

Sendromik Testler Nasıl Yorumlanmalı?

--Solunum Paneli--

Dr.Mahir Kapmaz
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İnfeksiyon Hastalıkları ve Klinik Mikrobiyoloji

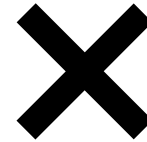
16.3.2019, KLİMİK 2019

Solunum yolu infeksiyonları için teste gerek var mı?

120 yıldır Gram boyama ve kültür

Ampirik tedaviler zaten çok geniş

Mikrobiyolojik bir etken saptama
İlgisi düşük



‘antimikrobiyal
yönetim’

Hastane infeksiyonları monomikrobiktir!

Yanılsama ?!

An Unmet Medical Need: Rapid Molecular Diagnostics Tests for Respiratory Tract Infections

Infectious Diseases Society of America^a

An Unmet Medical Need • CID 2011:52 (Suppl 4) • S385

IDSA:

Geleneksel mikrobiyoloji yavaş ve 'antika' kalmaktadır !

Bütün pnömoni
tipleri ve KOAH



Hızlı moleküler
tanı testleri
bir ihtiyaç!

++ FDA onaylı bile olsa hiçbir test, klinisyenin yerine geçmez: pnömoni tanısını ve etkenin klinik önemini klinisyen söyler

LOWERING DEMAND FOR ANTIMICROBIALS AND REDUCING UNNECESSARY USE



Public
awareness



Sanitation
and hygiene



Antibiotics in
agriculture and
the environment



Vaccines and
alternatives



Rapid
diagnostics



Human
capital

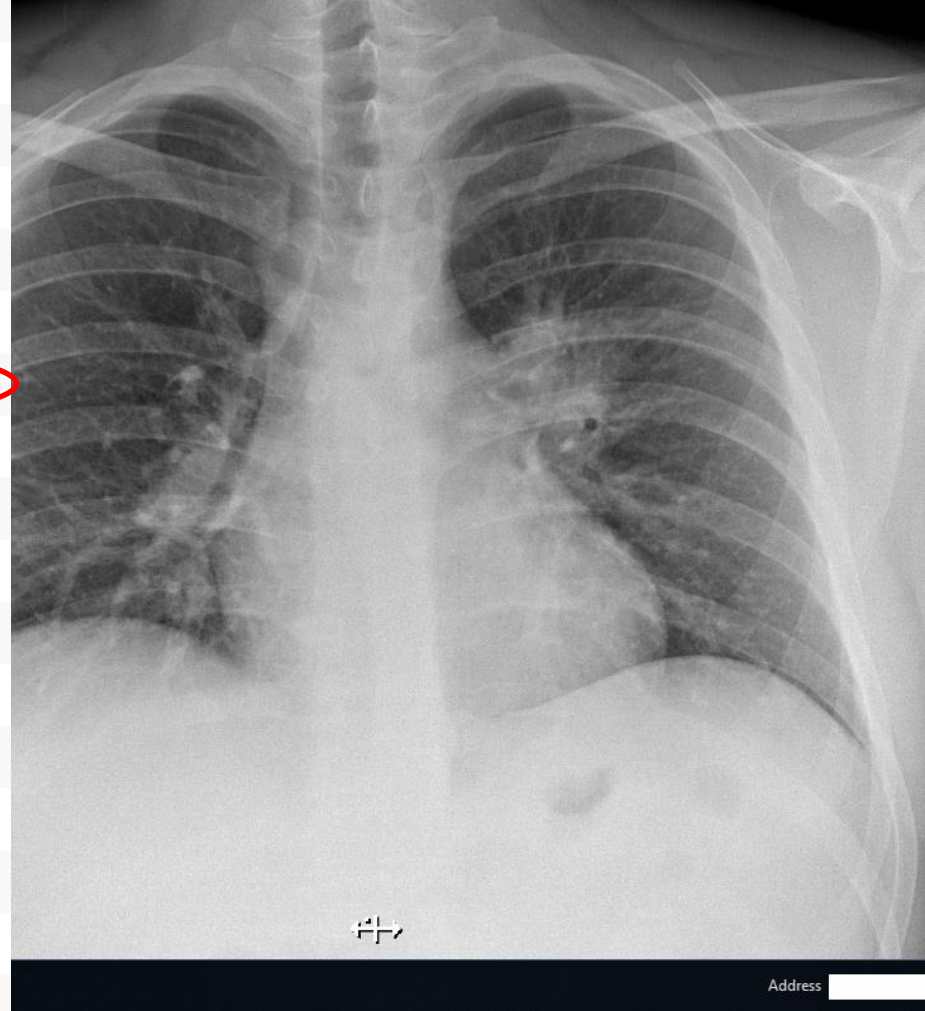
Bir öneri:

2020 yılında gelişmiş ülkelerde antibiyotik reçetesi
–mümkünse- sadece hızlı testler pozitif ise yazılsın !!

29 erkek, ateş, öksürük ile Klaritromisin almış, ishal

WBC:11500, Lenfosit: 800,
AST: 195, ALT: 199, Prokalsitonin: 0.23

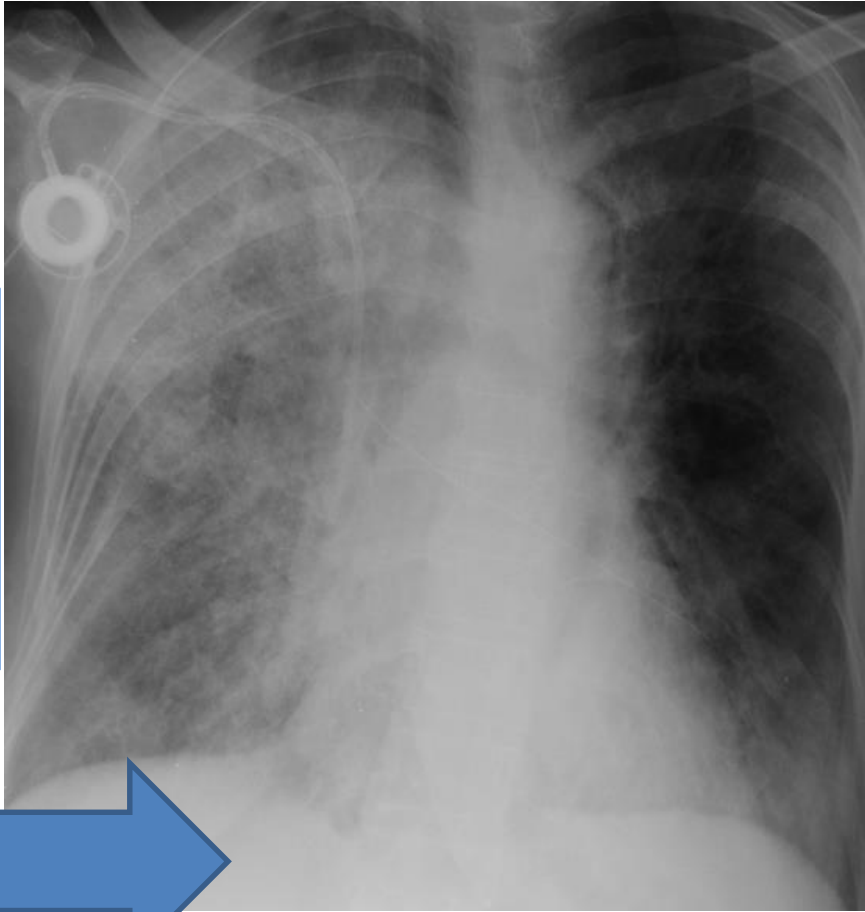
Solunum Yolları Virüsleri (Multiplex RT-PCR)	^	(N/A)
Adenovirus	Negatif	(N/A)
Coronavirus 229E	Negatif	(N/A)
Coronavirus HKU1	Negatif	(N/A)
Coronavirus NL63	Negatif	(N/A)
Coronavirus OC43	Negatif	(N/A)
Human Metapneumovirus	Negatif	(N/A)
Human Rhinovirus/Enterovirus	POZİTİF	(N/A)
Parainfluenza Virus 1	Negatif	(N/A)
Parainfluenza Virus 2	Negatif	(N/A)
Parainfluenza Virus 3	Negatif	(N/A)
Parainfluenza Virus 4	Negatif	(N/A)
Respiratory Syncytial Virus	Negatif	(N/A)
Bordetella pertussis	Negatif	(N/A)
Mycoplasma pneumoniae	Negatif	(N/A)
Chlamydia pneumoniae	Negatif	(N/A)
Influenza A	Negatif	(N/A)
Influenza B	Negatif	(N/A)



58, solid organ tm,
İnfluenza A pozitif



Piperasilin-tazobaktam
Klaritromisin
Ko-trimoksazol iv



Multiplex Respiratory Virus Testing for Antimicrobial Stewardship: A Prospective Assessment of Antimicrobial Use and Clinical Outcomes Among Hospitalized Adults

Makeda Semret,¹ Ian Schiller,² Barbara Ann Jardin,² Charles Frenette,¹ Vivian G. Loo,¹ Jesse Papenburg,¹ Shelly A. McNeil,⁴ and Nandini Dendukuri³

The Journal of Infectious Diseases®

2017;216:936–44

- 800 hasta SYE, 12 virus paneli, Kanada

Bireylerin %53'ünde influenza,
%10'unda diğer virüsler



İnfluenza için LOS kısa;
Diğer virüsler için fark yok

***Sonuç: Klinisyenler influenza sonucuna itibar ediyor;
ancak diğer virüslere kayıtsız!***

VICTORIA M. MADIGAN¹, VINCENT G. SINICKAS¹, DAWN GILTRAP¹,

Table 2 Health service outcomes for patients in the pre-implementation vs post-implementation period

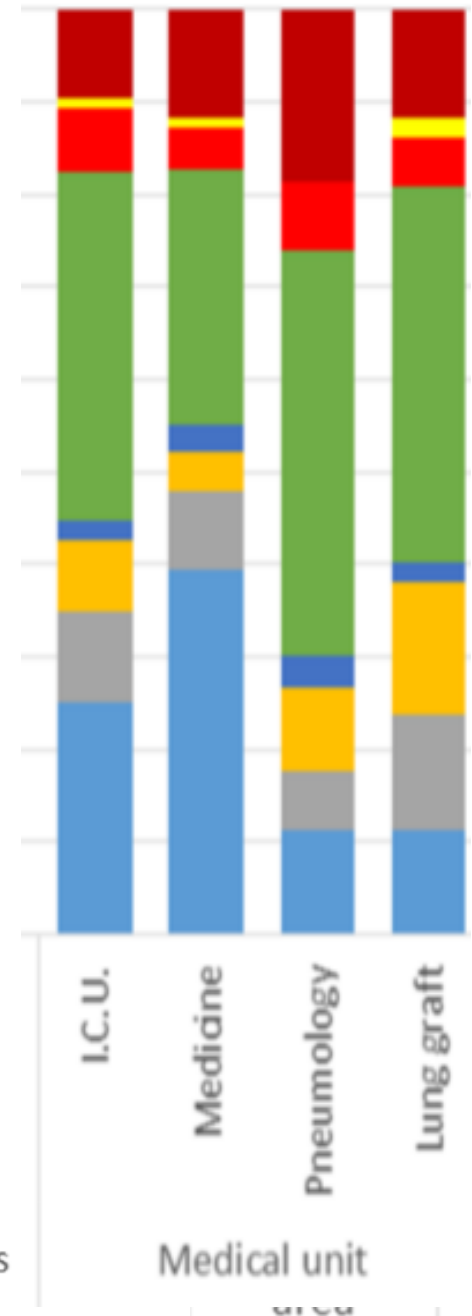
Characteristic	Pre-implementation <i>n</i> = 200	Post-implementation <i>n</i> = 124	<i>p</i> value
No. with positive result (%)	79 (39.5)	71 (57.3)	0.002
No. result released before discharge (%)	141 (70.5)	109 (87.9)	<0.001
Time to when result observed by clinician, hours, median (range)	27.0 (3.9–261.2)	9.4 (2.2–34.6)	<0.0001
Hospital LOS, hours, median (range)	52.8 (0.8–1361.7)	48.1 (2–855.9)	0.50
Isolation bed LOS, hours, median (range)	62.2 (1.1–455.5)	44.7 (0.32–267.2)	0.26

Sonuçta, TAT ve duyarlılık artmasına rağmen, LOS süresi iyileşmemiş !
Yetişkinler (Onko-hemato hastaları hariç)

Prevalence of respiratory viruses among adults, by season, age, respiratory tract region and type of medical unit in Paris, France, from 2011 to 2016

Benoit Visseaux^{1*}, Charles Burdet², Guillaume Voiriot³, François-Xavier Lescure²,

5 yıllık periyot
7196 örnek (4958 hasta)
29.2% pozitif
Viral ko-infeksiyon %1.6
Bakteriyel kültür yok.



Picornavirüsler (Rino- veya Enterovirus, 34.3%) ve İnfluenza (26.6%) = yaklaşık %60

Influenza RSV Parainfluenza Adenovirus
Picornaviridae Metapneumovirus Bocavirus Coronavirus

ORIGINAL ARTICLE

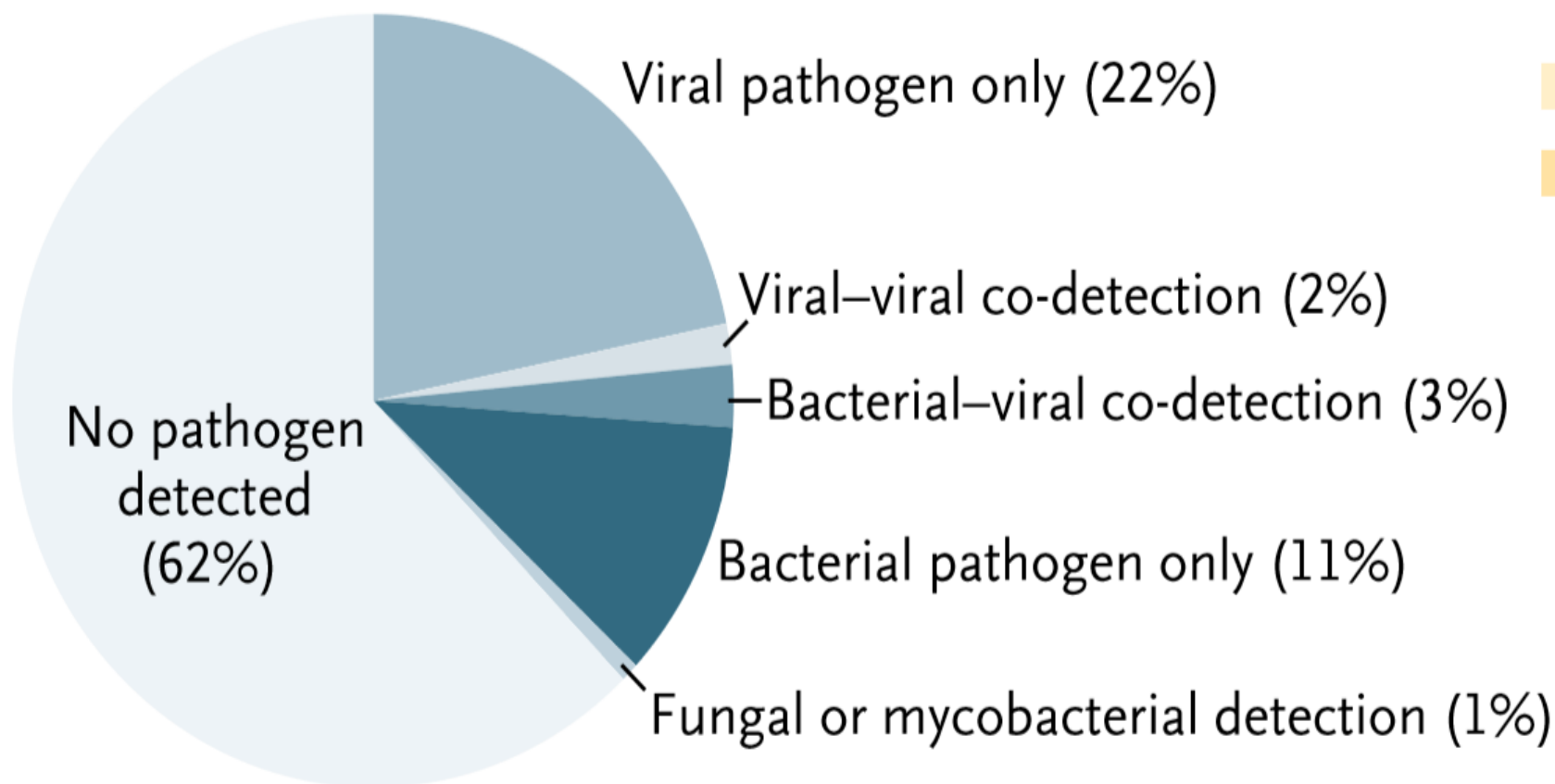
Community-Acquired Pneumonia Requiring Hospitalization among U.S. Adults

S. Jain, W.H. Self, R.G. Wunderink, S. Fakhran, R. Balk, A.M. Bramley, C. Reed,

2011- 2012

Hastalardan NF ve varsa balgam ve ETA ve BAL

Kontrol: NF ve OF örnekler alınmış



İlk FDA onaylı test

- xTAG RVP (Luminex Molecular Diagnostics)
2008'de ilk FDA onayı

2009 İnfluenza A H1N1 salgınında

%97.6 duyarlılık vs.
%88.9 --- R-Mix kültür vs.
%46.7 --- DFA
%17.8% --- RADT

RADT neden düşük?

Yaşlılarda mukozal
antikorlar, viral yük
düşüklüğüne yol açabilir?

Talbot et al. CID 2011

2014----- EV-D68 salgınında iyi performans!

Rapid molecular tests for influenza, respiratory syncytial virus, and other respiratory viruses: a systematic review of diagnostic accuracy and clinical impact studies

Vos LM et al. [Clin Infect Dis](#). 2019 Jan 28.

Laura M Vos¹, Andrea HL Bruning², Johannes B Reitsma³, Rob Schuurman⁴, Annelies

Antibiyotik
reçetelenmesi
azalmıyor

Outcome per study (author, year, country)	Study design	Sample size (n)	Effect - intervention vs control/ odds ratio (OR)	p-value	Conclusion
Antibiotic prescriptions					
Brendish, 2017 (UK)	RCT (1:1)	714	84% vs 83%	0.84	
Andrews, 2017 (UK)	RCT (quasi ^a)	522 ^l	75% vs 77%	0.99	
Chu, 2015 (USA)	Before-after, multivariate ^b	350	63% vs 76%	<.001	
Rogers, 2014 (USA)	Before-after, univariate	1136	72% vs 73%	0.61	
Rappo, 2016 (USA)	Before-after, univariate	337 ^c	66% vs 61%	0.35	
Linehan, 2017 (Ireland)	Before-after, univariate	67 ^e	33% vs 76%	<.001	
Busson, 2017 (Belgium)	Cohort, no control group	69	In 36.2% of patients antibiotic prescriptions were avoided	-	
Keske, 2017 (Turkey)	Cohort, no control group	359 ^c	45% of virus positive patients received antibiotics	-	

c. Subgroup analysis in virus positive patients. In the study of Gelfer (2015) among these virus positive patients only the patients who received antimicrobials were included. In the study of Keske (2017) these virus positive patients included only inpatients, and for the duration of antibiotic therapy only patients with inappropriate antibiotic use were included.

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Duration of antibiotic therapy

Branche, 2015 (USA)	RCT (1:1)	300	Median 3 days [IQR 1-7] vs 4 [0-8]	0.71
Brendish, 2017 (UK)	RCT (1:1)	714	Mean 7.2 days [SD 5.1] vs 7.7 [4.9]	0.32
Andrews, 2017 (UK)	RCT (quasi ^a)	522 ^l	Median 6 days [IQR 4-7] vs 6 [5-7.3]	0.23
Gilbert, 2016 (USA)	RCT (quasi ^d)	127	Mean 1053/1000 patient-days [SD 657] vs 472/1000 [1667]	0.07
Gelfer, 2015 (USA)	RCT (quasi ^d)	18 ^c	Mean 683/1000 patient-days [SD 317] vs 917/1000 [220]	0.052
Rogers, 2014 (USA)	Before-after, univariate	1136	Mean 2.8 days [SD 1.6] vs 3.2 [SD 1.6]	0.003
Rappo, 2016 (USA)	Before-after, univariate	212 ^e	Median 1 vs 2 days	0.24
Keske, 2017 (Turkey)	Cohort, no control group	160 ^c	Mean 6.5 days [SD 3.7] in virus positive patients	-

Antibiyotik süresi kısalıyor

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Study	group	positive patients	
Oseltamivir prescriptions			
Brendish, 2017 (UK)	RCT (1:1)	714	18% vs 14%
		94 ^e	91% vs 65%
Chu, 2015 (USA)	Before-after, univariate	350	55% vs 45%
		40 ^e	100% vs 100%
		136 ^f	45% vs 43%
Rappo, 2016 (USA)	Before-after, univariate	212 ^e	61% vs 61%
Linehan, 2017 (Ireland)	Before-after, univariate	68 ^e	95% vs 72%
Xu, 2013	Cohort, no control	97 ^e	81% of influenza positive patients

influenza
pozitif
hastalarda
uygun OSV
artıyor

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Length of hospital stay

Branche, 2015 (USA)	RCT (1:1)	300	Median 4 vs 4 days	NS
Brendish, 2017 (UK)	RCT (1:1)	714	Mean 5.7 days [SD 6.3] vs 6.8 [7.7] ^g	0.044
Andrews, 2017 (UK)	RCT (quasi ^a)	545	Median 4.1 days [IQR 2.0-9.1] vs 3.3 [1.7-7.9]	0.28
Rappo, 2016 (USA)	Before-after, multivariate ^h	212 ^e	Median 1.6 days [IQR 0.3-4.8] vs 2.1 [0.4-5.6]	0.040
Rogers, 2014 (USA)	Before-after, univariate	1136	Mean 3.2 days [SD 1.6] vs 3.4 [1.7]	0.16
Chu, 2015 (USA)	Before-after, univariate	350	Median 4 days [range 1-164] vs 5 [0-117]	0.33
Timbrook, 2015 (USA)	Cohort, no control group	601 ^c	Median 1 day [IQR 0-3] in virus positive patients	-

LOS
azalıyor

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Hospital admissions

Brendish, 2017 (UK)	RCT (1:1)	714	92% vs 92%	0.94
Rappo, 2016 (USA)	Before-after, univariate	337 ^c	76% vs 74%	0.60
Linehan, 2017 (Ireland)	Before-after, univariate	69 ^e	45% vs 88%	<.001
Busson, 2017 (Belgium)	Cohort, no control group	69	5.8% of hospitalizations was avoided	-

Hastaneye
yatış
azalmıyor

Safety

Branche, 2015 (USA)	RCT (1:1)	300	No difference in-hospital deaths, SAEs, new pneumonia cases or 90-day post-hospitalization visits	NS
Brendish, 2017 (UK)	RCT (1:1)	714	30-day readmission 13% vs 16%	0.28
			30-day mortality 3% vs 5%	0.15
			ICU admission 3% vs 2%	0.36
Andrews, 2017 (UK)	RCT (quasi ^a)	545	30-day readmission 19% vs 20%	0.70
			30-day mortality 4% vs 4%	0.79
Rogers, 2014 (USA)	Before-after, univariate	1136	Mortality 0% vs 0%	1.00
			ICU admission 0% vs 0%	1.00
Chu, 2015 (USA)	Before-after, univariate	350	Mortality 2% vs 4%	0.68
			ICU admission 31% vs 25%	0.19
Timbrook, 2015 (USA)	Cohort, no control group	601 ^c	ICU admission in 8.8% of virus positive patients	-

Hasta
güvenliği
etkilenmiyor

(1) Costs; (2a) no. of / (2b) any additional chest radiographs; (3a) use of / (3b) time in isolation

Gilbert, 2016 (USA)	RCT (quasi ^d)	127	(1) \$8308/1000 patient-days [SD 10165] vs \$11890/1000 [11712]	0.02
Rappo, 2016 (USA)	Before-after, multivariate ^h	188 ^e	(2a) Median 1 [IQR 1-1] vs 1 [1-2]	0.005
Busson, 2017 (Belgium)	Cohort, no control group	28 ^e	(2b) 25% reduction of X-rays in influenza positive patients	-
Brendish, 2017 (UK)	RCT (1:1)	385 ^m 50 ^e	(3a) 33% vs 25% 74% vs 57%	0.12 0.24
Rogers, 2014 (USA)	Before-after, univariate	1136	(3b) 2.9 days [SD 1.6] vs 3.0 [1.7]	0.27

Maliyet ve ek X-ray potansiyel azalıyor

Turnaround time

Brendish, 2017 (UK)	RCT (1:1)	714	Mean 2.3 hours [SD 1.4] vs 37.1 [21.5]	<.001
Andrews, 2017 (UK)	RCT (quasi ^a)	545	Median 19 hours [IQR 8.1-31.7] vs 39.5 [25.4-57.6] ^j	<.001
Gilbert, 2016 (USA)	RCT (quasi ^d)	127	Mean 2.1 hours [SD 0.7] vs 26.5 [15]	<.001
Gelfer, 2015 (USA)	RCT (quasi ^d)	59	Mean 1.8 hours [SD 0.3] vs 26.7 [16]	<.001
Chu, 2015 (USA)	Before-after, multivariate ^b	350	Median 1.7 hours [range 0.8-11.4] vs 25.2 [2.7-55.9]	<.001
Rogers, 2014 (USA)	Before-after, univariate	1136	Mean 6.4 hours [SD 4.9] vs 18.7 [8.2] ^k	<.001
Pettit, 2015 (USA)	Before-after, univariate	1102	Mean 3.1 hours vs 46.4	<.001
Rappo, 2016 (USA)	Before-after, univariate	212 ^e	Median 1.7 hours [IQR 1.6-2.2] vs 7.7 [0.8-14]	0.015
Muller, 2016 (Canada)	Before-after, univariate	125	Mean 3.6 hours vs 35.0	-
Xu, 2013 (USA)	Cohort, no control group	2537	Median 1.4 hours	-

Anlamli derecede daha hizli

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Vos LM et al. [Clin Infect Dis.](#) 2019 Jan 28.

Virüs sayısı arttıkça referans test ile uyumsuz sonuç ihtimali ↑

Bu testleri yorumlarken ve kafa-kafaya karşılaştırırken virüs sayısına dikkat

Klinik kafa karıştırıcı sonuçlar olmakla birlikte
LOS azaltabilir
influenzada OSV kullanımını artırabilir

Sonuçta
Hastanelerde kullanımı öneriliyor
ve
kalitesi yüksek randomize çalışmalara ihtiyaç (+)



Impact of antibacterials on subsequent resistance and clinical outcomes in adult patients with viral pneumonia: an opportunity for stewardship

Matthew P. Crotty¹, Shelby Meyers², Nicholas Hampton³, Stephanie Bledsoe⁴, David J. Ritchie^{1,2}, Richard S. Buller⁴,

Crotty et al. *Critical Care* (2015) 19:404

Toplam 174 hasta, immunokompromize (%56.3); Filmarray RP®

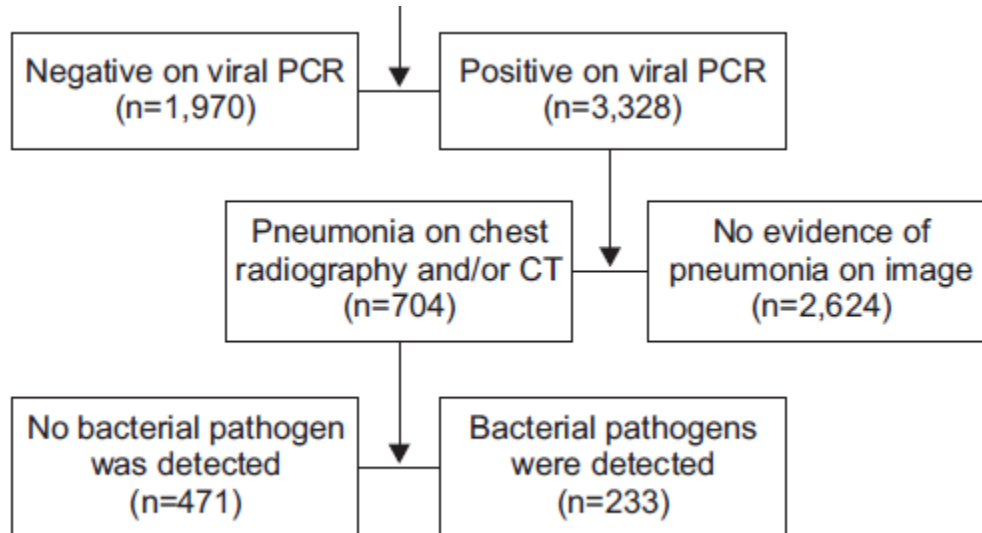
- 'long-course' antibiyotik, n = 67
- 'short-course' antibiyotik, n = 28
- mikst bakteriyel-viral, n = 79

Hastane içi mortalite viral gruplar arasında fark yok

MDRO infeksiyonu/kolonizasyonu uzun süreli tedavide daha sık (53.2 vs 21.1 %; P = 0.027)

Elucidation of Bacterial Pneumonia-Causing Pathogens in Patients with Respiratory Viral Infection

Hwa Sik Jung



SEKONDER infeksiyon ?

Influenza A-B, Rinovirus, hMPV	→	<i>S.aureus</i>
Coronavirus, PIV, RSV	→	Gram negatif
Çocuklarda viral pnömonide	→	makrolidler

**17 YBÜ’de izlenen 1011
hematoloji hastası 2010-2011**

**747 patients sampled using nasal
swabs and tested for viral PCR**

**Patients with ARF
N=447 (59.8%)**

**Patients without ARF
N=300 (40.2%)**

**114 (25.5%) patients with
positive virus detection**

**49 (16.3%) patients with
positive virus detection**

ICU mortality: 28.4%

ICU mortality 22.3%

**ePlex® Paneli:
163 vakada 179 patojen (21.8%):
%83.2 tek patojen**

The eSensor technology was originally developed in 1993 at the California Institute of Technology by Jon Faiz Kayyem.

1/6 hastada ve
akut solunum yetmezlikli 1/4 hastada (+)

ASY’li hastada virüs pozitifliği
(İnfluenza/PIV/RSV) →YBÜ Mortalitesi ↑

**Virus pozitif hastalar YBÜ erken alınıp
yakın takibe alınsa iyi olur !?**

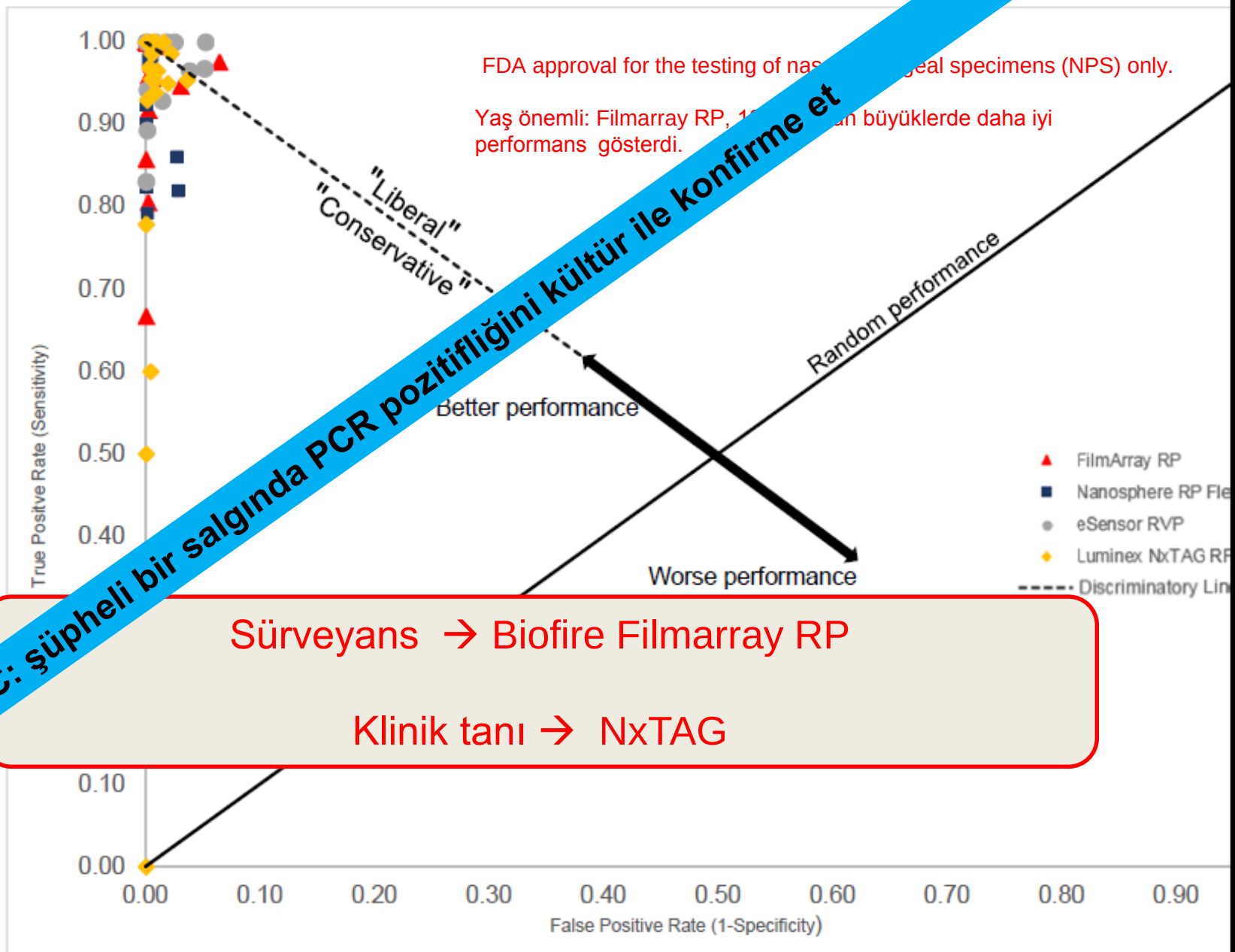


Figure 1. ROC Space of major FDA-approved respiratory panels showing "Liberal" and "Conservative" calls from discrimination. Better performing assays lie on the left of random chance; worse

Point-Counterpoint: Large Multiplex PCR Panels Should Be First-Line Tests for Detection of Respiratory and Intestinal Pathogens

Paul C. Schreckenberger,^a Alexander J. McAdam^b

Loyola University Medical Center, Maywood, Illinois, USA^a; Boston Children's Hospital, Boston, Massachusetts, USA^b

Devrimsel

VS.

Dehşetengiz

Tek bir test ile doğru tanı; hedefe yönelik tedavi
Hasta ve klinisyeni tatmin eder
Serbest bırak, klinisyen karar versin
Daha az yatış, tetkik ve görünmez maliyet ↓ (silo zihniyeti)



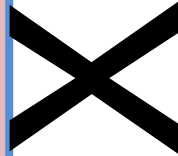
Teknik olarak yapabiliyor olmamız klinikte önemli olduğu anlamına gelmez!
Elbette işe yarar, akıllıca kullanırsak!
Kısıtla! Önce hızlı test, negatif gelirse PCR olabilir!
(Plk: İnflu; Pediatrik-KOAH: İnflu ve RSV)

The rise of syndromic molecular testing

Hastane içi bulaşı engeller

İnfluenza viral yük takibi ?

RSV-hMPV ko-infeksiyonu saptayabilir
(Kohorta dikkat, duyarlı birey risk altına girmesin)



En önemli eksiği ASYE'de bakteriyel ko-infeksiyonları dışlayamaz. Savaşın yarısı!?

Ağır hastada klinisyenin güveni kısıtlı ve antibiyotik kullanımının ve başka arayışların önüne geçememekte!

Ölü-canlı ayırımı yok, 'Tail end of previous infection'

Ramanan P, Bryson AL, Binnicker MJ, Pritt BS, Patel R. 2018. Syndromic panel-based testing in clinical microbiology. Clin Microbiol Rev 31:e00024-17. <https://doi.org/10.1128/CMR.00024-17>.

The Unyvero P55 'sample-in, answer-out' pneumonia assay: A performance evaluation

C. Ozongwu^{a,1}, Y. Personne^{a,1}, G. Platt^a, C. Jeanes^b, S. Aydin^a, N. Kozato^a, V. Gant^{c,d}, J. O'Grady^b, V.I. Enne^{a,c,*}

Unyvero P55 kartuşu,
20 patojen ve 19 direnç geni saptayabilmekte

Routine Culture Result	Unyvero P55 Result	Comprehensive Culture	16S rRNA Sequencing Results
<i>P. aeruginosa</i>	<i>P. aeruginosa</i> (+ + +) <i>S. marcescens</i> (+ + +) <i>S. aureus</i> (+ +) <i>S. maltophilia</i> (+ +)	<i>P. aeruginosa</i> <i>S. marcescens</i> <i>S. aureus</i>	<i>Pseudomonas</i> spp. 38.4% <i>Streptococcus</i> spp. (not including <i>S. pneumoniae</i>) 16.4% <i>Neisseria</i> spp. 16.4% <i>Serratia</i> spp. 12.5% <i>Stenotrophomonas</i> spp. 1.6% Others 14.0%

PPV düşük; NPV yüksek !

Keşke..

HSV, CMV, PCP gibi etkenler eklenirse
Viral yük saptayabilse (düşen yük hesaplayabilse!)
Bakteriyel etkenleri dışlayabilse

Klinik çalışmalara ihtiyaç (+)

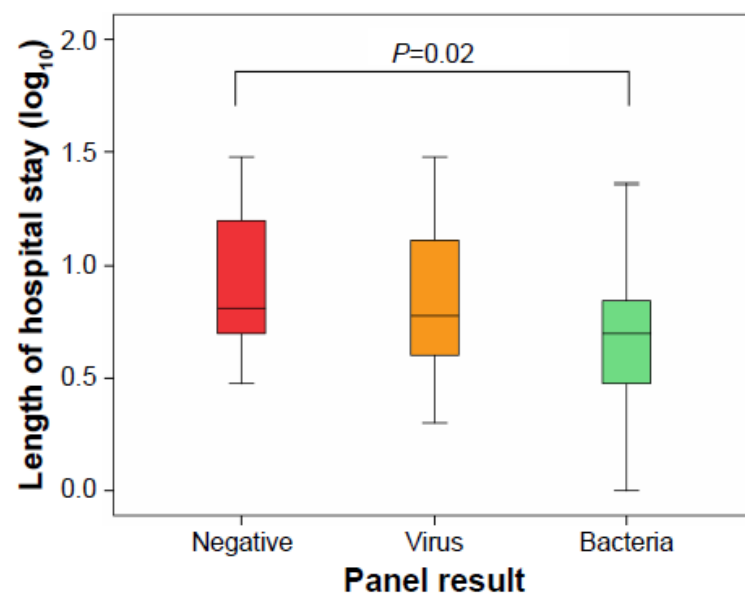
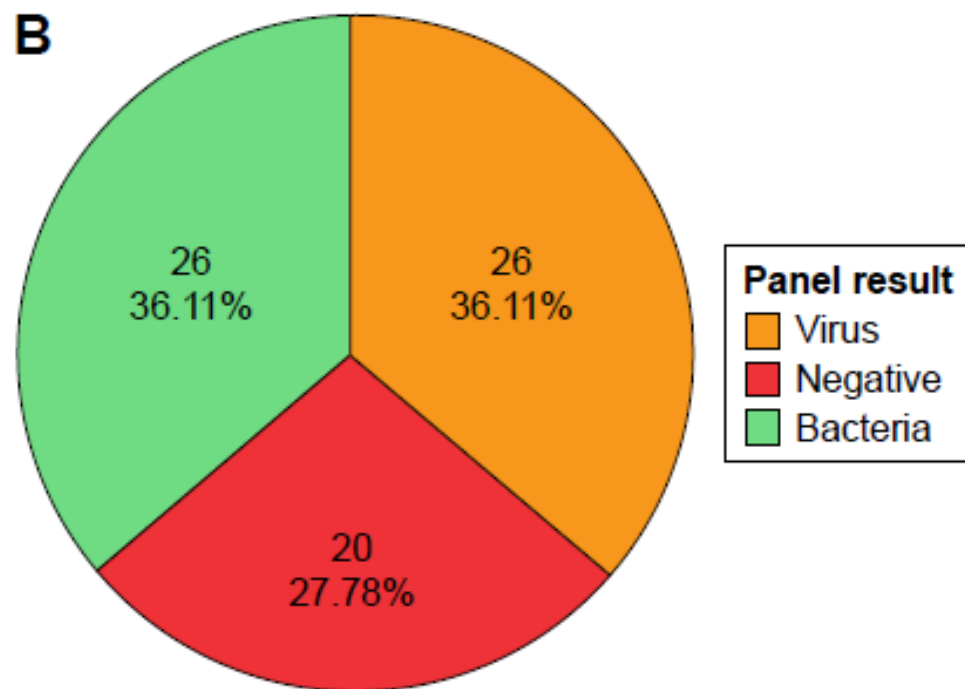
İmmünokompromize	vs.	Normal birey
Çocuk	vs.	Yetişkin
Yatan	vs.	Ayaktan

Phenotyping and outcomes of hospitalized COPD patients using rapid molecular diagnostics on sputum samples

This article was published in the following Dove Medical Press journal:

Table 2 Pathogens detected on the panel

	Total count	%
<i>Haemophilus influenzae</i>	28	33.7
<i>Streptococcus pneumoniae</i>	22	26.5
Rhinovirus	11	13.3
Influenza A virus	6	7.2
Influenza B virus	3	3.6
Respiratory syncytial virus A	3	3.6
<i>Moraxella catarrhalis</i>	2	2.4
Parainfluenza virus 4	2	2.4
Coronavirus	2	2.4
Adenovirus	1	1.2
Metapneumovirus	1	1.2
Parainfluenza virus 2	1	1.2
Parainfluenza virus 3	1	1.2
Total	83	100



The rapid diagnosis of viral respiratory tract infections and its impact on antimicrobial stewardship programs

Şiran Keske¹ • Önder Ergönül^{1,2} • Faik Tutucu² • Doruk Karaaslan² • Erhan Palaoğlu³ • Füsün Can⁴

European Journal of Clinical Microbiology & Infectious Diseases (2018) 37:779–783

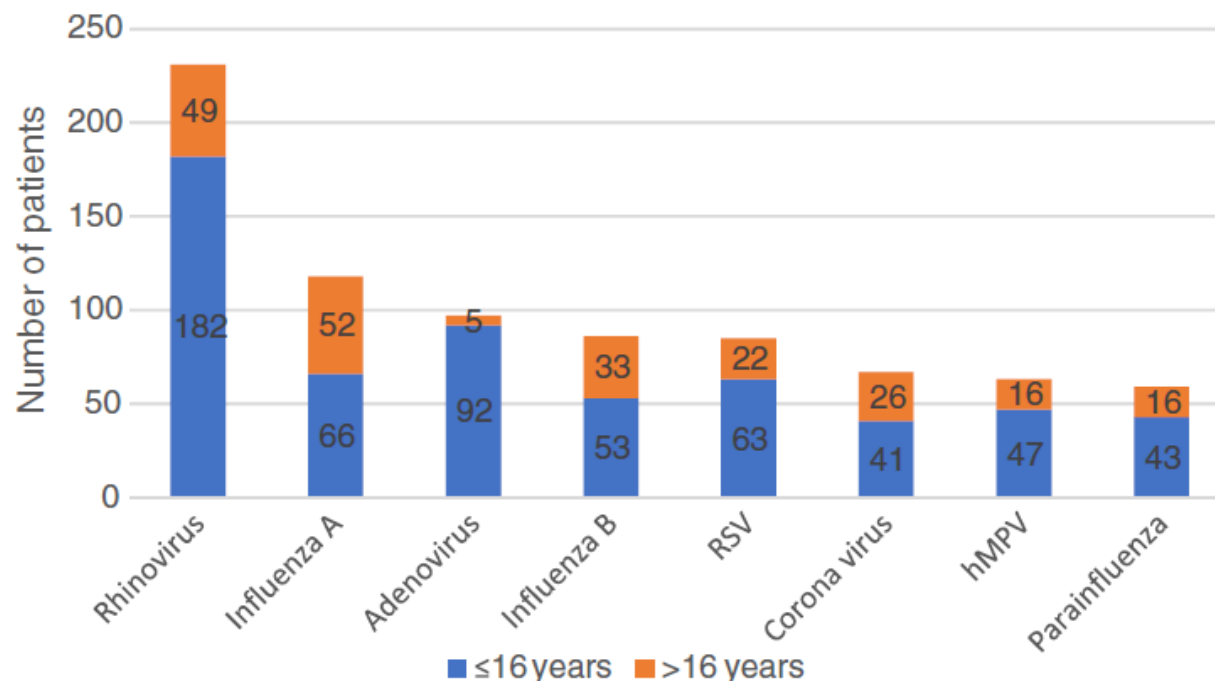


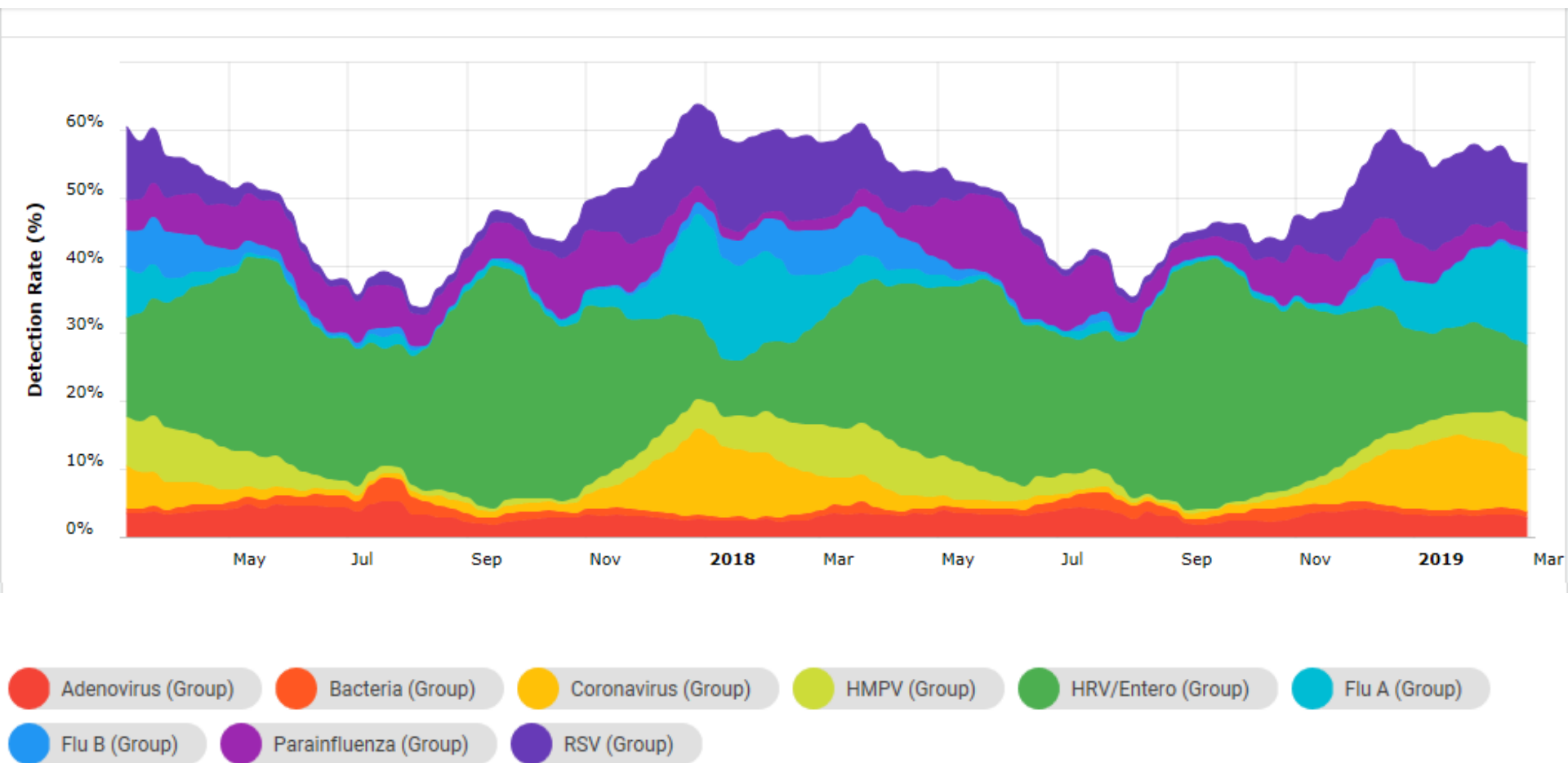
Table 2

	Children		<i>p</i> -Value	Adults		<i>p</i> -Value
	Before intervention (year 2015)	After intervention (year 2016)		Before intervention (year 2015)	After intervention (year 2016)	
Inappropriate antibiotic use (%)	53/119 (44.5)	40/139 (28.8)	0.009	28/39 (72)	39/62 (63)	0.36
Mean duration of inappropriate antibiotic use (days)	6.5 (SD 3.1)	4.6 (SD 2.0)	< 0.001	9.7 (SD 7.3)	6.2 (SD 3.7)	0.007

Gastro İntestinal sistem Patojenleri (Film Array, Multiplex PCR)	^	(N/A)
Campylobacter	Negatif	(N/A)
Clostridium difficile toxin A/B	POZİTİF	(N/A)
Plesiomonas shigelloides	Negatif	(N/A)
Salmonella	Negatif	(N/A)
Vibrio (V.parahaemolyticus/V.vulnificus/V.cholerae)	Negatif	(N/A)
Yersinia enterocolitica	Negatif	(N/A)
Enterotoxigenic E.coli (ETEC) lt/st	Negatif	(N/A)
Enteropathogenic Escherichia coli (EPEC)	POZİTİF	(N/A)
Shiga-like toxin-producing Escherichia coli (STEC) stx1/stx2 (E.coli O157)	Negatif	(N/A)
Shigella/Enteroinvasive E.coli (EIEC)	Negatif	(N/A)
Enteraggregative Escherichia coli (EAEC)	Negatif	(N/A)
Adenovirus F40/41	Negatif	(N/A)
Astrovirus	Negatif	(N/A)
Norovirus GI/GII	Negatif	(N/A)
Rotavirus A	Negatif	(N/A)
Sapovirus	Negatif	(N/A)
Cryptosporidium	Negatif	(N/A)
Cyclospora cayetanensis	Negatif	(N/A)
Entamoeba histolytica	Negatif	(N/A)
Giardia lamblia (G.intestinalis ve G.duodenalis)	Negatif	(N/A)
E.coli O157	^a Negatif	(N/A)

https://syndromictrends.com/metric/panel/respiratory/percent_positivity/organism/main

SyndromicTrends



FilmArray Respiratory Panel Assay: Comparison of Nasopharyngeal Swabs and Bronchoalveolar Lavage Samples

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- **86 hasta, YBÜ veya immünokompromize (nakil, lösemi/KİT) veya yanıtızsız hastalar**
- **NF (flocked eküvyonlar) ile patojen saptanır ise BAL alınması yeni mikrobiyolojik katkı sunmuyor**
- **Ancak NF negatif ise, 7 gün içinde yapılacak (median 1 gün) BAL yeni, faydalı bilgi sunabilir (İmmünökompromize veya YBÜ hastası 12/17 hasta)**
- Influenza virus (*n* 4), Parainfluenza virus (*n* 3), Respiratory syncytial virus (*n* 3), Coronavirus (*n* 3), Rhinovirus-Enterovirus (*n* 3), Adenovirus (*n* 1), and *Mycoplasma pneumoniae* (*n* 1).

Balgamda test Ø

İnflu, RSV, hMPV için yüksek viral yük

Dışkıda H5N1, H7N9 gibi etkenler

Citation Azadeh N, Sakata KK, Brighton AM, Vikram HR, Grys TE. 2015. FilmArray respiratory panel assay: comparison of nasopharyngeal swabs and bronchoalveolar lavage samples. J Clin Microbiol 53:3784–3787.

- NF örnekler ile pulmoner örnekler benzer duyarlılık göstermekte *Legionella pneumophila* istisna. !

Sylvie Roberta. Diagnostic performance of multiplex PCR on pulmonary samples versus nasopharyngeal aspirates in community-acquired severe lower respiratory tract infections

Rapid molecular tests for influenza, respiratory syncytial virus, and other respiratory viruses: a systematic review of diagnostic accuracy and clinical impact studies

Laura M Vos¹, Andrea HL Bruning², Johannes B Reitsma³, Rob Schuurman⁴, Annelies

Table 2. Accuracy estimates from s

Çocuklarda duyarlılık, yetişkinlerde özgüllük ↑

Characteristic	No. of studies	Pooled sensitivity % (95% CI)	P value ^a	Pooled specificity % (95% CI)	P value ^a
Population age group					
Children	8	93.0 (91.5-94.5)	0.010	80.8 (73.1-88.4)	0.001
Adults	7	79.8 (70.7-88.9)		98.6 (95.5-100)	
Population symptoms					
Respiratory/ ILI	34	90.4 (87.2-93.7)	0.655	96.2 (93.6-98.7)	0.478
Unclear	29	91.4 (88.6-94.2)		94.8 (91.9-97.7)	
Viruses					
Influenza	29	87.9 (83.7-92.1)	0.078 ^b	97.4 (94.2-100)	
Influenza + RSV	19	94.1 (90.9-97.4)		96.4 (93.6-99.2)	
Panel of viruses	14	91.8 (88.7-95.0)		88.8 (82.7-95.0)	
Index test					
Alere i Influenza A&B	14	81.6 (75.4-87.9)	0.000 ^c	94.0 (86.0-100)	
Cobas Liat Influenza A/B	5	98.1 (90.8-100)		99.7 (88.5-100)	
FilmArray	10	89.2 (86.4-92.0)		96.1 (90.5-100)	
Simplexa Flu A/B & RSV	9	99.0 (98.3-99.6)		98.2 (93.3-100)	
Verigene RV Plus test	5	96.2 (88.0-100)		97.1 (87.6-100)	
Cepheid Xpert Flu	9	94.9 (91.1-98.6)		100 (97.8-100)	

Mono testlere kıyasla özgüllük düşük !

Kohort çalışmalarında duyarlılığı vaka-kontrol çalışmalara kıyasla daha yüksek

Hızlı testler vs. sezon

İnfluenza sezonu → Yanlış negatiflikler
(Ancak yine de sezonda NPV yüksek)

Düşük sezon → Yanlış pozitiflikler

Hızlı testler sadece sezonda önerilmekte

- **NF nazik ama kuvvetli, 5 sn temas etmeli** Pozitiflik için 103 PFU (plak forming unit)
- Kültür: İnfluenza > Adeno = Rhino = RSV >> hMPV

Talbot et al 2011 CID

Bocavirus, Corona, PIV4, Rinovirus sadece NAAT ile tespit
C.pneumophila serolojisi güç

Ginocchio et al 2011 CID

Aleyhinde argumanlar

- Fiyat , raf ömrü kısa
- Kullandığın kadar öde, yok!
- Primer'lerde mutasyon ! Periyodik kalite programları yürütülmeli
- Doğası gereği 'kapalı' sistem. Yeni virüs saptayamaz
- HSV, CMV yok! Viral yük Ø, düşen yük hesaplayabilse!

Uzamış saçılım?

***B. pertussis* “pseudoepidemics” ??**

CDC: şüpheli bir salgında PCR pozitifliğini kültür ile konfirme et

Sommerville 2015

Kerri Basile.