Rapid diagnostics: an AMS tool?

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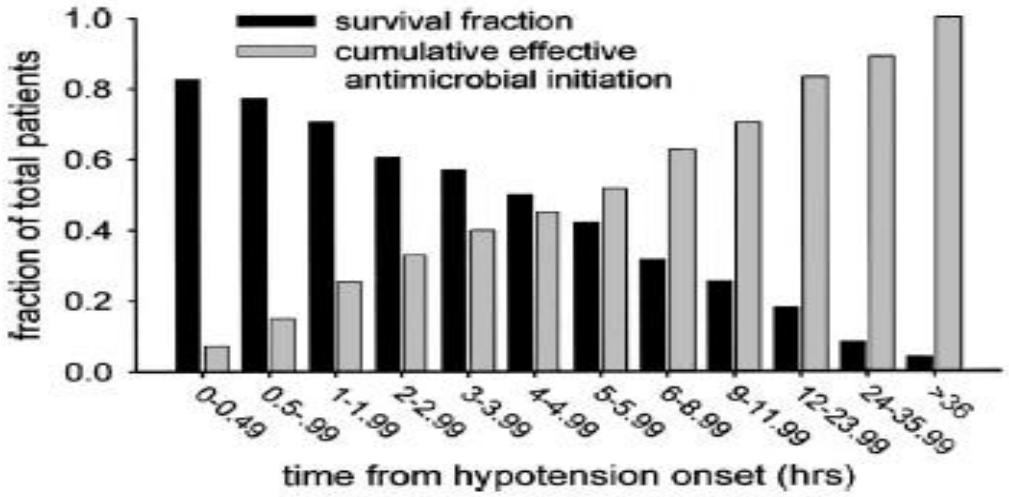
Rapid diagnostics (RDT): an AMS tool?

- **Outline**
  - **Why we need rapid diagnostics**
  - **What rapid diagnostics could test**
  - **Their usefulness for antimicrobial stewardship (AMS)**
  - **How we could use them in most efficient way**
    - **Diagnostic stewardship (DS)**

Why Do We Need RDT?

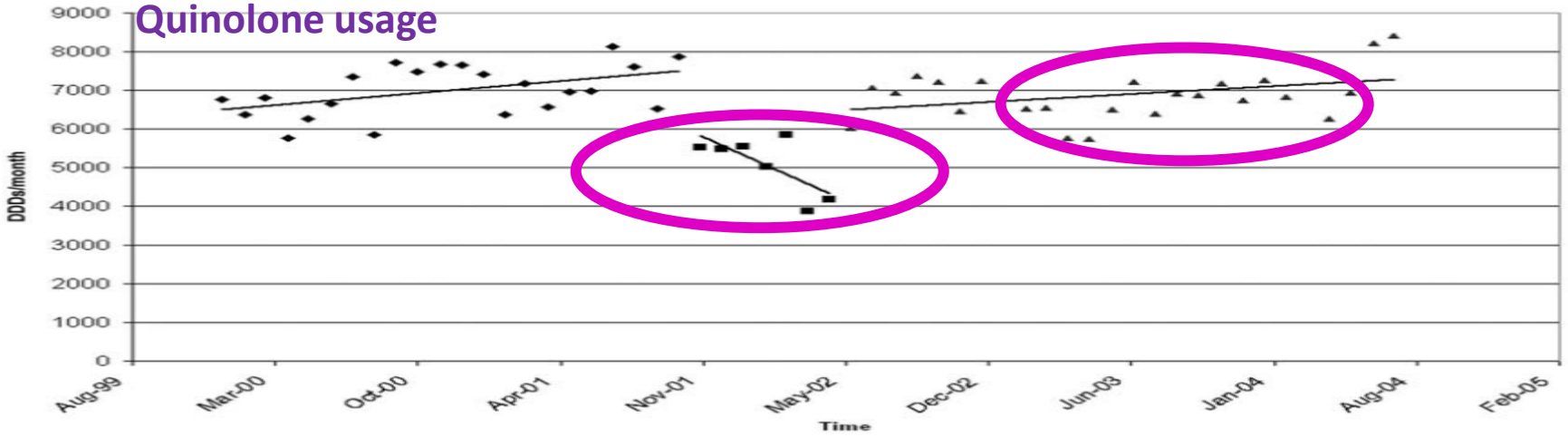
- **The perfect antimicrobial treatment of serious infections**
  - **Appropriate & Fast**
    - **Timely antimicrobial therapy improves the mortality of patients with sepsis**
    - **Each hour of delay resulting in a 8 % decrease in survival**

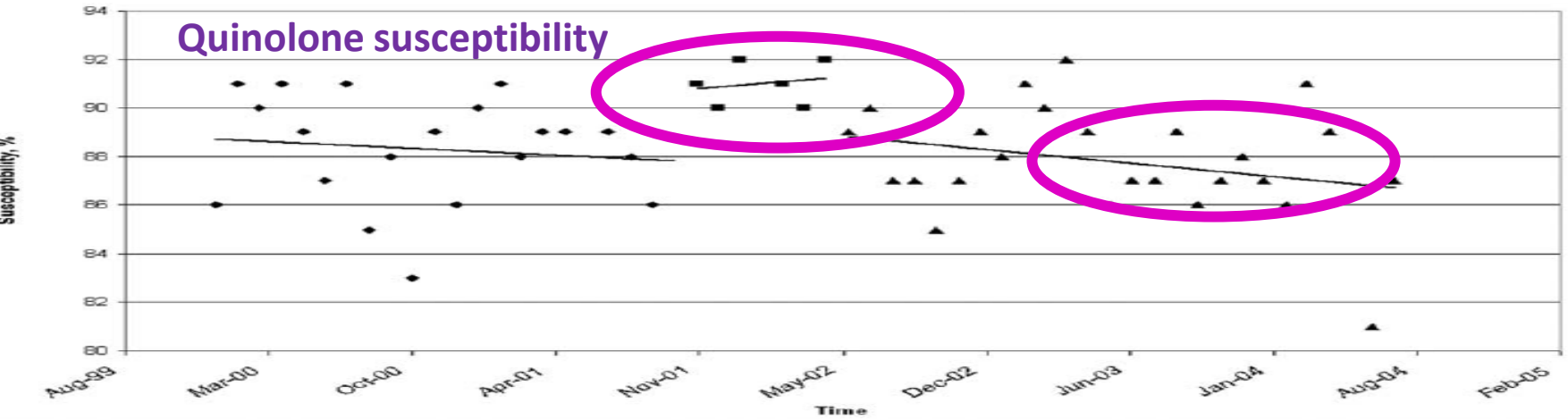


Kumar A.. Chest. 2009;136(5):1237-1248.
Kumar A. Crit Care Med. 2006;34(6):1589-1596.
Cosgrove SE. Clin Infect Dis. 2006;42(suppl 2):S82-S89
Ferrer R. Crit Care Med 2014; 42:1749–1755

Why Do We Need RDT?

Overuse leads to increase in antimicrobial resistance





Reducing quinolone consumption lead to an immediate significant increase in the susceptibility of E. coli urine isolates to quinolones.

The improved susceptibility pattern reversed immediately when quinolone consumption rose in the community.

Gottesman BS. Clin Infect Dis 2009; 49:869–75

Factors Affecting Appropriate Empiric Antimicrobial Selection

Clinical skills and knowledge + Local guidelines + Local susceptibility patterns + Basal MDR rates + Diagnostics

Appropriate antimicrobial selection

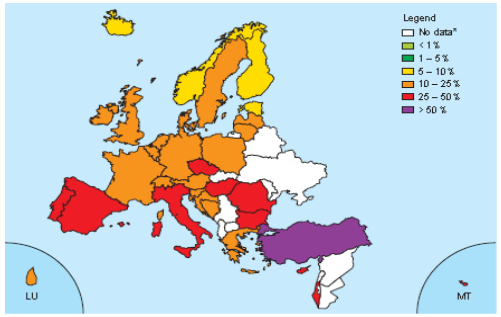
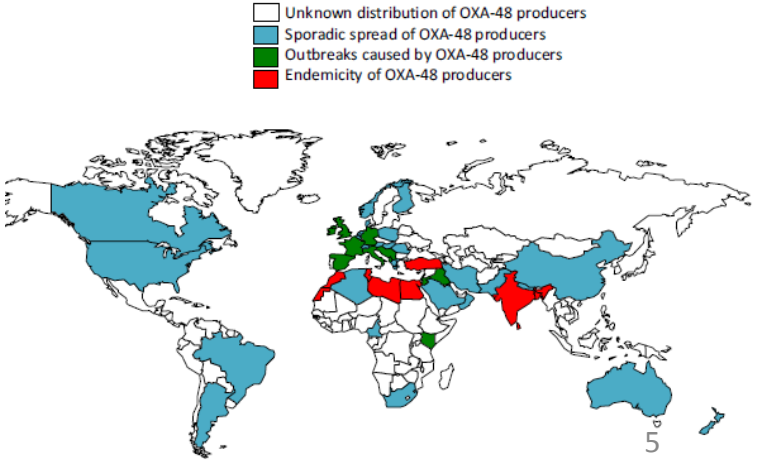
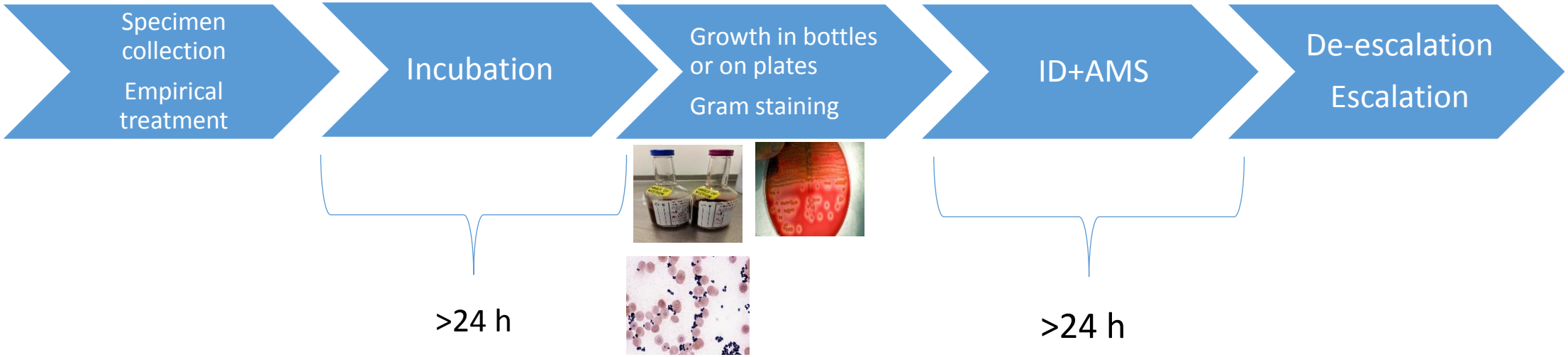


Figure 5.15. *Escherichia coli*: proportion of invasive isolates with resistance to fluoroquinolones in 2008.



Why Do We Need RDT?

- **Time-table for the diagnosis and treatment of infectious diseases with traditional diagnostics -culture+ID+susp**

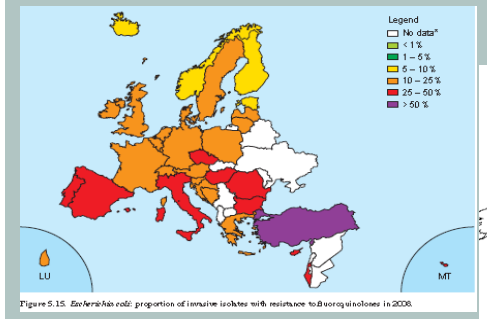


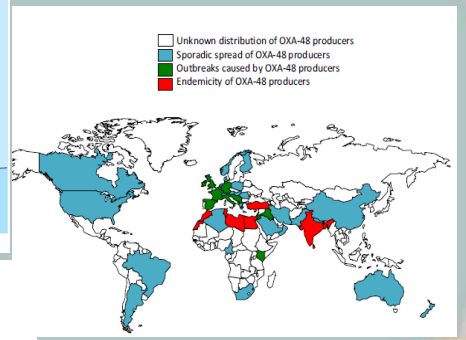
Traditional diagnostics
At least 48 h, usually 72-96 h to get the results

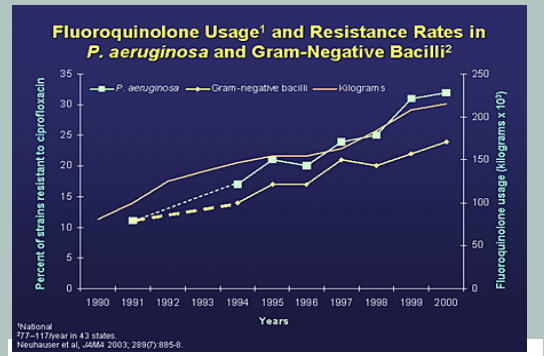
Why Do We Need RDT?

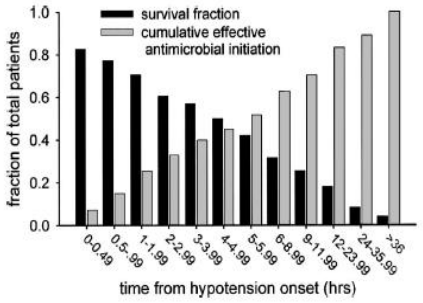
Meropenem-
colistin- vanco

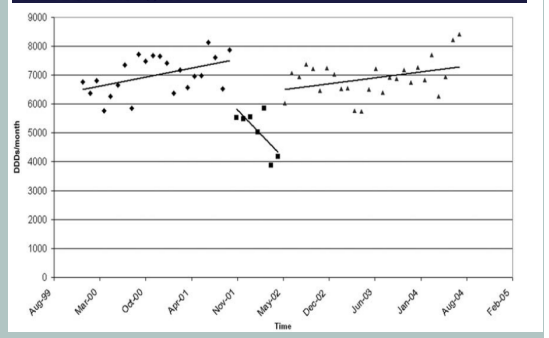
Ampicillin-
sulbactam





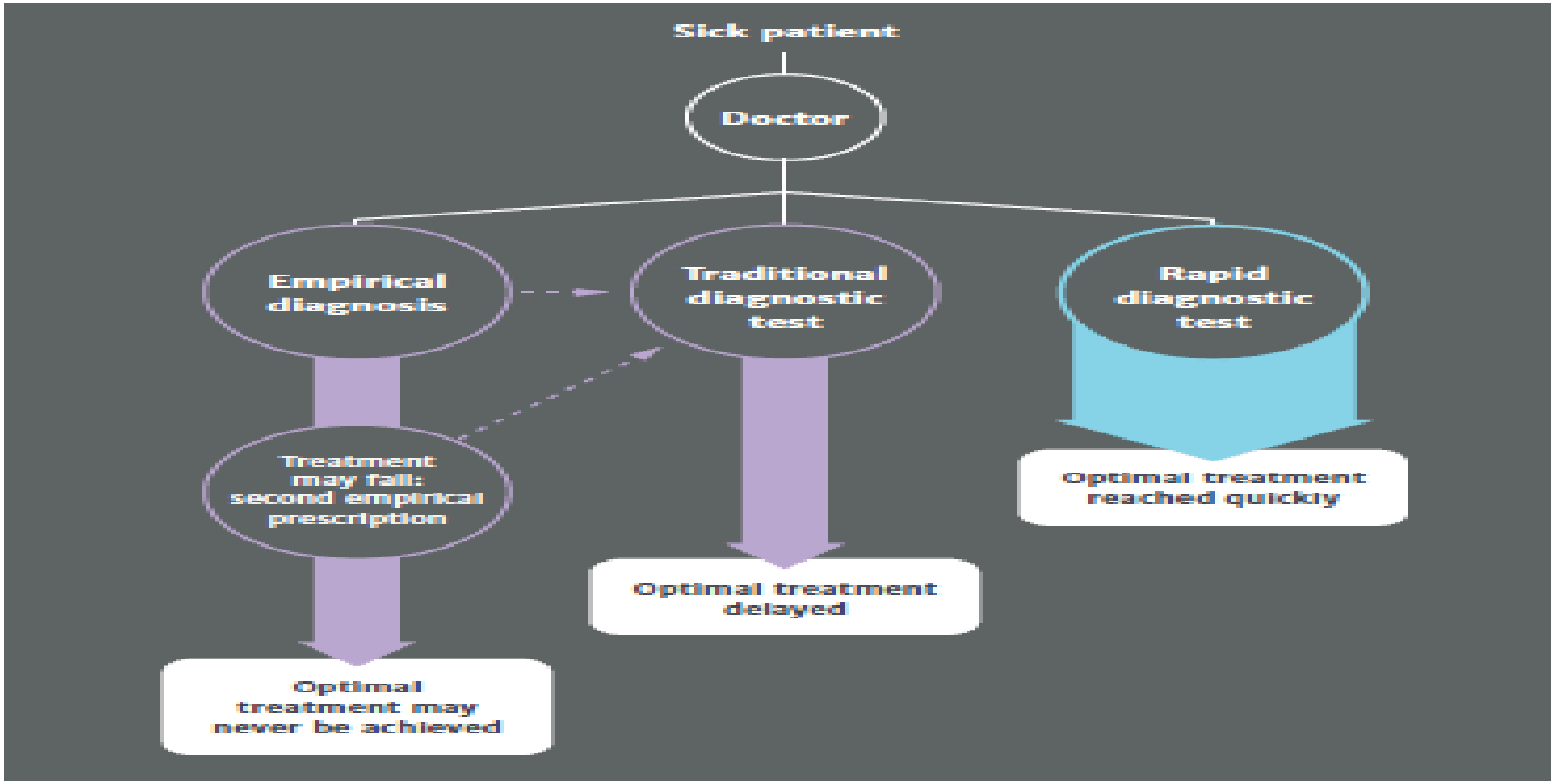






Why Do We Need RDT?

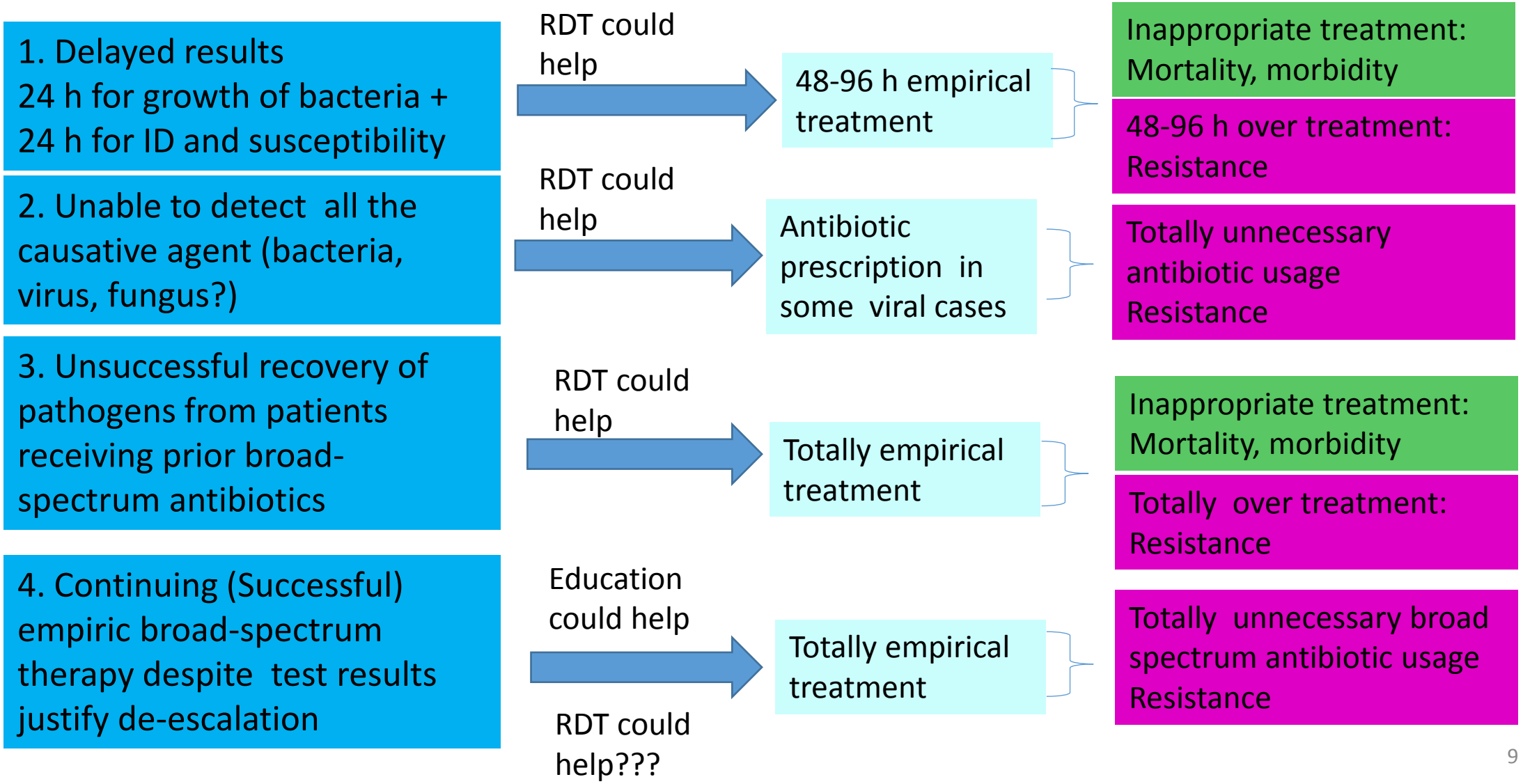
- **Hope (Dream): New rapid diagnostic tests could solve this dilemma by quickly providing the results and optimize the treatment.**



O'Neill J. https://amr-review.org/sites/default/files/Paper-Rapid-Diagnostics-Stopping-Unnecessary-Prescription-Low-Res.pdf

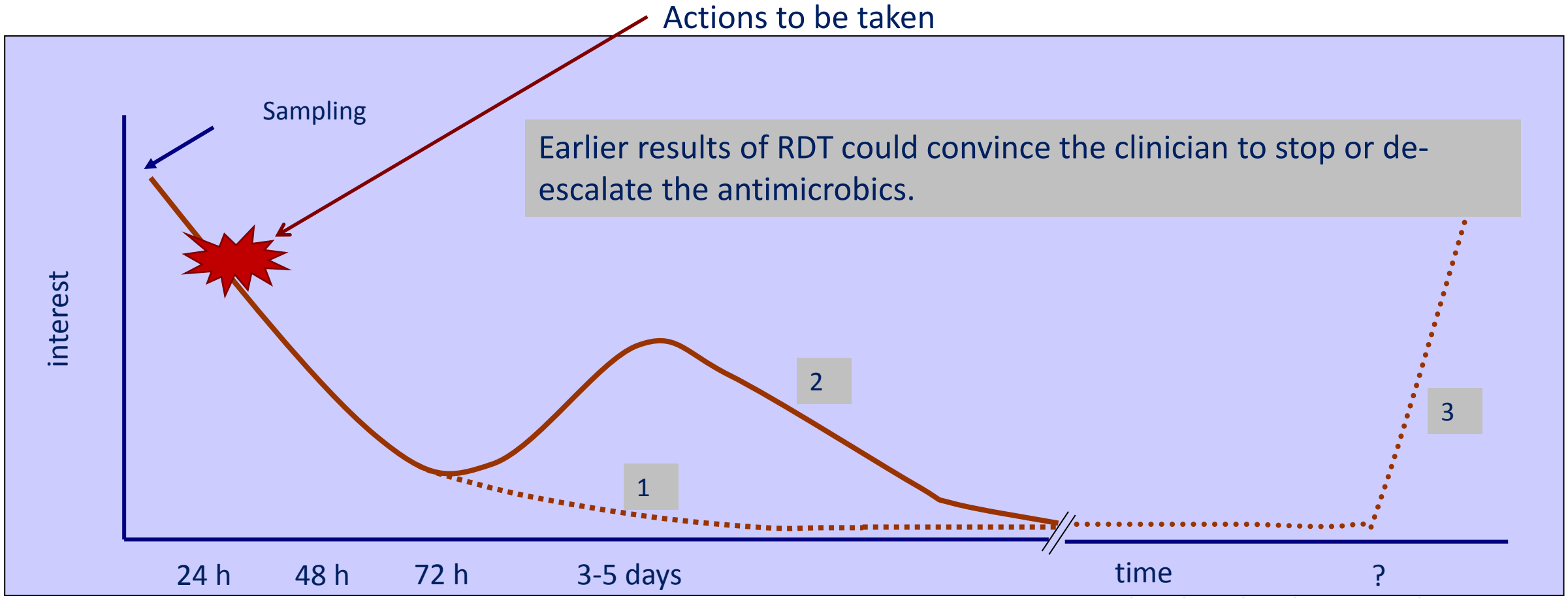
Why do we need RDT?

- **Problems with the traditional diagnostics (culture+ID+Susp) in infectious diseases**



Why do we need RDT?

Interest of the clinicians for microbiological reports

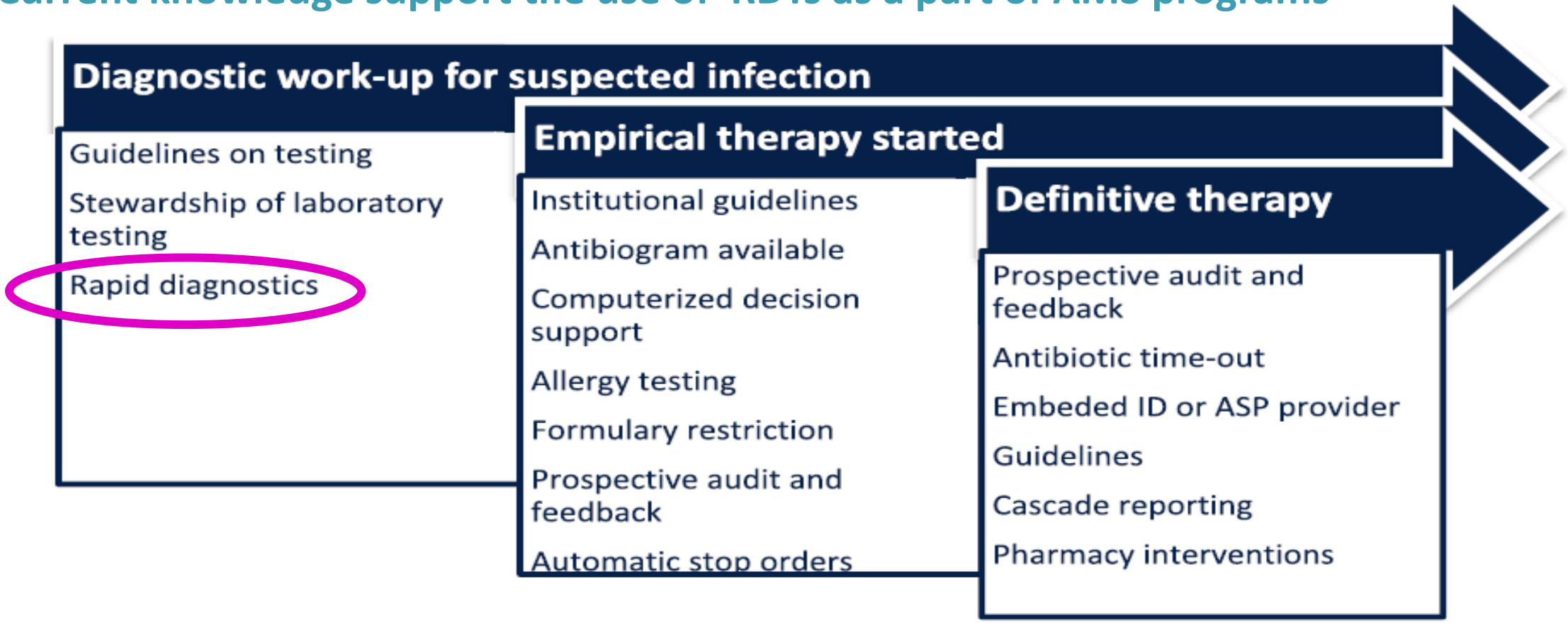


Edwards et al. Arch Intern Med 1973; 132:678-82
Spencely et al. J Infect 1979; 1:23-26
Cunney et al. Int J Antimicrob Chemother 2000; 14:13-9
R. Cantón (personal experience)

Slide from José Ramón Paño-Pardo

Opportunities for Antimicrobial Stewardship Interventions

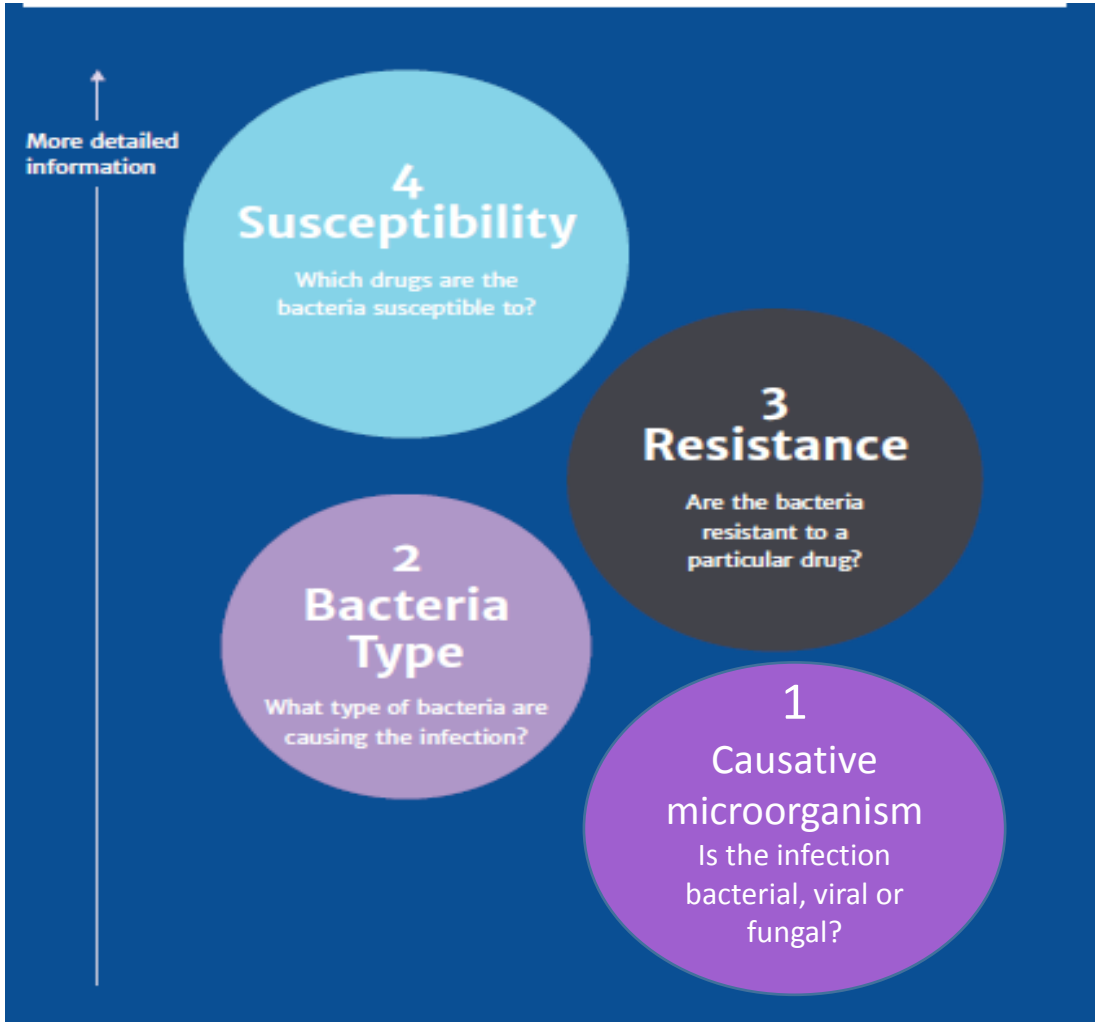
Current knowledge support the use of RDTs as a part of AMS programs



Doernberg SB. Infect Dis Clin N Am 2017; 31 513–534

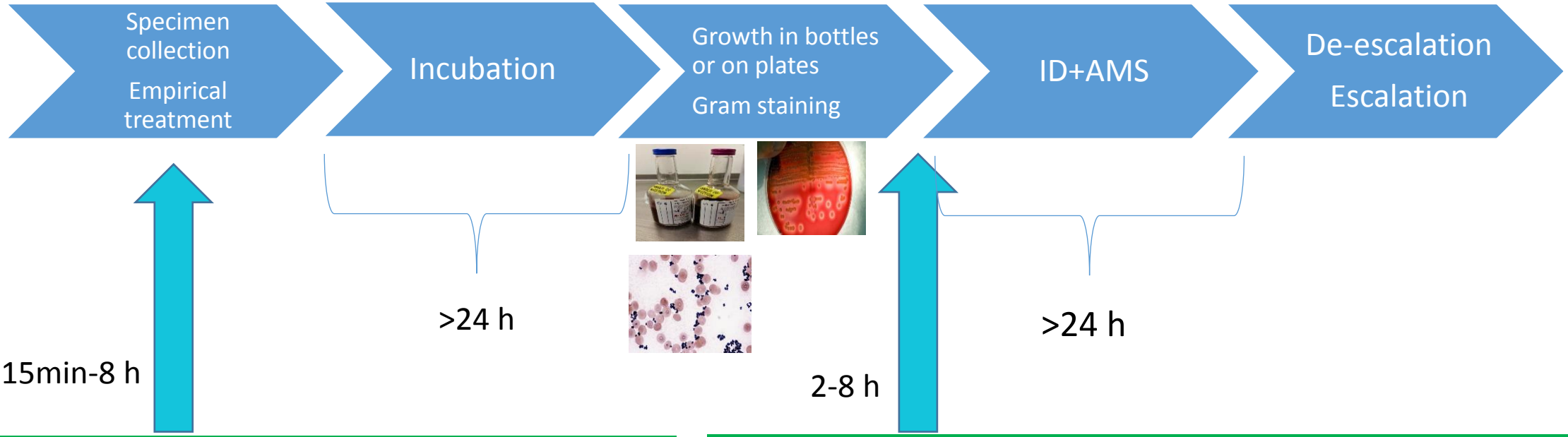
What Rapid Diagnostics Could Test

- In clinical samples
  - Presence/absence of microorganisms
    - Bacteria, virus, fungus
  - Biomarkers
- In positive blood culture bottles or culture plates
  - Bacteria type
  - Antimicrobial resistance
  - Antimicrobial susceptibility



What Rapid Diagnostics Could Test

- **Time-table for the diagnosis and treatment of infectious diseases (traditional diagnostics - culture+ID+susp)**



RAPID DIAGNOSTICS FOR CLINICAL SAMPLES (direct detection of microorganisms)

RAPID DIAGNOSTICS FOR POSITIVE BLOOD CULTURE BOTTLES AND CULTURE PLATES (ID, resistance, susceptibility)

What Rapid Diagnostics Could Test

Direct microorganism detection from clinical samples: Molecular or ICT

Syndrome	Test	Sample	Pathogen	Performance	TAT
Pneumonia	Multiplex PCR	Sputum	"Unlimited" pathogens	PPV????	2 h
	ICT	Urine	*S. pneumoniae* *Legionella*	PPV -> 0.8 -0.96 S: 76%; E: 99%	15 min
	Multiplex PCR	Nasal Swab	"Unlimited" virus	PPV???	2 h
Influenza	ICT	NP Swab	Influenza A and B	S:62%; E 98%	15 min
	PCR	NP Swab	Influenza A and B	S: ↑↑ E: ↑↑	1-6 h
Meningitis	Multiplex PCR	CSF	"Unlimited" virus and bacteria	S: ↑↑ E: ↑↑	2h
Diarrea	PCR	Stool	*C. diff*	S: >90% E: CDAD?	90 min
	ICT	Stool	*C. diff* Toxin A/B	S: 80-90%, E: 99%	<30 min
	ICT	Stool	Rotavirus, Adenovirus	S: ↑ E: ↑	<30 min
	ICT	Stool	Campylobacter		<30 min
	Multiplex PCR	Stool	"Unlimited" pathogens		2 h

1 Causative microorganism

1 Causative microorganism

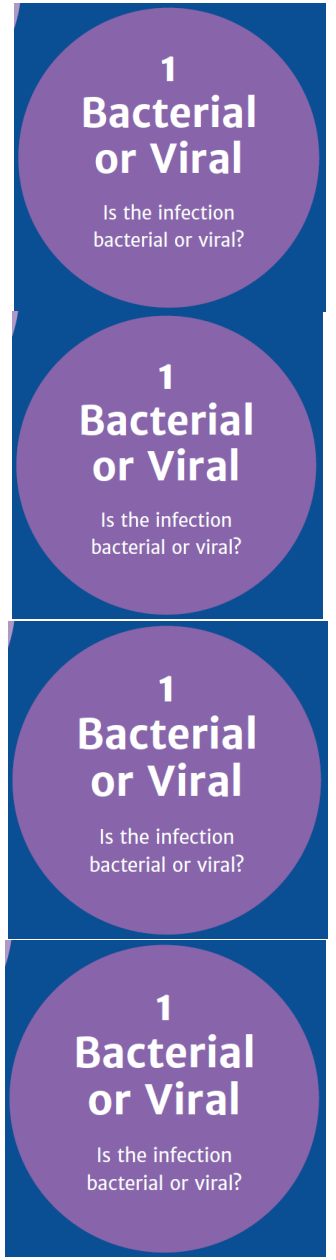
1 Causative microorganism

1 Causative microorganism

Slide from José Ramón Paño-Pardo

Direct Pathogen Detection From Clinical Samples

- **Multiplex PCR for respiratory infections as an AMS tool**
  - **The theory**
    - **Rapid, sensitive and specific detection of both bacterial and viral pathogens from a single specimen**
    - **They could help to avoid unnecessary antibacterial treatment if viral pathogens are detected**
  - **The real life**
    - **Identification of a single viral pathogen in respiratory samples did not result in immediate discontinuation of antimicrobial treatment in several studies.**
      - **Delayed communication**
      - **«He's doing well; let's continue the broad spectrum antibiotics»**



The reality

Contents lists available at ScienceDirect

American Journal of Infection Control

journal homepage: www.ajicjournal.org

Brief Report

Evaluating the impact of the multiplex respiratory virus panel polymerase chain reaction test on the clinical management of suspected respiratory viral infections in adult patients in a hospital setting

- **The impact of a multiplex respiratory virus panel PCR test in 186 adult patients with suspected influenza-like illness.**

		Antiviral treatment			Antibiotic treatment		
			Postresult treatment			Postresult treatment	
Test results	n	Empirically treated*	Continued†	Discontinued†	Empirically treated*	Continued†	Discontinued†
Hospitalized patients							
Negative	62	15 (24.2)	5 (33.3)	10 (66.7)	41 (66.1)	35 (85.4)	6 (14.6)
Positive noninfluenza	10	4 (40.0)	0 (0)	4 (100)	7 (70.0)	5 (71.4)	2 (28.6)
Positive influenza	17	7 (41.2)	7 (100)	0 (0)	12 (70.6)	9 (75.0)	3 (25.0)
Patients diagnosed in the emergency room							
Negative	31	8 (25.8)	1 (12.5)	7 (87.5)	22 (70.9)	17 (77.2)	5 (22.7)
Positive noninfluenza	22	7 (31.8)	2 (28.6)	5 (71.4)	11 (50.0)	7 (63.6)	4 (36.4)
Positive influenza	44	16 (36.4)	14 (87.5)	2 (12.5)	19 (43.2)	13 (68.4)	6 (31.6)

NOTE. Values are n (%) or as otherwise indicated.

- **Antivirals were discontinued nearly 70 % of patients with negative viral testing results, in 75% of patients with positive viral testing results**

RDT alone is not sufficient,
AMS efforts are required ☺)

Yee C. Am J Infect Control. 2016 ;44:1396-1398

Maurer F. Infect Dis Rep 2017; 9:6839

Direct Pathogen Detection From Clinical Samples

- Multiplex PCR for respiratory viruses&bacteria : PPV problem
  - Bacteria were found as causative agents for CAP

Causative microorganisms in 127 pts with CAP

Pathogen identified	Standard (47 pts)	FilmArray (43 pts)
Patients with viral pathogen only: Subtotal	**13**	**12**
- Adenovirus	0	0
- Coronavirus	0	1
- Human metapneumovirus	1	1
- Influenza	11	5
- Parainfluenza	0	1
- Respiratory syncytial virus	0	4
- Rhinovirus	1	0
Patients with bacterial pathogen only: Subtotal	**20**	**21**
- *S. pneumoniae*	8	6
- *S. aureus* (MSSA + MRSA)	4	6
- *S. pneumoniae* + *S. aureus*	1	2
- *H. influenzae*	3	5
- Streptococcus species	1	1
- *Moraxella catarrhalis*	0	1
- *Enterobacteriaceae* species	3	0
s with viral and bacterial pathogens: Subtotal	**14**	**10**
us + elevated procalcitonin serum concentration	2	1
neumoniae + adenovirus	0	0
neumoniae + coronavirus	0	0
neumoniae + hMPV*	0	0
neumoniae + influenza	3	2
neumoniae + parainfluenza	1	1
neumoniae + RSV*	2	2
neumoniae + rhinovirus	0	1
ureus + hMPV*	1	2
ureus + influenza	2	0
eptococcus species + influenza	1	0
ked bacterial flora + influenza	2	1

False-positive rapid molecular test results may even trigger antimicrobial therapy!!!!

RDT alone is not sufficient,
AMS and DS efforts are required ☺)

rt D. Diagn Microb Infect Dis 2016; 86: 102–107

Guideline Recommendation for Rapid Viral Testing

XVI. Should ASPs Advocate for Use of Rapid Viral Testing for Respiratory Pathogens to Reduce the Use of Inappropriate Antibiotics?

Recommendation

17. We suggest the use of rapid viral testing for respiratory pathogens to reduce the use of inappropriate antibiotics *(weak recommendation, low-quality evidence)*.

Comment: Although rapid viral testing has the potential to reduce inappropriate use of antibiotics, results have been inconsistent. Few studies have been performed to assess whether active ASP intervention would improve those results.

Barlam TF. Clin Infect Dis 2016;62:e51–e77

Original Investigation

Overdiagnosis of *Clostridium difficile* Infection in the Molecular Test Era

Christopher R. Polage, MD, MAS; Clare E. Gyorke, BS; Michael A. Kennedy, BS; Jhansi L. Leslie, BS;

1
Causative microorganism

- 293 hospitalized adult patients with a positive *C. difficile* PCR test
  - 45% Tox-
    - More
    - More
  - 55% Tox
    - Lower *C difficile* bacterial load (*P* < .001 for all)
    - Less antibiotic exposure, fecal inflammation, and diarrhea (*P* < .001)
    - Similar outcomes with Tox-/PCR+ patients

Exclusive reliance on molecular tests for CDI diagnosis without tests for toxins or host response is likely to result in overdiagnosis, overtreatment, and increased health care costs!!! 😮 😱

RDT alone is not sufficient,
AMS and DS efforts are required ☺)

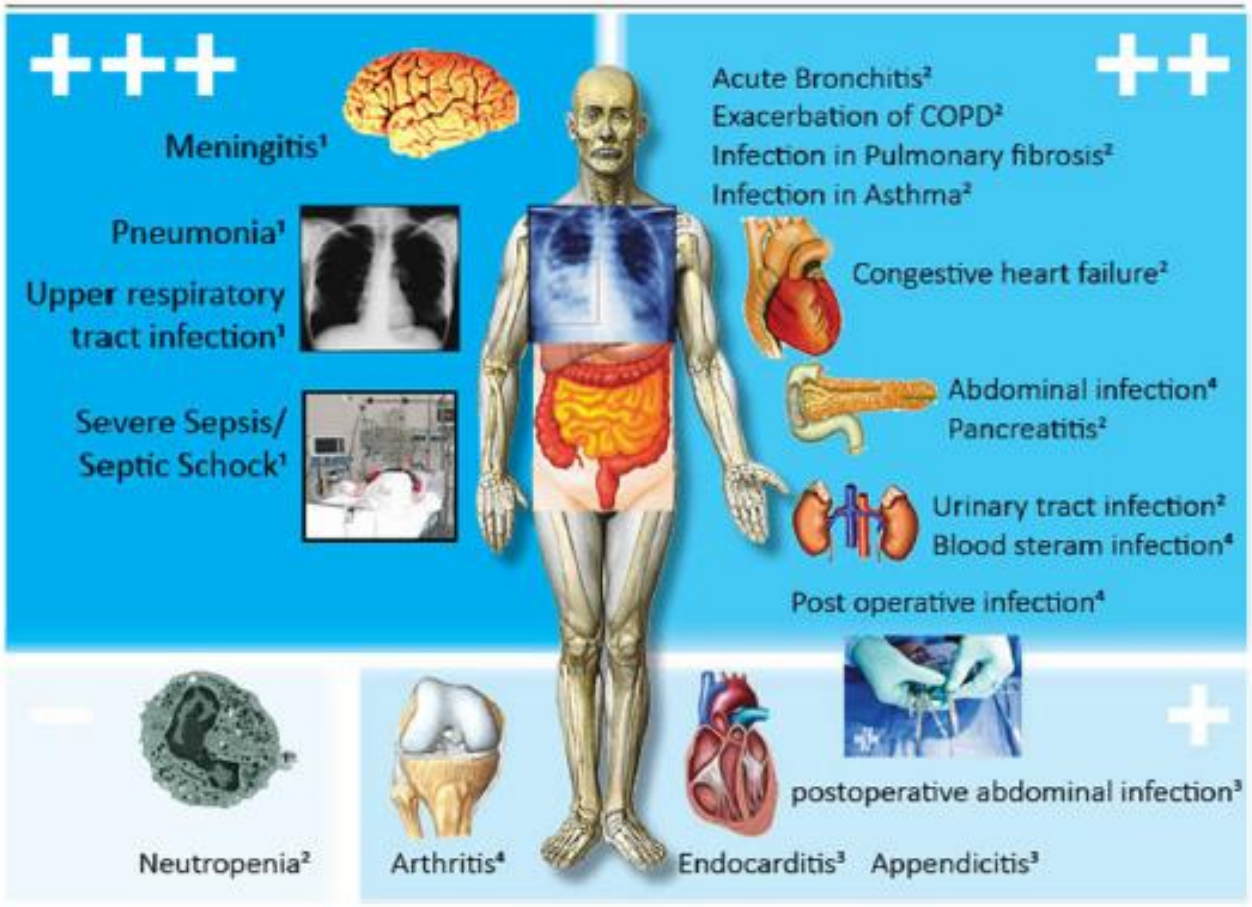
A Intern Med. 2015;175:1792-1801

1
Bacterial or Viral

Is the infection bacterial or viral?

Procalcitonin

The most studied RDT we have ever had.



Evidences Regarding PCT For Diagnosis and Antibiotic Stewardship in Organ-related Infections

+++: strong evidence in favor of PCT

++: good evidence in favor of PCT

+: moderate evidence in favor of PCT

– no evidence in favor of PCT

Sager R. BMC Medicine 2017; 15:15

Using Procalcitonin to Guide Antibiotic Therapy

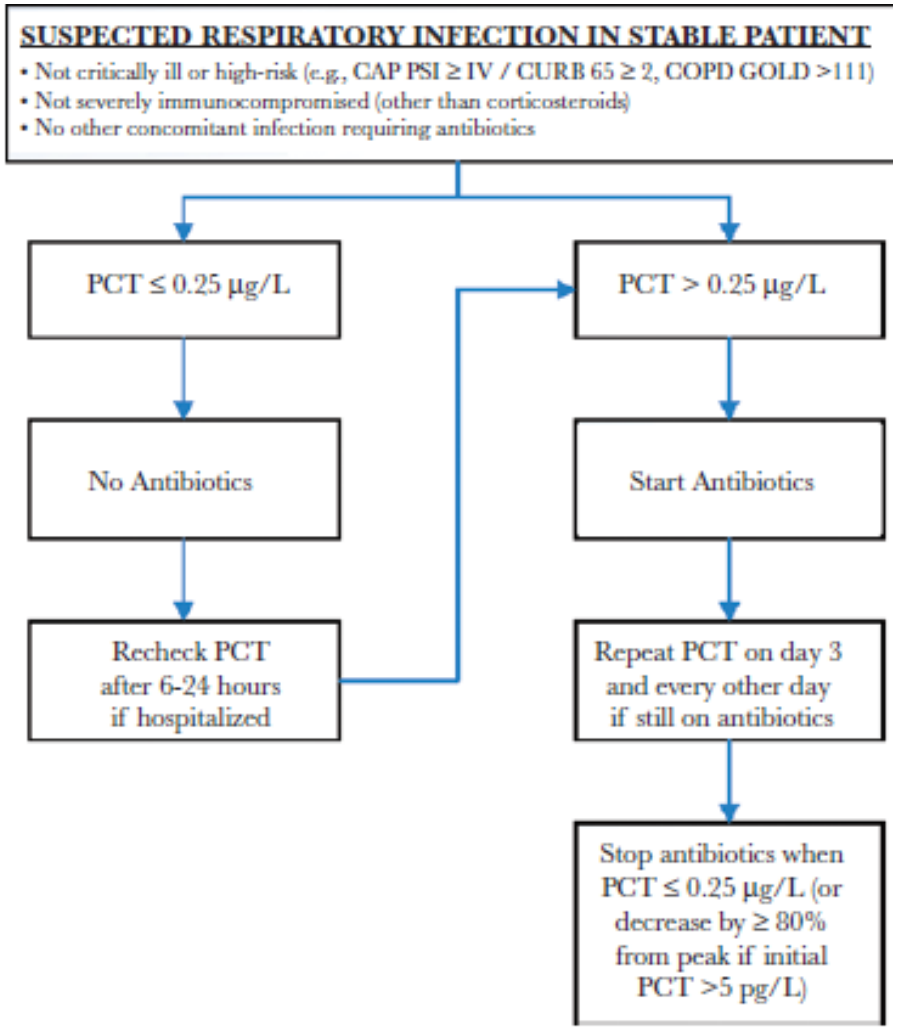
- **PCT for Respiratory Tract Infections in Adult Patients:10 RCT**
  - **PCT-based algorithms can safely reduce antibiotic use in stable, low risk patients with respiratory infections**
  - **PCT levels of <0.25 µg/L can guide the decision to withhold antibiotics or stop therapy early**
- **PCT for Infections in Critically Ill Adult Patients: 9 RCT**
  - **PCT-based algorithms can safely reduce antibiotic use in critically ill patients with suspected sepsis**
  - **Clinicians should not initially withhold antibiotics**
  - **PCT levels of <0.5 µg/L or levels that decrease by ≥80% from peak can guide discontinuation once patients stabilize**

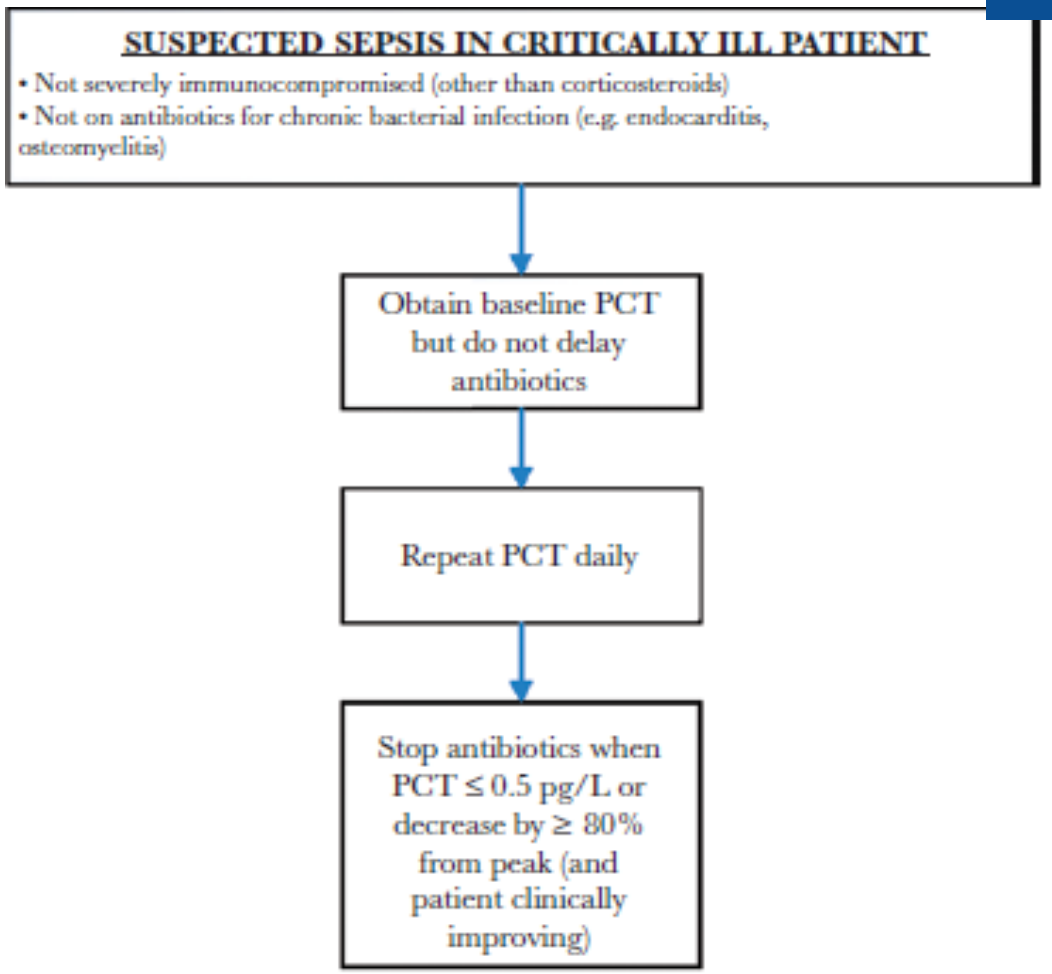
Rhee C. Open Forum Infect Dis 2016; DOI: 10.1093/ofid/ofw249

Using Procalcitonin to Guide Antibiotic Therapy

1 Bacterial or Viral

Is the infection bacterial or viral?





Rhee C. Open Forum Infect Dis 2016; DOI: 10.1093/ofid/ofw249

Efficacy and safety of procalcitonin guidance in reducing the duration of antibiotic treatment in critically ill patients: a randomised, controlled, open-label trial

1 Bacterial or Viral

Is the infection bacterial or viral?

- 1575 ICU patients were randomly assigned to the PCT-guided group (761) or to SOC (785)

Feature	Procalcitonin-guided group (761)	Standard-of-care (785)	Sig.
Median duration of treatment (days)	5	7	p<0.0001
Median antibiotic consumption of (DDD)	7.5	9.3	*P*<0 .0001
Mortality at 28 day	20%	25%	p=0.0122
1-year mortality	36%	43%	p=0.0188

- PCT guidance not only stimulates reduction of duration of treatment and daily defined doses in critically ill patients with a presumed bacterial infection, but it also reduces mortality significantly.

de Jong E. Lancet Infect Dis 2016; 16: 819–27

Guideline Recommendation for PCT

XVIII. In Adults in Intensive Care Units (ICUs) With Suspected Infection, Should ASPs Advocate Procalcitonin (PCT) Testing as an Intervention to Decrease Antibiotic Use?

Recommendation

19. In adults in ICUs with suspected infection, we suggest the use of serial PCT measurements as an ASP intervention to decrease antibiotic use *(weak recommendation, moderate-quality evidence)*.

Comment: Although randomized trials, primarily in Europe, have shown reduction in antibiotic use through implementation of PCT algorithms in the ICU, similar data are lacking for other regions including the United States where the patterns of antibiotic prescribing and approach to stewardship may differ. If implemented, each ASP must develop processes and guidelines to assist clinicians in interpreting and respond-
, and must determine if this inter-
s time and resources.

RDT alone is not sufficient,
AMS efforts are required ☺)

Barlam TF. Clin Infect Dis 2016;62:e51–e77

What Rapid Diagnostics Could Test

1
Causative microorganisms

Molecular assays directly on blood

Assay/ Time (h)	Detection technology	Sens%/Specif %	Pathogens
SeptiFast /2-6	PCR (16s, 23s , 18s rRNA)	68/86	19 b/6 f
Iridica/2-6	PCR + electrospray ionization MS	81/69	>750 b, >200 f, >130 v
SeptiTest/2-8	16S rDNA PCR + sequencing	26-87/83-86	>300
Looxter Vyoo/2-7	PCR + electrophoresis/ microarray		34 b, 7 f
Magicplex/2-6	Nested real time PCR	47/66	90
T2 Candida/2-3	PCR + NMR	100/98	5f
Polaris Idylla/ 1-2	Real time PCR		10 b, 6 f

Ziegler Z. PLoS ONE 2016; 11(12): e0167883
Vincent JL. Crit Care Med. 2015;43(11):2283–91.
Wenzler E. IDSE, Fall 2016; 35-45.
Dark P. Int Care Med 2015; 41: 21-33

Molecular assays directly on blood: **Pro/Con**

Pro

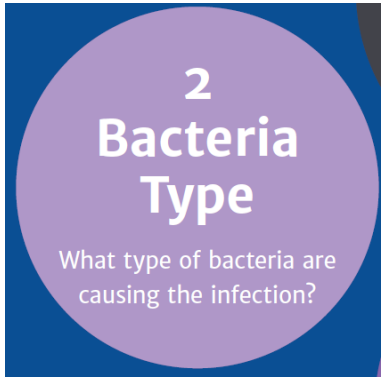
- **Timeliness**/Rapidness (potential influence on ABX prescribing)
- Better performance in **fastidious** microorganisms/**patients on antibiotics**

Con

- **Performance** = **unresolved** issue
- No/Limited susceptibility data
- **Cost**
- **Integration** with laboratory workflow
- **Unknown clinical value**

Slide from José Ramón Paño-Pardo

What Rapid Diagnostics Could Test



- **Rapid microorganism identification**
  - **From positive blood cultures and/or culture plates**
    - **Polymerase chain reaction (PCR)**
    - **Multiplex PCR**
    - **Nanoparticle probe technology (nucleic acid extraction and PCR amplification)**
    - **Peptide nucleic acid fluorescent in situ hybridization (PNA FISH)**
    - **Matrix assisted laser desarption/ionization time of flight mass spectrometry (MALDI-TOF)**

What Rapid Diagnostics Could Test

Microorganism ID and resistance determination directly from positive blood cultures.

Verigene®

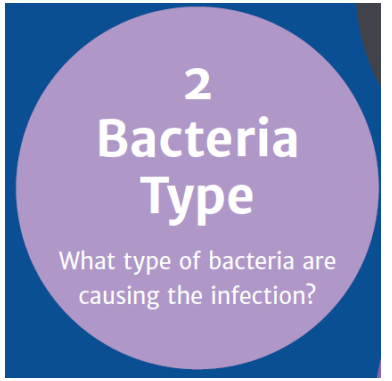
FilmArray®

MALDI-TOF MS

Short-term subculture + MALDI-TOF MS

Testing Time 2h

- 24 to 48h to ID/AST



What Rapid Diagnostics Could Test

Rapid phenotypic susceptibility testing

- Sensitive growth detection
  - Semi automated devices
  - Microcalorimetry
  - Impedence measurement
  - Spectrophotometry
  - Flow cytometry
  - Automated time-lapse microscopy
  - Two-photon excitation assays
  - Ultrahigh-resolution bacterial mass measurement
  - Luciferase express
  - Padlock probe detection of bacterial target DNA
  - Microfluidic channel method
  - High-throughput nanowell AST ……

Rapid molecular resistance testing

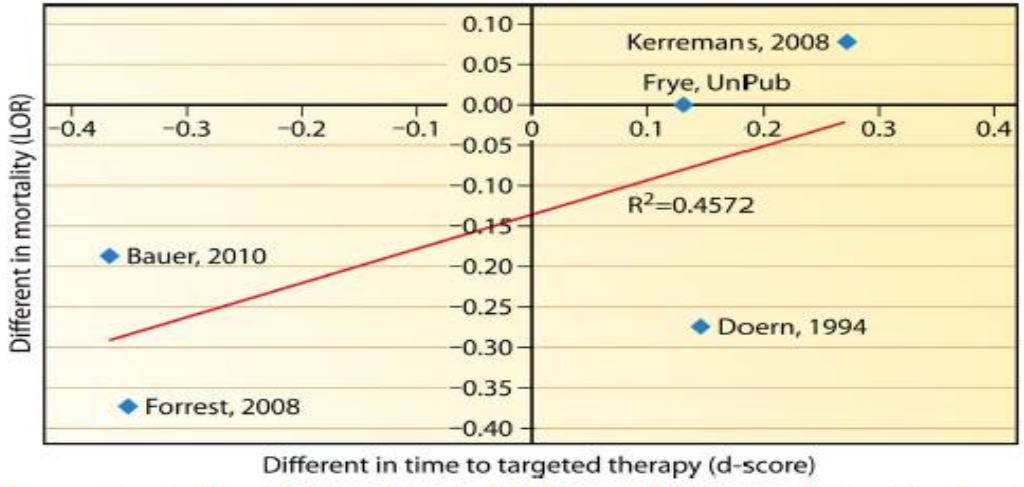
- *mecA: in* staphylococci
- *vanA/B* : in enterococci
- Various beta-lactamases (common carbapenemases) in Gram-negative rods

Maurer F. Infect Dis Rep 2017; 9:6839

Effectiveness of Practices To Increase Timeliness of Providing Targeted Therapy for Inpatients with Bloodstream Infections: a Laboratory Medicine Best Practices Systematic Review and Meta-analysis

The evidence for the effectiveness of rapid diagnostic practices in decreasing the time to targeted therapy (1994-2016)

- **Rapid molecular testing without direct communication of test results to clinicians is not significantly better in increasing timeliness than standard testing**
- **Rapid molecular testing with direct communication of test results to clinicians significantly improves timeliness**
- **Although a strong correspondence between the timeliness of targeted therapy and mortality can be observed, the relationship fails to reach significance**



Buehler SS. Clin Microb Rev 2016;29:60-101

Impact of same-day antibiotic susceptibility testing on time to appropriate antibiotic treatment of patients with bacteraemia: a randomised controlled trial

- A RCT evaluated the reduction in inappropriate antibiotic therapy using rapid ID and AMS testing (FAST) compared to standard of care (SOC) testing in patients with bloodstream infections.
- The FAST testing : ID-PCR and AMS-Semi molecular method
- SOC testing: BD Phoenix system

Outcome	FAST (129 patients)	SOC (121 patients)	Sig.
Mean time to result, h	50.7	66.3	P<0.001
Mean time to appropriate antibiotic, h	28.2	26.9	P=0.9
Hospital LOS, days	11	11	P=0.8
In hospital mortality, %	12.3	7.3	P=0.2

- greement with SOC was 94 %), they were only

RDT alone is not sufficient, AMS efforts are required ☺)

Beuving J. Eur J Clin Microbiol Infect Dis 2015 34:831–838

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

- **Randomization of 617 + blood cultures**

STANDARD BLOOD CULTURE ID (207)	RAPID MULTIPLEX PCR (198) (Filmarray®)	RAPID MULTIPLEX PCR (Filmarray®) + STEWARDSHIP* (212)

- **Stewardship***
  - **An ID clinician or pharmacist was paged with the result, 7d/24 h**
  - **The subject's rmPCR result and medical record were reviewed and the primary service contacted immediately over the 3 days following enrollment if a modification to antimicrobial therapy was deemed appropriate.**

Banerjee R. Clin Infect Dis 2015; 61(7):1071–80

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

(Rapid) **information does not** (necessarily) **lead to action, we should push☺)**

Time to ID, h	22.3	1.3	1.3	P<0.001
Ti				
Ti				
Ti				

Impact of targeted therapy on significant outcomes might not be obvious.

- **No significant differences in clinical outcomes (mortality, ICU admission, LOS) or cost**

RDT alone is not sufficient, AMS efforts are required ☺)

Banerjee R. Clin Infect Dis 2015; 61(7):1071–80

Effect of MALDI-TOF MS Alone versus MALDI-TOF MS Combined with Real-Time Antimicrobial Stewardship Interventions on Time to Optimal Antimicrobial Therapy in Patients with Positive Blood Cultures.

Features	MALDI (126)	MALDI+AMS (126)	Sig.
Time to optimal therapy, h	75.17	43.06	P<0.001
Gr (+) contaminant TTOT, h	48.21	11.75	P<0.001
Gr (-) TTOT, h	71.83	35.98	P<0.001
Hospital LOS, days	15.03	9.02	P=0.021
Gr (+) LOS, days	14.64	10.31	*P* = 0.002
Gr (-) time to microbiologic clearance, h	51.13	34.51	P<0.001
Gr (-) LOS, days	15.40	7.90	P=0.027

RDT alone is not sufficient, AMS efforts are required ☺)

Beganovic M. J Clin Microbiol. 2017 May;55:1437-1445

Original article

Impact of MALDI-TOF-MS-based identification directly from positive blood cultures on patient management: a controlled clinical trial

- **The impact of MALDI-TOF versus conventional identification … management in a setting with a well-est… …es**

Features			
			P=0.9
D… total AM therapy, h	16.4	15.9	P=0.8
Hospital LOS, days	17.9	16.1	P=0.3
Admission to ICU after BSI onset, %	37.2	23.1	P=0.02
In hospital mortality	9.3	9.3	P=1

Rapid identification using MALDITOF directly from positive BCs did not impact on duration of intravenous antimicrobial therapy in the setting of an established ASP.

In the setting of an established AST, RDT is not required at all☺)

Osthoff M. Clin Microb Inf 2017; 23:78-85.

What about from our old rapid diagnostics?

- **Gram-staining**
  - **Rapid**
  - **Cheap**
  - **Easy to perform**
  - **Available all the time**
  - **Could be reliable if you try**

SHORT REPORT

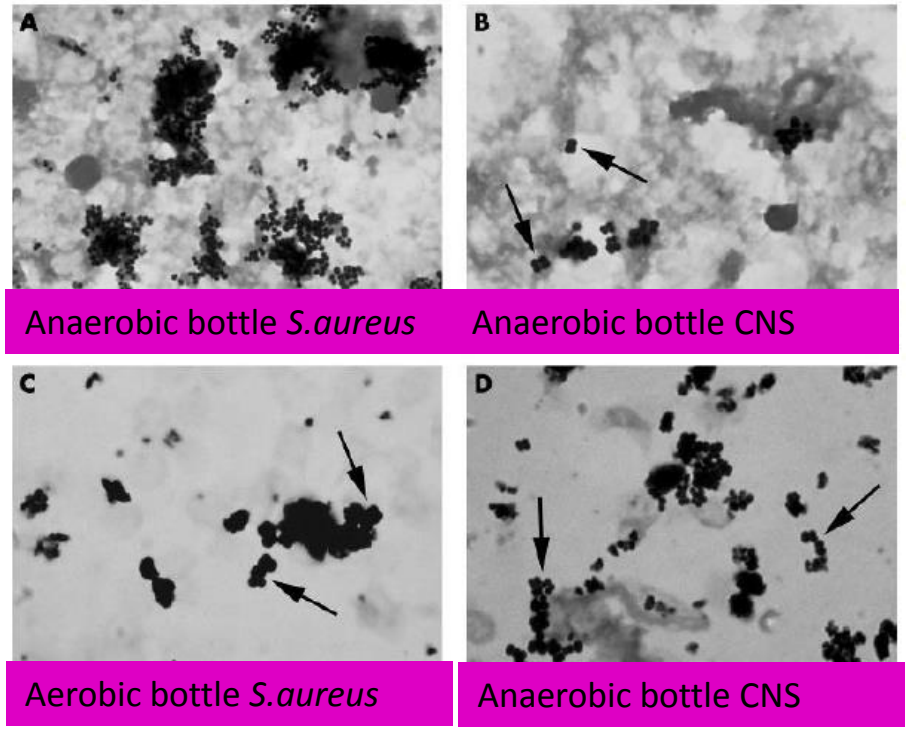
Rapid identification of *Staphylococcus aureus* from BacT/ALERT blood culture bottles by direct Gram stain characteristics

D R Murdoch, R L Greenlees

- **150 blood cultures in which a direct Gram stain showed Gram positive cocci resembling staphylococci were examined.**

Criteria used to distinguish *Staphylococcus aureus* from CNS in direct Gram stains from blood culture bottles

Bottle type	Organism	Cell size	Cluster characteristics
Anaerobic	*S aureus*	Small (<1 µm)	Irregularly clustered in large numbers (typically 200–300 cells)
	Coagulase-negative staphylococci	Large (≥1 µm)	Tetrads or small clusters up to 16 cells
Aerobic	*S aureus*	Large (≥1 µm)	Very tight clusters (typically 8–32 cells). Individual cells cannot be distinguished
	Coagulase-negative staphylococci	Variable (typically <1 µm)	Tetrads or small clusters up to 16 cells



Anaerobic bottle *S.aureus* | Anaerobic bottle CNS

Aerobic bottle *S.aureus* | Anaerobic bottle CNS

Murdoch DR. J Clin Pathol 2004;57:199–201

SHORT REPORT

Rapid identification of *Staphylococcus aureus* from BacT/ALERT blood culture bottles by direct Gram stain characteristics

D R Murdoch, R L Greenlees

- Using that criteria, an experienced microscopist was able to distinguish *S aureus* from other staphylococci isolated f s with an overall sensitivity of 89% and specificity of 98%.
- Testing time was 15 min

Table 2 Performance character ulture for identification of *Staphylococcus aureus* from BacT/ALERT blood culture bottle

Microscopist*	Blood culture bottle type	N N (%	m stains negative for *S aureus*/ ures negative for *S aureus*† ficity)	PPV (%)	NPV (%)
Technologist	All	5	98)	59/61 (97)	82/89 (92)
	Aerobic	26/31 (84)	49/50 (98)	26/27 (96)	49/54 (91)
				33/34 (97)	33/35 (94)
Microbiologist				58/65 (89)	77/85 (91)
				24/27 (89)	47/54 (87)
				34/38 (89)	30/31 (97)

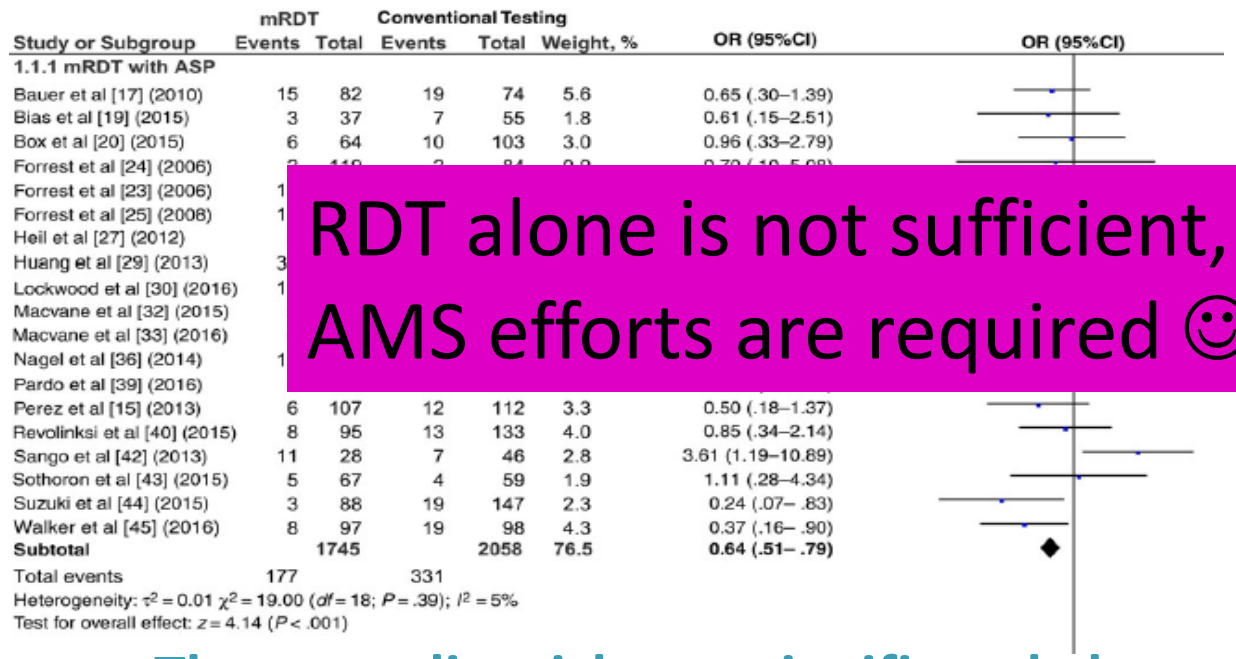
*Technologist e e staphylococci and micrococcus species.
NPV, negative predictive value; PPV, positive predictive value.

Gram staining: A lifebuoy RDT for resource limited settings☺)

Murdoch DR. J Clin Pathol 2004;57:199–201

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

- RDT with ASP

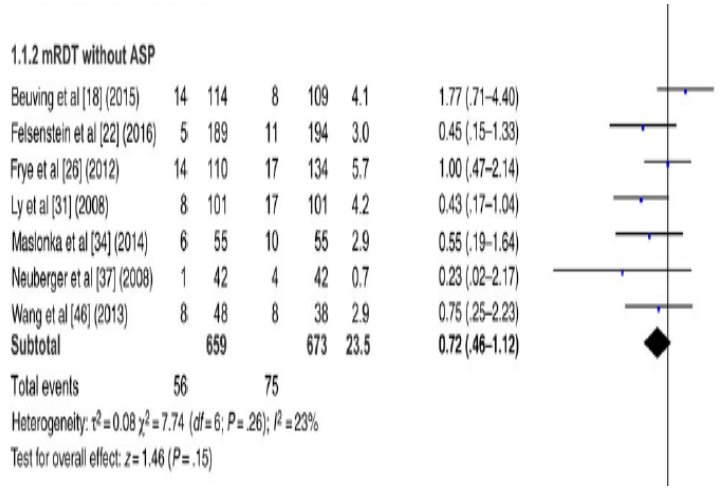


Study or Subgroup	mRDT Events	mRDT Total	Conventional Testing Events	Conventional Testing Total	Weight, %	OR (95%CI)
1.1.1 mRDT with ASP						
Bauer et al [17] (2010)	15	82	19	74	5.6	0.65 (.30–1.39)
Bias et al [19] (2015)	3	37	7	55	1.8	0.61 (.15–2.51)
Box et al [20] (2015)	6	64	10	103	3.0	0.96 (.33–2.79)
Forrest et al [24] (2006)						
Forrest et al [23] (2006)	1					
Forrest et al [25] (2008)	1					
Heil et al [27] (2012)						
Huang et al [29] (2013)	3					
Lockwood et al [30] (2016)	1					
Macvane et al [32] (2015)						
Macvane et al [33] (2016)						
Nagel et al [36] (2014)	1					
Pardo et al [39] (2016)						
Perez et al [15] (2013)	6	107	12	112	3.3	0.50 (.18–1.37)
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)
Sothoron et al [43] (2015)	5	67	4	59	1.9	1.11 (.28–4.34)
Suzuki et al [44] (2015)	3	88	19	147	2.3	0.24 (.07– .83)
Walker et al [45] (2016)	8	97	19	98	4.3	0.37 (.16– .90)
Subtotal		**1745**		**2058**	**76.5**	**0.64 (.51– .79)**
Total events	177		331			

Heterogeneity: $\tau^2 = 0.01$ $\chi^2 = 19.00$ ($df = 18$; $P = .39$); $I^2 = 5\%$
Test for overall effect: $z = 4.14$ ($P < .001$)

RDT alone is not sufficient, AMS efforts are required ☺)

- RDT without ASP



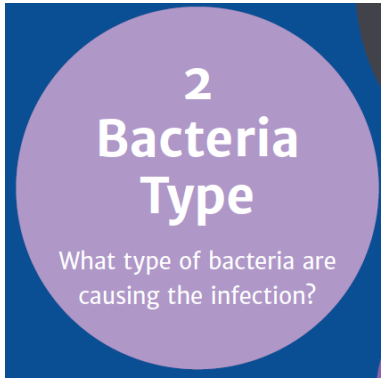
1.1.2 mRDT without ASP						
Beuving et al [18] (2015)	14	114	8	109	4.1	1.77 (.71–4.40)
Felsenstein et al [22] (2016)	5	189	11	194	3.0	0.45 (.15–1.33)
Frye et al [26] (2012)	14	110	17	134	5.7	1.00 (.47–2.14)
Ly et al [31] (2008)	8	101	17	101	4.2	0.43 (.17–1.04)
Maslonka et al [34] (2014)	6	55	10	55	2.9	0.55 (.19–1.64)
Neuberger et al [37] (2008)	1	42	4	42	0.7	0.23 (.02–2.17)
Wang et al [46] (2013)	8	48	8	38	2.9	0.75 (.25–2.23)
Subtotal		**659**		**673**	**23.5**	**0.72 (.46–1.12)**
Total events	56		75			

Heterogeneity: $\tau^2 = 0.08$ $\chi^2 = 7.74$ ($df = 6$; $P = .26$); $I^2 = 23\%$
Test for overall effect: $z = 1.46$ ($P = .15$)

The mortality risk was significantly lower in studies with mRDT+AMS programs with an OR of 0.64, but mRDT without ASP studies failed to demonstrate a significant decrease in mortality risk.

Timbrook TT. Clin Infect Dis 2017; 64(1):15–23

Guideline Recommendation for RDT on Blood Specimens



XVII. Should ASPs Advocate for Rapid Diagnostic Testing on Blood Specimens to Optimize Antibiotic Therapy and Improve Clinical Outcomes?

Recommendation

18. We suggest rapid diagnostic testing in addition to conventional culture and routine reporting on blood specimens if combined with active ASP support and interpretation *(weak recommendation, moderate-quality evidence)*.

Comment: Availability of rapid diagnostic tests is expected to increase; thus, ASPs must develop processes and interventions to assist clinicians in interpreting and responding appropriately to results.

Barlam TF. Clin Infect Dis 2016;62:e51–e77

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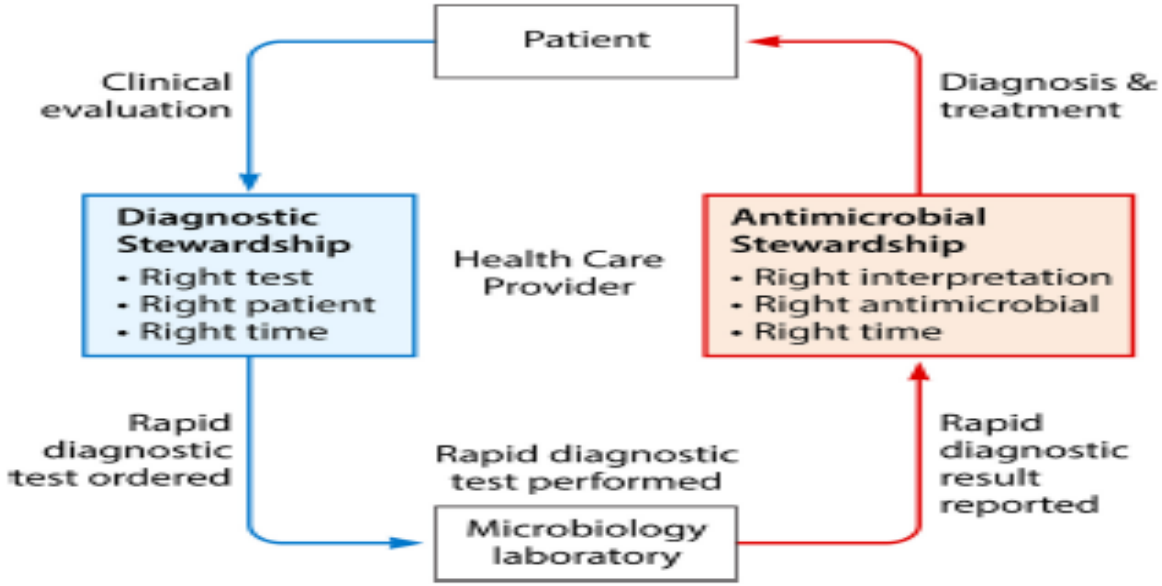
Implementation of Rapid Molecular Infectious Disease Diagnostics: the Role of Diagnostic and Antimicrobial Stewardship

"Our technical capabilities are exceeding our ability to apply them effectively and economically to human problems" Dr. Bartlett , 1974.

We need also diagnostic stewardship along with antimicrobial stewardship to ensure that these technologies conserve, rather than consume, additional health care resources and optimally affect patient care.



Messacar K. JClin Microbiol 2017; 5: 715–723.

Diagnostic and Antimicrobial Stewardship

Key antimicrobial stewardship considerations for implementation of rapid infectious disease diagnostics

Goal	Key question	Key considerations and potential strategies[a]
Right interpretation	Will the clinician understand the test result?	Result report language Selective reporting of relevant results AS prospective audit and feedback AS real-time decision support
Right antimicrobial	Will the clinician appropriately modify antimicrobials based on the test result?	Clinical practice guidelines EMR-based decision support with result reporting AS prospective audit and feedback AS real-time decision support
Right time	Will the clinician act upon the test result promptly?	EMR reporting Results called with readback reporting AS prospective audit and feedback AS real-time decision support

Messacar K. JClin Microbiol 2017; 5: 715–723.

Diagnostic and Antimicrobial Stewardship

Key diagnostic stewardship considerations for implementation of rapid infectious disease diagnostics

Goal	Key question	Key considerations and potential strategies
Right test	Is the test appropriate for the clinical setting?	Sensitivity and specificity Predictive values Testing volumes Diagnostic yield Laboratory feasibility Cost Clinical impact
Right patient	Will the clinical care of the patient be affected by the test result?	Laboratory test utilization committee Automatic laboratory reflex CPOE decision support Appropriate use criteria Indication selection Prior authorization Benchmarking Specimen rejection
Right time	Will the result be available in time to optimally affect care?	Time to specimen receipt Centralized vs point-of-care testing On-demand vs batched testing Specimen preparation time Run time Result reporting time

Messacar K. JClin Microbiol 2017; 5: 715–723.

Antimicrobial Stewardship Program Checklist for Rapid Diagnostic Tests

Preimplementation

- **Identify most useful RDT based on hospital pathogen prevalence**
- **Time to effective therapy**
- **Identify hospital cost of infection**

Bauer KA. CID 2014;59(S3):S134–45

Antimicrobial Stewardship Program Checklist for Rapid Diagnostic Tests

Implementation

- Microbiologist-validated RDT instrument
- Determine if test is done continuously (24/7) or at least in frequent batches
- Rapid notification and communication of RDT results from microbiologist to physician and ASP pharmacist is established
- ASP pharmacist-physician educates medical staff
- ASP documents interventions and acceptance rate

The most difficult part of the job!! Infectious Disease and Clinical Microbiology specialist could handle that better, at least in Turkey).

Bauer KA. CID 2014;59(S3):S134–45

Antimicrobial Stewardship Program Checklist for Rapid Diagnostic Tests

Postimplementation

- Time to effective therapy
- Time to discontinuation or de-escalation
- Time to ID consult
- Documented negative blood culture prior to hospital discharge
- 30-day readmission
- Mortality

Bauer KA. CID 2014;59(S3):S134–45

Diagnostic Stewardship Along with Antimicrobial Stewardship

Diagnostic Stewardship Along with Antimicrobial Stewardship

Nothing can be achieved by this way!!!

Birds fly not into our mouth ready roasted

Armut piş ağzıma düş

Diagnostic Stewardship Along with Antimicrobial Stewardship

- **To do this hardwork, all we need is ……..**

Cambridge Dictionary

the willingness to give a lot of time and energy to something (AMS) because it is <u>important</u> (not because it gives you power or money ☺))

Take-home Messages

- **Rapid diagnostics: an AMS tool?**
  - **Yes, they could be an AMS tool, if there are people who have dedicated themselves to protecting the antimicrobials.**
  - **RDTs are of little value if an AMS program does not have a role as an active messenger and educator of the results.**
  - **Along with AMS, diagnostic stewardship is needed to implement appropriate tests for the clinical setting and to direct testing toward appropriate patients.**
  - **PCT should be used to guide the therapy in sepsis and CA pneumonia.**