# Dr. Ronald Irwanto Natadidjaja, SpPD, Subsp.PTI(K), FINASIM

**Formal Education**

- **Universitas Indonesia**, Subspesialis / Konsultan Penyakit Tropik dan Infeksi, Lulus 2013
- **Universitas Indonesia**, Spesialis Penyakit Dalam (Internist), Lulus 2009
- **Universitas Trisakti**, Dokter Umum, Lulus 2002
- **SMP-SMA Kolese Kanisius**, Jakarta, Lulus 1994

**Organization**

- **Tim Covid-19,** RSPI Puri Indah, 2020 – sekarang
- **Bendahara**, Perhimpunan Ilmu Kedokteran Tropis dan Penyakit Infeksi Indonesia (PETRI) Jakarta, sejak 2016 - 2023
- **Sekretaris Jenderal (Sekjen)**, Pengurus Pusat Perhimpunan Pengendalian Infeksi Indonesia (PERDALIN), sejak 2016 - 2022
- **Tim Ahli** Pokja Pencegahan dan Pengendalian Infeksi (PPI), Kemenkes RI, sejak 2017-2024
- **Kepala Bagian** Ilmu Penyakit Dalam Fakultas Kedokteran Universitas Trisakti, 2013-2020
- **Pendiri dan Perintis** RASPRO Indonesia Study Group, **Yayasan Pelita RASPRO Indonesia** untuk studi resistensi antimikroba dan penggunaan antimikroba bijak Indonesia
- **Ketua PPI** RSPI Bintaro Jaya
- **Internist-Konsultan**, RSPI Puri Indah, RSPI Bintaro Jaya, dan Tzu Chi Hospital – Pantai Indah Kapuk, Jakarta Utara

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# MDR and Difficult to Treat Pathogen Approach in Critical Ill Patients

RASPRO Indonesia Study Group

**Ronald Irwanto Natadidjaja**

**Trisakti – RASPRO Indonesia Antimicrobial Stewardship (TRIASE) Learning Centre**

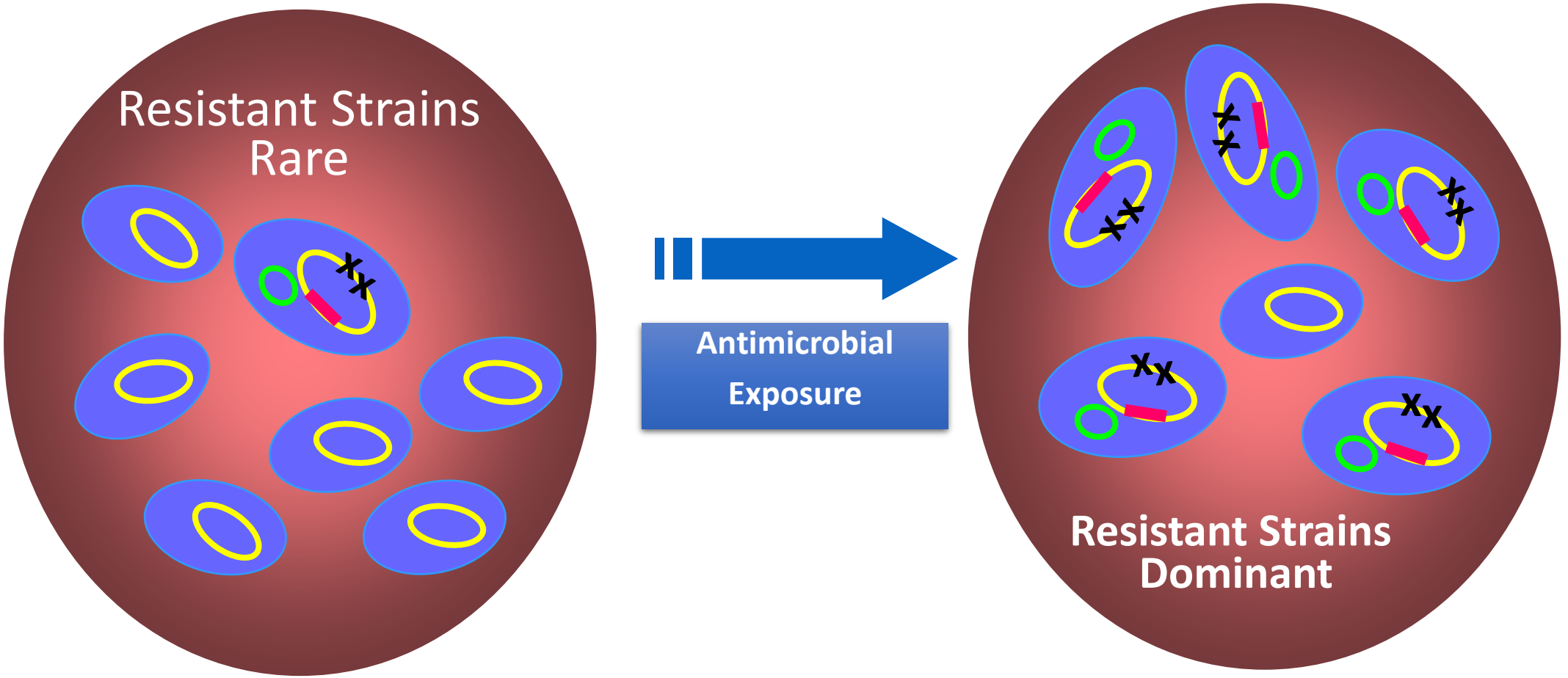
**Faculty of Medicine Universitas Trisakti**

# Predicting The Risk of MDR Pathogen Infection – Selective Pressure


***RI Natadidjaja***
***Infectious Disease (ID) Specialist***

# Selective Pressure

Campaign to Prevent Antimicrobial Resistance in Healthcare Settings, CDC 2002



## Community Based

Microorganism Pattern of Skin and Sof Tissue from 3 Emergency Rooms in Jakarta

Ronald Irwanto ,Suhendro, Khie Chen, Yeva Rosana, 2009

**GRAM Positive**

**OXA Sensitive S. aureus : 95.5%**

**GRAM NEGATIVE**

**Pseudomonas sp Sensitive to**

**MEM : 92.3%**
**IMP : 92.3%**
**TZP : 92.3%**
**LVX : 69.2%**
**AMK : 84.6%**

## Hospital Based

UNIVERSA MEDICINA

*January-April, 2013* *Vol.32 - No.1*

**Culture-and nonculture-based antibiotics for complicated soft tissue infections are comparable**

Ronald Irwanto*,**, Suhendro**, Khie Chen**, and Murdani Abdullah***

**GRAM Positive**

**OXA Sensitive S. aureus : 84.6 %**

**GRAM NEGATIVE**

**Pseudomonas sp Sensitive to**

**MEM : 68.2%**
**IMP : 78.7%**
**TZP : 50.0%**
**LVX : 54.5%**
**AMK : 68.2%**

Komisi Akreditasi Rumah Sakit

Journal of Hospital Accreditation, 2021
Vol 03, Edisi 2, hal 114-118
Tanggal Publikasi, 25 Juli 2021

Laporan Peningkatan Mutu

# PENINGKATAN MUTU PENGGUNAAN ANTIBIOTIK BIJAK MELALUI KESESUAIAN TEMUAN HASIL KULTUR DENGAN KAJIAN RISIKO PASIEN MENURUT MODEL REGULASI ANTIMIKROBA SISTEM PROSPEKTIF (RASPRO)

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[2]RASPRO Indonesia Study Group
[3]Ikatan Apoteker Indonesia

Tabel 3. Kesesuaian Temuan Hasil Kultur dengan Kajian Risiko Pasien Menurut Model RASPRO

| | Multisensitif | | MDR | | | | Prediksi | |
|---|---|---|---|---|---|---|---|---|
| | | | ESBL | | Non ESBL | | | |
| | n | % | n | % | n | % | Sesuai | Tidak Sesuai |
| **Gram Negatif** | | | | | | | | |
| Acinetobacter sp. | 0 | 0,00 | 0 | 0,00 | 4 | 10,00 | 4 | 0 |
| Pseudomanas sp. | 0 | 0,00 | 0 | 0,00 | 7 | 17,50 | 7 | 0 |
| Klebsiela pneumonia | 15 | 26,32 | 2 | 22,22 | 6 | 15,00 | 21 | 2 |
| Escheceria coli | 18 | 31,58 | 7 | 77,78 | 6 | 15,00 | 28 | 3 |
| Citrobacter koseri | 0 | 0,00 | 0 | 0,00 | 1 | 2,50 | 1 | 0 |
| Enterobacter sp. | 1 | 1,75 | 0 | 0,00 | 1 | 2,50 | 2 | 0 |
| Proteus sp. | 0 | 0,00 | 0 | 0,00 | 2 | 5,00 | 2 | 0 |
| Providencia stuartii | 0 | 0,00 | 0 | 0,00 | 1 | 2,50 | 1 | 0 |
| Pantoea agglomerans | 1 | 1,75 | 0 | 0,00 | 0 | 0,00 | 1 | 0 |
| Raoultella ornithinolytica | 0 | 0,00 | 0 | 0,00 | 1 | 2,50 | 1 | 0 |
| Serratia fonticola | 1 | 1,75 | 0 | 0,00 | 0 | 0,00 | 1 | 0 |
| **Total** | **36** | **63,15** | **9** | **100,00** | **29** | 72,50 | **69** | **5** |
| **Gram Positif** | | | | | | | | |
| Staphylococcus aureus | 4 | 7,02 | 0 | 0,00 | 1 * | 2,50 | 5 | 0 |
| Staphylococcus epidermidis | 1 | 1,75 | 0 | 0,00 | 2 ** | 5,00 | 3 | 0 |
| Enterococcus faecalis | 4 | 7,02 | 0 | 0,00 | 2 | 5,00 | 5 | 1 |
| Enterococcus faecium | 1 | 1,75 | 0 | 0,00 | 1 | 2,50 | 1 | 1 |
| Streptococcus sp. | 8 | 14,04 | 0 | 0,00 | 4 | 10,00 | 12 | 0 |
| Staphylococcus sp. | 3 | 5,26 | 0 | 0,00 | 1 | 2,50 | 3 | 1 |
| **Total** | **21** | **36,84** | 0 | 0,00 | **11** | 27,50 | **29** | **3** |
| **TOTAL** | **57** | **100,00** | **9** | **100,00** | **40** | **100,00** | **98** | **8** |

* MRSA ** MRSE

Tabel 4. Persentase Kesesuaian Hasil Kultur dengan Kajian Risiko Infeksi Multisensitif dan MDR Model RASPRO

| | Sesuai | | Tidak Sesuai | | Total | |
|---|---|---|---|---|---|---|
| | n | % | n | % | n | % |
| Multisensitif | 54 | 94,74 | 3 | 5,26 | 57 | 100,00 |
| MDR | 44 | 89,80 | 5 | 10,20 | 49 | 100,00 |

**Immunocompromised :**

**94.74%** showed multi-sensitive findings in “NAIVE” medical history, while :

**89.80%** showed MDR with :

< 90 days history of antibiotic usage AND / OR

< 90 days history of hospitalization AND / OR

< 90 days history of medical devices usage

# WHO- SEARO Webinar Series 6 :

## Role of Diagnostics in Antimicrobial Stewardship and Laboratory Surveillance

World Health Organization
Regional Office for South-East Asia

Fakultas Kedokteran TRIASE UNIVERSITAS TRISAKTI
RASPRO Indonesia
Antimicrobial Stewardship LEARNING CENTRE

ARUC Score
Shorr et al
Alberti et al
Tumbarelo for ESBL
Duke for ESBL
Gomila et al
Marchaim et al
Carmeli et al
etc

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ORIGINAL ARTICLE
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P-ISSN.2089-1180, E-ISSN: 2302-2914

Bali Medical Journal
Published by Bali Medical Journal

# The Association between Medical History-based Risks and Sepsis Events in Immunocompromised Patients according to Type III Stratification of the Indonesian Regulation on the Prospective Antimicrobial System (*Regulasi Antimikroba Sistem Prospektif / RASPRO*)

Ronald Irwanto Natadidjaja[1*], Armi Setia Kusuma[2], Gede Bangun Sudradjad[3], Lies Nugrohowati[4]

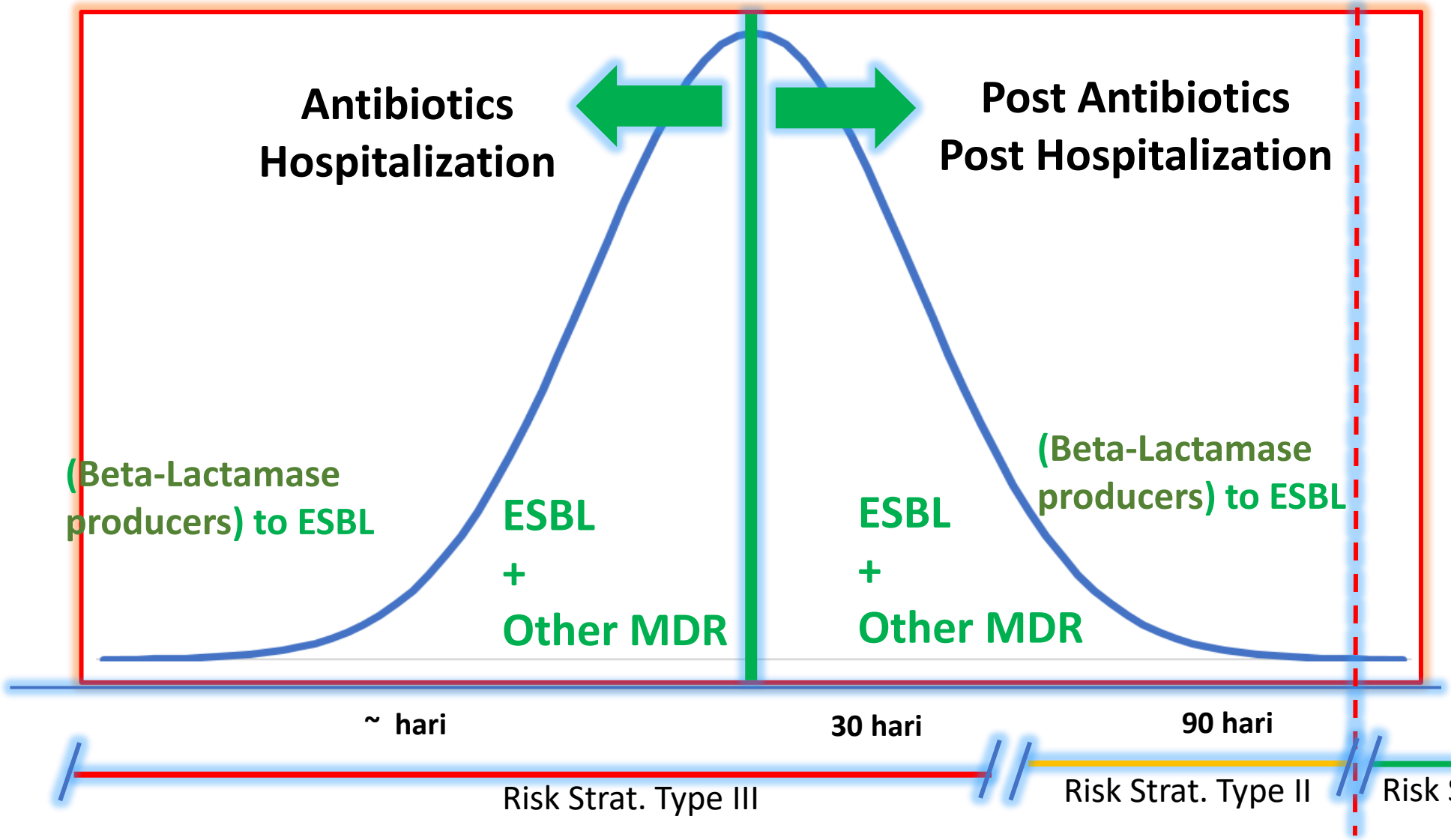
**Background:** The Indonesian Regulation on the Prospective Antimicrobial System (*Regulasi Antimikroba Sistem Prospektif/ RASPRO*) is a novel program. Its role has been reinforced by the Indonesian Ministry of Law and Human Rights Stipulation, which may predict the risk of sepsis events. Our study aimed to evaluate whether the risk factors listed in the *RASPRO* consensus have actual effects on sepsis events.

**Method:** The study was a retrospective cohort using secondary data with 98 subjects. The subjects were categorized into two groups, i.e., the *RASPRO* group with type III stratification (RASPRO Group) and Non-type III stratification *RASPRO* group (Non-RASPRO Group). Subjects with infection but with conditions other than the abovementioned criteria were categorized into the Non-RASPRO group.

**Results:** We found that among subjects in the RASPRO group, a history of antibiotic use over the past <30 days (OR 3.42; 95%CI 1.32–8.85; p=0.011) and a history of having procedure using medical instruments within the last <30 days (OR 2.62; 95%CI 1.06–6.45; p=0.037) seemed to be greatest risk factors for sepsis events.

**Conclusion:** The RASPRO group has a higher risk for sepsis events than the non-RASPRO with a history of antibiotic undergoing a procedure using a medical instrument within the last <30 days possessed the greatest risk factors for sepsis events.

RASPRO Indonesia File & Documents 2019 : Risk Stratification Consensus




ARUC
Aliberti et al
Gomila et al
Marchaim et al
Tumbarelo et al
etc

# Target for Decreasing the Risk of MDR Pathogen : RASPRO Indonesia to WHO AWaRe

***RI Natadidjaja***
***Infectious Disease (ID) Specialist***

# Futuristic Fashion in Antimicrobial Used - The WHO "Kick of" in 2023
# Shifting WATCH to ≥ 60% ACCESS

**RESERVED**

Aztrenonam
Ceftazidime Avibactam
Ceftaroline Fosamil
Ceftolozane Tazobactam

Imipenem cilastatin-relebactam

Fosfomycin IV
Colistin
Polymixin B
Tygecycline

This group includes antibiotics and antibiotic classes that should be reserved for treatment of confirmed or suspected infections due to multi-drug-resistant organisms. Reserve group antibiotics should be treated as "last resort" options.

**WATCH**

Quinolones
Azithromycin

2nd , 3rd& 4th Generation of Cephalosporin

Piperacillin Tazobactam
Carbapenems

This group includes antibiotic classes that have higher resistance potential and includes most of the highest priority agents among the Critically Important Antimicrobials for Human Medicine and/or antibiotics that are at relatively high risk of selection of bacterial resistance. These medicines should be prioritized as key targets of stewardship programs and monitoring. Selected Watch group antibiotics are recommended as essential first or second choice empiric treatment options for a limited number of specific infectious syndromes and are listed as individual medicines on the WHO Model Lists of Essential Medicines.

**ACCESS**

Ampicillin Sulbactam
Ampicillin
Amoxicillin Clavulanate
Amoxicillin

1st Generation of Cephalosporin

Amikacin
Gentamycin

This group includes antibiotics that have activity against a wide range of commonly encountered susceptible pathogens while also showing lower resistance potential than antibiotics in the other groups. Selected Access group antibiotics are recommended as essential first or second choice empiric treatment options for infectious syndromes reviewed by the EML Expert Committee and are listed as individual medicines on the Model Lists of Essential Medicines to improve access and promote appropriate use.

AWARE 2021

World Health Organization

HOSPITAL FACILITY
27. Community-acquired pneumonia – severe

ADULTS

# Community-acquired pneumonia



## CURB-65 Severity Scoring System

**Signs & Symptoms (1 point each)**

- Presence of Confusion (new onset)
- Urea > 19 mg/dL (or > 7 mmol/L)*
- Respiratory rate > 30/min
- Systolic BP < 90 mmHg (<12 kPa) or Diastolic BP ≤ 60 mmHg (<8 kPa)
- Age ≥ 65 years

**Score 0-1**
- Consider outpatient treatment

**Score 2**
- Consider inpatient treatment
- **Consider adding clarithromycin to beta-lactam for atypical coverage**
- Perform microbiology tests

**Score ≥3**
- Inpatient treatment (consider ICU)
- **Consider adding clarithromycin**
- Perform microbiology tests

*Other considerations such as severe comorbid illnesses or inability to maintain oral therapy should be taken into account. CURB-65 has not been extensively validated in low-income settings.*

**The **CRB-65** score, which does not require laboratory values for its calculation, can also be used, the score value interpretation is the same as for CURB-65*

## Mild to Moderate Cases

*All dosages are for normal renal function*

*Antibiotics are listed in alphabetical order and should be considered equal treatment options unless otherwise indicated*

**First Choice**

- ACCESS: Amoxicillin 1 g q8h **ORAL**

OR

- ACCESS: Phenoxymethylpenicillin (as potassium) 500 mg (800 000 IU) q6h **ORAL**

**Second Choice**

- ACCESS: Amoxicillin+clavulanic acid 875 mg+125 mg q8h **ORAL**

OR

- ACCESS: Doxycycline 100 mg q12h **ORAL**

## Treatment

### Antibiotic Treatment Duration

Treat for **5 days**

If severe disease, consider longer treatment and look for complications such as empyema, if patient not clinically stable at day 5

### Severe Cases

*All dosages are for normal renal function*

*Antibiotics are listed in alphabetical order and should be considered equal treatment options unless otherwise indicated*

**First Choice**

- WATCH: Cefotaxime 2 g q8h **IV/IM**

OR

- WATCH: Ceftriaxone 2 g q24h **IV** (1 g q24h **IM***)

**A larger volume would be painful to give as intramuscular injection*

IF CURB-65 ≥2, CONSIDER ADDING

- WATCH: Clarithromycin 500 mg q12h **ORAL** (or **IV**)

*Clarithromycin has excellent oral bioavailability and the intravenous route should be reserved for patients with impaired gastrointestinal function*

**Second Choice**

- ACCESS: Amoxicillin+clavulanic acid 1 g+200 mg q8h **IV**
  - A higher daily dose can be considered: 1 g+200 mg q6h

IF CURB-65 ≥2, CONSIDER ADDING

- WATCH: Clarithromycin 500 mg q12h **ORAL** (or **IV**)

*Clarithromycin has excellent oral bioavailability and the intravenous route should be reserved for patients with impaired gastrointestinal function*

**Table 2.2 – Common infections seen in primary health care settings and the antibiotic options recommended in the AWaRe book**

**Important**

Where more than one antibiotic is recommended for an infection, they are listed in alphabetical order and they should be considered equal treatment options, unless otherwise indicated.

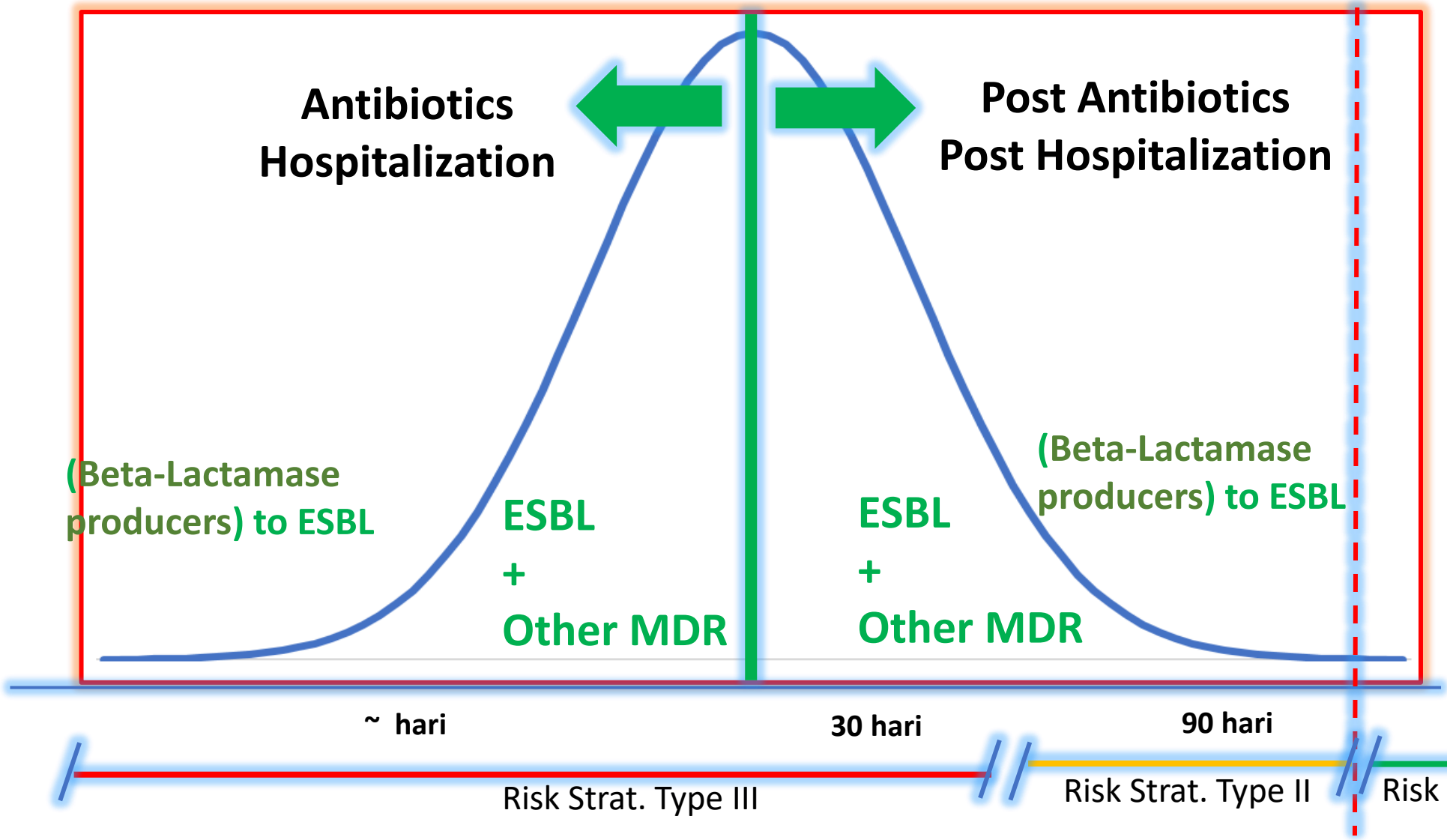
| Infection | ACCESS / WATCH | First-choice antibiotic option (when an antibiotic is indicated[a]) |
|---|---|---|
| Bronchitis | No antibiotic | No antibiotic |
| Community-acquired pneumonia (mild cases) | ACCESS | Amoxicillin OR Phenoxymethylpenicilli |
| Chronic obstructive pulmonary disease exacerbations | ACCESS | Amoxicillin (for most mild cases the fir symptomatic treatment an not necessary) |
| Dental infections | ACCESS | Amoxicillin OR Phenoxymethylpenicilli (for most cases the first ch procedure and antibiotics a |
| Infectious diarrhoea[b] | No antibiotic or WATCH | Most mild non-bloody diar by viral infections and antib necessary For acute severe bloody dia dysentery - Ciprofloxacin |
| Otitis media | ACCESS | Amoxicillin (for most mild cases the fir symptomatic treatment an not necessary) |

**Table 2.2** *continued*

| Infection | ACCESS / WATCH | First-choice antibiotic option (when an antibiotic is indicated[a]) |
|---|---|---|
| Pharyngitis | ACCESS | Amoxicillin OR Phenoxymethylpenicillin (for most mild cases the first choice is symptomatic treatment and antibiotics are not necessary) |
| Sinusitis | ACCESS | Amoxicillin OR Amoxicillin+clavulanic acid (for most mild cases the first choice is symptomatic treatment and antibiotics are not necessary) |
| Skin and soft tissue infection (mild cases)[c] | ACCESS | Amoxicillin+clavulanic acid OR Cefalexin OR Cloxacillin |
| Urinary tract infection, lower | ACCESS | Amoxicillin+clavulanic acid OR Nitrofurantoin OR Sulfamethoxazole+trimethoprim OR Trimethoprim |

[a] The decision to treat is based on assessment of the patient and on a minimum set of criteria to start antibiotics described in the chapters for each infection.
[b] Only oral antibiotic options are reported here.
[c] Cloxacillin and cefalexin have a narrower spectrum of antibacterial activity compared to amoxicillin+clavulanic acid with good efficacy in mild skin and soft tissue infections. Therefore, from an antibiotic stewardship perspective, these two antibiotics are the preferred options whenever possible (except for bite wounds).
Legend: ACCESS antibiotics are indicated in green, WATCH antibiotics in orange and RESERVE antibiotics in red.

RASPRO Indonesia File & Documents 2019 : Risk Stratification Consensus




ARUC
Aliberti et al
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Marchaim et al
Tumbarelo et al
etc

## Risk Stratification Type 3

Severe /HAIs / Febrile Neutropenia / Threatening Organ Perforation
AND / OR
Immunocompromized AND / OR Uncontrolled DM :
+
History of antibiotic use in the last 30 days
AND / OR
History of ≥ 48 hours hospitalization in the last 30 days
AND / OR
History medical devices use in the last 30 days

**Empiric Antibiotic for Severe Case or Suspected ESBLs or Other MDRO**

RESERVE | RESERVE | WATCH | WATCH

## Risk Stratification Type 2

Non Severe / Non Life Threatening – Non HAIs
Immunocompromized
AND / OR Uncontrolled DM :
.
History of antibiotic use in the last 90 days
AND / OR
History of ≥ 48 hours hospitalization in the last 90 days
AND / OR
History medical devices use in the last 90 days

**Empiric Antibiotic for Suspected (Beta Lactamase Producers) to ESBLs**

WATCH | WATCH | WATCH | ACCESS

## Risk Stratification Type 1

Non Risk Stratification Type 3 and / or 2

RASPRO indonesia
Risk Stratification


**Empiric Antibiotic for Multi-Sensitive Organism**

ACCESS | ACCESS | ACCESS | ACCESS

**Implementing the Empiric Antimicrobial Guidelines**

# Antibiogram + Antibiotic / PKPD

**Processing**

**Implemented by RASAL-RASLAN**

## Risk Stratification Type 3

**Anti-ESBLs and other MDRO**

**RESERVE**
- Linezolid
- Tygecycline
- Fosfomycin
- Polymixin
- Reserve BL /BLIs

**WATCH**
- Carbapenems group 2
- Piperacillin Tazobactam
- Vancomycin
- Quinolones
- 3th & 4th Gen Cephalosporins

**+/- Combination**
- Amikacin
- Gentamycin
- Metronidazole

**+/-** (for anaerobic suspected)

Empiric Antibiotic for Severe Case or Suspected ESBLs or Other MDRO

RESERVE RESERVE WATCH WATCH

## Risk Stratification Type 2

**Anti- (Beta-Lactamase Producers) to ESBLs**

**WATCH**
- Carbapenems group 1
- Piperacillin Tazobactam

**ACCESS**
- Amoxicillin Clavulanate
- Ampicillin Sulbactam

**+ Combination**
- Amikacin
- Gentamycin
- Metronidazole

**+/-** (for anaerobic suspected)

**Considering :**
**Carbapenem sparing regimen for ESBLs**

Empiric Antibiotic for Suspected (Beta Lactamase Producers) to ESBLs

WATCH WATCH WATCH ACCESS

## Risk Stratification Type 1

**ACCESS**
- Amoxicillin Clavulanate
- Ampicillin Sulbactam

**+/- Combination**
- Amikacin
- Gentamycin
- Metronidazole

**+/-** (for anaerobic suspected)

**WARNING!!**
**Avoid antibiotic use in**
**The case of viral infections**

Empiric Antibiotic for Multi-Sensitive Organism

ACCESS ACCESS ACCESS ACCESS

**RASPRO Alur Antibiotik Awal (RASAL 1.0)** Copyright: Ronald Irwanto

| NO. | SPESIFIKASI | FLOW | KET. | TINDAKAN | AB |
|---|---|---|---|---|---|
| 1. | Fokus infeksi dengan gejala infeksi | Tidak | henti | Tidak perlu antibiotik | |
| | | Ya | | Fokus Infeksi : ..... | |
| 2. | Klinis progresif Sepsis / Septic Shock / Febril Netropenia / Terkategori HAIs | Ya | henti | Antibiotik Stratifikasi Risiko Tipe III | |
| | | Tidak | | | |
| 3. | Perforasi organ mengancam | Ya | henti | Antibiotik Stratifikasi Risiko Tipe III | |
| | | Tidak | | | |
| 4. | Encephalopathy et causa infeksi bakterial | Ya | henti | Antibiotik Stratifikasi Risiko Tipe III | |
| | | Tidak | | | |
| 5. | (Immunocompromised dan / atau DM tidak terkontrol) + riwayat konsumsi antibiotik ≤ 30 hari yang lalu | Ya | henti | Antibiotik Stratifikasi Risiko Tipe III | |
| | | Tidak | | | |
| 6. | (Immunocompromised dan / atau DM tidak terkontrol) + riwayat perawatan ≥ 48 jam ≤ 30 hari yang lalu | Ya | henti | Antibiotik Stratifikasi Risiko Tipe III | |
| | | Tidak | | | |
| 7. | (Immunocompromised dan / atau DM tidak terkontrol) + penggunaan instrumen medis atau riwayat penggunaan instrumen medis ≤ 30 hari yang lalu | Ya | henti | Antibiotik Stratifikasi Risiko Tipe III | |
| | | Tidak | | | |
| 8. | (Immunocompromised dan / atau DM tidak terkontrol) + riwayat konsumsi antibiotik ≤ 90 hari yang lalu | Ya | henti | Antibiotik Stratifikasi Risiko Tipe II | |
| | | Tidak | | | |
| 9. | (Immunocompromised dan / atau DM tidak terkontrol) + riwayat perawatan ≥ 48 jam ≤ 90 hari yang lalu | Ya | henti | Antibiotik Stratifikasi Risiko Tipe II | |
| | | Tidak | | | |
| 10. | (Immunocompromised dan / atau DM tidak terkontrol) + riwayat penggunaan instrumen medis ≤ 90 hari yang lalu | Ya | henti | Antibiotik Stratifikasi Risiko Tipe II | |
| | | Tidak | | Antibiotik Stratifikasi Risiko Tipe I | |

**RASPRO Alur Antibiotik Lanjutan (RASLAN 1.0)** Copyright: Ronald Irwanto

| NO. | SPESIFIKASI | FLOW | KETERANGAN | TINDAKAN | AB AWAL | AB LANJUT |
|---|---|---|---|---|---|---|
| 1. | Gejala infeksi masih ada | Tidak | Henti (Isi AB awal - AB lanjut) | De-eskalasi antibiotik sesuai kultur / step-down antibiotik ke stratifikasi risiko yang lebih rendah / pindah IV ke oral / stop | | |
| | | Ya | Fokus Infeksi : ..... | | | |
| 2. | Klinis progresif Sepsis / Syok Sepsis / Febril Netropenia / Terkategori HAIs | Ya | Henti (Isi AB awal - AB lanjut) | Eskalasi antibiotik ke stratifikasi risiko tipe III | | |
| | | Tidak | | | | |
| 3. | Komplikasi perforasi organ | Ya | Henti (Isi AB awal - AB lanjut) | Eskalasi antibiotik ke stratifikasi risiko tipe III | | |
| | | Tidak | | | | |
| 4. | Komplikasi ensefalopati et causa infeksi bakterial | Ya | Henti (Isi AB awal - AB lanjut) | Eskalasi antibiotik ke stratifikasi risiko tipe III | | |
| | | Tidak | | | | |
| 5. | Gejala infeksi perbaikan pasca 3-7 hari pemberian antibiotik | Tidak | Henti (Isi AB awal - AB lanjut) | Eskalasi antibiotik ke stratifikasi risiko yang lebih tinggi / tambahkan antibiotik sesuai panduan | | |
| | | Ya | Henti (Isi AB awal - AB lanjut) | De-eskalasi antibiotik sesuai kultur / step-down antibiotik ke stratifikasi risiko yang lebih rendah / pindah IV ke oral / stop | | |

# e-RASPRO Model
# Digital Antimicrobial Stewardship
# Established in > 30 hospitals

- **Clinical**

**Site of infection:**

**Bacterial:**

"Big Four": Pneumonia, UTI, SSTI, Intra-Abdominal

Others: Intracranial, Central Line Associated BSIs, etc

**Viral:**

Upper respiratory tract

Lower respiratory tract – viral pneumonia

GI Tract

Unspecified

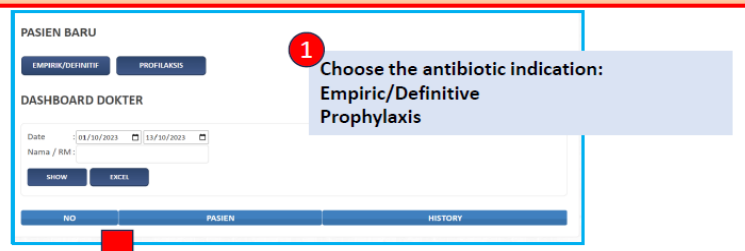
- **Laboratory**

Full Blood Count, CRP, Procalcitonin

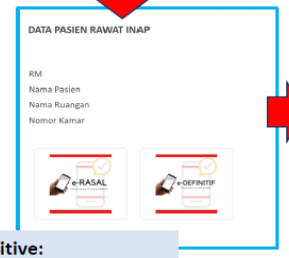
Culture Finding

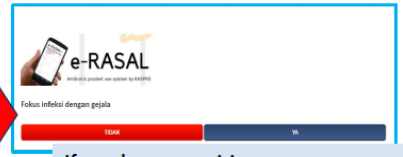
If the infection syndrome caused by viral such as Influenzae, COVID-19, others

→ The antibiotic would be **RESTRICTED**



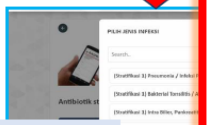

1 Choose the antibiotic indication:
Empiric/Definitive
Prophylaxis



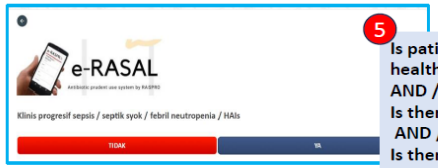




3 If we choose empiric:
Define the bact

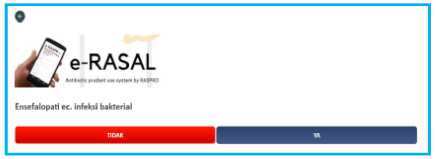
2 If we choose empiric/definitive:
Confirmation:
empiric (e-RASAL) or
definitive (e-definitive)



4 Choose the focus of infection
1,2,3 and more focus of infection can be covered by the system








5 Is patient sepsis / febrile neutropenia / healthcare associated infections?
AND / OR
Is there any threatening organ perforation?
AND / OR
Is there any bacterial encephalopathy?

**If Yes**

**Life threatening**

Request by system and local empiric guidelines for **WATCH** or **RESERVE** Group Antibiotic
Anti ESBLs / Pseudomonas sp / Anti MRSA
Note: by onsite consultation with ASP team

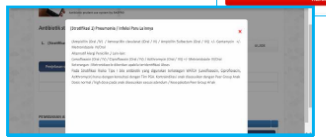
6 Is patient sepsis / febrile neutropenia / healthcare associated infections?
AND / OR
Is there any threatening organ perforation?
AND / OR
Is there any bacterial encephalopathy?

**If NO**

**Define the Patient Risk Stratification**

Type 3
Type 2 — Local empiric guidelines: WATCH Group Antibiotic
Type 1 — Local empiric guidelines: ACCESS Group Antibiotic





Digital Empiric Antibiotic Guidelines by Patient Risk Stratification (RASPRO Indonesia Model)

**Digital Antibiotic Guidelines based on Risk Stratification , Journal Synthesis & Microorganism Pattern**

**AWARE**

**Pre authorization - Digital Monitoring**

**Clinician – Pharmacist - PGA Team Connection**

**Antibiotic de-escalation timing**

**Difficult case notification**

**Data sorting & management**

**Evaluation**

# e-RASPRO Model
# Digital Antimicrobial Stewardship
# Established in > 30 hospitals

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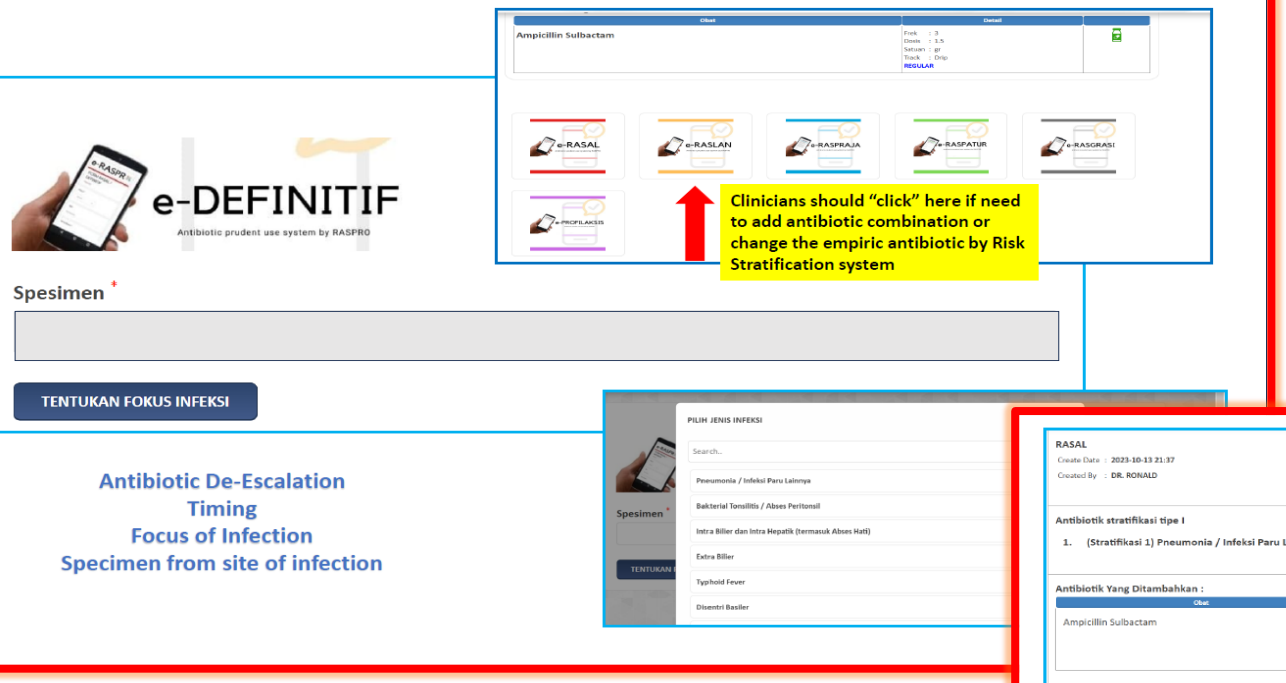
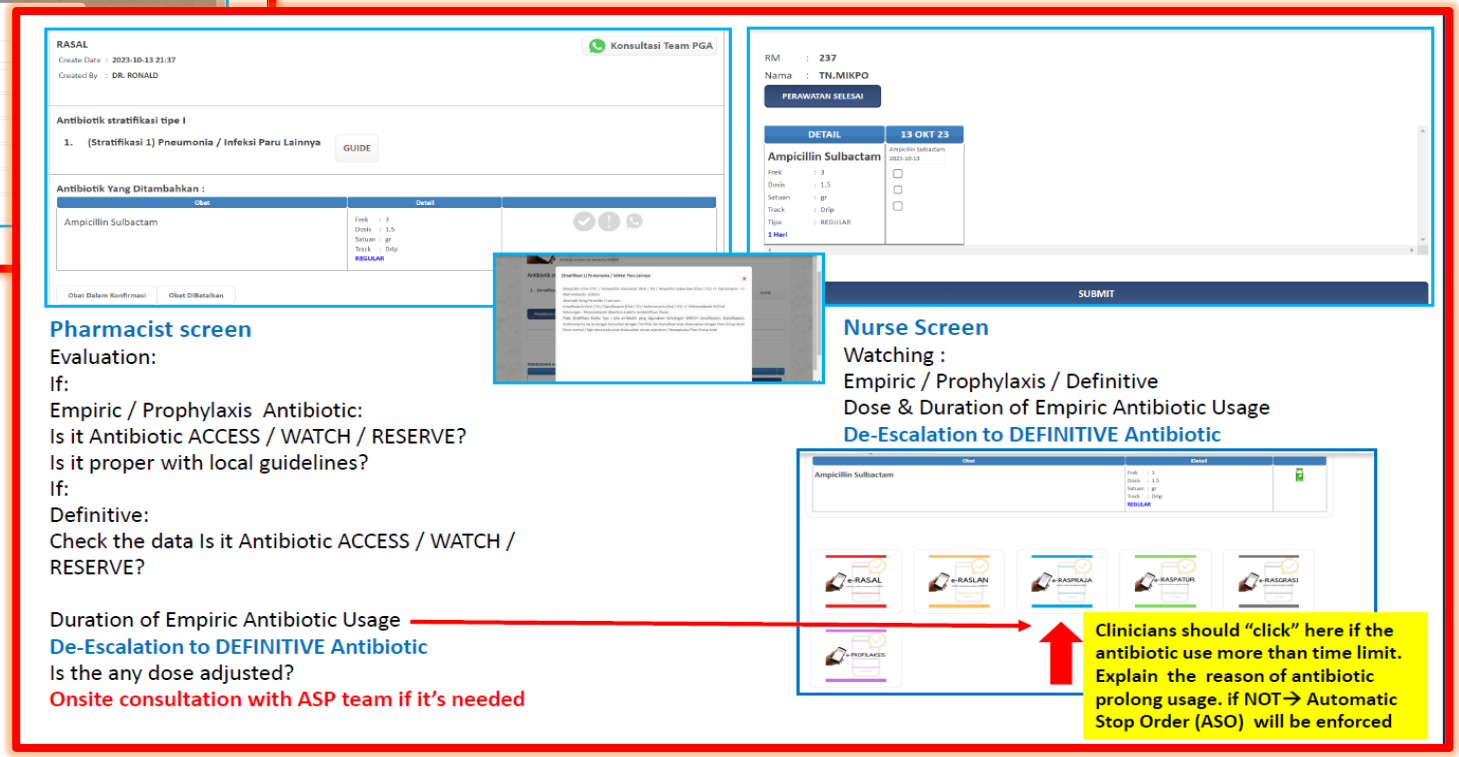



Antibiotic De-Escalation
Timing
Focus of Infection
Specimen from site of infection




**Pharmacist screen**
Evaluation:
If:
Empiric / Prophylaxis Antibiotic:
Is it Antibiotic ACCESS / WATCH / RESERVE?
Is it proper with local guidelines?
If:
Definitive:
Check the data Is it Antibiotic ACCESS / WATCH / RESERVE?

Duration of Empiric Antibiotic Usage
De-Escalation to DEFINITIVE Antibiotic
Is the any dose adjusted?
Onsite consultation with ASP team if it's needed

**Nurse Screen**
Watching :
Empiric / Prophylaxis / Definitive
Dose & Duration of Empiric Antibiotic Usage
De-Escalation to DEFINITIVE Antibiotic




## Digital Antibiotic Guidelines based on Risk Stratification , Journal Synthesis & Microorganism Pattern AWARE

## Pre authorization - Digital Monitoring

## Clinician – Pharmacist - PGA Team Connection

## Antibiotic de-escalation timing

## Difficult case notification

## Data sorting & management

## Evaluation

***Original Article***

# A Quantitative Survey on Antibiotic Prescribing Pattern in Three Indonesian Hospitals using Digital Antimicrobial Stewardship Tool (e-RASPRO)

Ronald Irwanto Natadidjaja[1,2], Aziza Ariyani[1], Hadianti Adlani[1,3,4], Raymond Adianto[1], Iin Indra Pertiwi[5], Grace Nerry Legoh[6], Alvin Rantung[6], Dianawati[5], Sri Mulyani[4], Ronaningtyas Maharani[4], Desi Anggiat[4], Triyoko Septio Marja[4], Hadi Sumarsono[1]

[1]RASPRO Indonesia Study Group, [2]Faculty of Medicine, Trisakti University, [3]Faculty of Medicine, Syarif Hidayatulah Islamic University, [4]Hermina Hospital Group Indonesia, [5]Tugu Ibu Hospital, [6]Advent Bandung Hospital

**Table 1. Demographic Characteristics of 3 Surveyed Hospitals**

| Demographic Characteristics of Hospitals | Hospital A | Hospital B | Hospital C |
|---|---|---|---|
| Number of Doctors | | | |
| General Physicians | 14 | 14 | 25 |
| Dentists | 5 | 15 | 8 |
| Specialist Doctors | 37 | 98 | 102 |
| Total | 56 | 127 | 135 |
| Number of Pharmacists | 9 | 26 | 39 |
| Number of Nurses | 115 | 74 | 368 |
| Number of Beds | | | |
| Wards | 124 | 168 | 259 |
| ICU + HCU + ICCU + NICU + PICU | 10 | 17 | 26 |
| Total | 134 | 185 | 285 |
| Ratio on numbers of specialist doctors : beds | 1 : 3.62 | 1 : 1.89 | 1 : 2.79 |
| Ratio on numbers of pharmacists : beds | 1 : 14.89 | 1 : 7.12 | 1 : 7.31 |
| Ratio on numbers of nurses : beds | 1 : 1.17 | 1 : 2.50 | 1 : 0.77 |
| The extent of the Buildings | 7,247.35 | 8,120.00 | 31,099.94 |

Data: sirs.kemkes.go.id

**Table 3. Initial Risk Stratification of Patients Receiving Antibiotics that Had Been Filled Out in the Digital Forms within 3 Months Following the Implementation of e-RASPRO in Three Hospitals**

| Risk Stratification | Hospital A 3 Months Oct – Dec 2021 | | Hospital B 3 Months Dec 2021 – Feb 2022 | | Hospital C 3 Months Nov 2022 – Jan 2023 | |
|---|---|---|---|---|---|---|
| | Number | % | Number | % | Number | % |
| Type 1 | 284 | 90.16% | 692 | 83.98% | 1,472 | 81.15% |
| Type 2 | 31 | 9.84% | 15 | 1.82% | 84 | 4.63% |
| Type 3 | - | 0.00% | 117 | 14.20% | 258 | 14.22% |
| Total | 315 | 100.00% | 824 | 100.00% | 1,814 | 100.00% |

***In progress publication***

**RASPRO Indonesia File & Documents 2022**

SSRN: https://ssrn.com/abstract=4822359 or http://dx.doi.org/10.2139/ssrn.4822359

# A Survey on Define Daily Dose of Watch- and Access-Category Antibiotics in Two Indonesian Hospitals Following the Implementation of Digital Antimicrobial Stewardship Tool

Ronald Irwanto Natadidjaja, Aziza Ariyani, Hadianti Adlani, Raymond Adianto, Iin Indah Pertiwi, Grace Nerry Legoh, Alvin Lekonardo Rantung, Hadi Sumarsono

**Background**: In 2023, the World Health Organization (WHO) began targeting a shift in antibiotic prescribing trends from WATCH to ACCESS category.

**Method**: This survey was a preliminary study, in which our study group designed a digital model of antimicrobial stewardship and the model was known as e-RASPRO. The survey on the use of antibiotic Define Daily Dose (DDD) was carried out in two hospitals in Indonesia at 3 months and 9 months of use, respectively. Data was retrieved retrospectively at the inpatient wards of both hospitals.

**Result**: Three months before and after the implementation of e-RASPRO in Hospital 1, the DDD of prophylactic antibiotic Cephazolin showed an increased of 167.18%. In hospital 2, Cephazolin had been used since the hospital applied the manual RASPRO concept. DDD of WATCH category antibiotics within 9 months following the implementation of e-RASPRO tool in hospital 1 showed a decrease of 49.01%. Meanwhile, the implementation of e-RASPRO for 3 months in Hospital 2 still showed an increase in WATCH category antibiotics by 20.18%; however, there was a decrease in DDD of Cephalosporin and Glycopeptide antibiotics by 7.63% and 49.30%, respectively. In the meantime, as a way of saving antibiotic use and shifting antibiotic prescribing to the ACCESS category, we found a decrease in DDD of ACCESS category antibiotics in Hospital 1 by 3.64% and an increase in Hospital 2 by 8.14%.

**Conclusion**: The survey may indicate that there are savings attempts in antibiotic use as well as an early change in DDD antibiotics from the WATCH category to the ACCESS category following the implementation of e-RASPRO tool in both hospitals. The time period of using the digital devices may still affect the results; however, this survey certainly has not illustrated a strong cause-and-effect correlation between the use of e-RASPRO tool and antibiotic DDD.

(Digital Model)

# Critical Ill and MDR Pathogen Treatment Strategy


***RI Natadidjaja***
***Infectious Disease (ID) Specialist***

# Prognostic accuracy of the quick Sequential Organ Failure Assessment (qSOFA)-lactate criteria for mortality in adults with suspected bacterial infection in the emergency department of a hospital with limited resources

http://orcid.org/0000-0003-3857-300X

**Robert Sinto, Suhendro Suwarto, Khie Chen Lie , Kuntjoro Harimurti, Djoko Widodo**
**Herdiman T Pohan**

**Results** Of 3026 patients screened, 1213 met the inclusion criteria. The AUROC of qSOFA-lactate criteria was 0.74 (95% CI 0.71 to 0.77). The AUROC of qSOFA-lactate was not statistically significantly different to the SOFA score (AUROC 0.75, 95% CI 0.72 to 0.78; p=0.462). The qSOFA-lactate was significantly higher than qSOFA (AUROC 0.70, 95% CI0.67 to 0.74; p=0.006) and SIRS criteria (0.57, 95% CI0.54 to 0.60; p<0.001).

**Conclusions** The prognostic accuracy of the qSOFA-lactate criteria is as good as the SOFA score in the emergency department of a hospital with limited resources. The performance of the qSOFA criteria is significantly lower than the qSOFA-lactate criteria and SOFA score.

Emergency Medicine Journal, Vol 37 issue 6, 2020

# Korelasi antara kadar *procalcitonin* dengan serum *transaminase* pada pasien sepsis: sebuah studi pendahuluan

Nur Hadi Kuswoyo[1] Ronald Irwanto Natadidjaja[2]

## RESULT

Mean age data is 47.5 ± 3.57 years old. Mean of PCT level in sepsis patient is 6.5083± 0.78 ng/ml, while the mean oftransaminase serum (SGPT) level each is 60.4167± 1.65 /mm3. The coefficient corelation of PCT to the SGPT show r = 0.812 ($p<0.05$).

## CONCLUSION

This research showed that liver dysfuunction may indicates the early event of sepsis. The high correlation between PCT and transamnase elevation resulted in this research.

*J Biomed Kesehat 2019 : 2 (1) : 15-19*

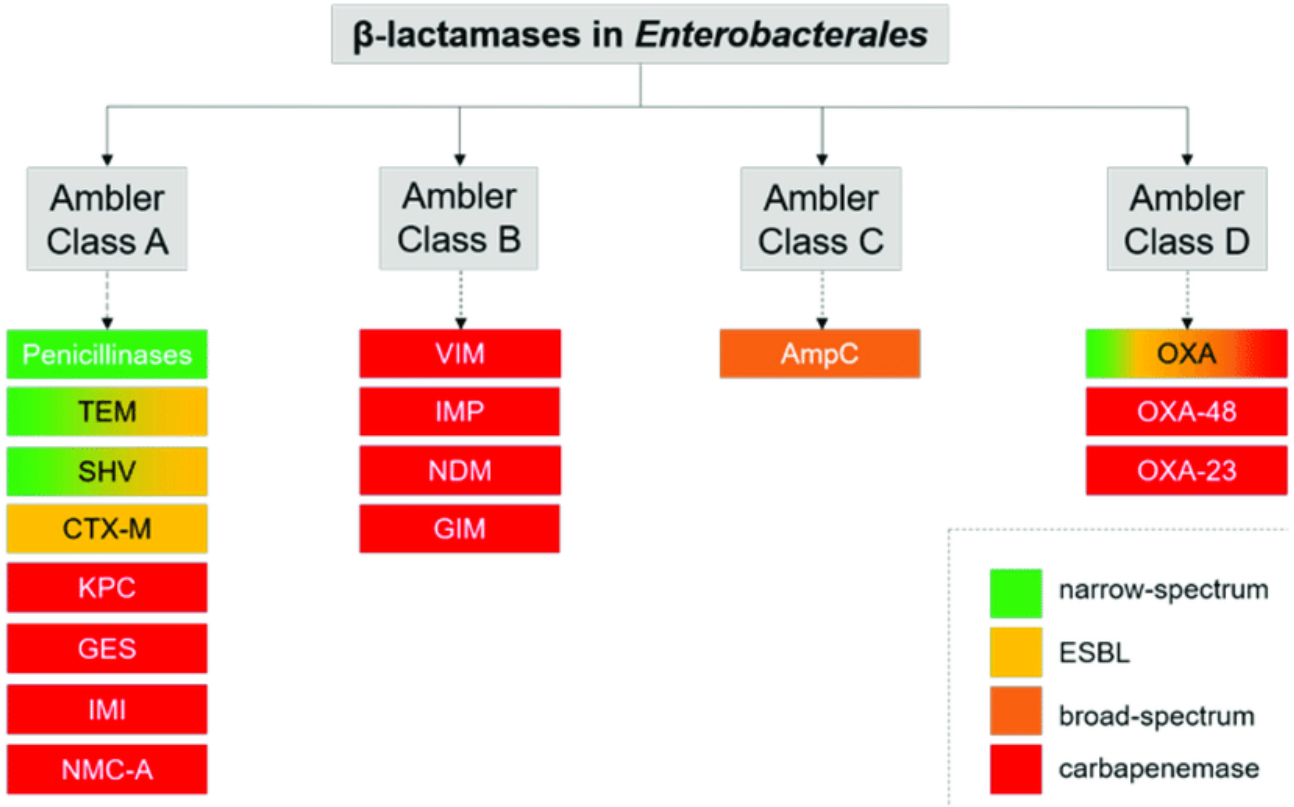
ORIGINAL ARTICLE BACTERIOLOGY

# Multidrug-resistant, extensively drug-resistant and pandrug-resistant bacteria: an international expert proposal for interim standard definitions for acquired resistance

A.-P. Magiorakos[1], A. Srinivasan[2], R. B. Carey[2], Y. Carmeli[3], M. E. Falagas[4,5], C. G. Giske[6], S. Harbarth[7], J. F. Hindler[8], G. Kahlmeter[9], B. Olsson-Liljequist[10], D. L. Paterson[11], L. B. Rice[12], J. Stelling[13], M. J. Struelens[1], A. Vatopoulos[14], J. T. Weber[2] and D. L. Monnet[1]

Many different definitions for multidrug-resistant (MDR), extensively drug-resistant (XDR) and pandrug-resistant (PDR) bacteria are being used in the medical literature to characterize the different patterns of resistance found in healthcare-associated, antimicrobial-resistant bacteria. A group of international experts came together through a joint initiative by the European Centre for Disease Prevention and Control (ECDC) and the Centers for Disease Control and Prevention (CDC), to create a standardized international terminology with which to describe acquired resistance profiles in *Staphylococcus aureus*, *Enterococcus* spp., *Enterobacteriaceae* (other than *Salmonella* and *Shigella*), *Pseudomonas aeruginosa* and *Acinetobacter* spp., all bacteria often responsible for healthcare-associated infections and prone to multidrug resistance. Epidemiologically significant antimicrobial categories were constructed for each bacterium. Lists of antimicrobial categories proposed for antimicrobial susceptibility testing were created using documents and breakpoints from the Clinical Laboratory Standards Institute (CLSI), the European Committee on Antimicrobial Susceptibility Testing (EUCAST) and the United States Food and Drug Administration (FDA). MDR was defined as acquired non-susceptibility to at least one agent in three or more antimicrobial categories, XDR was defined as non-susceptibility to at least one agent in all but two or fewer antimicrobial categories (i.e. bacterial isolates remain susceptible to only one or two categories) and PDR was defined as non-susceptibility to all agents in all antimicrobial categories. To ensure correct application of these definitions, bacterial isolates should be tested against all or nearly all of the antimicrobial agents within the antimicrobial categories and selective reporting and suppression of results should be avoided.

| Antimicrobial category | Antimicrobial agent | MDR | XDR | PDR |
|---|---|---|---|---|
| Aminoglycosides | Gentamicin | | X | X |
| | Tobramycin | | | X |
| | Amikacin | | | X |
| Carbapenem | Imipenem | X | X | X |
| | Meropenem | | X | X |
| | Doripenem | | X | X |
| Cephalosporins | Ceftazidime | | | X |
| | Cefepime | X | X | X |
| Fluoroquinolones | Ciprofloxacin | X | X | X |
| | Levofloxacin | | | X |
| Penicillins-βlactam | Pip-tazo | | | X |
| | Ticar-clav | | X | X |
| Monobactam | Aztreonam | | X | X |
| Phosphonic Acid | Fosfomycin | | | X |
| Polymycin | Colistin | | | X |
| | Polymyxin B | | | X |




**Detection of Multidrug-Resistant Enterobacterales—From ESBLs to Carbapenemases**

Antibiotics 2021, 10, 1140.
https://doi.org/10.3390/antibiotics10091140

## Multi-drug-resistant Gram-negative bacteria

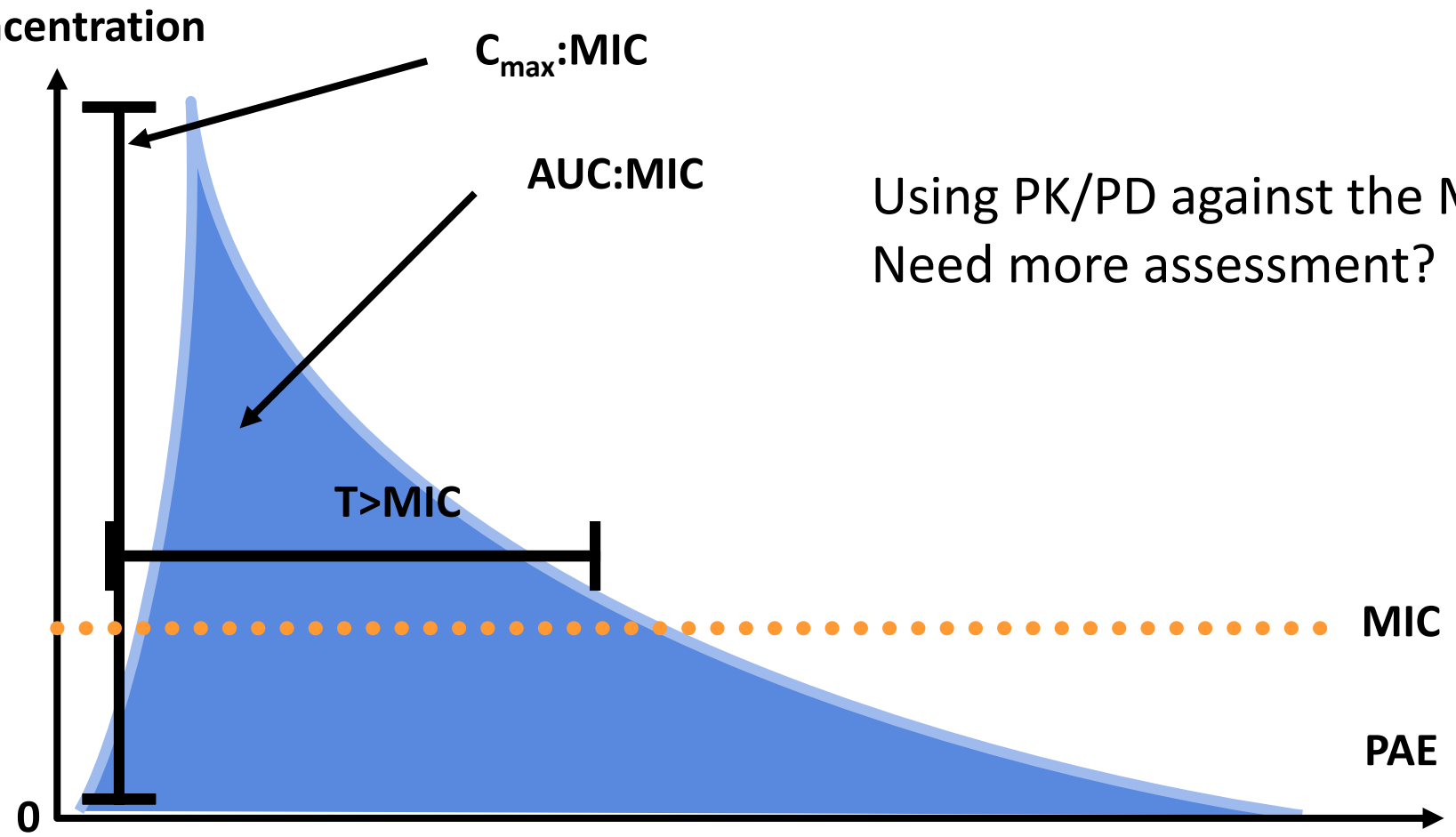
Hanna E Sidjabat , Witchuda Kamolvit , Alexander Wailan and David L Paterson+ Author Affiliations
*Microbiology Australia* 34(1) 43-46
https://doi.org/10.1071/MA13014
Published: 20 March 2013

| Ambler classification | Description or characteristics | Examples of enzymes | Bacterial strains |
|---|---|---|---|
| Class A (serine β-lactamase) | Cephalosporinases (ESBLs)<br>Usually clavulanic acid susceptible, except for KPC | TEM, SHV, CTX-M, **KPC**, VEB | *Enterobacteriaceae*, *Pseudomonas* spp. |
| Class B (metallo-β-lactamase or MBL) | Contain metal ion (Zn)<br>Carbapenemases<br>Not inhibited by clavulanic acid<br>Inhibited by aztreonam | **IMP, VIM, NDM** | *Enterobacteriaceae*, *Acinetobacter* spp., *Pseudomonas* spp. |
| Class C (AmpC β-lactamase – serine β-lactamase) | Resistant to clavulanic acid<br>Intrinsic in certain species of Gram-negative | CMY, DHA | *Enterobacteriaceae* |
| Class D (serine β-lactamase) | Oxacillinases<br>Susceptible to clavulanic acid<br>Carbapenemase | **OXA** | *Enterobacteriaceae* (OXA-48 like), *Acinetobacter* spp. |

Note: Enzymes in bold are carbapenemases.

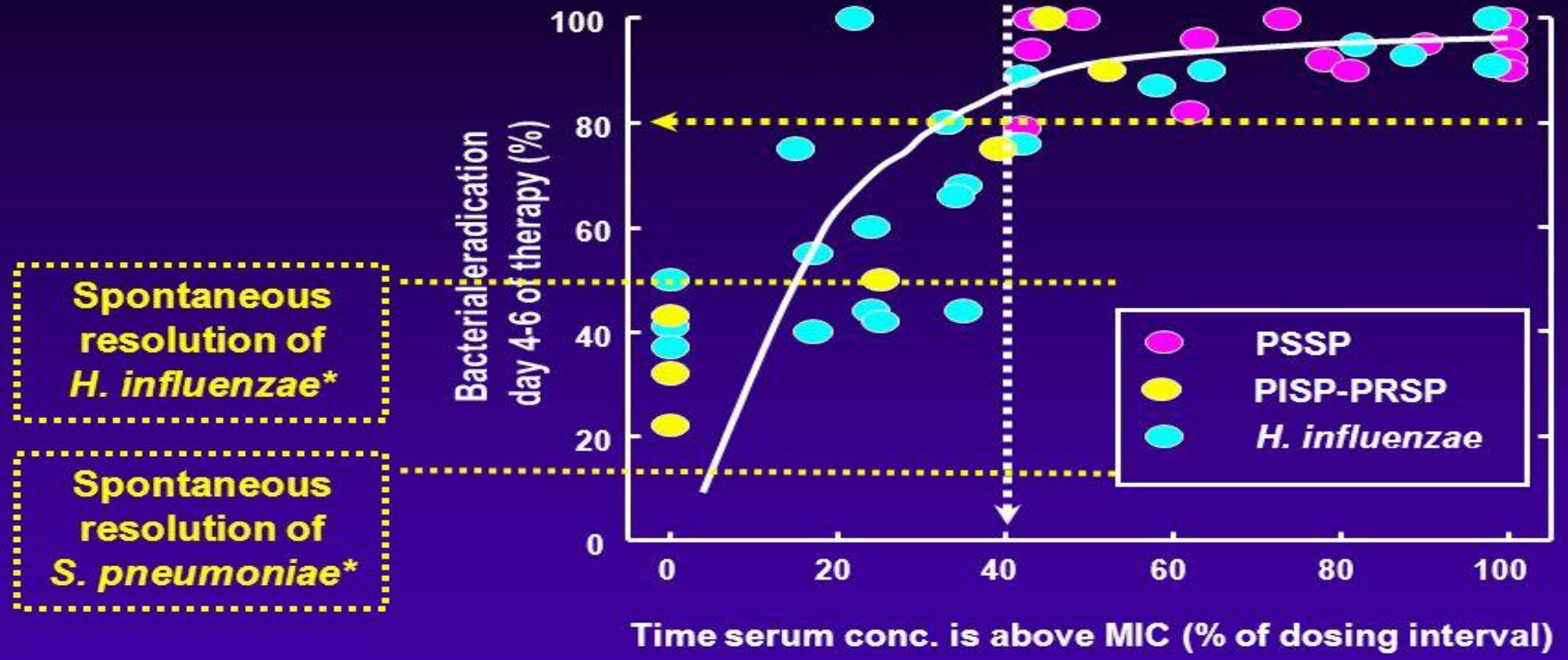
# Treat the MDR

## Strategy 1 : Using the PK/PD




Using PK/PD against the MDR bacteria?
Need more assessment?

# Relationship between time above MIC and bacterial eradication with β-lactams in otitis media




Craig W., Andes D. *Pediatr Infect Dis J* 1996; **15**:255–259.
Dagan R. et al. studies
*Howie, V. Clin Pediatr 1972, 11:205-214].

# Treat the MDR
# Strategy 2 : Find another Proper Broad Spectrum Antibiotic

## ESBL Treatment Option :

Carbapenem

Carbapenem Sparing Agent ( Combination therapy : BLI + Aminoglycosides, Piperacillin tazobactam, Ceftazidime Avibactam)

## MRSA Treatment Option :

Vancomycin, Teicoplanin

Linezolid

## S. maltophilia Treatment Option :

Levofloxacin

## MDR Pseudomonas Treatment Option

Carbapenem Combination Therapy – Aminoglicosides

Ceftazidime Avibactam

## Carbapenem Treatment Option :

Polimyxin

## MDR / XDR Acinetobacter Treatment Option

Tigecycline, Polimyxin

# Role of Ceftazidime Avibactam in Treating Severe Infection


***RI Natadidjaja***
***Infectious Disease (ID) Specialist***

# Ceftazidime Avibactam :

- **Reserve** category antibiotic
- The purpose?
- To decrease the carbapenem use – declining the risk of carbapenem resistant?
- Should be pre-authorized when it’s used both empirically or definitively!

# Ceftazidime/avibactam versus carbapenems for the treatment of infections caused by Enterobacteriaceae: A meta-analysis of randomized controlled trials

**Non Inferiority to Carbapenem Study**

Conclusion

CAZ-AVI is comparable with carbapenems in efficacy and safety for Enterobacteriaceae infections. More high-quality and large-scale RCTs are needed to further confirm the safety of CAZ-AVI. [PROSPERO ID: CRD42019116685.]

International Journal of Antimicrobial Agents
Volume 54, Issue 6, December 2019, Pages 809-813

# Ceftazidime-avibactam versus meropenem in nosocomial pneumonia, including ventilator-associated pneumonia (REPROVE): a randomised, double-blind, phase 3 non-inferiority trial

**Non Inferiority to Carbapenem Study**

**Interpretation:** Ceftazidime-avibactam was non-inferior to meropenem in the treatment of nosocomial pneumonia. These results support a role for ceftazidime-avibactam as a potential alternative to carbapenems in patients with nosocomial pneumonia (including ventilator-associated pneumonia) caused by Gram-negative pathogens.

. Lancet Infect Dis. 2018 Mar;18(3):285-295.
doi: 10.1016/S14733099(17)30747-8

# Ceftazidime/Avibactam versus Polymyxin B in the Challenge of Carbapenem-Resistant *Pseudomonas aeruginosa* Infection

**Conclusion:** CAZ/AVI therapy was superior to polymyxin B therapy for patients with CRPA infection, and provided significant survival benefits, but further larger studies were needed to substantiate our findings.

Infect Drug Resist. 2022 Feb 25:15:655-667.
doi: 10.2147/IDR.S350976. eCollection 2022

**Note :**

**Ceftazidime Avibactam is categorized into the Reserve Antibiotic**

**Should be pre-authorized with prospective audit when it's used both empirically or definitively**

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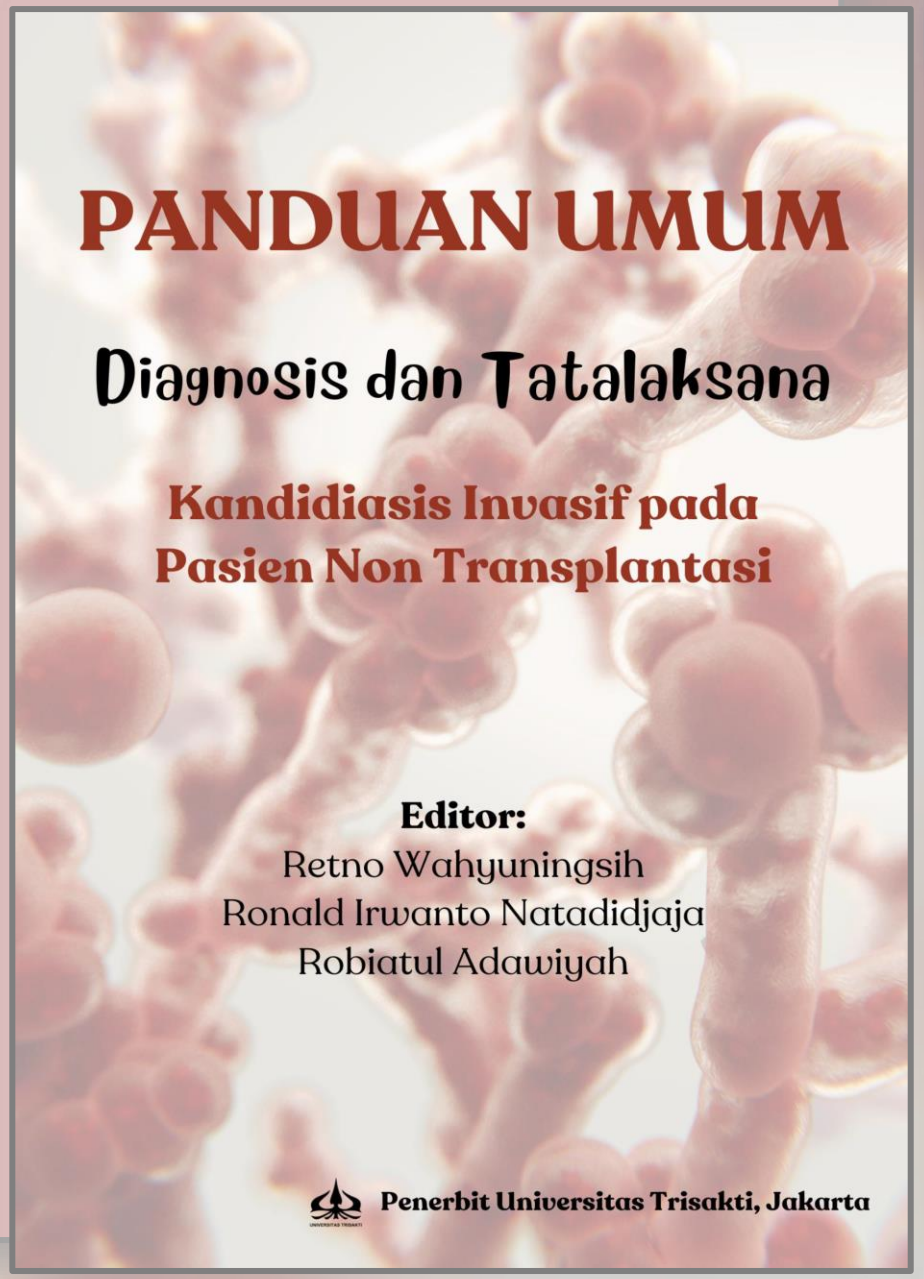
# Trisakti – RASPRO Indonesia Antimicrobial Stewardship (TRIASE) Learning Centre

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Thank You