Mikrobiyolog Gözü ile Hızlı Tanı Testleri

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Tıbbi Mikrobiyoloji Anabilim Dalı

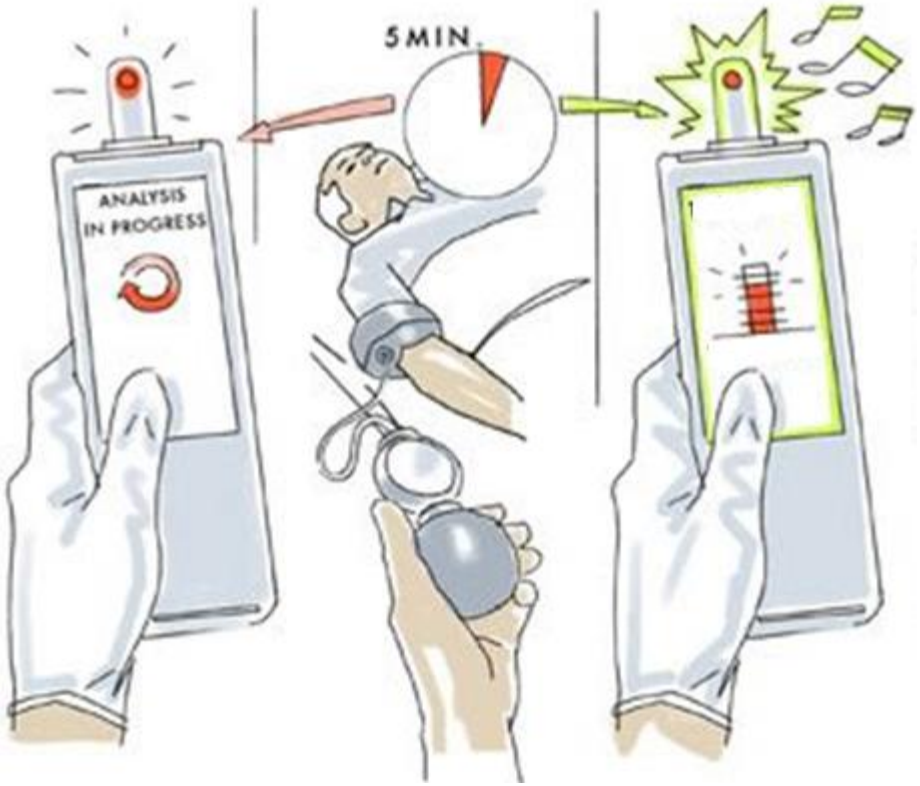
JOURNAL OF CLINICAL MICROBIOLOGY, Nov. 2002, p. 3889–3893 Vol. 40, No. 11
0095-1137/02/$04.00+0 DOI: 10.1128/JCM.40.11.3889–3893.2002

GUEST COMMENTARY

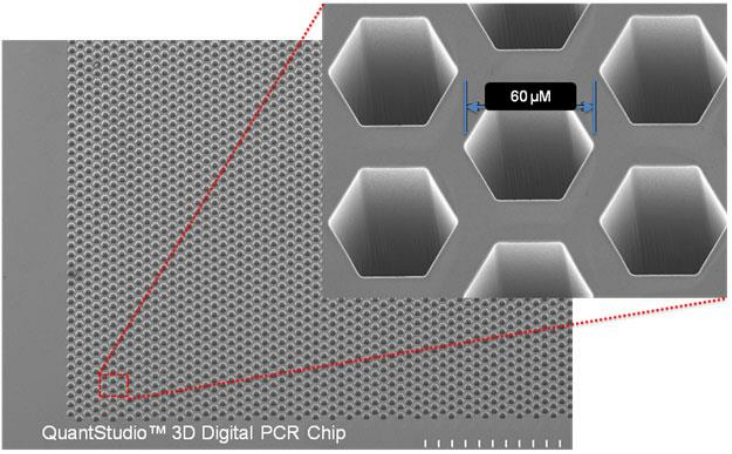
Clinical Microbiology in the Year 2025

W. Michael Dunne, Jr.,[1]* J. Keith Pinckard,[1] and Lora V. Hooper[2]

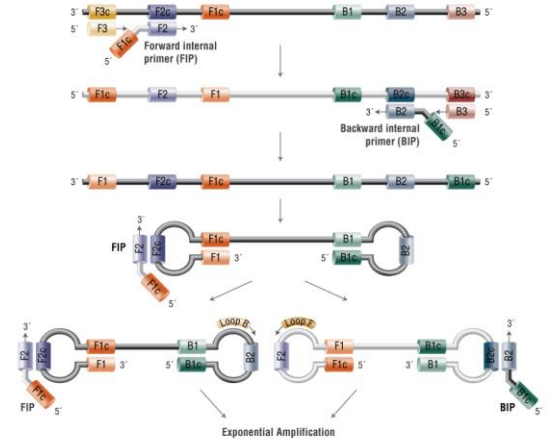
Departments of Pathology and Immunology[1] and Molecular Biology and Pharmacology,[2] Washington University School of Medicine, St. Louis, Missouri 63110

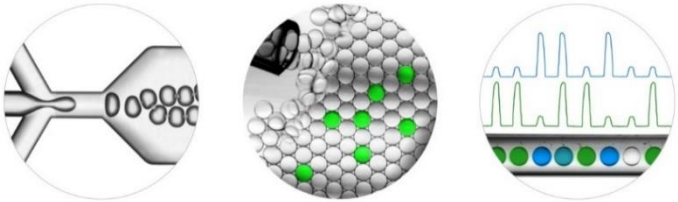


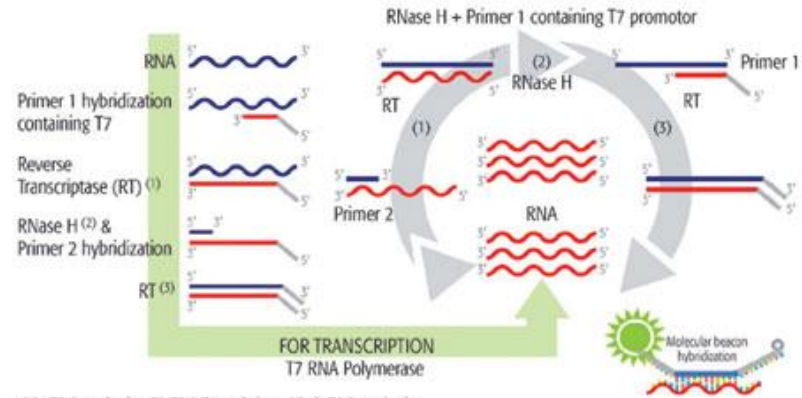
Mutfakta Neler Oluyor?

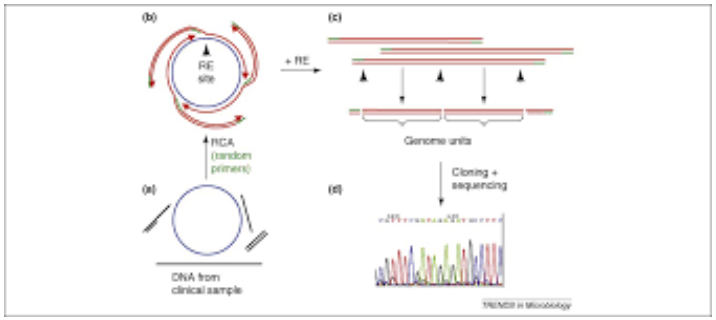


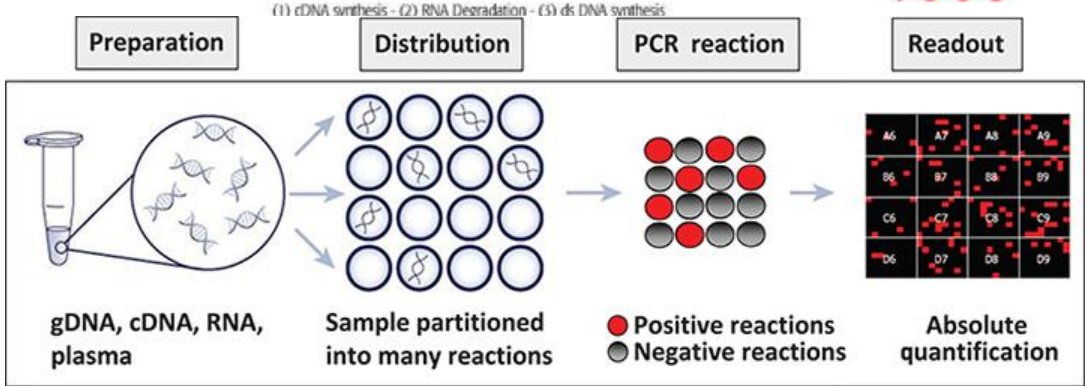
- PCR
- Real Time PCR
- Multiplex Testler
- LAMP
- TMA
- RPA
- RCA
- LCR



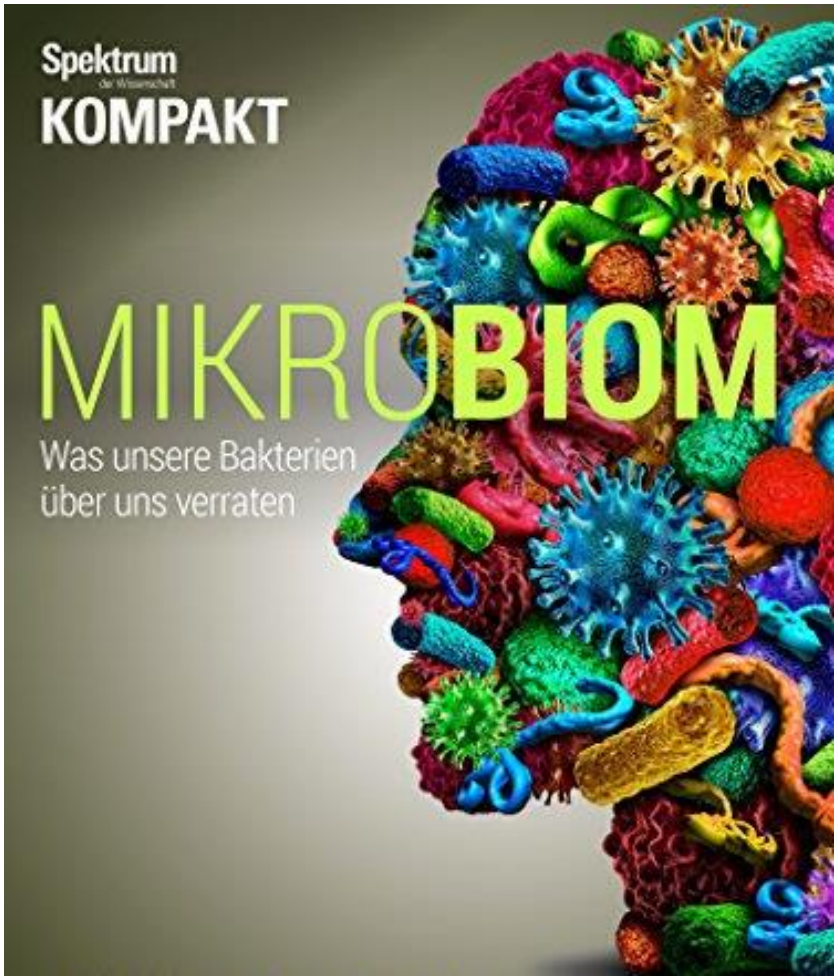


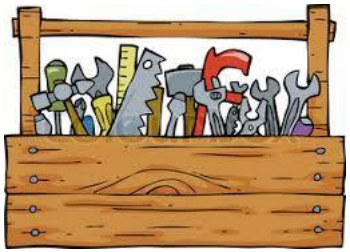






Alet Çantasındaki Pek Çok Alet; ve Yeni Kavramlar;



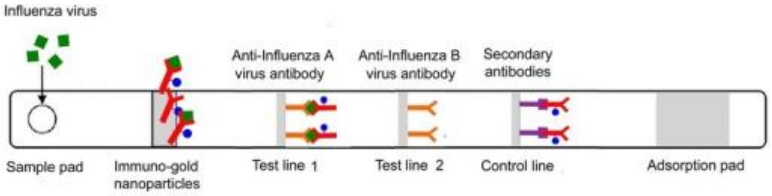


Point of Care Tests (Yerinde Bakım Testleri)

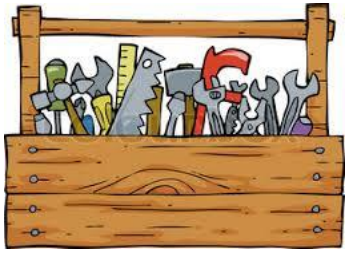
POC testlere olan gereksinimler sağlık altyapıları güçlü ve herkes için ulaşılabilir olan gelişmiş ülkelerle sağlık altyapısı zayıf ve çoğunlukla erişilebilir tek test seçeneği olan az gelişmiş ülkelerde farklı

Kolay uygulanabilir olmakla birlikte POC testler geçmişte genel olarak:

- Teknisyen hatalarına açık
- Duyarlılık ve özgüllükleri düşük



Affordable
Sensitive
Specific
User-friendly
Rapid
Equipment-free
Delivered to those in need

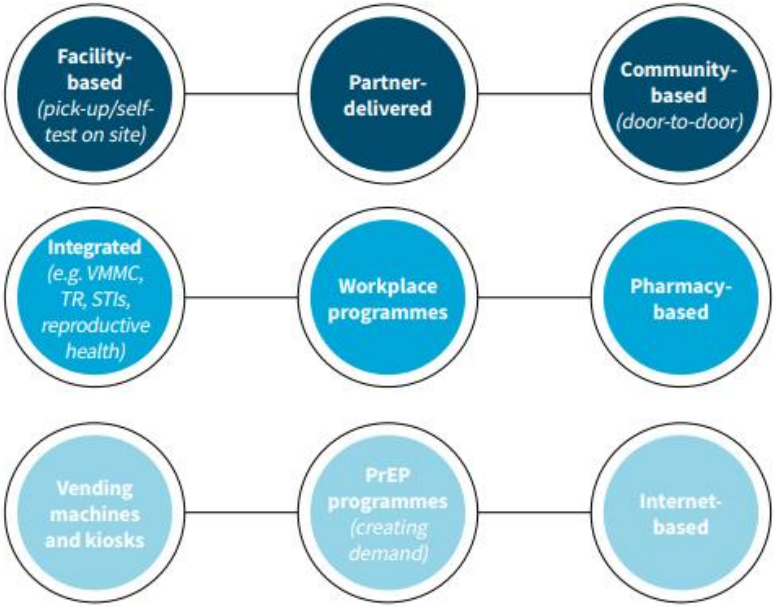


Point of Care Tests (Yerinde Bakım Testleri)

- Toplumda kullanımı???

- Eczanelerde test yapılması
- Kendi kendine testler ➔ Evde testler
- Mobil teknolojiler
- Sahada mobil teknolojiler

FIGURE 1.
HIVST service-delivery approaches



Source: WHO, 2016 [20].

diagnosed | on treatment | virally suppressed

AMERICAN SOCIETY FOR MICROBIOLOGY | Journal of Clinical Microbiology®

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

Kevin Messacar,[a,b] Sarah K. Parker,[b] James K. Todd,[b] Samuel R. Dominguez[b]

*the microbiology laboratory today is exceedingly "faced with a superabundance of academic information and pressure to perform exhaustive, expensive, clinically irrelevant [testing]", which, when misguided "**misleads physicians into erroneous diagnosis and inappropriate therapy**".*

"more practical, economical, clinically meaningful approach"

The clinical microbiology laboratory is in the midst of a diagnostic revolution.

Messacar K. J. Clin. Microbiol. doi:10.1128/JCM.02264-16

Lean Microbiology-Removing «Muda»

Artı Değer Üretmeyen Etkinliklerin Sonlandırılması

- Tip 1 Muda: «İşe yaramıyorsa yapma» yaklaşımı ile hemen elimine edilebilecekler.

- Tip 2 Muda: İşlerin şu an için yapılma şekli için gerekli olan ve elimine edilemeyecekler (denetim, gözetim, kalite kontrol için gerekli olanlar…)

Broad Assay Menu and Sample Types

Future Clinical Assay Menu Design Goals

NOW CE MARKED

ASSAY	INTENDED COVERAGE	INTENDED SAMPLE TYPE
BAC BSI	**780+ Bacteria**, Candida and 4 Antibiotic Resistance Markers: mecA, vanA, vanB and kpc	5ml EDTA whole blood
BAC Sterile Fluids & Tissues		Sterile fluid and tissues
BAC LRT	Identical coverage with **semi-quantitative threshold**	BAL and ETA
Fungal	**200+** fungi and yeast	BAL and Isolates
Viral IC	**13** distinct groups of viruses 130+ Viral species	Plasma

Clinical Infectious Diseases

Volume 66, Issue 3
1 February 2018

Demise of Polymerase Chain Reaction/Electrospray Ionization-Mass Spectrometry as an Infectious Diseases Diagnostic Tool

Volkan Özenci, Robin Patel ✉, Måns Ullberg, Kristoffer Strålin

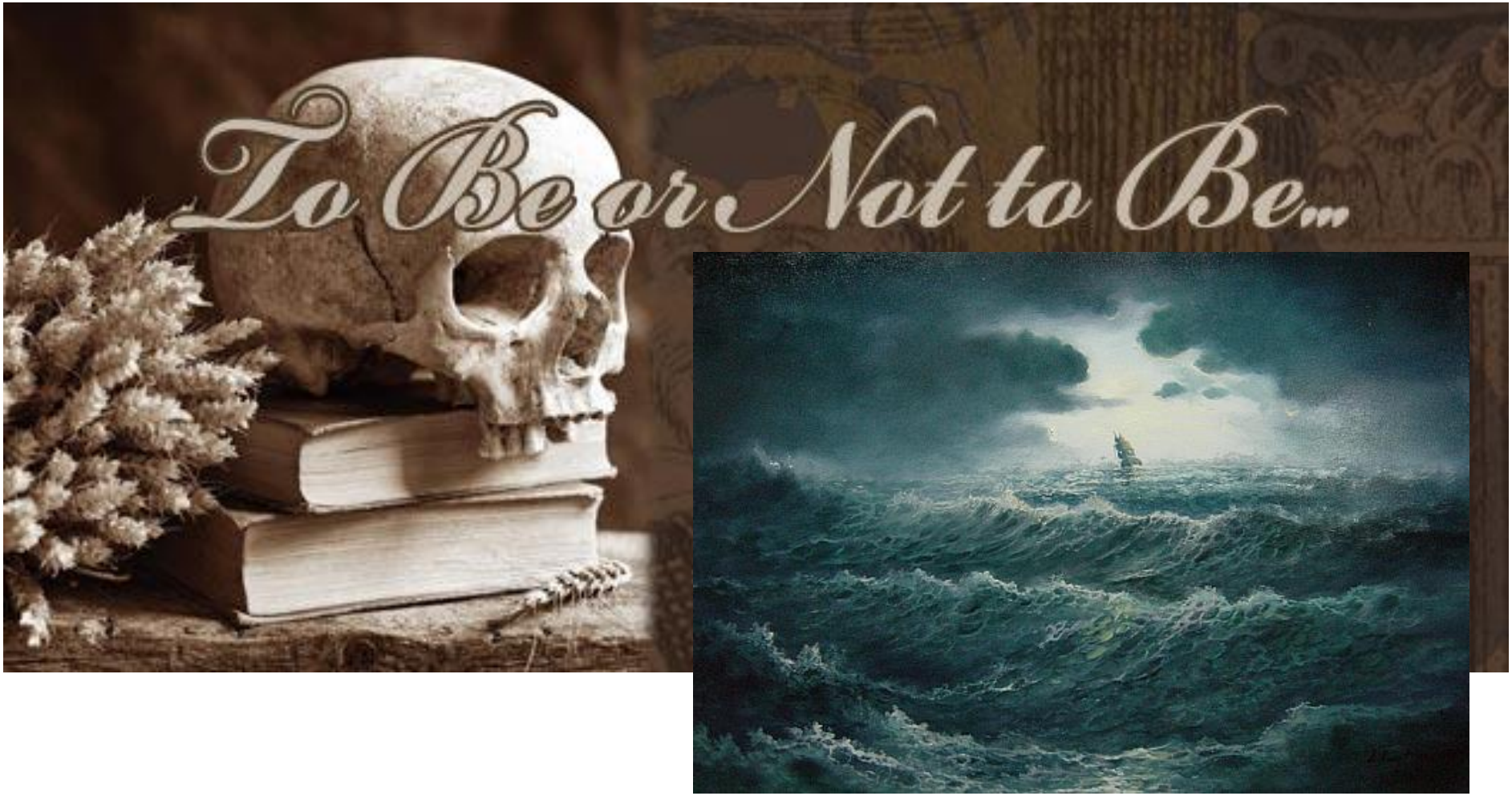
Clinical Infectious Diseases, Volume 66, Issue 3, 18 January 2018, Pages 452–455,
https://doi.org/10.1093/cid/cix743
Published: 21 August 2017 **Article history** ▾

Abstract

Although there are several US Food and Drug Administration (FDA)-approved/cleared molecular microbiology diagnostics for direct analysis of patient samples, all are single target or panel-based tests. There is no FDA-approved/cleared diagnostic for broad microbial detection. Polymerase chain reaction (PCR)/electrospray ionization-mass spectrometry (PCR/ESI-MS), commercialized as the IRIDICA system (Abbott) and formerly PLEX-ID, had been under development for over a decade and had become CE-marked and commercially available in Europe in 2014. Capable of detecting a large number of microorganisms, it was under review at the FDA when, in April 2017, Abbott discontinued it. This turn of events represents not only the loss of a potential diagnostic tool for infectious diseases but may be a harbinger of similar situations with other emerging and expensive microbial diagnostics, especially genomic tests.

Çözüm:

Hastanede Moleküler/Hızlı Testlerle Tanısal Yönetim



Kan Kültürü

Genel Olarak;

Organizma tanımlama sürelerinde azalma,
Sonuç olarak uygun antimikrobiyal tedaviye geçiş süresinde kısalma

Maliyetler de ciddi azalmalar

Mortalite oranlarında ve hastanede yatış süresinde çelişkili sonuçlar;

Hasta popülasyonu;
Lokal direnç oranları

TABLE 1 FDA-approved/cleared panel-based molecular assays for detection of select microorganisms and select resistance genes in positive blood culture bottles

Parameter	FilmArray BCID	Verigene Gram-positive blood culture	Verigene Gram-negative blood culture
Total no. of targets	27	15	14
Ability to detect pathogen			
Gram-positive bacteria			
Staphylococcus species	✓	✓	
Staphylococcus aureus	✓	✓	
Staphylococcus epidermidis		✓	
Staphylococcus lugdunensis		✓	
Streptococcus species	✓	✓	
Streptococcus agalactiae	✓	✓	
Streptococcus pyogenes	✓	✓	
Streptococcus pneumoniae	✓	✓	
Streptococcus anginosus group		✓	
Enterococcus species	✓		
Enterococcus faecalis		✓	
Enterococcus faecium		✓	
Listeria species		✓	
Listeria monocytogenes	✓		
Gram-negative bacteria			
Klebsiella oxytoca	✓		✓
Klebsiella pneumoniae	✓		✓
Serratia marcescens	✓		
Proteus species	✓		✓
Acinetobacter species			✓
Acinetobacter baumannii	✓		
Haemophilus influenzae	✓		
Neisseria meningitis	✓		
Pseudomonas aeruginosa	✓		✓
Enterobacteriaceae	✓		
Escherichia coli	✓		✓
Enterobacter species			✓
Enterobacter cloacae complex	✓		
Citrobacter species			✓
Yeasts			
Candida albicans	✓		
Candida glabrata	✓		
Candida krusei	✓		
Candida parapsilosis	✓		
Candida tropicalis	✓		
Ability to detect presence of resistance gene			
mecA	✓	✓	
vanA	✓	✓	
vanB	✓	✓	
bla_{KPC}	✓		✓
bla_{NDM}			✓
bla_{OXA}			✓
bla_{VIM}			✓
bla_{IMP}			✓
$bla_{CTX\text{-}M}$			✓
Time to result (h)	~1	~2.5	~2

Clinical Infectious Diseases

MAJOR ARTICLE

IDSA Infectious Diseases Society of America | hivma hiv medicine association | OXFORD

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.

Tanısal Yönetim

Antimikrobiyal Yönetim

Olgu

- 75 yaşında Vietnamlı erkek hasta, 40 yıl önce Kaliforniya’ya göç etmiş.
- 10 ay önce foliküler lenfoma tanısı var, 6 kür kemoterapi sonucu tam remisyon.
- Acil servise 2 hafta önce başlayan hafif bilinç bulanıklığı ve konuşma güçlüğü nedeni ile baş vuruyor.

Olgu

- Acilde konfüze, dezoryante fokal nörolojik bulgu yok,
- Nonkontrast MR’da önemli bulgu yok
- Bos Bulguları; pleositoz, 210 hücre/µL, glukoz 67 mg/dL, protein 587 mg/dL.
- Gram, kalkoflor beyazı, EZN negatif, Kültürlerde üreme yok.
- Çoklu test sonucu **HSV-1 POZİTİF**
- IV Asiklovir tedavisi başlandı

Olgu

- 7 Gün sonra durumunda iyileşme yok,
- MR hidrosefali. ➔ Yoğun bakım
- BOS tekrarı, artmış basınc, 35 cm H_2O, pleositoz, 99 hücre/uL, glikoz 39 mg/dL

Open Forum Infect Dis. 2017 Winter; 4(1): ofw245. PMCID: PMC5437853
Published online 2016 Dec 7. doi: 10.1093/ofid/ofw245

Delayed Diagnosis of Tuberculous Meningitis Misdiagnosed as Herpes Simplex Virus-1 Encephalitis With the FilmArray Syndromic Polymerase Chain Reaction Panel

Carlos A. Gomez,[1,2] Benjamin A. Pinsky,[1,2] Anne Liu,[1,3] and Niaz Banaei[1,2,4]

- Agresif klinik yönetime karşın trekeostomi, gastirik tüp
- ➔At the time of writing this report, he continued on tuberculosis therapy with severe neurological deficit.

Table 1. Positive Predicted Value of the FilmArray ME Panel*

Analyte	Confirmed Positives/Total Positives (%)
Streptococcus pneumoniae	9 of 16 (56)
Haemophilus influenzae	2 of 2 (100)
Streptococcus agalactiae†	No positives
Escherichia coli K1	2 of 3 (66)
Listeria monocytogenes†	No positives
Neisseria meningitidis†	No positives
HSV-1	2 of 4 (50)
HSV-2	11 of 12 (92)
CMV	4 of 6 (66)
VZV	6 of 7 (86)
HPeV	12 of 12 (100)
HHV-6	19 of 22 (79)
EV	49 of 51 (96)
Cryptococcus spp	3 of 5 (60)

Önlemler !!!

- Preanalitik:
  - Klinisyeni elektronik istem formunu doldururken popülasyon hakkında, kullanılan test performansı, limitleri ve pozitif sonuç sonrası uygulanacak refleks testler hakkında bilgilendir.
  - LP sırasında koruyucu maske takılması gerektiği hakkında bilgilendir.
  - Test kriterilerini anormal BOS bulguları doğrultusunda olabildiğince yönlendir.
  - Cerrahi sonrası hastaları dışla

Önlemler !!!

- Analitik
  - Biyogüvenlik kabininde çalış
  - Çalışma yüzeylerini temizle
  - Her örnek çalışmasından önce eldiven değiştir.
  - Her seferde bir BOS çalış.

Önlemler !!!

- Postanalitik
  - Pozitif sonuçları, Gram boyama ve diğer BOS bulguları ile tekrar değerlendir.
  - Laboratuvarlar ek bulgular ile sonuçları daha ileri konfirmasyon/araştırmalar için saklamalı
  - Pozitif testleri refleks testler ile (kültür, hedefe yönelik viral testler gibi) konfirme et.
  - Sonucu isteyen doktor ile tartış
  - Klinisyeni sonucu görüntüleme sırasında popülasyon hakkında, kullanılan test performansı, limitleri ve pozitif sonuç sonrası uygulanacak refleks testler hakkında bilgilendir.

Eur J Clin Microbiol Infect Dis
DOI 10.1007/s10096-014-2252-2

ARTICLE

Performance evaluation of the Verigene® (Nanosphere) and FilmArray® (BioFire®) molecular assays for identification of causative organisms in bacterial bloodstream infections

C. Ward · K. Stocker · J. Begum · P. Wade ·
U. Ebrahimsa · S. D. Goldenberg

Table 5 Details of all discrepant samples

Conventional methods identification	Verigene® identification	FIlmArray® identification	Number of occurrences
Staphylococcus epidermidis	*Staphylococcus epidermidis*	*Staphylococcus epidermidis* and *Pseudomonas aeruginosa* ✸	9
E. coli	*E. coli*	*E. coli* and *Pseudomonas aeruginosa* ✸	4
Staphylococcus hominis	*Staphylococcus* spp.	*Staphylococcus* spp. and *Pseudomonas aeruginosa* ✸	2
Klebsiella pneumoniae	*Klebsiella pneumoniae*	*Klebsiella pneumoniae* and *Pseudomonas aeruginosa* ✸	
Klebsiella oxytoca	*Klebsiella oxytoca*	*Klebsiella oxytoca* and *Pseudomonas aeruginosa* ✸	
Streptococcus bovis	*Streptococcus* spp.	*Streptococcus* spp. and *Pseudomonas aeruginosa* ✸	
Citrobacter braakii and *Klebsiella oxytoca*	*Citrobacter* spp. and *Klebsiella oxytoca*	*Enterobacter* spp. and *Pseudomonas aeruginosa* ✸	
Group C/G *Streptococcus*	*Streptococcus* spp.	*Streptococcus* spp. and *Pseudomonas aeruginosa* ✸	
Enterobacter cloacae	*Enterobacter* spp.	*Enterobacter cloacae* and *Pseudomonas aeruginosa* ✸	
Enterococcus faecium	*Enterococcus faecium*	*Enterococcus* spp. and *Pseudomonas aeruginosa* ✸	
Propionibacterium acnes	ND	*Pseudomonas aeruginosa* ✸	
Micrococcus luteus	*Micrococcus* spp.	ND	6
Corynebacterium spp.	ND	ND	4
Propionibacterium acnes	ND	ND	3
Haemophilus parainfluenzae	ND	ND	2
Brevibacterium casei	ND	ND	
Unidentified Gram-positive rod	ND	ND	
Aeromonas hydrophila	ND	ND	
Bacteroids fragilis	ND	ND	
Paenibacillus macerans	ND	ND	
Acinetobacter lwofii	ND	ND	
Prevotella denticola	ND	ND	
Morganella morganii	ND	ND	
Acinetobacter ursingii	*Acinetobacter* spp.	ND	
Staphylococcus hominis	*Staphylococcus* spp.	*Staphylococcus* spp. and *Klebsiella pneumoniae*	
Staphylococcus aureus and Group C/G *Streptococcus*	*Staphylococcus aureus*	*Staphylococcus aureus* and *Streptococcus* spp.	
Streptococcus viridans	*Streptococcus pneumoniae*	*Streptococcus* spp.	
Fusobacterium necrophorum	ND	*Pseudomonas aeruginosa* ✸	
Streptococcus viridans	*Streptococcus pneumoniae*	*Streptococcus* spp.	
Enterococcus avium	*Enterococcus faecium*	*Enterococcus* spp.	
Enterococcus faecalis	*Enterococcus faecalis* and *Staphylococcus* spp.	*Staphylococcus* spp. and *Enterococcus* spp.	
Enterococcus faecalis and *Citrobacter freundii*	*Citrobacter* spp.	*Enterococcus* spp. and *Enterobacter* spp.	

Aerop kan kültür şişelerinde Pseudomonas aeruginosa DNA Kontaminasyonu

Best Practices in Diagnosing Respiratory Viral Disease

Abraham J. Qavi, M.D., Ph.D.[1] and Neil W. Anderson, M.D.,[1] Assistant Professor of Pathology and Immunology, [1]Washington University School of Medicine, St. Louis, Missouri

Table 1. Broadly multiplexed respiratory virus tests available for syndromic testing

Name	Manufacturer	Technology	No. of targets	Workflow	Turnaround time (h)	Reference(s)
FilmArray Respiratory Virus Panel	Biofire Diagnostics, Salt Lake City, UT	Real-time PCR	20	Single assay per instrument or random access (FilmArray Torch), sample to answer	1	6-10
FilmArray Respiratory Panel EZ	Biofire Diagnostics, Salt Lake City, UT	Real-time PCR	14	Single assay per instrument, sample to answer	1	
Luminex xTAG RVP	Luminex Molecular Diagnostics, Austin, TX	PCR followed by bead-based/flow cytometry detection	12	Batched; separate amplification and detection instruments	7	6
Luminex xTAG RVP FAST	Luminex Molecular Diagnostics, Austin, TX	PCR followed by bead-based/flow cytometry detection	9	Batched; separate amplification and detection instruments	5-6	6, 8
Luminex NxTAG	Luminex Molecular Diagnostics, Austin, TX	PCR followed by bead-based/flow cytometry detection	20	Batched; separate amplification and detection instruments	4	9, 10
Verigene Respiratory Pathogens Flex Test	Luminex Molecular Diagnostics, Austin, TX	PCR followed by microarray hybridization	16	Single assay per instrument, sample to answer; ability to selectively test targets	2	
Genmark XT-8	GenMark Dx, Carlsbad, CA	PCR followed by electrochemical detection	14	Batched; separate amplification and detection instruments	6	6, 7
Genmark ePlex	GenMark Dx, Carlsbad, CA	PCR followed by electrochemical detection	21	Random access, sample to answer	1.5	

Best Practices in Diagnosing Respiratory Viral Disease

Abraham J. Qavi, M.D., Ph.D.[1] and Neil W. Anderson, M.D.,[1] Assistant Professor of Pathology and Immunology, [1]Washington University School of Medicine, St. Louis, Missouri

Table 2. Characteristics of most commonly used respiratory virus tests

	Characteristic[a]				
Test	**Turnaround time**	**Targets covered**	**Affordable**	**Sensitivity**	**Specificity**
Antigen testing	++++	+	++++	+	+++
Narrow-spectrum PCR (1-4 targets)	++	++	++	++++	++++
Highly multiplexed PCR (>5 targets)	++	++++	+	+++	++++
POC molecular testing	+++	+	++	++++	++++

[a]++++, favorable; +, less favorable.

Doğru tanı için:

Epidemiyolojik verileri ve kullandığın sistemi beraber değerlendir

https://www.cdc.gov/flu/professionals/diagnosis/rapidlab.htm

Resources

Work +

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Clinical Considerations of Testing When Influenza Prevalence is Low

When influenza prevalence is relatively low, the positive predictive value (PPV) is low and false-positive test results are more likely. By contrast, when influenza prevalence is low, the negative predictive value (NPV) is high, and negative results are more likely to be true.

If Influenza Prevalence is...	And Specificity is...	Then PPV is...	False Pos. rate[1] is...
VERY LOW (2.5%)	MODERATE (80%)	VERY LOW (6-12%)	VERY HIGH (88-94%)
VERY LOW (2.5%)	HIGH (98%)	LOW (39-56%)	HIGH (44-61%)
MODERATE (20%)	MODERATE (80%)	LOW (38-56%)	HIGH (44-62%)
MODERATE (20%)	HIGH (98%)	HIGH (86-93%)	LOW (7-14%)

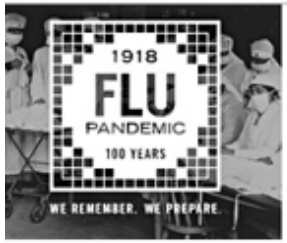
The false positive rate is the number of false positives divided by the number of total positives, or 1-PPV.

The interpretation of positive results should take into account the clinical characteristics of the patient and the prevalence of influenza in the patient population being tested (e.g., level of influenza activity in the community). If an important clinical decision is affected by the test result, the RIDT result should be confirmed by a molecular assay, such as reverse transcription polymerase chain reaction (RT-PCR).

Doğru tanı için:

Epidemiyolojik verileri ve kullandığın sistemi beraber değerlendir

https://www.cdc.gov/flu/professionals/diagnosis/rapidlab.htm



fluenza Types

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Clinical Considerations of Testing When Influenza Prevalence Is High

When influenza prevalence is relatively high, the NPV is low and false-negative test results are more likely. When influenza prevalence is high, the PPV is high and positive results are more likely to be true.

If Influenza Prevalence is...	And Sensitivity is...	Then NPV is...	False Neg. rate[2] is...
MODERATE (20%)	LOW (50%)	MODERATE (86-89%)	MODERATE (11-14%)
MODERATE (20%)	HIGH (90%)	HIGH(97-99%)	LOW (2-3%)
HIGH (40%)	LOW (50%)	MODERATE (70-75%)	MODERATE (25-30%)
HIGH (40%)	HIGH (90%)	HIGH (93-94%)	LOW (6-7%)

The false negative rate is the number of false negatives/number of total positives, or 1-NPV.

The interpretation of negative results should take into account the clinical characteristics of the patient and the prevalence of influenza in the patient population being tested (e.g., level of influenza activity in the community). If an important clinical decision is affected by the test result and influenza is still suspected, then the RIDT result should be confirmed by a molecular assay, such as RT-PCR.

Best Practices in Diagnosing Respiratory Viral Disease

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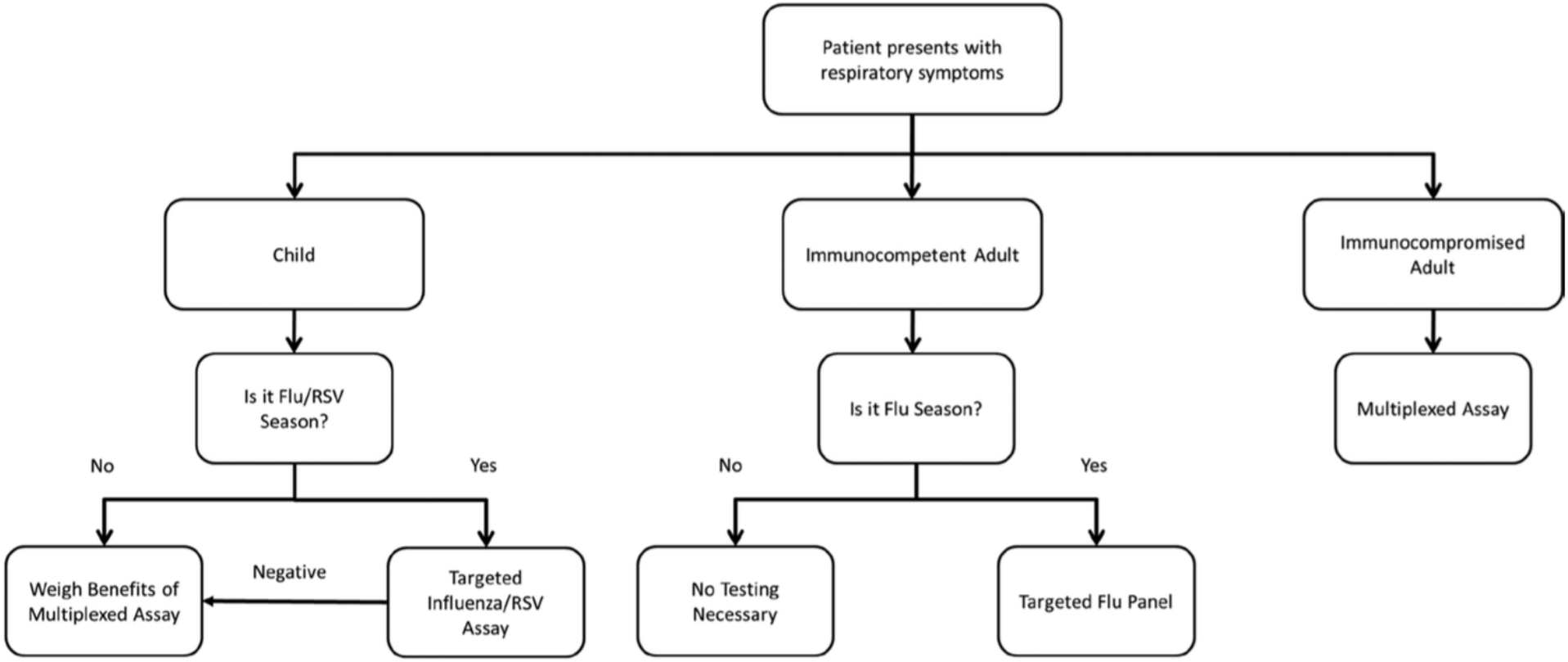
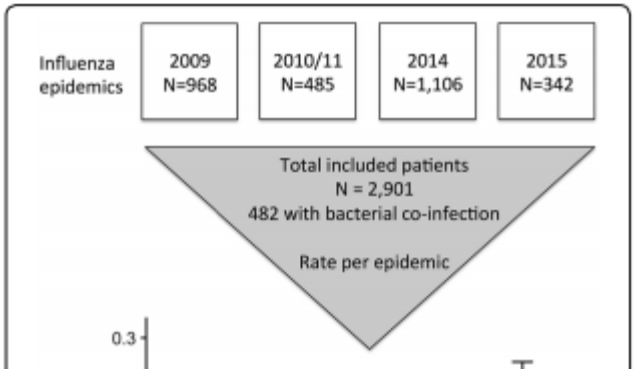


ORIGINAL

Increased incidence of co-infection in critically ill patients with influenza

Ignacio Martin-Loeches[1,2*], Marcus J Schultz[3], Jean-Louis Vincent[4], Francisco Alvarez-Lerma[5], Lieuwe D. Bos[3], Jordi Solé-Violán[6], Antoni Torres[7] and Alejandro Rodriguez[8,9]



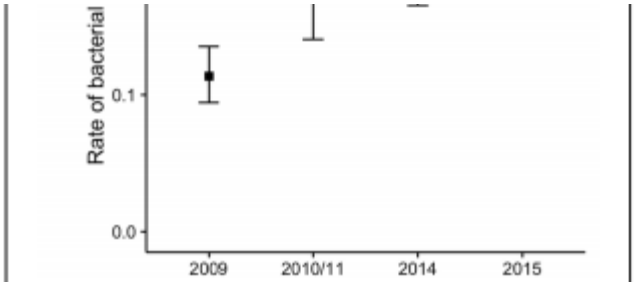


Fig. 1 Inclusion diagram and rate of bacterial co-infection per epidemic period. Patients from four influenza epidemics were included. The total number of patients with a positive PCR for influenza was 2901. Of these, 482 had a bacterial co-infection. The *lower panel* gives the rate of co-infection in each period. The *error bars* indicate the 95 % confidence interval

Table 2 Numbers and proportions of the pathogens isolated in critically ill patients with bacterial co-infection (N = 482)

Pathogen	N	%+	Definitive	Probable	Possible
S. pneumoniae	246	51.04	17	229	0
P. aeruginosa	55	11.4	2	53	0
MSSA	42	8.7	2	40	0
Aspergillus spp.	35	7.2	2*	25**	8
H. influenza	17	3.5	0	17	0
A. baumannii	14	2.9	0	14	0
MRSA	12	2.4	3	9	0
K. pneumoniae	12	2.4	1	11	0
E. cloacae	4	0.8	2	2	0
P. jirovecii	4	0.8	0	4	0
M. pneumoniae	4	0.8	1	3	0
C. pneumoniae	3	0.6	1	2	0
M. tuberculosis	3	0.6	0	3	0
S. maltophila	2	0.4	0	2	0
K. oxytoca	2	0.4	0	2	0
M. morganii	1	0.2	0	1	0
Shewanella spp.	1	0.2	0	1	0
B. fragilis	1	0.2	0	1	0
Nocardia spp.	1	0.2	0	1	0

MRSA methicillin-resistant *Staphylococcus aureus*, *MSSA* methicillin-sensitive *Staphylococcus aureus*

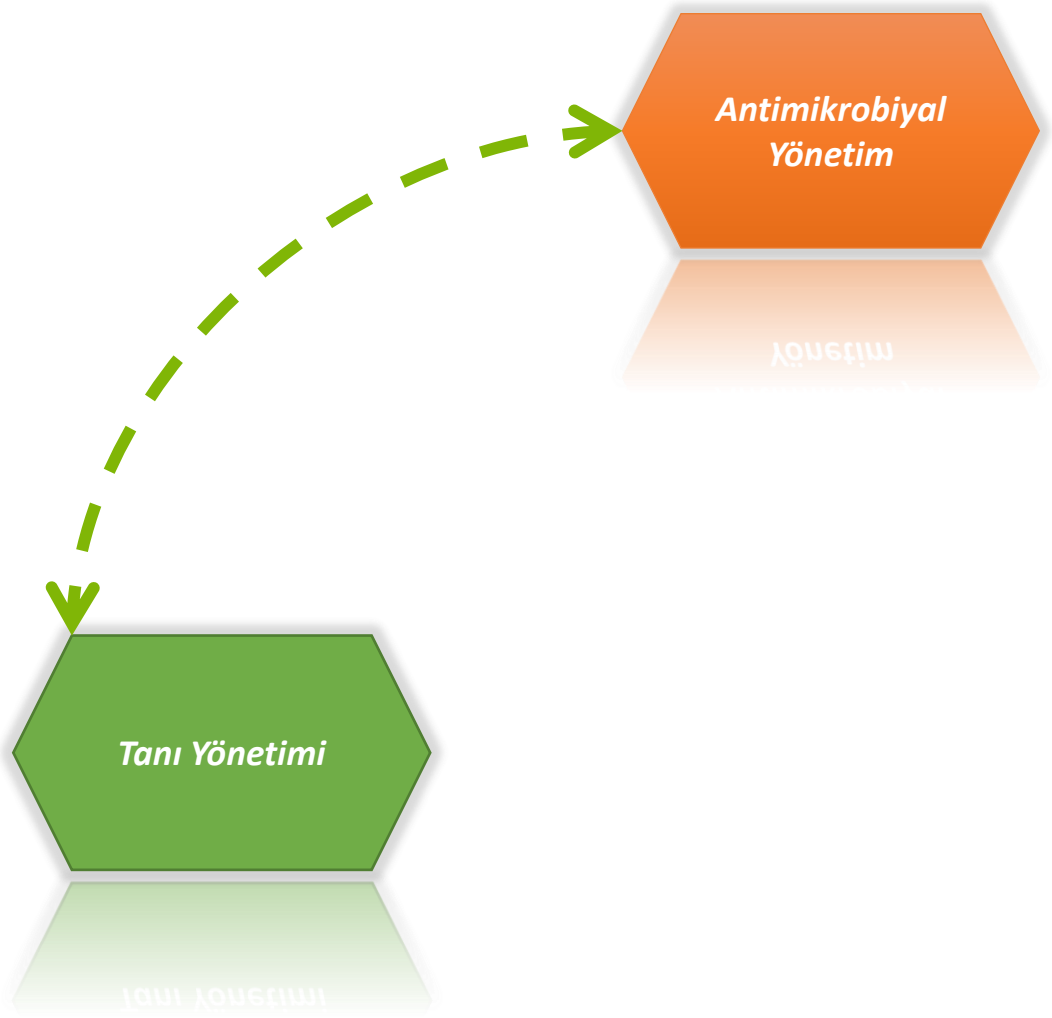
* Histopathological confirmation

** CT findings compatible with invasive aspergillosis

+ Percentage of all microorganisms

Conclusions: Co-infection in critically ill patients with influenza has increased in recent years. In this Spanish cohort age and immunosuppression were risk factors for co-infection, and co-infection was an independent risk factor for ICU, 28-day and hospital mortality.

Tanısal Yönetim



Hospital-Acquired Respiratory Viral Infections: Incidence, Morbidity, and Mortality in Pediatric and Adult Patients

Eric J. Chow[1,2,3] **and Leonard A. Mermel**[1,4]

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Background. Hospital-acquired respiratory viral infections can result in morbidity and mortality of hospitalized patients. This study was undertaken to better understand the magnitude of the problem of nosocomial respiratory viral infections in adult and pediatric patients.

Methods. This was a retrospective study at a tertiary care adult and pediatric teaching hospital. Study patients met a priori criteria for definite or possible nosocomial respiratory viral infection.

Results. From April 1, 2015 to April 1, 2016, we identified 40 nosocomial respiratory viral infections in 38 patients involving 14 definite and 3 possible cases in our adult hospital and 18 definite and 5 possible cases in our pediatric hospital. The incidence was 5 cases/10 000 admissions and 44 cases/10 000 admissions to our adult and pediatric hospitals, respectively. Only 6.8% of cases were due to influenza. Although 63% of cases occurred during the fall and winter, such infections were identified throughout the year. Five (13%) nosocomial respiratory viral infections occurred in 2 adult and 3 pediatric patients who died during the hospitalization.

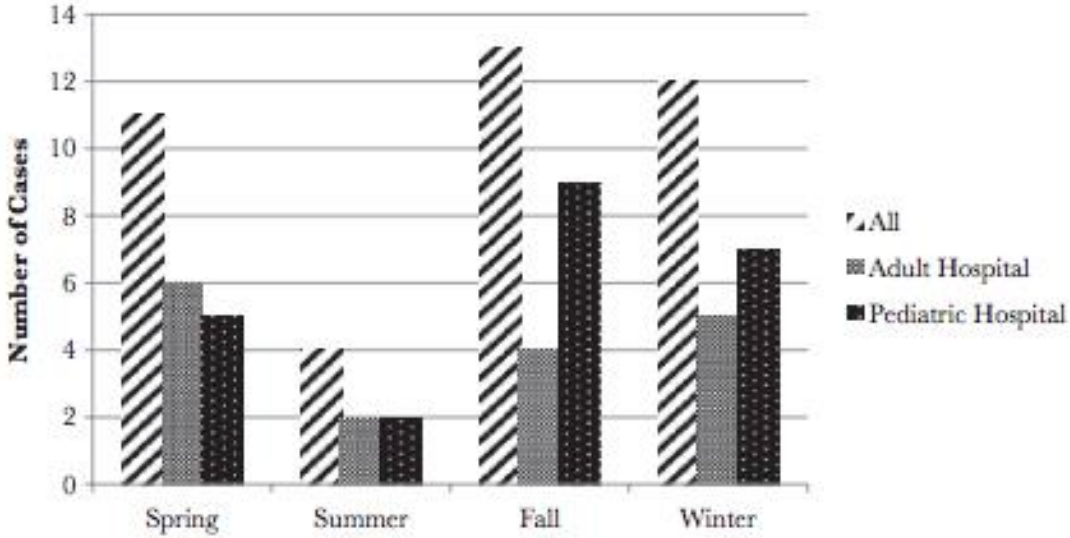
Conclusions. Nosocomial respiratory viral infections are an underappreciated cause of morbidity and mortality in hospitalized adult and pediatric patients. The incidence was nearly 10-fold higher in our pediatric hospital. We estimate there are approximately 18 955 pediatric and adult cases of nosocomial respiratory viral infections in US acute care hospitals each year.

Keywords. hospital-acquired; nosocomial; pneumonia; respiratory tract infection; viral.

Hospital-Acquired Respiratory Viral Infections: Incidence, Morbidity, and Mortality in Pediatric and Adult Patients

Eric J. Chow[1,2,3] and Leonard A. Mermel[1,4]

	All Viruses No. (%)	Adult Hospital No. (%)	Pediatric Hospital No. (%)	Seasons No.
	44	18	26	44
Adenovirus	3 (6.8)	2 (11)	1 (3.8)	Sp 1; Su 0; F 1; W 1
Coronavirus	2 (4.5)	0 (0)	2 (7.7)	Sp 0; Su 0; F 1; W 1
Influenza A	3 (6.8)	1 (5.6)	2 (7.7)	Sp 0; Su 0; F 0; W 3
Influenza B	0 (0)	0 (0)	0 (0)	N/A
Parainfluenza	1 (2.3)	0 (0)	1 (3.8)	Sp 1; Su 0; F 0; W 0
Respiratory syncytial virus A and B	6 (14)	2 (11)	4 (15)	Sp 3; Su 0; F 0; W 3
Rhino/enterovirus	25 (57)	11 (61)	14 (54)	Sp 6; Su 5; F 9; W 5
Metapneumovirus	4 (9)	2 (11)	2 (7.7)	Sp 2; Su 0; F 0; W 2



Clinical decision making in the emergency department setting using rapid PCR: Results of the CLADE study group

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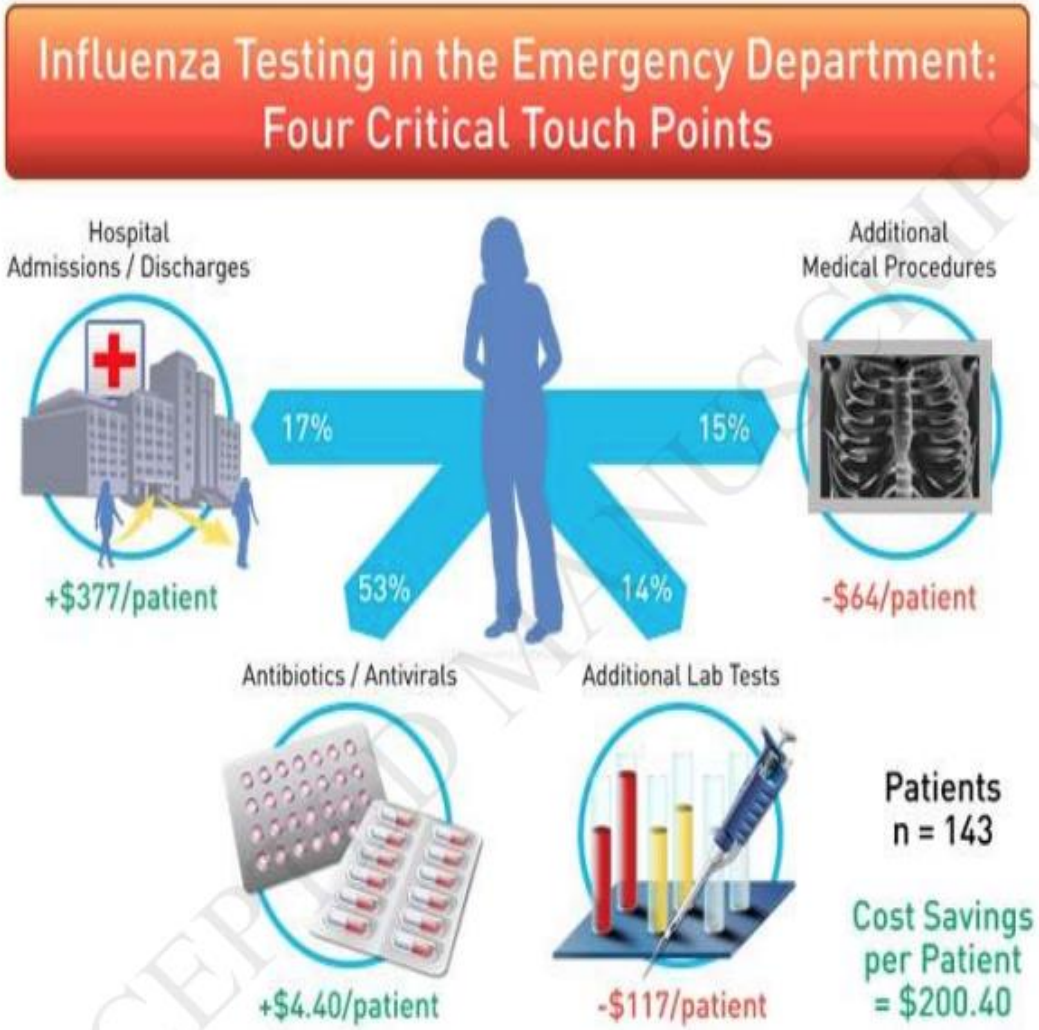
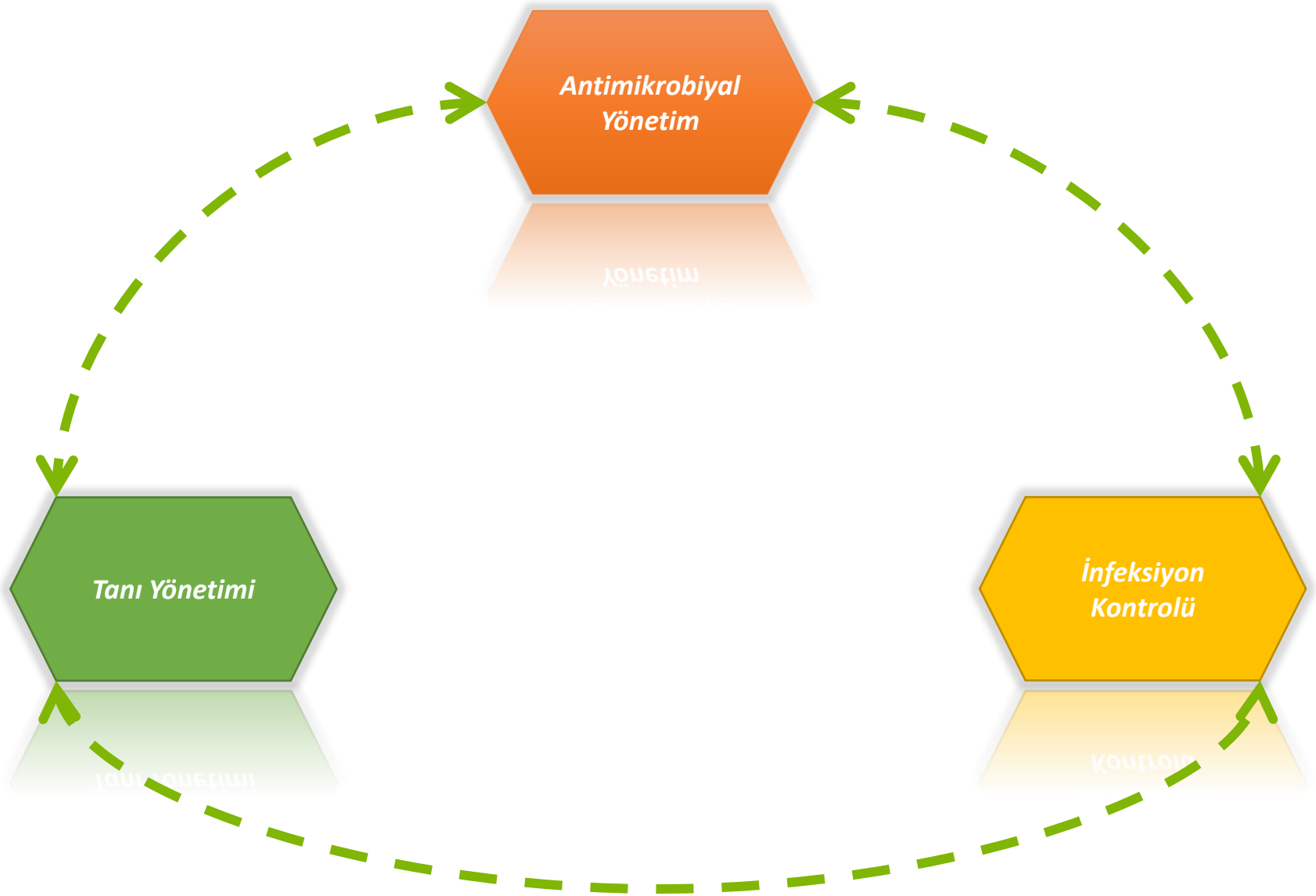
PlumX Metrics

DOI: https://doi.org/10.1016

Article Info



Tanısal Yönetim



Right-Sizing Technology in the Era of Consumer-Driven Health Care

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Table 1. Cost of mPOC implementation across 14 emergency departments

Expenditure	Cost[a]	No. needed	Estimated cost of implementation
Instrument	$15,000	14	$210,000
Tests	$35	6,000[b]	$210,000
Total			$420,000

[a]Hypothetical costs; not reflective of a specific platform.
[b]6,000 tests = 4.76 tests/day/ED over the 3-month flu season; does not include cost of controls, validation, or training materials.

Table 2. Cost of implementation and estimated cost avoidance to break even

Reagent costs	Instrument costs	Total cost of implementation	Estimated cost of avoidance of admission[a]	No. of admissions avoided required to break even
$210,000	$210,000	$420,000	$14,143	30 (2.12/ED)

[a]Average published cost per stay with a diagnosis of pneumonia. Healthcare Cost and Utilization Project (HCUP) Nationwide Emergency Department Sample (NEDS), HCUP, 2007, 2008, 2009. Agency for Healthcare Research and Quality, Rockville, MD (www.hcup-us.ahrq.gov/nedsoverview.jsp). The actual budget impact, depending on the payment schedule, is a saving of $6,715 due to $7,428 reimbursement if admitted, based on a blended rate of top diagnosis related group (DRG) associated with an influenza diagnosis.

Table 3. Estimated ROI based on hospital cost avoidance

Estimated no. of admissions avoided required to break even (0.5% over 3-month flu season)	Total estimated hospital cost avoidance	ROI[a]
30	$424,290	<3 months

[a]ROI, return on investment.

Maliyet Etkinlik

			SUT
4008	900.200	Alanin aminotransferaz (ALT)	1,09 ₺
4009	900.210	Albümin	0,99 ₺
4021	900.340	Alkalen fosfataz	1,09 ₺
4025	900.370	Amilaz	1,39 ₺
4047	900.580	Aspartat transaminaz (AST)	0,99 ₺
4059	900.690	Bilirubin Direkt	0,99 ₺
4059	900.690	Bilirubin Total	0,99 ₺
4081	900.901	CRP, nefelometrik	4,48 ₺
4089	901.020	Demir (Serum)	1,09 ₺
4091	901.040	Demir bağlama kapasitesi	1,09 ₺
4114	901.220	Ferritin	4,97 ₺
4119	901.260	Fosfor (P)	0,99 ₺
4141	901.500	Glukoz	0,99 ₺
4164	901.730	İdrar mikroskobisi	1,79 ₺
4168	901.780	TİT	4,97 ₺
4182	901.910	Kalsiyum (Ca)	1,09 ₺
4199	902.090	Klor (Cl)	0,99 ₺
4208	902.180	Kreatin	1,09 ₺
4209	902.190	Kreatin kinaz (CK)	1,39 ₺
4212	902.220	Kreatinin klerens testi	3,38 ₺
4217	902.260	Laktik Dehidrogenaz (LDH)	0,99 ₺
4296	903.130	Potasyum	1,09 ₺
4300	903.170	Procalcitonin	25,37 ₺
4323	903.400	Sedimentasyon	1,69 ₺
4330	903.470	Serbest T3	4,48 ₺
4331	903.480	Serbest T4	4,48 ₺
4153	901.620	Tam Kan (Hemogram)	2,98 ₺
		Toplam	77,01

4871	**908.732**	**ReverseTranscriptase PCR Multiplex**	**218,89**

Tanısal Yönetim

Impact of a Healthcare Provider Educational Intervention on Frequency of *Clostridium difficile* Polymerase Chain Reaction Testing in Children: A Segmented Regression Analysis

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Results. Hospital-wide, absolute TR reduction was 0.71 (P[level] = .0067; P[trend] = .0042) and absolute PR reduction was 0.14 (P[level] = .22; P[trend] = .018). In the outpatient setting, absolute TR reduction was 0.30 (P[level] = .0015; P[trend] < .001) and absolute PR reduction was 0.09 (P[level] = .0069; P[trend] = .046). The incidence density of healthcare facility-associated CDI did not significantly change after the EI. The EI was associated with avoidance of 574 tests and 113 positive tests (and subsequent antibiotic courses) during the postintervention period, which saved approximately $250 000 in patient charges related to CDI testing and treatment.

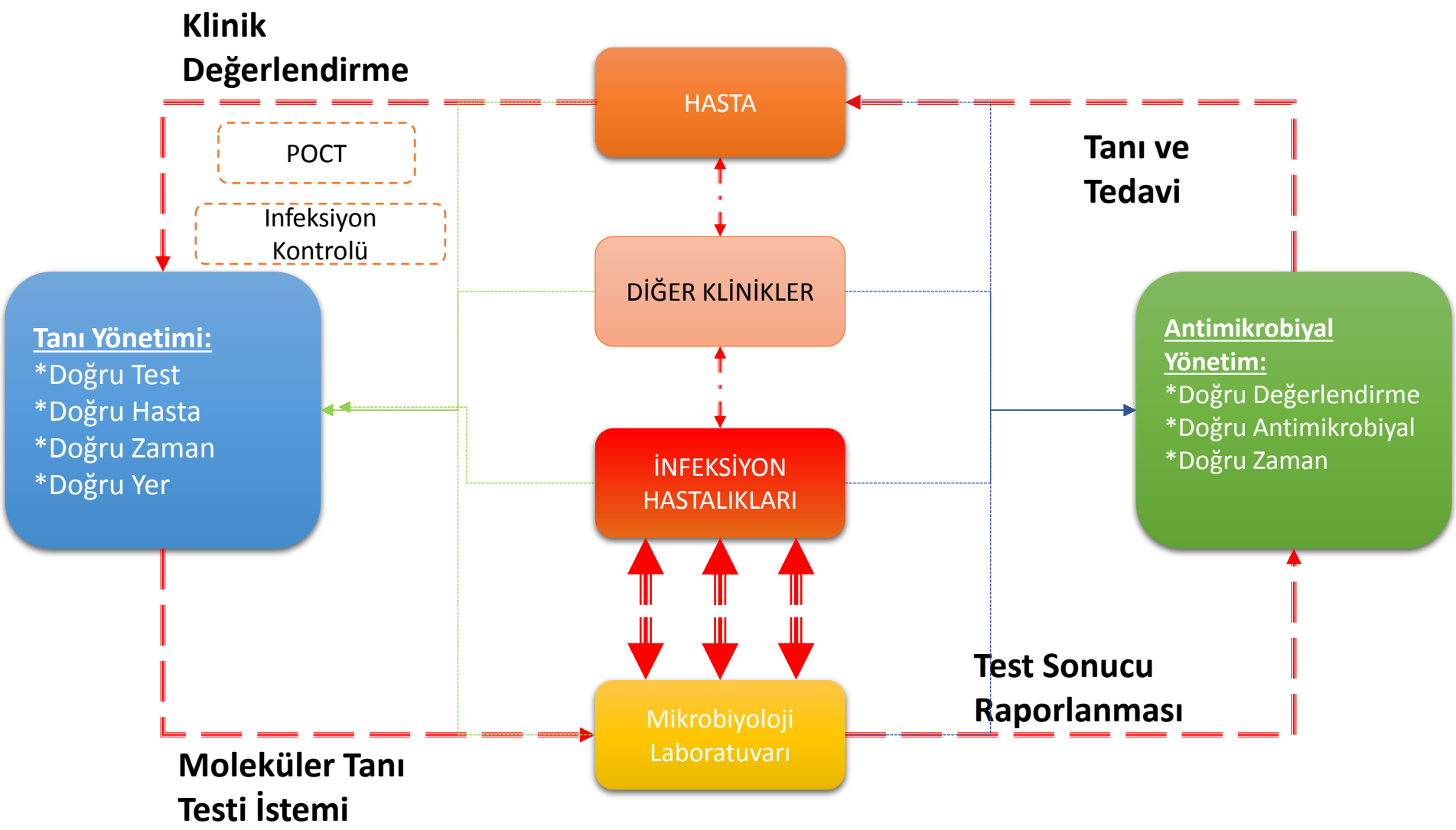
Table 1. Topics Included in the Healthcare Provider Didactic Education

Topics Included in 15-Minute Clinician Didactic Education
- Epidemiology of *Clostridium difficile* infection (CDI) and asymptomatic carriage
- *C difficile* polymerase chain reaction test interpretation
- American Academy of Pediatrics recommendations for CDI testing [19]
- Hospital CDI surveillance and *C difficile* testing data
- Impact of CDI misdiagnosis on patient care and hospital CDI surveillance
- Suggestions for improving CDI testing behaviors
- Questions and answers

Additional Topics Included in 30-Minute Microbiology Technologist Didactic Education
- Review of criteria for rejecting specimens for CDI testing
- Guidance for responding to healthcare provider inquiries after specimen rejection

Table 2. Electronic Medical Record Prompt When Ordering *Clostridium difficile* Polymerase Chain Reaction (PCR) Testing

Because *C difficile* PCR is highly sensitive and frequently identifies colonized patients, testing should NOT be ordered for patients with low probability of infection, such as the following:
- A patient without risk factors who has vomiting as a significant complaint.
- The stool is soft or formed.
- A patient has diarrhea and is prescribed stool softeners or laxatives.
- The test is ordered as a "test of cure" after treatment.
- A negative *C difficile* PCR result was reported within the last 7 days.


Klinik Değerlendirme
HASTA
POCT
Infeksiyon Kontrolü
Tanı ve Tedavi
DİĞER KLİNİKLER
Tanı Yönetimi:
*Doğru Test
*Doğru Hasta
*Doğru Zaman
*Doğru Yer
Antimikrobiyal Yönetim:
*Doğru Değerlendirme
*Doğru Antimikrobiyal
*Doğru Zaman
İNFEKSİYON HASTALIKLARI
Test Sonucu Raporlanması
Mikrobiyoloji Laboratuvarı
Moleküler Tanı Testi İstemi