13th ACCP 2023

Meeting on Antimicrobial Chemotherapy in Clinical Practice (ACCP)

Genova | 16 -17 novembre 2023
Starhotels President

Presidente del Congresso
Prof. Matteo Bassetti

Terapia antibiotica empirica e diagnostica molecolare rapida: una nuova convivenza

Prof. Ivan Gentile
Cattedra di Malattie Infettive
Università di Napoli Federico II

Il sottoscritto **GENTILE IVAN**

in qualità di relatore,

ai sensi dell’art. 76 sul Conflitto di Interessi, comma 4 dell'Accordo Stato-Regioni del 2 febbraio 2017 e del paragrafo 4.5. del Manuale nazionale di accreditamento per l'erogazione di eventi ECM

dichiara

che negli ultimi due anni ha avuto i seguenti rapporti anche di finanziamento con soggetti portatori di interessi commerciali in campo sanitario:

Abbvie, Abbott, Advanz, AstraZeneca, GSK, Jansenn, MSD, Gilead, Pfizer, Infectopharm, Angelini, SOBI, Basilea

AGENDA

- Introduzione
- Test rapidi: evidenze a supporto
- Pros, cons and pitfalls

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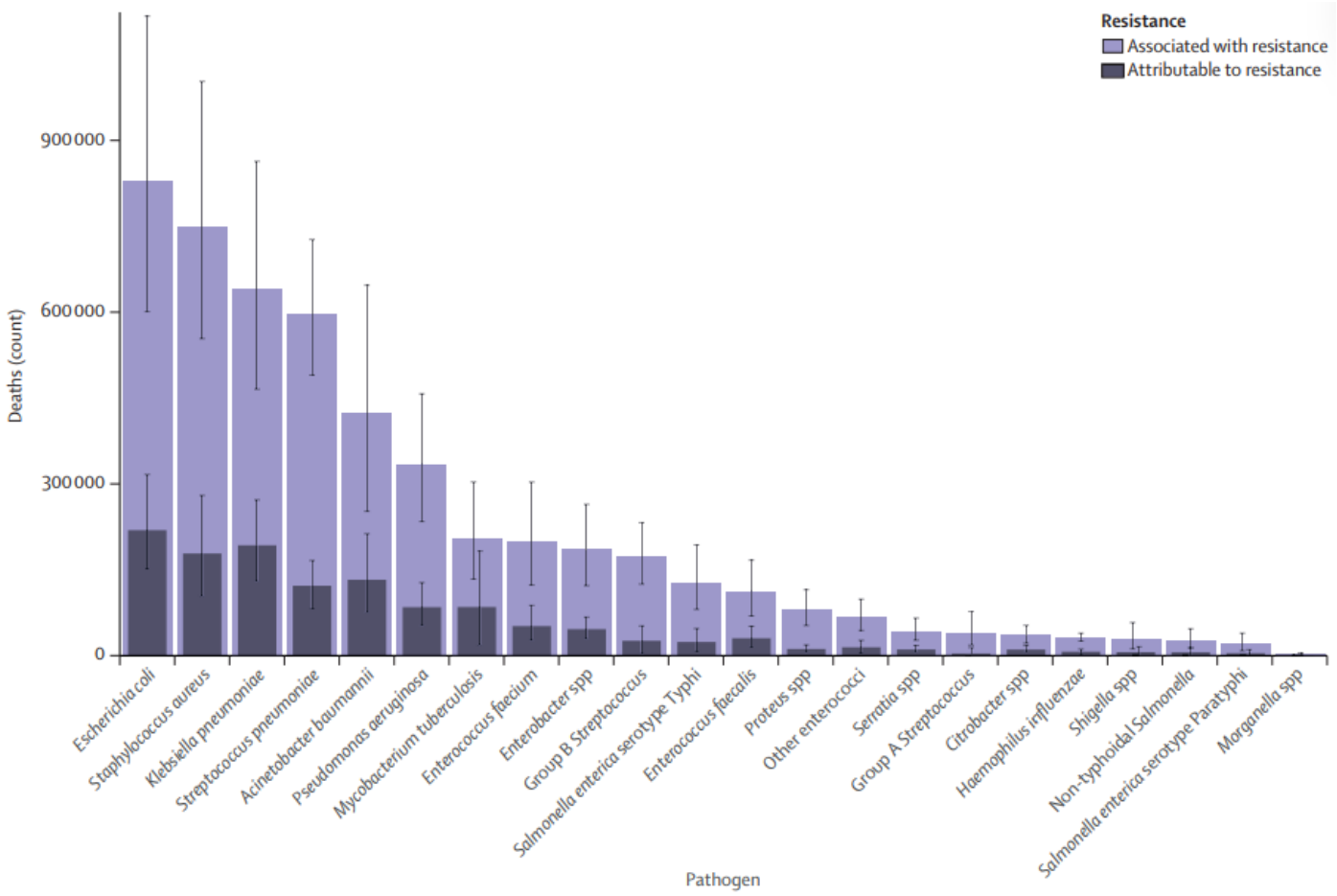
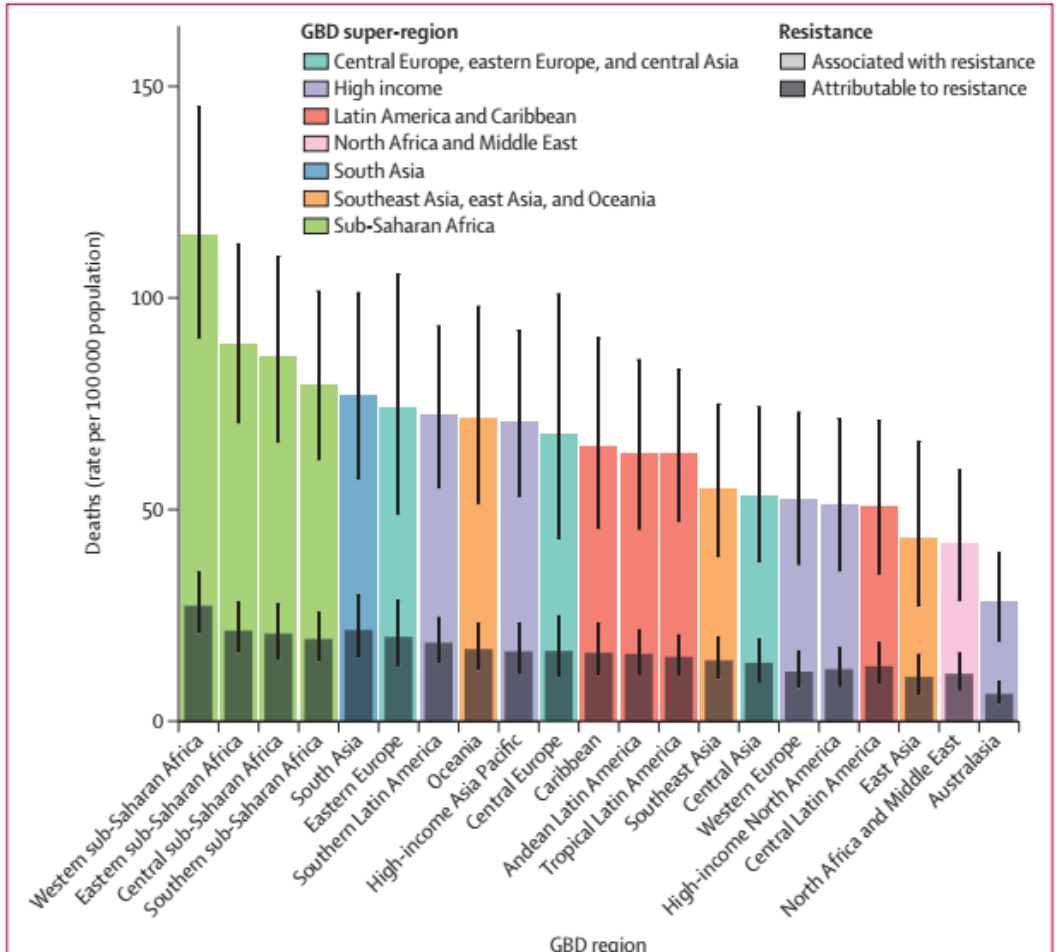
- Test rapidi: evidenze a supporto
- Pros, cons and pitfalls

Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis

*Antimicrobial Resistance Collaborators**

Findings On the basis of our predictive statistical models, there were an estimated 4·95 million (3·62–6·57) deaths associated with bacterial AMR in 2019, including 1·27 million (95% UI 0·911–1·71) deaths attributable to bacterial AMR. At the regional level, we estimated the all-age death rate attributable to resistance to be highest in western sub-





Intensive Care Med (2017) 43:1464–1475
DOI 10.1007/s00134-017-4878-x

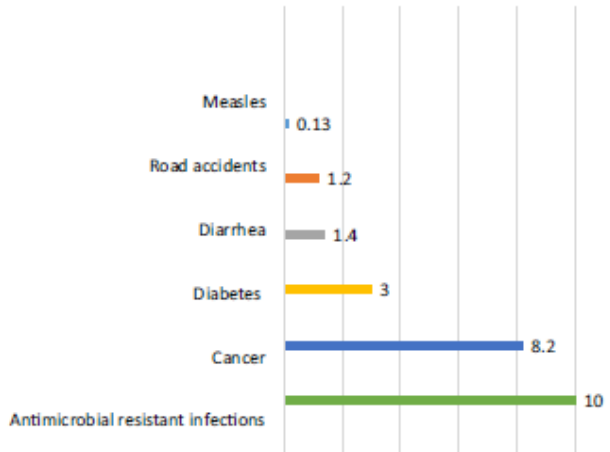
REVIEW

Antimicrobial resistance in the next 30 years, humankind, bugs and drugs: a visionary approach

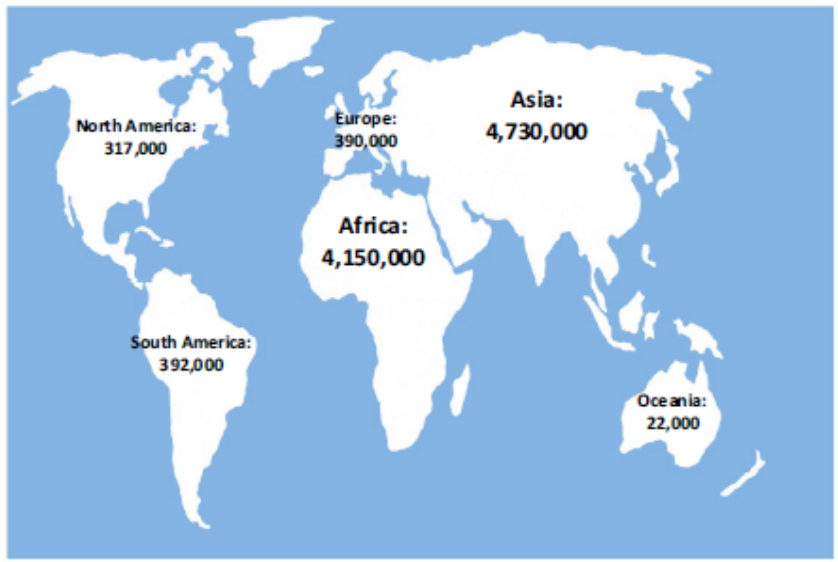
Matteo Bassetti[1*], Garyphallia Poulakou[2], Etienne Ruppe[3], Emilio Bouza[4,5,6,7], Sebastian J. Van Hal[8] and Adrian Brink[9,10]

The impact of antimicrobial resistance in 2050

DEATHS PER ANNUM FOR ANTIMICROBIAL RESISTANT INFECTIONS AND OTHER CAUSES BY 2050 IN MILLIONS. [1] AND HTTP://AMR-REVIEW.ORG/



Death attributable to antimicrobial resistance every year by 2050 in different countries [1]



Final Report

DRUG-RESISTANT INFECTIONS

A Threat to Our Economic Future

March 2017

WORLD BANK GROUP

FIGURE 6. Health Care Costs Reach Nearly $1.2 Trillion in the "High-AMR" Case

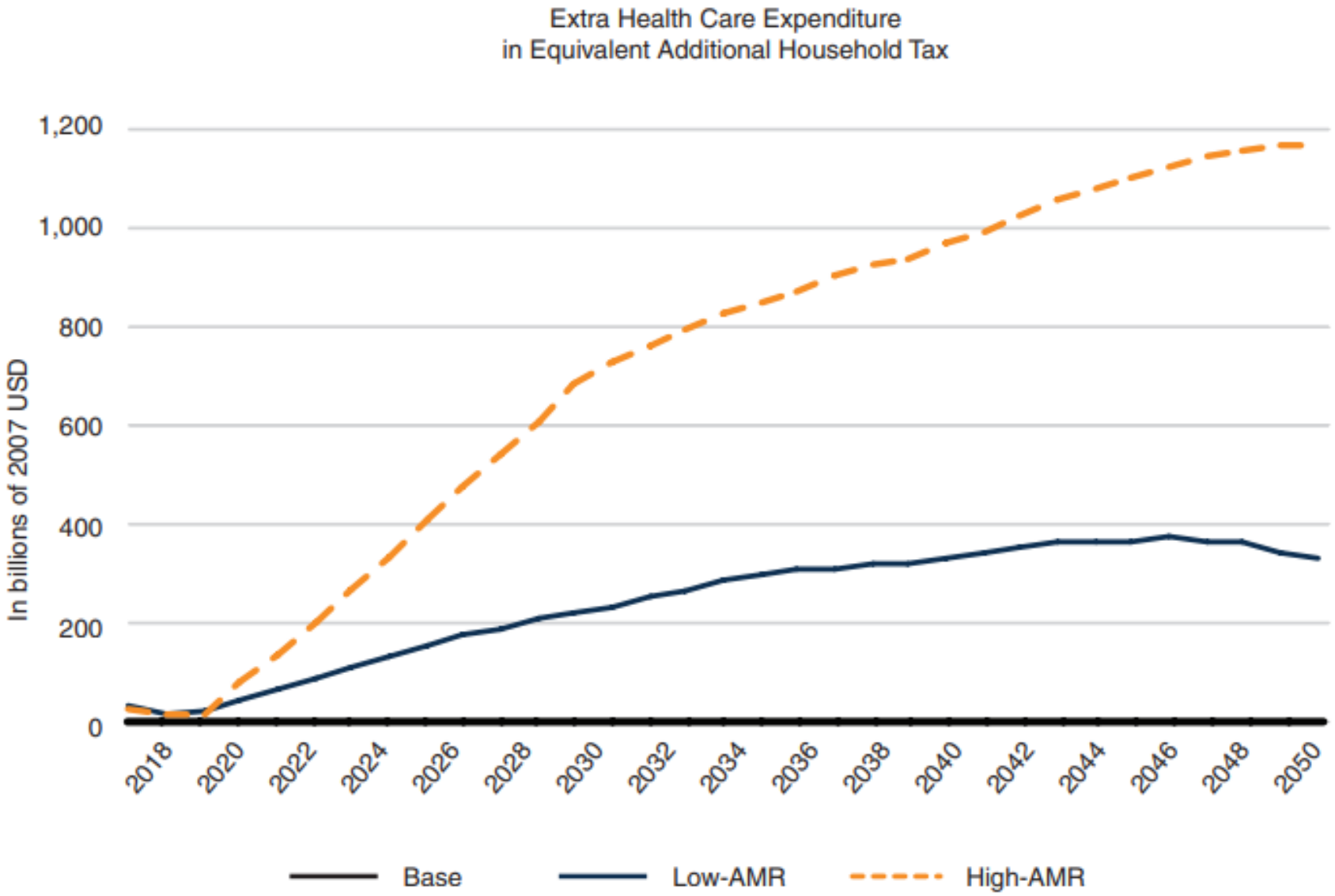
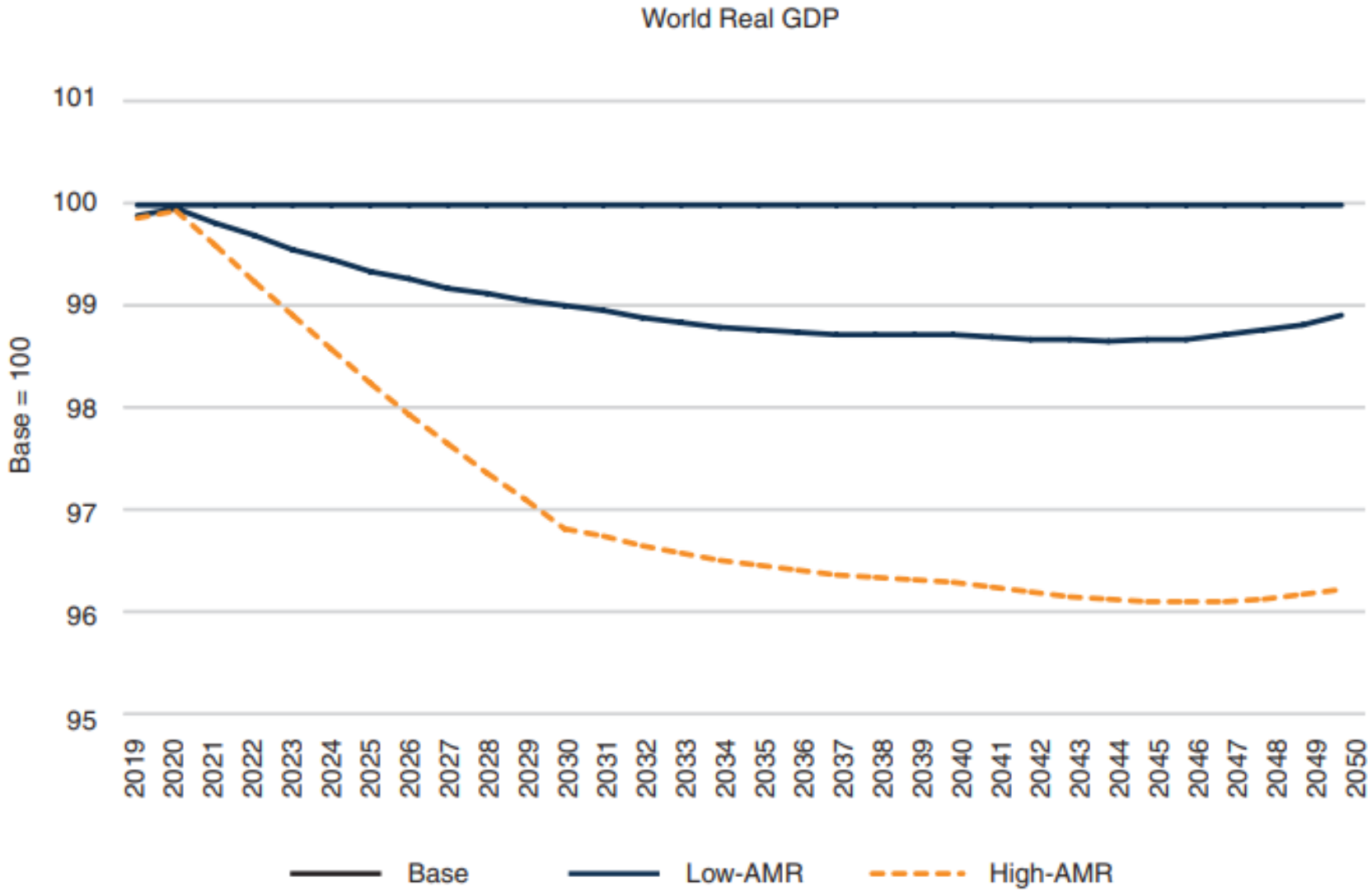
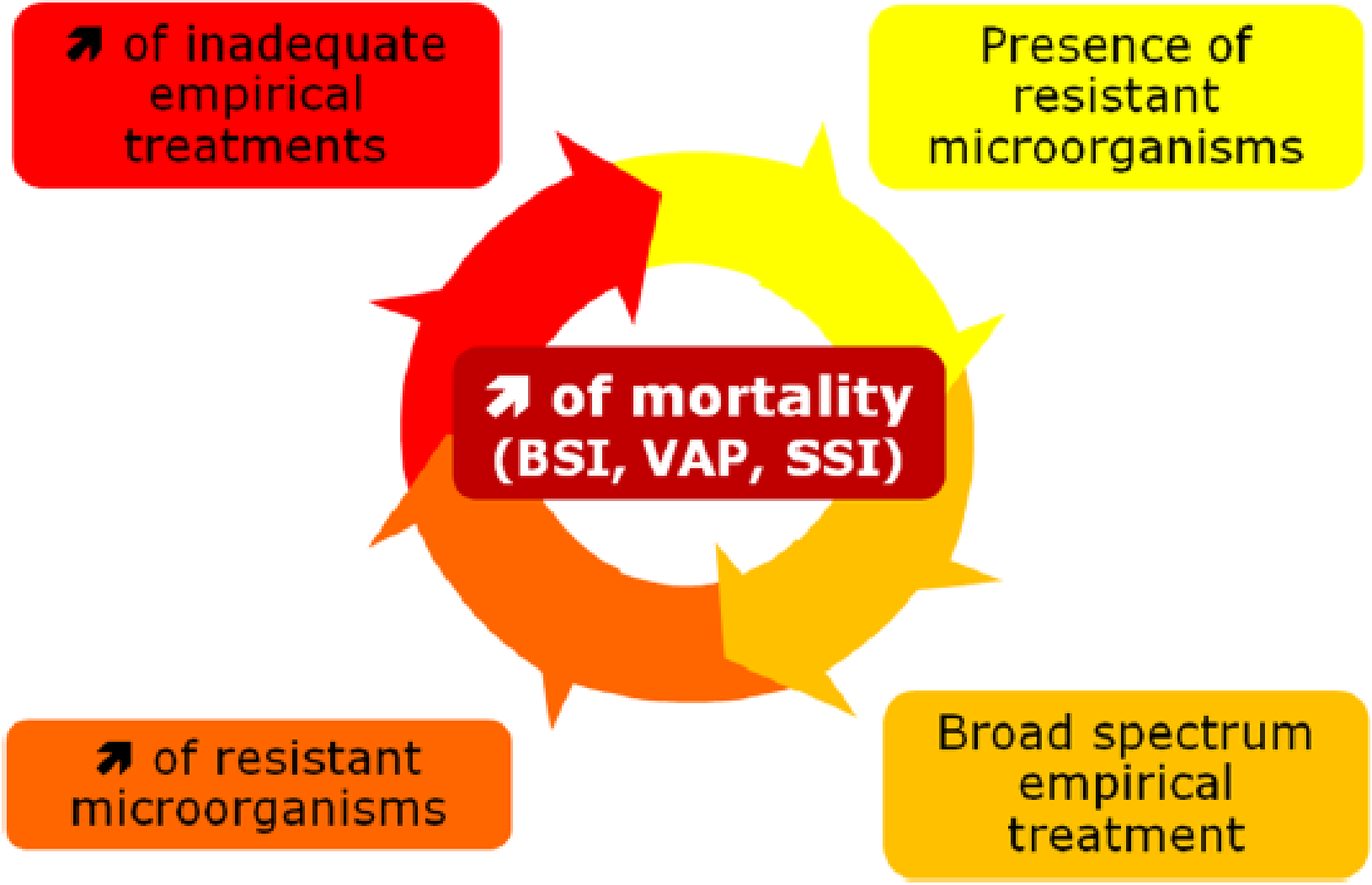


FIGURE ES1. Substantial and Protracted Shortfalls in Global Economic Output



The vicious circle of AMR development



Bassetti M et al. Intensive Care Med. 2015;41(5):776-95.

Van Goethem *et al. Microbiome* (2018) 6:40
https://doi.org/10.1186/s40168-018-0424-5

Microbiome

RESEARCH Open Access

A reservoir of 'historical' antibiotic resistance genes in remote pristine Antarctic soils

Marc W. Van Goethem[1†], Rian Pierneef[2†], Oliver K. I. Bezuidt[1], Yves Van De Peer[1,3,4,5], Don A. Cowan[1] and Thulani P. Makhalanyane[1*]

Abstract

Background: Soil bacteria naturally produce antibiotics as a competitive mechanism, with a concomitant evolution, and exchange by horizontal gene transfer, of a range of antibiotic resistance mechanisms. Surveys of bacterial resistance elements in edaphic systems have originated primarily from human-impacted environments, with relatively little information from remote and pristine environments, where the resistome may comprise the ancestral gene diversity.

Methods: We used shotgun metagenomics to assess antibiotic resistance gene (ARG) distribution in 17 pristine and remote Antarctic surface soils within the undisturbed Mackay Glacier region. We also interrogated the phylogenetic placement of ARGs compared to environmental ARG sequences and tested for the presence of horizontal gene transfer elements flanking ARGs.

Results: In total, 177 naturally occurring ARGs were identified, most of which encoded single or multi-drug efflux pumps. Resistance mechanisms for the inactivation of aminoglycosides, chloramphenicol and β-lactam antibiotics were also common. Gram-negative bacteria harboured most ARGs (71%), with fewer genes from Gram-positive *Actinobacteria* and *Bacilli* (*Firmicutes*) (9%), reflecting the taxonomic composition of the soils. Strikingly, the abundance of ARGs per sample had a strong, negative correlation with species richness ($r = -0.49$, $P < 0.05$). This result, coupled with a lack of mobile genetic elements flanking ARGs, suggests that these genes are ancient acquisitions of horizontal transfer events.

Conclusions: ARGs in these remote and uncontaminated soils most likely represent functional efficient historical genes that have since been vertically inherited over generations. The historical ARGs in these pristine environments carry a strong phylogenetic signal and form a monophyletic group relative to ARGs from other similar environments.

Keywords: Antibiotic resistance genes, Soil resistome, Antarctica, Metagenomics

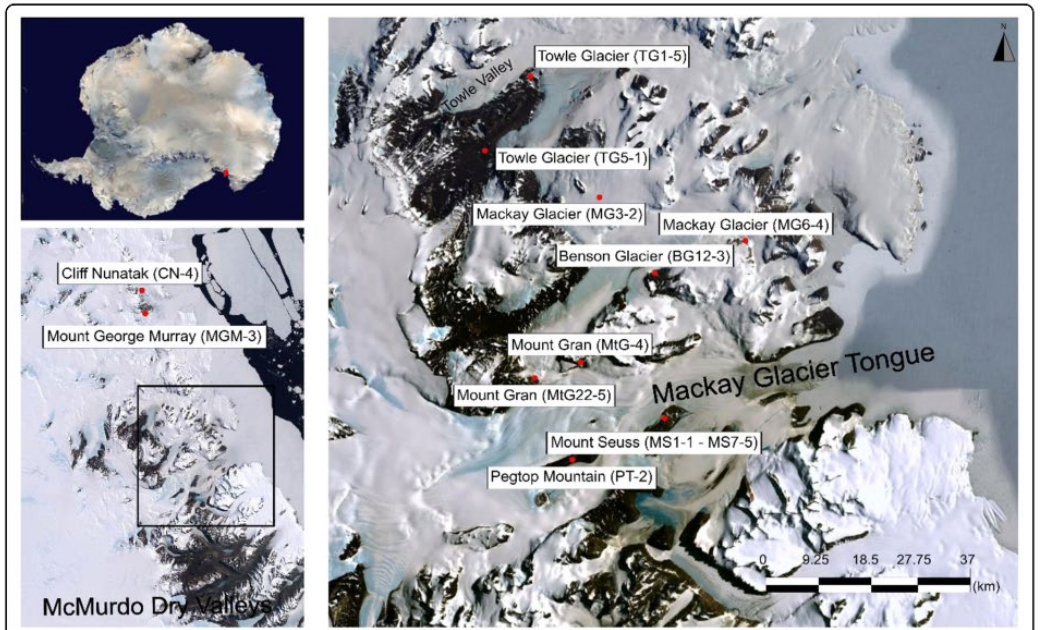


Fig. 1 Satellite image of the Mackay Glacier ecotone with the 17 sampling sites indicated. Source: Landsat Image Mosaic of Antarctica (LIMA) Digital Database and Google Earth

Table 2 ARG families found exclusively in a single community

Sample site	ARG family description
MS4-1	Multidrug efflux pump
MGM-3	Dihydrofolate reductase, which cannot be inhibited by trimethoprim
MS1-1	Tet35 is a tetracycline efflux pump found in the Gram-negative *Vibrio* and *Stenotrophomonas*. Unrelated to other tet resistance genes
TG5-1	Aminoglycoside 6-N-acetyltransferase, which modifies aminoglycosides by acetylation
CN-4	Adenine transferase/methyltransferase, conferring resistance to erythromycin/kasugamycin
	Mutation frequency decline (Mfd) protein

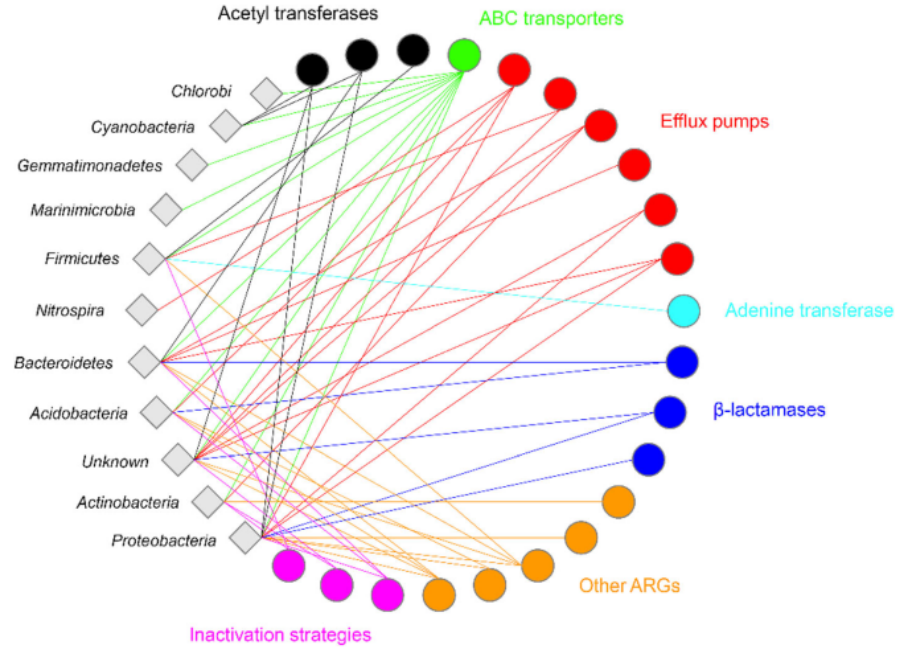


Fig. 3 Co-occurrence network of ARG mechanisms showing resistance mechanisms encoded by diverse soil bacterial phyla. Phyla from all 17 soils that were assigned an ARG are presented here (diamond-shaped nodes), with significant co-occurrences with a specific ARG (circles) indicated (edges)

Antibiotic resistance is often already present in nature, selective pressure with overuse of antibiotics greatly augment the diffusion

Van Goethem, et al. Microbiome 2018

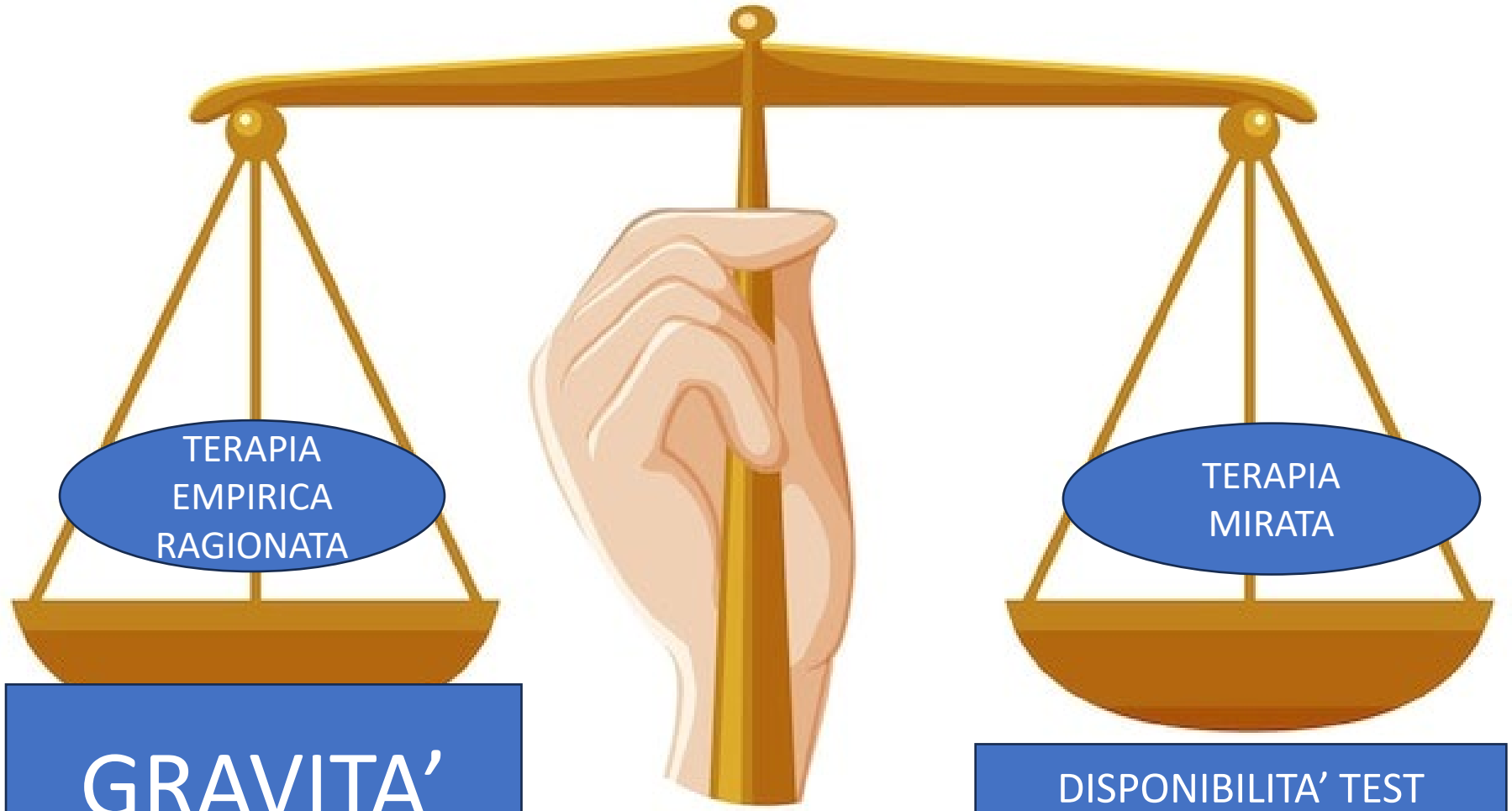
Antibiotic Timing

Shock is present

Shock is absent

	Shock is present	Shock is absent
Sepsis is definite or probable	✔ Administer antimicrobials ***immediately***, ideally within 1 hour of recognition.	✔ Administer antimicrobials ***immediately***, ideally within 1 hour of recognition.
Sepsis is possible	✔ Administer antimicrobials ***immediately***, ideally within 1 hour of recognition.	✔ Rapid assessment* of infectious vs. noninfectious causes of acute illness. ✔ Administer antimicrobials ***within 3 hours*** if concern for infection persists.

**Rapid assessment includes history and clinical examination, tests for both infectious and noninfectious causes of acute illness, and immediate treatment of acute conditions that can mimic sepsis. Whenever possible, this should be completed within 3 hours of presentation so that a decision can be made as to the likelihood of an infectious cause of the patient's presentation and timely antimicrobial therapy provided if the likelihood is thought to be high.*



GRAVITA’

FATTORI LOGISTICI

DISPONIBILITA’ TEST RAPIDI

ASP

AGENDA

- Introduzione
- Test rapidi: evidenze a supporto
- Pros, cons and pitfalls

TABLE 1
Rapid tests for identification and phenotypic/molecular antibiogram of Gram-negative bacteria (GNB) from positive blood cultures

Test	Technology Sensitivity (Se)[a] Specificity (Sp)[a]	Panel of GNB identification[b] and GNB phenotypic/molecular antibiogram	TAT from blood culture positivity[c]	Evidence from RCT and non-randomized, before–after studies on the actual[d] impact on therapeutic decisions, patients' outcomes and stewardship intervention, with focus on GNB or MDR-GNB BSI
MALDI-TOF MS	Laser desorption ionization plus mass spectrometry Se ≥75% Sp ≥95%	*Identification* • Most GNB *Molecular antibiogram* • Usually unavailable outside research laboratories, and needing further clinical evaluation	*Identification* • 0.5–2 hr if made from bacterial pellets • 2–6 hr if made after short incubation of positive cultures on a solid medium • Longer if made from isolated colonies	• In a recent RCT enrolling patients in 2 Vietnamese hospitals with invasive bacterial or fungal infection (mainly BSI, 421/628, 67%, of which 304/421,72%, caused by GNB, mostly *Enterobacterales*), MALDI-TOF MS did not improve proportion of optimal antimicrobial therapy within 24–48 hr after positivity of cultures vs. conventional methods, overall and in subgroups (including the GNB subgroup) [60]. Among *Enterobacterales*, prevalence of third-generation cephalosporin and carbapenem resistance were 48% and 5%, respectively. No subgroup analyses were performed according to antimicrobial resistance. The study was conducted in absence of AMS interventions. In another single-centre controlled trial (not randomized, allocation by weekdays) in Switzerland, no differences in duration of intravenous therapy (primary endpoint) were observed in the MALDI-TOF MS arm vs. conventional processing arm (13 vs. 14 days, p 0.7) in 242 patients with BSI [61]. Rates of admission to ICU (23 vs. 37%, 0.02) and the mean time from Gram-stain to active therapy (3.7 vs. 6.7 hr, p 0.003) were reduced in the MALDI-TOF MS arm vs. conventional processing arm. GNB were isolated in 37% of enrolled patients. The trial was conducted in a background of very rare prevalence of MDR in GNB (<5 episodes of MDR infection/year) • Before-after studies (focused or not focused only on GNB BSI) support a positive effect of MALDI-TOF plus AMS interventions in terms of increased clinical cure rates and reductions in time to optimal therapy, time to microbiological clearance, and length of stay in patients with BSI [8,16,62]
PNA-FISH Quick-FISH	FISH Se ≥95% Sp ≥90%	*Identification* • *Escherichia coli* • *Klebsiella pneumoniae* • *Pseudomonas aeruginosa* *Antibiogram*• Not available	*Identification* • 30 min to 3 hr (depending on the method)	• Clinical studies reporting reductions in antibiotic use, mortality, and costs are mostly focused/limited to Gram-positive organisms [15,63]
ALFRED60	Light scattering technology Se 97-98% Sp NA	*Identification* • Not available *Phenotypic antibiogram* • Some antibiotics used for MDR-GNB are currently not included in the AST panel	*Phenotypic antibiogram* • 3–5 hr	• Currently no RCT or quasi-experimental before-after studies evaluating the actual impact on therapeutic choices, patients' outcomes, and epidemiology of GNB and MDR-GNB BSI
Accelerate Pheno system	FISH/time-lapse microscopy Se 96% Sp 99–100%	*Identification (FISH)* • *E. coli* • *K. pneumoniae* • *P. aeruginosa* • *Acinetobacter baumannii* • Other GNB [20] *Phenotypic antibiogram* • Some antibiotics used for MDR-GNB are currently not included in the AST panel	*Identification* • 1.5–3 hr *Phenotypic antibiogram* • 7–9 hr	• The RCT RAPIDS-GN (NCT03218397), conducted in patients with GNB BSI, and evaluating the clinical impact of the Accelerate Pheno system® plus AMS vs. standard blood culture work-up plus AMS in terms of time to first antibiotic modification (primary endpoint) and various secondary outcomes, including amongst others the development of novel infections due to MDR organisms, has been completed and results are awaited • Another RCT (NCT03745014) is expected to start in September 2019 that will compare the clinical impact of the Accelerate Pheno system® vs. standard blood culture work-up for patients with GNB BSI. The primary endpoint is a composite of patients' outcomes evaluated through the desirability of outcome ranking (DOOR) methodology • Duration of antipseudomonal therapy is one of the 2 major endpoints (the other one is duration of anti-MRSA therapy) of an ongoing RCT (NCT03744728) comparing the use of the Accelerate Pheno system® vs. standard processing plus Verigene BC-GN/GP®
Verigene BC-GN	NAAT/microarrays Se 97% Sp 100%	*Identification* • *E. coli* • *K. pneumoniae* • *P. aeruginosa* • *Acinetobacter* spp. • Other GNB [24] *Molecular antibiogram* • CTX-M • KPC • NDM	*Identification* • <2 hr *Molecular antibiogram* • <2 hr	• In non-randomized, before-after studies, reductions in time to effective therapy, mortality, and length of stay in patients with GNB and/or MDR-GNB BSI were observed after the implementation of the Verigene BC-GN® assay [27,64,65]

TABLE 1 (*continued*)

Test	Technology Sensitivity (Se)[a] Specificity (Sp)[a]	Panel of GNB identification[b] and GNB phenotypic/molecular antibiogram	TAT from blood culture positivity[c]	Evidence from RCT and non-randomized, before–after studies on the actual[d] impact on therapeutic decisions, patients' outcomes and stewardship intervention, with focus on GNB or MDR-GNB BSI
		• OXA-23, -40, -48 and -58 groups • IMP • VIM		
FilmArray BCID	NAAT/microarrays Se >90% Sp 100%	*Identification* • *E. coli* • *K. pneumoniae* • *P. aeruginosa* • *A. baumannii* • Other GNB [30] *Molecular antibiogram* • KPC	*Identification* • 1 hr *Molecular antibiogram* • 1 hr	• In an RCT, 617 patients with BSI (of which 33% due to GNB) were randomized in 3 arms: (a) standard processing; (b) FilmArray BCID®; (c) FilmArray BCID® plus AMS. The primary endpoint was duration of selected antimicrobial therapies, with duration of piperacillin-tazobactam therapy been lower in the FilmArray BCID® and FilmArray BCID® plus AMS arms than in the standard processing arm (44 hr and 45 hr vs. 56 hr, respectively, p 0.012) [66]. The study was conducted in a setting with low prevalence of MDR organisms. No KPC production was reported. Other RCT (NCT02743585, NCT03255759) exploring patient-level relevant outcomes are ongoing • In non-randomized, before–after studies, reductions in time to effective therapy and time to de-escalation were observed after the implementation of the FilmArray BCID® assay in samples including either only GNB BSI or both GPB and GNB BSI [33,67,68]
LFIA methods	LFIA Se >95% Sp >95%	*Identification* • Not available *Molecular antibiogram* • NDM • KPC • IMP • VIM • OXA-48-like and OXA-23	*Molecular antibiogram* • <30 min	• Currently no RCT or quasi-experimental before-after studies evaluating the actual impact on therapeutic choices, patients' outcomes, and epidemiology of GNB and MDR-GNB BSI
Unyvero System	NAAT Se 100% Sp 99.75%	*Identification* • *E. coli* • *K. pneumoniae* • *P. aeruginosa* • *A. baumannii* • Other GNB [34] *Molecular antibiogram* • KPC • NDM • IMP • VIM • OXA-48, -23, -24, -58 • CTX-M-14, CTX-M-15 • *aac* (6′)/*aph* (2″) • *aac*A4	*Identification* • 4–5 hr *Molecular antibiogram* • 4–5 hr	• Currently no RCT or quasi-experimental before-after studies evaluating the actual impact on therapeutic choices, patients' outcomes, and epidemiology of GNB and MDR-GNB BSI

TABLE 2
Rapid tests for identification and molecular antibiogram of Gram-negative bacteria (GNB) directly from whole blood

Test	Technology Sensitivity (Se)[a] Specificity (Sp)[a]	Panel of GNB identification[b] and GNB molecular antibiogram	TAT from blood draw[c]	Evidence from RCT and non-randomized, before-after studies on the actual[d] impact on therapeutic decisions, patients' outcomes, and stewardship intervention, with focus on GNB or MDR-GNB BSI
LightCycler SeptiFast	NAAT Se 50-75% Sp 86-92%	*Identification* • *Escherichia coli* • *Klebsiella pneumoniae* • *Pseudomonas aeruginosa* • *Acinetobacter baumannii* • Other GNB [41]	*Identification* • 4–5 hr	• In a recent, single-centre RCT in 200 patients with sepsis comparing the use of the LightCycler SeptiFast® vs. conventional cultures, no difference was observed in antimicrobial consumption (primary endpoint). In the subgroup of patients with microbiological diagnosis in both arms (44, of which 68% were GNB) a reduction in antimicrobial consumption was observed in the SeptiFast® arm (1429 vs. 1889 DOT per 1000 patient-days). Statistically significant reductions were also observed in the time to de-escalation (8 vs. 54 hr) and in the duration of antimicrobial therapy (12 vs. 15 days), but not in mortality [69]. Antimicrobial costs were reduced for anti-GPB but not for anti-GNB agents. The trial was conducted in a setting of high prevalence of MDR (no further details provided) • In a multicentre, cluster-randomized, crossover trial, appropriate antimicrobial treatment in patients with severe infections (mostly severe sepsis) and microbiological diagnosis (n = 478) was similar in the intervention (SeptiFast®) and the control (conventional cultures) periods (92% vs. 91%) [70]. GNB were 14% of identified pathogens. Overall, SeptiFast® increased the number of septic patients with microbial diagnosis. No information on resistance prevalence in GNB was provided. • Patient-level outcomes and costs including those assigned to future resistance are among the endpoints of the Optimal Antibiotic Treatment of Moderate to Severe Bacterial Infections (CDSS) RCT, evaluating the use of SeptiFast® plus a computerized decision support system for antibiotic treatment (NCT01338116, last updated as recruiting patients in April 2016)
Magicplex Sepsis	NAAT Se 33-65% Sp 66-92%	*Identification* • *E. coli* • *K. pneumoniae* • *P. aeruginosa* • *A. baumannii* • Other GNB [43]	*Identification* • 3–6 hr	• Currently no RCT or quasi-experimental before-after studies evaluating the actual impact on therapeutic choices, patients' outcomes, and epidemiology of GNB and MDR-GNB BSI
VYOO	NAAT Se 60% Sp 75%	*Identification* • *E. coli* • *K. pneumoniae* • *P. aeruginosa* • *A. baumannii* • Other GNB [47] *Molecular antibiogram* • CTX-M • SHV	*Identification* • 7 hr	• Currently no RCT or quasi-experimental before-after studies evaluating the actual impact on therapeutic choices, patients' outcomes, and epidemiology of GNB and MDR-GNB BSI
SepsiTest	NAAT Se 21-85% Sp 53-100%	*Identification* • *E. coli* • *K. pneumoniae* • *P. aeruginosa* • *A. baumannii* • Other GNB [51]	*Identification* • 8 hr	• Currently no RCT or quasi-experimental before-after studies evaluating the actual impact on therapeutic choices, patients' outcomes, and epidemiology of GNB and MDR-GNB BSI
IRIDICA BAC BSI (production discontinued)	NAAT/ESI-MS Se 81% Sp 84%	*Identification* • *E. coli* • *K. pneumoniae* • *P. aeruginosa* • *A. baumannii* • Other GNB [52] *Molecular antibiogram* • KPC	*Identification* • 6–8 hr *Molecular antibiogram* • 6–8 hr	• No RCT or quasi-experimental before-after studies evaluating the actual impact on therapeutic choices, patients' outcomes, and epidemiology of GNB and MDR-GNB BSI
T2Bacteria panel	NAAT/T2MR Se 83–90% Sp 90–98%	*Identification* • *A. baumannii* • *P. aeruginosa* • *E. coli* • *K. pneumoniae*	*Identification* • 5–6 hr	• Currently no RCT or quasi-experimental before-after studies evaluating the actual impact on therapeutic choices, patients' outcomes, and epidemiology of GNB and MDR-GNB BSI

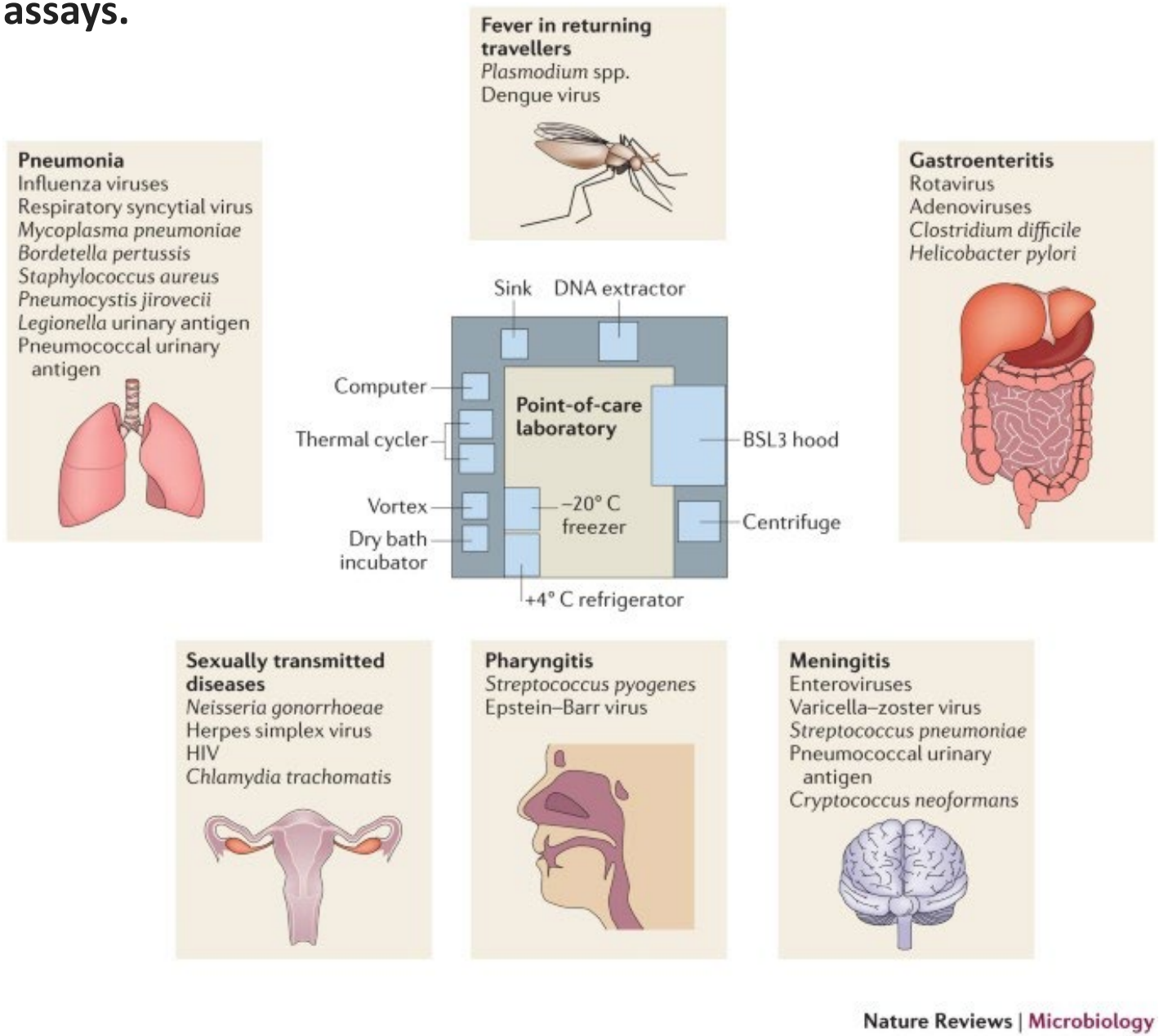
Table 3. Different infectious polymicrobial diseases: a comparison of molecular diagnostic technologies.

Technology	Cost-Effective	Sensitivity	Specificity	Turnaround Time	Multiplexing Capability	Refs.
Microbiological Methods						
Blood Culture/Gram Staining	★★★	★	★	★★★	★	[179]
BactecFx/VITEK 2	★★	★★	★★	★★★	★★	[180]
Biochemical Methods	★★★	★	★	★★★	★	[181]
Modern Methods						
Molecular Methods						
Real-Time PCR	★★	★★★	★★	★★★	★★	[182]
SERS	★★	★★	★★	★★	★★	[183]
MALDI-TOF	★	★	★★	★	★	[184]
AMR Detection Methods						
HRM	★★	★★	★★	★★★	★	[185]
Sequencing	★	★★★	★★★	★	★★★	[173]
DNA Microarray	★	★★	★★	★★	★★★	[186]
Advanced Methods						
Biosensors	★	★★	★★	★	★★★	[187]
POCT	★	★★	★★	★	★★★	[186,187]
CRISPR/Cas9	★	★★	★★	★★	★★★	[188]
CRISPR/Cas9						

(★ More stars suggest more cost effective, less sensitive and specificity, more turnaround time and vice-versa according to the technology).

Diagnostics **2023**, *13*(2), 277; https://doi.org/10.3390/diagnostics13020277

Diagnosis of infectious diseases using point-of-care assays.



Nature Reviews Microbiology **volume 11**, pages574–585 (2013)

| Review | 14 December 2016

Antimicrobial Stewardship: How the Microbiology Laboratory Can Right the Ship

Authors: Philippe Morency-Potvin, David N. Schwartz, Robert A. Weinstein | AUTHORS INFO & AFFILIATIONS

Point of Care diagnostics

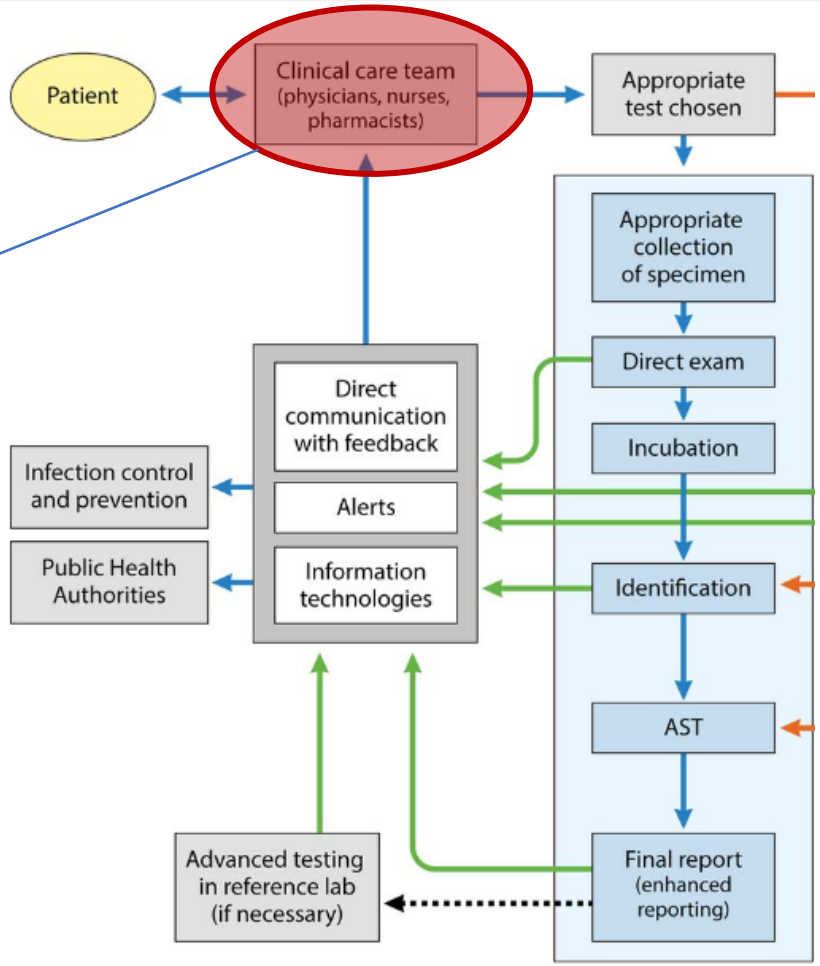


FIG 1 Workflow pathways for conventional microbiology and RDT. Implementation of RDT increases laboratory workflow complexity but can hasten the availability of results. Communication of results is a key factor. Blue arrows represent the conventional microbiology pathway, orange arrows represent the RDT pathway, and green arrows represent opportunities for the laboratory and antimicrobial stewardship teams to improve communication of results. AST, antimicrobial susceptibility testing.

Clinical Microbiology Reviews, 2016

Clinical Infectious Diseases

MAJOR ARTICLE

Clinical Impact of a Multiplex Gastrointestinal Polymerase Chain Reaction Panel in Patients With Acute Gastroenteritis

Robert J. Cybulski Jr,[1,a] Allen C. Bateman,[1,a,b] Lori Bourassa,[1] Andrew Bryan,[1] Barb Beail,[1] Jason Matsumoto,[2] Brad T. Cookson,[1,3] and Ferric C. Fang[1,2,3,4]

[1]Department of Laboratory Medicine, University of Washington, [2]Harborview Medical Center Clinical Microbiology Laboratory, [3]Department of Microbiology, University of Washington, and [4]University of Washington School of Medicine, Seattle

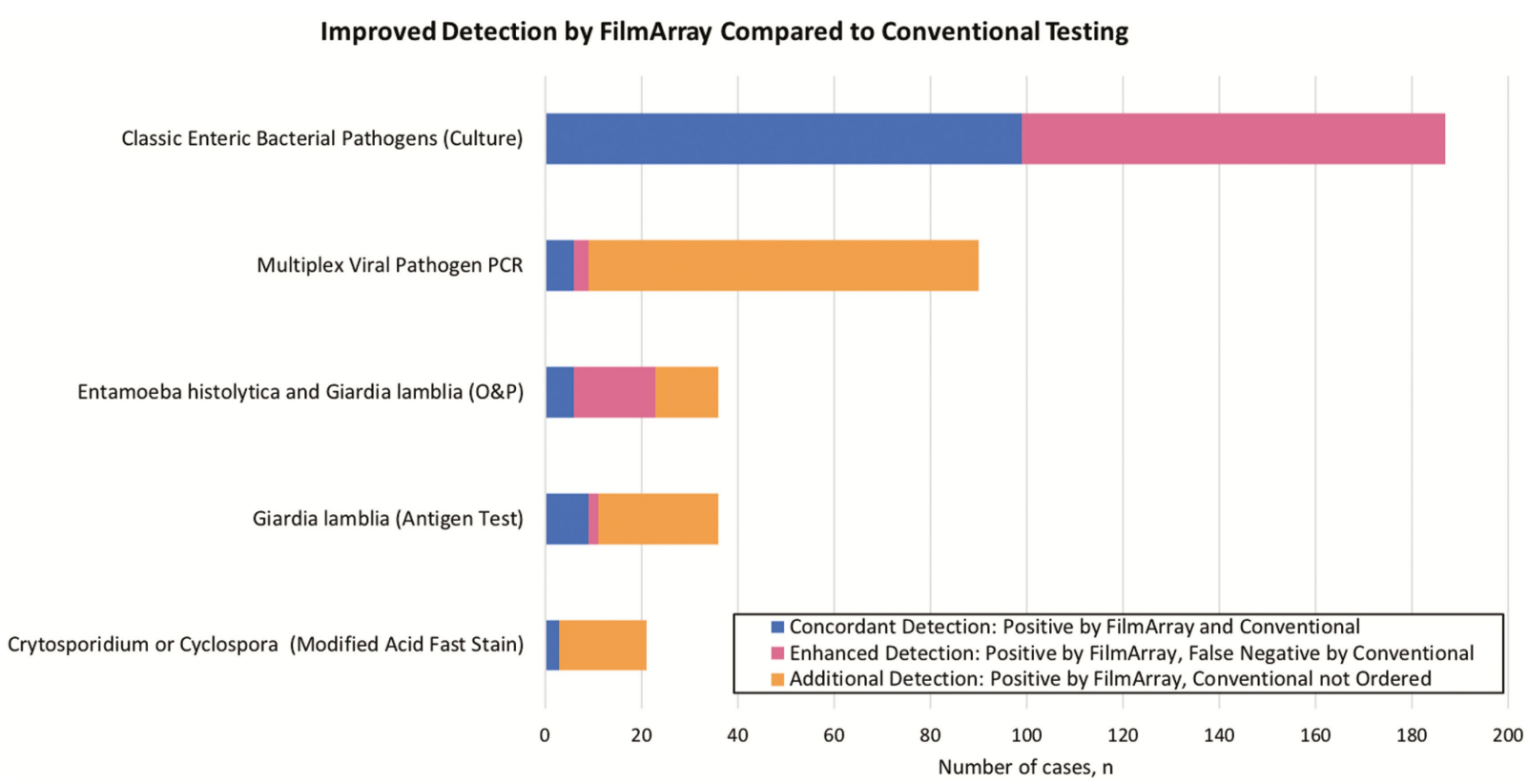
Background. Molecular syndromic diagnostic panels can enhance pathogen identification in the approximately 2–4 billion episodes of acute gastroenteritis that occur annually worldwide. However, the clinical utility of these panels has not been established.

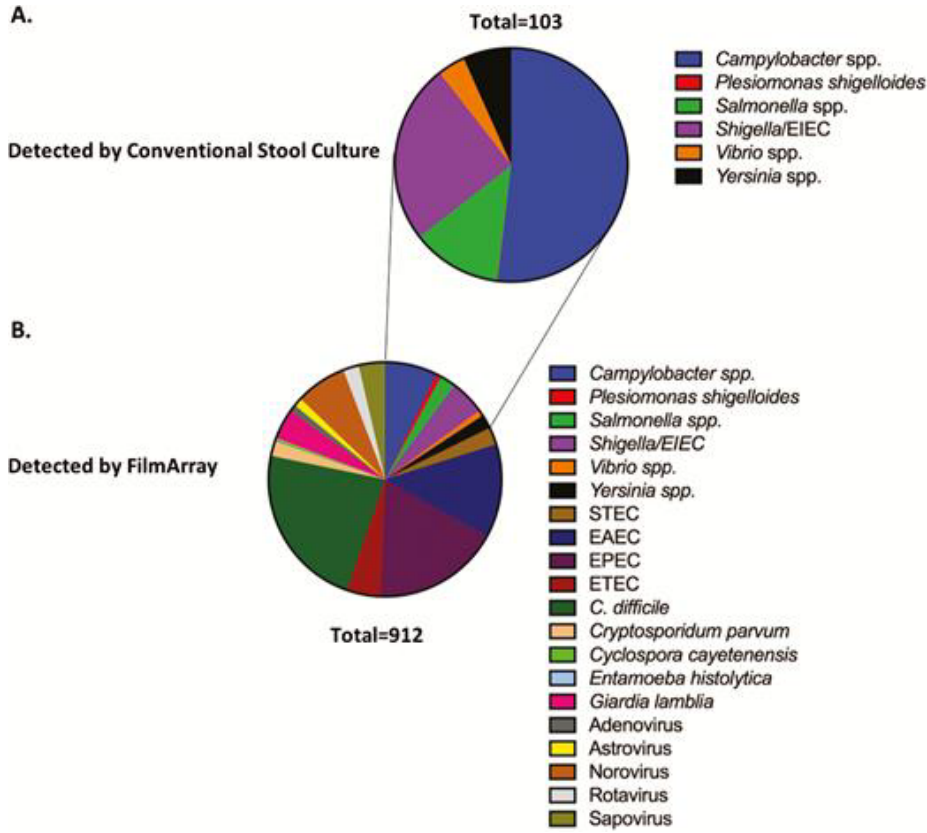
Methods. We conducted a prospective, multi-center study to investigate the impact of the BioFire FilmArray Gastrointestinal polymerase chain reaction panel on clinical diagnosis and decision-making, and compared the clinical acuity of patients with positive results obtained exclusively with the FilmArray with those detected by conventional stool culture. A total of 1887 consecutive fecal specimens were tested in parallel by FilmArray and stool culture. Laboratory and medical records were reviewed to determine rates of detection, turnaround times, clinical features, and the nature and timing of clinical decisions.

Results. FilmArray detected pathogens in 35.3% of specimens, compared to 6.0% for culture. Median time from collection to result was 18 hours for FilmArray and 47 hours for culture. Median time from collection to initiation of antimicrobial therapy was 22 hours for FilmArray and 72 hours for culture. Patients diagnosed by FilmArray were more likely to receive targeted rather than empirical therapy, compared to those diagnosed by culture ($P = .0148$). Positive Shiga-like toxin-producing *E. coli* results were reported 47 hours faster with FilmArray and facilitated discontinuation of empirical antimicrobials. Patients diagnosed exclusively by FilmArray had clinical characteristics similar to those identified by culture.

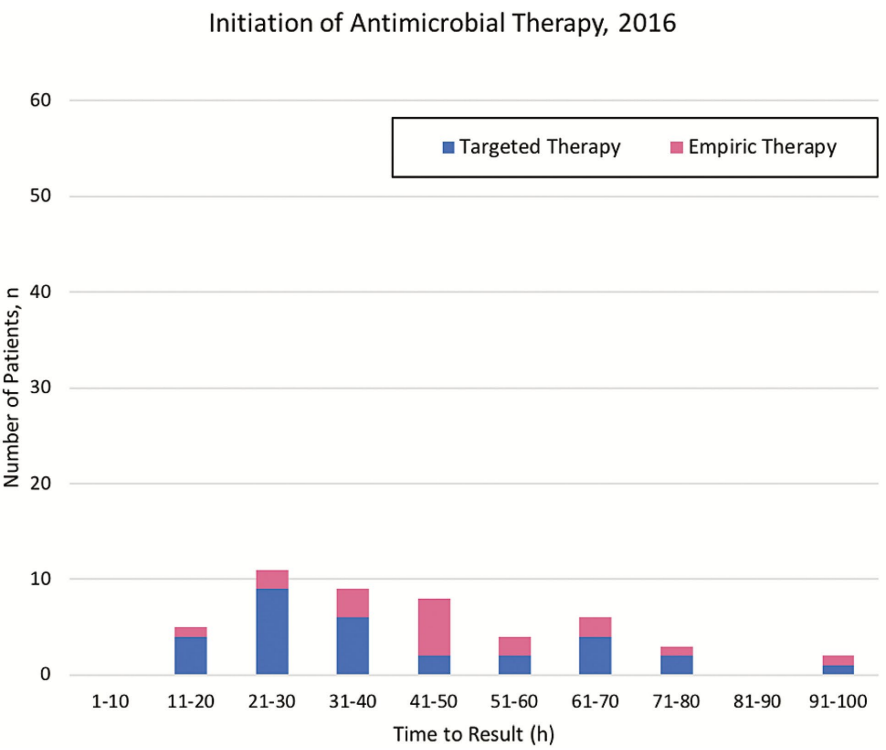
Conclusions. FilmArray markedly improved clinical sensitivity in patients with acute diarrhea, identified cases with clinical acuity comparable to those identified by culture, and enabled clinicians to make more timely and targeted therapeutic decisions.

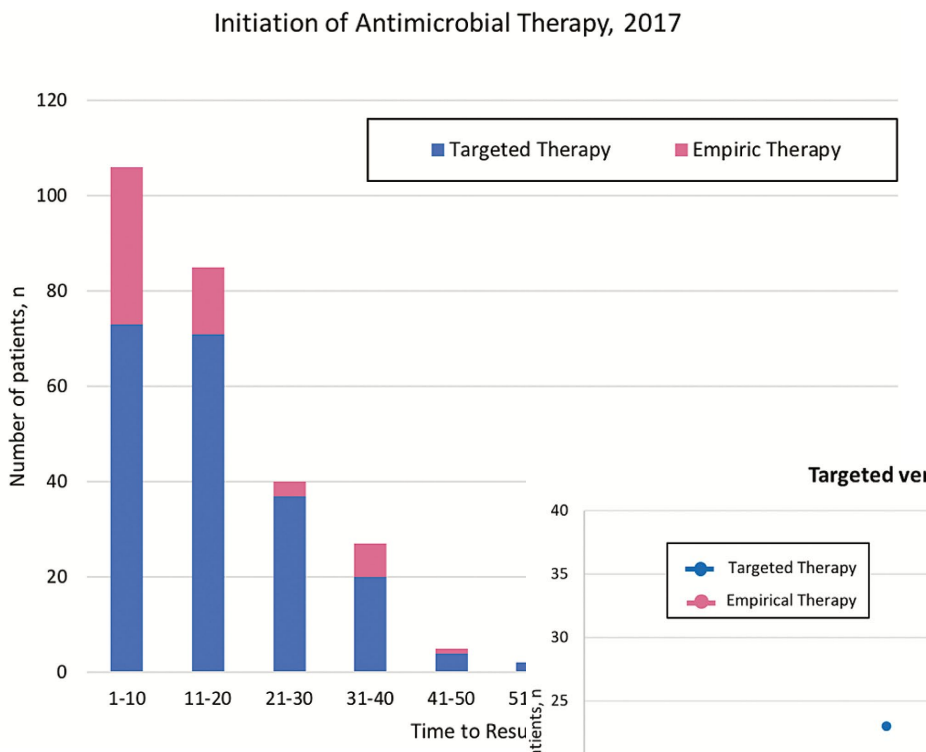
Keywords. acute gastroenteritis; multiplex PCR panel; syndromic testing; culture-independent diagnostic test.

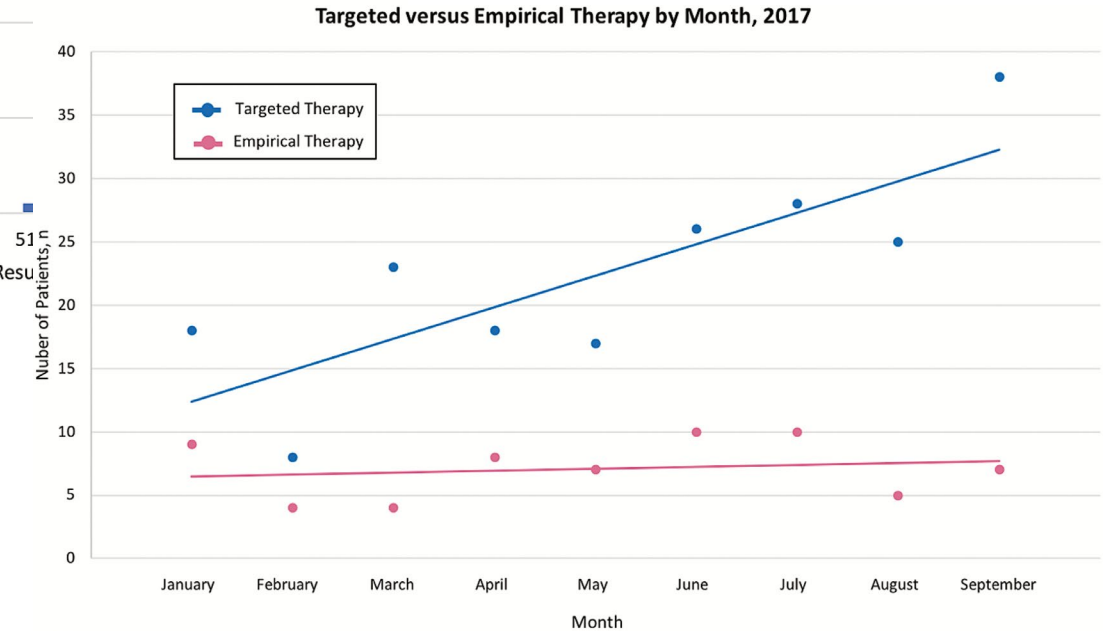




Cybulski et al. Clinical Infectious Diseases, Volume 67, Issue 11, 1 December 2018, Pages 1688–1696,







The estimated median time from collection to antibiotic initiation was 26 hours in 2017 compared to 72 hours in 2016 ($P < .0001$). In 2017, 64 of 272 (23.5%) antimicrobial prescriptions were initiated empirically at the time of encounter. This proportion is lower ($P = .0148$) than the 20 of 50 (40.0%) cases of empirical therapy in 2016 The use of Film Array resulted in a significant ($r^2 = 0.65$, $P = .009$ by linear regression) trend toward targeted rather than empirical therapy over the course of the study period

Journal of Clinical Microbiology®

BACTERIOLOGY

J Clin Microbiol 58:e00135-20. https://doi.org/10.1128/JCM.00135-20.

Practical Comparison of the BioFire FilmArray Pneumonia Panel to Routine Diagnostic Methods and Potential Impact on Antimicrobial Stewardship in Adult Hospitalized Patients with Lower Respiratory Tract Infections

Blake W. Buchan,[a] Sam Windham,[a] Joan-Miquel Balada-Llasat,[b] Amy Leber,[c] Amanda Harrington,[d] Ryan Relich,[e] Caitlin Murphy,[f] Jennifer Dien Bard,[g] Samia Naccache,[g] Shira Ronen,[a] Amanda Hopp,[a] Derya Mahmutoglu,[a] Matthew L. Faron,[a] Nathan A. Ledeboer,[a] Amanda Carroll,[b] Hannah Stone,[b] Oluseun Akerele,[b] Kathy Everhart,[c] Andrew Bonwit,[d] Christina Kwong,[d] Rebecca Buckner,[e] Del Warren,[e] Randal Fowler,[f] Sukantha Chandrasekaran,[h] Holly Huse,[h] Shelley Campeau,[h]* Romney Humphries,[h]* Corrin Graue,[i] Angela Huang[a,j]

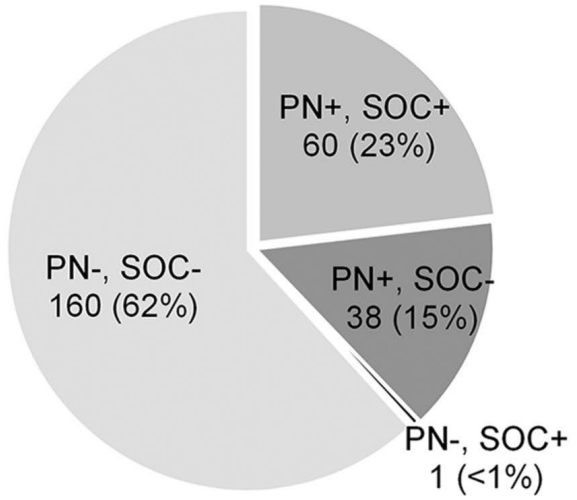
ABSTRACT Lower respiratory tract infections, including hospital-acquired and ventilator-associated pneumonia, are common in hospitalized patient populations. Standard methods frequently fail to identify the infectious etiology due to the polymicrobial nature of respiratory specimens and the necessity of ordering specific tests to identify viral agents. The potential severity of these infections combined with a failure to clearly identify the causative pathogen results in administration of empirical antibiotic agents based on clinical presentation and other risk factors. We examined the impact of the multiplexed, semiquantitative BioFire FilmArray Pneumonia panel (PN panel) test on laboratory reporting for 259 adult inpatients submitting bronchoalveolar lavage (BAL) specimens for laboratory analysis. The PN panel demonstrated a combined 96.2% positive percent agreement (PPA) and 98.1% negative percent agreement (NPA) for the qualitative identification of 15 bacterial targets compared to routine bacterial culture. Semiquantitative values reported by the PN panel were frequently higher than values reported by culture, resulting in semiquantitative agreement (within the same $\log_{10}$ value) of 43.6% between the PN panel and culture; however, all bacterial targets reported as $>10^5$ CFU/ml in culture were reported as $\geq 10^5$ genomic copies/ml by the PN panel. Viral targets were identified by the PN panel in 17.7% of specimens tested, of which 39.1% were detected in conjunction with a bacterial target. A review of patient medical records, including clinically prescribed antibiotics, revealed the potential for antibiotic adjustment in 70.7% of patients based on the PN panel result, including discontinuation or de-escalation in 48.2% of patients, resulting in an average savings of 6.2 antibiotic days/patient.

TABLE 1 BioFire PN panel targets

Category (result type)	Target
Viruses (qualitative)	Adenovirus
	Coronavirus
	Human metapneumovirus
	Human rhinovirus/enterovirus
	Influenza A virus
	Influenza B virus
	Parainfluenza virus
	Respiratory syncytial virus
	Bacteria (qualitative result)
Bacteria (qualitative)	*Chlamydia pneumoniae*
	Legionella pneumophila
	Mycoplasma pneumoniae
Bacteria (semiquantitative[a])	*Acinetobacter calcoaceticus-A. baumannii* complex
	Enterobacter cloacae complex
	Escherichia coli
	Haemophilus influenzae
	Klebsiella aerogenes
	Klebsiella oxytoca
	Klebsiella pneumoniae group
	Moraxella catarrhalis
	Proteus spp.
	Pseudomonas aeruginosa
	Serratia marcescens
	Staphylococcus aureus
	Streptococcus agalactiae
	Streptococcus pneumoniae
	Streptococcus pyogenes
Antimicrobial resistance markers (qualitative, conditionally reported)	
Carbapenemases	KPC[b]
	NDM[b]
	IMP[b]
	VIM[b]
	OXA-48-like[c]
Extended-spectrum beta-lactamases	CTX-M[b]
Methicillin resistance genes	*mecA*/*mecC* and MREJ[d]

Buchan BW, JCM 2020

A Total number of BAL Specimens (n=259) with Bacterial Target(s) Detected



B Number of Bacterial Targets (n=151) Detected in all BAL Specimens

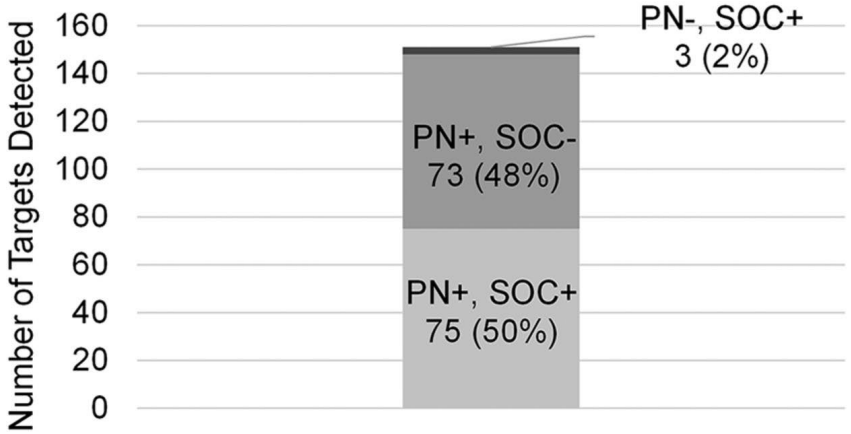
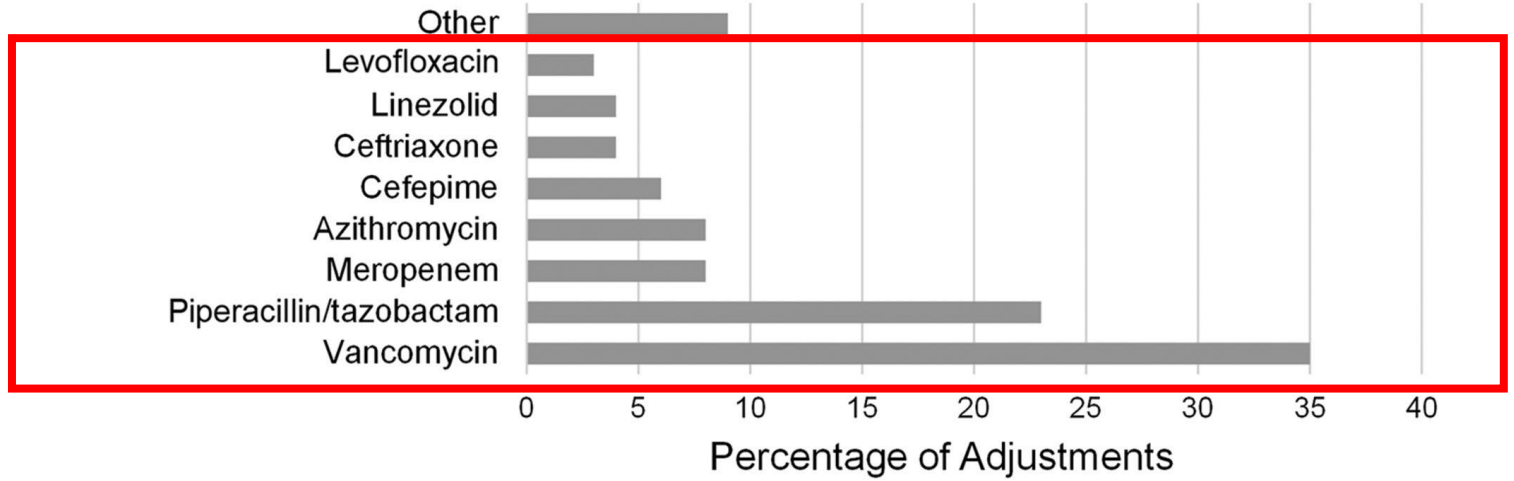


TABLE 7

TABLE 7 Potential impact of the BioFire PN panel result on antibiotic utilization

Potential modification	No. of antimicrobials	No. (%) of patients	No. of hrs
Appropriate de-escalation/discontinuation	206	122 (48.2)	18,284.07
Appropriate escalation/initiation	11	11 (4.3)	184.66
Inappropriate de-escalation/discontinuation	4	4 (1.6)	
Inappropriate escalation/continuation	42	42 (16.6)	
No change		74 (29.2)	
Unable to assess[a]		16	

Appropriate Antibiotic De-escalation/Discontinuation



JOURNAL ARTICLE

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

Ritu Banerjee, Christine B. Teng, Scott A. Cunningham, Sherry M. Ihde, James M. Steckelberg, James P. Moriarty, Nilay D. Shah, Jayawant N. Mandrekar, Robin Patel Author Notes

Clinical Infectious Diseases, Volume 61, Issue 7, 1 October 2015, Pages 1071–1080, https://doi.org/10.1093/cid/civ447

Published: 20 July 2015 **Article history**

(See the Editorial Commentary by Caliendo on pages 1081–3.)

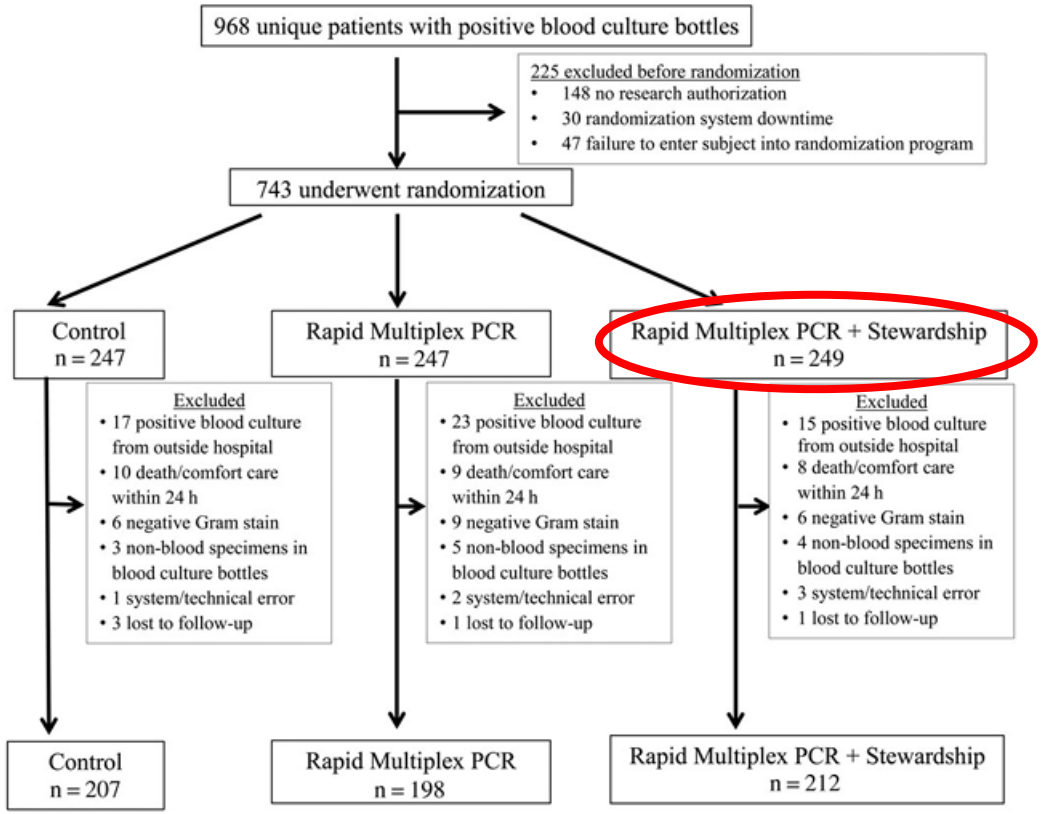
Background. The value of rapid, panel-based molecular diagnostics for positive blood culture bottles (BCBs) has not been rigorously assessed. We performed a prospective randomized controlled trial evaluating outcomes associated with rapid multiplex PCR (rmPCR) detection of bacteria, fungi, and resistance genes directly from positive BCBs.

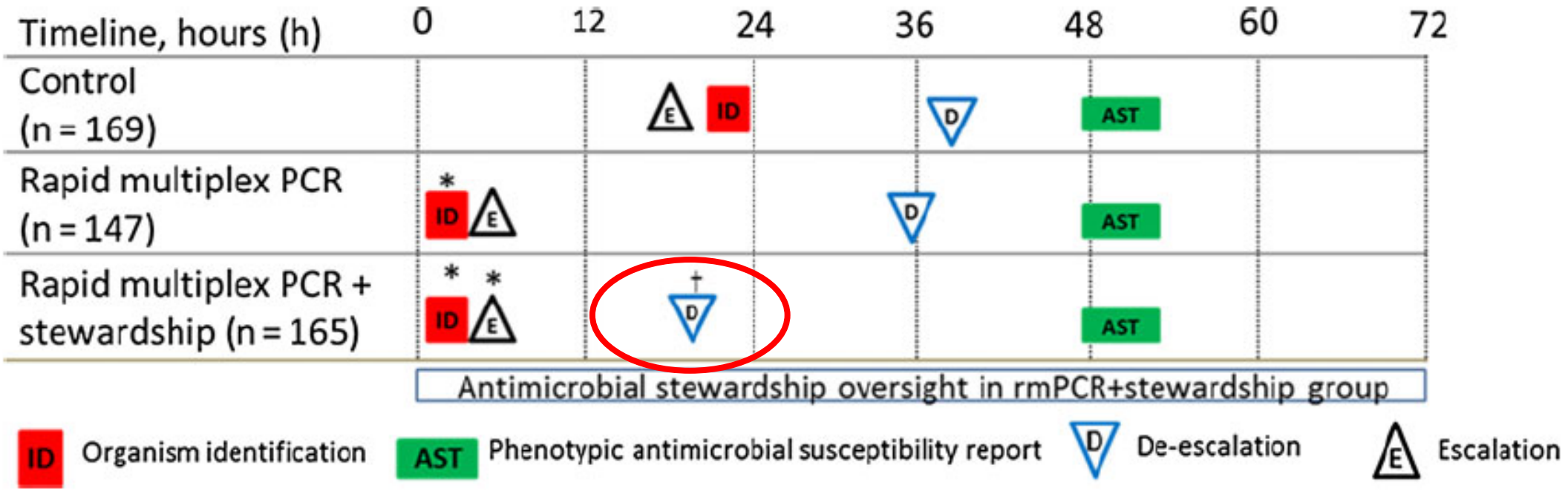
Methods. A total of 617 patients with positive BCBs underwent stratified randomization into 3 arms: standard BCB processing (control, n = 207), rmPCR reported with templated comments (rmPCR, n = 198), or rmPCR reported with templated comments and real-time audit and feedback of antimicrobial orders by an antimicrobial stewardship team (rmPCR/AS, n = 212). The primary outcome was antimicrobial therapy duration. Secondary outcomes were time to antimicrobial de-escalation or escalation, length of stay (LOS), mortality, and cost.

Results. Time from BCB Gram stain to microorganism identification was shorter in the intervention group (1.3 hours) vs control (22.3 hours) ($P < .001$). Compared to the control group, both intervention groups had decreased broad-spectrum piperacillin-tazobactam (control 56 hours, rmPCR 44 hours, rmPCR/AS 45 hours; $P = .01$) and increased narrow-spectrum β-lactam (control 42 hours, rmPCR 71 hours, rmPCR/AS 85 hours; $P = .04$) use, and less treatment of contaminants (control 25%, rmPCR 11%, rmPCR/AS 8%; $P = .015$). Time from Gram stain to appropriate antimicrobial de-escalation or escalation was shortest in the rmPCR/AS group (de-escalation: rmPCR/AS 21 hours, control 34 hours, rmPCR 38 hours, $P < .001$; escalation: rmPCR/AS 5 hours, control 24 hours, rmPCR 6 hours, $P = .04$). Groups did not differ in mortality, LOS, or cost.

Conclusions. rmPCR reported with templated comments reduced treatment of contaminants and use of broad-spectrum antimicrobials. Addition of antimicrobial stewardship enhanced antimicrobial de-escalation.

Clinical Trials Registration. NCT01898208.





Time from Gram stain to appropriate antimicrobial de- escalation or escalation was shortest in the rmPCR/AS group

De- escalation ($p < .001$)

- rmPCR/AS 21 hours,
- control 34 hours,
- rmPCR 38 hours,

Escalation ($P < .004$)

- rmPCR/AS 5 hours,
- control 24 hours,
- rmPCR 6 hours

Table 3. Antibiotic Utilization Among All Study Subjects in the First 96 Hours Following Enrollment

Outcome	Control	Rapid Multiplex PCR	Rapid Multiplex PCR + Stewardship	*P* Value Comparing 3 Groups
Duration of therapy[a], h				
Vancomycin				
All patients (n = 357)	44 (22–72)	42 (21–93)	42 (19–90)	.92
Organisms not requiring vancomycin[b] (n = 169)	8.2 (0–26)	0 (0–16)	0 (0–3)[c]	.032
Vancomycin-susceptible enterococci (n = 32)	20 (1–59)	70 (48–88)[c]	82 (40–96)[c]	.037
Methicillin-susceptible *Staphylococcus aureus* (n = 42)	23 (20–53)	11 (0–26)	8 (0–44)	.2
Nafcillin, oxacillin, or cefazolin (n = 50)	42 (24–57)	71 (51–79)[c]	85 (42–92)[c]	.035
Piperacillin-tazobactam (n = 214)	56 (39–82)	44 (27–74)[c]	45 (19–78)[c]	.012
Cefepime (n = 181)	55 (28–96)	71 (43–96)	58 (32–96)	.56
Antibiotic modifications				
Time to first appropriate de-escalation[d] (n = 344)	34 (21–55)	38 (22–66)	21 (7–37)[c,e]	<.0001
Time to first appropriate escalation[f] (n = 122)	24 (3–67)	6 (2–36)	5 (2–22)[c]	.04
Time to administration of active antibiotics (n = 123)[g]	11 (2–51)	6 (2–31)	4 (2–20)	.55
Contaminated blood cultures not treated or treated for <24 h, No. (%)[h]	47 (75)	49 (89)[c]	57 (92)[c]	.015

Groups **did not differ in** mortality, LOS, or cost.

J Antimicrob Chemother 2018; **73** Suppl 4: iv20–iv26
doi:10.1093/jac/dky049

Journal of Antimicrobial Chemotherapy

T2Bacteria magnetic resonance assay for the rapid detection of ESKAPEc pathogens directly in whole blood

Giulia De Angelis[1]†, Brunella Posteraro[2]†, Elena De Carolis[1], Giulia Menchinelli[1], Francesco Franceschi[3], Mario Tumbarello[4], Gennaro De Pascale[5], Teresa Spanu[1] and Maurizio Sanguinetti[1]*

[1]Institute of Microbiology, Università Cattolica del Sacro Cuore, Fondazione Policlinico Universitario Agostino Gemelli, Rome, Italy; [2]Institute of Public Health (Section of Hygiene), Università Cattolica del Sacro Cuore, Fondazione Policlinico Universitario Agostino Gemelli, Rome, Italy; [3]Department of Emergency Medicine, Università Cattolica del Sacro Cuore, Fondazione Policlinico Universitario Agostino Gemelli, Rome, Italy; [4]Institute of Infectious Diseases, Università Cattolica del Sacro Cuore, Fondazione Policlinico Universitario Agostino Gemelli, Rome, Italy; [5]Department of Anaesthesiology and Intensive Care, Università Cattolica del Sacro Cuore, Fondazione Policlinico Agostino Gemelli, Rome, Italy

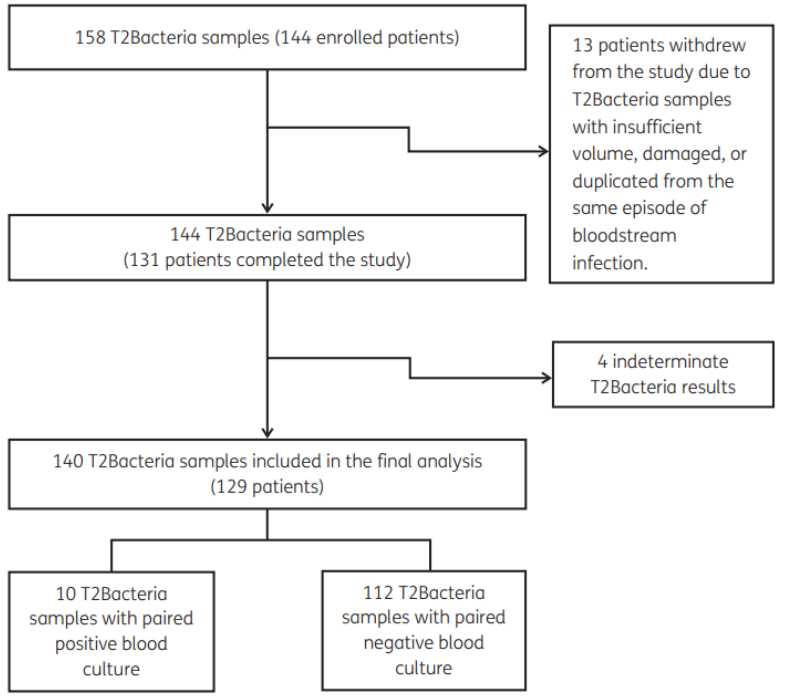
The T2 Magnetic Resonance (T2MR) system

Objectives: To evaluate the magnetic resonance-based T2Bacteria Panel assay for direct detection of ESKAPEc (*Enterococcus faecium*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa* and *Escherichia coli*) pathogens in blood samples of patients with suspected bloodstream infection (BSI).

Patients and methods: Adult patients admitted to the Emergency Medicine Department, Infectious Diseases Unit and ICU of a large tertiary-care hospital were included if they had a blood culture (BC) ordered concomitantly with a whole-blood sample for T2Bacteria testing. Results were compared with those of BC and other clinically relevant information.

Results: A total of 140 samples from 129 BSI patients were studied. Single bacteria were detected in 15.7% (22/140) and 12.1% (17/140), and multiple bacteria in 2.9% (4/140) and 1.4% (2/140), of samples tested by T2Bacteria and BC, respectively. With respect to the six target (ESKAPEc) species, overall sensitivity and specificity of T2Bacteria across all detection channels in comparison with BC were 83.3% and 97.6%, respectively; these values increased to 89.5% and 98.4%, respectively, when a true-infection criterion (i.e. the same microorganism detected only by T2Bacteria was cultured from another sample type reflecting the source of infection) was used as the comparator. There were 808 T2Bacteria detection results across 112 samples, with concordant negative results, yielding a negative predictive value of 99.8%. The mean time to negative result was 6.1±1.5 h, whereas the mean time to detection/species identification was 5.5±1.4 h.

Conclusions: The T2Bacteria Panel assay has the potential to provide accurate and timely diagnosis of ESKAPEc bacteraemia, which might support the direct therapeutic management of BSI patients.



J Antimicrob Chemother 2018; **73** Suppl 4: iv20–iv26
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Journal of Antimicrobial Chemotherapy

T2Bacteria magnetic resonance assay for the rapid detection of ESKAPEc pathogens directly in whole blood

Giulia De Angelis[1]†, Brunella Posteraro[2]†, Elena De Carolis[1], Giulia Menchinelli[1], Francesco Franceschi[3], Mario Tumbarello[4], Gennaro De Pascale[5], Teresa Spanu[1] and Maurizio Sanguinetti[1]*

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The T2 Magnetic Resonance (T2MR) system

Table 3. Performance of the T2Bacteria Panel in clinical blood samples according to the BC used as the gold standard assessed by detection channel

	T2Bacteria results by detection channel						
	Ab	Eci	Efm	Kp	Pa	Sa	Total
Matched positives, *n*	0	4	2	1	1	2	10
Matched negatives, *n*	135	128	134	138	135	138	808
T2Bacteria overdetections, *n*	5	7	4	0	4	0	20
T2Bacteria misses, *n*	0	1	0	1	0	0	2
Overall agreement, %	96.4	94.3	97.1	99.3	97.1	100.0	97.4
Sensitivity, %	–	80.0	100.0	50.0	100.0	100.0	83.3
Specificity, %	96.4	94.8	97.1	100.0	97.1	100.0	97.6
PPV, %	0.0	36.4	33.3	100.0	20.0	100.0	33.3
NPV, %	100.0	99.2	100.0	99.3	100.0	100.0	99.8

Ab, *A. baumannii*; Eci, *E. coli*; Efm, *E. faecalis*; Kp, *K. pneumoniae*; Pa, *P. aeruginosa*; Sa, *S. aureus*; PPV, positive predictive value; NPV, negative predictive value.

Assessment of variables potentially influencing T2Bacteria Panel performance

Subgroup analysis of the BC results showed that a previous antibiotic treatment, a SOFA or qSOFA score of >2 and a procalcitonin level of >2 ng/mL were significantly associated with culture-negative but T2Bacteria-positive cases compared with cases in which both culture and T2Bacteria results were negative [88.2% (15/17) versus 29.4% (33/112), 82.3% (14/17) versus 21.4% (24/112) and 70.6% (12/17) versus 13.4% (15/112), respectively; $P < 0.001$ for all comparisons]. In contrast, subgroup analysis of the T2Bacteria

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Original Article

Integration of antimicrobial stewardship intervention with rapid organism identification improve outcomes in adult patients with bloodstream infections

Tzu-Ping Weng [a b], Ching-Lung Lo [a b], Wen-Liang Lin [d], Jen-Chieh Lee [a], Ming-Chi Li [a b], Wen-Chien Ko [a b c], Nan-Yao Lee [a b c]

Materials and methods

A pre–post quasi-experimental study was conducted to analyze the impact of ASI with organism identification via matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF-MS) among patients with BSIs. Outcomes were compared to a historic pre-intervention group. The 30-day mortality was the primary endpoint. Secondary outcomes included time to first antibiotic modification, length of hospital stay.

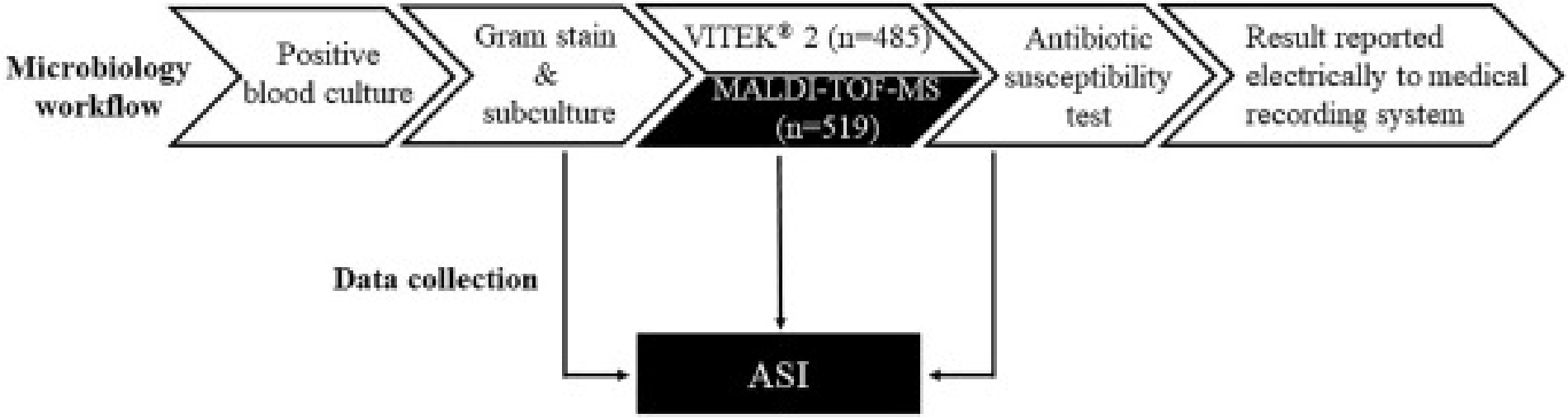

Table 2 Multivariate logistic regression analysis of the variables associated with the 30-day mortality.

Variables	Survivors (n = 783)	Non-survivors (n = 221)	Univariate analysis		Multivariate analysis	
			OR (95% CI)	*p* values	OR (95% CI)	*p* values
Age; median (IQR), year	67 (57–78)	68 (62–77)	–	0.42		
Male gender	427 (54.5)	116 (52.5)	0.92 (0.68–1.24)	0.59		
Diabetes mellitus	305 (39.0)	87 (39.4)	1.02 (0.75–1.38)	0.94		
Chronic kidney disease	245 (31.3)	65 (29.4)	0.92 (0.66–1.27)	0.62		
Malignancy	497 (63.5)	132 (59.7)	0.85 (0.63–1.16)	0.31		
Chronic hepatitis	108 (13.8)	24 (10.9)	0.76 (0.48–1.22)	0.31		
Pneumonia	34 (4.3)	20 (9.0)	2.19 (1.24–3.89)	0.01	2.25 (1.19–4.26)	0.01
Critical Illness (Pitt score ≥4 points)	210 (26.8)	141 (63.8)	4.81 (3.50–6.60)	<0.001	5.39 (3.86–7.53)	<0.001
Antibiotic stewardship intervention	443 (56.6)	76 (34.4)	0.40 (0.30–0.55)	<0.001	0.33 (0.24–0.47)	<0.001
Multidrug resistant isolates	451 (57.6)	120 (54.3)	0.88 (0.65–1.18)	0.40		
Appropriate antimicrobial therapy	774 (98.9)	211 (95.5)	0.25 (0.10–0.61)	0.003	0.25 (0.09–0.67)	<0.001

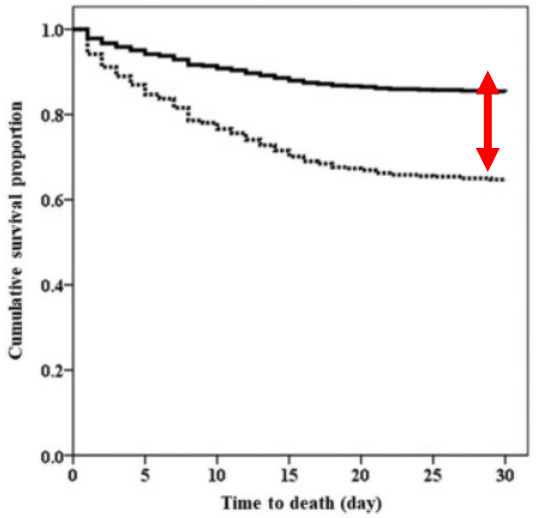

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Figure2. The survival analysis curves for the BSIs in the intervention (solid line) and pre-intervention period (dot line) (*P*<0.001, log rank test).

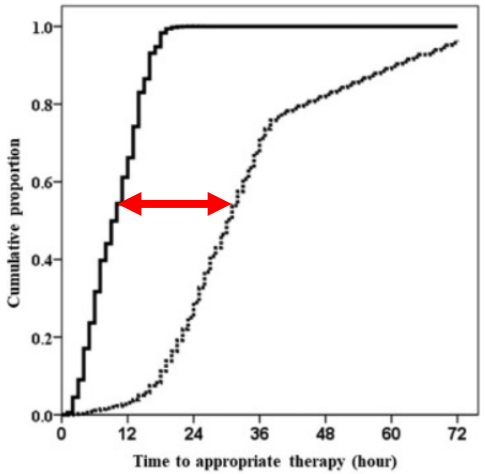

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Figure3. The Kaplan–Meier analysis of the time from blood culture positivity to optimal antibiotic therapy in the intervention (solid line) and pre-intervention period (dot line) (*P*<0.001, log-rank test).

Results

A total of 1004 adult patients with BSIs were included in the final analysis, 519 patients classified into the intervention group and 485 patients in the preintervention group. The patients in the intervention group were younger (66 vs. 70 years, *P* = 0.02). **The 30-day crude mortality (14.6% vs. 29.9%, P < 0.001) was lower, the time to organism identification (72.25 vs. 83.6 h, *P* < 0.001) and length of hospital stay (12 days vs. 14 days, *P* < 0.001) were shorter in the intervention group**. Acceptance of an ASI was associated with a trend toward a reduced 30-day mortality on multivariable analysis (odds ratio 0.33; 95% CI: 0.24–0.47; *P* < 0.001).

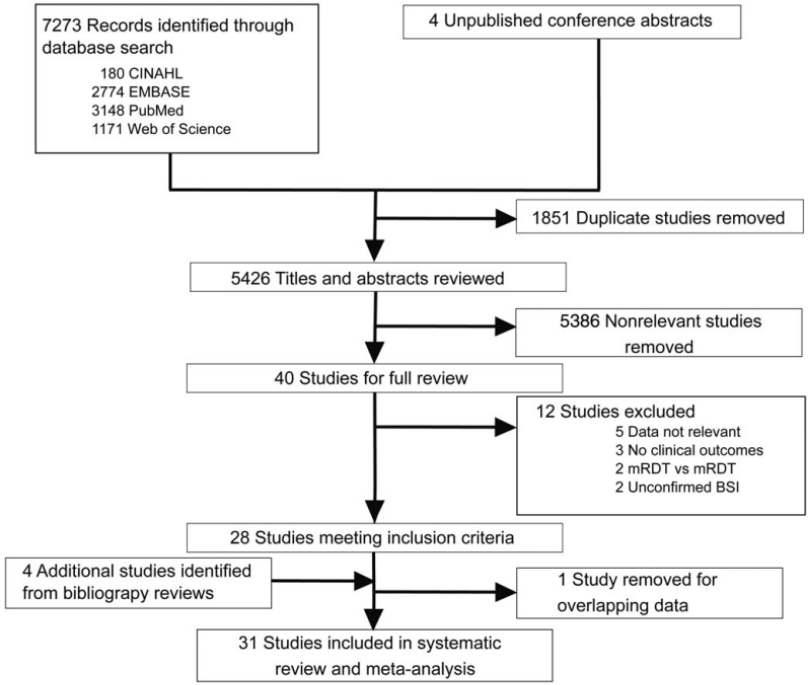


Figure 1. Flow diagram. Abbreviations: BSI, bloodstream infection; mRDT, molecular rapid diagnostic testing.

Clinical Infectious Diseases

MAJOR ARTICLE

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

Tristan T. Timbrook,[1,4] Jacob B. Morton,[1,4] Kevin W. McConeghy,[2] Aisling R. Caffrey,[1,2,4] Eleftherios Mylonakis,[3] and Kerry L. LaPlante[1,2,4]

[1]Rhode Island Infectious Diseases Research Program, Providence Veterans Affairs Medical Center, [2]Center of Innovation in Long Term Services and Supports, Providence Veterans Affairs Medical Center, [3]Infectious Diseases Division, Warren Alpert Medical School of Brown University, Providence, and [4]College of Pharmacy, University of Rhode Island, Kingston

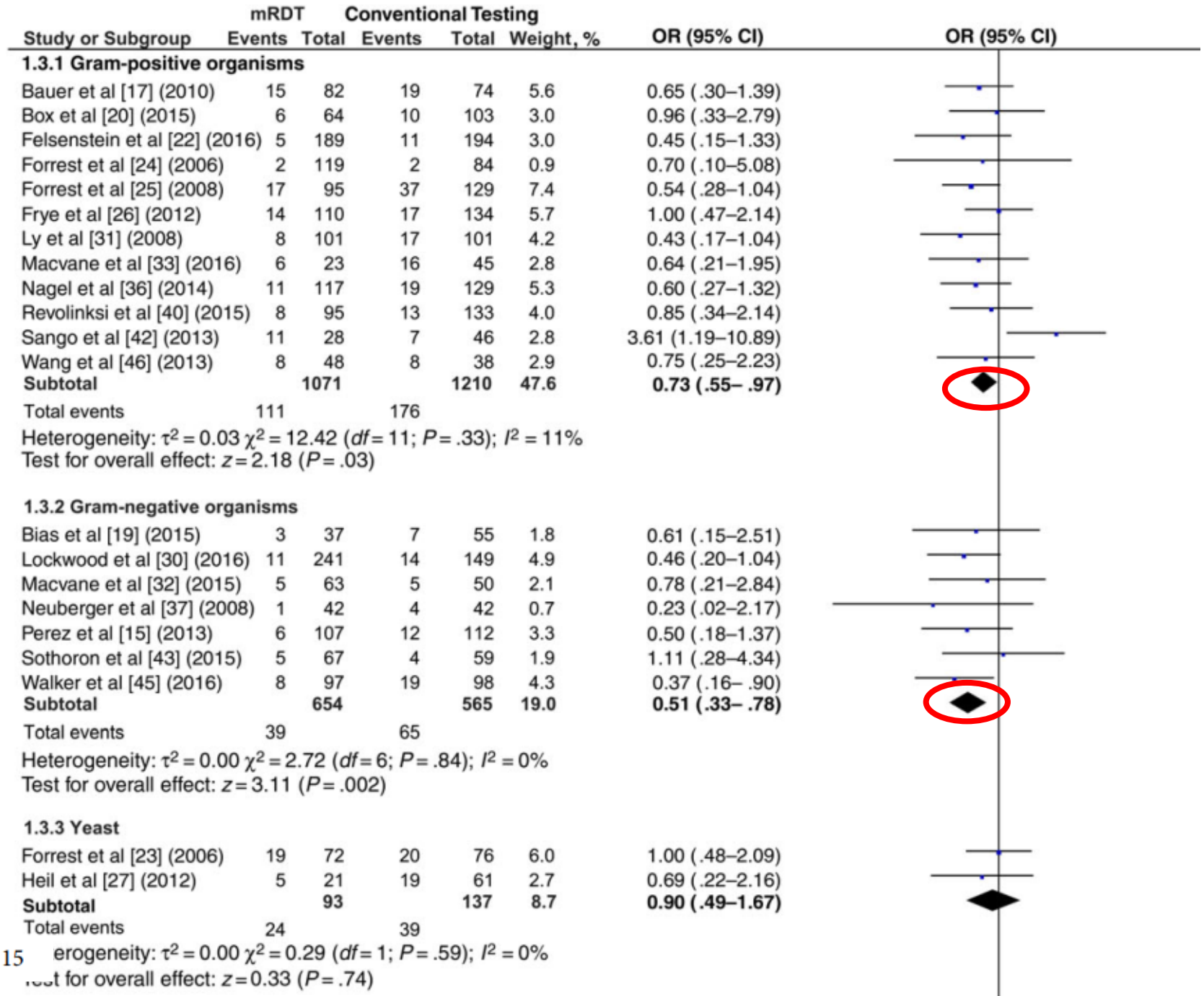
Background. Previous reports on molecular rapid diagnostic testing (mRDT) do not consistently demonstrate improved clinical outcomes in bloodstream infections (BSIs). This meta-analysis seeks to evaluate the impact of mRDT in improving clinical outcomes in BSIs.

Methods. We searched PubMed, CINAHL, Web of Science, and EMBASE through May 2016 for BSI studies comparing clinical outcomes between mRDT and conventional microbiology methods.

Results. Thirty-one studies were included with 5920 patients. The mortality risk was significantly lower with mRDT than with conventional microbiology methods (odds ratio [OR], 0.66; 95% confidence interval [CI], .54–.80), yielding a number needed to treat of 20. The mortality risk was slightly lower with mRDT in studies with antimicrobial stewardship programs (ASPs) (OR, 0.64; 95% CI, .51–.79), and non-ASP studies failed to demonstrate a significant decrease in mortality risk (0.72; .46–1.12). Significant decreases in mortality risk were observed with both gram-positive (OR, 0.73; 95% CI, .55–.97) and gram-negative organisms (0.51; .33–.78) but not yeast (0.90; .49–1.67). Time to effective therapy decreased by a weighted mean difference of −5.03 hours (95% CI, −8.60 to −1.45 hours), and length of stay decreased by −2.48 days (−3.90 to −1.06 days).

Conclusions. For BSIs, mRDT was associated with significant decreases in mortality risk in the presence of a ASP, but not in its absence. mRDT also decreased the time to effective therapy and the length of stay. mRDT should be considered as part of the standard of care in patients with BSIs.

Keywords. rapid diagnostic tests; bloodstream infections; meta-analysis; antimicrobial stewardship.


mRDT
Conventional Testing
Study or Subgroup Events Total Events Total Weight, % OR (95% CI)
OR (95% CI)
1.3.1 Gram-positive organisms
Bauer et al [17] (2010) 15 82 19 74 5.6 0.65 (.30–1.39)
Box et al [20] (2015) 6 64 10 103 3.0 0.96 (.33–2.79)
Felsenstein et al [22] (2016) 5 189 11 194 3.0 0.45 (.15–1.33)
Forrest et al [24] (2006) 2 119 2 84 0.9 0.70 (.10–5.08)
Forrest et al [25] (2008) 17 95 37 129 7.4 0.54 (.28–1.04)
Frye et al [26] (2012) 14 110 17 134 5.7 1.00 (.47–2.14)
Ly et al [31] (2008) 8 101 17 101 4.2 0.43 (.17–1.04)
Macvane et al [33] (2016) 6 23 16 45 2.8 0.64 (.21–1.95)
Nagel et al [36] (2014) 11 117 19 129 5.3 0.60 (.27–1.32)
Revolinksi et al [40] (2015) 8 95 13 133 4.0 0.85 (.34–2.14)
Sango et al [42] (2013) 11 28 7 46 2.8 3.61 (1.19–10.89)
Wang et al [46] (2013) 8 48 8 38 2.9 0.75 (.25–2.23)
Subtotal 1071 1210 47.6 0.73 (.55– .97)
Total events 111 176
Heterogeneity: τ² = 0.03 χ² = 12.42 (df = 11; P = .33); I² = 11%
Test for overall effect: z = 2.18 (P = .03)
1.3.2 Gram-negative organisms
Bias et al [19] (2015) 3 37 7 55 1.8 0.61 (.15–2.51)
Lockwood et al [30] (2016) 11 241 14 149 4.9 0.46 (.20–1.04)
Macvane et al [32] (2015) 5 63 5 50 2.1 0.78 (.21–2.84)
Neuberger et al [37] (2008) 1 42 4 42 0.7 0.23 (.02–2.17)
Perez et al [15] (2013) 6 107 12 112 3.3 0.50 (.18–1.37)
Sothoron et al [43] (2015) 5 67 4 59 1.9 1.11 (.28–4.34)
Walker et al [45] (2016) 8 97 19 98 4.3 0.37 (.16– .90)
Subtotal 654 565 19.0 0.51 (.33– .78)
Total events 39 65
Heterogeneity: τ² = 0.00 χ² = 2.72 (df = 6; P = .84); I² = 0%
Test for overall effect: z = 3.11 (P = .002)
1.3.3 Yeast
Forrest et al [23] (2006) 19 72 20 76 6.0 1.00 (.48–2.09)
Heil et al [27] (2012) 5 21 19 61 2.7 0.69 (.22–2.16)
Subtotal 93 137 8.7 0.90 (.49–1.67)
Total events 24 39
erogeneity: τ² = 0.00 χ² = 0.29 (df = 1; P = .59); I² = 0%
t for overall effect: z = 0.33 (P = .74)

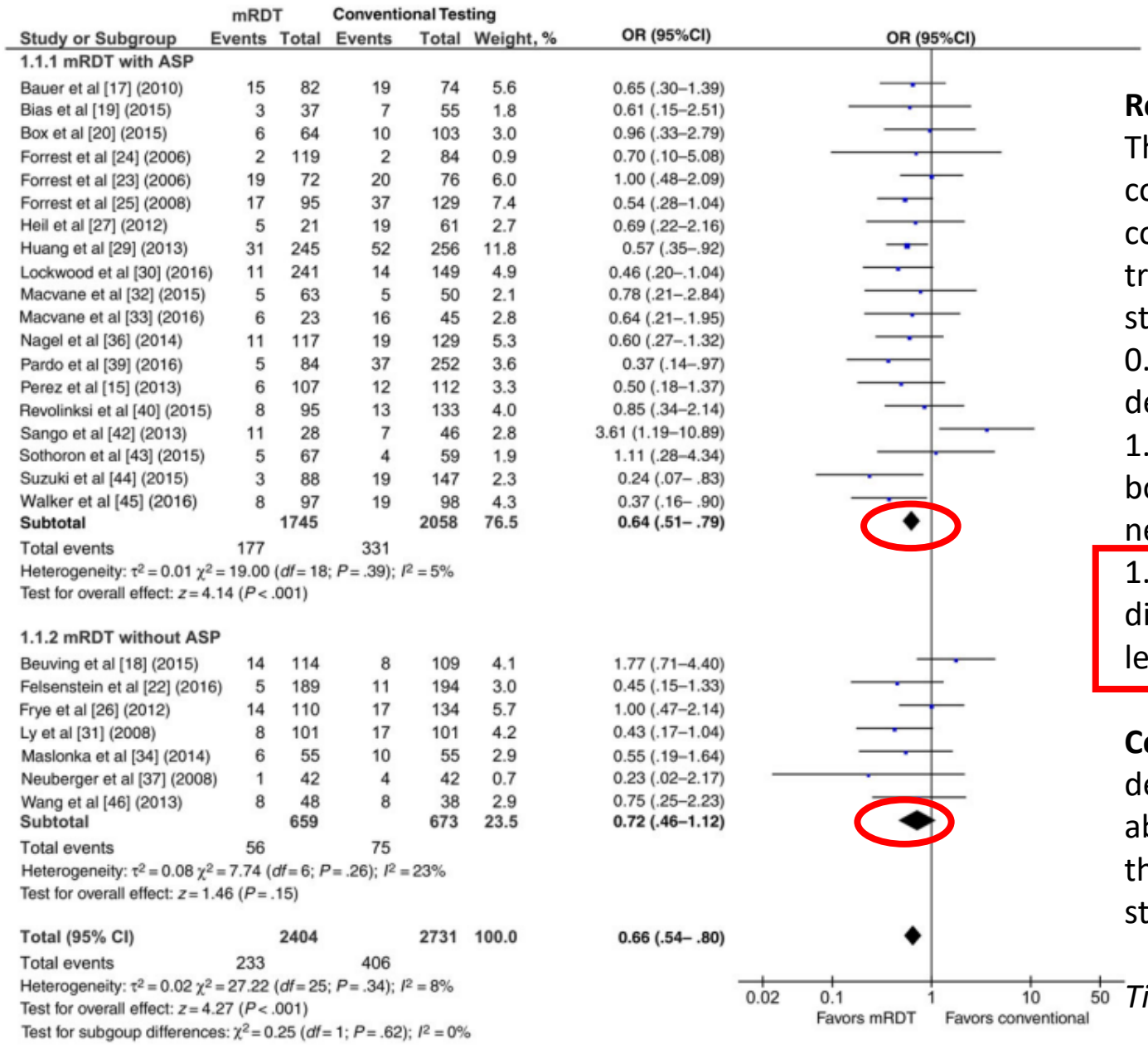


Figure 2. Mortality outcomes with molecular rapid diagnostic testing (mRDT) versus conventional testing in bloodstream infection. Odds ratios (ORs) were determined with the Mantel-Haenszel random-effects method. Abbreviations: ASP, antimicrobial stewardship program; CI, confidence interval.

Results. Thirty-one studies were included with 5920 patients. The mortality risk was significantly lower with mRDT than with conventional microbiology methods (odds ratio [OR], 0.66; 95% confidence interval [CI], .54–.80), yielding a number needed to treat of 20. The mortality risk was slightly lower with mRDT in studies with antimicrobial stewardship programs (ASPs) (OR, 0.64; 95% CI, .51–.79), and non-ASP studies failed to demonstrate a significant decrease in mortality risk (0.72; .46–1.12). Significant decreases in mortality risk were observed with both gram-positive (OR, 0.73; 95% CI, .55–.97) and gram-negative organisms (0.51; .33–.78) but not yeast (0.90; .49–1.67). Time to effective therapy decreased by a weighted mean difference of −5.03 hours (95% CI, −8.60 to −1.45 hours), and length of stay decreased by −2.48 days (−3.90 to −1.06 days).

Conclusions. For BSIs, mRDT was associated with significant decreases in mortality risk in the presence of a ASP, but not in its absence. mRDT also decreased the time to effective therapy and the length of stay. mRDT should be considered as part of the standard of care in patients with BSIs.

Timbrook et al. Clinical Infectious Diseases® 2017;64(1):15–23

AGENDA

- Introduzione
- Test rapidi: evidenze a supporto
- Pros, cons and pitfalls

Contents lists available at ScienceDirect

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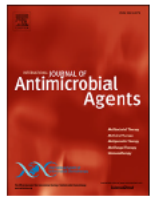
journal homepage: www.elsevier.com/locate/ijantimicag



Review

Diagnosis and management of infections caused by multidrug-resistant bacteria: guideline endorsed by the Italian Society of Infection and Tropical Diseases (SIMIT), the Italian Society of Anti-Infective Therapy (SITA), the Italian Group for Antimicrobial Stewardship (GISA), the Italian Association of Clinical Microbiologists (AMCLI) and the Italian Society of Microbiology (SIM)

QUESTION #1: Do rapid microbiological diagnostics impact on the management and clinical outcome of critically ill/septic patients?

Recommendation 1.1:

In critically ill patients, the use of rapid diagnostic microbiological tests (RDTs) should be adopted since they have the potential to improve the timing to initiate appropriate therapy and possibly improve the patient outcome.

Strength of recommendations: **STRONG** Certainty of evidence: **LOW**

Recommendation 1.2:

Rapid molecular identification of micro-organisms from blood cultures as well as rapid detection of their resistance mechanisms should be carefully integrated in the laboratory workflow scheme. These tests may be useful tools for 24 hour/day monitored care.

Strength of recommendation: **STRONG** Certainty of evidence: **MODERATE**

QUESTION #2: Do rapid microbiological diagnostics favour the adjustment of empirical therapy and the transition to targeted therapy?

Recommendation 2.1:

In hospitalised patients, the use of rapid diagnostic tests (RDTs) is recommended to improve time to initiate appropriate antimicrobial therapy.

Strength of recommendation: **STRONG** Certainty of evidence: **LOW**

Recommendation 2.3:

The implementation of rapid diagnostic tests (RDTs) should include activation of an antimicrobial stewardship programme (ASP) (including an action plan to ensure correct interpretation, real-time reporting and guidance on optimal therapy).

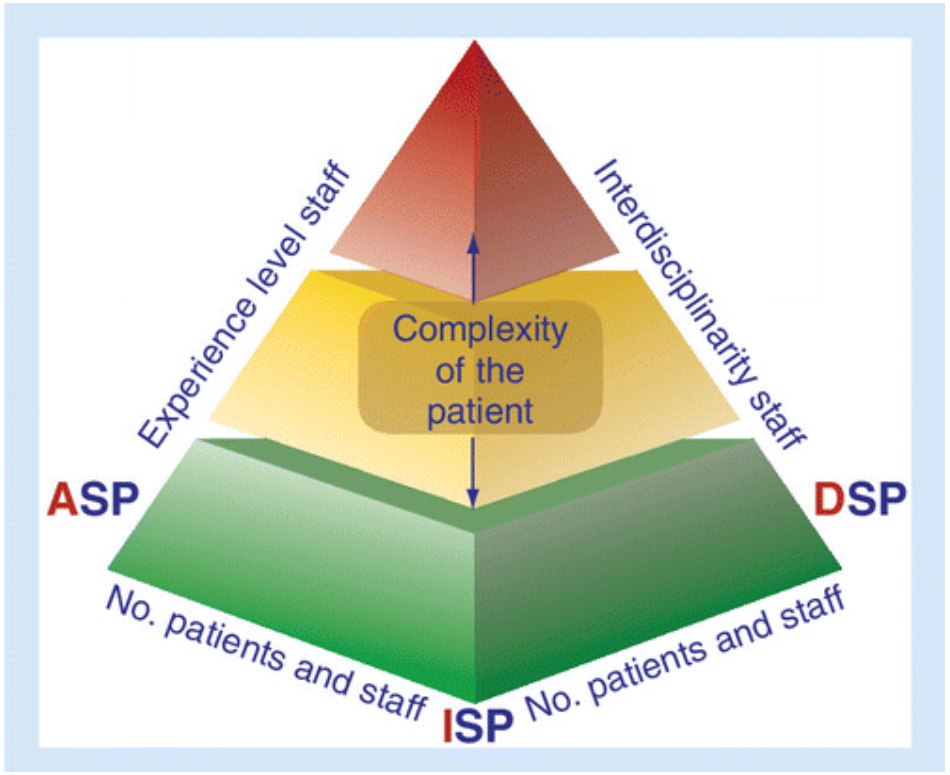
Strength of recommendation: **STRONG** Certainty of evidence: **MODERATE**

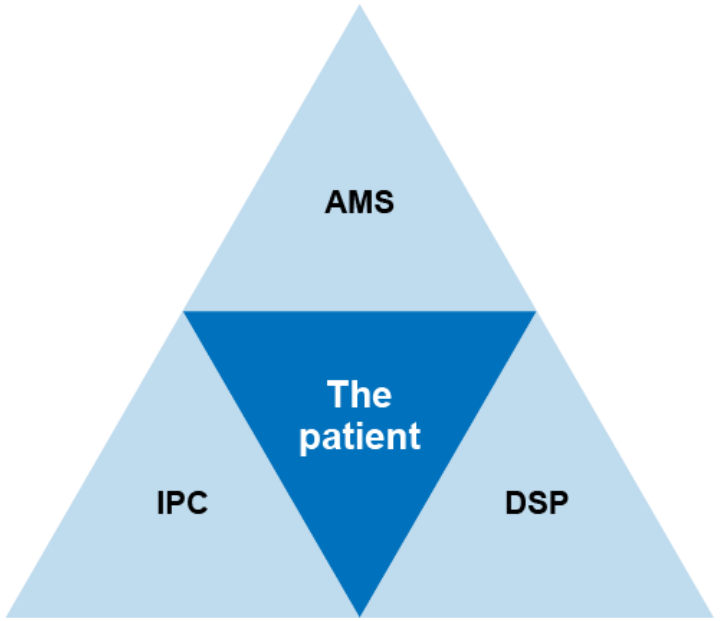
bination with an ASP.

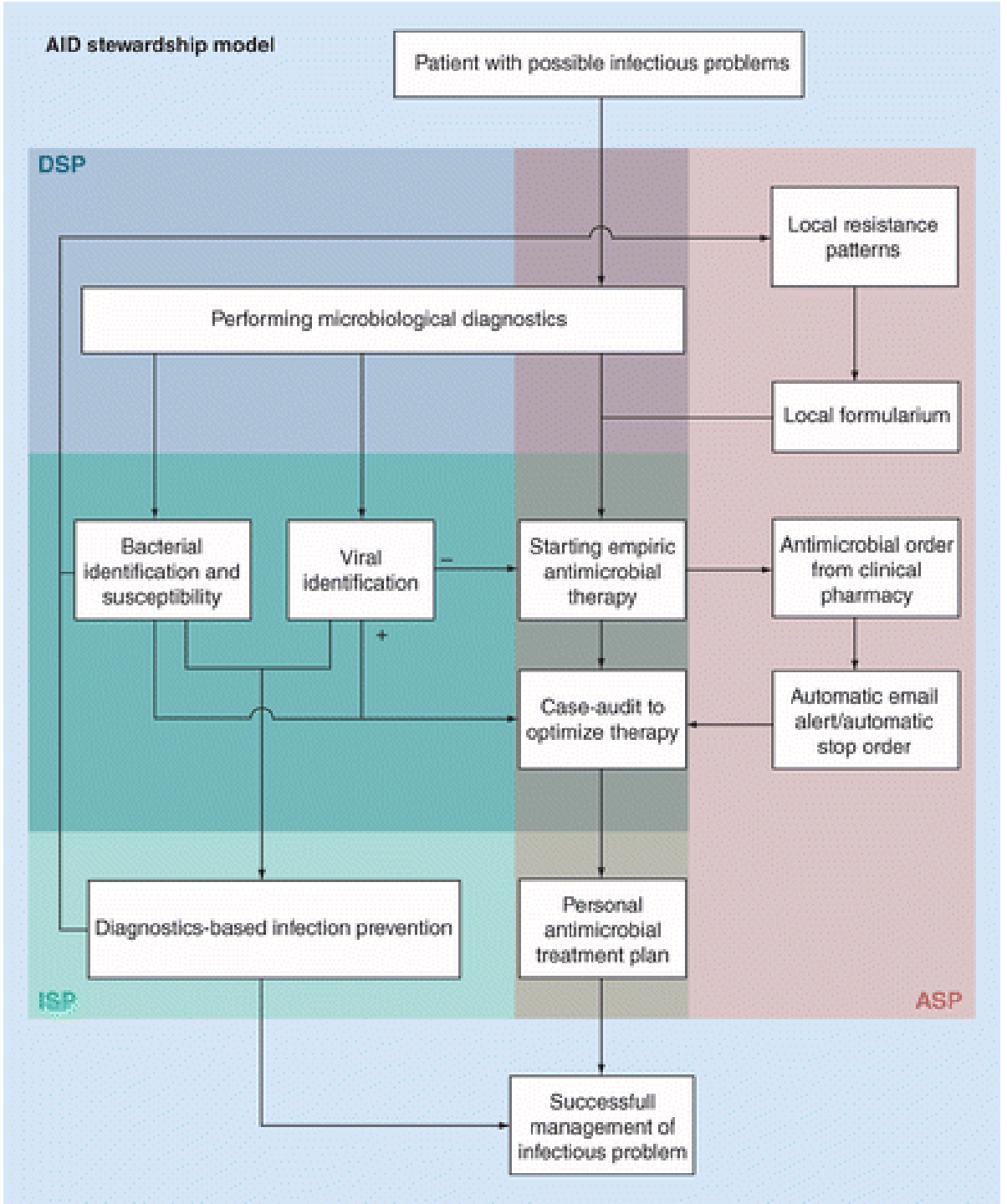
Recommendation 2.4:

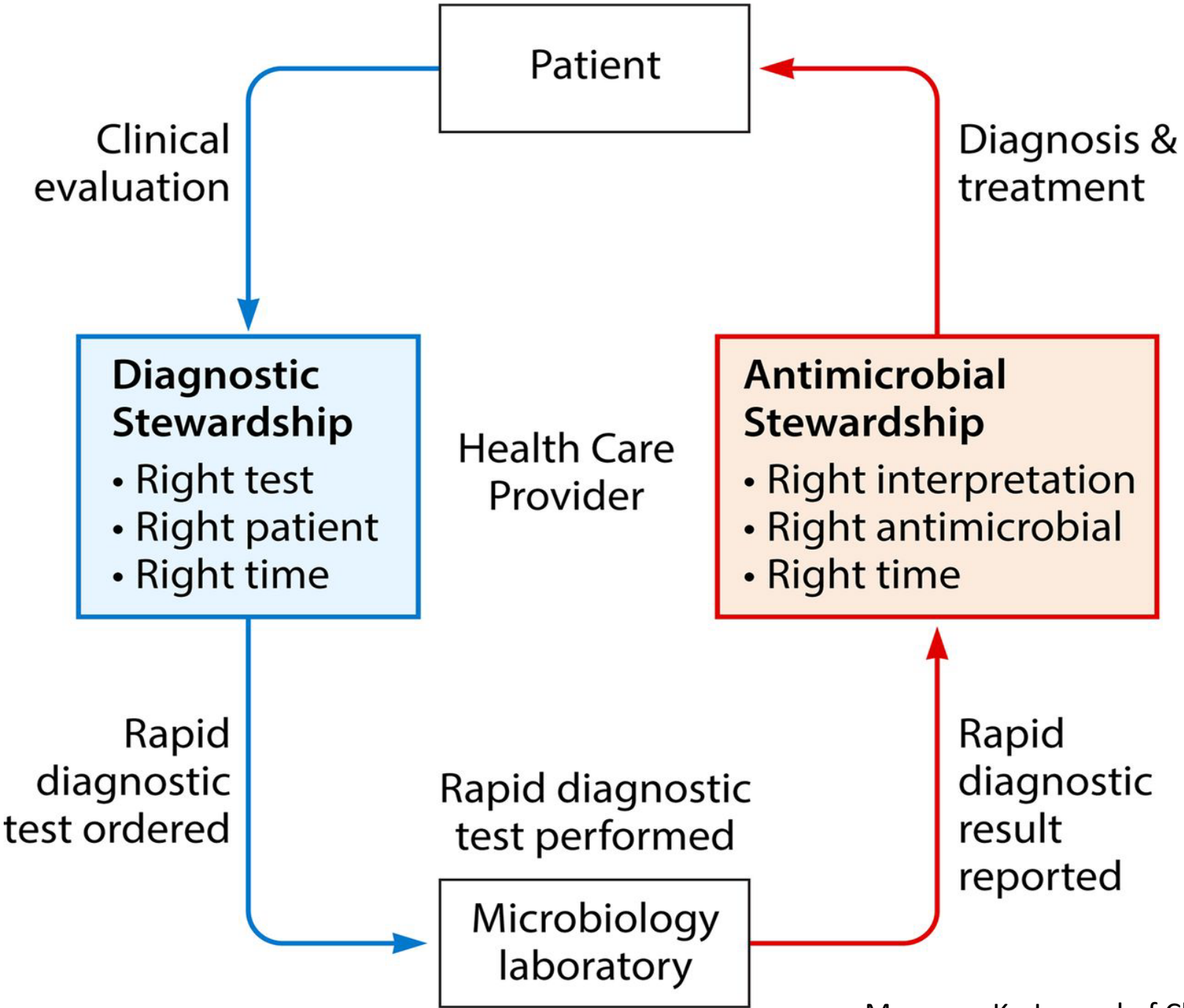
The use of rapid diagnostic tests (RDTs) is recommended since it can lead to a more judicious use of antibiotics; it should be part of the standard of care in patients with bloodstream infections (BSIs).

Strength of recommendation: **CONDITIONAL** Certainty of evidence: **LOW**


Experience level staff
Interdisciplinarity staff
Complexity of the patient
ASP
DSP
No. patients and staff
No. patients and staff
ISP


AMS
The patient
IPC
DSP


AID stewardship model
Patient with possible infectious problems
DSP
Local resistance patterns
Performing microbiological diagnostics
Local formularium
Bacterial identification and susceptibility
Viral identification
Starting empiric antimicrobial therapy
Antimicrobial order from clinical pharmacy
Case-audit to optimize therapy
Automatic email alert/automatic stop order
Diagnostics-based infection prevention
Personal antimicrobial treatment plan
ISP
ASP
Successfull management of infectious problem



Messacar K., Journal of Clinical Microbiology (2017)

Punti critici della Diagnostic Stewardship

1. **Pre-analitica**
   - Scelta del sito da campionare e del tipo di campione
   - Storia ed esame clinico del paziente
   - Corretto prelevamento del campione
   - Corretto trasporto del campione
   - Comunicazione con il microbiologo
2. **Analitica**
3. **Post-analitica**
   - Modalità di report del dato microbiologico
   - Fruibilità del dato in tempi congrui
   - Inquadramento del dato nel giusto contesto clinico
   - Scelta terapia (e soprattutto NON-terapia) in base al dato

Pitfalls della diagnostica rapida

- **Sito di campionamento sbagliato** (*siti non sterili, metodiche non sterili, campioni inidonei…*)
- **Tempo di campionamento sbagliato** (*dopo terapia antibiotica prolungata…)*
- **Campionamento nonostante assenza segni sintomi di infezione**
- **Eccessiva richiesta di metodiche rapide** (*cost-effectiveness sbilanciata, laboratorio sovraccarico*)
- **Scarsa conoscenza della tecnica** (*aspettarsi qualcosa di diverso da quello che la metodica può dare, avviare un test costoso senza vantaggi…)*
- **Erronea comunicazione con il microbiologo**
- **Conservazione e trasporto inadeguati**
- **Erronea interpretazione di un risultato negativo o positivo** (*escalation terapeutica inutile, rischio di non trattare infezioni gravi con rapidi negativi…*)
- **Erronea interpretazione determinazione assenza di resistenze** (*Pseudomonas, Acinetobacter…)*

Conclusioni

- La diagnostica microbiologica rapida può essere di ausilio soprattutto nel paziente grave per una migliore scelta della terapia antibiotica e per *early de-escalation*.

- La scelta del tipo di test e del percorso nonché l'integrazione con i sistemi tradizionali va individualizzata in percorsi di Stewardship Diagnostica, considerando la realtà locale clinica e laboratoristica.

- I migliori risultati in termini di *outcome* robusti (mortalità, LOS) sono ottenuti con un'integrazione dei test rapidi in percorsi di ASP.

GRAZIE!!!


Personal care and clinical care
Services and supports for daily living
Organisation's service environment
Feedback and complaints
Human resources
Organisational governance
Ongoing assessment and planning with consumers
Consumer dignity and choice
1
2
3
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5
6
7
8