient should be documented in the medical records when antibiotics are prescribed.
3. Patients with a history of anaphylaxis after penicillin therapy should be prescribed an alternative drug class
4. Medical staff should be educated regarding cross-allergy with cephalosporins in patients with penicillin allergy.

Safety/Interaction

1. Identified interactions between antibiotic regimen and concurrent medications should be documented in the medical record with a recommended management plan to deal with the interaction.

Safety/Toxicity

1. Duration of administration of intravenous antibiotics should be compliant with guidelines.

Selective Reporting

1. The microbiological laboratory should report individual selective susceptibly reports\* (or antibiograms) adapted to local guidelines.
A selective susceptibly report (or antibiogram) is a report of a selection of antibiotic sensitivities, based on bacteriological activity, broadness of spectrum or toxicity.

Spectrum

1. The prescribed antibiotic should be active against all the likely causative pathogens.

Streamlining/De-escalation

1. Broad-spectrum empirical antibiotic therapy should be changed to pathogen-directed therapy as soon as culture results become available.
2. The choice of antibiotic treatment should be reviewed and modified based on clinical response.
3. Antibiotics for empirical therapy should be reviewed within the third day of treatment or when microbiological results become available.

Surgical prophylaxis

1. Prophylactic antibiotics should be added to a pre-operative checklist.

Therapeutic Drug Monitoring

1. Therapeutic Drug Monitoring should be performed for antibiotics with a narrow therapeutic spectrum and an increased risk of toxicity according to guidelines.
2. If antibiotic Therapeutic Drug Monitoring levels are not in the reference range, doses should be adjusted appropriately after the results become available.
3. Therapeutic Drug Monitoring levels of antibiotics should be documented in the medical records.

Timing

1. Timeliness of administration of antibiotic therapy and prophylaxis should be compliant with guidelines.

**Pollack 2016**

**Infrastructure**

1. Does your facility have a formal antimicrobial stewardship program accountable for ensuring appropriate antimicrobial use?
2. Does your facility have a formal organizational structure responsible for antimicrobial stewardship (eg, a multidisciplinary committee focused on appropriate antimicrobial use, pharmacy committee, patient safety committee, or other relevant structure)?
3. Is an antimicrobial stewardship team available at your facility (eg, greater than one staff member supporting clinical decisions to ensure appropriate antimicrobial use)?
4. Is there a physician identified as a leader for antimicrobial stewardship activities at your facility?
5. Is there a pharmacist responsible for ensuring appropriate antimicrobial use at your facility?
6. Does your facility provide any salary support for dedicated time for antimicrobial stewardship activities (eg, percentage of full-time equivalent [FTE] staff for ensuring appropriate antimicrobial use)?
7. Does your facility have the information technology (IT) capability to support the needs of the antimicrobial stewardship activities?

**Policy and practice**

1. Does your facility have facility-specific treatment recommendations based on local antimicrobial susceptibility to assist with antimicrobial selection for common clinical conditions?
2. Does your facility have a written policy that requires prescribers to document an indication in the medical record or during order entry for all antimicrobial prescriptions?
3. Is it routine practice for specified antimicrobial agents to be approved by a physician or pharmacist in your facility (eg, preauthorization)?
4. Is there a formal procedure for a physician, pharmacist, or other staff member to review the appropriateness of an antimicrobial at or after 48 hours from the initial order (post-prescription review)?

**Monitoring and feedback**

1. Has your facility produced a cumulative antimicrobial susceptibility report in the past year?
2. Does your facility monitor if the indication is captured in the medical record for all antimicrobial prescriptions?
3. Does your facility audit or review surgical antimicrobial prophylaxis choice and duration?
4. Are results of antimicrobial audits or reviews communicated directly with prescribers?
5. Does your facility monitor antimicrobial use by grams (Defined Daily Dose [DDD]) or counts (Days of Therapy [DOT]) of antimicrobial(s) by patients per days?
6. Has an annual report focused on antimicrobial stewardship (summary antimicrobial use and/or practices improvement initiatives) been produced for your facility in the past year?

**Schouten 2005**

CAP

1. Timely initiation of antibiotic therapy (within 4 h after presentation)
2. Empirical antibiotic regimen at correct indication and according to guidelines
3. Stop antibiotic therapy if no fever for 3 consecutive days
4. Obtaining two sets of blood samples for culture
5. Urine antigen testing for Legionella species on clinical suspicion

COPD alone

1. Prescribe antibiotic therapy for exacerbations only when indicated
2. Optimal duration of antibiotic therapy from 5-7 days

Both CAP & COPD

1. Adapting dose and dose interval of antibiotics according to renal function
2. Switch from intravenous to oral therapy according to existing criteria and clinical stability
3. Changing broad-spectrum, empirical therapy to pathogen-directed therapy (streamlining therapy)
4. Obtaining sputum samples for Gram staining and culture

**Schouten 2012**

1. Clinical rationale of starting AB documented in the chart (day 1)

2. Appropriate microbiological cultures according to local and/or internaional guidelines (day 1);

3. Choice of empiric therapy according to local and/or international guidelines (day 1)

4. Review of diagnosis according to microbiological results (day 2, 3, 4, 5)

5. De-escalation therapy to be considered in patients with microbiological diagnosis according to the susceptibility pattern of the isolate (day 2, 3, 4, 5)

6. Withdrawal of therapy to be considered in patients with a definitive non-infectious diagnosis (day 3, 4, 5)

**Sneddon 2012**

1. Indication recorded and empirical antibiotic choice compliant with local policy. Target ≥95% compliance.

2. Duration of surgical prophylaxis <24 hours and choice compliant with local policy. Target ≥95% compliance.

**Ten Oever 2019** (**Antimicrobial therapeutic interventions only)**

Blood cultures

1. Follow-up blood cultures after initiation of antimicrobial therapy should be done regardless of clinical evolution.
2. Collection of repeat blood cultures should be performed until first negative blood culture.

Antibiotic treatment

1. Initial antibiotic therapy should be administered intravenously in patients with SAB.
2. Initial therapy should be intravenous (flu)cloxacillin (or nafcillin or oxacillin) or cefazolin in the case of methicillin-susceptible strains in patients with SAB.
3. Antibiotic therapy should be initiated within 24 h after first positive blood culture.
4. Appropriate treatment should be adapted within the first 24 h after a methicillin susceptibility result is available, if so required.
5. The dosage of antibiotic treatment should be according to (national) guidelines in patients with SAB.
6. Appropriate duration of intravenous antibiotic treatment should be at least 14 days for uncomplicated SAB.
7. Appropriate duration of intravenous antibiotic treatment should be at least 28 days for SAB complicated by metastatic abscesses or deep foci of infection
8. Therapeutic drug monitoring should be performed when SAB is treated with vancomycin.
9. Antibiotic treatment therapy for patients with SAB should be adjusted according renal function.
10. Intravenous-to-oral switch should not be performed in uncomplicated SAB after 48–72 h.
11. Intravenous-to-oral switch should not be performed in complicated SAB after 48–72 h.

Other management aspects

1. Infectious disease specialist consultation should be performed in patients with SAB.
2. SAB should be documented in the medical discharge summary.

**Van der Bosch 2014**

1. Antimicrobial therapy in adult patients with sepsis should be started intravenously.
2. Antimicrobial therapy should be started as soon as possible, preferably within the first hour in adult patients with severe sepsis and septic shock.
3. Before starting antimicrobial therapy, at least two sets of blood cultures and specimens for culture from suspected sites of infection should be taken.
4. Empiric systemic antimicrobial therapy should be changed to pathogen-directed therapy if culture results become available.
5. Empiric systemic antimicrobial therapy (only choice of antimicrobial agent) should be prescribed according to the national guideline. The local guidelines should correspond to the national guideline but should deviate based on local resistance patterns.

**Van der Bosch 2015**

1. Before starting systemic antibiotic therapy, at least two sets of blood cultures should be taken.

2. When starting systemic antibiotic therapy, specimens for culture from suspected sites of infection should be taken as soon as possible, preferably before antibiotics are started (cultures should be taken until a maximum of 24 h after antibiotics are started).

3. Empirical systemic antibiotic therapy should be prescribed according to the local guidelines.

4. A current local antibiotic guideline should be present in the hospital and an evaluation whether an update should be considered should be done every three years.

5. Local antibiotic guidelines should correspond to the national antibiotic guidelines, but should deviate based on local resistance patterns.

6. Empirical antibiotics should be changed to pathogen-directed therapy if culture results become available.

7. Dose and dosing intervals of systemic antibiotics should be adapted to renal function.

8. Systemic antibiotic therapy should be switched from intravenous to oral antibiotic therapy within 48–72 h on the basis of the clinical condition and when oral treatment is adequate.

9. An antibiotic plan should be documented on the case notes at the start of systemic antibiotic treatment.

10. Therapeutic drug monitoring should be performed when the treatment duration is more than three days for aminoglycosides and more than five days for vancomycin.

11. Empirical antibiotic therapy for presumed bacterial infection should be discontinued based on the lack of clinical and/or microbiological evidence of infection. The maximum duration of empirical systemic antibiotic treatment should be seven days.

**Vera 2014**

1. **Antimicrobial use in the intensive care unit Formula**: Total number of days of use of antimicrobial agent /Total number of days of ICU patients ×100
2. **Non-empirical antimicrobial use Formula**: Total antimicrobials used to treat infections in a directed manner /Total of antimicrobials used to treat infections ×100
3. **Changes in antimicrobials used as treatment Formula:** Total number of antimicrobials changed to another antimicrobial / Total of antimicrobials used to treat infections × 100
4. **Days without antimicrobial use in ICU Formula:** Total number of ICU days without antimicrobials / Total number of days of ICU patients × 100
5. **Days free of antimicrobials in patients on antimicrobial treatment Formula**: Number of days free of antimicrobials in patients on antimicrobial treatment / Total days in ICU of patients on antimicrobial treatment × 100
6. **Number of days of antimicrobials for surgical prophylaxis Formula**: Number of days of use of antimicrobials for surgical prophylaxis / Total number of patients with surgical prophylaxis treatment × 100
7. **Inappropriate empirical antimicrobial treatment Formula:** Total number of inappropriate empirical antimicrobials / Total number of empirical antimicrobials used to treat infections × 100
8. **Empirical antimicrobials changed because they are inadequate Formula:** Number of empirical antimicrobials changed because they are inadequate Total number of empirical antimicrobials used to treat infections × 100
9. **Empirical antimicrobial changed for de-escalation Formula:** Number of empirical antimicrobials changed by adjustment or de-escalation Total number of empirical antimicrobials used to treat infections × 100
10. **Patients with severe sepsis/septic shock treated with antimicrobials in the first three hours Formula:** Number of patients with severe sepsis/septic shock, treated with antimicrobials in the first 3 hours / Total number of patients with severe sepsis/septic shock