

# Geleneksel Yaklaşımlar: RAST ve Gram Boyaması

KLİMİK Kongresi  
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Seniha BAŞARAN

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# Gram Boyaması

- 1884 - Hans Christian Gram
- 1980'ler- özellikle pnömoni tedavisinde yönlendirici
- 1988- 'Clinical Laboratory Improvement Amendments'
  - Gram boyamasının değerlendirilmesi yetkilendirilmiş kişiler tarafından yapılmalı
- Solunum kinolonların kullanıma girmesi
- ABD'de 1986'da %50, 2004'te %5-klinisyenlerin rutinde balgam Gram boyaması kullanımı



Pnömoni  
tedavisinde  
balgamin Gram  
boyaması ile  
değerlendirilme  
azalmış

## Diagnosis and Treatment of Adults with Community-acquired Pneumonia

An Official Clinical Practice Guideline of the American Thoracic Society and Infectious Diseases Society of America

**TABLE 3: Diagnostic Testing for Community-acquired Pneumonia (CAP) by Disease Severity<sup>1</sup>**

|                                                        | Non-severe CAP*                                                                                                                                                                                                                         | Severe CAP*                                                                                                                                                                                           |
|--------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>Blood</b>                                           |                                                                                                                                                                                                                                         |                                                                                                                                                                                                       |
| Blood culture                                          | Not routinely recommended <sup>†</sup>                                                                                                                                                                                                  | Yes                                                                                                                                                                                                   |
| Procalcitonin <sup>‡</sup>                             | Consider if available and recommended by hospital guidelines                                                                                                                                                                            | Yes, if available and recommended by hospital guidelines                                                                                                                                              |
| <b>Respiratory</b>                                     |                                                                                                                                                                                                                                         |                                                                                                                                                                                                       |
| Respiratory culture                                    | Not routinely recommended unless:<br>• hospitalization and parenteral antibiotics in the last 90 days<br>OR<br>• anti-MRSA or anti- <i>P. aeruginosa</i> coverage is initiated<br>OR<br>• advanced structural lung disease <sup>§</sup> | Yes                                                                                                                                                                                                   |
| Molecular testing for bacterial pathogens <sup>†</sup> | Not routinely recommended <sup>†</sup>                                                                                                                                                                                                  | Yes, if available and recommended by hospital guidelines                                                                                                                                              |
| MRSA nasal swab (marker of MRSA colonization)*         | Yes, if:<br>• hospitalization and parenteral antibiotics in the last 90 days<br>OR<br>• anti-MRSA coverage is initiated                                                                                                                 | Yes, if<br>• hospitalization and parenteral antibiotics in the last 90 days<br>OR<br>• history of MRSA colonization or infection at any site within 1 year<br>OR<br>• anti-MRSA coverage is initiated |

### Gerekçe

- Daha iyi bir klinik sonuca katkısı yok
- Kaliteli balgam elde etmek güç
- Daha önce antibiyotik kullanımına bağlı olarak performansı değişmekte

# Eriřkinlerde Toplumda Geliřen Pnömoniler Tanı ve Tedavi Uzlařı Raporu 2021

- Tanı- Klinik, radyolojik bulguların yanı sıra yapılabiliyorsa balgam Gram boyamasının sonuçlarının dikkate alınması gereklidir.

## *Balgamın Gram boyama yöntemi ile deęerlendirilmesi*

Balgam veya alt solunum yolundan alınan dięer örneklerin mikroskopik incelemesi tanıda yardımcıdır. Ağız içindeki flora yükünü azaltmak için steril su veya serum fizyolojik ile gargara yapılır. Dış macunu kullanmadan dış fırçası ile dişler, mukoza, dil, dış etleri fırçalanır. Bu işlem etkenin izolasyon şansını artırır. Antiseptik içeren gargaralar kullanılmamalıdır. Elde edilen örnek en kısa sürede (<2saat) laboratuvara ulaştırılmalıdır. Bu sürede laboratuvara transportu sağlanamayacak örnekler 24 saat süresince 2-8 °C'da saklanabilir.

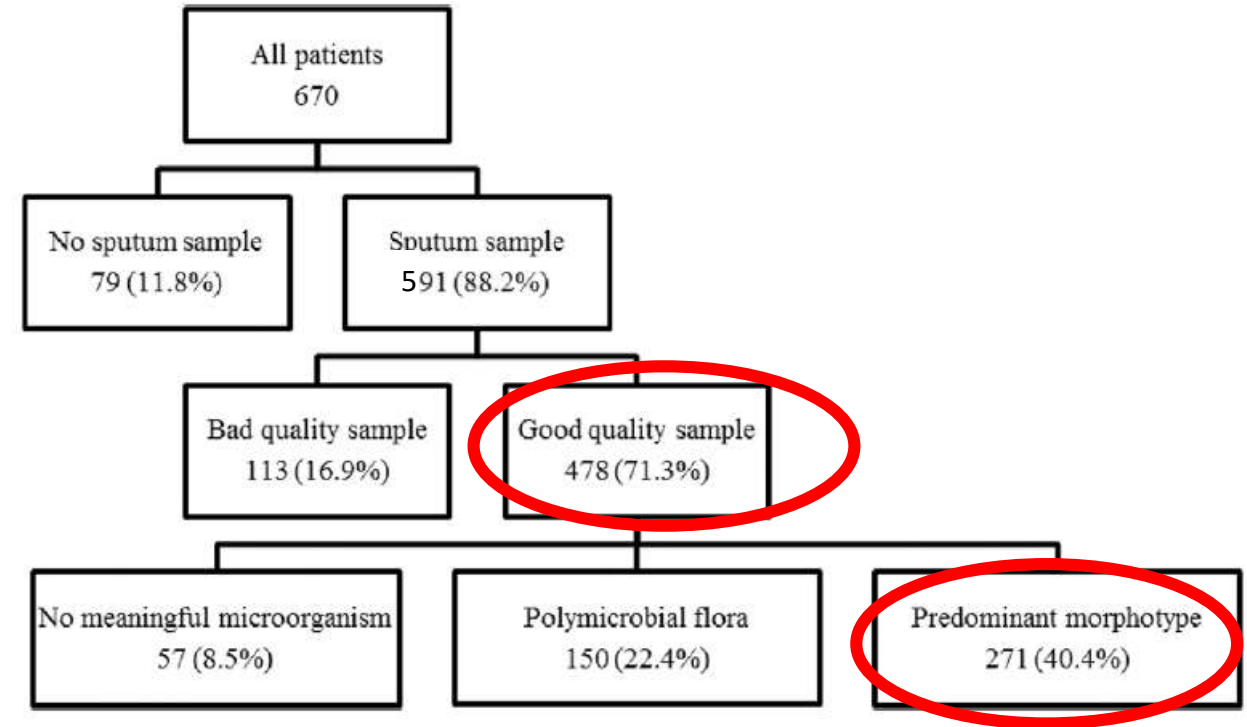
Deęerlendirmeye elverişli bir örnek olabilmesi için, balgam mikroskopisinde küçük büyütmele objektifle (10x) görülen yassı epitel hücre sayısının 10'dan az, polimorfonükleer lökosit (PNL) sayısının 25'in üzerinde olması gereklidir. Nötropenik olgularda PNL sayısının 25'in altında olabileceęi unutulmamalıdır (17).

# Solunum örneklerin Gram boyaması

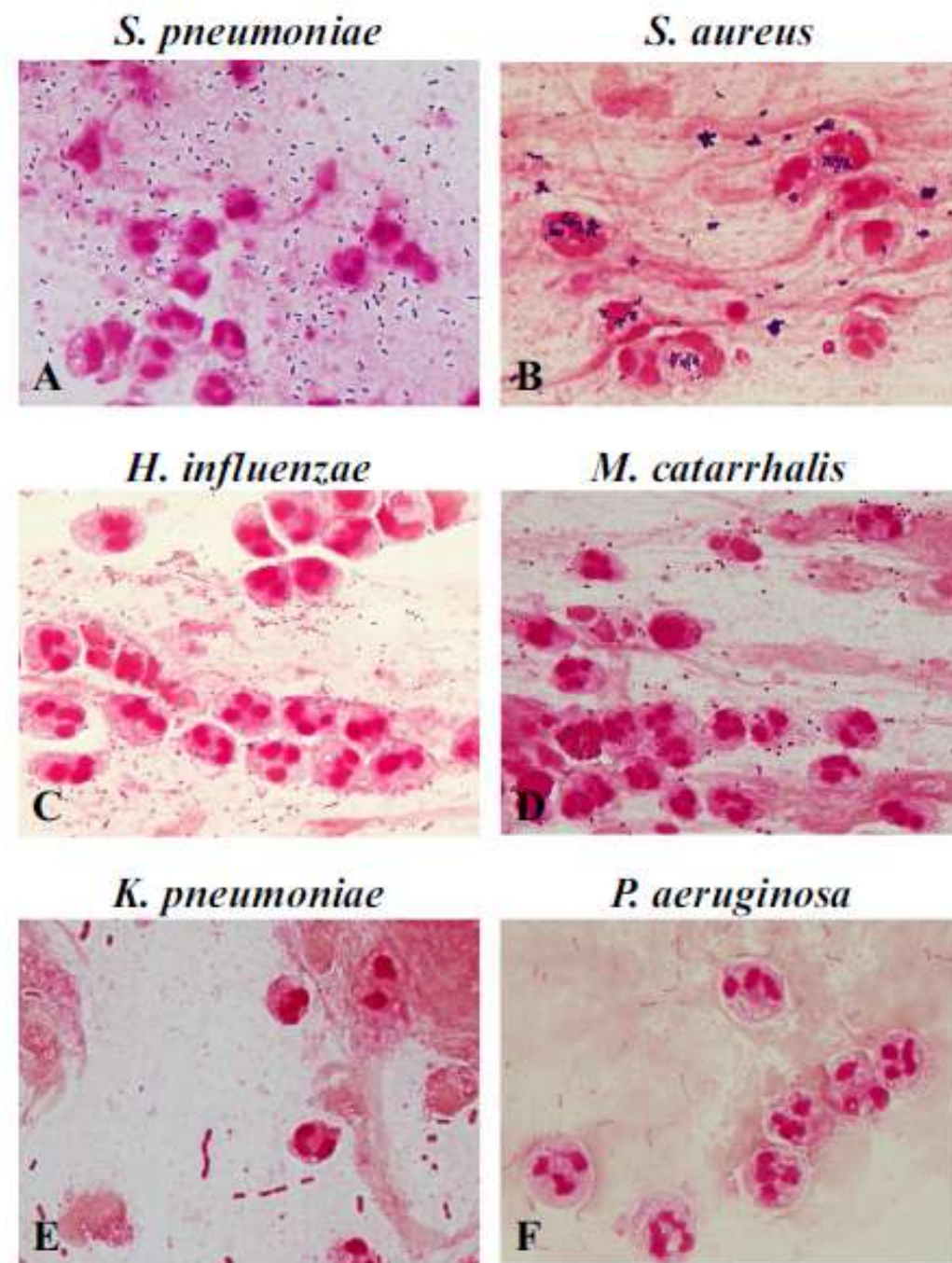


# Validation of sputum Gram stain for treatment of community-acquired pneumonia and healthcare-associated pneumonia: a prospective observational study

- 550 yataklı hastane, Acil serviste pnömoni tanısı alan tüm hastalar, 2010-12 yıllarında
- Acil biriminde en az 1-2 yıllık deneyimi olan doktorlar 24 saat boyunca Gram boyaması yapıp değerlendirmişler
- Balgam veremeyen şuuru bozuk hastalardan nazotrakeal aspirat alınıp değerlendirilmiş
- Balgam Gram boyamasının tanısal değeri araştırılmış
  - balgamda kültüründe orta-yoğun derecede üreyen etken, kan kültüründe üreyen, plevra sıvısında üreyen, idrarda pozitif pnömokok antijeni ile kıyaslanmış
- Balgam Gram boyamasına göre tedaviyle, tamamen ampirik tedavi seçimlerin hasta sonuçları üzerine etkileri kıyaslanmış



- Gram pozitif lanset biçiminde diplokoklar - *S. pneumoniae*  
\*Ampisilin
- Gram negatif kokobasil - *H. influenzae*  
\*3. kuşak sefalosporin
- Gram negatif diplokok - *M. catarrhalis*  
\* Ampisilin-sulbaktam
- Gram negatif büyük çomaklar - *K. pneumoniae*  
\* 2./3. kuşak sefalosporin
- Gram negatif küçük çomak - *P. aeruginosa*  
\*Antipsödomonal antibiyotik
- Gram pozitif küme koklar - *S. aureus*  
\* Vankomisin



**Table 3 Predictive accuracy of sputum Gram stain for the etiologic diagnosis**

|                                              | Sensitivity   | Specificity    | PPV           | NPV            |
|----------------------------------------------|---------------|----------------|---------------|----------------|
| GPDC ( <i>Streptococcus pneumoniae</i> )     | 62.5 (70/112) | 91.5 (335/365) | 69.3 (70/101) | 88.9 (335/377) |
| GNCB ( <i>Haemophilus influenzae</i> )       | 60.9 (67/110) | 95.1 (350/368) | 78.8 (67/85)  | 89.1 (350/393) |
| GNDC ( <i>Moraxella catarrhalis</i> )        | 68.2 (30/44)  | 96.1 (417/434) | 63.8 (30/47)  | 96.8 (417/431) |
| GNR-large ( <i>Klebsiella pneumoniae</i> )   | 39.5 (15/38)  | 98.2 (432/436) | 65.2 (15/23)  | 95.0 (432/455) |
| GNR-small ( <i>Pseudomonas aeruginosa</i> )  | 22.2 (6/27)   | 99.8 (450/451) | 85.7 (6/7)    | 95.5 (450/471) |
| GPC-cluster ( <i>Staphylococcus aureus</i> ) | 9.1 (1/11)    | 100 (467/467)  | 100 (1/1)     | 97.1 (467/477) |

- Sağlık bakımıyla ilişkili pnömonide daha çok balgam elde edilebiliyor, ancak kalitesi daha düşük ve polimikrobiyal flora daha sık.
- Toplum kökenli pnömonide balgam Gram boyamasının pozitif prediktif değeri daha yüksek.

**Table 4 Diagnostic performance of sputum Gram stain in patients with CAP and HCAP**

|                                    | CAP<br>n = 328 | HCAP<br>n = 342 | p value |
|------------------------------------|----------------|-----------------|---------|
| No sputum sample, n (%)            | 55 (16.8)      | 24 (7.0)        | <0.001  |
| Poor quality sample, n (%)         | 43 (13.1)      | 70 (20.5)       | 0.011   |
| Good quality sample, n (%)         | 230 (70.1)     | 248 (72.5)      | 0.49    |
| No meaningful microorganism, n (%) | 30 (9.1)       | 27 (7.9)        | 0.56    |
| Polymicrobial flora, n (%)         | 56 (17.1)      | 94 (27.5)       | 0.001   |
| Predominant morphotype, n (%)      | 144 (43.9)     | 127 (37.1)      | 0.0744  |
| Positive predict, n (%)            | 107 (32.6)     | 82 (24.0)       | 0.013   |

Balgam Gram boyaması sonucuna göre tedavi alanlarla ampirik tedavi alanlar kıyaslandığında :

- İstenmeyen etki daha az
- Mortalitede fark yok

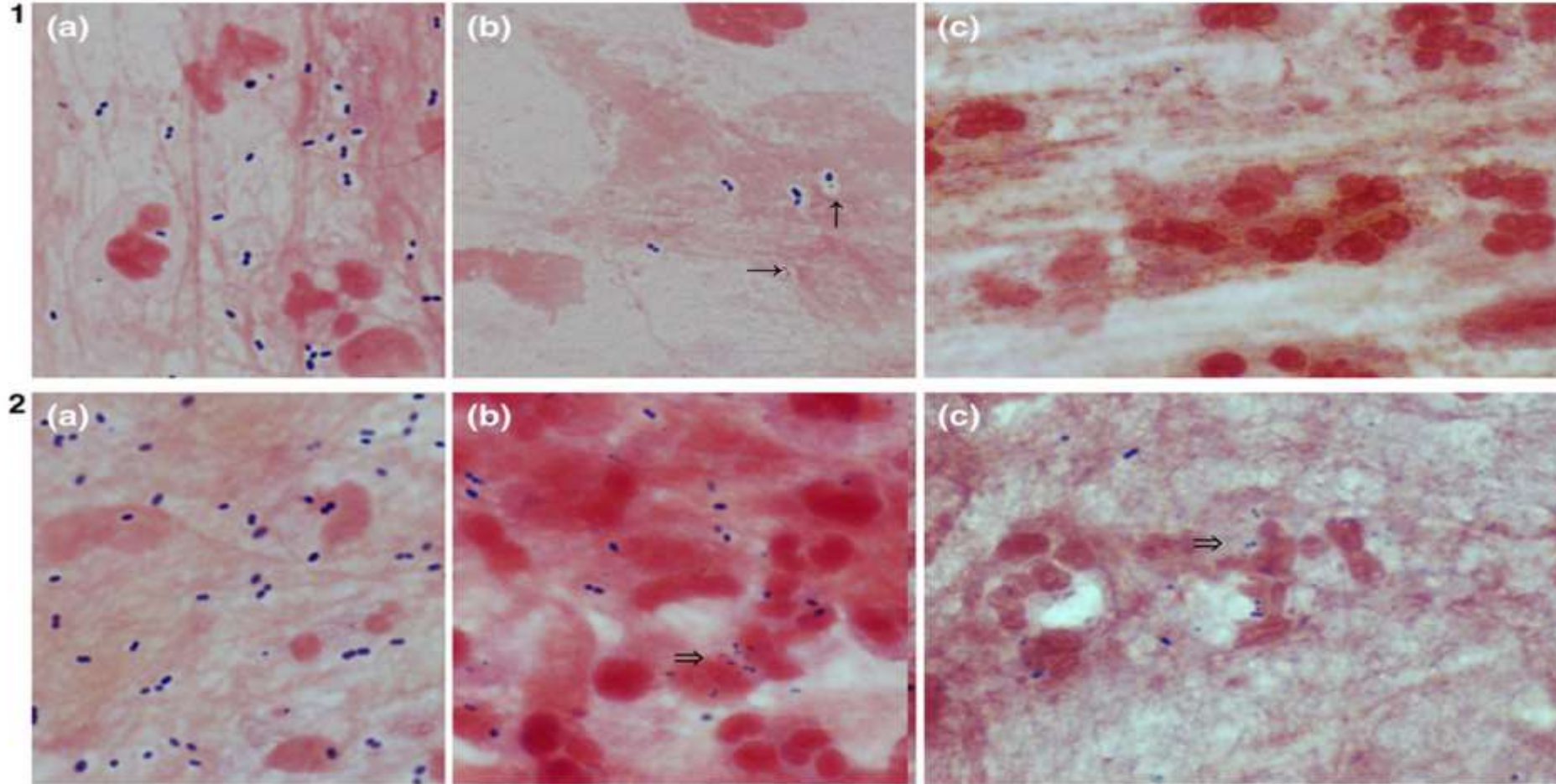
### Sonuç olarak :

- Balgam Gram boyaması etyolojik tanı için oldukça spesifik, TKP ve sağlık bakımıyla ilişkili pnömonide patojen hedefli antibiyotik tedavisine rehberlik edebilir.

|                                                 | Pathogen-targeted<br>treatment<br>n = 172 | Empirical<br>treatment<br>n = 498 | p value |
|-------------------------------------------------|-------------------------------------------|-----------------------------------|---------|
| Patient background                              |                                           |                                   |         |
| Age, median (IQR), y                            | 80 (72–88)                                | 76 (63–85)                        | 0.064   |
| Male, n (%)                                     | 90 (52.3)                                 | 340 (68.3)                        | <0.001  |
| Comorbid conditions, n (%)                      | 163 (94.8)                                | 472 (94.8)                        | 0.157   |
| CAP, n (%)                                      | 100 (58.1)                                | 228 (45.8)                        | 0.005   |
| Previous antibiotics treatment,<br>n (%)        | 14 (8.1)                                  | 83 (16.7)                         | 0.006   |
| Immunosuppressed, n (%)                         | 8 (4.7)                                   | 32 (6.4)                          | 0.40    |
| Suspected aspiration, n (%)                     | 43 (25.0)                                 | 203 (40.8)                        | <0.001  |
| Severity scores                                 |                                           |                                   |         |
| PSI score, median (IQR)                         | 108 (89–128)                              | 112 (90–142)                      | 0.012   |
| PSI class, median (IQR)                         | 4 (3–4)                                   | 4 (4–5)                           | 0.002   |
| Clinical outcomes                               |                                           |                                   |         |
| Initial treatment failure, n (%)                | 13 (7.6)                                  | 61 (12.2)                         | 0.091   |
| Antibiotics adverse events,<br>n (%)            | 5 (2.9)                                   | 35 (7.0)                          | 0.049   |
| ICU admission, n (%)                            | 12 (7.0)                                  | 69 (13.9)                         | 0.017   |
| Length of intravenous<br>treatment, median(IQR) | 8 (6–9)                                   | 9 (7–13)                          | <0.001  |
| Length of hospital stay,<br>median (IQR)        | 9 (7–13)                                  | 11 (8–21)                         | <0.001  |
| In-hospital mortality, n (%)                    | 14 (8.1)                                  | 45 (9.0)                          | 0.72    |

# Tedavi etkinliğini deęerlendirmede Gram boyaması

- *Streptococcus pneumoniae*



15 dakika sonra

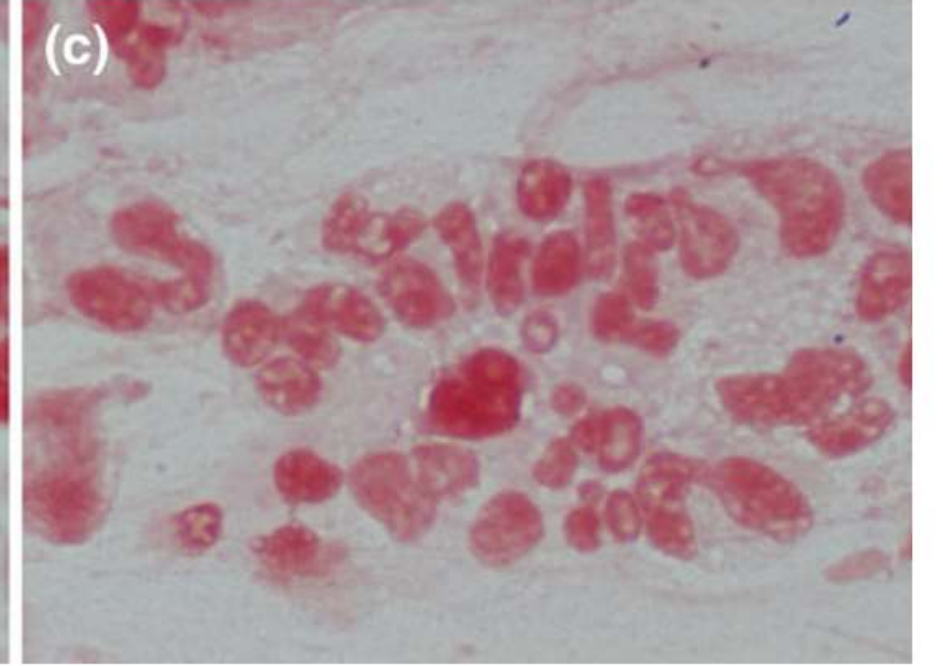
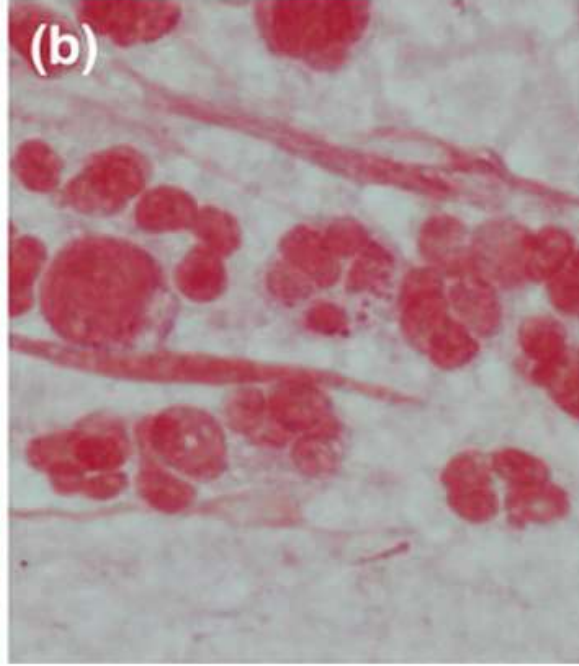
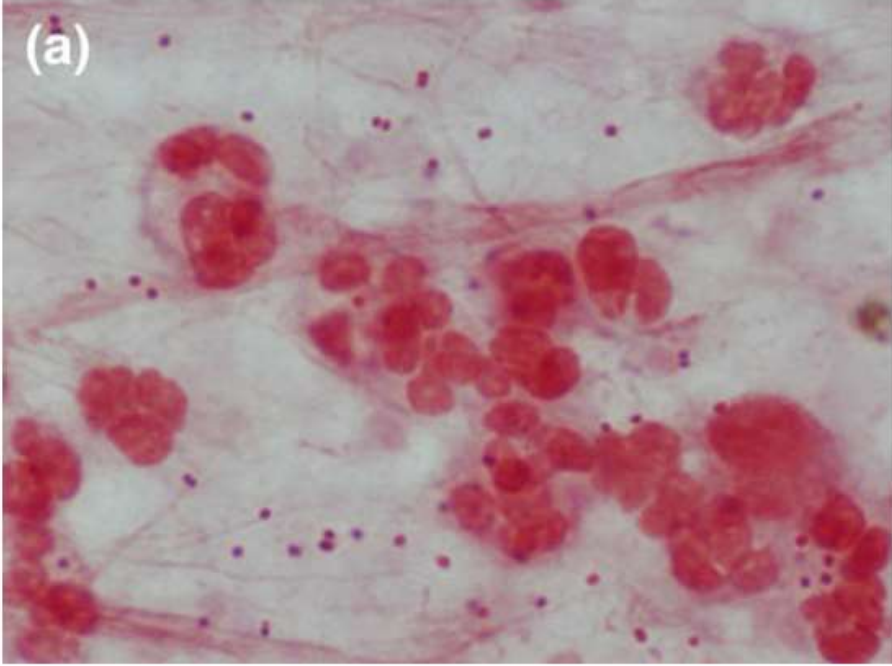
1 saat sonra

# Tedavi etkinliđini deęerlendirmede Gram boyaması

- *Moraxella catarrhalis*

30 dakika sonra

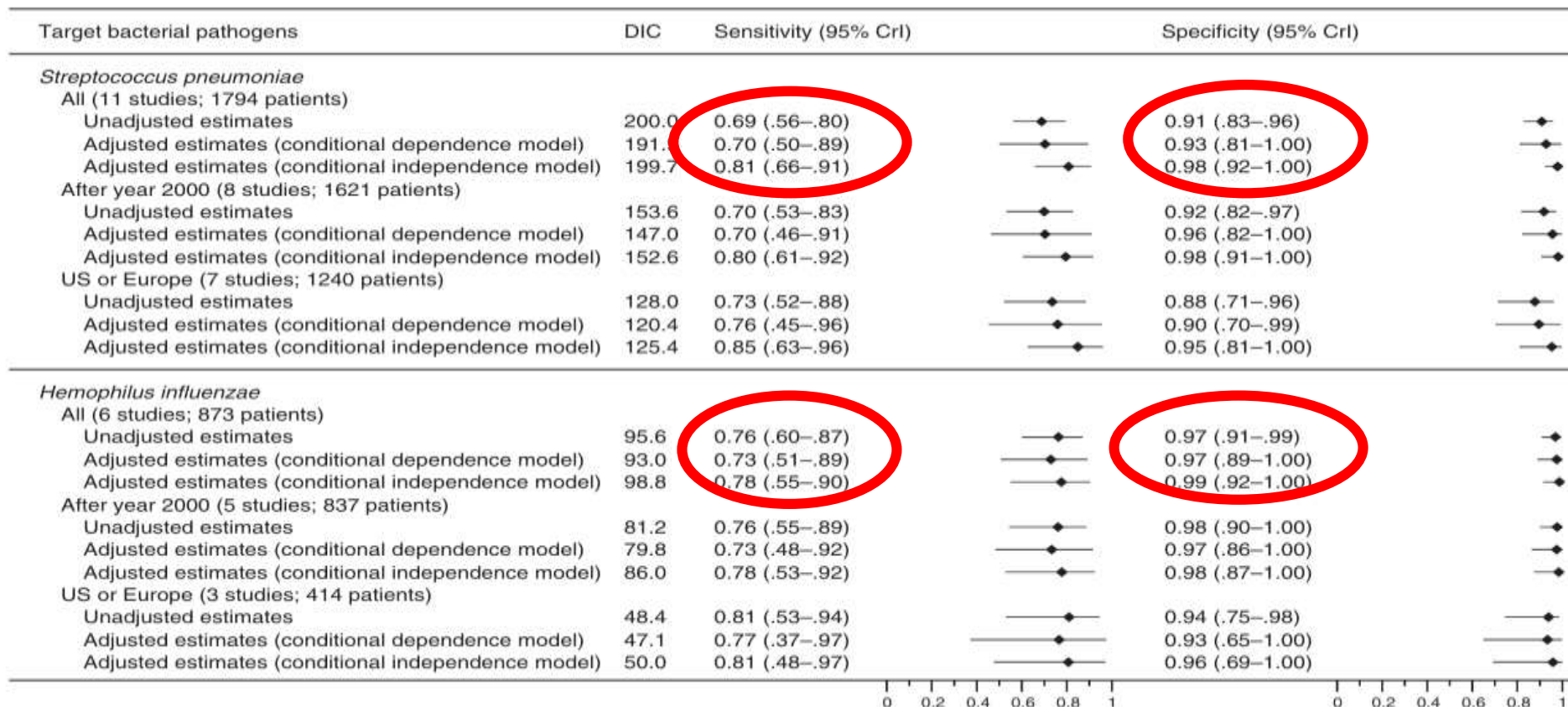
2 saat sonra



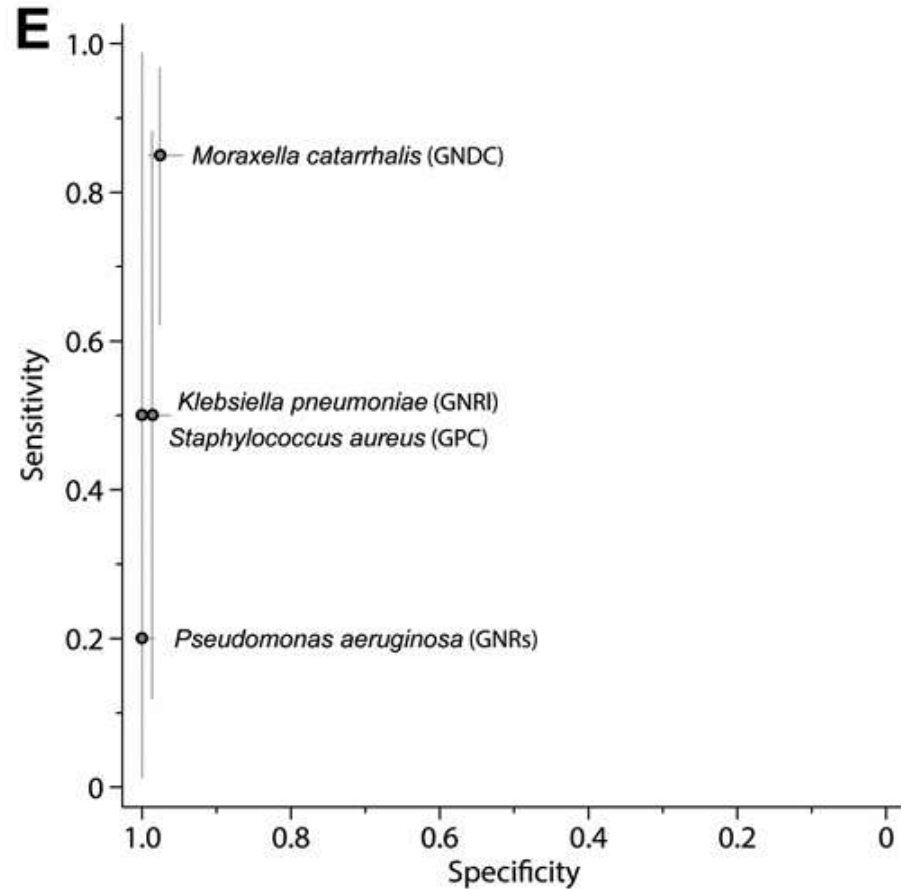
- Tedavi etkinliđinin deęerlendirilmesinde
  - CRP ve lkosit sayısından daha erken bilgi verir

# Sputum Gram Stain for Bacterial Pathogen Diagnosis in Community-acquired Pneumonia: A Systematic Review and Bayesian Meta-analysis of Diagnostic Accuracy and Yield

- 24 makale, 4533 TKP hasta, kaliteli balgam örneği değerlendiren çalışmalar



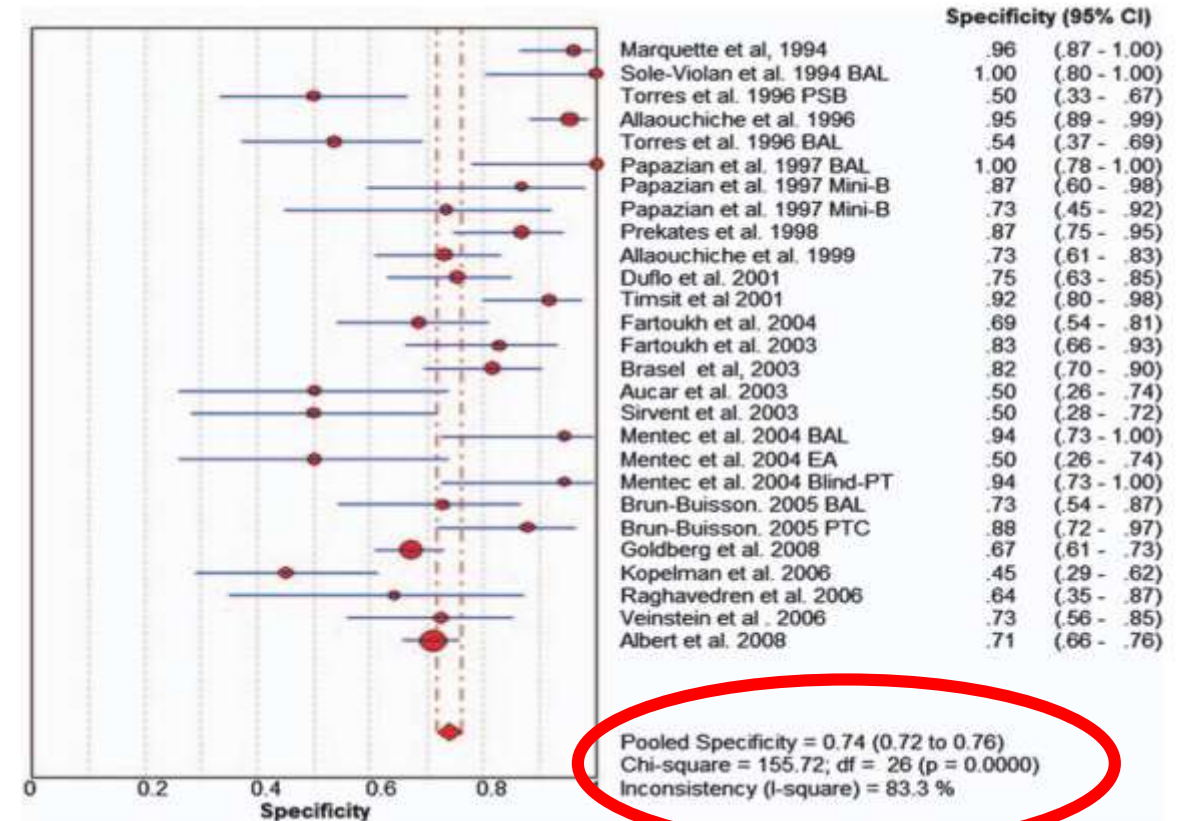
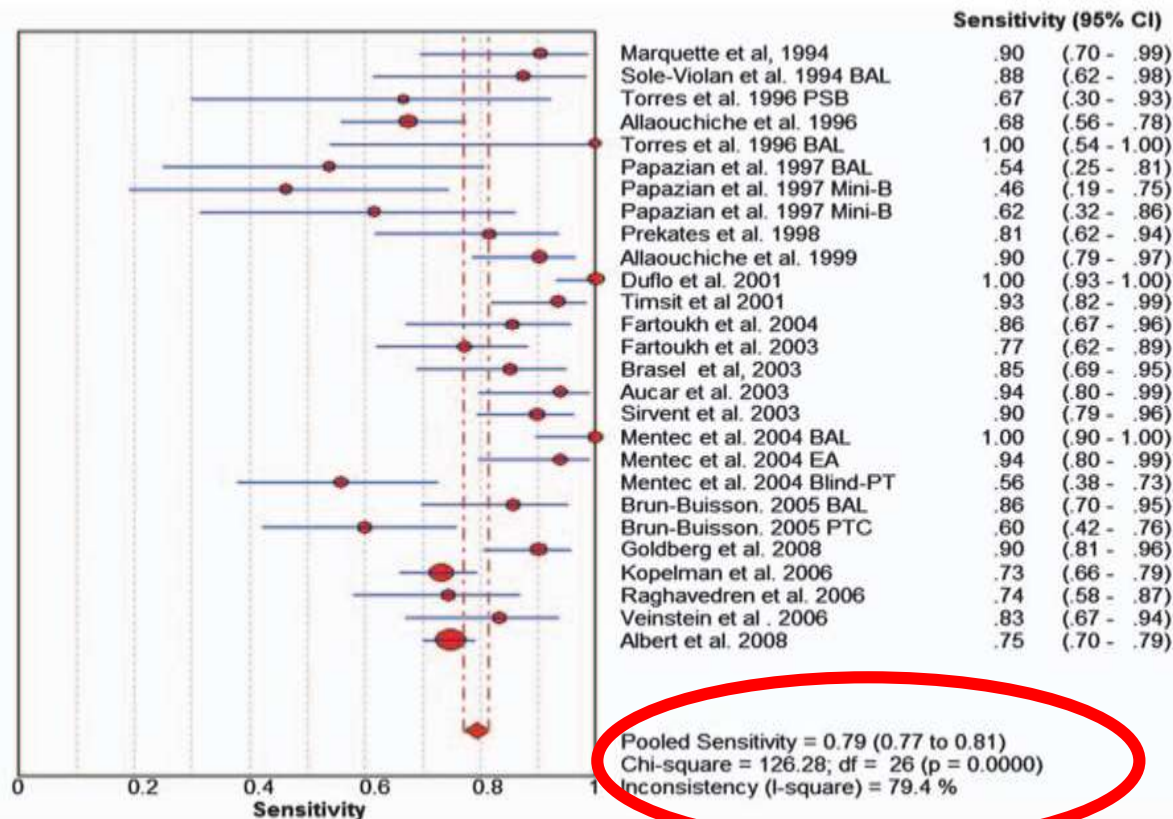
# Sputum Gram Stain for Bacterial Pathogen Diagnosis in Community-acquired Pneumonia: A Systematic Review and Bayesian Meta-analysis of Diagnostic Accuracy and Yield



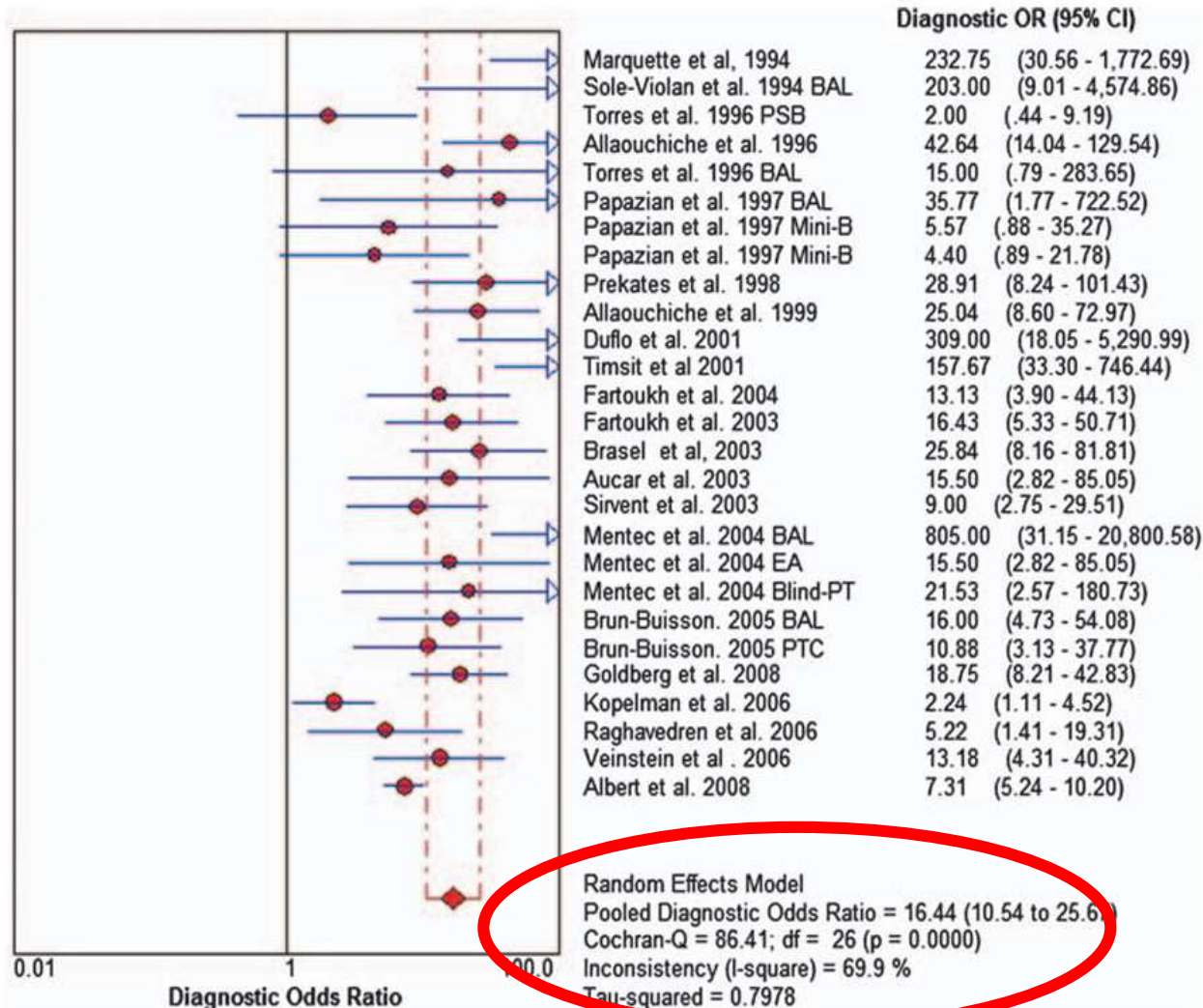
- *S. pneumoniae* ve *H. influenzae* ile ilişkili TKP tanısında balgam Gram boyaması oldukça spesifik
- Kaliteli balgam örneklerin Gram boyaması patojen odaklı antibiyotik tedavisi için klinikte destek sağlayabilir

# Is the Gram Stain Useful in the Microbiologic Diagnosis of VAP? A Meta-analysis

- 24, çoğu prospektif BAL (TA olanlar da var) örneğin değerlendirildiği çalışmalar



# Is the Gram Stain Useful in the Microbiologic Diagnosis of VAP? A Meta-analysis



## VİP tanısında

Gram boyamasında bakteri bulunmaması

- yüksek negatif öngörü değerine sahip (NPV %91, PPV %40)

Gram boyamasında gösterilen etkenle, kültürde elde edilen mikroorganizma arasında

- zayıf korelasyon

(Gram pozitif etkenlerde

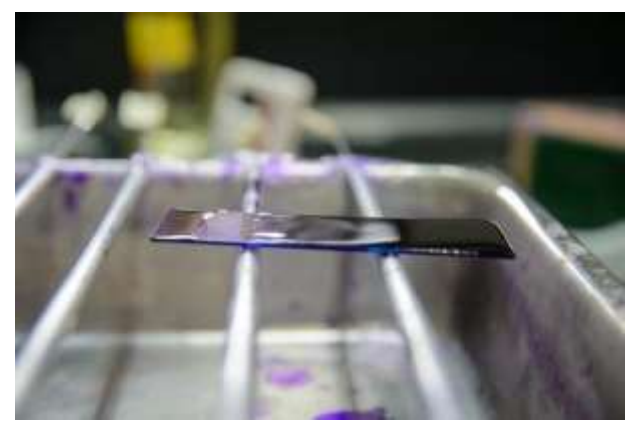
kappa katsayısı 0.42

Gram negatif etkenlerde

kappa katsayısı 0.34)

## Effect of Gram Stain-Guided Initial Antibiotic Therapy on Clinical Response in Patients With Ventilator-Associated Pneumonia The GRACE-VAP Randomized Clinical Trial

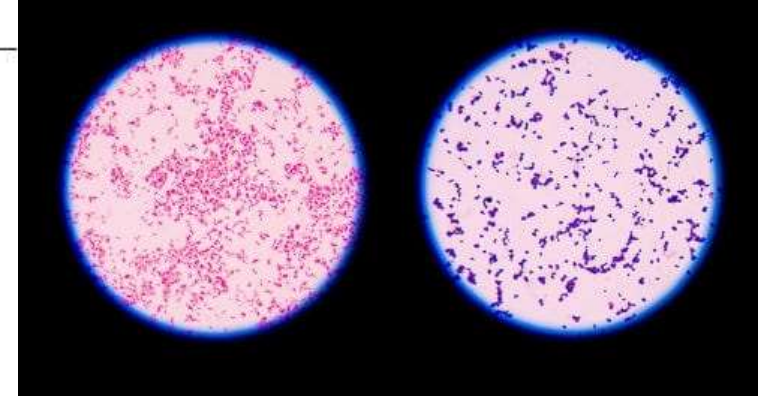
Jumpei Yoshimura, MD; Kazuma Yamakawa, MD, PhD; Yoshinori Ohta, MD, PhD; Kensuke Nakamura, MD, PhD; Hideki Hashimoto, MD, PhD; Masahiro Kawada, MD; Hiroki Takahashi, MD; Takeshi Yamagiwa, MD, PhD; Akira Kodate, MD; Kyohei Miyamoto, MD, PhD; Satoshi Fujimi, MD, PhD; Takeshi Morimoto, MD, PhD, MPH



- Gram Stain-Guided Antibiotics Choice for VAP (GRACE-VAP)
- Üçüncü basamak hastane YBÜ, 12 merkez, Japonya
- Nisan 2018 - Mayıs 2020, toplam 206 hasta
- COVID-19 enfeksiyon tanısı alanlar dışlanmış
- Açık etiketli, randomize klinik çalışma
- Endotrakeal aspiratın Gram boyaması sonucuna göre tedavi seçimi ile kılavuz önerilerine göre yapılan seçimler kıyaslanmış

# Effect of Gram Stain-Guided Initial Antibiotic Therapy on Clinical Response in Patients With Ventilator-Associated Pneumonia The GRACE-VAP Randomized Clinical Trial

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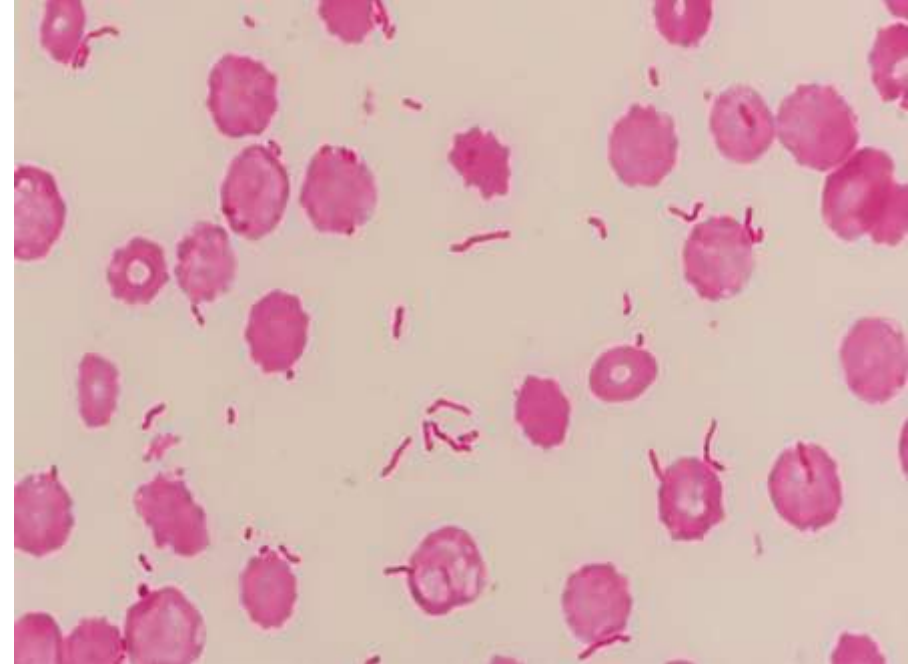
| Endotrakeal aspiratın Gram boyaması sonucu         | Verilen antibiyotikler                                            |
|----------------------------------------------------|-------------------------------------------------------------------|
| Gram-pozitif zincir kok ve/veya Gram-pozitif basil | Anti-pseudomonas etkisi olmayan beta-laktam antibiyotik           |
| Sadece Gram-pozitif küme kok                       | Anti-MRSA etkili antibiyotik                                      |
| Sadece Gram-negatif çomak                          | Anti-pseudomonal etkili antibiyotik                               |
| Gram-pozitif küme kok + Gram-negatif çomak         | Anti-pseudomonal + anti-MRSA etkili antibiyotiklerin kombinasyonu |
| Etken saptanamazsa                                 | Anti-pseudomonal + anti-MRSA etkili antibiyotiklerin kombinasyonu |

VİP'in Gram boyaması rehberliğindeki tedavi kılavuzuna dayalı tedaviden **daha az etkin olmayıp**, bu hastalarda **geniş spektrumlu antibiyotik kullanımını** önemli ölçüde **azalttığını** göstermektedir.

| Outcome                                                                           | No. (%)                           |                                 | P value            |
|-----------------------------------------------------------------------------------|-----------------------------------|---------------------------------|--------------------|
|                                                                                   | Gram stain-guided group (n = 103) | Guideline-based group (n = 103) |                    |
| Primary outcome                                                                   |                                   |                                 |                    |
| Clinical response rate                                                            | 79 (76.7)                         | 74 (71.8)                       | <.001 <sup>a</sup> |
| Completion of antibiotic therapy within 14 d <sup>b</sup>                         | 98 (95.1)                         | 94 (91.3)                       | NA                 |
| Improvement or lack of progression of baseline radiographic findings <sup>b</sup> | 85 (82.5)                         | 78 (75.7)                       | NA                 |
| Resolution of signs and symptoms of pneumonia <sup>b</sup>                        | 87 (84.5)                         | 85 (82.5)                       | NA                 |
| Lack of antibiotic agent readministration <sup>b</sup>                            | 85 (82.5)                         | 85 (82.5)                       | NA                 |
| Secondary outcomes                                                                |                                   |                                 |                    |
| 28-d mortality                                                                    | 14 (13.6)                         | 18 (17.5)                       | .44                |
| 28-d ventilator-free days, median (IQR)                                           | 21 (0-24)                         | 21 (4-25)                       | .63                |
| 28-d ICU-free days, median (IQR)                                                  | 18 (11-22)                        | 17 (5-22)                       | .61                |
| Administration of antibiotic therapy                                              |                                   |                                 |                    |
| Antipseudomonal agents                                                            | 72 (69.9)                         | 103 (100)                       | <.001              |
| Anti-MRSA agents                                                                  | 63 (61.2)                         | 103 (100)                       | <.001              |
| Coverage rate of initial antibiotic therapy                                       | 89 (86.4)                         | 95 (92.2)                       | .18                |
| Escalation <sup>b</sup>                                                           | 7 (6.8)                           | 1 (1.0)                         | .03                |
| De-escalation                                                                     | 67 (65.0)                         | 79 (76.7)                       | .07                |
| Antibiotic therapy days until de-escalation, median (IQR)                         | 3 (2-4)                           | 3 (2-4)                         | .22                |
| Antibiotic therapy days, median (IQR)                                             | 8 (7-11)                          | 8 (7-11)                        | .09                |

# Kan k lt r 

## Gram boyaması



## The 24-h reporting of Gram stains from positive blood cultures contributes to physician's use of appropriate antimicrobials: Experience at a university hospital

- Ocak-Aralık 2016, Tokyo, 1020 yataklı, 33 kliniği olan üniversite hastanesi
- 24 saat boyunca pozitif kan kültürün Gram boyamasının bildirilmesi ile klinisyenlerin antibiyotik seçimine etkisi incelenmiş
- 11 profesyonel laboratuvar çalışanı ve 53 tıbbi tekniker (Gram boyaması konusunda eğitilmiş, mesai saatleri dışında destek olan) dahil edilmiş
- Gram boyamasını ilk değerlendiren kişi ilgili hekime telefonla ulaşip bilgi vermiş
- Bir sonraki gün sabah laboratuvarda kıdemli biri kontrol edip son değerlendirme infeksiyon kontrol ekibi (İKE) yapmış
- İKE - İV antibiyotik tedavisi alan tüm hastalara sabah vizitini yapan ekip, kan kültüründe üremesi olanlar dahil (2007'den itibaren)

## The 24-h reporting of Gram stains from positive blood cultures contributes to physician's use of appropriate antimicrobials: Experience at a university hospital

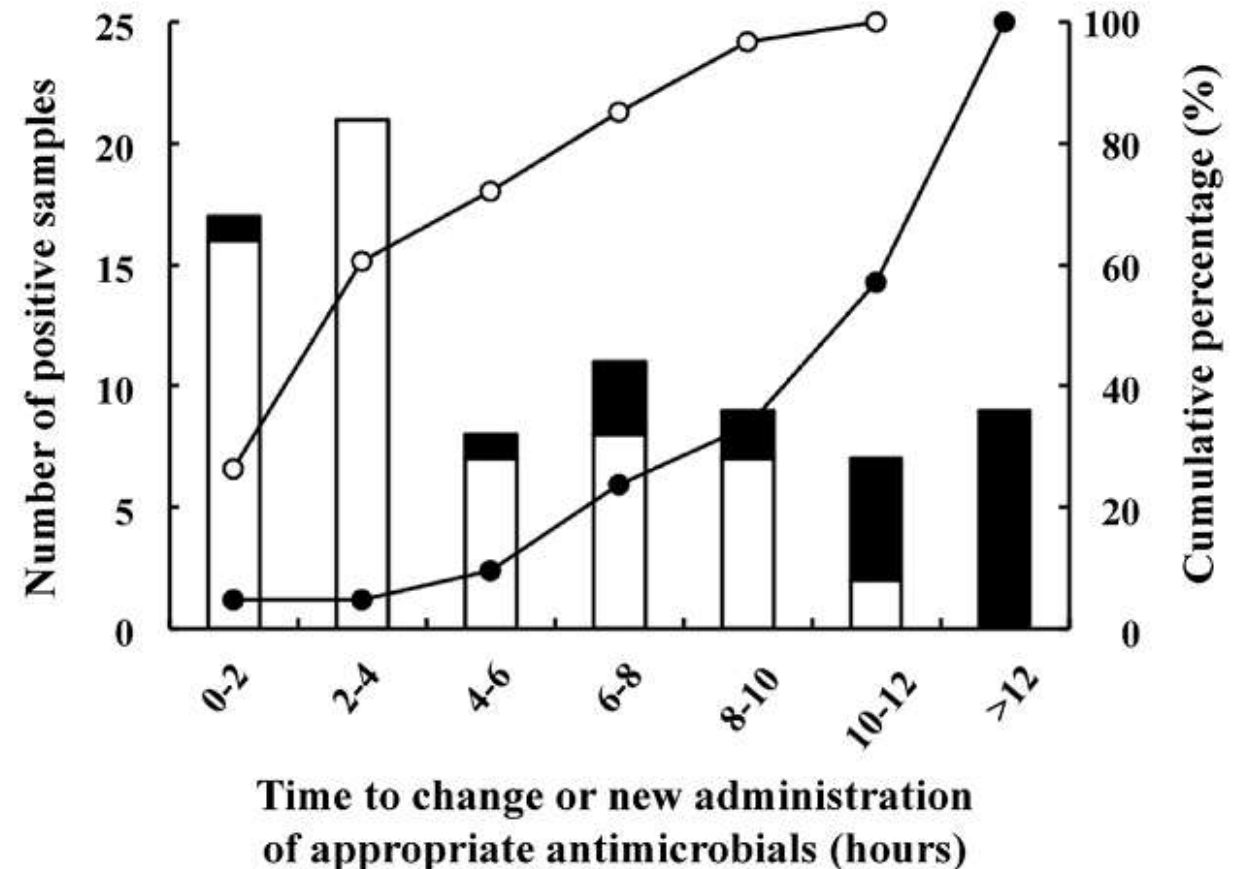
- 627 pozitif kan kültürü (%50'si ilk 6 saatte, %67'si mesai saatlerin dışında pozitifleşmiş), **Gram boyamasıyla nihai etken morfolojisi tam uyumluymuş**
- **İlk raporlamadan sonra tedavisi değişen veya yeni başlananlar, İKE ziyaretinden sonra başlananlara göre daha fazla olmuş (61'e karşı 21 hastada,  $p < 0.001$ )**

Impact of first laboratory report of Gram stain from positive blood cultures or ICT intervention on physician's use of appropriate antimicrobials.

| Antimicrobial use                                | BSI (%)            | CLA-BSI (%)    | Contamination (%) | Undetermined (%) | Subtotal (%)          | Total (%) |
|--------------------------------------------------|--------------------|----------------|-------------------|------------------|-----------------------|-----------|
| No change during administration                  | 318 (51)           | 79 (13)        | 97 (15)           | 8 (1)            | 502 (80) <sup>b</sup> | 502 (80)  |
| Change after first laboratory report             | 16 (3)             | 20 (3)         | 0                 | 0                | 36 (6) <sup>b</sup>   | 61 (10)   |
| New administration after first laboratory report | 19 (3)             | 6 (1)          | 0                 | 0                | 25 (4)                |           |
| New administration after ICT-intervention        | 12 (2)             | 8 (1)          | 0                 | 1                | 21 (3)                | 21 (3)    |
| No administration                                | 6 (1) <sup>a</sup> | 1 <sup>a</sup> | 33 (6)            | 3                | 43 (7)                | 43 (7)    |
| Overall (%)                                      | 371 (59)           | 114 (18)       | 130 (21)          | 12 (2)           | 627 (100)             | 627 (100) |

## The 24-h reporting of Gram stains from positive blood cultures contributes to physician's use of appropriate antimicrobials: Experience at a university hospital

- Telefonla bildirim sonrası uygun antibiyotik başlanma süresi (**4 saat**, 2–7)
- İKE ziyareti sonrası uygun antibiyotik başlanma süresi (**12 saat**, 10–17)
- **$p < 0.001$**

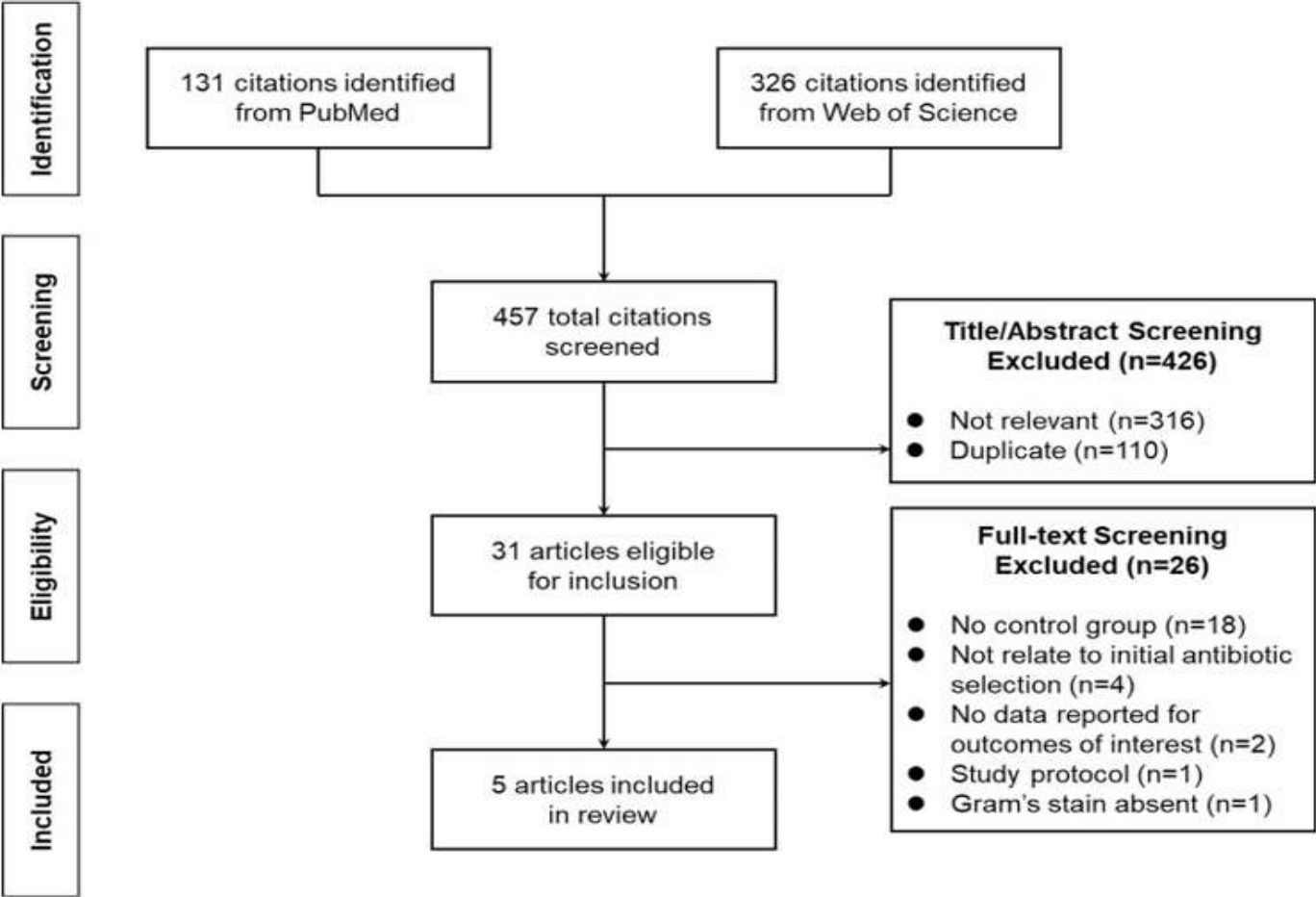


# Gram boyaması



Geniş spektrum antibiyotikler kullanımının azalması

# The role of gram stain in reducing broad-spectrum antibiotic use: A systematic literature review and meta-analysis



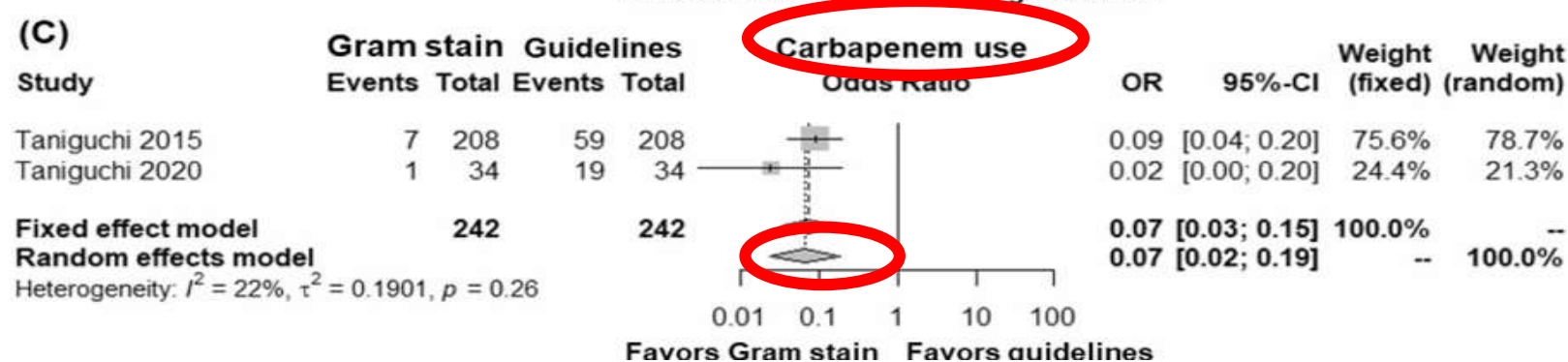
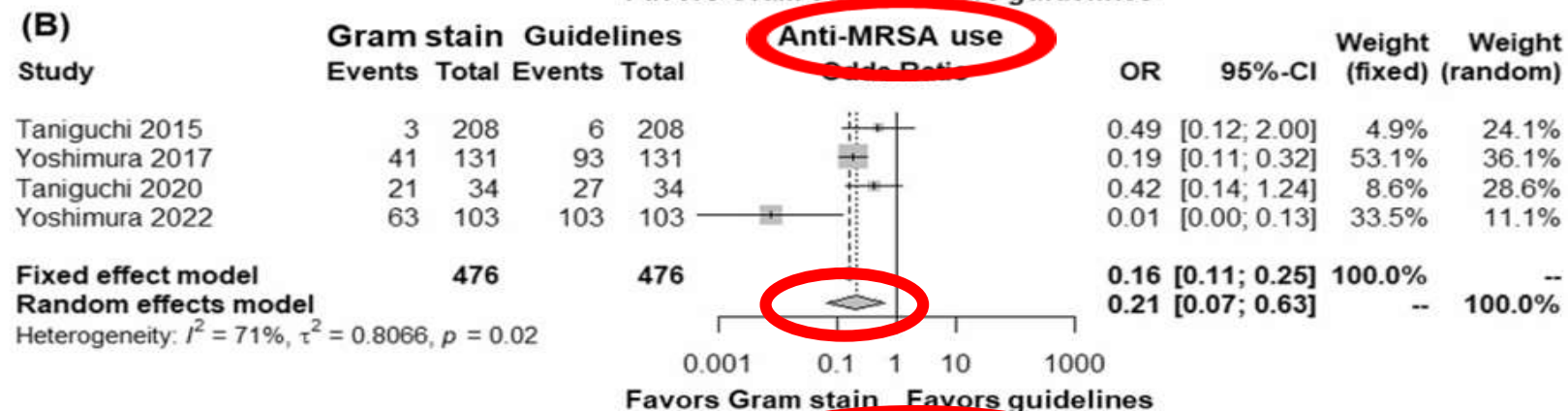
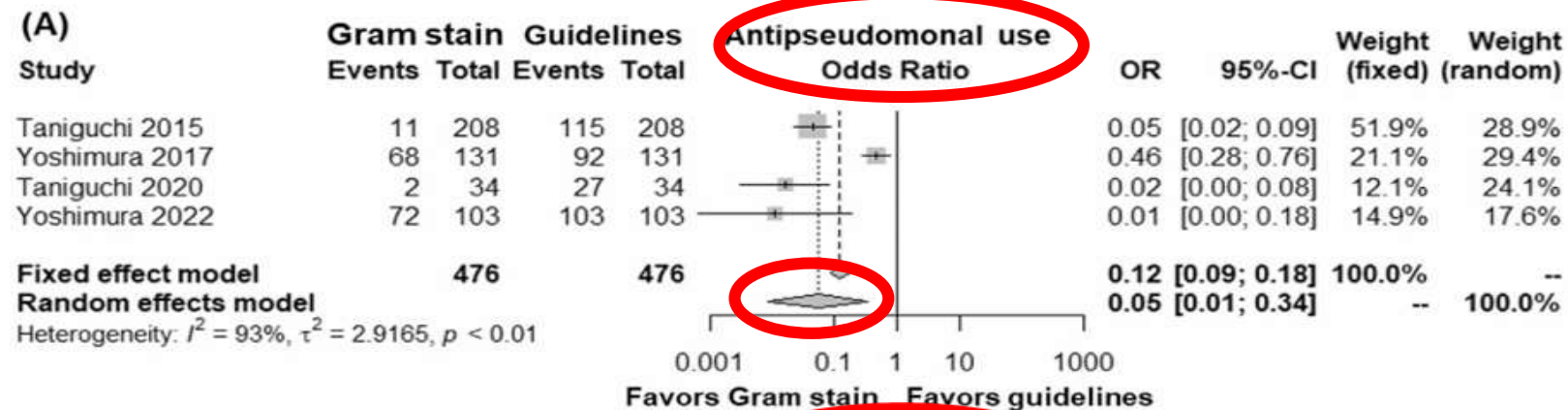
**Fig. 1. PRISMA Flowchart of Search Results Summarizing the Study Selection Process.** NA, not applicable; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

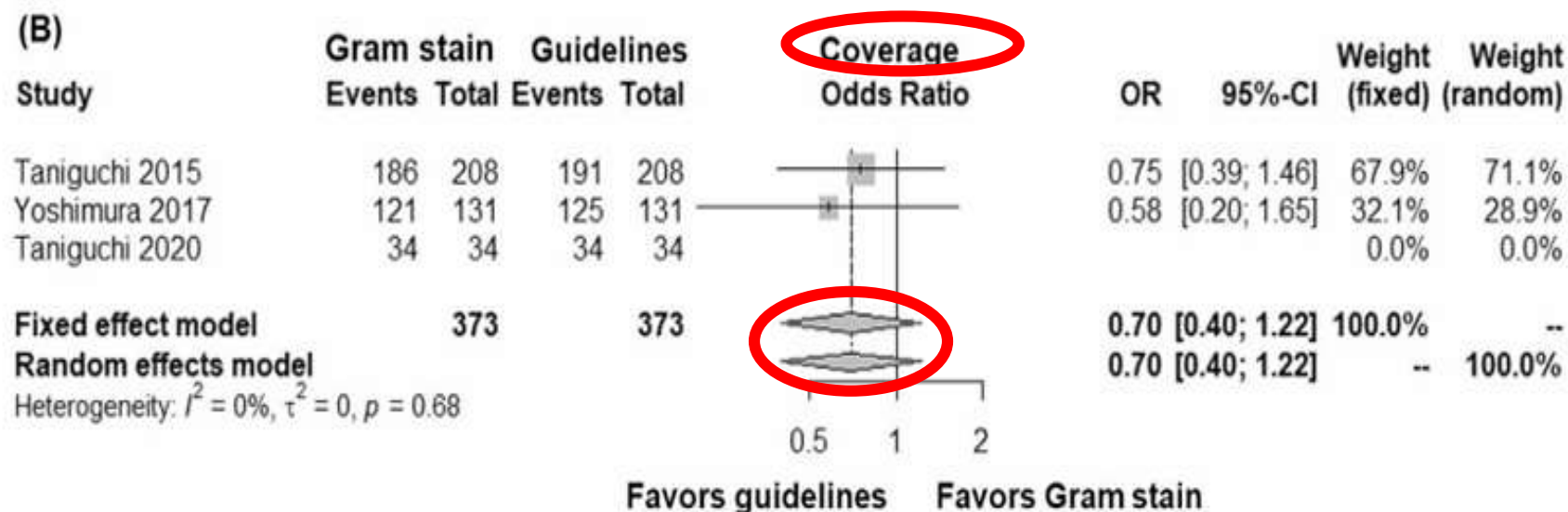
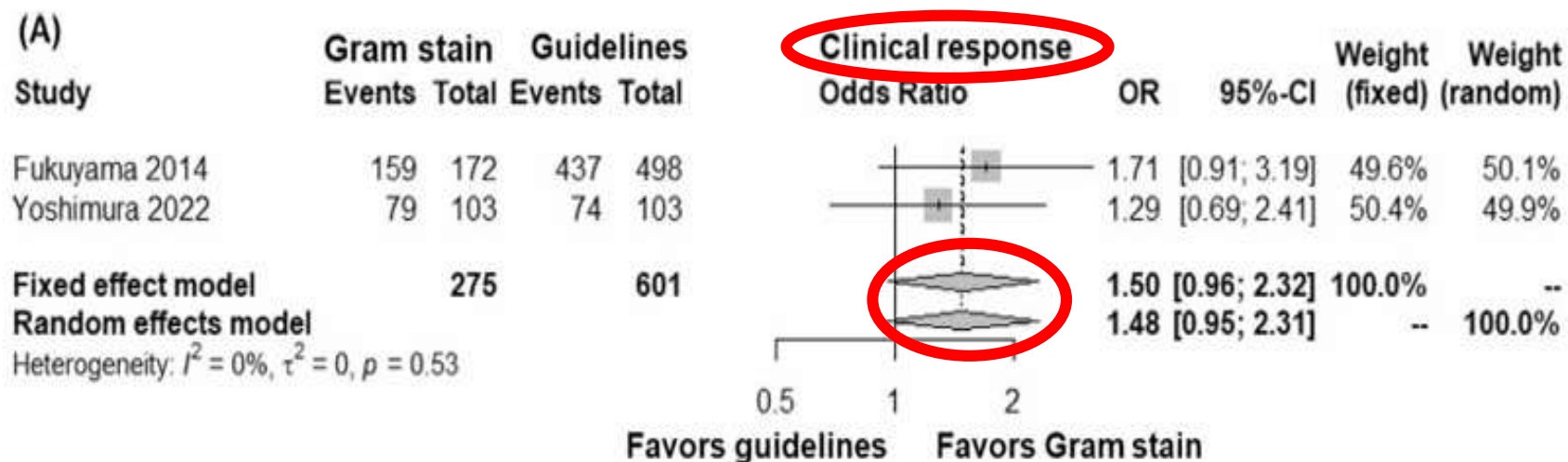
# The role of gram stain in reducing broad-spectrum antibiotic use: A systematic literature review and meta-analysis

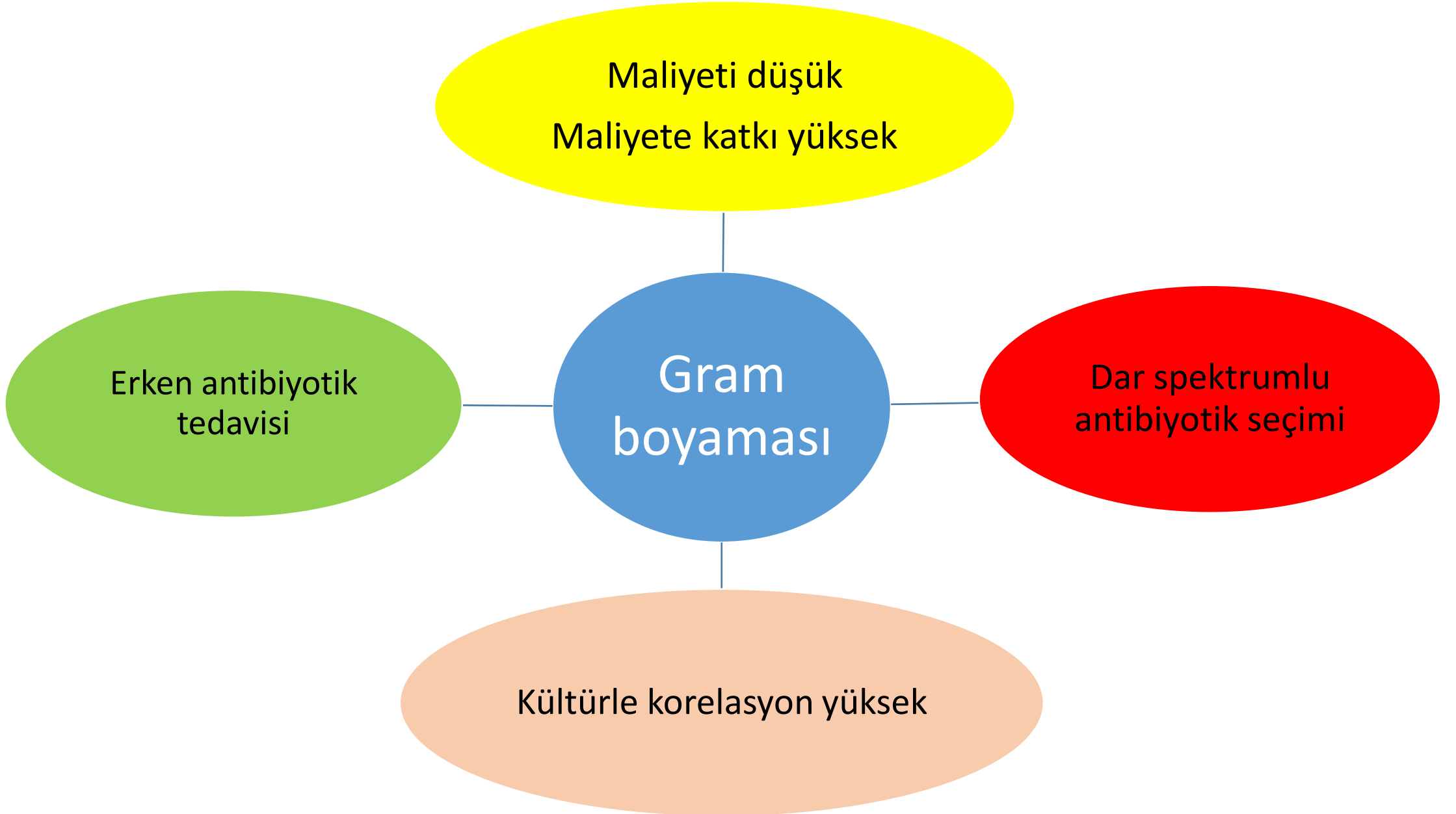


Description of studies included in the systematic review.

| Reference                      | Country | Patient population and size                                                                                   | Study setting                             | Study design and period                                                                          | Infection site                                                 | Exposure (intervention) vs. comparison                                                                                                |
|--------------------------------|---------|---------------------------------------------------------------------------------------------------------------|-------------------------------------------|--------------------------------------------------------------------------------------------------|----------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------|
| <b>Fukuyama et al. (2014)</b>  | Japan   | Adult hospitalized patients with pneumonia (n = 670)                                                          | A tertiary care hospital                  | A single-center, prospective observational study (August 2010–July 2012)                         | Pneumonia (both CAP and HCAP)                                  | Sputum Gram stain-guided antibiotic therapy (n = 172) vs. JRS guidelines-guided antibiotic therapy (n = 498)                          |
| <b>Taniguchi et al. (2015)</b> | Japan   | Adult hospitalized patients with suspected bacterial infection (n = 208)                                      | A tertiary care hospital                  | A single-center, prospective descriptive study (May 2013–April 2014)                             | Suspected respiratory, urinary tract, or soft tissue infection | Sputum, urine, or blood Gram stain-guided antibiotic therapy (n = 208) vs. JAID/JSC guidelines-guided antibiotic therapy (n = 208)    |
| <b>Yoshimura et al. (2017)</b> | Japan   | Adult hospitalized patients in the ICU with microbiologically confirmed VAP (n = 131)                         | A tertiary care hospital with 18 ICU beds | A single-center, retrospective observational study (February 2013–February 2016)                 | VAP                                                            | Endotracheal aspirate Gram stain-guided antibiotic therapy (n = 131) vs. ATS/IDSA guidelines-guided antibiotic therapy (n = 131)      |
| <b>Taniguchi et al. (2020)</b> | Japan   | Adult hospitalized patients with bacterial meningitis (n = 34)                                                | A tertiary care hospital                  | A single-center, retrospective observational study (January 1995–January 2015)                   | Meningitis                                                     | CSF Gram stain-guided antibiotic therapy (n = 34) vs. Japanese guidelines for bacterial meningitis-guided antibiotic therapy (n = 34) |
| <b>Yoshimura et al. (2022)</b> | Japan   | Adult hospitalized patients with VAP with a modified Clinical Pulmonary Infection Score of $\geq 5$ (n = 206) | ICUs of 12 tertiary referral hospitals    | A multicenter, open-label, noninferiority randomized clinical trial (April 1, 2018–May 31, 2020) | VAP                                                            | Endotracheal aspirate Gram stain-guided antibiotic therapy (n = 103) vs. ATS/IDSA guidelines-guided antibiotic therapy (n = 103)      |







# RAST

## Hızlı Antibiyotik Duyarlılık Testleri

# EUCAST RAST

European Committee on Antimicrobial Susceptibility Testing

## Zone diameter breakpoints for rapid antimicrobial susceptibility testing (RAST) directly from blood culture bottles

Version 1.0, valid from 2018-11-28

This document should be cited as "The European Committee on Antimicrobial Susceptibility Testing. Zone diameter breakpoints for rapid antimicrobial susceptibility testing (RAST) directly from blood culture bottles. Version 1.0, 2018. <http://www.eucast.org>."

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| <i>Enterococcus faecalis</i>                      | 10   |                        |
| <i>Enterococcus faecium</i>                       | 11   |                        |
| <i>Streptococcus pneumoniae</i>                   | 12   |                        |

**4. / 6. / 8. saat**

European Committee on Antimicrobial Susceptibility Testing

## Zone diameter breakpoint tables for rapid antimicrobial susceptibility testing (RAST) directly from blood culture bottles

Version 5.1, valid from 2022-05-02

This document should be cited as "The European Committee on Antimicrobial Susceptibility Testing. Zone diameter Breakpoint Tables for rapid antimicrobial susceptibility testing (RAST) directly from blood culture bottles. Version 5.1, 2022. <http://www.eucast.org>."

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| <i>Klebsiella pneumoniae</i>                      | 7    | Breakpoints for 4, 6, 8 and 16-20 h |
| <i>Pseudomonas aeruginosa</i>                     | 8    | Breakpoints for 6, 8 and 16-20 h    |
| <i>Acinetobacter baumannii</i>                    | 9    | Breakpoints for 4, 6 and 8 h        |
| <i>Staphylococcus aureus</i>                      | 10   | Breakpoints for 4, 6, 8 and 16-20 h |
| <i>Enterococcus faecalis</i>                      | 11   | Breakpoints for 4, 6 and 8 h        |
| <i>Enterococcus faecium</i>                       | 12   | Breakpoints for 4, 6 and 8 h        |
| <i>Streptococcus pneumoniae</i>                   | 13   | Breakpoints for 4, 6, 8 and 16-20 h |

**16. - 20. saat**

# EUCAST RAST

European Committee on Antimicrobial Susceptibility Testing

## Zone diameter breakpoint tables for rapid antimicrobial susceptibility testing (RAST) directly from blood culture bottles

Version 8.0, valid from 2025-03-18

**This document should be cited as** "The European Committee on Antimicrobial Susceptibility Testing. Zone diameter Breakpoint Tables for rapid antimicrobial susceptibility testing (RAST) directly from blood culture bottles. Version 8.0, 2025. <http://www.eucast.org>."

The RAST Breakpoint Tables are updated each year after the EUCAST standard Breakpoint Tables have been updated.

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| <a href="#">Staphylococcus aureus</a>                             | 11   | Breakpoints for 4, 6, 8 and 16-20 h |
| <a href="#">Enterococcus faecalis</a>                             | 12   | Breakpoints for 4, 6, 8 and 16-20 h |
| <a href="#">Enterococcus faecium</a>                              | 13   | Breakpoints for 4, 6, 8 and 16-20 h |
| <a href="#">Streptococcus pneumoniae</a>                          | 14   | Breakpoints for 4, 6, 8 and 16-20 h |

# CLSI RAST

- CLSI S31 / 2021
- Enterobacterales disk duyarlılık sınırları - **8-10 saat**

## CLSI S32 / 2022

- *Pseudomonas* sp ve ek antibiyotiklerin duyarlılık sınırları - **8-10 saat**

## CLSI S34/ 2024

- *Acinetobacter* sp disk duyarlılık sınırları - **8-10 saat**

# EUCAST RAST

- Pozitifleşen kan kültürlerine 0-18 saat içinde uygulanabilir.
- Otomatize sistemden çıkarıldıktan sonra hemen, en geç 3 saat içinde uygulanmalı
- Kan kültürü şişesine herhangi bir işlem yapılmadan  $125 \pm 25$  µl alınır, 90 mm Mueller Hinton agara yayılır
- Her bir plak agara maksimum 4-6 antibiyotik diski yerleştirilir
- 4., 6. ve 8. saatlerden sonra tekrar inkübe edilecekse her okumada sonra 10 dakika içinde hemen geri yerleştirilmeli

# EUCAST RAST

## *Escherichia coli*

Zone diameter breakpoints for RAST directly from blood culture bottles

| Antimicrobial agent           | Disk content (µg) | 4 hours |         |      | 6 hours |         |      | 8 hours |         |      | 16-20 hours |         |      |
|-------------------------------|-------------------|---------|---------|------|---------|---------|------|---------|---------|------|-------------|---------|------|
|                               |                   | S ≥     | ATU     | R <  | S ≥     | ATU     | R <  | S ≥     | ATU     | R <  | S ≥         | ATU     | R <  |
| Ampicillin                    | 10                | 12      | 10-11   | 10   | 13      | 11-12   | 11   | 13      | 11-12   | 11   | 14          | 12-13   | 12   |
| Amoxicillin-clavulanic acid   | 20-10             | 16      | 14-15   | 14   | 17      | 15-16   | 15   | 17      | 15-16   | 15   | 19          | 17-18   | 17   |
| Piperacillin-tazobactam       | 30-6              | 17      | 14-16   | 14   | 18      | 15-17   | 15   | 18      | 15-17   | 15   | 17          | 15-16   | 15   |
| Temocillin                    | 30                | 50      | 13-14   | 13   | 50      | 15-16   | 15   | 50      | 15-16   | 15   | 50          | 17-18   | 17   |
| Cefotaxime <sup>1</sup>       | 5                 | 15      | 13-14   | 13   | 16      | 14-15   | 14   | 17      | 15-16   | 15   | 16          | 14-15   | 14   |
| Ceftazidime <sup>1</sup>      | 10                | 15      | 12-14   | 12   | 16      | 14-15   | 14   | 17      | 15-16   | 15   | 17          | 15-16   | 15   |
| Ceftazidime-avibactam         | 10-4              | 12      | 10-11   | 10   | 12      | 10-11   | 10   | 12      | 10-11   | 10   | 13          | 11-12   | 11   |
| Ceftolozane-tazobactam        | 30-10             | 16      | 14-15   | 14   | 18      | 16-17   | 16   | 18      | 16-17   | 16   | 20          | 16-19   | 16   |
| Imipenem <sup>2</sup>         | 10                | 16      | 12-15   | 12   | 17      | 13-16   | 13   | 17      | 13-16   | 13   | 17          | 12-16   | 12   |
| Imipenem-relebactam           | 10-25             | 13      | 11-12   | 11   | 15      | 13-14   | 13   | 15      | 13-14   | 13   | 17          | 15-16   | 15   |
| Meropenem <sup>2</sup>        | 10                | 17      | 15-16   | 15   | 17      | 15-16   | 15   | 17      | 15-16   | 15   | 15          | 13-14   | 13   |
| Meropenem-vaborbactam         | 20-10             | 16      | 12-15   | 12   | 16      | 14-15   | 14   | 17      | 15-16   | 15   | 16          | 14-15   | 14   |
| Ciprofloxacin                 | 5                 | 17      | 14-16   | 14   | 19      | 16-18   | 16   | 20      | 17-19   | 17   | 21          | 18-20   | 18   |
| Levofloxacin                  | 5                 | 16      | 14-15   | 14   | 18      | 15-17   | 15   | 18      | 15-17   | 15   | 23          | 15-22   | 15   |
| Amikacin <sup>3</sup>         | 30                | (15)    | (13-14) | (13) | (15)    | (13-14) | (13) | (15)    | (13-14) | (13) | (13)        | (11-12) | (11) |
| Gentamicin <sup>3</sup>       | 10                | (14)    | (12-13) | (12) | (14)    | (12-13) | (12) | (14)    | (12-13) | (12) | (13)        | (11-12) | (11) |
| Tobramycin <sup>3</sup>       | 10                | (14)    | (12-13) | (12) | (15)    | (13-14) | (13) | (15)    | (13-14) | (13) | (13)        | (11-12) | (11) |
| Trimethoprim-sulfamethoxazole | 1.25-23.75        | 12      | 10-11   | 10   | 14      | 12-13   | 12   | 14      | 12-13   | 12   | 14          | 12-13   | 12   |

# RAST

- Tanımlanan tüm etkenlerde güvenilir sonuç verir mi?
- Tanımlanan tüm antibiyotiklerde aynı oranda güvenilir sonuç verir mi?

# Test güvenirliliğin değerlendirilmesi

Yeni testle standart test karşılaştırıldığında (FDA):

- Kategorik uyum (CA)  $\geq$  %90
- Çok büyük hata oranı (VME)  $\leq$  % 1.5
  - **Standart test dirençli, RAST duyarlı**
- Büyük hata oranı (ME)  $\leq$  % 3.0
  - **Standart test duyarlı, RAST dirençli**
- Küçük hata oranı (mE)  $<$  % 10
  - **Standart test ara değer, RAST duyarlı/dirençli**

# Fully Automated EUCAST Rapid Antimicrobial Susceptibility Testing (RAST) from Positive Blood Cultures: Diagnostic Accuracy and Implementation

- İsviçre merkezli tam otomatize sistemle disk zonları okunmuş ve RAST sınır değerleri değerlendirilmiş
- 779 suş kan kültürlerine inoküle edilerek
- 539 prospektif ardışık pozitifleşen kan kültür örneklerinden elde edilen suşlar çalışılmış
- Suşların arasında
  - Karbapenemaz üreten Enterobacterales
  - Çoğul dirençli *A. baumannii* ve *P. aeruginosa*
  - Vankomisine dirençli *E. faecalis* ve *E. faecium*
  - Metisilin dirençli, indüklenebilen klindamisin dirençli *S. aureus*

**TAB 3** *Escherichia coli* spiked BC results (n = 207 isolates)<sup>a</sup>

| <i>E. coli</i> spiked BC parameters    | Piperacillin-tazobactam |      |      | Ceftazidime |      |      | Imipenem |      |      | Meropenem |      |      | Ciprofloxacin |      |      | Gentamicin |      |      | Amikacin |      |      | Co-trimoxazole |      |      |
|----------------------------------------|-------------------------|------|------|-------------|------|------|----------|------|------|-----------|------|------|---------------|------|------|------------|------|------|----------|------|------|----------------|------|------|
|                                        | 4 h                     | 6 h  | 8 h  | 4 h         | 6 h  | 8 h  | 4 h      | 6 h  | 8 h  | 4 h       | 6 h  | 8 h  | 4 h           | 6 h  | 8 h  | 4 h        | 6 h  | 8 h  | 4 h      | 6 h  | 8 h  | 4 h            | 6 h  | 8 h  |
| Isolates by category (n)               |                         |      |      |             |      |      |          |      |      |           |      |      |               |      |      |            |      |      |          |      |      |                |      |      |
| Resistant                              | 30                      | 36   | 34   | 8           | 21   | 32   | 6        | 11   | 9    | 7         | 9    | 9    | 56            | 63   | 62   | 24         | 26   | 26   | 33       | 14   | 12   | 69             | 74   | 74   |
| ATU                                    | 81                      | 54   | 51   | 23          | 13   | 7    | 3        | 6    | 7    | 8         | 5    | 4    | 20            | 23   | 16   | 5          | 3    | 2    | 128      | 83   | 54   | 2              | 1    | 2    |
| Susceptible                            | 89                      | 117  | 122  | 169         | 173  | 168  | 191      | 190  | 191  | 185       | 193  | 194  | 124           | 121  | 129  | 171        | 178  | 179  | 39       | 110  | 141  | 129            | 132  | 131  |
| Inhibition zone not readable           | 7                       | 0    | 0    | 7           | 0    | 0    | 7        | 0    | 0    | 7         | 0    | 0    | 7             | 0    | 0    | 7          | 0    | 0    | 7        | 0    | 0    | 7              | 0    | 0    |
| Isolates by category (%)               |                         |      |      |             |      |      |          |      |      |           |      |      |               |      |      |            |      |      |          |      |      |                |      |      |
| Resistant                              | 15.0                    | 17.4 | 16.4 | 4.0         | 10.1 | 15.5 | 3.0      | 5.3  | 4.3  | 3.5       | 4.3  | 4.3  | 28.0          | 30.4 | 30.0 | 12.0       | 12.6 | 12.6 | 16.5     | 6.8  | 5.8  | 34.5           | 35.7 | 35.7 |
| ATU                                    | 40.5                    | 26.1 | 24.6 | 11.5        | 6.3  | 3.4  | 1.5      | 2.9  | 3.4  | 4.0       | 2.4  | 1.9  | 10.0          | 11.1 | 7.7  | 2.5        | 1.4  | 1.0  | 64.0     | 40.1 | 26.1 | 1.0            | 0.5  | 1.0  |
| Susceptible                            | 44.5                    | 56.5 | 58.9 | 84.5        | 83.6 | 81.2 | 95.5     | 91.8 | 92.3 | 92.5      | 93.2 | 93.7 | 62.0          | 58.5 | 62.3 | 85.5       | 86.0 | 86.5 | 19.5     | 53.1 | 68.1 | 64.5           | 63.8 | 63.3 |
| Inhibition zone not readable           | 3.4                     | 0.0  | 0.0  | 3.4         | 0.0  | 0.0  | 3.4      | 0.0  | 0.0  | 3.4       | 0.0  | 0.0  | 3.4           | 0.0  | 0.0  | 3.4        | 0.0  | 0.0  | 3.4      | 0.0  | 0.0  | 3.4            | 0.0  | 0.0  |
| Categorical agreement (%) <sup>b</sup> |                         |      |      |             |      |      |          |      |      |           |      |      |               |      |      |            |      |      |          |      |      |                |      |      |
| ATU included                           | 98.5                    | 98.1 | 98.6 | 98.0        | 98.1 | 98.6 | 100.0    | 99.5 | 99.5 | 99.5      | 99.5 | 99.5 | 99.5          | 99.5 | 99.5 | 99.5       | 98.1 | 98.1 | 94.0     | 98.1 | 97.6 | 98.0           | 97.6 | 97.6 |
| ATU not included                       | 97.5                    | 97.4 | 98.1 | 97.7        | 97.9 | 98.5 | 100.0    | 99.5 | 99.5 | 99.5      | 99.5 | 99.5 | 99.4          | 99.5 | 99.5 | 99.5       | 98.0 | 98.0 | 83.3     | 96.8 | 96.7 | 98.0           | 97.6 | 97.6 |
| Discordant results (n)                 |                         |      |      |             |      |      |          |      |      |           |      |      |               |      |      |            |      |      |          |      |      |                |      |      |
| Minor error                            |                         |      |      | 1           | 1    | 1    |          |      |      |           |      |      |               |      |      |            |      |      |          |      |      |                |      |      |
| Major error                            | 1                       | 2    | 1    |             |      |      |          | 1    | 1    | 1         | 1    | 1    |               | 1    | 1    |            | 1    | 1    | 10       | 1    | 1    | 4              | 5    | 5    |
| Very major error                       | 2                       | 2    | 2    | 3           | 3    | 2    |          |      |      |           |      |      | 1             |      |      | 1          | 3    | 3    | 2        | 3    | 4    |                |      |      |
| Discordant results (%)                 |                         |      |      |             |      |      |          |      |      |           |      |      |               |      |      |            |      |      |          |      |      |                |      |      |
| Minor error                            | 0.0                     | 0.0  | 0.0  | 0.5         | 0.5  | 0.5  | 0.0      | 0.0  | 0.0  | 0.0       | 0.0  | 0.0  | 0.0           | 0.0  | 0.0  | 0.0        | 0.0  | 0.0  | 0.0      | 0.0  | 0.0  | 0.0            | 0.0  | 0.0  |
| Major error                            | 0.5                     | 1.0  | 0.5  | 0.0         | 0.0  | 0.0  | 0.0      | 0.5  | 0.5  | 0.5       | 0.5  | 0.5  | 0.0           | 0.5  | 0.5  | 0.0        | 0.5  | 0.5  | 4.8      | 0.5  | 0.5  | 1.9            | 2.4  | 2.4  |
| Very major error                       | 1.0                     | 1.0  | 1.0  | 1.4         | 1.4  | 1.0  | 0.0      | 0.0  | 0.0  | 0.0       | 0.0  | 0.0  | 0.5           | 0.0  | 0.0  | 0.5        | 1.4  | 1.4  | 1.0      | 1.4  | 1.9  | 0.0            | 0.0  | 0.0  |

**TABLE 5** *Klebsiella pneumoniae* spiked BC results (n = 118 isolates)<sup>a</sup>

| <i>K. pneumoniae</i> spiked BC parameters | Piperacillin-tazobactam |      |      | Ceftazidime |       |       | Imipenem |       |      | Meropenem |      |      | Ciprofloxacin |       |       | Gentamicin |       |      | Amikacin |      |       | Cotrimoxazole |      |      |
|-------------------------------------------|-------------------------|------|------|-------------|-------|-------|----------|-------|------|-----------|------|------|---------------|-------|-------|------------|-------|------|----------|------|-------|---------------|------|------|
|                                           | 4 h                     | 6 h  | 8 h  | 4 h         | 6 h   | 8 h   | 4 h      | 6 h   | 8 h  | 4 h       | 6 h  | 8 h  | 4 h           | 6 h   | 8 h   | 4 h        | 6 h   | 8 h  | 4 h      | 6 h  | 8 h   | 4 h           | 6 h  | 8 h  |
| Isolates by category (n)                  |                         |      |      |             |       |       |          |       |      |           |      |      |               |       |       |            |       |      |          |      |       |               |      |      |
| Resistant                                 | 45                      | 51   | 52   | 46          | 50    | 49    | 27       | 27    | 30   | 24        | 30   | 31   | 41            | 36    | 44    | 29         | 30    | 27   | 23       | 13   | 22    | 43            | 43   | 46   |
| ATU                                       | 23                      | 18   | 15   | 4           | 2     | 3     | 3        | 4     | 1    | 5         | 4    | 3    | 18            | 16    | 9     | 5          | 3     | 6    | 50       | 13   | 27    | 4             | 4    | 1    |
| Susceptible                               | 50                      | 49   | 51   | 68          | 66    | 66    | 88       | 87    | 87   | 89        | 84   | 84   | 59            | 66    | 65    | 84         | 85    | 85   | 45       | 92   | 69    | 71            | 71   | 71   |
| Inhibition zone not readable              | 0                       | 0    | 0    | 0           | 0     | 0     | 0        | 0     | 0    | 0         | 0    | 0    | 0             | 0     | 0     | 0          | 0     | 0    | 0        | 0    | 0     | 0             | 0    | 0    |
| Isolates by category (%)                  |                         |      |      |             |       |       |          |       |      |           |      |      |               |       |       |            |       |      |          |      |       |               |      |      |
| Resistant                                 | 38.1                    | 43.2 | 44.1 | 39.0        | 42.4  | 41.5  | 22.9     | 22.9  | 25.4 | 20.3      | 25.4 | 26.3 | 34.7          | 30.5  | 37.3  | 24.6       | 25.4  | 22.9 | 19.5     | 11.0 | 18.6  | 36.4          | 36.4 | 39.0 |
| ATU                                       | 19.5                    | 15.3 | 12.7 | 3.4         | 1.7   | 2.5   | 2.5      | 3.4   | 0.8  | 4.2       | 3.4  | 2.5  | 15.3          | 13.6  | 7.6   | 4.2        | 2.5   | 5.1  | 42.4     | 11.0 | 22.9  | 3.4           | 3.4  | 0.8  |
| Susceptible                               | 42.4                    | 41.5 | 43.2 | 57.6        | 55.9  | 55.9  | 74.6     | 73.7  | 73.7 | 75.4      | 71.2 | 71.2 | 50.0          | 55.9  | 55.1  | 71.2       | 72.0  | 72.0 | 38.1     | 78.0 | 58.5  | 60.2          | 60.2 | 60.2 |
| Inhibition zone not readable              | 0.0                     | 0.0  | 0.0  | 0.0         | 0.0   | 0.0   | 0.0      | 0.0   | 0.0  | 0.0       | 0.0  | 0.0  | 0.0           | 0.0   | 0.0   | 0.0        | 0.0   | 0.0  | 0.0      | 0.0  | 0.0   | 0.0           | 0.0  | 0.0  |
| Categorical agreement (%) <sup>b</sup>    |                         |      |      |             |       |       |          |       |      |           |      |      |               |       |       |            |       |      |          |      |       |               |      |      |
| ATU included                              | 96.6                    | 96.6 | 96.6 | 100.0       | 100.0 | 100.0 | 100.0    | 100.0 | 99.2 | 99.2      | 99.2 | 98.3 | 100.0         | 100.0 | 100.0 | 99.2       | 100.0 | 99.2 | 99.2     | 95.8 | 100.0 | 98.3          | 98.3 | 98.3 |
| ATU not included                          | 95.8                    | 96.0 | 96.1 | 100.0       | 100.0 | 100.0 | 100.0    | 100.0 | 99.1 | 99.1      | 99.1 | 98.3 | 100.0         | 100.0 | 100.0 | 99.1       | 100.0 | 99.1 | 98.5     | 95.2 | 100.0 | 98.2          | 98.2 | 98.2 |
| Discordant results (n)                    |                         |      |      |             |       |       |          |       |      |           |      |      |               |       |       |            |       |      |          |      |       |               |      |      |
| Major error                               |                         |      |      |             |       |       |          |       | 1    | 1         | 1    | 2    |               |       |       |            |       | 1    |          |      | 1     | 1             | 1    |      |
| Very major error                          | 4                       | 4    | 4    |             |       |       |          |       |      |           |      |      |               |       |       | 1          |       | 1    |          | 5    |       | 1             | 1    | 1    |
| Discordant results (%)                    |                         |      |      |             |       |       |          |       |      |           |      |      |               |       |       |            |       |      |          |      |       |               |      |      |
| Major error                               | 0.0                     | 0.0  | 0.0  | 0.0         | 0.0   | 0.0   | 0.0      | 0.0   | 0.8  | 0.8       | 0.8  | 1.7  | 0.0           | 0.0   | 0.0   | 0.0        | 0.0   | 0.0  | 0.8      | 0.0  | 0.0   | 0.8           | 0.8  | 0.8  |
| Very major error                          | 3.4                     | 3.4  | 3.4  | 0.0         | 0.0   | 0.0   | 0.0      | 0.0   | 0.0  | 0.0       | 0.0  | 0.0  | 0.0           | 0.0   | 0.0   | 0.8        | 0.0   | 0.8  | 0.0      | 4.2  | 0.0   | 0.8           | 0.8  | 0.8  |

**TABLE 7** *Acinetobacter baumannii* spiked BC results (*n* = 63 isolates)<sup>a</sup>

| <i>A. baumannii</i> spiked BC parameters | Imipenem |       |       | Meropenem |       |       | Ciprofloxacin <sup>c</sup> |       |       | Levofloxacin |       |       | Gentamicin |       |       | Amikacin |      |      | Cotrimoxazole |      |      |
|------------------------------------------|----------|-------|-------|-----------|-------|-------|----------------------------|-------|-------|--------------|-------|-------|------------|-------|-------|----------|------|------|---------------|------|------|
|                                          | 4 h      | 6 h   | 8 h   | 4 h       | 6 h   | 8 h   | 4 h                        | 6 h   | 8 h   | 4 h          | 6 h   | 8 h   | 4 h        | 6 h   | 8 h   | 4 h      | 6 h  | 8 h  | 4 h           | 6 h  | 8 h  |
| Isolates by category ( <i>n</i> )        |          |       |       |           |       |       |                            |       |       |              |       |       |            |       |       |          |      |      |               |      |      |
| Resistant                                | 48       | 50    | 50    | 46        | 50    | 50    | 47                         | 49    | 48    | 47           | 48    | 48    | 47         | 49    | 50    | 26       | 33   | 33   |               | 43   | 44   |
| ATU                                      | 1        | 1     | 1     | 5         | 2     |       | 3                          | 2     | 1     | 3            | 3     | 4     | 4          | 2     | 1     | 35       | 12   | 12   | 48            | 4    | 4    |
| Susceptible                              | 12       | 12    | 12    | 10        | 11    | 13    | 11                         | 12    | 14    | 11           | 12    | 11    | 10         | 12    | 12    | 18       | 18   | 13   | 16            | 15   |      |
| Inhibition zone not readable             | 2        | 0     | 0     | 2         | 0     | 0     | 2                          | 0     | 0     | 2            | 0     | 0     | 2          | 0     | 0     | 2        | 0    | 0    | 2             | 0    | 0    |
| Isolates by category (%)                 |          |       |       |           |       |       |                            |       |       |              |       |       |            |       |       |          |      |      |               |      |      |
| Resistant                                | 78.7     | 79.4  | 79.4  | 75.4      | 79.4  | 79.4  | 77.0                       | 77.8  | 76.2  | 77.0         | 76.2  | 76.2  | 77.0       | 77.8  | 79.4  | 42.6     | 52.4 | 52.4 | 0.0           | 68.3 | 69.8 |
| ATU                                      | 1.6      | 1.6   | 1.6   | 8.2       | 3.2   | 0.0   | 4.9                        | 3.2   | 1.6   | 4.9          | 4.8   | 6.3   | 6.6        | 3.2   | 1.6   | 57.4     | 19.0 | 19.0 | 78.7          | 6.3  | 6.3  |
| Susceptible                              | 19.7     | 19.0  | 19.0  | 16.4      | 17.5  | 20.6  | 18.0                       | 19.0  | 22.2  | 18.0         | 19.0  | 17.5  | 16.4       | 19.0  | 19.0  | 0.0      | 28.6 | 28.6 | 21.3          | 25.4 | 23.8 |
| Inhibition zone not readable             | 3.2      | 0.0   | 0.0   | 3.2       | 0.0   | 0.0   | 3.2                        | 0.0   | 0.0   | 3.2          | 0.0   | 0.0   | 3.2        | 0.0   | 0.0   | 3.2      | 0.0  | 0.0  | 3.2           | 0.0  | 0.0  |
| Categorical agreement (%) <sup>b</sup>   |          |       |       |           |       |       |                            |       |       |              |       |       |            |       |       |          |      |      |               |      |      |
| ATU included                             | 100.0    | 100.0 | 100.0 | 100.0     | 100.0 | 100.0 | 100.0                      | 100.0 | 100.0 | 100.0        | 100.0 | 100.0 | 100.0      | 100.0 | 100.0 | 98.4     | 98.4 | 98.4 | 98.4          | 98.4 | 98.4 |
| ATU not included                         | 100.0    | 100.0 | 100.0 | 100.0     | 100.0 | 100.0 | 100.0                      | 100.0 | 100.0 | 100.0        | 100.0 | 100.0 | 100.0      | 100.0 | 100.0 | 96.2     | 98.0 | 98.0 | 92.3          | 98.3 | 98.3 |
| Discordant results ( <i>n</i> )          |          |       |       |           |       |       |                            |       |       |              |       |       |            |       |       |          |      |      |               |      |      |
| Major error                              |          |       |       |           |       |       |                            |       |       |              |       |       |            |       |       |          |      |      |               |      |      |
| Very major error                         |          |       |       |           |       |       |                            |       |       |              |       |       |            |       |       | 1        | 1    | 1    | 1             | 1    | 1    |
| Discordant results (%)                   |          |       |       |           |       |       |                            |       |       |              |       |       |            |       |       |          |      |      |               |      |      |
| Major error                              | 0.0      | 0.0   | 0.0   | 0.0       | 0.0   | 0.0   | 0.0                        | 0.0   | 0.0   | 0.0          | 0.0   | 0.0   | 0.0        | 0.0   | 0.0   | 0.0      | 0.0  | 0.0  | 0.0           | 0.0  | 0.0  |
| Very major error                         | 0.0      | 0.0   | 0.0   | 0.0       | 0.0   | 0.0   | 0.0                        | 0.0   | 0.0   | 0.0          | 0.0   | 0.0   | 0.0        | 0.0   | 0.0   | 1.6      | 1.6  | 1.6  | 1.6           | 1.6  | 1.6  |

**TABLE 8** *Pseudomonas aeruginosa* spiked BC results (*n* = 129 isolates)<sup>a</sup>

| <i>P. aeruginosa</i> results           | Piperacillin-tazobactam <sup>b</sup> |      | Ceftazidime <sup>b</sup> |      | Cefepime <sup>b</sup> |      | Imipenem <sup>b</sup> |      | Meropenem |      | Ciprofloxacin <sup>b</sup> |      | Levofloxacin |      | Amikacin |      | Tobramycin |      |
|----------------------------------------|--------------------------------------|------|--------------------------|------|-----------------------|------|-----------------------|------|-----------|------|----------------------------|------|--------------|------|----------|------|------------|------|
|                                        | 6 h                                  | 8 h  | 6 h                      | 8 h  | 6 h                   | 8 h  | 6 h                   | 8 h  | 6 h       | 8 h  | 6 h                        | 8 h  | 6 h          | 8 h  | 6 h      | 8 h  | 6 h        | 8 h  |
| Isolates by category ( <i>n</i> )      |                                      |      |                          |      |                       |      |                       |      |           |      |                            |      |              |      |          |      |            |      |
| Resistant                              | 20                                   | 17   | 13                       | 13   | 37                    | 13   | 11                    | 16   | 10        | 8    | 7                          | 10   | 15           | 16   | 13       | 6    | 3          | 2    |
| ATU                                    | 43                                   | 37   | 38                       | 23   | 42                    | 25   | 5                     | 6    | 9         | 9    | 8                          | 10   | 8            | 12   | 17       | 15   | 3          | 6    |
| Susceptible                            | 62                                   | 75   | 74                       | 93   | 46                    | 91   | 109                   | 107  | 106       | 112  | 110                        | 109  | 102          | 101  | 95       | 108  | 119        | 121  |
| Inhibition zone not readable           | 4                                    | 0    | 4                        | 0    | 4                     | 0    | 4                     | 0    | 4         | 0    | 4                          | 0    | 4            | 0    | 4        | 0    | 4          | 0    |
| Isolates by category (%)               |                                      |      |                          |      |                       |      |                       |      |           |      |                            |      |              |      |          |      |            |      |
| Resistant                              | 16.0                                 | 13.2 | 10.4                     | 10.1 | 29.6                  | 10.1 | 8.8                   | 12.4 | 8.0       | 6.2  | 5.6                        | 7.8  | 12.0         | 12.4 | 10.4     | 4.7  | 2.4        | 1.6  |
| ATU                                    | 34.4                                 | 28.7 | 30.4                     | 17.8 | 33.6                  | 19.4 | 4.0                   | 4.7  | 7.2       | 7.0  | 6.4                        | 7.8  | 6.4          | 9.3  | 13.6     | 11.6 | 2.4        | 4.7  |
| Susceptible                            | 49.6                                 | 58.1 | 59.2                     | 72.1 | 36.8                  | 70.5 | 87.2                  | 82.9 | 84.8      | 86.8 | 88.0                       | 84.5 | 81.6         | 78.3 | 76.0     | 83.7 | 95.2       | 93.8 |
| Inhibition zone not readable           | 3.1                                  | 0.0  | 3.1                      | 0.0  | 3.1                   | 0.0  | 3.1                   | 0.0  | 3.1       | 0.0  | 3.1                        | 0.0  | 3.1          | 0.0  | 3.1      | 0.0  | 3.1        | 0.0  |
| Categorical agreement (%) <sup>c</sup> |                                      |      |                          |      |                       |      |                       |      |           |      |                            |      |              |      |          |      |            |      |
| ATU included                           | 96.0                                 | 98.4 | 93.6                     | 96.1 | 80.8                  | 97.7 | 92.8                  | 89.9 | 98.4      | 99.2 | 97.6                       | 96.9 | 98.4         | 98.4 | 98.4     | 99.2 | 98.4       | 98.4 |
| ATU not included                       | 93.9                                 | 97.8 | 90.8                     | 95.3 | 71.1                  | 97.1 | 92.5                  | 89.4 | 98.3      | 99.2 | 97.4                       | 96.6 | 98.3         | 98.3 | 98.1     | 99.1 | 98.4       | 98.4 |
| Discordant results ( <i>n</i> )        |                                      |      |                          |      |                       |      |                       |      |           |      |                            |      |              |      |          |      |            |      |
| Major error                            | 5                                    | 1    | 6                        | 4    | 24                    | 2    | 4                     | 9    | 2         | 1    | 1                          | 2    | 1            | 1    | 2        | 1    |            |      |
| Very major error                       |                                      | 1    | 2                        | 1    |                       | 1    | 5                     | 4    |           |      | 2                          | 2    | 1            | 1    |          |      | 2          | 2    |
| Discordant results (%)                 |                                      |      |                          |      |                       |      |                       |      |           |      |                            |      |              |      |          |      |            |      |
| Major error                            | 3.9                                  | 0.8  | 4.7                      | 3.1  | 18.6                  | 1.6  | 3.1                   | 7.0  | 1.6       | 0.8  | 0.8                        | 1.6  | 0.8          | 0.8  | 1.6      | 0.8  | 0.0        | 0.0  |
| Very major error                       | 0.0                                  | 0.8  | 1.6                      | 0.8  | 0.0                   | 0.8  | 3.9                   | 3.1  | 0.0       | 0.0  | 1.6                        | 1.6  | 0.8          | 0.8  | 0.0      | 0.0  | 1.6        | 1.6  |

# RAST

- ESBL'yi gösterebilir mi?
- Karbapenemaz varlığını gösterebilir mi?

# **Screening** for ESBL and carbapenemases in *Escherichia coli*, *Klebsiella pneumoniae* and *Salmonella enterica* for epidemiological purposes as part of the RAST procedure.

**EUCAST Guidelines for detection of resistance mechanisms and specific resistance of clinical and/or epidemiological importance using EUCAST rapid antimicrobial susceptibility testing (RAST) directly from positive blood culture bottles.**

**Version 3.0  
March 2025**

**Table 1. Screening cut-off values (mm) for ESBL-producing *E. coli*, *K. pneumoniae* and *S. enterica*.**

| Species              | Antimicrobial agent | Conduct ESBL testing if |         |         |             |
|----------------------|---------------------|-------------------------|---------|---------|-------------|
|                      |                     | 4 hours                 | 6 hours | 8 hours | 16-20 hours |
| <i>E. coli</i>       | Cefotaxime 5 µg     | <15                     | <16     | <17     | <16         |
|                      | Ceftazidime 10 µg   | <15                     | <16     | <17     | <17         |
| <i>K. pneumoniae</i> | Cefotaxime 5 µg     | <15                     | <18     | <18     | <16         |
|                      | Ceftazidime 10 µg   | <15                     | <16     | <16     | <18         |
| <i>S. enterica</i>   | Cefotaxime 5 µg     | <13                     | <14     | <14     | <14         |
|                      | Ceftazidime 10 µg   | <12                     | <16     | <17     | <18         |

**TABLE 1** Phenotypes of the bacterial isolates analyzed in the spiked BCs phase<sup>a</sup>

| Phenotype (n)                    | Species        |                      |                      |                     |                  |                    |                   |
|----------------------------------|----------------|----------------------|----------------------|---------------------|------------------|--------------------|-------------------|
|                                  | <i>E. coli</i> | <i>K. pneumoniae</i> | <i>P. aeruginosa</i> | <i>A. baumannii</i> | <i>S. aureus</i> | <i>E. faecalis</i> | <i>E. faecium</i> |
| ESBL                             | 51             | 50                   |                      |                     |                  |                    |                   |
| OXA-23-like producers            |                |                      |                      | 27                  |                  |                    |                   |
| OXA-48-like producers            | 3              | 7                    |                      |                     |                  |                    |                   |
| OXA-58-like producers            | 1              |                      |                      | 2                   |                  |                    |                   |
| OXA-181-like producers           | 10             | 1                    |                      |                     |                  |                    |                   |
| KPC-like producers               | 1              | 12                   |                      |                     |                  |                    |                   |
| NDM-like producers               | 2              | 13                   |                      | 7                   |                  |                    |                   |
| VIM-like producers               |                |                      | 2                    |                     |                  |                    |                   |
| MRSA                             |                |                      |                      |                     | 17               |                    |                   |
| Inducible clindamycin resistance |                |                      |                      |                     | 47               |                    |                   |
| VanA producers <sup>b</sup>      |                |                      |                      |                     |                  | 6                  | 14                |
| VanB producers <sup>c</sup>      |                |                      |                      |                     |                  |                    | 9                 |
| High-level gentamicin resistance |                |                      |                      |                     |                  | 16                 | 20                |
| Total <sup>d</sup>               | 207            | 118                  | 129                  | 63                  | 148              | 66                 | 48                |

**TABLE 2** Independent positive BC broken down by species and phenotype<sup>a</sup>

| Phenotype (n)                    | Species        |                      |                      |                     |                  |                    |                   |
|----------------------------------|----------------|----------------------|----------------------|---------------------|------------------|--------------------|-------------------|
|                                  | <i>E. coli</i> | <i>K. pneumoniae</i> | <i>P. aeruginosa</i> | <i>A. baumannii</i> | <i>S. aureus</i> | <i>E. faecalis</i> | <i>E. faecium</i> |
| Isolates                         | 198            | 80                   | 12                   | 2                   | 122              | 46                 | 40                |
| ESBL                             | 18             | 3                    |                      |                     |                  |                    |                   |
| OXA-48-like producers            |                | 1                    |                      |                     |                  |                    |                   |
| MRSA                             |                |                      |                      |                     | 3                |                    |                   |
| Inducible clindamycin resistance |                |                      |                      |                     | 2                |                    |                   |
| VanB producers <sup>b</sup>      |                |                      |                      |                     |                  |                    | 1                 |
| High-level gentamicin resistance |                |                      |                      |                     |                  | 4                  | 3                 |
| Total <sup>c</sup>               | 216            | 83                   | 12                   | 2                   | 127              | 50                 | 44                |

# RAST- ESBL tarama

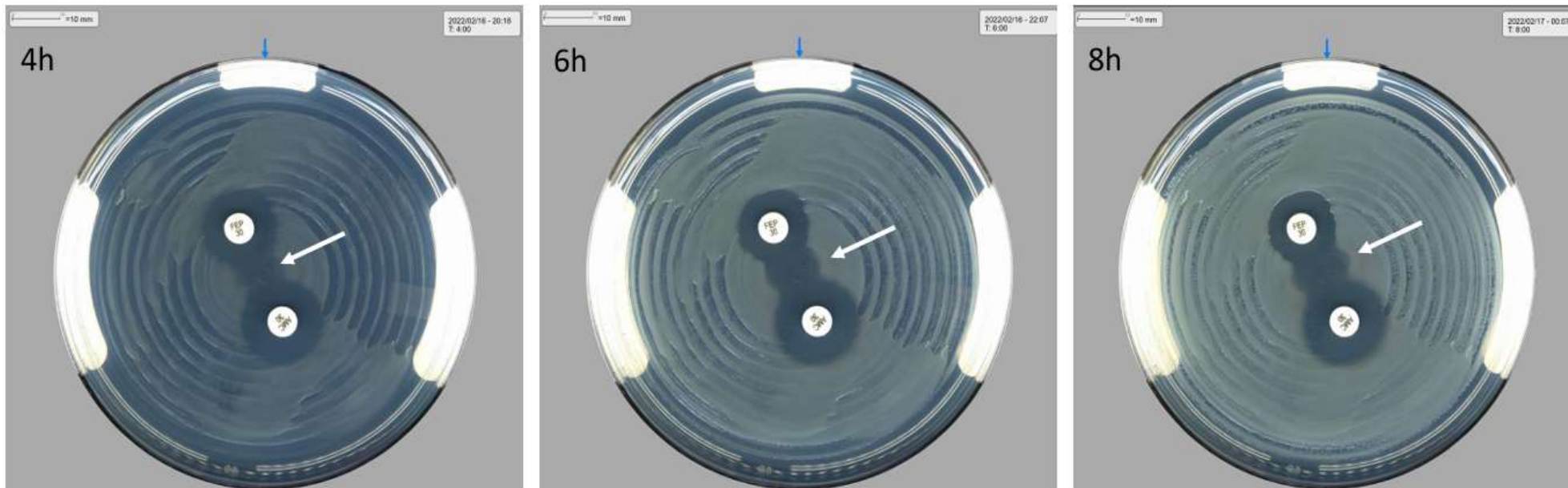
- *K.pneumoniae*
  - Standart yöntemle sefotaksim/seftazidime dirençli
  - RAST ile tümü sefotaksim/seftazidime dirençli / ATU
- *E. coli*
  - Standart yöntemle sefotaksim/seftazidim dirençli
  - RAST - 3 suş **seftazidim** duyarlı (**çok büyük hata**)
  - RAST - Sefotaksimde tümü dirençli/ATU

# RAST- ESBL doğrulama

ESBL-producing *E. coli* and *K. pneumoniae*

DDS<sub>20mm</sub> Test performances for the **122 ESBL** isolates analyzed

**Results :** 67% POS at 4h and 100% POS at 6h



The inhibition zone around FEP disks is enhanced, highly suggesting the production of ESBL (white arrow)

# Screening for ESBL and carbapenemases in *Escherichia coli*, *Klebsiella pneumoniae* and *Salmonella enterica* for epidemiological purposes as part of the RAST procedure.

EUCAST Guidelines for detection of resistance mechanisms and specific resistance of clinical and/or epidemiological importance using EUCAST rapid antimicrobial susceptibility testing (RAST) directly from positive blood culture bottles.

**Version 3.0**  
**March 2025**

Table 2. Screening cut-off values (mm) for carbapenemase-producing *E. coli* and *K. pneumoniae*.

| Species              | Antimicrobial agent | Screening cut-off |         |         |             |
|----------------------|---------------------|-------------------|---------|---------|-------------|
|                      |                     | 4 hours           | 6 hours | 8 hours | 16-20 hours |
| <i>E. coli</i>       | Meropenem 10 µg     | -                 | <20     | <20     | <20         |
| <i>K. pneumoniae</i> | Meropenem 10 µg     | -                 | <18     | <18     | <20         |

# RAST- Karbapenemaz tarama

**TABLE 3** *Escherichia coli* spiked BC results (n = 207 isolates)<sup>a</sup>

| <i>E. coli</i> spiked BC parameters    | Piperacillin-tazobactam |      |      | Ceftazidime |      |      | Imipenem |      |      | Meropenem |      |      |
|----------------------------------------|-------------------------|------|------|-------------|------|------|----------|------|------|-----------|------|------|
|                                        | 4 h                     | 6 h  | 8 h  | 4 h         | 6 h  | 8 h  | 4 h      | 6 h  | 8 h  | 4 h       | 6 h  | 8 h  |
| Isolates by category (n)               |                         |      |      |             |      |      |          |      |      |           |      |      |
| Resistant                              | 30                      | 36   | 34   | 8           | 21   | 32   | 6        | 11   | 9    | 7         | 9    | 9    |
| ATU                                    | 81                      | 54   | 51   | 23          | 13   | 7    | 3        | 6    | 7    | 8         | 5    | 4    |
| Susceptible                            | 89                      | 117  | 122  | 169         | 173  | 168  | 191      | 190  | 191  | 185       | 193  | 194  |
| Inhibition zone not readable           | 7                       | 0    | 0    | 7           | 0    | 0    | 7        | 0    | 0    | 7         | 0    | 0    |
| Isolates by category (%)               |                         |      |      |             |      |      |          |      |      |           |      |      |
| Resistant                              | 15.0                    | 17.4 | 16.4 | 4.0         | 10.1 | 15.5 | 3.0      | 5.3  | 4.3  | 3.5       | 4.3  | 4.3  |
| ATU                                    | 40.5                    | 26.1 | 24.6 | 11.5        | 6.3  | 3.4  | 1.5      | 2.9  | 3.4  | 4.0       | 2.4  | 1.9  |
| Susceptible                            | 44.5                    | 56.5 | 58.9 | 84.5        | 83.6 | 81.2 | 95.5     | 91.8 | 92.3 | 92.5      | 93.2 | 93.7 |
| Inhibition zone not readable           | 3.4                     | 0.0  | 0.0  | 3.4         | 0.0  | 0.0  | 3.4      | 0.0  | 0.0  | 3.4       | 0.0  | 0.0  |
| Categorical agreement (%) <sup>b</sup> |                         |      |      |             |      |      |          |      |      |           |      |      |
| ATU included                           | 98.5                    | 98.1 | 98.6 | 98.0        | 98.1 | 98.6 | 100.0    | 99.5 | 99.5 | 99.5      | 99.5 | 99.5 |
| ATU not included                       | 97.5                    | 97.4 | 98.1 | 97.7        | 97.9 | 98.5 | 100.0    | 99.5 | 99.5 | 99.5      | 99.5 | 99.5 |
| Discordant results (n)                 |                         |      |      |             |      |      |          |      |      |           |      |      |
| Minor error                            |                         |      |      | 1           | 1    | 1    |          |      |      | 1         | 1    | 1    |
| Major error                            | 1                       | 2    | 1    |             |      |      |          | 1    | 1    |           |      |      |
| Very major error                       | 2                       | 2    | 2    | 3           | 3    | 2    |          |      |      |           |      |      |
| Discordant results (%)                 |                         |      |      |             |      |      |          |      |      |           |      |      |
| Minor error                            | 0.0                     | 0.0  | 0.0  | 0.5         | 0.5  | 0.5  | 0.0      | 0.0  | 0.0  | 0.0       | 0.0  | 0.0  |
| Major error                            | 0.5                     | 1.0  | 0.5  | 0.0         | 0.0  | 0.0  | 0.0      | 0.5  | 0.5  | 0.5       | 0.5  | 0.5  |
| Very major error                       | 1.0                     | 1.0  | 1.0  | 1.4         | 1.4  | 1.0  | 0.0      | 0.0  | 0.0  | 0.0       | 0.0  | 0.0  |

**TABLE 5** *Klebsiella pneumoniae* spiked BC results (n = 118 isolates)<sup>a</sup>

| <i>K. pneumoniae</i> spiked BC parameters | Piperacillin-tazobactam |      |      | Ceftazidime |       |       | Imipenem |       |      | Meropenem |      |      |
|-------------------------------------------|-------------------------|------|------|-------------|-------|-------|----------|-------|------|-----------|------|------|
|                                           | 4 h                     | 6 h  | 8 h  | 4 h         | 6 h   | 8 h   | 4 h      | 6 h   | 8 h  | 4 h       | 6 h  | 8 h  |
| Isolates by category (n)                  |                         |      |      |             |       |       |          |       |      |           |      |      |
| Resistant                                 | 45                      | 51   | 52   | 46          | 50    | 49    | 27       | 27    | 30   | 24        | 30   | 31   |
| ATU                                       | 23                      | 18   | 15   | 4           | 2     | 3     | 3        | 4     | 1    | 5         | 4    | 3    |
| Susceptible                               | 50                      | 49   | 51   | 68          | 66    | 66    | 88       | 87    | 87   | 89        | 84   | 84   |
| Inhibition zone not readable              | 0                       | 0    | 0    | 0           | 0     | 0     | 0        | 0     | 0    | 0         | 0    | 0    |
| Isolates by category (%)                  |                         |      |      |             |       |       |          |       |      |           |      |      |
| Resistant                                 | 38.1                    | 43.2 | 44.1 | 39.0        | 42.4  | 41.5  | 22.9     | 22.9  | 25.4 | 20.3      | 25.4 | 26.3 |
| ATU                                       | 19.5                    | 15.3 | 12.7 | 3.4         | 1.7   | 2.5   | 2.5      | 3.4   | 0.8  | 4.2       | 3.4  | 2.5  |
| Susceptible                               | 42.4                    | 41.5 | 43.2 | 57.6        | 55.9  | 55.9  | 74.6     | 73.7  | 73.7 | 75.4      | 71.2 | 71.2 |
| Inhibition zone not readable              | 0.0                     | 0.0  | 0.0  | 0.0         | 0.0   | 0.0   | 0.0      | 0.0   | 0.0  | 0.0       | 0.0  | 0.0  |
| Categorical agreement (%) <sup>b</sup>    |                         |      |      |             |       |       |          |       |      |           |      |      |
| ATU included                              | 96.6                    | 96.6 | 96.6 | 100.0       | 100.0 | 100.0 | 100.0    | 100.0 | 99.2 | 99.2      | 99.2 | 98.3 |
| ATU not included                          | 95.8                    | 96.0 | 96.1 | 100.0       | 100.0 | 100.0 | 100.0    | 100.0 | 99.1 | 99.1      | 99.1 | 98.3 |
| Discordant results (n)                    |                         |      |      |             |       |       |          |       |      |           |      |      |
| Major error                               |                         |      |      |             |       |       |          |       | 1    | 1         | 1    | 2    |
| Very major error                          | 4                       | 4    | 4    |             |       |       |          |       |      |           |      |      |
| Discordant results (%)                    |                         |      |      |             |       |       |          |       |      |           |      |      |
| Major error                               | 0.0                     | 0.0  | 0.0  | 0.0         | 0.0   | 0.0   | 0.0      | 0.0   | 0.8  | 0.8       | 0.8  | 1.7  |
| Very major error                          | 3.4                     | 3.4  | 3.4  | 0.0         | 0.0   | 0.0   | 0.0      | 0.0   | 0.0  | 0.0       | 0.0  | 0.0  |

Karbapenemaz pozitif olan tüm suşlar tarama testiyle saptandı  
Suşlar ya dirençli ya da ATU kategorisindeydi

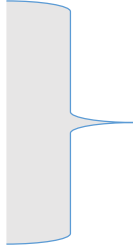
RAST

Klinik yararı var mı?

## Implementation of rapid antimicrobial susceptibility testing combined with routine infectious disease bedside consultation in clinical practice (RAST-ID): a prospective single-centre study

Thomas Valentin<sup>1\*</sup>, Elisabeth Koenig<sup>1,2</sup>, Juergen Prattes<sup>1</sup>, Stefanie Wunsch<sup>1</sup>, Tobias Loizenbaur<sup>1</sup>, Robert Krause<sup>1</sup> and Ines Zollner-Schwetz<sup>1</sup>

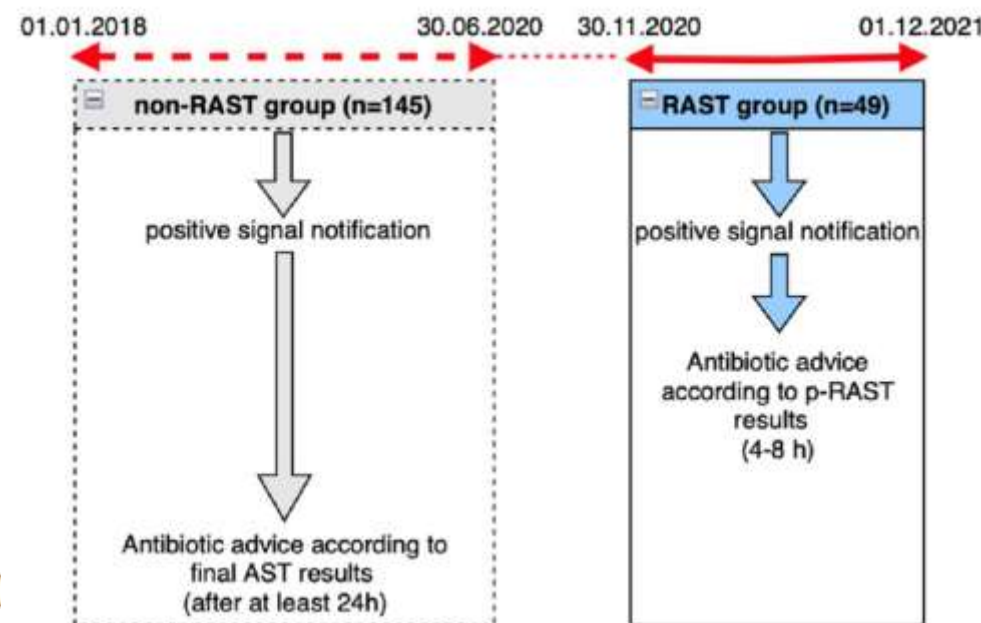
- Avusturya’da, 2019 yılında, yatan ve kan kültürü pozitif olan hastalar
- Çalışma saatleri içinde RAST için uygun olan **152** kan kültürü  
(58 *E.coli*, 52 *S. aureus*, 13 *K.pneumoniae*, 12 *P. aeruginosa*, 7 *S. pneumoniae*, 7 *E.faecium* ve 3 *E.faecalis*)
- RAST’la değerlendirilebilen antibiyotik sayısı **6. saatte % 95, 4. saatte % 75,  $p < 0.001$**
- **6. saat RAST** sonucuna göre hastaların
  - **% 88.2 enfeksiyon konsültasyonu** istenmiş
  - **% 54.5’ine antibiyotik değişimi** yapılmış
  - **% 46.3’üne ek tetkikler** istenmiş



Bir önceki yıla kıyasla  
**mortalitede fark yok**

# Implementation of the EUCAST rapid antimicrobial susceptibility test (RAST) for carbapenemase/ESBL-producing *Escherichia coli* and *Klebsiella pneumoniae* isolates, and its effect on mortality

- Dışkapı Yıldırım Beyazıt Eğitim ve Araştırma Hastanesi
- **Antibiyotik değişimi** – RAST (tüm hastalar en geç 8 saat)  
Kontrol ( En erken 24 saat sonra hastaların %45.5'i)
- **30 günlük mortalite** - RAST grubunda % 28.6  
Kontrol grubunda - %51.7



**Table 2.** Baseline patient characteristics by 30 day all-cause mortality (univariate analysis)

| Characteristic      | Non-survivors (N=89)<br>n (%) | Survivors (N= 105)<br>n (%) | RR (95% CI)   | P value <sup>a</sup> |
|---------------------|-------------------------------|-----------------------------|---------------|----------------------|
| RAST implementation |                               |                             |               |                      |
| p-RAST              | 14 (28.6)                     | 35 (71.4)                   | 1             |                      |
| Non-RAST            | 75 (51.7)                     | 70 (48.3)                   | 1.8 (1.1–2.9) | 0.005                |

# Impact of EUCAST Rapid Antimicrobial Susceptibility Testing (RAST) on optimal antimicrobial therapy in gram-negative bloodstream infections

Özge Özgen Top<sup>a,\*</sup>, Beyza Çifci<sup>a</sup>, Merve Büyükkörük<sup>a</sup>, Handan Can<sup>b</sup>, Pınar Aysert Yıldız<sup>a</sup>, Halil Furkan Martlı<sup>c</sup>, Elif Ayça Şahin<sup>c</sup>, Kayhan Çağlar<sup>c</sup>, Hasan Selçuk Özger<sup>a</sup>

- Gazi Üniversitesi hastanesi, Ağustos-Aralık 2023
- RAST- seftazidim, piperasilin-tazobaktam, meropenem, siprofloksasin, amikasin
- Hastalarda kullanılan antibiyotikler
  - Grup 1: Siprofloksasin, amikasin, seftazidim ve diğer 3. kuşak sefalosporinler, fosfomisin
  - Group 2: Piperasilin-tazobaktam
  - Group 3: Meropenem, tigesiklin, polimiksinler

Antibiotic susceptibility results according to reference test (VITEK 2).

|                                      | <i>P. aeruginosa</i><br>n = 8 | <i>A. baumannii</i><br>n = 13 | <i>E.coli</i><br>n = 44 | <i>Klebsiella</i><br>spp.<br>n = 38 | Total n<br>= 103 |
|--------------------------------------|-------------------------------|-------------------------------|-------------------------|-------------------------------------|------------------|
| <b>CAZ, n (%)</b>                    |                               |                               |                         |                                     |                  |
| Susceptible, standard dosing regimen | 6 (75)                        | –                             | 19 (43.2)               | 10 (26.3)                           | 38 (36.9)        |
| Susceptible, increased exposure      | –                             | –                             | 3 (6.8)                 | –                                   |                  |
| Resistant                            | 2 (25)                        | 13 (100)                      | 22 (50)                 | 28 (73.7)                           | 65 (63.1)        |
| <b>AMK, n (%)</b>                    |                               |                               |                         |                                     |                  |
| Susceptible, standard dosing regimen | 8 (100)                       | 1 (7.7)                       | 37 (84)                 | 25 (65.7)                           | 76 (73.8)        |
| Susceptible, increased exposure      | –                             | –                             | 4 (9)                   | 1 (2.6)                             |                  |
| Resistant                            | –                             | 12 (92.3)                     | 3 (6.8)                 | 12 (31.6)                           | 27 (26.2)        |
| <b>CIP, n(%)</b>                     |                               |                               |                         |                                     |                  |
| Susceptible, standard dosing regimen | –                             | –                             | 11 (25)                 | 11 (28.9)                           | 35 (34.0)        |
| Susceptible, increased exposure      | 6 (75)                        | –                             | 4 (9)                   | 3 (7.8)                             |                  |
| Resistant                            | 2 (25)                        | 13 (100)                      | 29 (65.9)               | 24 (63.2)                           | 68 (66.0)        |

Antibiotic susceptibility results according to reference test (VITEK 2).

|                                      | <i>P. aeruginosa</i><br>n = 8 | <i>A. baumannii</i><br>n = 13 | <i>E.coli</i><br>n = 44 | <i>Klebsiella</i><br>spp.<br>n = 38 | Total n<br>= 103 |
|--------------------------------------|-------------------------------|-------------------------------|-------------------------|-------------------------------------|------------------|
| <b>TZP, n (%)</b>                    |                               |                               |                         |                                     |                  |
| Susceptible, standard dosing regimen | 1 (12.5)                      | –                             | 37 (84.1)               | 15 (39.5)                           | 57 (55.3)        |
| Susceptible, increased exposure      | 4 (50)                        | –                             | –                       | –                                   |                  |
| Resistant                            | 3 (37.5)                      | 13 (100)                      | 7 (15.9)                | 23 (60.5)                           | 46 (44.7)        |
| <b>MEM, n (%)</b>                    |                               |                               |                         |                                     |                  |
| Susceptible, standard dosing regimen | 7 (87.5)                      | –                             | 42 (95.4)               | 22 (57.8)                           | 73 (70.9)        |
| Susceptible, increased exposure      | –                             | –                             | 1 (2.3)                 | 1 (2.6)                             |                  |
| Resistant                            | 1 (12.5)                      | 13 (100)                      | 1 (2.3)                 | 15 (39.5)                           | 30 (29.1)        |
| <b>MDR, n (%)</b>                    | 1 (12.5)                      | 13 (100)                      | 4 (9.1)                 | 20 (52.6)                           | 38 (36.9)        |

Appropriateness of empirical antibiotics and empirical therapy according to microorganism types.

|                                                        | Appropriate<br>Empirical Treatment,<br>n (%) | Inappropriate<br>Empirical Treatment, n<br>(%) |
|--------------------------------------------------------|----------------------------------------------|------------------------------------------------|
| <b>Empirical antibiotics</b>                           |                                              |                                                |
| <b>Monotherapy (n = 62)</b>                            |                                              |                                                |
| Piperacillin-tazobactam<br>(n = 32)                    | 23 (76.6)                                    | 7 (23.4)                                       |
| Meropenem (n = 23)                                     | 22 (95.6)                                    | 1 (4.4)                                        |
| 3rd generation<br>cephalosporins (n = 6)               | 1 (16.7)                                     | 5 (83.3)                                       |
| Other (n = 3)*                                         | 3 (100)                                      | 0                                              |
| <b>Combination therapy (n = 40)</b>                    |                                              |                                                |
| Combination with<br>piperacillin-tazobactam<br>(n = 5) | 5 (100)                                      | 0                                              |
| Combination with<br>meropenem (n = 19)                 | 16 (84.2)                                    | 3 (15.8)                                       |
| Other combination (n =<br>16)*                         | 14 (87.5)                                    | 2 (12.5)                                       |
| <b>Microorganism type</b>                              |                                              |                                                |
| <i>Escherichia coli</i> (n = 44)                       | 39 (88.6)                                    | 5 (11.4)                                       |
| <i>Klebsiella</i> spp. (n = 38)                        | 31 (81.5)                                    | 7 (18.5)                                       |
| <i>Pseudomonas</i> spp. (n = 8)                        | 7 (87.5)                                     | 1 (12.5)                                       |
| <i>Acinetobacter</i> spp. (n = 13)                     | 7 (53.8)                                     | 6 (46.1)                                       |

Impact of 6 h RAST results on antimicrobial therapy.

|                                                                                                  | n (%)            |
|--------------------------------------------------------------------------------------------------|------------------|
| Antibiotic management                                                                            |                  |
| De-escalation, n (%)                                                                             | 63 (61.2)        |
| Switch to narrow-spectrum antibiotics                                                            | 47 (45.6)        |
| From group 2 to group 1                                                                          | 22 (21.3)        |
| From group 3 to group 1                                                                          | 19 (18.4)        |
| From group 3 to group 2                                                                          | 6 (5.8)          |
| Switch to narrow-spectrum antibiotics and from combination to monotherapy                        | 13 (12.6)        |
| False de-escalation                                                                              | 3 (2.9)          |
| Carbapenem-sparing therapy                                                                       | 25 (24.3)        |
| Escalation, n (%)                                                                                | 19 (18.4)        |
| From group 2 to group 3                                                                          | 7 (6.7)          |
| From group 1 to group 3                                                                          | 10 (9.7)         |
| From group 1 to group 2                                                                          | 2 (1.9)          |
| Continuing treatment without change                                                              | 21 (20.4)        |
| Continuing treatment incorrectly                                                                 | 1 (1.0)          |
| Reduction in antibiotic susceptibility reporting time, h (median, 25–75 % IQR)                   | 41.5 (38.8–63.2) |
| Reduction in antibiotic susceptibility reporting time for de-escalation, h (median, 25–75 % IQR) | 41.5 (38.8–43.9) |
| Reduction in antibiotic susceptibility reporting time for escalation, h (median, 25–75 % IQR)    | 44.1 (39.8–70.6) |

