Antibiogram based guidelines in Antimicrobial stewardship: RASPRO Concept, An Indonesian alternative solution to some key challenges of LMICs

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Background

Internist - Infectious Disease Specialist : **77 members** (PETRI, 2022)
Clinical Pathologist : **1753 members** (IDI, 2022)
Clinical Microbiologist : **214 members** (IDI, 2022)

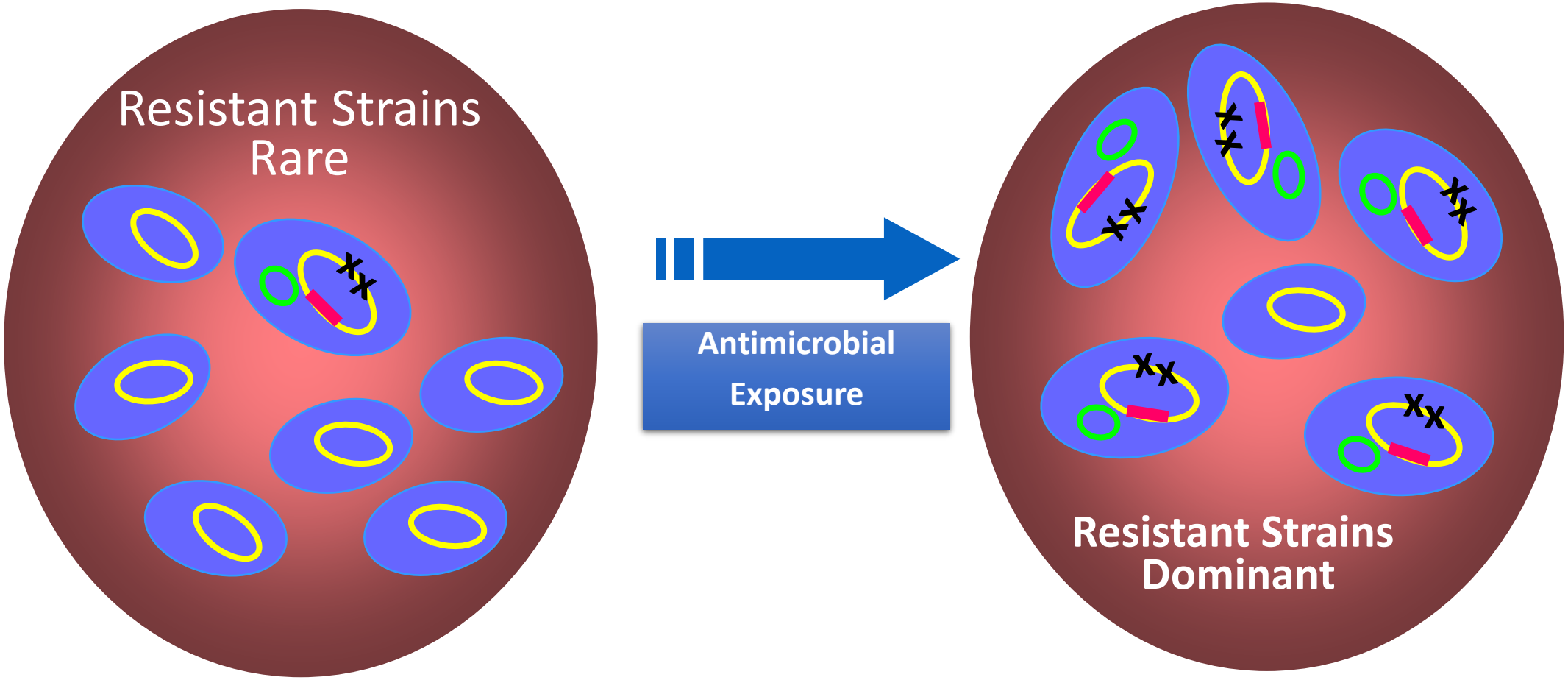
Hospitals : **3112 units** (BPS, 2021)

Indonesia & ASP

“ How we make it ? “

Background

Mechanism of Antimicrobial Resistance:
"Selective Pressure" for Antimicrobial-Resistant Strains



Setting Based Antibiogram

Community Based

Microorganism pattern of Skin and Soft 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%

Risk Stratification based Microorganism Pattern

	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

	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

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RONALD IRWANTO NATADIDJAJA[1,2], HADIANTI ADLANI[2], HADI SUMARSONO[2,3]

ORIGINAL ARTICLE

Bali Medical Journal (*Bali MedJ*) 2021, Volume 10, Number 3: 1031-1036
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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.

ARUC Score

Shorr et al

Alberti et al

Tumbarelo for ESBL

Duke for ESBL

Gomila et al

Marchaim et al

Carmeli et al
etc

Antibiogram Based Guidelines

- Considering :
  - Risk Stratification
  - Pharmacokinetic & Pharmacodynamic
  - Microorganism pattern

Good Diagnostic Stewardship for Good Antimicrobial Stewardship

RASPRO Antibiogram Based Guidelines (Example)

Org	Organism	No.	AMK	AMP	SAM	ATM	MEM	CTX	CAZ	CRO	CIP
eco	E.coli	164	95.4	23.5	89.3	15.3	100	78.8	98.5	88.7	80.5
kpn	K.pneumoniae	123	96.7	34.5	78.9	56.7	100	89.8	94.5	83.3	88.2
ecl	E.cloacae	73	93.3	23.3	80.8	40.5	100	78.3	91.1	77.7	100
aba	A.baumannii	45	74.3	11.1	24.4	10.1	88.9	15.4	15.4	12.3	75
pae	P.aeruginosa	42	85.4	15.3	15.1	10.3	90.1	45.3	80.9	15.2	50

Risk Stratification Type III (Group with possibility ESBL / Pseudomonas sp Infection)
Meropenem / Imipenem ± Ciprofloxacin / Amikacin

Ceftazidime + Ciprofloxacin / Amikacin

Risk Stratification Type II (Group with possibility ESBL infection)
Ertapenem /
Piperacillin Tazobactam

Risk Stratification Type I (Group with possibility of multi-sensitive microorganism) infection)
Ampisulbactam / Ceftriaxone / Cefotaxime / Amoxyclav

Risk Stratification Type III (Group with possibility ESBL / Pseudomonas sp Infection)
Meropenem / Imipenem ±
Ciprofloxacin / Amikacin

Ceftazidime + Ciprofloxacin / Amikacin

Risk Stratification Type II (Group with possibility ESBL infection)
Ertapenem /
Piperacillin Tazobactam

Risk Stratification Type I (Group with possibility of multi-sensitive microorganism) infection)
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Antibiotic usage at a private hospital in Central Java: results of implementing the Indonesian Regulation on the Prospective Antimicrobial System (Regulasi Antimikroba Sistem Prospektif Indonesia [RASPRO])

Ronald Irwanto Natadidjaja[1,2*], Tarcisius Henry[1], Hadianti Adlani[1], Aziza Ariyani[1] and Rika Bur[1]

[1]RASPRO Indonesia Study Group, Jakarta, Indonesia; [2]Infectious Disease Division, Trisakti School of Medicine, Trisakti University, Jakarta, Indonesia

NO.	SPECIFICATION	FLOW	STOP	TREATMENT	AB
1.	Bacterial infection site(s) & symptoms clearly explained	No	STOP	No AB Treatment	
		Yes	Site(s):		
2.	Sepsis/Febrile Neutropenia/Categorized into HAIs	Yes	STOP	Stratification Type III	
		No			
3.	Organ perforation	Yes	STOP	Stratification Type III	
		No			
4.	Bacterial infection encephalopathy	Yes	STOP	Stratification Type III	
		No			
5.	Immunocompromised and/or uncontrolled DM with history of antibiotic(s) taking in the last 30 days	Yes	STOP	Stratification Type III	
		No			
6.	Immunocompromised and/or uncontrolled DM with history of hospitalization more than 48 hours in the last 30 days	Yes	STOP	Stratification Type III	
		No			
7.	Immunocompromised and/or uncontrolled DM with history of medical devices usage in the last 30 days	Yes	STOP	Stratification Type III	
		No			
8.	Immunocompromised and/or uncontrolled DM with history of antibiotic(s) taking in the last 90 days	Yes	STOP	Stratification Type II	
		No			
9.	Immunocompromised and/or uncontrolled DM with history of hospitalization more than 48 hours in the last 90 days	Yes	STOP	Stratification Type II	
		No			
10.	Immunocompromised and/or uncontrolled DM with history of medical devices usage in the last 90 days	Yes	STOP	Stratification Type II	
		No	Stratification Type I		

AB = Antibiotic
HAIs = Healthcare Associated Infections
DM = Diabetes Mellitus

Fig. 1. RASAL flowchart.

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[1]RASPRO Indonesia Study Group, Jakarta, Indonesia; [2]Infectious Disease Division, Trisakti School of Medicine, Trisakti University, Jakarta, Indonesia

NO.	SPECIFICATION	FLOW	STOP	TREATMENT	FIRST AB	ADVANCE AB
1.	Clinical symptom(s) of infection still present	No	Stop	De-escalation due to the culture result/AB step-down to the lower stratification/switch from IV to oral/AB stop		
		Yes	Site(s):			
2.	Sepsis/Febrile Neutropenia/ Categorized into HAIs	Yes	Stop	Antibiotic escalation to stratification type 3		
		No				
3.	Organ perforation	Yes	Stop	Antibiotic escalation to stratification type 3		
		No				
4.	Bacterial infection encephalopathy	Yes	Stop	Antibiotic escalation to stratification type 3		
		No				
5.	Clinical symptom(s) improved between 3 to 7 days antibiotic treatment	No	Stop	AB escalation to the next stratification/AB added due to the guidelines		
		Yes	De-escalation due to the culture result/AB step-down to the lower stratification/switch from IV to oral/AB stop			

AB = Antibiotic
IV = Intravenous
HAIs = Healthcare Associated Infections

Fig. 2. RASLAN flowchart.

RASPRAJA

I. **Patient**
Name : .....
Age : .....
Gender : .....
Medical Record Number : .....

II. **Infection Site** : .....
1. .....
2. .....
3. .....

III. **Antibiotics**
Type Start date : .....
1. .....
2. .....
3. .....

IV. **Planning for to Stop Antibiotic**
Type Stop date : .....
1. .....
2. .....
3. .....

V. **Reason of Prolong Use of Antibiotic**
1. .....
2. .....
3. .....

Physician / Surgeon,

Name & Signature

Fig. 3. RASPRAJA form.

RASPATUR

I. **Patient**
Name : .....
Age : .....
Gender : .....
Medical Record Number : .....

II. **Specimen Taken from** : .....
1. .....
2. .....
3. .....

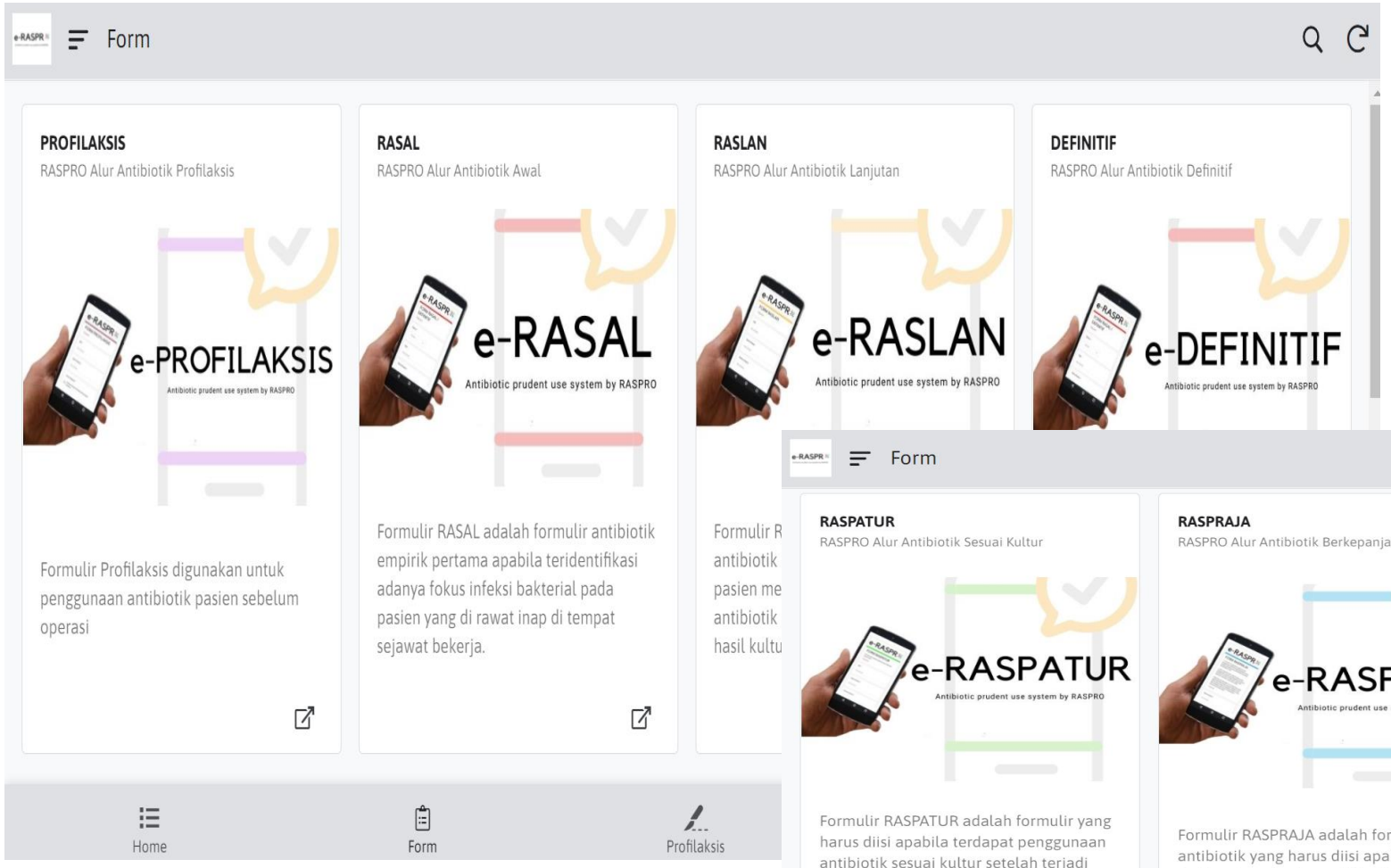
III. **Culture Based Antibiotics**
Type Start date : .....
1. .....
2. .....
3. .....

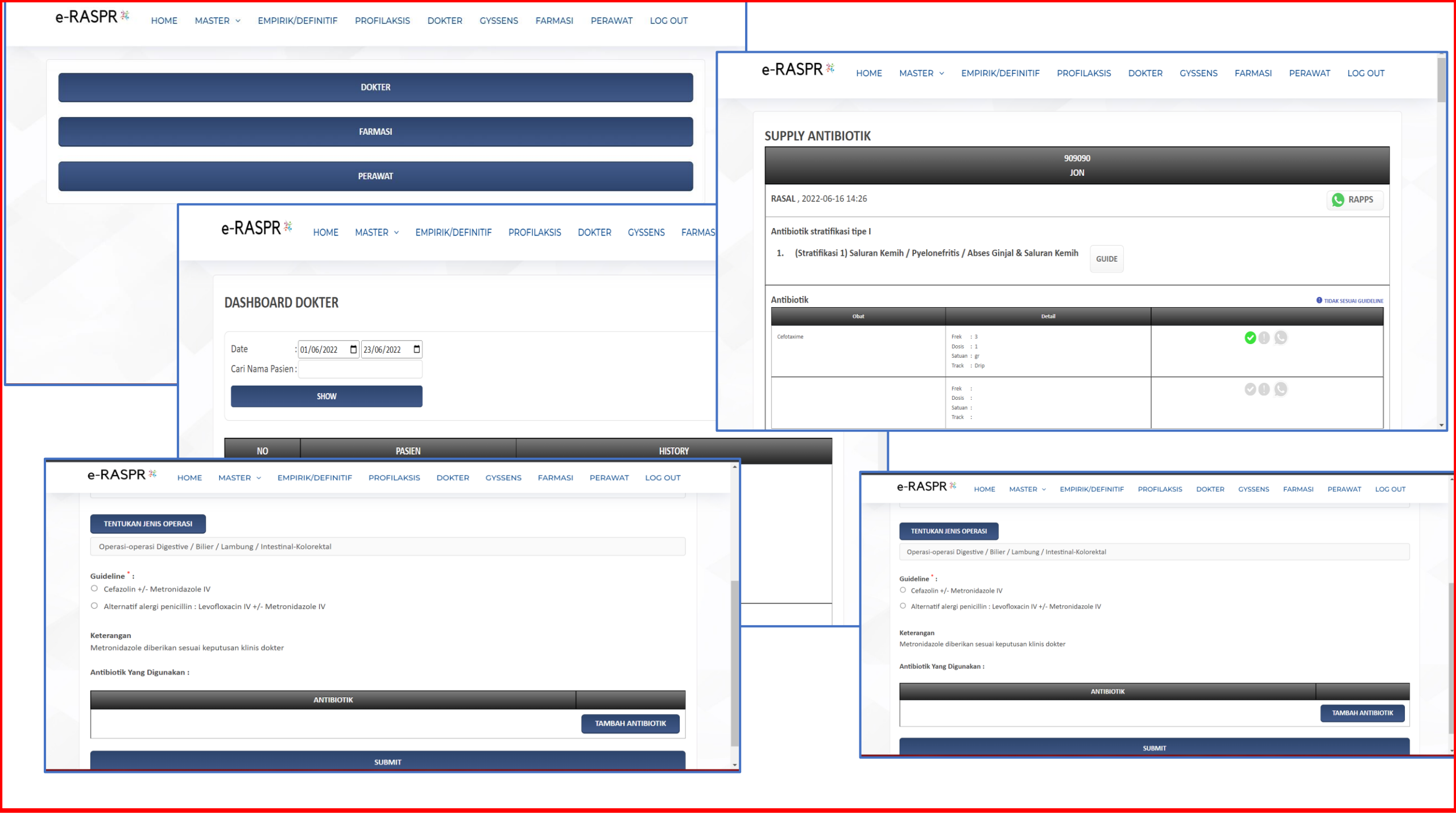
Physician / Surgeon,

Name & Signature

Fig. 4. RASPATUR form.

Electronic RASPRO (e-RASPRO) : an effort for ASP digitization




e-RASPR
HOME
MASTER
EMPIRIK/DEFINITIF
PROFILAKSIS
DOKTER
GYSSENS
FARMASI
PERAWAT
LOG OUT
DOKTER
FARMASI
PERAWAT
DASHBOARD DOKTER
Date : 01/06/2022 23/06/2022
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SHOW
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HISTORY
SUPPLY ANTIBIOTIK
909090
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RASAL , 2022-06-16 14:26
RAPPS
Antibiotik stratifikasi tipe I
1. (Stratifikasi 1) Saluran Kemih / Pyelonefritis / Abses Ginjal & Saluran Kemih
GUIDE
Antibiotik
TIDAK SESUAI GUIDELINE
Obat
Detail
Cefotaxime
Frek : 3
Dosis : 1
Satuan : gr
Track : Drip
TENTUKAN JENIS OPERASI
Operasi-operasi Digestive / Bilier / Lambung / Intestinal-Kolorektal
Guideline * :
Cefazolin +/- Metronidazole IV
Alternatif alergi penicillin : Levofloxacin IV +/- Metronidazole IV
Keterangan
Metronidazole diberikan sesuai keputusan klinis dokter
Antibiotik Yang Digunakan :
ANTIBIOTIK
TAMBAH ANTIBIOTIK
SUBMIT

Pre-Post Study

Decreasing the Broad Spectrum Antibiotics Unit Sold: The Prospective Antimicrobial Stewardship of RASPRO Model in A Private Hospital, Indonesia

Ronald Irwanto Natadidjaja*#, Yuhana Fitra, Yudianto Budi Saroyo**, Augustine Matatula**, Rinna Wamila Sundariningrum**

J Antimicrobiol Resist & Inf Control. 2019. 8(suppl 1) : P357

Results.

Three months observation and comparison before-after RASPRO-RASAL flowchart implemented :

0.5g Meropenem unit sold decreased 63.83%, 1g Meropenem decreased 75.42% while Imipenem showed 100% reduction.

A 93.80% decreasing of Ceftazidime and 70.05% Cefepime unit sold also reported.

Overall, we noted 76.10% broad spectrum reduced before-after RASPRO-RASAL implemented.

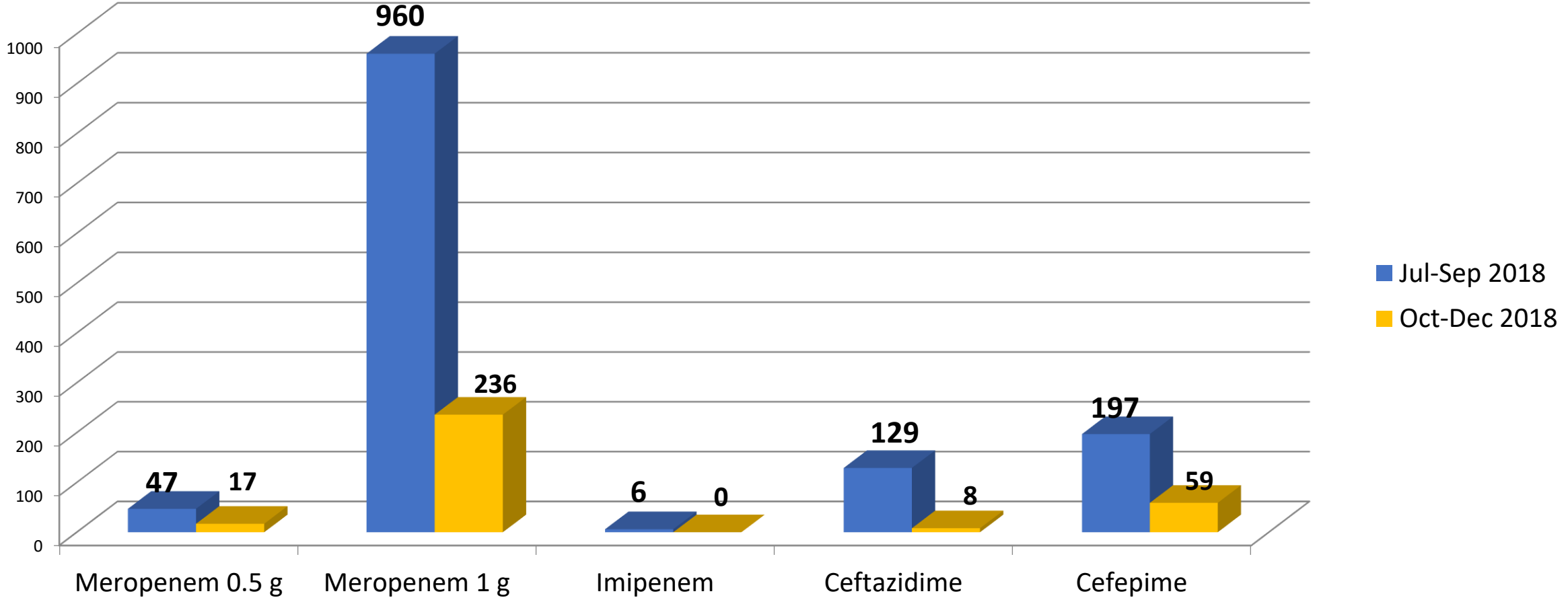
Conclusion.

Decreasing of broad spectrum antibiotics unit sold was reported in 3 months after RASPRO-RASAL used.

This result might not be a fully improvement of RASPRO-RASAL tools, but in our experience and opinion, this significant result should be considered as part of RASPRO-RASAL implementation.

Ronald Irwanto Natadidjaja*#, Yuhana Fitra, Yudianto Budi Saroyo**,
Augustine Matatula**, Rinna Wamila Sundariningrum**

Three Months Comparison of Broad Antibiotics Unit Sold: Before and After RASPRO-RASAL Criteria Implemented



J Antimicrobiol Resist & Inf Control. 2019. 8(suppl 1) : P357

Comparison of Antibiotic Expenditure 3rd Gen of Cephalosporine and Meropenem
Before- After 3 months RASPRO Concept Implemented in a Hospital, Indonesia

	2018	2019	Penurunan	
	Okt - Des	Jan - Mar	Unit	%
Ceftriaxone	7.887	5.588	2.299	29,15
Cefoperazone	5.699	3.627	2.072	36,36
Cefotaxime	860	649	211	24,53
Cefuroxime	1.068	969	99	9,27
Meropenem	1.196	1.048	148	12,37
Total	16.710	11.881	4.829	28,90

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RONALD IRWANTO NATADIDJAJA[1,2], YUHANA FITRA[1], AZIZA ARIYANI[1], RIKA BUR[1], NUGROHO BUDI SANTOSO[1]

Qualitative Evaluation of Antibiotic with Gyssens Method by RASPRO Concept for Pneumonia at Pediatric Intensive Care Unit

Rinna W. Sundariningrum,[1] Darmawan Budi Setyanto,[2] **Ronald Irwanto Natadidjaja** [3]

1Bagian Ilmu Kesehatan Anak Rumah Sakit Hermina Bekasi, 2Departemen Ilmu Kesehatan Anak Fakultas Kedokteran Universitas Indonesia/RSUPN Dr. Cipto Mangunkusumo, **3Departemen Ilmu Penyakit Dalam Fakultas Kedokteran Trisakti dan Yayasan Pelita RASPRO Indonesia**

Background. Pneumonia remains the commonest infective reason for admission to intensive care as well as being the most common secondary infection acquired whilst in the pediatric intensive care unit. Inappropriate use of antibiotics can increase morbidity, mortality, patient cost, and antibiotic resistance.
Objective. To qualitatively evaluate antibiotic use in pneumonia with The Gyssens method by RASPRO concept.
Methods. We performed a descriptive, retrospective study data based on medical records of patients with pneumonia who admitted to the pediatric intensive care unit in Hermina Bekasi Hospital from May to October 2019. Records were evaluation its qualitative antibiotic using the Gyssens method by RASPRO concept.
Result. This study discovered 51 cases (14,46%) of severe pneumonia. We found 119 antibiotics uses including 90 (75,63%) empirical therapies and 29 (24,37%) devinitive therapies. Ampicilin sulbactam was the most common antibiotic used (15,98%), followed by cefotaxime (15,12%), meropenem (13,44%), azithromycin (11,78%) and ceftriaxone (10,92%). Based on Gyssens method by RASPRO concept, appropriate antibiotic use (category 0) accounted for 63,02%, while inappropriated use accounted for 1,68% category IVa (improper; other antibiotics were more effective), 22,69% category IIIa (improper; duration too long), 9,24% category IIIb (improper; duration too short) and 3,36% category IIa (improper; incorrect dose).
Conclusion. Appropriate use of antibiotics showed quite good results, namely 63,03%. The RASPRO concept can be used to reduce subjectivity bias in qualitative antibiotic assessments by the Gyssens method for pneumonia treated in the pediatric intensive care unit.

Sari Pediatri 2020; 22(2): 109-14

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Table 1. The average antibiotic consumption (DDD/100 patient-days) in the 3-month period before and after the implementation of the RASPRO

Year 2019	Defined Daily Dose (DDD) /100 patient days							
	Levofloxacin	Carbapenem	Ceftriaxone	Cefuroxime	Cefotaxime	Ampicillin Sulbactam	Gentamicin	Amikacin
3 Months Before								
April	1.83	0.44	36.45	16.65	10.33	1.68	2.68	3.87
May	2.30	0.60	27.06	13.67	9.92	1.10	3.89	1.18
June	3.00	0.50	32.78	21.42	10.73	0.65	2.98	1.75
Average	**2.38**	**0.51**	**32.10**	**17.25**	**10.33**	**1.14**	**3.18**	**2.27**
3 Months After								
July	15.34	1.97	38.81	1.50	8.37	1.36	2.50	2.05
August	16.44	2.46	38.50	2.60	5.42	1.40	1.11	2.68
September	14.10	2.49	36.77	0.04	6.71	0.77	2.13	1.65
Average	**15.29**	**2.31**	**38.03**	**1.38**	**6.83**	**1.18**	**1.91**	**2.13**

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Table 2. Reduced average monthly cephalosporin consumption (DDD/100 patient-days) in the 3-month period before and after the implementation of the RASPRO

Year	Defined Daily Dose(DDD)/100 patient days			
	Ceftriaxone	Cefuroxime	Cefotaxime	Average
3 Months Before				
April	36.45	16.65	10.33	**21.14**
May	27.06	13.67	9.92	**16.88**
June	32.78	21.42	10.73	**21.64**
Average	**32.10**	**17.25**	**10.33**	**19.89**
3 Months After				
July	38.81	1.50	8.37	**16.23**
August	38.50	2.60	5.42	**15.51**
September	36.77	0.04	6.71	**14.51**
Average	**38.03**	**1.38**	**6.83**	**15.41**

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Table 3. A comparison of antibiotic expenditure in the 3-month period before and after the implementation of the RASPRO for inpatient settings

Year 2019	Inpatients	Antibiotic Expenditure	Antibiotic Expenditure/Inpatients
3 Months Before			
April	2,409	21,730	**9.02**
May	2,209	21,156	**9.58**
June	2,230	21,913	**9.83**
Total	**6,848**	**64,799**	
Average	**2,283**	**21,600**	**9.47**
3 Months After			
July	1,996	17,049	**8.54**
August	2,118	16,658	**7.86**
September	2,269	17,954	**7.91**
Total	**6,383**	**51,661**	
Average	**2,128**	**17,220**	**8.11**
Average % of Decreasing	**6.79**	**20.28**	**14.44**

RASPRO Concept Technical Guidance for ASP in Indonesian Hospitals

JAKARTA

National Cardiac Center Harapan Kita Hospital
Tebet Government General Hospital
Cempaka Putih Government General Hospital
Pasar Rebo Government General Hospital
Hermina Group Hospitals (40 hospitals)
Koja Government General Hospital
Pertamina Center Hospital
Jakarta Eye Center (JEC) Hospital
Primaya Group Hospitals (6 hospitals)
RSIA Kemang Hospital

Papua

Abepura Government General Hospital

Province of East Borneo

AW.Sjahranie Government General Hospital

Province of Central Java

Mardi Rahayu Hospital, Kudus
Tjitrowardojo Government General Hospital

Province of North Sumatera

Bunda Thamrin Hospital

Province of West Sumatera

National Stroke Bukit Tinggi Hospital
Prof Ali Hanafiah Government General Hospital

Province of West Java

Bandung Adventist Hospital
Immanuel Hospital
Sayang Hospital, Cianjur
Cicendo National Eye Center
Syamsudin Government General Hospital

Province of Jambi

HAMBA Government General Hospital
Kolonel Abundjani Government General Hospital

Province of East Java

Soedono Government General Hospital Madiun
Sudomo, Government General Hospital, Trenggalek
Syamrabu Government Hospital, Bangkalan
Bangil Government Hospiital, Pasuruan

Province of Kepulauan Riau

Awal Bros Batam Hospital

Thank You