BIOMÉRIEUX

EVIDENCE-BASED DIAGNOSTICS FOR ANTIMICROBIAL STEWARDSHIP

Selection of publications

2021 EDITION

PIONEERING DIAGNOSTICS

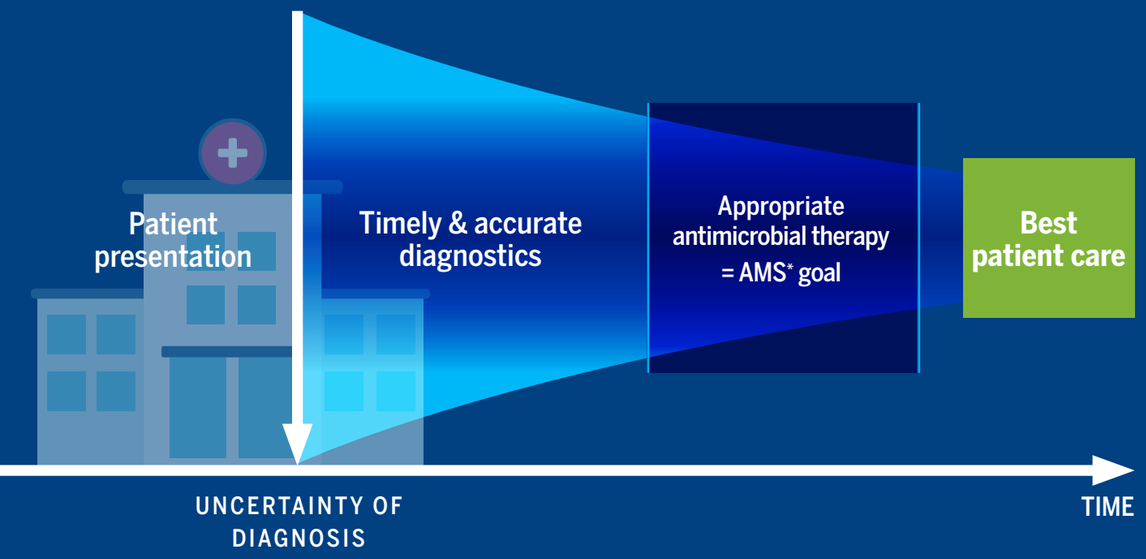
How can Appropriate Therapy be defined?

> **“ The right antibiotic for the right patient, at the right time, with the right dose, and the right route, causing the least harm to the patient and future patients.[1] ”**

What is the Value of Diagnostics-guided Antimicrobial* Prescribing?

The sooner the appropriate therapy, the better the patient outcome!
By reducing the window of clinical uncertainty, rapid diagnostic test results support earlier prescription of the appropriate antimicrobial therapy.

DIAGNOSTICS CONTRIBUTE TO HIGHER MEDICAL VALUE LEADING TO BETTER PATIENT CARE [2]



*** AMS: antimicrobial stewardship**

1. CDC. https://www.cdc.gov/media/releases/2017/safe-antibiotic-prescribing.html Accessed on Feb 8 2021.
2. bioMérieux.

** In this document, the term "antimicrobials", encompassing antibiotics, antifungals and antiviral drugs, will be frequently replaced by "antibiotics", which represent the most commonly prescribed therapy.*

PREFACE

Antimicrobial resistance (AMR) is one of the major global public health threats of modern times[1], due to overuse and misuse of existing antimicrobials, the lack of new antibiotics in the development pipeline and multidrug-resistant infections becoming untreatable. In recent years, greater awareness of the scope of the problem has led governments, global and national health organizations, and healthcare institutions to increase their efforts to tackle the problem.

Antimicrobial stewardship (AMS) has emerged over the past two decades as a vital activity to combat antimicrobial resistance. It involves the careful and responsible management of antimicrobial prescribing practices and antibiotic use in hospitals and healthcare settings worldwide. A key component of antimicrobial stewardship is the availability of **clinical prescribing guidelines** to support empiric and targeted therapies.[2,3]

An **antimicrobial stewardship program (ASP)** with a dedicated multi-disciplinary team is now an essential and accepted component in an increasing number of hospital management policies. In some countries, it is now a mandatory requirement for hospitals and other healthcare facilities to put in place a stewardship team with clear objectives and policies to appropriately monitor and improve antimicrobial prescribing practices. This sometimes comes with financial incentives or penalties. However, in many low- and middle-income countries (LMICs), developing and implementing ASP interventions remains an immense challenge given the limited healthcare and economic resources as well as the lack of hospital/laboratory infrastructures.[4] However, a full discussion of these challenges is beyond the scope of this publication.

The main objective of ASPs is to achieve the prescription of the most appropriate antimicrobial therapy in order to provide three main benefits:

- optimize patient outcomes, and reduce risk of adverse drug events (ADE)
- reduce resistance and sustain antibiotic efficacy thereby supporting public health and modern medicine
- generate cost-savings.

The uncertainty of diagnosis is one of the key drivers of antimicrobial overuse and misuse. Therefore, **diagnostic tests are instrumental for antimicrobial stewardship programs**, since they have a decisive impact on clinical decision-making and patient care. When appropriate tests are ordered in a timely way, rapid diagnostic results can be translated into tailored antibiotic therapy to optimize patient health outcomes. Moreover, integrating diagnostic results into clinical decision support systems (CDSS) can help increase compliance with evidence-based care guidelines and antibiotic susceptibility test results, resulting in optimized antibiotic prescribing decisions.[5]

The articles summarized in this **Selection of Publications** provide real-world evidence and scientific proof that support the effectiveness of ASPs, and demonstrate the key role diagnostics play in defining and prescribing responsible and appropriate therapy to improve ASP goals.

We hope that this document will be a useful, informative resource to encourage and support healthcare professionals in their pursuit of optimal antimicrobial prescribing practices.

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1. World Health Organization. Available at https://www.who.int/news-room/fact-sheets/detail/antimicrobial-resistance Oct 13 2020. Accessed on Jan 14 2021.
2. CDC. Core Elements of Hospital Antibiotic Stewardship Programs. Atlanta, GA: US Department of Health and Human Services, CDC; 2019.
Available at https://www.cdc.gov/antibiotic-use/core-elements/hospital.html. Accessed on Jan 14 2021.
3. Pulcini C, *et al*. Developing core elements and checklist items for global hospital antimicrobial stewardship programmes: a consensus approach. *Clinical Microbiology and Infection* 2019;25(1):20-25
4. Yusuf E, Hamers RL. What the WHO's List of Essential Diagnostics means for clinical microbiology laboratories and antimicrobial stewardship practice worldwide. *Clinical Microbiology and Infection* 2019;25:6-9
5. Laka M, *et al*. Can Evidence-Based Decision Support Tools Transform Antibiotic Management? A Systematic Review and Meta-Analyses. *Journal of Antimicrobial Chemotherapy* 2020;75(5):1099-1111

ABBREVIATIONS & ACRONYMS

ADE	adverse drug events
AMR	antimicrobial resistance
AMS	antimicrobial stewardship
ARI	acute respiratory infection
ASP	antimicrobial stewardship program
AST	antimicrobial susceptibility testing
BSI	bloodstream infection
CAP	community-acquired pneumonia
CDSS	clinical decision support system
COPD	chronic obstructive pulmonary disease
CPE	carbapenemase-producing *Enterobacterales*
CRE	carbapenem-resistant *Enterobacterales*
DDD	daily defined dose
DOT	duration of therapy
ESBL	extended spectrum beta-lactamase
GNB	gram-negative bacteria
HAI	healthcare-associated infections
HAP	hospital-acquired pneumonia
ID	identification
LMIC	low- and middle-income countries
LOS	length of stay
MALDI-TOF	matrix-assisted laser desorption/ionization-time of flight
MDR	multi-drug resistant
MIC	minimum inhibitory concentration
MRSA	methicillin-resistant *Staphylococcus aureus*
NPV	negative predictive value
PAF	prospective audit and feedback
PCR	polymerase chain reaction
PCT	procalcitonin
PK/PD	pharmacokinetics/pharmacodynamics
PNA-FISH	peptide nucleic acid fluorescent *in situ* hybridization
POCT	point of care testing
PPS	point prevalence survey
PPV	positive predictive value
RCT	randomized controlled trial
RDT	rapid diagnostic testing
SOC	standard of care
TTAT/TTET	time to appropriate/effective therapy
TTR	time to result
VAP	ventilator-associated pneumonia
VRE	vancomycin-resistant enterococci

GLOSSARY

ANTIMICROBIAL THERAPY

Empiric therapy: educated decision based on patient presentation and local antibiogram

Targeted/oriented therapy based on initial rapid testing results providing evidence of the nature of the infectious micro-organism (none, bacteria, fungus, virus, parasite) and sometimes resistant determinants

Appropriate therapy (optimal, effective, definitive therapy): microbiologically active therapy based on antimicrobial susceptibility testing and antibiotic sustainability

Personalized therapy: optimizing antimicrobial exposure in selected patient populations (using biomarkers, PK/PD targets, MIC,...)

MEDICAL INDICATORS AND OUTCOMES

ANTIMICROBIAL PRESCRIBING INDICATORS

- Antibiotic therapy initiation rate
- Time to appropriate therapy
- Proportion of appropriate antibiotic therapy
- Antibiotic exposure (duration & quantity of antibiotic used during a course of treatment)
- Length/duration of therapy
- Antibiotic de-escalation/escalation
- Time to oral switch
- Reduction in antimicrobial usage: days of therapy (DOT), defined daily dose (DDD)

PATIENT OUTCOMES

- Clinical resolution/cure rate
- Length of stay (LOS)
- Morbidity
- 30-day mortality
- Time to discharge
- Re-admission at 30 days
- Patient safety
- Adverse effects (HAI, *C. difficile*, acute kidney injury)
- Quality of life post-care

CONTENTS

BENEFITS OF ANTIMICROBIAL STEWARDSHIP

Figure 1. Goals of antimicrobial stewardship programs (ASPs)
Source: bioMérieux

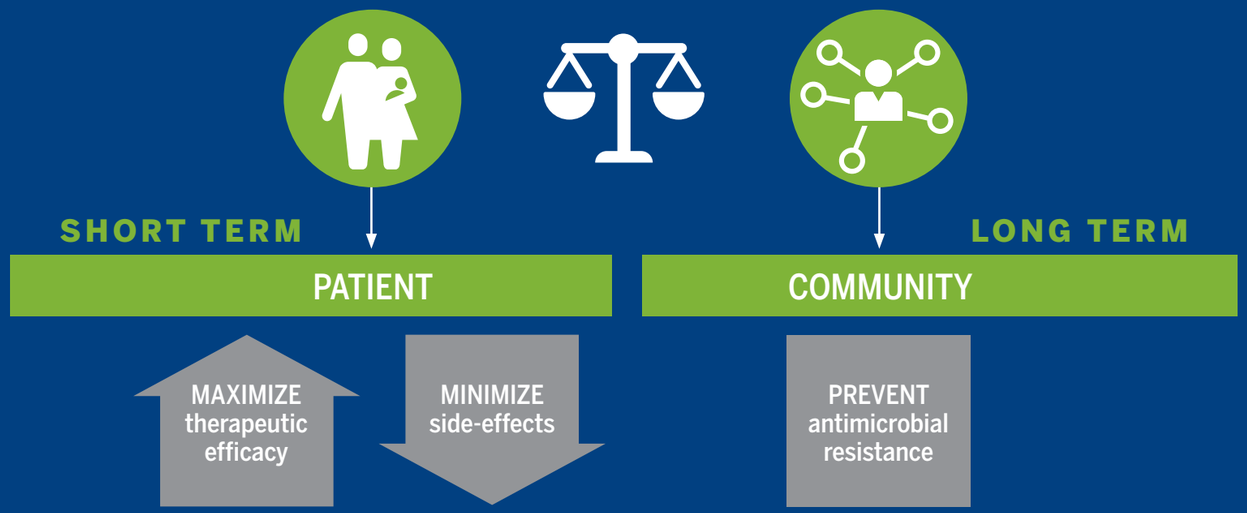
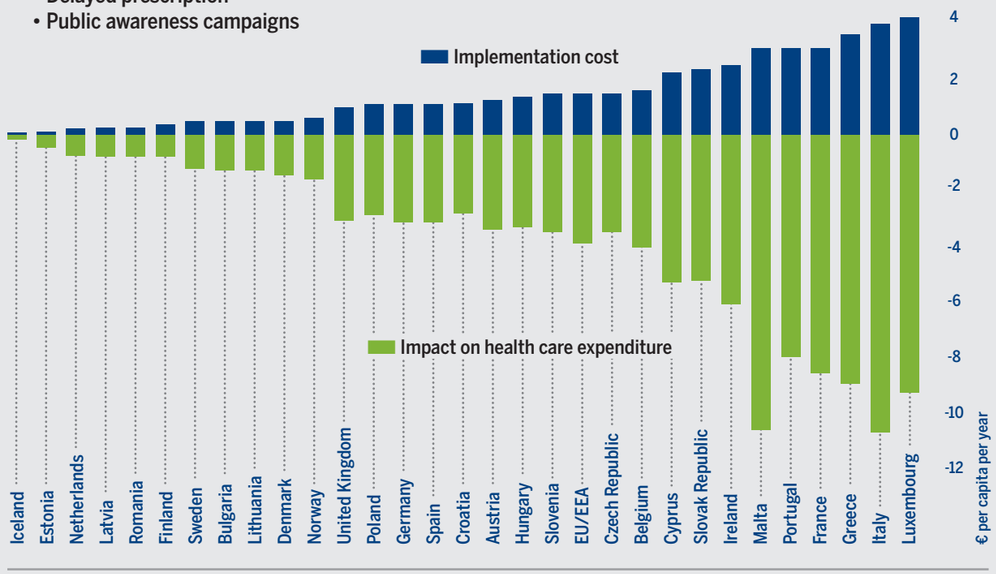


Figure 2. Economic assessment* of the "mixed-intervention" package: just a few euros more produce substantial savings in health care expenditure
Adapted from OECD Policy Brief: Stemming the Superbug Tide: Just a Few Dollars More. 2018

"MIXED-INTERVENTION" PACKAGE:

- **Improve hospital hygiene** (starting with hand hygiene)
- **Antimicrobial stewardship**
- **Rapid diagnostic tests** (bacterial *vs.* viral infection)
- **Delayed prescription**
- **Public awareness campaigns**



* Including effects on susceptible infections.

BENEFITS OF ANTIMICROBIAL STEWARDSHIP

Antimicrobial stewardship (AMS) involves the careful and responsible management of antimicrobial prescribing practices and antibiotic use in hospitals and healthcare settings worldwide.

AMS efforts are generally led by a dedicated multi-disciplinary team which develops and implements an **antimicrobial stewardship program (ASP)**.

The main objective of ASPs is to achieve the prescription of the **most appropriate antimicrobial therapy** with both short-term and long-term goals (**Figure 1**).

- **SHORT-TERM GOAL** improve individual patient outcomes through optimal therapy.
- **LONG-TERM GOAL** support public health and modern medicine by reducing antimicrobial resistance and sustaining the efficacy of existing antibiotics.

Indirectly, appropriate prescribing also **generates cost-savings**, by enabling, for example, shorter length of stay, lower 30-day readmission rates and optimized hospital resource management. Reports[1,2] have demonstrated that investing 1.5 Euros or 2 USD per capita per year in a package of mixed public health measures, would avoid about 27,000 deaths per year in EU/EEA* countries and about 47,000 deaths annually in OECD** countries (**Figure 2**). Furthermore, such a public health package could pay for itself within just one year and end up **saving about 1.4 billion Euros per year in EU/EEA countries**, and **4.8 billion USD per year in OECD countries**.

ASPs positively impact antimicrobial prescribing practices globally, although implementation is more challenging in low- and middle-income countries (LMICs). Investment in basic infrastructure, the development of affordable, rapid diagnostics with more robust systems for their procurement, supply and storage as well as overall quality assurance are essential to successfully implement ASPs in these settings.

The publications in this section demonstrate how antimicrobial stewardship programs improve patient safety and outcomes, decrease antimicrobial resistance and generate cost-savings. The specific challenges and levers for action in LMICs are also addressed in a review by Cox *et al*.[3]

* EU/EEA: European Union/European Economic Area
** OECD: Organisation for Economic Co-operation and Development
1. OECD/ECDC Briefing Note for EU/EAA Countries. 2019 Antimicrobial Resistance: Tackling the Burden in the European Union.
2. OECD Policy brief. 2018 Stemming the Superbug Tide: Just a Few Dollars More.
3. Cox JA, *et al*. Antibiotic stewardship in low- and middle-income countries: the same but different? *Clinical Microbiology and Infection* 2017;23:812-818

THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES
2019;357(2):103-110

Impact of Delayed Appropriate Antibiotic Therapy on Patient Outcomes by Antibiotic Resistance Status from Serious Gram-negative Bacterial Infections.

Bonine NG, Berger A, Altincatal A, Wang R, Bhagnani T, Gillard P, Lodise T.

OBJECTIVE

This study consisted of the retrospective analysis of a large in-patient hospital database to assess the clinical and economic burdens associated with delayed receipt of appropriate therapy among patients with serious infections caused either by resistant or susceptible gram-negative bacteria (GNB).

STUDY DESIGN

This analysis studied data from the Premier Hospital Database from over 56,000 patients treated in 150 hospitals throughout the United States. The study population included adult patients admitted from July 2011 to September 2014 with evidence of complicated urinary tract infection, complicated intra-abdominal infection, hospital-associated pneumonia, or bloodstream infection who also had (1) a positive culture for gram-negative bacteria from a site consistent with the infection type and (2) a length of stay (LOS) of ≥1 day. Patients were divided into two groups based on the antibiotic resistance status of the infecting pathogen (resistant or susceptible).

The group with GNB-resistant infections included patients showing evidence of infection with one or more of the following pathogens: carbapenem-resistant *Enterobacterales* (CRE), carbapenem-resistant *Pseudomonas* sp, multidrug-resistant *P. aeruginosa* and extended spectrum beta-lactamase producing *Enterobacterales.*

Therapy was defined as timely and appropriate when used antibiotics had relevant microbiological activity (matching identification and susceptibility based on culture) and were administered within 2 days of the index date. Delayed appropriate therapy was defined when antibiotics with relevant microbiological activity were administered beyond 2 days of the index date.

RESULTS

A total of 56,357 patients with GNB infections were included in the analysis: 6,055 with infections caused by resistant GNB and 50,302 with infections caused by susceptible GNB.

Delayed appropriate therapy was received by 2,800 patients out of 6,055 (46.2%) with resistant infections and 16,585 patients out of 50,302 (33.0%) with susceptible infections **(Table 1)**.

When compared to timely therapy, delayed appropriate therapy was associated with:

- longer duration of antibiotic therapy: +4.5 days and +4.9 days, respectively, for patients with resistant infections and those with susceptible infections;
- longer LOS: +4.9 days and +5.5 days, respectively;
- higher hospital costs: $11,508 and $9,507, respectively;
- higher risk of in-hospital mortality or discharge to hospice: an increase of 16% and 24%, respectively;
- less likelihood of discharge to home: a decrease of 31% and 35%, respectively.

CONCLUSIONS

Firstly, these study findings show that delays in delivering appropriate therapy are linked to worse clinical and economic outcomes among patients with gram-negative infections, regardless of resistance status.

Secondly, ensuring timely initial therapy has a greater influence on clinical and economic outcomes than does the difference between the resistant or susceptible status of the pathogen.

Thirdly, the negative impact of delayed appropriate therapy was similar on outcomes of both resistant and susceptible infections. Consequently, this study also highlights the importance of rapid pathogen identification to prescribe the appropriate antibiotic(s) as early as possible in the treatment pathway.

Diagnostics play a key role in the prescription of responsible appropriate antibiotic therapy, contributing to optimized patient outcomes and cost savings. Once identification and susceptibility data are available, physicians can streamline therapy and minimize the duration of broad-spectrum antibiotics use to reduce growing antimicrobial resistance and sustain antibiotic efficacy.

ANTIMICROBIAL STEWARDSHIP – PATIENT OUTCOME BENEFITS

Table 1. Association of delayed appropriate therapy *vs.* timely appropriate therapy with infection-related outcomes.
Adapted from Bonine NG, *et al. The American Journal of the Medical Sciences* 2019;357(2):103-110

Outcome[a]	Serious infections due to resistant pathogens (CRE, CRP, MDRP or ESBL)		Serious infections due to susceptible pathogens	
	Delayed appropriate therapy (n=2,800)	Timely appropriate therapy (n=3,255)	Delayed appropriate therapy (n=16,585)	Timely appropriate therapy (n=33,717)
Mean (95% CI) duration of antibiotic therapy, days	12.7 (12.4-13.0)[b]	8.2 (8.0-8.4)	11.3 (11.2-11.4)[b]	6.4 (6.4-6.5)
Mean (95% CI) LOS, days	13.6 (13.3-14.0)[b]	8.7 (8.5-9.0)	12.1 (12.0-12.2)[b]	6.6 (6.5-6.6)
Mean (95% CI) total in-hospital costs to hospital to render care, $	32,518 (31,491-33,579)[b]	21,010 (20,348-21,695)	21,852 (21,648-22,058)[b]	12,345 (12,231-12,460)
Multivariate OR (95% CI)				
Discharged home	0.7 (0.6-0.8)		0.7 (0.6-0.7)	
In-hospital death or discharged to hospice	1.2 (1.1-1.3)		1.2 (1.2-1.3)	

CI, confidence interval; CRE, carbapenem-resistant *Enterobacterales*; CRP, carbapenem-resistant *Pseudomonas* sp; ESBL, extended spectrum beta-lactamase producing *Enterobacterales*; LOS, length of stay; MDRP, multi-drug-resistant *Pseudomonas* sp; OR, odds ratio.

[a] All values were estimated from the index date to discharge; in all instances, reference group was patients who received timely appropriate therapy. Each outcome was adjusted for variables that were included in the inverse probability weighting: age, Charlson Comorbidity Index score, preindex LOS, resource intensity cost index, complicated urinary tract index, complicated intra-abdominal infection index, admission type, sex, asthma, congestive heart failure, chronic pulmonary disease, myocardial infarction+coronary heart disease, hemiplegia/paraplegia, immunocompromising conditions, cancer, malnutrition, peripheral vascular disease, chronic renal disease, type diabetes, community-acquired infection *vs.* other source of infections, healthcare-associated infection, nosocomial infection, culture drawn in the intensive care unit, infection-related hospitalizations in prior 3 months.

[b] $p<0.01$

"Results of these analyses therefore suggest that better methods of early pathogen identification can reduce time to appropriate therapy, thereby improving outcomes and reducing in-hospital costs among hospitalized patients with serious infections due to gram-negative bacteria."

KEY FINDINGS

- **Incidence of delayed appropriate therapy for adult patients hospitalized for serious GNB infections is relatively high in both antibiotic-susceptible and antibiotic-resistant cases.**
- **In both cases, outcomes for patients with GNB infections improve significantly when timely appropriate therapy is provided.**
- **Improved early pathogen identification methods (diagnostics) make it possible to reduce time to appropriate therapy, contributing to lower costs and better outcomes for patients at risk for serious GNB infections.**

LANCET INFECTIOUS DISEASES
2017;17(9):990-1001

Effect of antibiotic stewardship on the incidence of infection and colonisation with antibiotic-resistant bacteria and *Clostridium difficile* infection: a systematic review and meta-analysis.

Baur D, Gladstone BP, Burkert F, Carrara E, Foschi F, Döbele S, Tacconelli E.

OBJECTIVE

The goal of this study was to determine the effectiveness of antibiotic stewardship programs (ASPs) to reduce the incidence of infections and colonization with antibiotic-resistant bacteria and *C. difficile* infections among hospitalized patients.

STUDY DESIGN

The authors undertook a systematic review and meta-analysis of evidence of the effect of ASPs among hospital inpatients. They performed a search of PubMed, the Cochrane Database of Systematic Reviews, the Cochrane Central Register of Controlled Trials, and Web of Science for studies published between January 1960 and May 2016.

The primary outcome was the difference in the incidence ratio (IR) of bacterial colonization or infection per 1,000 patient-days following implementation of ASPs. Bacterial species evaluated included targeted antibiotic-resistant bacteria (colonization or infection) and *C. difficile* (infection).

To determine the types of measures that were most effective in inpatient settings, the study also looked at different care settings, different types of antibiotic stewardship initiatives, and what happened when ASPs were combined with various infection-control interventions.

RESULTS

A total of 32 studies were included in the meta-analysis, representing 9,056,241 patient days and 159 estimates of IR. The studies were conducted in 20 countries between 1992 and 2014.

The findings showed that implementing ASPs in hospital settings led to reduced IR of infection and colonization with antibiotic-resistant bacteria and *C. difficile* infections **(Table 1)**. Specifically, antibiotic stewardship was associated with:

- 51% reduction in the incidence of infection and colonization with multidrug-resistant gram-negative bacteria (MDR GNB);
- 48% reduction in the incidence of extended-spectrum β-lactamase (ESBL)-producing GNB;
- 37% reduction in the incidence of methicillin-resistant *Staphylococcus aureus* (MRSA) infections;
- 32% reduction in the incidence of *C. difficile* infections.

No significant reduction was observed in the incidence of vancomycin-resistant enterococci, nor of quinolone- or aminoglycoside-resistant GNB.

Antibiotic stewardship programs were more effective at reducing antibiotic resistance when combined with other infection-control measures than when used alone. The measure with the greatest impact was hand hygiene (IR reduced by 66%). Other effective measures included antibiotic cycling (51% reduction), audit with feedback (34% reduction), and restricting specific antibiotics (23% reduction). The impact of such interventions generally increased over time.

CONCLUSIONS

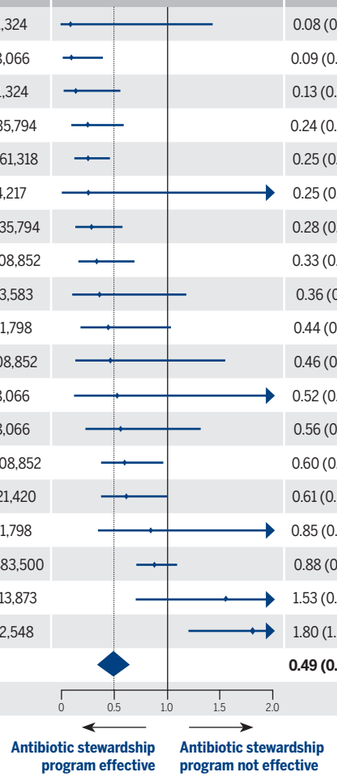
Antibiotic stewardship programs have been shown to reduce antibiotic use and hospital costs. In this study, they are also associated with a significant reduction in the incidence of infections and colonization with antibiotic-resistant bacteria and *C. difficile* infections. The greatest impact observed in this analysis was the reduced incidence of MDR GNB.

For stakeholders responsible for designing new antibiotic stewardship programs, this study highlights the value of combining such programs with infection-control measures, especially those to promote hand hygiene. The findings indicate that combined interventions have the strongest impact to reduce the burden of antibiotic-resistant bacteria.

ANTIMICROBIAL STEWARDSHIP – PUBLIC HEALTH BENEFITS

Table 1. Forest plot of the incidence ratios for studies of the effect of antibiotic stewardship on the incidence of MDR GNB.
Adapted from Baur D, *et al. Lancet Infectious Diseases* 2017;17(9):990-1001

	MDR GNB	Events/patient-day		Incidence ratio (95% CI)
		Before	After	
Apisarnthanarak *et al.*	MDR *Pseudomonas aeruginosa*	13/2,889	1/1,324	0.08 (0.00–1.41)
Marra *et al.*	Imipenem-resistant *Acinetobacter baumannii*	23/8,421	2/8,066	0.09 (0.02–0.39)
Apisarnthanarak *et al.*	XDR *A baumannii*	33/2,889	2/1,324	0.13 (0.03–0.55)
Takesue *et al.*	Metallo-β-lactamase GNB	27/698,794	6/635,794	0.24 (0.10– 0.59)
Cook and Gooch	Carbapenem-resistant *P aeruginosa*	44/220,474	13/261,318	0.25 (0.13–0.46)
Peto *et al.*	MDR *P aeruginosa*	2/4,280	1/4,217	0.25 (0.01–5.63)
Takesue *et al.*	MDR GNB	39/698,794	10/635,794	0.28 (0.14–0.56)
Arda *et al.*	Meropenem-resistant *Acinetobacter* spp	28/285,606	10/308,852	0.33 (0.16–0.68)
Leverstein-van Hall *et al.*	MDR Enterobacteriaceae	9/19,142	4/23,583	0.36 (0.11–1.17)
Yeo *et al.*	Carbapenem-resistant *P aeruginosa*	17/20,469	8/21,798	0.44 (0.19–1.02)
Arda *et al.*	Meropenem-resistant *P aeruginosa*	8/285,606	4/308,852	0.46 (0.14–1.54)
Marra *et al.*	Imipenem-resistant *Klebsiella pneumoniae*	6/8,421	3/8,066	0.52 (0.13–2.09)
Marra *et al.*	Imipenem-resistant *P aeruginosa*	15/8,421	8/8,066	0.56 (0.24–1.31)
Arda *et al.*	Meropenem-resistant *A baumannii*	45/285,606	29/308,852	0.60 (0.37–0.95)
Meyer *et al.*	Imipenem-resistant *P aeruginosa*	34/13,502	33/21,420	0.61 (0.38–0.99)
Yeo *et al.*	Carbapenem-resistant *A baumannii*	10/20,469	9/21,798	0.85 (0.34–2.08)
Zou *et al.*	Meropenem-resistant *P aeruginosa*	185/834,560	172/883,500	0.88 (0.71–1.08)
Niwa *et al.*	Imipenem-resistant *P aeruginosa*	11/128,146	15/113,873	1.53 (0.70–3.34)
Aubert *et al.*	Imipenem-resistant *P aeruginosa*	49/5,100	44/2,548	1.80 (1.20–2.70)
Overall				**0.49 (0.35–0.68)**
I^2=76·2%, p=0·000				



CI, confidence interval; MDR GNB, multidrug-resistant gram-negative bacteria; XDR, extensively drug-resistant

"...our meta-analysis shows that antibiotic stewardship programmes have an essential role in combating the development of antibiotic resistance, especially for MDR gram-negative bacteria, and emphasizes the importance of promoting antimicrobial stewardship programmes at the hospital level to reduce the spread of antibiotic-resistant bacteria among the inpatient population."

KEY FINDINGS

- This study showed the following public health impact of antibiotic stewardship programs:
  - 51% reduction in the incidence of infections and colonization with MDR GNB,
  - 32% reduction in the incidence of *C. difficile*.
- Combining antibiotic stewardship programs with other interventions (infection control, especially hand hygiene) has the greatest impact on reducing antibiotic resistance.

ANTIMICROBIAL RESISTANCE AND INFECTION CONTROL
2019;8:35

Value of hospital antimicrobial stewardship programs [ASPs]: a systematic review.

Nathwani D, Varghese D, Stephens J, Ansari W, Martin S, Charbonneau C.

OBJECTIVE

Hospital antimicrobial stewardship programs (ASPs) are primarily designed to improve patient outcomes and safety, and promote appropriate antimicrobial prescribing to fight antimicrobial resistance (AMR). Demonstrating the cost-effectiveness of such a program is, however, also an important factor to ensure adoption and implementation of ASPs. This systematic review aimed to assess the economic and clinical impact of ASPs.

STUDY DESIGN

The study took as its starting point a previous systematic literature review conducted by J-W Dik *et al*., providing an assessment of methods used for published economic evaluations of hospital ASP studies, 2000-2014.

For the present study, the authors conducted a systematic review on Embase and Medline, using the same framework used by Dik *et al*., and limiting their review to primary research studies from September 2014 to December 2017. Following ASP implementation, various criteria were evaluated, including length of stay (LOS), antimicrobial costs and total hospital costs (including ASP implementation and operational costs).

RESULTS

A total of 146 primary research studies were reviewed, originating from North America (49%), Europe (25%) and Asia (14%). A majority of the studies were conducted in hospitals with 500 to 1,000 beds.

Overall, after implementation of ASPs, 92% of studies showed a reduction of antibiotic costs, and 85% a reduction in LOS. LOS was the key driver of cost savings. The mean cost reduction varied by hospital size and geographic region. Hospitals with comprehensive ASPs, including therapy review and antibiotic restrictions, reported higher cost savings.

Outcomes were classified into three categories:

- **ANTIMICROBIAL OUTCOMES**
  - 68% of relevant studies reported changes in antibiotic use, including defined daily dose, days of therapy, and proportion of patients on antimicrobial treatment.
  - Overall antibiotic use decreased in most studies.
  - 61% of the 18 statistically-significant studies measuring antimicrobial resistance found a significant change in AMR post-ASP implementation after a mean interval period of 24 months.
- **PATIENT OUTCOMES**
  - 85% of studies saw a reduction or no change in LOS, ranging from 0 to 22 days after ASP implementation. An average decrease in LOS or 3.24 days or 20.6% per patient following ASP intervention was noted for statistically significant studies.
  - 10.5% and 11.3% decreases in all-cause mortality rates and infection-related mortality rates, respectively, were observed.
- **ECONOMIC OUTCOMES**
  - Antibiotic expenditure: 97% of studies showed a decrease in antimicrobial costs, averaging 36%.
  - LOS costs: all studies documenting this point showed reductions ranging from $18,300 in a small hospital to €93,000 and $2,000,000 for 2 large-sized hospitals.
  - Overall aggregated hospital costs associated with patient treatment for bacterial infection, typically including LOS, diagnostics, treatment, and ASP costs were documented in 1/3 of all studies (49) and all generated cost savings.
  - Cost savings averaged $435,000 (range: $9,110 to $2 million) per year for the hospital, or $732 per patient (range: $2.50 to $2,640) in studies measuring costs in USD.
  - Cost savings averaged €41,500 (range: €19,000 to €66,200) per year for the hospital, or €198 (range: €40 to €529) per patient for data in EUR. In particular, in Europe the proportion of a bed stay saved through ASP represents 60-80% of the cost of a bed stay **(Table 1)**.
  - Higher cost savings were generated at hospitals implementing comprehensive ASPs with therapy review and antibiotic restrictions.

ANTIMICROBIAL STEWARDSHIP – ECONOMIC BENEFITS

CONCLUSIONS

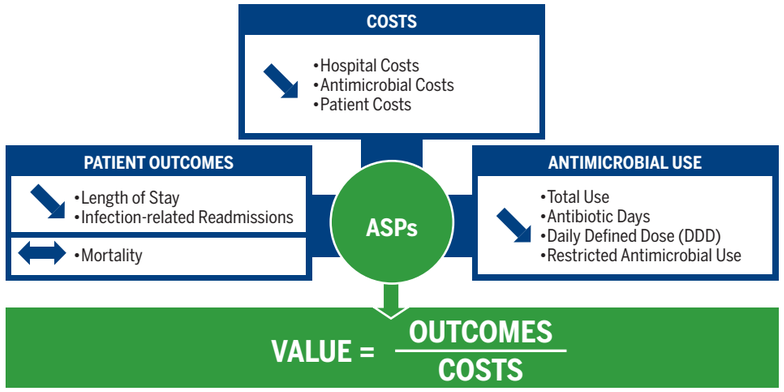
The economic and clinical value of hospital antimicrobial stewardship programs is supported by this systematic review, which analyzes specific beneficial health outcomes achieved per dollar spent **(Figure 1)**. The review indicates that the cost of implementing ASPs can be offset by subsequent savings. For a full critical appraisal of the value of ASPs, more research is needed, in particular real-world studies in diverse resource settings and geographies.

Table 1. Cost savings compared with bed day costs around the world.
Adapted from Nathwani D, *et al*. *Antimicrobial Resistance and Infection Control* 2019;8:35

	United States	European Union	United Kingdom
Annual Per Patient Cost Savings with ASP	$732.00	€198.00	£304.00
Average Hospital Bed Day Cost, 2015	$2,271 [2]	€328.64 [154, 155][a]	£375.86 [154, 155][a]
Estimated Cost Offset as a Bed Day Saved Annually	32%	60%	80%

[a]Original WHO 2008 costs in US$ were inflated to 2015 costs and converted to Euro or Pound Sterling

Figure 1. Value framework for ASP implementation.
Adapted from Nathwani D, *et al*. *Antimicrobial Resistance and Infection Control* 2019;8:35



" The findings [...] suggest that costs associated with start-up and implementation of ASPs are potentially offset by subsequent cost-savings."

KEY FINDINGS

Economic benefits of ASP interventions:

- 85% of relevant studies showed a decrease in LOS (3.24 days on average). Shorter LOS was a key driver in cost savings.
- 92% of relevant studies showed a decrease in spending on antimicrobials. Cost savings were higher in hospitals with comprehensive ASPs focused on therapy review and antibiotic restrictions.
- Mean cost savings in the US were $435,000 per hospital per year.
- Initial investment in an ASP can be paid off by the cost-savings generated.

CLINICAL MICROBIOLOGY AND INFECTION
2017;23:812-818

Antibiotic stewardship in low- and middle-income countries: the same but different?

Cox JA, Vlieghe E, Mendelson M, Wertheim H, Ndegwa L, Villegas MV, Gould I, Levy Hara G.

OBJECTIVE

Antimicrobial stewardship (AMS) is a cornerstone of the World Health Organization's global action plan to combat antimicrobial resistance. It is widely recognized that global collaborative action is needed across all resource settings to tackle the problem. To date, most studies on AMS have been performed in high-income settings, however, many LMICs are in the process of developing antimicrobial stewardship programs (ASPs). This review set out to identify the main challenges for AMS initiatives in LMICs, highlight examples of effective interventions and identify key actions for progress.

STUDY DESIGN

In this review, the authors searched PubMed for articles on AMS interventions in LMICs, published in English or Spanish within the last 5 years. Relevant websites and experts were consulted for additional sources.

RESULTS

The main challenges identified included:

- diagnostic capabilities with limited availability of clinical microbiology laboratories, and lack of basic infrastructure, materials, well-trained staff, standard operating procedures and quality control systems;
- limited use of rapid, point-of-care diagnostics, largely due to cost factors and short shelf-lives;
- insufficient level of knowledge and awareness of antimicrobial resistance and optimal antibiotic use among medical students and healthcare workers;
- lack of local high-level evidence and experience in developing evidence-based guidelines;
- access to quality-assured antibiotics, with a double challenge of limited access to essential quality antibiotics and widespread poorly-regulated over-the-counter availability of antibiotics, including sub-standard or counterfeit products;
- healthcare facilities, facing lack of basic infrastructure and equipment, shortage of qualified staff and high turnover, and large patient numbers.

The review cites impactful benefits of national AMS initiatives and action plans, as well as effective ASP interventions in both hospital-based and primary care/community settings in a large number of LMICs.

The authors also identified a number of strategic actions which could be progressively addressed, notably:

- ensuring availability of diagnostic testing;
- providing dedicated education on antibiotic resistance for healthcare workers and the public;
- creating or strengthening (inter)national agencies towards better regulations and audit on production, distribution and dispensing of drugs;
- strengthening healthcare facilities;
- exploring broader synergy between policy makers, academia, professional bodies and civil society;
- designing and studying easy and scalable AMS interventions for both hospital and community settings.

CONCLUSIONS

Although many implementation challenges remain, and published evidence on effective AMS interventions in LMICs is limited, ASPs are demonstrated to be feasible and effective in LMICs (see selected examples opposite).

ANTIMICROBIAL STEWARDSHIP – BENEFITS FOR LMICs

Table 1. Selected examples of benefits of national AMS initiatives, hospital-based ASPs and community healthcare initiatives.
Adapted from Cox JA, *et al. Clinical Microbiology and Infection* 2017;23:812-818

COLOMBIA	SOUTH AFRICA	VIETNAM	KENYA
A Nosocomial Resistance network, covering 32 hospitals in 11 cities, introduced actions such as surveillance reporting on resistance patterns to each hospital every six months, together with antibiotic treatment suggestions and outbreak analyses. These recommendations enable regular updates of antibiotic guidelines and comparison over time.	Measures including audit and feedback for complex patients and restricted use of certain antibiotics were introduced by AMS and IPC specialists in a university hospital. The measures led to a sustainable drop in total antibiotic consumption, significant cost savings (215,000 USD over 4 years) with no significant changes in mortality or 30-day readmission rates.	Patients with acute respiratory tract symptoms in ten urban and rural community healthcare centers were randomly assigned to a point-of-care testing group *vs.* standard care group. Use of POC testing to guide treatment decisions less to less antibiotic use within 14 days after presentation: 64% *vs.* 78% in standard care group.	A program was introduced in a rural hospital to reduce overprescribing of antibiotic injections by switching from IV to oral metronidazole in the medical and surgical wards. Education on medical record documentation, good antibiotic prescribing practices and a checklist were given to clinicians, together with twice-weekly ward rounds with a pharmacist. This resulted in improved documentation and an increase in oral metronidazole use, helping to reduce costs, patient discomfort and iatrogenic infections.

"... several initiatives at the international and local levels in Latin America, Africa and Asia have shown that AMS [antimicrobial stewardship] effective interventions are feasible in LMICs, although contextualization is essential."

KEY FINDINGS

- Effective antimicrobial stewardship initiatives are feasible in LMICs.
- Benefits of ASPs are illustrated in multiple examples of national, hospital-based and community initiatives.
- There is an on-going need to develop specific guidance for setting up ASPs in LMICs.

ROLE OF DIAGNOSTICS IN ANTIMICROBIAL STEWARDSHIP

Figure 1. Role of diagnostics to support responsible antibiotic prescribing
Adapted from Messacar *et al*. *Journal of Clinical Microbiology* 2017;55:715-723

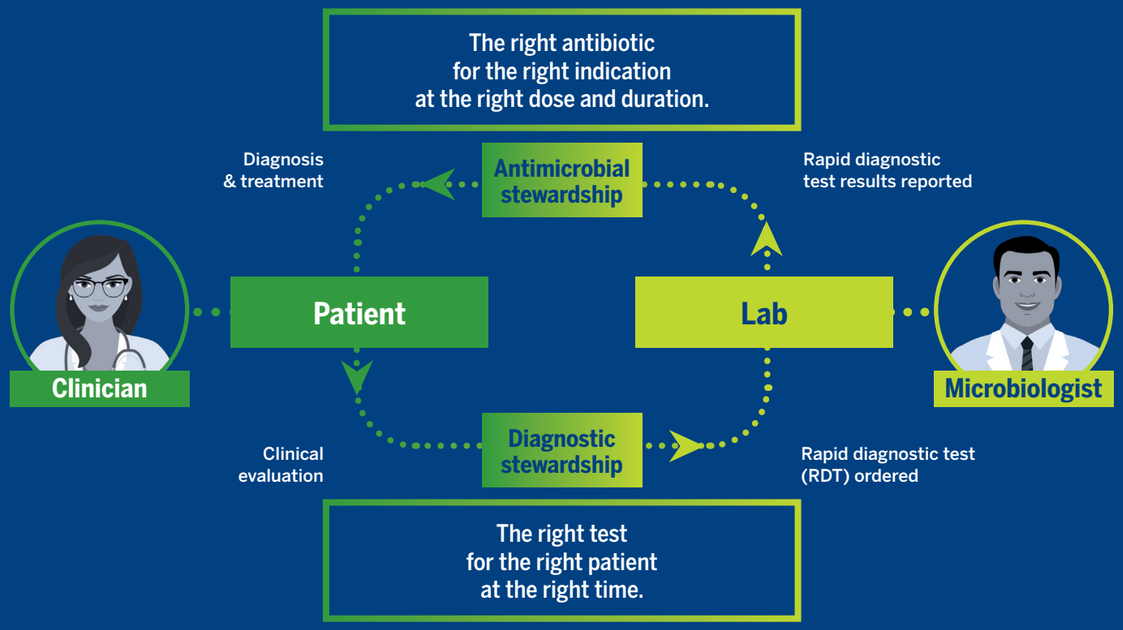


Figure 2. How Rapid Diagnostics Optimize Treatment
Adapted from O'Neill *et al*. *The Review on Antimicrobial Resistance.* 2015

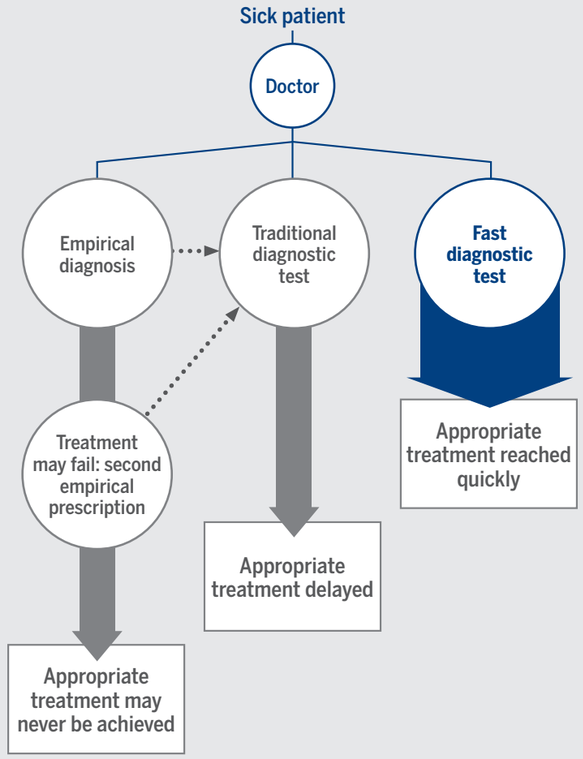
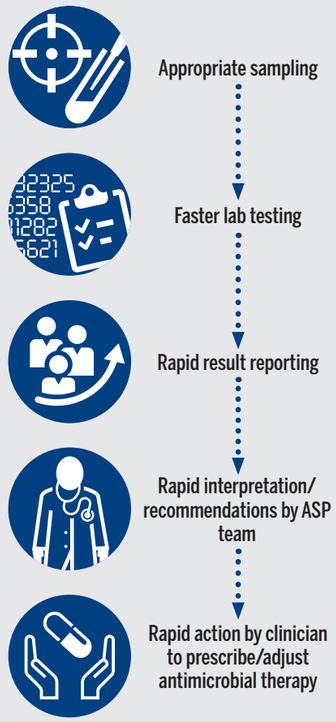


Figure 3. The "Optimal Equation" for appropriate antimicrobial prescribing
Source: bioMérieux



ROLE OF DIAGNOSTICS IN ANTIMICROBIAL STEWARDSHIP

Diagnostic tests are instrumental for antimicrobial stewardship programs (ASPs), and have a decisive impact on clinical decision-making and patient care. They enable clinicians and pharmacists to more accurately tailor appropriate antibiotic therapy to maximize patient health outcomes.

To combat antimicrobial resistance and support antimicrobial stewardship efforts, diagnostics can play a key role on 2 different levels:

- 1. For the optimal diagnosis and appropriate management of a patient,
- 2. For the benefit and improvement of Public Health through screening and surveillance of antimicrobial resistance in order to maintain the effectiveness of existing antibiotics.

DETERMINING THE RIGHT TREATMENT FOR THE RIGHT PATIENT AT THE RIGHT TIME

To determine the most appropriate treatment for the patient, the clinician needs timely and accurate diagnostic test results.
The microbiology laboratory plays a crucial role in identifying precisely and rapidly the infectious agent, as well as ensuring its susceptibility to antibiotics, in order to help clinicians prescribe the right treatment at the right time **(Figure 1)**.

IMPROVED PATIENT OUTCOMES DEMAND FASTER RESULTS, REPORTING AND ACTION

Studies[1,2,3] have demonstrated that new fast, accurate and reliable diagnostic technologies enable earlier prescription of responsible, appropriate antimicrobial therapy **(Figure 2)**. Additionally, new digital tools, such as clinical decision support systems (CDSS), can efficiently support the work of the ASP teams.[4]
However, the optimal patient benefits of these new diagnostics can only be achieved if leveraged by an effective ASP team - with rapid reporting and translation of test results into actionable information for clinicians - through an optimized hospital workflow.

This requires a seamless partnership between clinical laboratories, pharmacists, and infectious disease clinicians, so that appropriate tests are ordered, appropriate samples are collected and diagnostic information is translated into appropriate patient management in real time (Figure 3).

The following summary of a publication by Timbrook *et al*. illustrates how appropriate use and management of rapid diagnostics can positively impact appropriate therapy and patient outcomes.[1]

In many low- and middle-income countries **(LMICs)**, however, diagnostic capabilities to support AMS initiatives are still severely lacking and there is an urgent need to develop simplified, affordable and rapid diagnostic tools. Diagnostics need to be better integrated into routine patient management, and clinical microbiologists have a central role to play in strengthening the role of diagnostic laboratories in these settings.[5]

A summary of a Global Point Prevalence Survey in Nigeria reveals the need for a cohesive national ASP as well as increased laboratory testing to guide antimicrobial prescribing.[6]

1. Timbrook TT, *et al*. *Clinical Infectious Diseases* 2017;64(1):15-23
2. Pliakos EE, *et al*. *Clinical Microbiology Reviews* 2018;31(3):e00095-17
3. Beganovich M, *et al*. *Journal of Applied Laboratory Medicine* 2019;3(4):601-616
4. Nault V, *et al*. *Journal of Antimicrobial Chemotherapy* 2016;72:933-940
5. Yusuf E, *et al*. *Clinical Microbiology and Infection* 2019;25:6-9
6. Oduyebo OO, *et al*. *Annals of Tropical Pathology* 2017;8(1):42-46

CLINICAL INFECTIOUS DISEASES
2017;64(1):15-23

The Effect of Molecular Rapid Diagnostic Testing on Clinical Outcomes in Bloodstream Infections: A Systematic Review and Meta-analysis.

Timbrook TT, Morton JB, McConeghy KW, Caffrey AR, Mylonakis E, LaPlante KL.

OBJECTIVE

In bloodstream infections (BSIs), timely administration of appropriate antibiotic therapy is critical to achieve improved clinical outcomes. Yet, reports on molecular rapid diagnostic testing (mRDT) in BSIs have not consistently described improvement in clinical outcomes. In this systematic review and meta-analysis, the authors assessed the impact of mRDT on improvement of BSI clinical outcomes, including time to effective (i.e. appropriate) therapy (TTET), associated or not with an antimicrobial stewardship program (ASP).

STUDY DESIGN

A web search of PubMed, CINAHL, Web of Science, and Embase was performed for studies published through May 2016 assessing outcomes of mRDT *versus* conventional microbial techniques in BSIs.

Eligible studies defined mRDT as commercially available molecular tests providing results in ≤24 hours. Evaluated outcomes included: overall mortality risk, mortality risk in studies with ASPs, mortality risk by organism, TTET and length of stay (LOS). Studies were considered to be ASP-driven if antimicrobial selection was reviewed by an infectious disease physician or pharmacist.

RESULTS

Per search criteria, the meta-analysis extracted data from 31 studies, with a total of 5,920 patients. Most of the studies were from academic medical center settings and adult patients were the most common cohort studied. Gram-positive organisms were the most commonly reported BSI type included (17 studies; 55%).

The types of mRDT technology utilized included PCR or other microarray technologies (65% of studies), PNA-FISH (19%), and MALDI-TOF (13%) analyses. A majority of studies (65%) provided ASP-compliant mRDT-result notification.

Assessment of clinical outcomes in BSIs demonstrated the benefit of mRDT over conventional microbiologic methodology **(Table 1)**. In 26 studies, mortality was significantly lower with mRDT (odds ratio* [OR] 0.66; 95% confidence interval [CI] 0.54-0.80); with a calculated number-needed-to-treat of 20**. In addition:

- mortality was significantly lower for BSIs using mRDT with ASPs (OR 0.64, 95% CI 0.51-0.79); whereas mortality risk without ASPs failed to achieve significance (OR 0.72, 95% CI 0.46-1.12);
- odds of mortality were reduced using mRDT in studies of gram-negative, gram-positive, and multiple organism types (OR 0.58; 95% CI 0.32-1.04).

Among 9 studies, TTET was significantly shorter (by 5 hours) when using mRDT *versus* conventional microbiology, and LOS was reduced by nearly 2.5 days.

CONCLUSIONS

Molecular rapid diagnostic testing was associated with significant decreases in mortality risk in the presence of an ASP in BSIs. In the absence of ASPs, however, no such significance was demonstrated. A decrease in mortality risk was observed in studies that included gram-positive, gram-negative, and multiple organism types. Additionally, mRDT was found to be associated with decreased TTET and LOS. Based on these clinical outcomes, the authors conclude that mRDT should be considered as a component of the standard of care bundle for patients with BSIs.

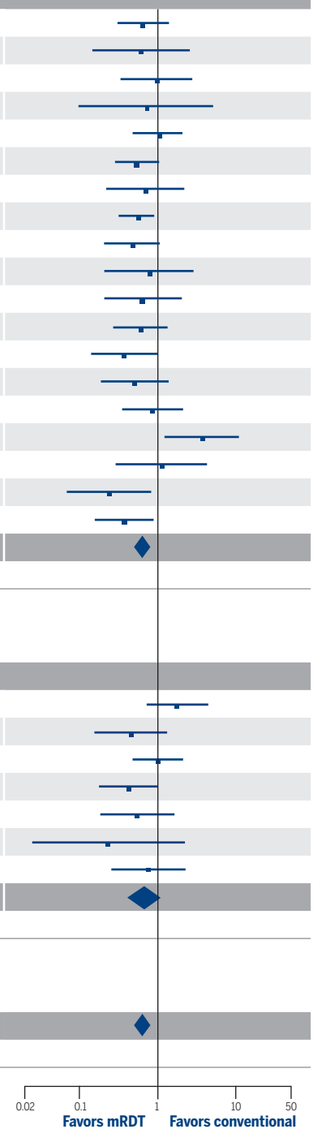
"In conclusion, mRDT was associated with significant decreases in mortality risk in the presence of an ASP, but not in its absence. [...] In addition, mRDT was associated with decreased time to effective therapy and LOS."

* Odds ratios (ORs) were determined with the Mantel-Haenszel random-effects method.
** Number needed to treat of 20 means that twenty patients need to be diagnosed for one to have the expected medical outcome benefit.

RAPID DIAGNOSTICS IN AMS – APPROPRIATE THERAPY

Table 1. Mortality outcomes with mRDT *versus* conventional testing in bloodstream infection.
Adapted from Timbrook TT, *et al*. *Clinical Infectious Diseases* 2017;64(1):15-23

Study or Subgroup	mRDT Events	mRDT Total	Conventional Testing Events	Conventional Testing Total	Weight, %	Odds Ratio M-H, Random, 95% CI
mRDT with ASP						
Bauer 2010	15	82	19	74	5.6%	0.65 [0.30, 1.39]
Bias 2015	3	37	7	55	1.8%	0.61 [0.15, 2.51]
Box 2015	6	64	10	103	3.0%	0.96 [0.33, 2.79]
Forrest 2006 (CoNS)	2	119	2	84	0.9%	0.70 [0.10, 5.08]
Forrest 2006 (Yeast)	19	72	20	76	6.0%	1.00 [0.48, 2.09]
Forrest 2008	17	95	37	129	7.4%	0.54 [0.28, 1.04]
Heil 2012	5	21	19	61	2.7%	0.69 [0.22, 2.16]
Huang 2013	31	245	52	256	11.8%	0.57 [0.35, 0.92]
Lockwood 2016	11	241	14	149	4.9%	0.46 [0.20, 1.04]
Macvane 2015	5	63	5	50	2.1%	0.78 [0.21, 2.84]
Macvane 2016	6	23	16	45	2.8%	0.64 [0.21, 1.95]
Nagel 2014	11	117	19	129	5.3%	0.60 [0.27, 1.32]
Pardo 2016	5	84	37	252	3.6%	0.37 [0.14, 0.97]
Perez 2013	6	107	12	112	3.3%	0.50 [0.18, 1.37]
Revolinski 2015	8	95	13	133	4.0%	0.85 [0.34, 2.14]
Sango 2013	11	28	7	46	2.8%	3.61 [1.19, 10.89]
Sothoron 2015	5	67	4	59	1.9%	1.11 [0.28, 4.34]
Suzuki 2015	3	88	19	147	2.3%	0.24 [0.07, 0.83]
Walker 2016	8	97	19	98	4.3%	0.37 [0.16, 0.90]
Subtotal (95% CI)		**1,745**		**2,058**	**76.5%**	**0.64 [0.51, 0.79]**
Total events	177		331			
Heterogeneity: Tau² = 0.01; Chi² = 19.00, df = 18 (*p*=0.39); I² = 5%						
Test for overall effect: Z = 4.14 (*p*<0.0001)						
mRDT without ASP						
Beuving 2015	14	114	8	109	4.1%	1.77 [0.71, 4.40]
Felsenstein 2016	5	189	11	194	3.0%	0.45 [0.15, 1.33]
Frye 2012	14	110	17	134	5.7%	1.00 [0.47, 2.14]
Ly 2008	8	101	17	101	4.2%	0.43 [0.17, 1.04]
Maslonka 2014	6	55	10	55	2.9%	0.55 [0.19, 1.64]
Neuberger 2008	1	42	4	42	0.7%	0.23 [0.02, 2.17]
Wang 2013	8	48	8	38	2.9%	0.75 [0.25, 2.23]
Subtotal (95% CI)		**659**		**673**	**23.5%**	**0.72 [0.46, 1.12]**
Total events	56		75			
Heterogeneity: Tau² = 0.08; Chi² = 7.74, df = 6 (*p*=0.26); I² = 23						
Test for overall effect: Z = 1.46 (*p*=0.15)						
Total (95% CI)		**2,404**		**2,731**	**100.0%**	**0.66 [0.54, 0.80]**
Total events	233		406			
Heterogeneity: Tau² = 0.02; Chi² = 27.22, df = 25 (*p*=0.34); I² = 8%						
Test for overall effect: Z = 4.27 (*p*<0.0001)						
Test for subgroup differences: Chi² = 0.25, df = 1 (*p*=0.62), I² = 0%						



KEY FINDINGS

- Significantly lower mortality was observed for BSIs when using mRDT in association with ASPs *versus* without ASPs.
- Time to effective therapy decreased by an average 5 hours with mRDT *versus* conventional microbiology, and length of stay decreased by nearly 2.5 days.
- In BSI patients, mRDT should be considered as part of the standard care package.

ANNALS OF TROPICAL PATHOLOGY
2017;8(1):42-46

A Point Prevalence Survey of Antimicrobial Prescribing in Four Nigerian Tertiary Hospitals.

Oduyebo OO, Olayinka AT, Iregbu KC, Versporten A, Goossens H, Nwajiobi-Princewill PI, Jimoh O, Ige TO, Aigbe AI, Ola-Bello OI, Aboderin AO, Ogunsola FT.

OBJECTIVE

The aim of this study was to acquire baseline information about antimicrobial-prescribing practices in Nigeria, a prerequisite to the implementation of a cohesive antimicrobial stewardship program (ASP).

STUDY DESIGN

From April to June 2015, the Global Point Prevalence Survey (Global-PPS) was conducted across all clinical departments at four tertiary hospitals in Nigeria.

Information was collected about the rate and characteristics of antibiotic use including prevalence, types of antibiotics prescribed, treatment indications, quality indicators and compliance with guidelines.

RESULTS

A total of 828 patients were included in the survey, of whom 69.7% received at least one antimicrobial on the day of the Global-PPS.

The most commonly prescribed antibiotics were third-generation antimicrobials, particularly cephalosporins (21.4% of prescriptions) and mainly ceftriaxone (18.9%), followed by metronidazole (18.0%) and quinolones (14.1%), especially ciprofloxacin (9.9%).

Antibiotics were most often prescribed in adult ICUs (88.9%), followed by pediatric medical wards (84.6%) and neonatal ICUs (76.7%). Just over half of prescriptions (51.2%) were based on therapeutic indications; of these, 89.5% were for community-acquired infections.

The survey showed low use of quality indicators:

- compliance with local antibiotic guidelines was 7.1% for medical and 4.1% for surgical indications;
- indication for antibiotic prescription in notes in 61.8% of cases;
- a stop/review date was documented for 27.8% of prescriptions;
- in 95% of cases, surgical prophylaxis was given for more than 1 day.

Use of biomarkers, such as procalcitonin, to guide antibiotic prescribing was very low (0.5%), despite their inclusion in current infection management guidelines. This was partly attributed to availability and cost. The authors highlighted their utility to guide and monitor antibiotic therapy, particularly in patients with severe bacterial infections and suspicion of sepsis.

CONCLUSIONS

The Point Prevalence Survey (PPS) is a popular and widely accepted method that is less expensive, less time-consuming, and easier to conduct than incidence studies, and can be used to identify and assess quality indicators to evaluate antimicrobial prescribing issues. This survey highlighted the need to improve awareness among prescribers of the importance of targeted antimicrobial therapy and the use of evidence-based antibiotic guidelines in Nigeria. Furthermore, it provided evidence that the country needs to institute a cohesive antimicrobial stewardship intervention program.

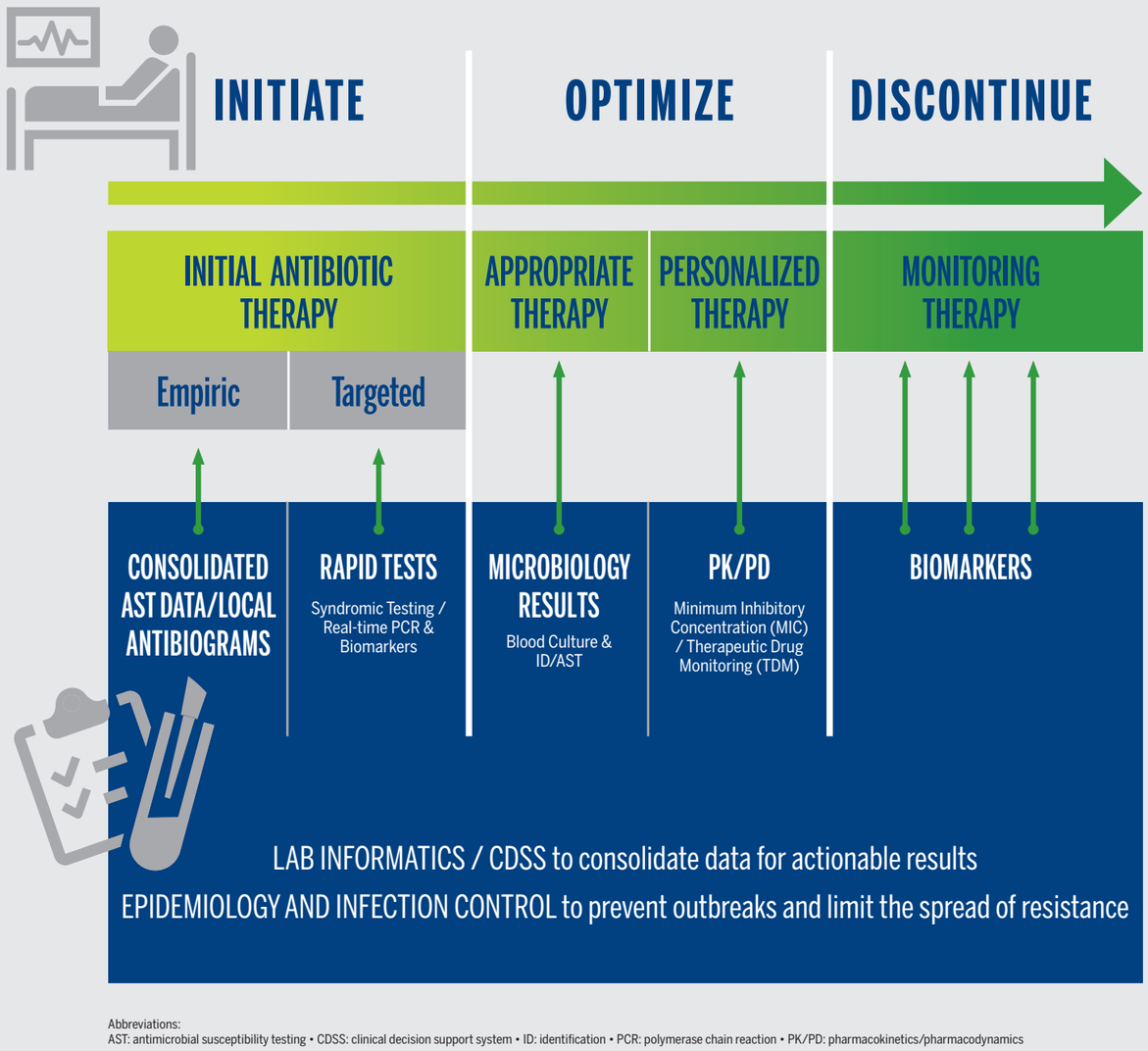
"There is clearly a need to improve prescribing practices in the country by developing evidence-based guidelines, improving laboratories, and retraining prescribers on the importance of definitive or targeted therapy."

KEY FINDINGS

- This Global Point Prevalence Survey represents the first objective pan-hospital antimicrobial prescription evaluation in Nigeria.
- Prevalence of antibiotic prescription in Nigerian hospitals was observed to be high with only about 50% of prescriptions based on clear therapeutic indications.
- Laboratory tests, and biomarkers in particular, remain widely underused, although recommended in guidelines for infection management and appropriate antibiotic prescribing.

EVIDENCE-BASED IMPACT OF DIAGNOSTICS ON ANTIMICROBIAL THERAPY

Figure 1. How diagnostics support the antibiotic prescribing process and optimal patient care
Source: bioMérieux



Abbreviations:
AST: antimicrobial susceptibility testing • CDSS: clinical decision support system • ID: identification • PCR: polymerase chain reaction • PK/PD: pharmacokinetics/pharmacodynamics

EVIDENCE-BASED IMPACT OF DIAGNOSTICS ON ANTIMICROBIAL THERAPY

Diagnostics support clinical decision-making and appropriate antibiotic therapy prescribing along the continuum of patient care, from diagnosis to discharge and from antibiotic initiation to treatment optimization and discontinuation (Figure 1).

INITIATE ANTIBIOTIC THERAPY

KEY MEDICAL QUESTIONS

• Signs and symptoms suggestive of infection? • Is suspected infection likely viral or bacterial?	• What is the site of infection and which are the most common pathogens to be covered?	• Are there severity signs/organ failure? • Are there risk factors for MDROs? • Which antibiotic? Dose and duration?

Diagnostic test results help confirm bacterial origin of the infection and identify the causative pathogen to avoid unnecessary antibiotic use and ensure optimal patient outcomes.

OPTIMIZE ANTIBIOTIC THERAPY

KEY MEDICAL QUESTIONS

• Can I safely de-escalate? • Should I add an antibiotic or an antifungal drug? • Can I stop the treatment ?	• Is there a situation that requires: - a precise MIC? e.g. critical condition, challenging micro-organism, multi-drug resistance, ... - therapeutic drug monitoring (TDM)? e.g. high risk patients with altered pharmaco-kinetics: critical care, obese, organ transplantation, pediatrics and elderly populations	• How can I monitor emerging resistant strains in my ward? • How can I characterize them in order to take infection prevention actions?

Diagnostic test results determine a pathogen's susceptibility profile to select the most appropriate treatment, limit use of broad-spectrum antibiotics and avoid adverse side effects.

DISCONTINUE ANTIBIOTIC THERAPY

KEY MEDICAL QUESTIONS

• Can I safely stop antibiotic therapy and reduce selection pressure?	• Should I reconsider my treatment?

Diagnostic test results help monitor the patient's response to personalized treatment duration and support safe discontinuation of antibiotic therapy as early as possible.

The publications summarized in the following sections demonstrate the high medical value of diagnostics to reinforce clinical decision-making and support clinicians in their therapeutic choice.

INITIATION OF ANTIBIOTIC THERAPY

LANCET INFECTIOUS DISEASES
2018;18:95-107

Effect of Procalcitonin-Guided Antibiotic Treatment on Mortality in Acute Respiratory Infections: A Patient Level Meta-Analysis.

Schuetz P, Wirz Y, Sager R, Christ-Crain M, Stolz D, Tamm M, Bouadma L, Luyt CE, Wolff M, Chastre J, Tubach F, Kristoffersen KB, Burkhardt O, Welte T, Schroeder S, Nobre V, Wei L, Bucher HC, Annane D, Reinhart K, Falsey AR, Branche A, Damas P, Nijsten M, de Lange DW, Deliberato RO, Oliveira CF, Maravić-Stojković V, Verduri A, Beghé B, Cao B, Shehabi Y, Jensen JS, Corti C, van Oers JAH, Beishuizen A, Girbes ARJ, de Jong E, Briel M, Mueller B.

OBJECTIVE

This meta-analysis comprehensively assessed the safety of procalcitonin-guided treatment in patients with acute respiratory infections (ARIs) in primary care, intensive care, surgical intensive care, or emergency department settings.

STUDY DESIGN

The analysis combined data from 6,708 patients enrolled in 26 separate randomized controlled trials in which patients with respiratory infections were randomly assigned to either a PCT-guided antibiotic treatment group or a control group. The meta-analysis relied on individual patient data rather than aggregated patient data, which allowed for harmonization of outcomes definitions. The primary endpoints were 30-day mortality and setting-specific treatment failure, secondary endpoints were antibiotic exposure, side-effects and length of stay.

RESULTS

The analysis demonstrated significant improvements in patient outcomes for the PCT-guided treatment group. Mortality at 30 days was significantly lower (9% *vs.* 10%, p=0.037), and antibiotic related side effects were significantly reduced (16% *vs.* 22%, p<0.0001) in PCT-guided patients compared to control patients. Mean total antibiotic exposure was also significantly lower in the PCT-guided group (5.7 days *vs.* 8.1 days, p<0.0001). Treatment failure, as specifically defined for each clinical setting, was less frequent in the PCT-guided patients, but not significantly (23.0% *vs.* 24.9%, p=0.068). Mean total antibiotic exposure was significantly lower in the PCT-guided group (5.7 days *vs.* 8.1 days, p<0.0001) and, side-effects were also lower (16% *vs.* 22%, p<0.001). No significant differences in length of hospital stay or ICU stay were observed between the two groups.

CONCLUSIONS

This meta-analysis found that implementation of PCT-guided protocols in patients with ARIs led to positive effects on clinical outcomes and reduced antibiotic exposure. Given these positive findings, and the increasing threat of multi-drug resistance, this report strengthens the rationale to use procalcitonin to support antibiotic stewardship decisions in patients with ARIs.

"... [This patient-level meta-analysis] is the first report to describe significant and relevant improvements in clinical outcomes and specifically a decreased risk for mortality for patients with acute respiratory infections, when procalcitonin was used to guide antibiotic treatment decisions."

KEY FINDINGS

- This study demonstrates for the first time that PCT-guided treatment significantly improved clinical outcomes in patients with ARIs from different clinical settings.
- PCT-guided treatment was associated with:
  - a decreased risk of mortality (9% *vs.* 10%),
  - reduced antibiotic exposure (5.7 days *vs.* 8.1 days),
  - fewer antibiotic-related side effects compared to treatment without PCT guidance (16% *vs.* 22%).
- The meta-analysis described in this paper is the basis for a Cochrane Systematic Review (Schuetz P, *et al.* Cochrane Database Syst Rev. 2017;10(10):CD007498) which concluded that the quality of the evidence for the mortality and antibiotic exposure outcomes was high.

CLINICAL CHEMISTRY AND LABORATORY MEDICINE
2018;56(8):1200-1209

Procalcitonin guidance in patients with lower respiratory tract infections: a systematic review and meta-analysis.

Hey J, Thompson-Leduc P, Kirson NY, Zimmer L, Wilkins D, Rice B, Iankova I, Krause A, Schonfeld SA, DeBrase CR, Bozzette S, Schuetz P.

OBJECTIVE

This study was conducted to summarize existing evidence on the safety and efficacy of PCT guidance in adult patients with lower respiratory tract infections (LRTI), comprising acute bronchitis, exacerbations of chronic obstructive pulmonary disease (COPD), and pneumonia.

STUDY DESIGN

As part of a regulatory submission to the US FDA, a systematic review and meta-analysis of randomized controlled trials of PCT-guided therapy *versus* standard of care was performed. Eleven English-language papers evaluating PCT use in this population and published between 2004 and 2016 were included.

In the PCT-guided treatment arm of these studies, physicians used both clinical judgment and PCT values when deciding whether to initiate and when to discontinue antibiotic use. To evaluate the effectiveness of PCT in guiding antibiotic (AB) therapy among adults with LRTI compared to standard care, the study examined the proportion of patients initiating ABs and length of AB treatment. Safety was measured by length of hospital stay (LOS) and all-cause mortality.

RESULTS

When compared to patients treated according to standard care, patients whose treatment was guided by PCT had lower odds of initiating AB treatment (odds ratio [OR]: 0.26, 95% confidence interval [CI]: 0.13 ; 0.52); and fewer days of AB use (weighted mean difference [WMD]: -2.15 days, 95% CI: -3.30 ; -0.99). Patients in the PCT arm did not have a statistically different length of hospital stay (WMD: -0.15, 95% CI: -0.60 ; 0.30); or a statistically different risk of mortality (relative risk [RR]: 0.94, 95% CI: 0.69 ; 1.28).

CONCLUSIONS

The use of PCT as a biomarker for adults with LRTI reduced antibiotic use with no adverse effects on LOS or mortality.

"The findings of the present study are consistent with the prior analyses and further strengthen the evidence for the potential benefit of PCT as part of AB stewardship programs."

KEY FINDINGS

- PCT can help guide decision-making for both the initiation and discontinuation of antibiotics in patients with LRTIs.
- PCT-guidance had no adverse impact on mortality or LOS in this population.
- The reduction in antibiotic use achieved using PCT can have important implications for antimicrobial resistance and side-effects from prescribing unnecessary antibiotics.

CLINICAL MICROBIOLOGY AND INFECTION
2019;25(11):1430.E5-1430.E12

Copan WASPLab automation significantly reduces incubation times and allows earlier culture readings.

Cherkaoui A, Renzi G, Vuilleumier N, Schrenzel J.

OBJECTIVE

The aim of this study was to assess whether the use of WASPLab® automation (automated inoculation and incubation combined with digital imaging) combined with chromogenic media can help reduce the time to result (TTR) compared to conventional diagnostic methods in order to improve patient care.

STUDY DESIGN

The authors compared the results obtained on 1,294 clinical samples when using either WASPlab full automation or WASP-based inoculation coupled to conventional incubation and manual diagnostic. The samples included urine, genital tract, non-sterile specimens and swabs obtained at Geneva University Hospitals between October 2018 and March 2019. The samples were screened for different types of resistant microorganisms. A first set of data was used to determine the reading time points and the methodology was then validated on an independent dataset.

RESULTS

The use of WASPLAB combined to chromogenic media allows to reduce the length of incubation time for urine, genital tract and non-sterile site specimens as well as the time needed to screen methicillin-resistant *Staphylococcus aureus* (MRSA), methicillin-susceptible *S. aureus* (MSSA), extended spectrum beta-lactamases (ESBL) and carbapenemase-producing *Enterobacterales* (CPE) without affecting the analytical performance **(Table 1)**.

Table 1. Times for final reading for fully automated vs. conventional diagnostic methods.
Adapted from Cherkaoui A, *et al. Clinical Microbiology and Infection* 2019;25(11):1430.E5-1430.E12

TYPE OF SAMPLES	CHROMOGENIC MEDIA	TIME FOR FINAL READING: FULL AUTOMATION	TIME FOR FINAL READING: CONVENTIONAL
Urine	CHROMID® CPS ELITE	18* and 24h	24* and 48h
Nasal and inguinal/perineal swabs	CHROMID® MRSA	18h	18/24* and 48h
Rectal screening swab	CHROMID® ESBL AND CHROMID® OXA 48	16h	18/24h* and 48h

CONCLUSIONS

The use of automated incubators, digital imaging and chromogenic media can improve the TTR for all specimens tested compared to conventional methods, without compromising the analytical performance.

Implementation of established and validated incubation times enables improved efficiency in laboratory workflows.

A reduced TTR could potentially improve patient outcomes and medical decision-making and may also have a positive impact on treatment de-escalation.

"...Shortening the turn-around times could positively improve the patient's outcome. This implies providing earlier medically actionable results to the treating physician (e.g. switches from empiric to targeted drug regimens)"

KEY FINDINGS

- The use of automation combined with chromogenic media reduced incubation times without compromising analytical performance.
- The reduced TTR could have a positive impact on patient outcomes and treatment de-escalation.

CRITICAL CARE
2020;24:434

Multicenter Evaluation of a Syndromic Rapid Multiplex PCR Test for Early Adaptation of Antimicrobial Therapy in Adult Patients with Pneumonia.

Monard C, Pehlivan J, Auger G, Alviset C, Tran Dinh A, Duquaire P, Gastli N, d'Humières C, Maamar A, Boibieux A, Baldeyrou M, Loubinoux J, Dauwalder O, Cattoir V, Armand-Lefèvre L, Kernéis S, ADAPT study group.

OBJECTIVE

This study aimed to evaluate the relevance of a new syndromic rapid multiplex test (rm-PCR) on respiratory samples to guide empirical antimicrobial therapy in adult patients with community acquired pneumonia (CAP), hospital-acquired pneumonia (HAP), and ventilator-acquired pneumonia (VAP).

STUDY DESIGN

This retrospective multicenter study was conducted in four French university hospitals. Respiratory samples obtained from adults with clinically diagnosed pneumonia were simultaneously tested with standard-of-care (SOC) methods and the BIOFIRE® FILMARRAY® Pneumonia *plus* (PN*plus*) Panel to evaluate the potential impact on antibiotic prescription.

In each study site, a committee composed of an intensivist, an ID specialist and a microbiologist was formed to retrospectively review all medical files, including patient's history, previous antimicrobials, MDRO risk and clinical and radiological findings. For each episode, the committee, blinded to the empiric therapy and microbiology results, agreed on the most appropriate therapy, based on the results of the BIOFIRE PN*plus* Panel, as well as medical files. The BIOFIRE guided therapy was compared with the real treatment administered to the patient.

The primary endpoint was the number of pneumonia episodes in which PCR-guided therapy differed from empirical therapy.

RESULTS

A total of 159 pneumonia episodes were included. The type of pneumonia episodes were HAP (n=68, 43%), CAP (n=54, 34%), and VAP (n=37, 23%). SOC methods identified at least one microorganism in 95 (60%) patients; while the BIOFIRE PN*plus* Panel detected at least one bacterial pathogen in 132 (83%) episodes.

Based on the results of the BIOFIRE PN*plus* Panel, the committee agreed on a theoretical change of empiric antimicrobials in 123 (77%) episodes: de-escalation in 63 (40%) and escalation in 35 (22%). Moreover, in patients where culture identified a pathogen (n=95), the BIOFIRE PN*plus* Panel would have increased appropriateness of therapy in 10% of the episodes compared to empirical regimes: 83 (87%) *vs* 73 (77%). The potential changes in therapy by pneumonia type are shown in **Table 1**.

The use of the BIOFIRE PN*plus* Panel would have decreased the use of β-lactams from 92% to 82%, and the use of β-lactam companion therapies from 50% to 31%.

Table 1. Impact of rm-PCR results on antibiotic prescription, according to multidisciplinary committee (n=159).
Adapted from Monard C, *et al. Critical Care* 2020;24:434

	Overall n=159	CAP n=54	HAP n=68	VAP n=37
Antibiotic modification	123 (77%)	37 (69%)	54 (79%)	32 (87%)
De-escalation	63 (40%)	20 (37%)	25 (37%)	18 (49%)
Escalation	35 (22%)	8 (15%)	18 (27%)	9 (24%)
Undetermined	25 (16%)	9 (17%)	11 (16%)	5 (14%)
No change	36 (23%)	17 (32%)	14 (21%)	5 (14%)

CONCLUSIONS

Use of a syndromic rm-PCR test has the potential to reduce unnecessary antimicrobial exposure and increase the appropriateness of empirical antibiotic therapy in adult patients with pneumonia.

"Early use of [BIOFIRE PNplus Panel] in pneumonia could reduce unnecessary antimicrobial exposure...Together with an expert advice, this promising diagnostic tool could improve the quality of care."

KEY FINDINGS

- The BIOFIRE PN*plus* Panel increased diagnostic yield from 60 to 83%.
- The BIOFIRE PN*plus* Panel led to a potential change in therapy in 77% of the episodes and a reduction in the use of β-lactams.
- The use of the BIOFIRE PN*plus* Panel has the potential to reduce unnecessary antimicrobial exposure.

LANCET RESPIRATORY MEDICINE
2017;5(5):401-411

Routine Molecular Point-Of-Care Testing For Respiratory Viruses In Adults Presenting To Hospital With Acute Respiratory Illness (ResPOC): A Pragmatic, Open-Label, Randomised Controlled Trial.

Brendish N, Malachira A, Armstrong L, Houghton R, Aitken S, Nyimbili E, Ewings S, Lillie P, and Clark T.

OBJECTIVE

The objective of this parallel-group, open-label, randomized controlled trial was to compare patient outcomes when a highly multiplexed, rapid point-of-care (POCT) PCR test for respiratory pathogens, BIOFIRE® FILMARRAY® Respiratory (RP) Panel, was used *versus* routine clinical care.

STUDY DESIGN

In total, 720 patients (age ≥ 18 years) presenting to the emergency department with acute respiratory illness or fever higher than 37.5°C (≤7 days duration), or both were enrolled during two consecutive respiratory seasons. Patients were randomly assigned to either the POCT arm (n=362) or to routine care (n=358).

The primary outcome was the proportion of patients who received antibiotics while hospitalized (up to 30 days). Secondary outcomes included duration of antibiotics, proportion of patients receiving single doses or brief courses of antibiotics, length of stay, antiviral use, isolation facility use, and safety.

RESULTS

While the proportion of patients treated with antibiotics did not change, the study shows the following findings for the POCT group *vs.* the control group:

- a higher pathogen detection rate (45% *vs* 15%, $p<0.0001$);
- faster time to diagnostic results (2.3 hours *vs* 37.1 hours, $p<0.0001$);
- shorter length of hospital stay (5.7 days *vs* 6.8 days, $p=0.0443$);
- more patients on short antibiotic courses (<48 hours) or single doses (17% *vs* 9%, $p=0.0047$);
- more efficient use of neuraminidase inhibitors;
- more appropriate use of isolation resources:
  - shorter time to isolation (0.5 days *vs* 1.0 day, $p=0.0071$);
  - shorter time to de-isolation (1.0 day *vs* 3.1 days, $p=0.0057$).

CONCLUSIONS

Routine molecular POCT was associated with more patients in the POCT group receiving single doses or short courses of antibiotics, reduced length of hospital stay, improved detection of influenza and use of antivirals, and appeared to be safe.

"Rapid and appropriate assignment of hospital side rooms for patients with respiratory virus infection is hugely important to reduce the risk of nosocomial transmission to other vulnerable hospitalised patients and to improve the flow of patients through acute areas within the hospital"

KEY FINDINGS

- Use of the BIOFIRE RP Panel shortened antibiotic use in patients without any evidence of harm and improved influenza detection and antiviral use.
- The BIOFIRE RP Panel allowed for faster turnaround time for results and was associated with a reduced length of stay of around 1 day (equating to around 200,000 bed days/year saving around £80 million/year).

OPTIMIZATION OF ANTIBIOTIC THERAPY

CLINICAL INFECTIOUS DISEASES
2015;61(7):1071-1080

Randomized Trial of Rapid Multiplex Polymerase Chain Reaction-Based Blood Culture Identification and Susceptibility Testing.

Banerjee R, Teng CB, Cuningham SA, Ihde SM, Steckelberg JM, Moriarty JP, Shah ND, Mandrekar JN, Patel R.

OBJECTIVE

This paper describes a prospective randomized controlled trial evaluating outcomes associated with BIOFIRE® FILMARRAY® Blood Culture Identification (BCID) Panel detection of bacteria, fungi, and resistance genes directly from positive blood culture bottles (BCBs). The primary outcome was antimicrobial therapy duration. Secondary outcomes were time to antimicrobial de-escalation or escalation, length of stay (LOS), mortality, and cost.

STUDY DESIGN

A total of 617 adults and children with positive BCBs were randomized into three arms: standard BCB processing (207) and two intervention groups using the BIOFIRE BCID Panel: BIOFIRE BCID Panel testing reported with template comments (198), or BIOFIRE BCID Panel testing reported with template comments and real-time audit and feedback of antimicrobial orders by an antimicrobial stewardship team (212).

RESULTS

Time from BCB Gram stain to microorganism identification was shorter in the groups using BIOFIRE BCID Panel testing (1.3 hours) *vs* control (22.3 hours). Additionally, both intervention groups had decreased use of broad spectrum antibiotics and increased use of narrow spectrum antibiotics compared to the control group. Furthermore, time from Gram stain to appropriate antimicrobial escalation was reduced by 14 hours in both intervention groups and time to de-escalation was reduced by 19 hours in the group that included BIOFIRE BCID Panel test results with an audit from the antimicrobial stewardship team. Groups did not differ in the secondary outcomes (mortality, LOS, and cost) with this study design.

CONCLUSIONS

Use of the BIOFIRE BCID Panel, along with templated comments or oversight from an antimicrobial stewardship team, may optimize antibiotic prescribing for bloodstream infections.

"Faster identification and resistance characterization of pathogens may lead to earlier administration of directed antimicrobial therapy, promote earlier de-escalation of broad-spectrum agents, and potentially result in better outcomes."

KEY FINDINGS

- Antibiotic escalation improved with use of the BIOFIRE BCID Panel with or without antimicrobial stewardship.
- Antibiotic de-escalation occurred earlier when the BIOFIRE BCID Panel was used in conjunction with antimicrobial stewardship.
- Use of the BIOFIRE BCID Panel increased laboratory testing costs, but there was no significant difference in overall healthcare costs.

DIAGNOSTIC MICROBIOLOGY AND INFECTIOUS DISEASE
2016;86:102-107

The Potential of Molecular Diagnostics and Serum PCT Levels to Change the ATB Management of CAP.

Gilbert D, Gelfer G, Wang L, Myers J, Bajema K, Johnston M, Leggett J.

OBJECTIVE

The objective of this study was to evaluate if physicians would alter therapy (switch from empiric therapy to either no therapy or a targeted antimicrobial regimen) in response to the combination of procalcitonin (PCT) levels (VIDAS® B·R·A·H·M·S· PCT™ immunoassay), and results generated with the BIOFIRE® FILMARRAY® Respiratory (RP) Panel.

STUDY DESIGN

The study was a non-blinded cluster randomized trial performed at a 480 bed community-teaching hospital in the USA. Patients enrolled had a diagnosis of community acquired pneumonia requiring admission as determined by the emergency room physician.

The study enrolled 127 patients, randomized to two arms. Both arms had standard of care (SOC) testing that consisted of two blood cultures, sputum culture, serum PCT level, urinary antigen testing for *Legionella pneumophila*, *Streptococcus pneumoniae*, nasal swabs for PCR detection of *Streptococcus pneumoniae* and *Staphylococcus aureus*. In addition, the SOC arm had a 5 virus PCR panel. The second arm of the study had BIOFIRE RP Panel testing performed in lieu of the 5 viral PCR. All results were delivered to the clinician within 48 hours of admission.

RESULTS

- Combining the 2 arms of the study, 71% (90) of the patients had an etiology determined: 32% (40) were only bacterial, 20% (25) only viral and 19% (24) had bacterial and viral infections. There was a significant difference in the time to results for the BIOFIRE RP Panel testing (2.1 hours ± 0.7 hours) *versus* the internal PCR (26.5 hours ± 15 hours).
- PCT levels were significantly less ($p<0.003$) in patients identified with just viral infection *versus* those with bacterial or bacterial and viral infections.
- The length of therapy, duration of therapy, cost of antibiotics and antivirals were calculated and normalized. The median cost for therapy was lower in the BIOFIRE group ($3,037 *versus* $7,932; $p=0.02$). For each etiology group, the cost and duration were significantly lower in patients with combined bacterial and viral infections as identified by the BIOFIRE RP Panel ($p=0.03$).
- There were no difference in both groups relating to length of stay.
- In the 25 patients with only viral detection, PCT levels were consistent with the diagnosis of viral pneumonia. However, the discontinuation of empiric therapy within 48 hours only occurred in 8 patients.

CONCLUSIONS

The potential for improved antibiotic stewardship using molecular diagnostics was demonstrated in 25 patients (20%) with only detectable respiratory virus and normal levels of PCT.

The one-day shorter time to result of the BIOFIRE RP Panel *versus* the internal PCR enabled an additional reduction in terms of duration and median cost of therapy.

"The fast turnaround time of the [BIOFIRE] FilmArray offers quick assistance to antibiotic stewardship activities."

KEY FINDINGS

- The requirement for respiratory isolation and a second dose of empiric antimicrobials can be altered when laboratory results that distinguish viral from bacterial infections are available within 8 hours of hospital admission.
- Overall duration of therapy and cost of therapy were lower in groups with faster pathogen identification.
- Positive viral PCR and low PCT levels strongly suggest the absence of invasive bacterial infections and should be a help to reconsider antimicrobial therapy strategy.

CLINICAL INFECTIOUS DISEASES
2020;71(5):1142-1148

Determining the utility of Methicillin-Resistant *Staphylococcus aureus* Nares screening in Antimicrobial Stewardship.

Mergenhagen KA, Starr KE, Wattengel BA, Lesse AJ, Sumon Z, Sellick JA.

OBJECTIVE

The aim of this study was to assess if the nasal screening of every patient for methicillin-resistant *Staphylococcus aureus* (MRSA) colonization at admission, transfer and discharge can be a powerful antimicrobial stewardship tool for de-escalation and avoidance of MRSA empirical therapy. The relationship between the presence or absence of MRSA nasal carriage and the presence of MRSA in clinical cultures was established for a variety of anatomical sites.

STUDY DESIGN

Data from 245,833 patients with MRSA nares screening were obtained from a large national database across Veterans Affairs hospitals in the United States. The subsequent 561,325 clinical cultures within 7 days were analyzed for the presence of MRSA. The sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were calculated to determine the use of MRSA nasal screening in predicting MRSA in a clinical culture. Cultures from urine (40%), wound (24.7%), respiratory (16.2%) and blood (12.5%) were included in the cohort.

RESULTS

Table 1. Efficacy characteristics of MRSA nares screening for the whole cohort and for the main culture sites.
Adapted from Mergenhagen KA, *et al. Clinical infectious Disease* 2020;71(5):1142-1148

Sample type	Number	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
All	561,325	67.4	81.2	24.6	**96,5**
Blood	70,185	69.8	81.9	27.8	**96.5**
Respiratory tract	90,912	76.2	80.3	35	**96.1**
Renal system	201,443	72.5	80.2	7.6	**99.2**
Wound	136,078	59.8	82.5	34.2	**93.1**

CONCLUSIONS

The data confirmed that a negative MRSA nares swab is useful for predicting the absence of MRSA in a subsequent clinical culture in a variety of samples and could therefore be used as a tool to deescalate or avoid empirical antimicrobial therapy.

"...Use of MRSA nares screening may improve patient care by avoiding potential nephrotoxicity with unnecessary antibiotics."

KEY FINDINGS

- Nasal screening is a powerful tool to rule out MRSA infection in many different types of samples.
- This test could be used to avoid the use of, or deescalate, an anti-MRSA therapy, thereby contributing to patient care and the fight against antimicrobial resistance.

JOURNAL OF INFECTION
2012;65(4):302-309

Clinical and economic evaluation of the impact of rapid microbiological diagnostic testing.

Galar A, Leiva J, Espinosa M, Guillén-Grima F, Hernáez S, Yuste JR.

OBJECTIVE

This study evaluated the clinical and economic impact of rapid reporting of results from the clinical microbiology lab.

STUDY DESIGN

The study included 574 hospitalized patients with diverse bacterial infections, 284 of which were included in a control group where, following the laboratory's normal practice, results were made available to clinicians one day after the analysis was initiated. The remaining 290 patients made up the experimental group. Their respective microbiology results were reported to clinicians the same day of the analysis using a rapid, same-day workflow. The VITEK® 2 System was used for both identification and antimicrobial susceptibility testing for all results in this study.

RESULTS

The data generated showed that reporting microbiology results faster allowed clinicians to provide antibiotic treatment sooner (p<0.001). In 9.0% of cases of 702 cases reviewed, the initial empirical treatment had not included an antibiotic to which the isolate was susceptible. Upon receipt of the microbiological results, the physicians were able to make antibiotic substitutions (most common action taken), initiations or discontinuations. For the intervention group, there was a higher number of changes in antibiotic treatment within 24 hours of introduction of the organism into the VITEK 2. For the control group, significant changes did not occur until 24 to 48 hours. In addition, for the group whose results were reported according to the rapid protocol, there was a significant reduction in the reporting turnaround time (17.6 hours), resulting in a reduction in the number of tests performed, decreased duration of hospital stay, and lower intubation rates for patients. Additionally, costs incurred for the patients including those associated with microbiology testing, antibiotic costs, length of hospitalization, and miscellaneous patient costs were lower (mean savings of 3,588€ or $4,542 USD* per patient) for the group of patients whose results were reported via the rapid protocol. Mortality rates did not differ significantly between the two groups.

CONCLUSIONS

In conclusion, the authors described that rapid reporting of microbiology results was associated with quality improvement as seen by earlier optimization of patient antibiotic therapy, an improved clinical outcome and financial benefits.

* USD calculated using exchange rate of $1.226 USD per 1.0€

"Rapid microbiological information was associated with quality improvement seen in earlier changes in antibiotic use, an improved clinical outcome and financial benefits."

KEY FINDINGS

- Rapid microbiology results from the VITEK 2 significantly impacted antibiotic use which can lead to improved patient outcomes and reduced length of stay.

DIAGNOSTIC MICROBIOLOGY AND INFECTIOUS DISEASE
2019;95(2):208-211

Effect of antimicrobial stewardship with rapid MALDI -TOF identification and Vitek® 2 antimicrobial susceptibility testing on hospitalization outcome.

Cavalieri SJ, Kwon S, Vivekanandan R, Ased S, Carroll C, Anthone J, Schmidt D, Baysden M, Destache CJ.

OBJECTIVE

The aim of this study was to assess the time needed to obtain identification (ID) and antimicrobial susceptibility testing (AST) results and to initiate appropriate therapy before and after the implementation of VITEK® MS, VITEK® 2 and a dedicated antimicrobial stewardship (ASP) team in patients with bloodstream, respiratory and urinary infections.

STUDY DESIGN

For the 2017 time period, organism ID and AST were performed on 77 patients using the Microscan microdilution system and limited ASP was available.

For the 2018 time period, organism ID and AST were performed on 77 patients using VITEK MS / VITEK 2 and a dedicated ASP team was hired.

Time to obtain ID and AST results as well as length of stay (LOS) and length of antimicrobial therapy were compared between the two periods.

RESULTS

Table 1. Comparison of time to ID/AST results and time to appropriate therapy before and after implementation of VITEK MS, VITEK 2 and an ASP team.

Adapted from Cavalieri SJ, *et al. Diagnostic Microbiology and Infectious Disease* 2019;95(2):208-211

TIME VARIABLE	MICROSCAN AND NO DEDICATED ASP TEAM	VITEK® MS / VITEK® 2 ASP +	STATISTICAL SIGNIFICANCE
Identify and report organism (hours)	33.8 +/- 17	24.9 +/- 14.4	*p*=0.001
Perform and report AST (hours)	28.5 +/- 14.9	18.2 +/- 14	*p*<0.001
Length of hospitalization (days)	15.5 +/- 18.1	10.7 +/- 11.1	*p*=0.05
Length of in-patient antimicrobial therapy (days)	8.8 +/- 7.8	6.7 +/- 3.8	*p*=0.036

CONCLUSIONS

Use of VITEK MS / VITEK 2 leads to an average 21.5 hours faster ID and AST results and in conjunction with a dedicated ASP team leads to significant reduction in antimicrobial therapy duration (or antimicrobial exposure) and hospital LOS.

"...Use of ASP and MALDI-TOF/Vitek2 rapid identification and AST demonstrated a significant reduction in time to isolate identification and AST results, which translated into significant reduction in antibiotic length of therapy and hospital LOS."

KEY FINDINGS

- The time to obtain both ID and AST results was significantly faster in 2018 than in 2017 (21.5 hours less on average) which, in conjunction with workflow optimization, allowed the ASP team to recommend significantly more adjustments for appropriate antimicrobial therapy.
- The consequence was a significant reduction in LOS (4 days for general ward and 7 days in ICU) and length of antimicrobial therapy (2 days).

ANTIMICROBIAL AGENTS AND CHEMOTHERAPY
2012;56(8):4214-4222

Impact of Antibiotic MIC on Infection Outcome in Patients With Susceptible Gram-negative Bacteria: A Systematic Review and Meta-Analysis.

Falagas ME, Tansarli GS, Rafailidis PI, Kapaskelis A, Vardakas KZ.

OBJECTIVE

In this meta-analysis of 13 published articles, the authors reviewed available evidence to examine whether, for patients with infections caused by gram-negative bacteria (GNB), infections with higher antibacterial MIC values that were within the defined "susceptible" range were associated with worse outcomes than those with a lower MIC.

STUDY DESIGN

A PubMed and Scopus electronic database search was conducted in January 2012 to analyze the impact of antibiotic MIC values on the outcomes of infections. Articles considered for review reported clinical or microbiological outcomes of patients with infections due to antibiotic-susceptible GNB isolates (per CLSI and EUCAST criteria), stratified by antibiotic MIC, and receiving the corresponding antimicrobial therapy.

Primary outcomes were all-cause mortality and clinical or microbiological treatment failure. Treatment failure was defined as a persistence of symptoms/signs, failure to eradicate the implicated bacterial pathogen (based on cultures), infection recurrence, or death.

Patients were allocated into 2 groups: high MICs *vs.* low MICs. Patients with infections due to high-MIC isolates included those with isolates with the breakpoint value and those with an MIC value 1 dilution lower; the remaining isolates comprised the low-MIC group. Patients infected with strains that were resistant to the administered antibiotics were excluded.

RESULTS

From a total of 3,177 reviewed, 13 articles were included, and data from 1,469 patients were analyzed.

Enterobacterales

- More treatment failures were observed for infections due to *Salmonella enterica* strains with high fluoroquinolone MICs of ≥0.125 μg/ml than for those with MICs <0.125 μg/ml (relative risk [RR], 5.75; 95% confidence interval [CI], 1.77 to 18.71) with no difference in mortality.
- For infections due to *Enterobacterales* other than *Salmonella* spp., pooled data showed a higher mortality rate associated with high-MIC strains (RR, 2.03; 95% CI, 1.05 to 3.92).

Non-fermentative bacilli

- Pooled data revealed more treatment failures for patients infected with high-MIC strains (RR, 5.54; 95% CI, 2.72 to 11.27).
- The mortality rate for patients with high-MIC isolates was higher than that for patients with low-MIC isolates (RR, 2.39; 95% CI, 1.19 to 4.81).

Other GNB

- Pooled outcomes of patients with *Haemophilus influenzae* infections showed no difference in treatment failures between patients infected high- or low-MIC strains (RR, 1.66; 95% CI, 0.87 to 3.14).

CONCLUSIONS

An association was observed between high MIC values within the currently accepted "susceptible" range and adverse infection outcomes, particularly those caused by *S. enterica* and *P. aeruginosa*; for these infections, more treatment failures were reported for strains with high MICs of fluoroquinolones and of piperacillin-tazobactam or meropenem. The mortality rate was also higher for patients infected with *P. aeruginosa* strains with high MICs. The data for *Enterobacterales* other than *S. enterica* also showed a higher mortality rate for patients infected with high MICs of various antibiotics.

The authors note that the association between high MIC values and adverse outcomes requires confirmation in larger, prospective studies.

"The limited data regarding the outcomes of infections due to gram-negative bacteria according to the MIC value suggested that high MIC values within the currently accepted 'susceptible' range were associated with worse outcomes."

KEY FINDINGS

- Among non-*Salmonella Enterobacterales*, a higher all-cause mortality was observed for the patients infected with strains with high MICs.
- With non-fermentative gram-negative bacilli, the strains with high MICs had:
  - More treatment failures occurring in infected patients
  - A higher mortality rate than for those with low MIC strains.

JOURNAL OF ANTIMICROBIAL CHEMOTHERAPY
2020;75(5):1099-1111

Can Evidence-Based Decision Support Tools Transform Antibiotic Management? A Systematic Review and Meta-Analyses.

Laka M, Milazzo A, Merlin T.

OBJECTIVE

This systematic review and meta-analysis assessed the impact of using clinical decision support systems (CDSSs) on appropriate antibiotic prescribing in different care settings, including hospitals and primary care.

STUDY DESIGN

Seven databases were searched for peer-reviewed articles from database inception to August 2018. The protocol was developed using the PRISMA-P* checklist and pre-determined study selection criteria. Where sufficient outcome data was available, meta-analyses were performed using a random-effects model to evaluate whether use of CDSS could impact antibiotic prescribing. The review studied the following parameters: inappropriate antibiotic prescriptions, volume of antibiotic use, antibiotic exposure, length of hospital stay, mortality and cost of therapy.

RESULTS

Out of 6,410 studies, 57 studies were included in the review, comprised of 13 randomized controlled trials (RCTs) and 44 non-randomized controlled studies. Meta-analysis showed that appropriate antibiotic therapy was twice as likely to be prescribed following implementation of a CDSS compared with standard care (pooled odds ratio [OR] 2.28, 95% confidence interval [CI] 1.82–2.86).

Furthermore, a CDSS was associated with an 18% relative reduction in mortality (OR 0.82, 95% CI 0.73–0.91), as well as decreases in overall volume of antibiotic use in 11 studies **(Table 1)**, length of hospital stay in 12 studies, antibiotic exposure in 5 studies in both hospital and primary care settings and cost of therapy in 8 studies **(Table 2)**.

The findings of this review and meta-analysis are consistent with findings of previous systematic reviews of CDSSs, and additionally, covered both hospital and primary care settings.

CONCLUSIONS

This study demonstrated that a CDSS has the potential to optimize antibiotic prescribing by increasing compliance with evidence-based care (guidelines and antibiotic susceptibility test results). A positive impact was observed on appropriate prescribing and clinical and economic outcomes in a variety of different healthcare settings and with different types of CDSSs.

"Our study demonstrates that a CDSS has great potential to optimize antibiotic management by increasing adherence to evidence-based care. [...] antibiotics prescribed using a CDSS may be up to twice as likely to be compliant with guidelines or in vitro susceptibility test results."

KEY FINDINGS

- CDSSs can be effective in improving antibiotic prescribing.
- Using a CDSS, antibiotic prescribing is twice as likely to be appropriate and in compliance with guidelines or antibiotic susceptibility test results.
- Most studies also reported reductions in overall volume of antibiotic use, antibiotic exposure, length of stay, and cost of therapy.

Table 1. Impact of CDSS intervention on the overall volume of antibiotic use.
Adapted from Laka M, *et al*. *Journal of Antimicrobial Chemotherapy* 2020;75(5):1099-1111

Study	Study setting	Unit	Non-CDSS	CDSS	Change	*p* Value
Agwu *et al*. 2008	Hospital	Doses/day (restricted antibiotics)	125.8	111.8	↓ -11.13%	NR
Bourgeois *et al*. 2010	Primary care	Proportion of total visits	46%	39.7%	↓ -6.30%	0.84
Burke and Pestotnik 1999	Hospital	DDD/1000 PDs[a]	226	299	↑ +32%	NR
Evans *et al*. 1999	Hospital	DDD/1000 PDs[a]	2009	1956	↓ -2.64%	NR
Evans *et al*. 1998	Hospital	DDD/1000 BDs[b]	1852	1619	↓ -12.58%	NR
Nault *et al*. 2018	Hospital	Difference in DDD/1000 PDs (%)[a]	NA	NA	↓ -12.2%	0.02
Okumura *et al*. 2016	Hospital	DDD/1000 BDs	63.1	21.5	↓ -65.93%	NR
Pestotnik *et al*. 1996	Hospital	DDD/1000 OBDs[a]	359	277	↓ -22.84%	NR
Rattinger *et al*. 2012	Primary care	Proportion of unwarranted antibiotic prescriptions	22%	3.3%	↓ -18.7%	<0.0001
Tafelski *et al*. 2010	Hospital	Antibacterial agents administered/day	1.5	1.3	↓ -13.33%	<0.05
Thursky *et al*. 2006	Hospital	DDD/1000 ICU BDs[c]	1670	1490	↓ -10.78%	NA

a. Defined daily dosage/1000 occupied bed days (OBDs)
b. Defined daily dosage/1000 patient days (PDs)
c. Defined daily dosage/1000 bed days (BDs)

Table 2. Impact of CDSS intervention on the cost of antibiotic therapy.
Adapted from Laka M, *et al*. *Journal of Antimicrobial Chemotherapy* 2020;75(5):1099-1111

Study	Study setting	Study location	Unit of measure	Non-CDSS	CDSS	Change	*p* Value
Buising *et al*. 2008	Hospital	Australia	Mean cost per patient for pneumonia (AUD)	72.07	84.04	16.60%	NR
Evans *et al*. 1998	Hospital	USA	Mean cost per patient (USD)	340	102	-70%	<0.001
Evans *et al*. 1999	Hospital	USA	Mean cost per patient (USD)	92.96	80.62	-13.27%	<0.02
Evans *et al*. 1994	Hospital	USA	Mean cost per patient (USD)	51.93	41.08	-20.89%	<0.001
Kofoed *et al*. 2008	Hospital	Denmark	Mean cost per treatment (Euro)	624	528	-15.38%	0.06
McGregor *et al*. 2006	Hospital	USA	Total cost of antibiotics for study period (USD)	370,006	285,812	-22.75%	NR
Mullet *et al*. 2001	Hospital	USA	Total cost per patient (USD)	274.79	289.60	-5.39%	NS
Paul *et al*. 2006	Hospital	Israel, Germany and Italy	Mean cost per patient (Euro)	623.2	565.4	-9.27%	0.473
Pestotnik *et al*. 1996	Hospital	USA	Mean cost per treated patient (USD)	122.66	51.90	-57.69%	NR

JOURNAL OF ANTIMICROBIAL CHEMOTHERAPY
2016;72:933-940

Sustained impact of a computer-assisted antimicrobial stewardship intervention on antimicrobial use and length of stay.

Nault V, Beaudoin M, Perron J, Moutquin JM, Valiquette L.

OBJECTIVE

This study aimed to evaluate the longitudinal impact of a novel computerized clinical decision support system, Antimicrobial Prescription Surveillance System (APSS) designed to assist an antimicrobial stewardship program (ASP) team with Prospective Audit and Feedback (PAF) on hospital length of stay (LOS), antimicrobial use and costs and quality of antimicrobial prescription.

STUDY DESIGN

Between 2008 and 2013, a retrospective cohort study was conducted at the Centre Hospitalier Universitaire de Sherbrook, Canada (677 beds), on hospitalized adult patients receiving antimicrobials (intravenous and oral). ASP hospital intervention started in 2010, led by a pharmacist.

The APSS (Lumed Inc.) was able to receive and analyze clinical data from the electronic record system including demographics, admission, vital signs, pharmacy, radiology, laboratory and microbiology data.

Using its knowledge base rules (derived from published and local guidelines), the APPS verified whether the antimicrobial treatment was appropriate according to drug-drug interactions, redundant spectrums, drug-bug mismatches, cheaper alternatives, dose adjustments, duration of treatment and switch from intravenous to oral therapy. Statistical analysis were performed by segmented regression analysis.

RESULTS

The APSS collected and reviewed 40,605 hospitalizations for 35,778 patients who received antimicrobials. The system generated 5,665 recommendations which were validated by pharmacists with a 91% acceptance rate by the prescribers.

Dosing adjustment (26%), switch from intravenous to oral therapy (16%) and immediate discontinuation of the treatment (13%) were the most frequent interventions generated.

Piperacillin/tazobactam (20%), vancomycin (18%), ciprofloxacin (17%) and meropenem (5%) were the most frequently prescribed antimicrobials targeted by recommendations.

A positive impact was observed on several outcomes after the implementation of the APSS for the ASP team, persisting over 3 years post-intervention:

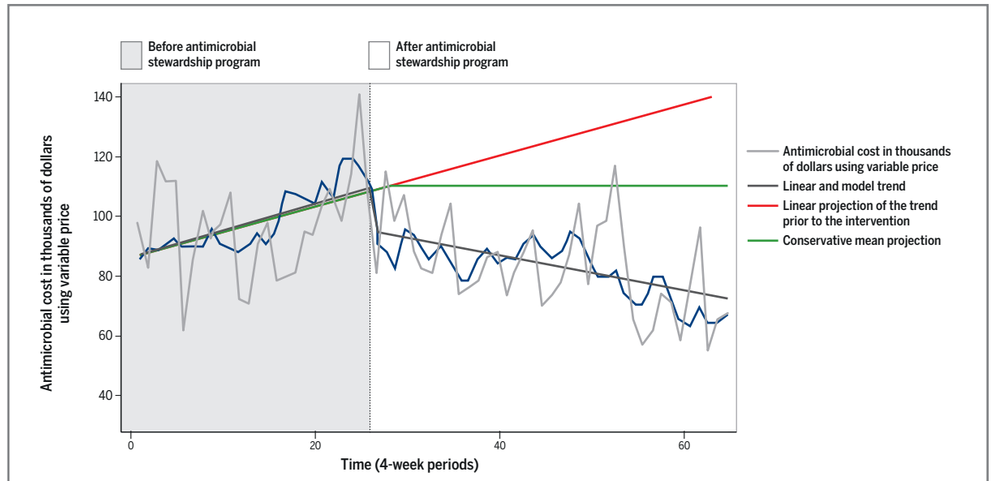
- A decrease in average LOS for patients receiving antimicrobial treatment (between -18.6% and -27.4% from conservative and maximum outcome prediction, respectively). This translated into 2.3 days average decrease in LOS, representing indirect savings of $2,085 per hospitalization in which the patient received antimicrobials.
- A reduction in antimicrobial consumption: for days of therapy per 1,000 inpatients days, the decrease was comprised between -11.0% and -21.8% (from conservative and maximum outcome prediction, respectively).
- A decrease in antimicrobial spending of around 28%, generating annual direct savings of $350,000 (20.5% of the hospital's antimicrobial budget). Savings outweighed the cost of the intervention, which includes the APSS license, a full-time pharmacist and an hour a day of an infectious diseases physician.
- A reduction of the non-concordance with antimicrobial prescribing guidelines (between -4.2% and 5.5% from conservative and maximum outcome prediction, respectively).

CONCLUSIONS

The implementation of APSS to support the ASP team demonstrated a sustainable positive impact for clinical and financial aspects on the prescription of antimicrobials in the hospital. The high rate of acceptance by prescribers plays a key role in these results.

OPTIMIZATION OF ANTIBIOTIC THERAPY

Figure 1. Antibiotic spending using variable pricing over a 4 week period.
Adapted from Nault V, *et al. Journal of Antimicrobial Chemotherapy* 2016;72:933-94



"Our intervention was well received by the prescribing physicians. The impacts of the ASP articulated around APSS, a computerized clinical decision-support system that performs a systematic review of all prescribed antimicrobials, were financially and clinically significant for the hospital."

KEY FINDINGS

- One of the first studies to evaluate a CDSS able to demonstrate a sustainable reduction in LOS of patients receiving antimicrobials following a PAF initiative.
- The reduction in LOS results from a combination of interventions targeting the switch from intravenous to oral and the discontinuation and reduction in the duration of antimicrobial therapy.
- This study confirmed that clinical decision support can sustainably improve quality of antimicrobial prescribing.

DISCONTINUATION OF ANTIBIOTIC THERAPY

LANCET INFECTIOUS DISEASES
2016;16(7):819–827

Efficacy and Safety of Procalcitonin Guidance in Reducing the Duration of Antibiotic Treatment in Critically Ill Patients: A Randomised, Controlled, Open-Label Trial.

de Jong E, van Oers JA, Beishuizen A, Vos P, Vermeijden WJ, Haas LE, Loef BG, Dormans T, van Melsen GC, Kluiters YC, Kemperman H, van den Elsen MJ, Schouten JA, Streefkerk JO, Krabbe HG, Kieft H, Kluge GH, van Dam VC, van Pelt J, Bormans L, Otten MB, Reidinga AC, Endeman H, Twisk JW, van de Garde EM, de Smet AM, Kesecioglu J, Girbes AR, Nijsten MW, de Lange DW.

OBJECTIVE

This trial evaluated the safety and efficacy of procalcitonin guidance in reducing duration of antibiotic use in critically ill ICU patients with a presumed bacterial infection.

STUDY DESIGN

This was a prospective, multicenter, randomized, controlled, open-label intervention trial in 15 hospitals in the Netherlands, where 1,575 patients were randomized (1:1 ratio) to a PCT-guided (n=776) or standard-of-care antibiotic (n=799) group.

The primary outcome for this study was consumption of antibiotics and duration of antibiotic treatment. The primary safety outcome was mortality at 28 days and 1 year. Secondary outcomes were the percentage of patients with recurrent infections, hospital and ICU length of stay (LOS), cost of antibiotics, and cost of PCT. The analyses for this study were intent-to-treat.

RESULTS

71% of the patients in the PCT-guided therapy group discontinued antibiotics in the ICU, with a median consumption of antibiotics of 7.5 daily doses *vs.* 9.3 daily doses for the standard of care group ($p<0.0001$). Mortality at 28 days was less at 19.6% for the PCT-guided group *vs.* 25% for the standard of care group ($p=0.0122$) and mortality at 1 year was 34.8% for the PCT group *vs.* 40.9% for standard of care ($p=0.0158$). A median reduction of antibiotic costs in the PCT-guided group was 34 Euros per patient ($p=0.0006$).

CONCLUSIONS

This large multi-center study in critically ill patients shows that PCT concentrations help physicians in deciding whether or not a presumed bacterial infection is truly of bacterial origin. Furthermore, use of a PCT-guided algorithm reduces duration of antibiotic therapy, which is one of the pillars of antibiotic stewardship. This reduction of antibiotic duration was associated with a significant decrease in mortality.

"Procalcitonin guidance stimulates reduction of duration of treatment and daily defined doses in critically ill patients with a presumed bacterial infection. This reduction was associated with a significant decrease in mortality."

KEY FINDINGS

- This trial demonstrated that PCT-guided antibiotic therapy strategy can reduce antibiotic treatment duration (<2 days) and consumption (<19%).
- Procalcitonin-guided therapy in critically ill ICU patients was associated with a reduction in 28-day and 1-year mortality as compared to standard of care.

OPEN FORUM INFECTIOUS DISEASES
2019;6(11):OFZ355

Impact of Procalcitonin Levels Combined with Active Intervention on Antimicrobial Stewardship in a Community Hospital.

Newton JA, Robinson S, Ling CLL, Zimmer L, Kuper K, Trivedi KK.

OBJECTIVE

The objective of this study was to measure the impact of PCT with an antimicrobial stewardship program (ASP) on patient length of stay (LOS) and antimicrobial therapy (ABX) duration in a community hospital.

STUDY DESIGN

Patients with at least 1 PCT value and an ASP recommendation to alter medications were included in the study. Between May 2013 and April 2014, 857 patients were eligible. The most common diagnoses were pneumonia, cystitis and undifferentiated sepsis. ASP recommendations were made based upon evidence-based guidelines, clinical experience and PCT results. No specific PCT algorithm was used. LOS, length of ABX after ASP recommendations and total length of ABX were evaluated.

Patients were stratified into two groups based upon treating physician acceptance or rejection of ASP guidance (compliers *versus* non-compliers). Patients were also stratified by initial PCT level (normal *versus* elevated).

RESULTS

Providers complied with 73.7% of ASP recommendations. Although mean LOS did not differ significantly between the ASP complier group compared to the ASP non-complier group, there was a significantly shorter mean LOT after ASP recommendations and a significantly shorter mean total LOT **(Table 1)**.

Table 1. Length of stay, duration of antibiotic after ASP recommendations and total duration of ABX therapy among ASP Compliers and ASP Non-compliers in days.

Adapted from Newton JA, *et al*. *Open Forum Infectious Diseases* 2019;6(11):ofz355

Variable	Compliers (N=632)		Noncompliers (N=225)		*p* Value
	Mean	SD	Mean	SD	
Length of stay (days)	8.46	6.66	8.21	7.61	.6493
Length of antimicrobial therapy* (after ASP recommendation) (days)	2.50	3.33	3.93	4.38	<.0001
Total length of antimicrobial therapy (days)*	5.10	3.74	6.55	4.96	<.0001

SD, standard deviation
*indicates statistically significant difference between compliers and non-compliers at $p<0.05$ significance level utilizing analysis of variance and Kruskal-Wallis procedure

CONCLUSIONS

PCT-guided recommendations, when accepted by providers, resulted in shorter duration of antibiotic therapy irrespective of whether PCT values were normal or elevated.

"In this study, we demonstrate that incorporation of PCT with ASP recommendations reduced LOT in a large community hospital, despite limited resources"

KEY FINDINGS

- In a 'real world' setting, compliance with PCT-guided recommendations provided by an ASP can decrease ABX duration.
- Duration of antibiotic therapy after ASP recommendations was significantly shorter (2.5 *vs* 3.9 days, $p<0.0001$) in the ASP complier group.
- ASPs play a key role in reducing inappropriate antibiotic use.

A SELECTION OF ANTIMICROBIAL STEWARDSHIP RESOURCES

GUIDELINES

CDC Guidelines: Core Elements of Hospital Antibiotic Stewardship Programs
https://www.cdc.gov/antibiotic-use/core-elements/hospital.html

IDSA/SHEA Guidelines: Implementing an antibiotic stewardship program
https://www.idsociety.org/practice-guideline/implementing-an-ASP/

Guide to Infection Control in the Healthcare Setting by International Society for Infectious Diseases (ISID)
https://isid.org/guide/amr/

NICE guideline: Antimicrobial stewardship: systems and processes for effective antimicrobial medicine use.
https://www.nice.org.uk/guidance/ng15

EU-Joint Action on Antimicrobial Resistance and Healthcare-Associated Infections (EU-JAMRAI): Guidelines, tools and implementation methods for antibiotic stewardship
https://eu-jamrai.eu/increasing-prudent-use-of-antibiotics-human-health/

Pan American Health Organization (PAHO) / Florida International University (FIU) Recommendations for Implementing Antimicrobial Stewardship in Latin America and the Caribbean: Manual for Public Health Decision-Makers
https://www.paho.org/en/documents/recommendations-implementing-antimicrobial-stewardship-programs-latin-america-and

India: Treatment Guidelines for Antimicrobial Use in Common Syndromes
https://www.ijmm.org/documents/Treatment_Guidelines_2019_Final.pdf
India: Treatment Guidelines for Antimicrobial Use in Infectious Diseases
https://ncdc.gov.in/WriteReadData/l892s/File622.pdf

Guidelines for the prevention and containment of antimicrobial resistance in South African hospitals
https://www.knowledgehub.org.za/elibrary/guidelines-prevention-and-containment-antimicrobial-resistance-south-african-hospitals

AMR/AMS REPORTS

O'Neill report: Review on Antimicrobial Resistance. Tackling Drug-Resistant Infections Globally: Final Report and Recommendations. 2016
https://amr-review.org/

OECD (2018), Stemming the Superbug Tide: Just A Few Dollars More, OECD Publishing, Paris
https://doi.org/10.1787/9789264307599-en

**Inter-Agency Coordination Group (IACG) on Antimicrobial Resistance.
No time to wait: Securing the Future from Drug-Resistant Infections.
Report to the Secretary-General of the United Nations. April 2019.**
https://www.who.int/antimicrobial-resistance/interagency-coordination-group/final-report/en/

RESOURCE DATABASES

ECDC Global and European repository on AMS
https://www.ecdc.europa.eu/en/publications-data/directory-guidance-prevention-and-control/prudent-use-antibiotics/antimicrobial

**CIDRAP-ASP (Center for Infectious Disease Research and Policy)
web-based resource: Antimicrobial stewardship project with emphasis on news, commentary, webinars, podcasts, etc.**
http://www.cidrap.umn.edu/asp

BSAC Infection Learning Hub; a global open access learning hub
https://infectionlearninghub.co.uk

BSAC Antimicrobial Resistance Centre (ARC): resource database for guidelines, MOOC courses, publications, research papers, etc.
http://www.bsac-arc.com

BSAC JAC -AMR, open access repository of peer reviewed and non-peer reviewed resources for educational and research in antimicrobial stewardship and resistance
https://academic.oup.com/jacamr

ON-LINE COURSES

WHO - Antimicrobial stewardship: a competency- based approach
https://openwho.org/courses/AMR-competency

CDC - Antibiotic Stewardship Training Series
https://www.train.org/cdctrain/training_plan/3697

The role of Diagnostics in the Antimicrobial Resistance Response
https://www.futurelearn.com/courses/role-of-diagnostics-in-the-amr-response

Point Prevalence Survey (PPS) course: Analysis of data from a PPS
https://www.futurelearn.com/info/courses/point-prevalence-surveys/0/steps/25690

BSAC with University of Dundee and FutureLearn – Massive Open Online Courses (MOOCs)

**Antimicrobial Stewardship: Managing Antibiotic Resistance
(available in English, Mandarin, Spanish, Russian. Pending Portuguese and Japanese translations)**
https://www.futurelearn.com/courses/antimicrobial-stewardship

Antimicrobial Stewardship for Africa
https://www.futurelearn.com/courses/antimicrobial-stewardship-for-africa

Antimicrobial Stewardship for the Gulf, Middle East and North Africa
https://www.mooc-list.com/course/antimicrobial-stewardship-gulf-middle-east-and-north-africa-futurelearn

E-BOOKS / TOOLKITS / PRACTICAL GUIDANCE

Ebook- Antimicrobial Stewardship: From Principles to Practice:
http://bsac.org.uk/antimicrobialstewardship-from-principles- to-practice-e-book/

Antimicrobial Stewardship in Australian Health Care (the AMS Book)
https://www.safetyandquality.gov.au/our-work/antimicrobial-stewardship/antimicrobial-stewardship-australian-health-care-ams-book_

Antimicrobial Stewardship (AMS), Volume 2, 1st Edition.
https://www.elsevier.com/books/antimicrobial-stewardship/pulcini/978-0-12-810477-4

WHO Practical Toolkit: Antimicrobial Stewardship Programmes in Healthcare Facilities in Low- and Middle-Income Countries
https://apps.who.int/iris/bitstream/handle/10665/329404/9789241515481-eng.pdf

Wellcome Trust Toolkit on Communicating Antimicrobial Resistance
https://wellcome.org/reports/reframing-antimicrobial-resistance-antibiotic-resistance

REACT: Toolbox for action on antibiotic resistance
https://www.reactgroup.org/toolbox/

Stewardship playbook from National Quality Forum
https://store.qualityforum.org/collections/antibiotic-stewardship

Antimicrobial stewardship: a practical guide to implementation in hospitals; and other educational booklets
https://www.biomerieux.com/en/education/antimicrobial-resistance-antimicrobial-stewardship/educational-materials

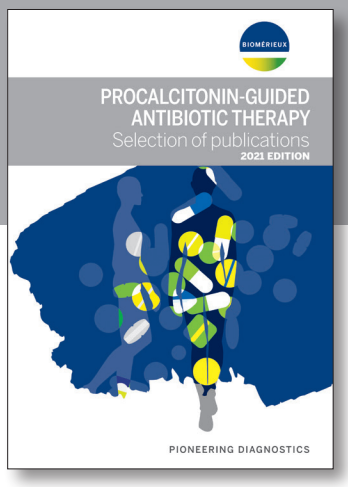
POINT PREVALENCE SURVEY RESOURCES

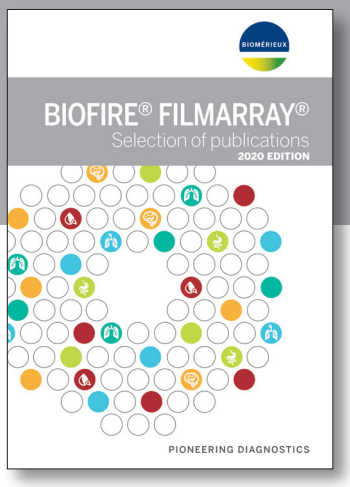
WHO Point Prevalence Survey (PPS) methodology
https://apps.who.int/iris/bitstream/handle/10665/280063/WHO-EMP-IAU-2018.01-eng.pdf?ua=1

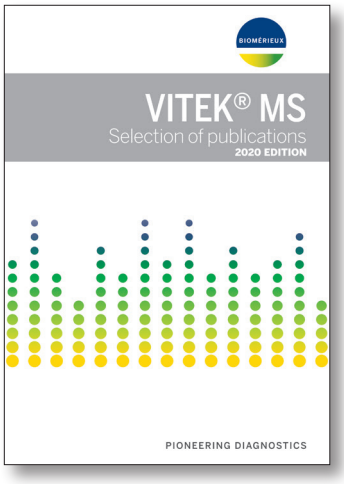
Global Point Prevalence Survey (Global-PPS) initiative led by the University of Antwerp
https://www.global-pps.com/

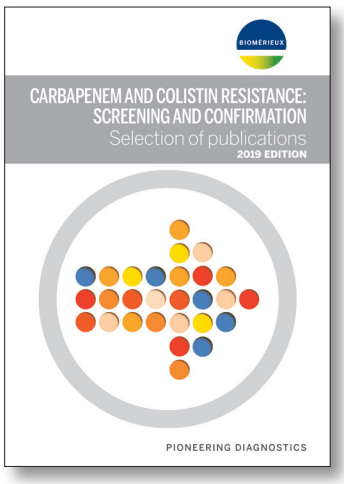
Other “Selection of Publications” available

Contact your local bioMérieux representative to find out more about available literature









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