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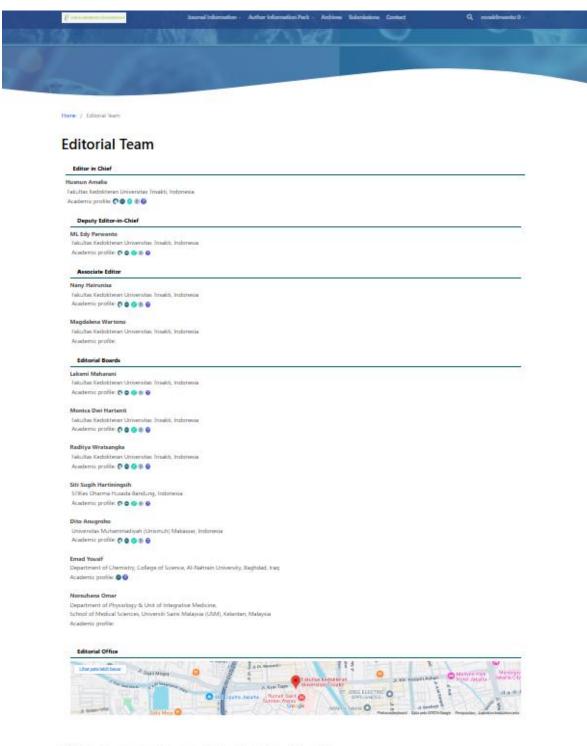
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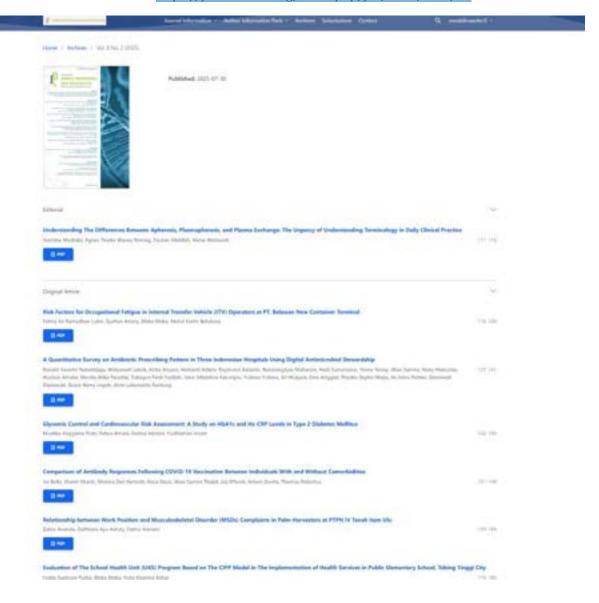


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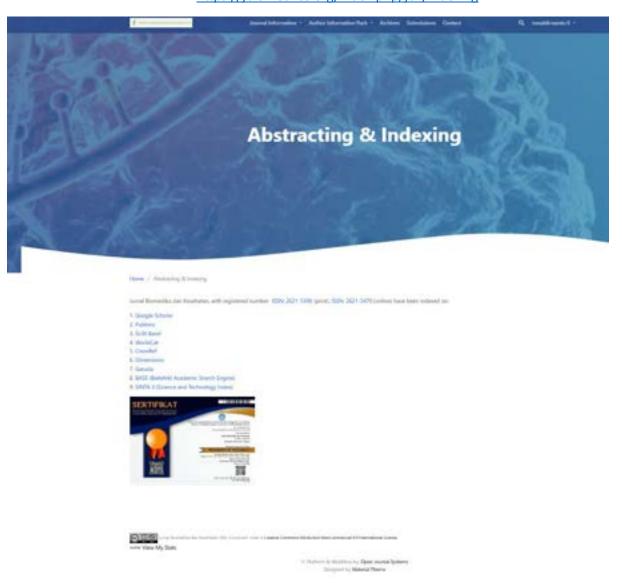
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BUKTI KORESPONDENSI

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[JBK] Submission Acknowledgement



Ronald Irwanto Natadidjaja:

Thank you for submitting the manuscript, "A Quantitative Survey on Antibiotic Prescribing Pattern in Three Indonesian Hospitals using Digital Antimicrobial Stewardship" to Jurial Biomedika dan Kesehatan. With the online journal management system that we are using, you will be able to track its progress through the editinal process by logging in to the journal web site.

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If you have any questions, please contact me. Thank you for considering this journal as a venue for your work.

Dr. dr. Huston Amatia, Sp.M.

Aurus Giomedica dan Kesehatan

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[JBK] Editor Decision @



Husmun Amaka

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Ronald Invanto Nataddaja, Widyawati Lekok, Aciza Ariyani, Hadanti Adlani, Raymond Adlanto, Ronaningtyas Mahanani, Hadi Sumarsono, Yenny Yenny, Jihan Samira, Nany Hasunisa, Hussun Amalia, Meutia Alka Faradila, Tubagus Fertii Fadilah, Joce Wiladelwa Kalumpia, Yuliana Yukina, Sri Mutyan, Desi Anggiat, Tinyoko Septio Marja, Ini tridra Pertiivi, Dianawati Dianawati, Orace Neny Legoh, Alvin Lekonando Rantung

We have reached a decision regarding your submission to Jurnal Biomedika dan Kesehafan, "A Quantitative Survey on Antibiotic Prescribing Pattern in Three Indonesian. Hospitals using Digital Antimicrobial Stewardship".

Our decision is: Revisions Required

Junal Biomedika dan Kesehatan

Ji. Kysi Tapa No. 260 Kampus B, Grogol, DKI Jakarta 11440

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Manuscript review checklist		
Title: A Quantitative Survey on Antibiotic Prescribing Pattern in Three Indonesian Hospitals using Digital Antimicrobial Stewardship		
Sent Date: 7 July 2025		
Due Date for Review: 14 July 2025	Adequate	Needs revision

TITLE	V	
Not more than 15 words		
Clearly describes the article		
Abstracts should be of approximately 200-300 words Reflects the content of the article	V	
Keywords: provide 3 – 10 keywords		
INTRODUCTION		
1. Rationale for study (need and significance)	V	
2. Summarizes relevant research to provide context,		√
and explains other authors' findings		
3. Describe the novelty of the study	V	
4. Objective of the study		V
METHODS		
1. The design is suitable for answering the question	V	
2. The sampling is appropriate	V	
3. Data Collection Procedures	V	
4. Measurements have been described	V	
5. Data Analysis (Description of Statistical Evaluation)		V
C. RESULTS		
Detail in narrative of the findings	V	
2. Descriptive quality of figures and tables (if relevant)	V	
3. Clearly laid out and in a logical sequence	V	
4. The analysis has been conducted appropriately	V	
DISCUSSION		
Findings compared and contrasted with relevant literature		√
2. The results support or contradict previous theories	V	
3. Limitations of the study	V	
4. Clinical implications of the study		V
5. Future directions of the study	V	
CONCLUSIONS		

1. Drawn logically	$\sqrt{}$	
ACKNOWLEDGEMENT	V	
AUTHOR CONTRIBUTION	V	
FUNDING STATEMENT	V	
CONFLICT OF INTEREST	$\sqrt{}$	
REFERENCES		
1. Compliance with journal format (Vancouver style)	$\sqrt{}$	
2. The minimal number of references should be 20 and 85% of them should be	$\sqrt{}$	
recent (published during the last 10 years, with the majority during the last 5 years)		
3. Abbreviate journal names according to the Index Medicus system	V	
4. The total number of tables and figures not more than 5	V	

advise for the author(s)

This article is quite relevant and useful regarding the assessment of antibiotic prescription quantity patterns with Digital Antimicrobial Stewardship in Indonesia. However, there are some notes related to this article that need revision.

1. Introduction

- It should be added with more relevant research to provide context and explain other authors' findings.
- The aim of the study should be stated clearly, usually at the end of the introduction

2. Method

- What are the criteria for selecting hospitals? For example, based on the locations, government/private hospitals, or the duration of applying that system?
- Locations of the hospitals should be stated, at least to the province/ city, since Indonesia is too large.
- When was the research conducted?
- What kind of statistical analysis is used? univariate/ bivariate?

3. Result

The results are quite numerous and detailed. The table number should be written in narration following the tables, although all the narratives are sited below the table in question

4. Discussion

- All subtitles in the discussion section should be deleted, since the table number is already stated, and it is not common.

- It should be elaborated with more references to discuss the gap in findings and clinical implications.
- Limitations must be written, which may affect the results, apart from the fact that this research is a preliminary study.

5. Conclusion

- Since the survey has not been able to describe the causal-effect correlation between e-RASPRO implementation and the quantity of antibiotic prescribing. What is your suggestion/recommendation for the next?

RESPONSE TO REVIEWER'S COMMENT

antitiootics that have greater potency on resistance and antitiootics in Neserve category are types of antibiotics that are used only when there is an infection caused by suspected Multi-Drug Resistant. (VIDR) bacteria; these antibiotics should not be used carelessly, particularly in large quantity.

In this case, the RASPRO indonesia Study Group has tried to develop a system, which is called as RASPRO system that can guide clinicians in antibletic prescribing based on local guideline. The RASPRO system was made by using risk stratification of patients and it directs clinicians in initial prescribing of empirical antibiotics as well as a guideline in changing antibiotics and providing definitive antibiotic treatment including filling out compulsory specialized forms when there is any prolonged use of antibiotics.)

Our survey is a continuation of previous survey conducted in a hospital in Central Java, indonesta. The hospital has implemented a manual RASPRO system to carry out the ASP. The survey, which was carried out before and after the manual system had been implemented for three months, showed that there was a decrease in antibiotic prescribing from 64,799 ampules/vials to 51,661 ampules/vials with reduced mean percentage of artibiotic use within 3 months of implementation reaching 14,443. The previous RASPRO system using the manual guideline forms was then tested into a digital form of electronic RASPRO (e-RASPRO); therefore, e-RASPRO has become a digital tool in Indonesia designed to carry out ASP in hospitals. Through e-RASPRO, a local antimicrobial guideline is developed digitally by filling out RASPRO forms, which is also made digitally that consists of electronic forms for empirical antibiatics and defeative antibiotics figurable survey of a PASPRO implementation showed a 45 or fill decrease of Watch, category antibiotics Define Dalls Date (2001) within a martin implementation and stiff showed an increase in Watch sategory antibiotics 2000 by as a 65 within a morths implementation.

Clinical pharmacles can also perform direct verification on indication appropriateness, time limitation of antibiotic use and appropriateness of using empirical antibiotics by utilizing the digital guideline on antibiotic between the state of the properties of the support of the properties of antibiotic prescribing, i.e. prioritizing the use of Access category antibiotics in order to suppress the risk of widespread resistance against antibiotics, particularly the wide-spectrum antibiotics. The aim of this attack is to show the comparison of antibiotic prescription pattern among a months and a months implementation of a RASPEC in a bountals. Ronald treamto July 14, 2025 Formattind: Fort: Carders, 13 pt

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METHODS

A survey was conducted at 3 hospitals in indonesia, i.e. Hospital A, Hospital B and Hospital C.

All hospitals are located in West Leva, and were chanse by their service level category. One of them
is a primary hospital (Hospital A) and other two hospitals are, secondary hospitals (Hospital B and
C). Previously, various socialization on implementing digital antimicrobial stewardship program
using e-RASPRO has been performed that includes socialization on digital prescribing of emphical
antibiotics as well as definitive antibiotics, socialization on patient grouping based on the Risk
Stratification in order to perform empirical antibiotics prescribing using digital tool and socialization
on the digital guideline on using empirical antimicrobial agents, and socialization on prolonged
antibiotic use in digital tools.

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Socialization on Digital Prescribing of Empirical Antibiotics in e-RASPRO

Socialization was performed on implementing e-RASPRO in three hospitals to prescribe empirical antibiotics. In prescribing empirical antibiotics, clinicians were guided to determine risk stratification of hospitalized patients based on their immune status, severity of infection and medical history such as history of previous antibiotic use, history of previous hospitalization and history of previous medical instrument usage.

Socialization was also carried out about the guideline and procedure on how to fill out the forms of escalating and stepping down empirical antibiotics, which was consistent with the digital middline on the use of antipological prenty in a PASCRO. When appoint a pathiotic operations use through a digital form in e-RASPRO. It would then be verified by clinical pharmacy and it was reported to the ASP team in the hospitals.

When there was a prolonged antibiotic use without any filled out electronic form in e-RASPRO about the concerned issue or without any clear indication, then the clinical pharmacy in accordance with the consent issued by Hospital ASP team could perform Automatic Stop Order (ASO). Socialization was carried out by the investigators for the Antimicrobial Resistance Control Program Committee of the three hospitals and it was continued for clinicians at each hospital. The socialization was performed online and offline.

Survey Setting and Time Period of Data Collection

The retrieved data was secondary data, univariate analyses, which was obtained from reports on the use of injected antibiotics at hospital wards of the three hospitals. Data was taken from January 2021 – June 2022 in Hospital A, March 2021 – August 2022 in Hospital B and August 2021 – January 2022 in Hospital C. Through implementation of e-RASPRO, initial data collection was performed within the first three-month, which included percentage of patients in each risk stratification group based on the digital e-RASPRO forms as well as appropriateness of initial empirical antibiotic prescribing with the digital guidelines on the use of antimicrobial agents.

The survey was followed by collecting all quantitative data on empirical antibiotic prescribing as well as injected definitive antibiotics prescribing for hospitalized patients within 9 months before and after the implementation of e-RASPRO in two hospitals (Hospital A and B) and within 3 months before and after utilizing e-RASPRO in another hospital (Hospital C). When the data was retrieved, Hospital C had just implemented e-RASPRO for 3 months. Interviews and discussions with the Antimicrobial Resistance Control Program Committee of the three hospitals were carried out during the initial utilization of e-RASPRO as well as when the survey data was retrieved.

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RESULTS

The following was data obtained from the survey conducted within the first 3 months of implementing e-RASPRO at 3 hospitals in Indonesia:

Table 1. Demographic Characteristics of 3 Surveyed Hospitals

Demographic Characteristics of Hospitals		Hospital	4.0	
	A	8	C	
Number of Doctors				
General Physicians	14	14	25	
Dentists	5	15	25 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	111.89	122.79	
Ratio on numbers of pharmacists; beds	1:14.89	117.12	117.31	
Ratio on numbers of nurses; beds	111.17	113.50	1: 0.77	
The extent of the Buildings	7,247-35	8,120.00	31,099.94	
Data: sirs.kemkes.go.id	N/min/min	2.0	AL INVESTIGATION	

Table s. Actual demographic data of the three surveyed hospitals, which was collected from sirs.kemkes.go.id, Ministry of Health Republic of Indonesia, was as the following: Hospital A, B and C had +34 beds, +85 beds and 254 beds, respectively; with ratio of specialist doctors per bed of each hospital was + per 3.62 beds, + per +.89 beds and + per 2.79 beds.

Table 2, 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 Hospital A Hospital B

Table 2. 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	3 Mc	ital A onths sec 2021	000000000000000000000000000000000000000	ital B inths - Feb 2022	Hospital C 3 Months Nov 2022 – Jan 2023	
	Number	*	Number	*	Number	X
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	#00.00t	1,814	100.00%

Table 2. In the digital e-RASPRO form, which was filled out within 3 months during initial utilization of e-RASPRO, majority of patients were in the Type 1 Risk Stratification category with the percentage in Hospital A, B and C reached 90.16%, 83.98% and 81.15%, respectively.

guideline of antimicrobial use in e- RASPRO						
Empirical antibiotic prescribing has unidentified consistency in e- RASPRO	,	0,525		soot	348	19,125
Total of forms had been filled out	375	100.00%	814	100,00%	ÇE14	100.00\$

Tabel 3. The appropriateness of empirical antibiotic prescribing with the digital guideline on the use of antimicrobial agents contained in e-RASPRO, which was documented in Hospital A, B and C within 3 months before and after implementation of e-RASPRO, reached \$1,59%, 76.09% and 24.45%, respectively. Empirical antibiotic prescribing with non-identified appropriateness, which was documented in the digital forms, was defined as antibiotic prescribing using e-RASPRO with vague appropriateness, for example combined antibiotics prescribing in which one of the antibiotic was appropriate; while the other was not consistent with the digital guideline of antimicrobial agents or other variant condition, in which the appropriateness could not be concluded during data collection. Such condition was documented as much as 19.48% in Hospital C.

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Metronidacole	USA	1,006	14.92%	1,731	2,424	40.03%	1,610	4339	16.83%
Cefurosime	1000	0.014(0.0)	100000	838	3,074	HOUX	0.00		1000
Total Access	2,149	3,416	19.42%	4,679	15,401	213.47%	2,113	1,959	6.86
Total Access /	0.5098	0.5232	3.645	0.6034	3.3256	168.83%	0.7533	0.7364	0.19%
In Policet				10.00					

When the data was collected, e-RASPRO had been implemented for g months in Hospital A and B, but it has only been implemented for g months in Hospital C; the results were as follows:

Table 1. The use of antibiotic included in Reserve category such as <u>Polymbin</u> and <u>Typecycline</u> was not found in this survey. There was reduced quantity of Ceftriaxone prescribing significantly in Hospital A, B and C as much as 62.91%, 40.58% and +0.66%, respectively. Nevertheless, there was a very significant increase of Cefotaxime prescribing in Hospital A and B with increased percentages of 35.32 % and >100% each.

A significant increase also occurred for Ciprofloxacin prescribing in three hospitals. The quantity of you mg Levefloxacin prescribing in Hospital A, B and C had some decrease of 45.44%, 64.84% and 76.25% respectively. The quantity of 750 mg Levefloxacin reduced in Hospital A and B as much as 65.45% and 13.26% each; however, it increased significantly >100% in Hospital C. The quantity of prescribing 1.gram Meropenem in Hospital A and B reduced as much as 41.32% and 13.45%, respectively; however, it still increased in Hospital C as much as 10.00%. The quantity of Acthromycin prescribing also decreased very significantly in Hospital B, Le. 93.26%. Piperacilin Tazobactam seemed to be very rarely used. The minimum use was found in Hospital B i.e.

as many as as ampules/vials within 9 months period before e-RASPRO tool was implemented. In general, there was reduced quantity of antibiotic use included in Watch category at Hospital A, B and C of 54,93% (-58.86% per impatient), 21.11% (-9.91% per impatient) and 8.59% (-4.15% per impatient), respectively. The quantity of Access category antibiotic prescribing in Hospital A, B and C was as follows: there was tools increase of Ampicilin and Amossicilin-Clarelanate prescribing in the implementation of ASPIIII This survey is a limited survey conducted at three hospitals in Indonesia which have different characteristics as shown in table v.

in table s, it can be seen that Hospital C is the hospital with the greatest resources regarding number of physicians, pharmacists and nurses compared to Hospital A and B. It also has the largest building compared to the other two hospitals. Various human resources in the hospital and its large size had brought their own difficulties in terms of socializing antimicrobial stewardship program, either using manual or digital method. In daily practice, unevenly distributed level of socialization may affect the level of appropriateness of antibiotic use with the digital guideline on the use of antimiorobial agents contained in e-RASPRO.

in table 2, we can see that most patients who would receive early empirical antibiotic escribing at hospital admission are those who had Type + Risk Stratification as documented in e-RASPRO. These patients include a group of immunocompetent patients or immunocompromized patients who had unthreathering bacterial infection or those who are not at risk of having infection caused by MDR microorganisms. Prescribing wide spectrum antibiotics should be avoided as much as possible in patients who were mostly included in the group with Type + Risk Stratification. It should be taken into caution considering that using various type of antibiotics may increase the risk of developing resistance. As the diseases progress, empirical antibiotic treatment certainly can be escalated in accordance with the patient's condition.

Table 3 describes the appropriateness of initial empirical antibiotic prescribing with the digital antimicrobial guideline as documented in Hospital A, B and C within 3 months of using a-RASPRO, which reach \$1.59%, 76.09% and 24.48%. It is categorized as "appropriate prescribing" when the empirical antibiotic is given in accordance with the digital guideline of antimicrobial use included in e-RASPRO that is compliant with patient's risk stratification. There is a high percentage of a group of patients with Type + Risk Stratification. This result is expected to bring some changes in the quantitative pattern of antibiotic prescribing from the type of antibiotics included in the Watch category to those in Access category.

The appropriateness of antibiotic prescribing in Hospital C, which is documented in digital e-

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Access category such as Ampicillin Subactam or Amoxycillin Clavulanate with or without combination of Aminoglycosides as the anti-ESBLs often serve as empirical antibiotic of choice to be given for patients who are included in the Type a Risk Stratification. Nevertheless, in reality, the initial 3-month survey on the implementation of e-RASPRO in three hospitals has shown that the number of patients included in the Type 2 Risk Stratification group were minority. Overall, there is a reduced quantity of Watch category antibiotic prescribing in Hospital A, B and C as much as 54.93% (-58.86% per inpatient), 24.4% (-9.97% per inpatient) and 6.59% (-4.45% per inpatient) following the implementation of e-RASPRO.

in Table 4 a survey conducted for 9 months before and after the utilization of e-RASPRO in Hospital A and B and 3 months before and after implementing e-RASPRO in Hospital C has demonstrated a significant increase in the quantity of antibiotic prescribing of Ampicilin, Amoxycillin Clavulanate and s.5 g Ampkillin Sulbactam, which are antibiotics included in Access category in the three hospitals. The survey conducted within the first 3 months of e-RASPRO utilization has demonstrated that the majority of patients are included in the Type i Risk Stratification group of those three hospitals (Table 2), in which the majority of empirical antibiotic choices indeed are antibiotics included in the Access category. Nevertheless, it certainly requires futher surveys to be carried out on the following months in Hospital A and B.

The significant increase of o.75 g Ampicilin Sulbactam prescribing may also still be associated with the continuity of s.5 g Ampicillin Sulbactam availability in Hospital B. Some sources in Hospital B, through a discussion with the investigators, suggest that there is often shortage supply of 1.5 Ampicilin Subactam in Hospital B. Therefore, considering this reasoning, the Antimicrobial Resistance Control Program Committee in Hospital B has included Cefuroxime in Access category of its guideline on antimicrobial use. This condition explains the presence of increased quantity of Cefuroxime prescribing, which is included in Access category in Hospital 8.

Based on the digital guideline on antimicrobial use in ##ASPRO of the three hospitals, Aminoglycosides has actually been used as combined antibiotics. It has not been identified clearly about the cause of reduced Gentamycin prescribing in Hospital A, while in Hospital C, the use of Gentamycin and Amikacin indeed have not been documented either before or after the

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on the quantity of Watch category antibiotic prescribing in three hospitals as well as increased percentage of quantity of Access category antibiotic prescribing in two hospitals (Hospital A and B) following the implementation of e-RASPRO. The increased quantity of Access category antibiotic prescribing, particularly in Hospital B, is extremely significant.

Altered quantity of Watch and Access category antibiotics prescribing, particularly in Hospital. A and B, is probably still affected by the appropriateness of empirical antibiotic use, in which it is lead by the digital guideline on antimicrobtal use included in e-HASPRO. However, it certainly requires further studies. Hospital characteristics such as the number of hospital bed, the number of physicians and other facilities of each hospital may also affect the pattern of antibiotic prescribing. A potentials, review showed a decrease in antimicrobial DDO range from -B.asS to do.apS related to the digital antimicrobial stewardship tool.

Some studies have demonstrated that the utilization of digital tool to implement ASP can reduce the use of antimicrobial agents and it also can reduce the DOD Mill in other previous study the duration of digital antimicrobial stewardship teoplementation may alone a different antibiotic DOD result. However, we still cannot conclude what type of digital intervention that will certainly reduce the use of antimicrobial agents. If Our study is an initial survey on the utilization of e-RASPRO as one of digital antimicrobial stewardship program that has been used in indonesia. This study is only a survey and still cannot describe the consistion between e-RASPRO using and the artificial because duration of e-RASPRO certainly should be carried out along with compulsory disciplines and full support from hospital management team. Demographic characteristics of the hospitals can also affect the effectiveness of e-RASPRO diffication. In order to provide good explanation on this issue, more extensive studies with full support from managerial beam are required to further analyze causal effect correlation between utilization of e-RASPRO and altered quantitative pattern on antibiotic prescribing.

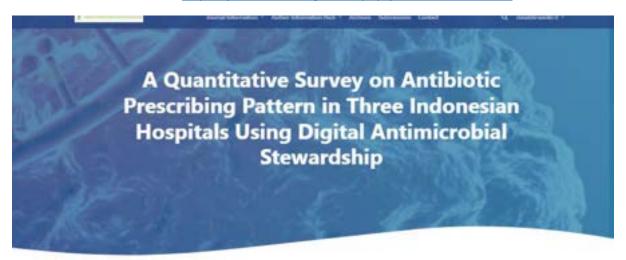
CONCLUSIONS

The survey has not been able to describe the causal effect correlation between e-RASPRO implementation and the quantity of antibiotic prescribing. However, in general, there is an altered

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ORIGINAL ARTICLE

A Quantitative Survey on Antibiotic Prescribing Pattern in Three Indonesian Hospitals Using Digital Antimicrobial Stewardship

Survei Pola Kuantitas Peresepan Antibiotik di Tiga Rumah Sakit di Indonesia dengan Penatagunaan Antimikroba Digital

Ronald Irwanto Natadidjaja 12014, Widyawati Lekoki, Aziza Ariyani', Hadianti Adlani'46, Raymond Adianto', Ronaningtyas Maharani', Hadi Sumarsono', Yenny Yenny^{2,3}, Jihan Samira^{3,3}, Nany Hairunisa^{3,3}, Husnun Amalia^{3,3}, Meutia Atika Faradilla^{3,3}, Tubagus Ferdi Fadilah^{2,3}, Joice Viladelvia Kalumpiu^{2,3}, Yuliana Yuliana², Sri Mulyani³, Desi Anggiat³, Triyoko Septio Marja⁵, lin Indra Pertiwi⁶, Dianawati Dianawati⁶, Grace Nerry Legoh⁷, Alvin Lekonardo Rantung?

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ABSTRACT

Background

Antimicrobial Stewardship Program (ASP) is very essential. There are three categories of antimicrobial agents as recommended by WHO: Access, Watch and Reserve. e-RASPRO, a digital ASP model, may alter antibiotic prescribing patterns by prioritizing Access category antibiotic prescribing.

Methods

Our manuscript presented a quantitative survey on antibiotic prescribing patterns within 3 months and 9 months before and after implementing digital electronic-RASPRO (e-RASPRO) in three Indonesian hospitals, utilizing retrospective inpatient data. This analysis included the appropriateness of empirical antibiotic prescribing and the quantity of antibiotic prescribing based on each category.

In the first 3 months, we found that 90.16%, 83.98%, and 81.15% of patients were included in Type 1 Risk Stratification. The appropriateness of initial empirical antibiotic prescribing with the digital guideline on antimicrobial use of e-RASPRO in three hospitals was 81.59%, 76.09% and 24.48%, respectively. Within 9 months after implementing e-RASPRO in Hospital A and B and within 3 months in Hospital C, there was a trend of reduced quantity of Watch category antibiotic prescribing of 54.93% (-58.86% per inpatient), 21.11% (-9.97% per inpatient), and 8.59% (-4.15% per inpatient), respectively. There was a 12.42% (+2.61 % per inpatient) and 223.17% (+268.83% per inpatient) increase in the quantity of Access category antibiotic prescribing in Hospitals A and B, while in Hospital C, the quantity decreased by 6.81% (-2.29% per inpatient).

Conclusions

There are changes in antibiotic prescribing patterns, particularly in the antibiotics included in the Watch and Access categories following the implementation of e-RASPRO. The relationship between digital antimicrobial stewardship use and the results still needs further research.

Keywords: Access; Digital Antimicrobial Stewardship; Quantity; Survey; Watch.

ABSTRAK

Latar Belakang

Penatagunaan antimikroba (PGA) merupakan hal yang urgen dilakukan. World Health Organization (WHO) telah mengkategori antimikroba ke dalam 3 golongan yaitu: Access, Watch, dan Reserve. Perangkat PGA digital e-RASPRO diharapkan dapat merubah pola peresepan antibiotik dengan mengedepankan peresepan antibiotik kategori Access.

Metode

Artikel ini merupakan survei pola kuantitas peresepan antibiotik 3 bulan dan 9 bulan sebelum dan sesudah terapan perangkat digital elektronik-RASPRO (e-RASPRO) dengan data retrospektif pada rawat inap di 3 rumah sakit di Indonesia, mencakup kesesuaian peresepan antibiotik empirik, dan kuantitas peresepan antibiotik berdasarkan masing-masing kategori.

Hasil

Dalam 3 bulan pertama, didapatkan 90.16%, 83.98% dan 81.15% dari pasien yang diberikan antibiotik termasuk dalam Stratifikasi Risiko Tipe 1. Kesesuaian peresepan antibiotik empirik inisiasi dengan panduan penggunaan antimikroba digital perangkat e-RASPRO pada ketiga rumah sakit masing-masing mencapai 81.59%, 76.09%, dan 24.48%. 9 bulan sesudah terapan perangkat e-RASPRO di Rumah Sakit C terdapat tren penurunan kuantitas peresepan antibiotik kategori Watch masing-masing sebesar 54.93% (-58.86% per pasien rawat inap), 21.11% (-9.97% per pasien rawat inap) dan 8.59% (-4.15% per pasien rawat inap). Kuantitas peresepan antibiotik kategori Access di Rumah Sakit A dan B meningkat 12.42% (+2.61% per pasien rawat inap) and 223.17% (+268.83% per pasien rawat inap), sementara itu di Rumah Sakit C menurun 6.81% (-2.29% per pasien rawat inap).

Kesimpulan

Terdapat perubahan pola peresepan antibiotik kategori Watch dan Access paska terapan perangkat e-RASPRO. Analisis hubungan antara penggunaan perangkat PGA digital dengan hasil yang ada masih membutuhkan penelitian lebih lanjut.

Kata Kunci: Access; Penatagunaan Antimikroba Digital; Kuantitas; Survei; Watch.

INTRODUCTION

The implementation of the Antimicrobial Stewardship Program (ASP) has been planned globally with the aim of promoting the prudent use of antimicrobial agents and reducing the risk of antimicrobial resistance development. The World Health Organization (WHO) has categorized antibiotics into three categories: Access, Watch, and Reserve (AWARE). Antibiotics included in Access category are antibiotics that have potency of lower incidence on resistance; while those in Watch category are types of antibiotics that have greater potency on resistance and antibiotics in Reserve category are types of antibiotics that are used only when there is an infection caused by suspected Multi-Drug Resistant (MDR) bacteria; these antibiotics should not be used carelessly, particularly in large quantity.

In this case, the RASPRO Indonesia Study Croup has attempted to develop a system, known as the RASPRO system, that can guide clinicians in antibiotic prescribing based on local guidelines.' The RASPRO system was made by using risk stratification of patients, and it directs clinicians in initial prescribing of empirical antibiotics, as well as a guideline in changing antibiotics and providing definitive antibiotic treatment, including filling out compulsory specialized forms when there is any prolonged use of antibiotics.'

Our survey is a continuation of a previous survey conducted in a hospital in Central Java, Indonesia. The hospital has implemented a manual RASPRO system to carry out the ASP. The survey, conducted before and after the manual system had been implemented for three months, revealed a decrease in antibiotic prescribing from 64,799 ampules/vials to 51,661 ampules/vials, with a reduced mean percentage of antibiotic use within three months of implementation reaching 14.44%. The previous RASPRO system, which used manual guideline forms, was then converted into an electronic form of RASPRO (e-RASPRO); therefore, e-RASPRO has become a digital tool in Indonesia designed to facilitate ASP in hospitals. Through e-RASPRO, a local antimicrobial guideline is developed digitally by completing RASPRO forms, which are also created digitally and comprise electronic forms for empirical antibiotics and definitive antibiotics. A previous survey of e-RASPRO implementation showed a 49.01% decrease in Watch category antibiotics Define Daily Dose (DDD) within 9 months of implementation, but still showed an increase in Watch category antibiotics DDD by 20.18% within 3 months of implementation.³

Clinical pharmacies can also perform direct verification on the appropriateness of indications, time limitations of antibiotic use, and the appropriateness of using empirical antibiotics by utilizing the digital guidelines on antimicrobial use that are applicable in hospitals where e-RASPRO has been implemented. By utilizing e-RASPRO, it is expected that there will be an altered pattern of antibiotic prescribing, i.e., prioritizing the use of Access category antibiotics to suppress the risk of widespread antibiotic resistance, particularly against wide-spectrum antibiotics. The aim of this study is to show the comparison of antibiotic prescription patterns among 9 months and 3 months of implementation of e-RASPRO in 3 hospitals.

METHODS

A survey was conducted at three hospitals in Indonesia: Hospital A, Hospital B, and Hospital C. All hospitals are located in West Java and were selected based on their service level category. One of them is a primary hospital (Hospital A), and the other two hospitals are secondary hospitals (Hospital B and C). Previously, various socialization on implementing digital antimicrobial stewardship program using e-RASPRO has been performed that includes socialization on digital prescribing of empirical antibiotics as well as definitive antibiotics, socialization on patient grouping based on the Risk Stratification in order to perform empirical antibiotics prescribing using digital tool and socialization on the digital guideline on using empirical antimicrobial agents, and socialization on prolonged antibiotic use in digital tools.

Socialization on Digital Prescribing of Empirical Antibiotics in e-RASPRO

Socialization was conducted on the implementation of e-RASPRO in three hospitals to guide the prescription of empirical antibiotics. When prescribing empirical antibiotics, clinicians were advised to determine the risk stratification of hospitalized patients based on their immune status, severity of infection, and medical history, such as previous antibiotic use, prior hospitalizations, and history of medical instrument usage.

Socialization also covered the guidelines and procedures for filling out forms for escalating and stepping down empirical antibiotics, aligning with the digital guideline on antimicrobial agent use in e-RASPRO. When empirical antibiotic prescribing did not follow the digital guideline, clinical pharmacy would confirm with clinicians and the ASP team in the hospital to decide if the antibiotic could be used. The socialization was conducted by the investigators for the Antimicrobial Resistance Control Program Committee of the three hospitals and continued for clinicians at each hospital. It was held both online and offline.

Socialization on Patient Grouping based on Risk Stratification for Empirical Antibiotics Prescribing in e-RASPRO

Socialization was conducted on patient grouping based on their risk stratification in e-RASPRO. The socialization was carried out by the investigators for the Antimicrobial Resistance Control Program Committee of the three hospitals and was continued with the clinicians at each hospital. The socialization was performed both online and offline.

The administration of initial empirical antibiotics in hospitalized patients should be based on patients' risk stratification, as recommended by the digital guideline on the use of antimicrobial agents, which has been incorporated into e-RASPRO. The e-RASPRO categorized patients into three groups for risk stratification in initial empirical antibiotic treatment. (4)

The Group of Patients with Type 1 Risk Stratification was a group of patients who could receive empirical antibiotics covering multidrug-resistant microorganisms. This group included immunocompetent patients and immunocompromised patients with a non-threatening severity of bacterial infection or without a risk of MDR, as classified by Non-Type 2 and/or Type 3 Risk Stratification.

The Group of Patients with Type 2 Risk Stratification was a group of (immunocompromised patients and/or uncontrolled diabetes mellitus with unthreatening severity of bacterial infection) PLUS (a history of receiving antibiotic treatment within 90 days ago (31-90 days in the system) and/or a history of having treatment at a healthcare facility of ≥48 days within 90 days ago (31-90 days in the system), and/or a history of using medical instrumentation within 90 days ago (31-90 days in the system)). This group was at risk of having a multidrug-resistant (MDR) Extended-Spectrum Beta-Lactamase (ESBL) infection. 10-16

The Group of Patients with Type 3 RIsk Stratification was a group of (patients with threatening infection, and/or immunocompromised individuals and/or individuals with uncontrolled diabetes mellitus) PLUS (a history of receiving antibiotic treatment within 30 days ago and/or having treatment at a healthcare facility 248 hours within 30 days ago, and/or a history of using medical instrument within 30 days ago). This group was a group with high severity of infection or a group that was at risk of having ESBL infection and infection caused by other Multi-Drug Resistant (MDR) microorganisms, including MDR Pseudomonas sp. **Agroup of patients with Healthcare-Associated Infections (HAIs) was also included in the group with Type 3 Risk Stratification. The group with the HAI category was a group with a period of infection of 248 hours of treatment at a healthcare facility, even within 90 days following a surgery.**

Socialization on the Digital Guideline of Using Empirical Antimicrobial Agents in e-RASPRO

Socialization was conducted on the implementation of e-RASPRO, which included the digital guideline on the use of antimicrobial agents in three Indonesian hospitals. The socialization was carried out by the investigators for the Antimicrobial Resistance Control Program Committee of each hospital and was continued for clinicians at each facility.

A digital guideline on the use of antimicrobial agents was developed, incorporating antibiotic categories based on the AWARE category proposed by the World Health Organization (WHO) in 2021. The guideline was then mutually agreed upon by the hospital management and the Antimicrobial Resistance Control Program Committee, which was subsequently incorporated into

e-RASPRO. The three hospitals used similar digital guidelines on using antimicrobial agents, which were developed by the RASPRO Indonesia Study Group by considering the WHO AWARE category as follows:

Empirical Antibiotic Choice for Patients with Type 1 Risk Stratification in e-RASPRO Digital Guidelines on the Use of Antimicrobial Agents

Most of empirical antibiotic choice included in the digital guideline on antimicrobial use for patients with type-1 risk stratification were the Access category antibiotics such as: Ampicillin, Ampicillin Sulbactam, Amoxycillin Clavulanate, Amikacin and Gentamicin; with the exception of Hospital B, in accordance with and on consideration of the continuity of drug availability as well as based on the agreement made by the Antimicrobial Resistance Control Program Committee, Cefuroxime (second generation of Cephalosporin) was included as the Access category antibiotic. Whenever necessary, most empirical antibiotic choices for the Type 1 Risk Stratification patient group could include antibiotics in the Watch category, i.e., third-generation cephalosporins such as Cefotaxime and Ceftizoxime.

Empirical Antibiotic Choice for Patients with Type 2 Risk Stratification in e-RASPRO Digital Guidelines on the Use of Antimicrobial Agents

For the group of patients with Type 2 Risk Stratification in e-RASPRO, the empirical antibiotic options included anti-ESBL antibiotics. Most of the antibiotic choices fell into either the Access category, such as Ampicillin-Sulbactam / Amoxicillin-Clavulanate combined with Amikacin / Gentamicin, or the Watch category, as outlined in the digital guidelines for antimicrobial use, which include Piperacillin-Tazobactam or the single use of Ertapenem.

Empirical Antibiotic Choice for Patients with Type 3 Risk Stratification in e-RASPRO Digital Guidelines on the Use of Antimicrobial Agents

Patients included in the Type 3 Risk Stratification group of the e-RASPRO system were a group of patients at risk of having sepsis. Therefore, for this group, the empirical antibiotic choice was an antibiotic capable of eradicating ESBL-producing bacteria and other MDR bacteria, with the majority of antibiotic selection following the digital guidelines on antimicrobial agents. These guidelines include categories such as Watch to Reserve, which encompasses antibiotics like Meropenem and Imipenem, with or without combination with Access category antibiotics, including Amikacin or Gentamicin, or with the use of Polymyxin or Tigecycline.

The e-RASPRO system with digital guidelines also guide clinicians if they need to step down or escalate the antibiotic empirically while the culture result still in progress. 10

Socialization on Prescribing Definitive Antibiotics in e-RASPRO

Socialization was performed by implementing e-RASPRO in three hospitals to prescribe definitive antibiotics, in e-RASPRO, a digital form was used to administer definitive antibiotics, which clinicians were required to fill out when prescribing antibiotics in accordance with culture findings. The socialization was conducted by the investigators for the Antimicrobial Resistance Control Program Committee of the three hospitals, and it was subsequently continued for clinicians at each hospital. The socialization was performed online and offline.

Socialization on Prolonged Antibiotic Use in e-RASPRO

Socialization was performed by implementing e-RASPRO in three hospitals. When there is a prolonged antibiotic prescribing, a clinician must describe the indication for prolonged antibiotic use through a digital form in e-RASPRO.¹⁰ It would then be verified by the clinical pharmacy, and the results would be reported to the ASP team in the hospital.

When prolonged antibiotic use occurred without a completed electronic form in e-RASPRO regarding the concerned issue or without clear indication, the clinical pharmacy, in accordance with the consent issued by the Hospital ASP team, could perform an Automatic Stop Order (ASO). Socialization was conducted by the investigators for the Antimicrobial Resistance Control Program Committee of the three hospitals, and it was also continued for clinicians at each hospital. The socialization was performed online and offline.

Survey Setting and Time Period of Data Collection

The retrieved data were secondary, univariate analyses obtained from reports on the use of injected antibiotics in the hospital wards of the three hospitals. Data was taken from January 2021 – June 2022 in Hospital A, March 2021 – August 2022 in Hospital B and August 2021 – January 2022 in Hospital C. Through implementation of e-RASPRO, initial data collection was performed within the first three-month, which included percentage of patients in each risk stratification group based on the digital e-RASPRO forms as well as appropriateness of initial empirical antibiotic prescribing with the digital guidelines on the use of antimicrobial agents.

The survey was followed by collecting all quantitative data on empirical antibiotic prescribing, as well as definitive antibiotic prescribing, for hospitalized patients within 9 months before and after the implementation of e-RASPRO in two hospitals (Hospital A and B), and within 3 months before and after utilizing e-RASPRO in another hospital (Hospital C). When the data was retrieved, Hospital C had just implemented e-RASPRO for 3 months. Interviews and discussions with the Antimicrobial Resistance Control Program Committee of the three hospitals were conducted during the initial implementation of e-RASPRO, as well as when the survey data were retrieved.

RESULTS

The following was data obtained from the survey conducted within the first 3 months of implementing e-RASPRO at 3 hospitals in Indonesia:

Table 1. Demographic Characteristics of 3 Surveyed Hospitals

Demographic Characteristics of Hospitals		Hospital	
	A	В	C
Number of Doctors			
General Physicians	14	14	25
Dentists	5	15	25 8
Specialist Doctors	37	98	102
Total	56 9	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	117.42	117.31
Ratio on numbers of nurses : beds	1147	112.50	110.77
The extent of the Buildings	7,247.35	8,120.00	31,099.94

Data: sirs.kemkes.go.id

Table 1. Actual demographic data of the three surveyed hospitals, which was collected from sirs.kemkes.go.id, Ministry of Health, Republic of Indonesia, was as follows: Hospital A, B, and C had 134 beds, 185 beds, and 254 beds, respectively; with a ratio of specialist doctors per bed of each hospital was 1 per 3.62 beds, 1 per 1.89 beds, and 1 per 2.79 beds.

Table 2. 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	10000	ital A nths ec 2021	3 Mo	ital B inths - Feb 2022	Hospital C 3 Months Nov 2022 – Jan 2023	
	Number	X	Number	X	Number	X.
Type i	284	90.16%	692	83.98%	1,472	81.15%
Type 3	31	9.84%	15	1.82%	84	4.63%
Турез	- 3	200.0	117	14.20%	258	14.22%
Total	315	100.00%	824	100.00%	1,814	100.003

Table 2. In the digital e-RASPRO form, which was completed within 3 months during the initial utilization of e-RASPRO, the majority of patients were in the Type 1 Risk Stratification category, with percentages of 90.16%, 83.98%, and 81.15% in Hospitals A, B, and C, respectively.

Table 3. Appropriateness of Initial Empirical Antibiotic Prescribing with the Digital Guideline on the Use of Antimicrobial Agents within 3 Months Following the Implementation of e-RASPRO in Three Hospitals

	Hospital A 3 Months Oct – Dec 2021		3 Me	Hospital B 3 Months Dec 2021 – Feb 2022		pital C onths - Jan 2023	
	Number	*	Number	X	Number	1	
Empirical antibiotic prescribing is consistent with the digital guideline of antimicrobial use in e-RASPRO	257	81.59%	627	76.09\$	444	24.481	
Empirical antibiotic prescribing is not consistent with the digital guideline of antimicrobial use in e-RASPRO	57	Zeo,81	197	23.91%	1,022	56,341	
Empirical antibiotic prescribing has unidentified consistency in e- RASPRO		0.32%		0.00%	348	19.183	
Total of forms had been filled out	315	100,00%	524	200.001	1,514	100.00%	

Table 3. The appropriateness of empirical antibiotic prescribing, as documented in Hospitals A, B, and C, using the digital guideline on the use of antimicrobial agents contained in e-RASPRO, reached 81.59%, 76.09%, and 24.48%, respectively, within 3 months before and after the implementation of e-RASPRO. Empirical antibiotic prescribing with non-identified appropriateness, which was documented in the digital forms, was defined as antibiotic prescribing using e-RASPRO with vague appropriateness, for example combined antibiotics prescribing in which one of the antibiotic was appropriate; while the other was not consistent with the digital guideline of antimicrobial agents or other variant condition, in which the appropriateness could not be concluded during data collection. Such a condition was documented in as many as 19.18% of cases at Hospital C.

Table 4. The Quantity of Intravenous Watch and Access Category Antibiotic Prescribing for Inpetient within 9 Months and 3 Months Before and After Implementing e-RASPRO

Arrebiodos	Tright Tright Tright Tright C									
	Fire templatementation of #4ASPRO ton-1apt zone of patients: quiry	g marchs post triplementation of +6ACHRO CNI 200n - June 2000 Number of patients 4,548	Decrease /	Free templementation of e-RASPRO Mar- Non-2001 Number of patients (1754)	g moretis post implementation of +AACPRO Dec 2001 - August 2022 Number of pathetes 6,754	Increase / Decrease	Free Implementation of #RASPINO Reguet - Oct 1888 Number of patients subsy	y morethy peak implementation of #RASPRO New 2012 - Jan 1943 Number of patients 1,475	Decrease Decrease	
	Ampulashiati	Ampulas/state	Ampulet/Visis	Ampulashish	Ampulasidals	Ampulanivish	Ampulas/visis	Ampulashiah	Ampulasivisis	
Ceftrisione	15.514	3-258	40 grit	ryles:	5,594	411.525	4.5/3	6.0%	-market	
ng Cefutpaine	298	V/00	mark.	999	4,459	reet	Life	Liter	dent.	
6.5 E Cellistavime			12	76	165	84.186			+	
Ceftanidine			63	sie :	300	-skett	796	774	6.65	
Celoperacino			100	100	419	y6.m/E				
Catoperazone Subactam			5				± .	ugit .	rescore)	
Caffingtime		ofic	100,005	407	194	19.095	109		100,000	
Cefegime			2000	14	4	direct.	1465	sale	105.60%	
yearing Levellonacie	1,407	241	45.495	1279	3,400	-1.96%	364	854	rest	
young Levoforace	F35	457	45.44	5/97	504	44.64	5,000	ayl.	96.158	
Oprofissacie		146	rem.est	106	NAME.	rest.		194	Posterior	
Mosflowsin			Same	alty	The Control	24.60	4		-	
1g Meropeners	968	968	41,005	Allen	2881	-9-498	1/mg	sale.	med	
n-s g Management				*		net	104	425	maket.	
Intperem + Oligetatin			FE.	99	0	49.698	4	4		

Antibiotics	Hospital A			Prospilal B			Hospital C		
	Fruit Implementation of +9ASPE() Jan - Sept asix Number of patients: 4,315	a murths post implementation of a BASING Oct 2014 - June 2003 Fumber of partners g.full Arapulary value	Propesse / Decresse	Fre Implementation of #AACPRO Mar-Nov 2021 Number of patients: 7,756 Angulasinols	g months part implementation of +845790 Dec 2021 - August 2021 founder of patients: 6,794 Angules/vish	Decrease / Decrease	Pre- implementation of +AASPRO August - Oct 1033 Number of patients: Lifes Auguste/state	a months pool implementation of #AACPBO Nov 2013 - Jan 2015 - Novider of patients Lifys. Airgulas/stati	Decrease / Decrease
Pperaction Tecobectum				41		-100%	4		
Acithromycin	100	6.5		2,660	179	251.69			
8.5 Vancompile				945	579	Rs.mpt.	396	ngd.	****
Total Watch	20,218	9,443	54.90%	30,649	19,707	med.	10,000	15,040	A.ggli
Social Watch / In Fatient	67987	1800	98,865	gainte	3389	+4/1	4.0759	8401	4:51
Angistin	654	967	200.00		10	roof	9 1		636
s 5 g Ampicillie Sulbactim		-0.	-	296	efe	1400%	107	466	HONB
4-75.g Ampicitie Subsctom				746	6.000	years.	196	164	*****
Amonyotto - Clandario		205	F94,000						
Gentamiste	969	100	-79.49%	3887	1,550	Heek.	9 0		611
Amiliacin		63	277	418	689	resoli	ALC: U		
Metrorstansle	spile.	since:	74 0 ft	5291	NAME.	Rene	splints .	5339	-6.8)\$
Cefurosime	S. Carrier	- C. C.	75.00	818	3474	14005			100
Total Access	3,445	2.66	11.415	4,509	Y5.404	105.05	3,89	4,059	4.86
Total Access / to Patient	nort	H-5191	1.6c%	n-8454	0.0096	esk.byt	e-7101	0.7584	4.09%

When the data was collected, e-RASPRO had been implemented for 9 months in Hospitals A and B, but it had only been implemented for 3 months in Hospital C; the results were as follows:

Table 4. The use of antibiotics included in the Reserve category, such as Polymixin and Tetracycline, e was not found in this survey. There was a significant reduction in the quantity of Ceftriaxone prescribed in Hospitals A, B, and C, by 62.92%, 40.58%, and 11.06%, respectively. Nevertheless, there was a significant increase in Cefotaxime prescribing in Hospitals A and B, with increases of 35.32% and more than 100%, respectively. A significant increase also occurred for Ciprofloxacin prescribing in three hospitals. The quantity of 500 mg Levofloxacin prescribed in Hospitals A, B, and C decreased by 45.14%, 64.84%, and 76.25%, respectively. The quantity of 750 mg Levofloxacin was reduced in Hospitals A and B by 65.49% and 13.36%, respectively; however, it increased significantly by more than 100% in Hospital C. The quantity of prescribing 1 gram of Meropenem in Hospitals A and B decreased by 41.32% and 13.45%, respectively; however, it increased in Hospital C by 10.01%. The quantity of azithromycin prescribed also decreased significantly in Hospital B, by 93.28%. Piperacillin-Tazobactam seemed to be used very rarely. The minimum use was found in Hospital B i.e.

as many as 45 ampules/vials within 9 9-month period before the e-RASPRO tool was implemented. In general, the quantity of antibiotic use included in the Watch category at Hospitals A, B, and C was reduced by 54.93% (-58.86% per inpatient), 21.11% (-9.97% per inpatient), and 8.59% (-4.15% per inpatient), respectively. The quantity of Access category antibiotic prescribing in Hospitals A, B, and C was as follows: there was a 100% increase in Ampicillin and Amoxicillin-Clavulanate prescribing in Hospital A. While the prescribing of 1.5 g Ampicillin Sulbactam had also increased by>100% in Hospitals B and C.

Antibiotic prescribing of 0.75 g ampicillin-sulbactam increased by more than 100% in Hospital B; however, there was a decrease of 44.59% in Hospital C. The quantity of Gentamycin prescribing had a reduction of 79.15% in Hospital A; nevertheless, there was a significant increase up to >100% in Hospital B. Meanwhile, in Hospital C, Gentamycin had not been used before and after the implementation of e-RASPRO. Increased Cefuroxime prescribing was also found very significant in Hospital B, based on the agreement made by the Antimicrobial Resistance Control Program Committee, as well as continuity of drug availability in Hospital B, Cefuroxime was included in the Access category. In general, the quantity of Access category antibiotic prescribing in Hospitals A and B increased by 12.42% (+2.61 % per inpatient) and 223.17% (+268.83% per inpatient), respectively. Meanwhile, in Hospital C, it decreased by 6.81% (-2.29% per inpatient)

DISCUSSION

An integrated survey on Antimicrobial Resistance (AMR) and Antimicrobial Use (AMU) is very essential, and it should be carried out in order to evaluate the effectiveness of policy, evidence and the implementation of ASP. 21,22 This survey is a limited survey conducted at three hospitals in Indonesia, which have different characteristics as shown in Table 1.

In Table 1, it is evident that Hospital C has the greatest resources in terms of the number of physicians, pharmacists, and nurses compared to Hospitals A and B. It also has the largest building compared to the other two hospitals. The various human resources in the hospital, along with its large size, presented their own challenges in implementing the antimicrobial stewardship program, whether using manual or digital methods. In daily practice, unevenly distributed levels of socialization may affect the level of appropriateness of antibiotic use with the digital guideline on the use of antimicrobial agents contained in e-RASPRO.

In Table 2, we can see that most patients who would receive early empirical antibiotic prescribing at hospital admission are those who have a Type 1 Risk Stratification, as documented in e-RASPRO. These patients include a group of immunocompetent patients or

immunocompromised patients who had unthreatening bacterial infection or those who are not at risk of having infection caused by MDR microorganisms.' Prescribing wide-spectrum antibiotics should be avoided as much as possible in patients who were mostly included in the group with Type 1 Risk Stratification. It should be taken into consideration that using various types of antibiotics may increase the risk of developing resistance. The disease progresses, empirical antibiotic treatment certainly can be escalated in accordance with the patient's condition.

Table 3 describes the appropriateness of initial empirical antibiotic prescribing using the digital antimicrobial guideline as documented in Hospitals A, B, and C within 3 months of implementing e-RASPRO, which achieved rates of 81.59%, 76.09%, and 24.48%. It is categorized as "appropriate prescribing" when the empirical antibiotic is given in accordance with the digital guideline of antimicrobial use included in e-RASPRO that is compliant with the patient's risk stratification. There is a high percentage of patients in a group with Type 1 Risk Stratification. This result is expected to bring some changes in the quantitative pattern of antibiotic prescribing from the type of antibiotics included in the Watch category to those in the Access category.

The appropriateness of antibiotic prescribing in Hospital C, which is documented in digital e-RASPRO forms, is still relatively low. Through discussions and interviews with the investigators, it may be caused by the socialization associated with e-RASPRO implementation that has not been thoroughly conducted for the clinicians, or there might be other unidentified obstacles.

Table 4 is a table describing the quantity of antibiotic prescribing, both empirical and definitive antibiotics prescribed using e-RASPRO. The absence of Reserve category antibiotic prescribing in our survey may be due to difficulties in supplying those antibiotics in the three hospitals, or it may also be attributed to the extremely small number of cases associated with this issue in the three hospitals.

Table 4 describes the quantity of Watch category antibiotic prescribing within 9 months before and after implementing e-RASPRO in Hospital A and B as well as within 3 months before and after implementing the tool in Hospital C. There was a significant decrease of Ceftriaxone prescribing in Hospital A, B and C since those three hospitals had carried out some efforts to lower Ceftriaxone prescribing either as empirical or definitive antibiotics; therefore, in the digital guidelines on the antimicrobial use in e-RASPRO of the three hospitals, the use of Ceftriaxone could be minimized

In some group of patients with Type 1 Risk Stratification when the Third Generation of Cephalosporins should be administered, Cefotaxime becomes the appropriate choice as recommended by the digital antimicrobial guidelines in the three hospitals; therefore, although in most cases the empirical antibiotics used in patients with Type 1 Risk Stratification are those in the Access category, but there are some focal infection that can be treated with Cefotaxime as the empirical antimicrobial agent of choice. The Antimicrobial Resistance Control Program Committee of Hospitals A and B has obviously included Ceftizoxime as the Cephalosporin that has been commonly used, and it can be administered when necessary. This might explain the relatively significant increase in Cefotaxime and Ceftizoxime prescribing in Hospital A and B. Meanwhile, in Hospital C, Ceftizoxime had not been included in the digital antimicrobial guideline; therefore, Ceftizoxime had not been used within 3 months following the implementation of e-RASPRO.

The significant increase in Ciprofloxacin prescribing in three hospitals may occur because the prescribing was less consistent with the recommendation included in the digital antimicrobial guideline of e-RASPRO. Nevertheless, the guideline recommends that Ciprofloxacin may serve as a β-lactam antibiotic, which is optional for all types of risk stratifications when patients have a Penicillin allergy. Based on the digital guidelines for antimicrobial use in e-RASPRO, Ciprofloxacin has also been used as the antibiotic of choice for tropical infectious diseases in the three hospitals, such as typhoid fever, and many cases have been reported in Indonesia. For such

infections, according to the digital guideline of antimicrobial use in e-RASPRO, Ciprofloxacin is recommended as one of the antibiotics of choice. Moreover, increased prescribing of Cefotaxime and Ciprofloxacin may also be caused by clinicians who have prescribed definitive antimicrobial treatments using e-RASPRO. However, we still require additional data to confirm this event.

In general, there is a significant decrease in the quantity of Meropenem and Levofloxacin prescribing in hospitals A and B. This is consistent with the digital guideline on antimicrobial use included in e-RASPRO of the three hospitals, which minimizes the use of Levofloxacin for patients with Type 1 Risk Stratification, who are the majority in the three hospitals. Meanwhile, Meropenem can only be administered to patients with Type 3 Risk Stratification. The use of Meropenem cannot be separated from the possibility of escalating antibiotic treatment, which is in accordance with the digital guideline on antimicrobial use included in e-RASPRO.

The increased prescribing quantity of 750 mg Levofloxacin and 1 g Meropenem in Hospital C still persists. It is probably caused by a compliance issue or inconsistency with the digital guideline on antimicrobial use. In the first 3 months of survey conducted in Hospital C, the appropriateness level of antimicrobial prescribing with the digital guideline on the use of antimicrobial agents is still considered to be low; while the majority of patients actually are included in the Type 1 Risk Stratification group, in which most of their empirical antibiotic choices are those included in the Access category. Nevertheless, further review should be conducted to assess the situation that has occurred at Hospital C.

This survey has not found antimicrobial prescribing of Piperacillin-Tazobactam and Ertapenem for patients included in the Type 2 Risk Stratification group following the implementation of e-RASPRO. Through various discussions with those hospitals, we identified that it is difficult to provide antimicrobial agents of Piperacillin Tazobactam and Ertapenem; therefor antibiotics of Access category such as Ampicillin Sulbactam or Amoxycillin Clavulanate with or without combination of Aminoglycosides as the anti-ESBLs often serve as empirical antibiotic of choice to be given for patients who are included in the Type 2 Risk Stratification. Nevertheless, in reality, the initial 3-month survey on the implementation of e-RASPRO in three hospitals has shown that the number of patients included in the Type 2 Risk Stratification group was a minority. Overall, there is a reduction in the quantity of antibiotic prescribing in the Watch category at Hospitals A, B, and C, by 54.93% (-58.86% per inpatient), 21.1% (-9.97% per inpatient), and 8.59% (-4.15% per inpatient), respectively, following the implementation of e-RASPRO.

In Table 4 a survey conducted for 9 months before and after the utilization of e-RASPRO in Hospital A and B and 3 months before and after implementing e-RASPRO in Hospital C has demonstrated a significant increase in the quantity of antibiotic prescribing of Ampicillin, Amoxycillin Clavulanate and 1.5 g Ampicillin Sulbactam, which are antibiotics included in Access category in the three hospitals. The survey conducted within the first 3 months of e-RASPRO utilization has demonstrated that the majority of patients are included in the Type 1 Risk Stratification group at those three hospitals (Table 2), in which the majority of empirical antibiotic choices are indeed antibiotics included in the Access category. Nevertheless, further surveys are certainly required to be carried out in Hospitals A and B in the following months.

The significant increase of 0.75 g Ampicillin Sulbactam prescribing may also still be associated with the continuity of 1.5 g Ampicillin Sulbactam availability in Hospital B. Some sources at Hospital B, through discussions with investigators, suggest that there is often a shortage of 1.5 Ampicillin-Sulbactam in the hospital. Therefore, considering this reasoning, the Antimicrobial Resistance Control Program Committee in Hospital B has included Cefuroxime in the Access category of its guideline on antimicrobial use. This condition explains the presence of an increased quantity of Cefuroxime prescribing, which is included in the Access category in Hospital B.

Based on the digital guideline on antimicrobial use in e-RASPRO of the three hospitals, Aminoglycosides have actually been used as combined antibiotics. It has not been identified clearly about the cause of reduced Gentamycin prescribing is in Hospital A, while in Hospital C, the use of Gentamycin and Amikacin has not been documented either before or after the implementation of e-RASPRO. Increased Gentamycin and Amikacin prescribing in Hospital B could occur because the digital guideline on antimicrobial use for those three hospitals recommends using aminoglycosides as combined empirical antibiotics for some focal infections in patients with Type 1 risk stratification and almost all focal infections in patients with Type 3 Risk Stratification. Overall, there is increased quantity of Access category antibiotic prescribing in Hospital A and B of 12.42% (+2.61% per inpatient) and 223.17% (+268.83% per inpatient), respectively. A survey conducted within 3 months before and after the implementation of e-RASPRO in Hospital C demonstrated a reduction in Access category antibiotic prescribing of 6.81% (-2.29% per inpatient).

In Table 4, regarding the number of patients before and after the implementation of e-RASPRO in those three hospitals, it can also be seen that the numbers were not significantly different. This survey has not correlated the quantity of prescribing with the duration of antibiotic use; furthermore, it has not calculated the percentage of escalating and stepping down empirical antibiotic treatment. However, in this survey, we observed a reduced percentage of Watch category antibiotic prescribing in three hospitals, as well as an increased percentage of Access category antibiotic prescribing in two hospitals (Hospital A and B) following the implementation of e-RASPRO. The increased quantity of Access category antibiotic prescribing, particularly in Hospital B, is extremely significant.

The altered quantity of Watch and Access category antibiotics prescribed, particularly in Hospitals A and B, is likely still influenced by the appropriateness of empirical antibiotic use, which is guided by the digital guideline on antimicrobial use included in e-RASPRO. However, it certainly requires further studies. Hospital characteristics, such as the number of hospital beds, the number of physicians, and other facilities, may also affect the pattern of antibiotic prescribing. A systematic review showed a decrease in the antimicrobial DDD range from -8.42% to -61.29% related to the use of a digital antimicrobial stewardship tool.²⁴

Some studies have demonstrated that the utilization of digital tools to implement ASP can reduce the use of antimicrobial agents and also decrease the DDD.^{24,25} In other previous study the duration of digital antimicrobial stewardship implementation may show a different antibiotic DDD result.³ However, we still cannot conclude what type of digital intervention will certainly reduce the use of antimicrobial agents.¹⁵ Our study is an initial survey on the utilization of e-RASPRO, one of the digital antimicrobial stewardship programs used in Indonesia. This study is a survey only and cannot yet describe the correlation between e-RASPRO use and antibiotic prescribing patterns. To achieve good results, the utilization of e-RASPRO should be carried out in conjunction with compulsory disciplines and with full support from the hospital management team. Demographic characteristics of the hospitals can also affect the effectiveness of e-RASPRO utilization. To provide a comprehensive explanation of this issue, more extensive studies with full support from the managerial team are required to further analyze the causal correlation between the utilization of e-RASPRO and the altered quantitative pattern in antibiotic prescribing.

CONCLUSION

The survey has not been able to describe the causal-effect correlation between e-RASPRO implementation and the quantity of antibiotic prescribing. However, in general, there is an altered quantitative pattern in the quantity of empirical antibiotic prescribing, particularly for those included in the Watch and Access categories, following the implementation of e-RASPRO. We

suggest a broader scope of research on digital antimicrobial stewardship tools to evaluate their effectiveness in implementing antimicrobial stewardship programs.

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AUTHORS CONTRIBUTION

The authors confirm their contribution to the paper as follows: study conception and design: RIN; data collection: WL, RA, RM, HS, SM, DA, TSM, IIP, DD, GNL, ALR; analysis and interpretation of results: RIN, WL, AA, HA; draft manuscript preparation: RIN, WL, YY, JS, NH, HA, MAF, TFF, JVK, YY. All authors reviewed the results and approved the final version of the manuscript.

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CONFLICT OF INTEREST

Competing interests: No relevant disclosures.

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A Quantitative Survey on Antibiotic Prescribing Pattern in Three Indonesian Hospitals Using Digital Antimicrobial Stewardship

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A Quantitative Survey on Antibiotic Prescribing Pattern in Three Indonesian Hospitals Using Digital Antimicrobial Stewardship

Survei Pola Kuantitas Peresepan Antibiotik di Tiga Rumah Sakit di Indonesia dengan Penatagunaan Antimikroba Digital

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BSTRACT

Background

Antimicrobial Stewardship Program (ASP) is try essential. There are three categories of antimicrobial agents as recommended by WHO: Access, Watch and Reserve. e-RASPRO, a digital ASP model, may alter antibiotic prescribing patterns by prioritizing Access category antibiotic prescribing.

Methods

Our manuscript presented a cantitative survey on antibiotic prescribing patterns within 3 months and 9 months before and after implementing digital electronic-RASPRO (e-RASPRO) in three Indonesian hospitals, utilizing retrospective inpatient data. This analysis included the appropriateness of empirical antibiotic prescribing and the quantity of antibiotic prescribing based on each category.

Results

In the first 3 months, we found that 90.16%, 83.98%, and 81.15% of patients were included in Type 1 Risk Stratification. The appropriateness of initial empirical antibiotic prescribing with the digital guideline on intrinsical problems of e-RASPRO in three hospitals was 81.59%, 76.09% and 24.48%, respectively. Within 9 months after implementing e-RASPRO in Hospital A and B and within 3 months in Hospital C, there was a trend of reduced quantity of Watch category antibiotic prescribing of 54.93% (-58.86% per inpatient), 21.11% (-9.97% per inpatient), and 8.59% (-4.15% per inpatient), respectively. There was a 12.42% (+2.61% per inpatient) and 223.17% (+268.83% per inpatient) increase in the quantity of Access category antibiotic prescribing in Hospitals A and B,

while in Hospital C, the quantity decreased by 6.81% (-2.29% per inpatient).

Conclusions

There are changes in antibiotic prescribing patterns, particularly in the antibiotics included in the Watch and Access categories following the implementation of e-RASPRO. The relationship between digital antimicrobial stewardship use and the results still needs further research.

Keywords: Access; Digital Antimicrobial Stewardship; Quantity; Survey; Watch.

ABSTRAK

Latar Belakang

Penatagunaan antimikroba (PGA) merupakan hal yang urgen dilakukan. World Health Organization (WHO) telah mengkategori antimikroba ke dalam 3 golongan yaitu: Access, Watch, dan Reserve. Perangkat PGA digital e-RASPRO diharapkan dapat merubah pola peresepan antibiotik dengan mengedepankan peresepan antibiotik kategori Access.

Metode

Artikel ini merupakan survei pola kuantitas peresepan antibiotik 3 bulan dan 9 bulan sebelum dan sesudah terapan perangkat digital elektronik-RASPRO (e-RASPRO) dengan data retrospektif pada rawat inap di 3 rumah sakit di Indonesia, mencakup kesesuaian peresepan antibiotik empirik, dan kuantitas peresepan antibiotik berdasarkan masing-masing kategori.

Hasil

Dalam 3 bulan pertama, didapatkan 90.16%, 83.98% dan 81.15% dari pasien yang diberikan antibiotik termasuk dalam Stratifikasi Risiko Tipe 1. Kesesuaian peresepan antibiotik empirik inisiasi dengan panduan penggunaan antimikroba digital perangkat e-RASPRO pada ketiga rumah sakit masingmasing mencapai 81.59%, 76.09%, dan 24.48%. 9 bulan sesudah terapan perangkat e-RASPRO di Rumah Sakit A dan B dan 3 bulan sesudah terapan perangkat e-RASPRO di Rumah Sakit C terdapat tren penurunan kuantitas peresepan antibiotik kategori Watch masing-masing sebesar 54.93% (-58.86% per pasien rawat inap), 21.11% (-9.97% per pasien rawat inap) dan 8.59% (-4.15% per pasien rawat inap). Kuantitas peresepan antibiotik kategori Access di Rumah Sakit A dan B meningkat 12.42% (+ 2.61% per pasien rawat inap) and 223.17% (+26.8.83% per pasien rawat inap), sementara itu di Rumah Sakit C menurun 6.81% (-2.29% per pasien rawat inap).

Kesimpulan

Terdapat perubahan pola peresepan antibiotik kategori Watch dan Access paska terapan perangkat e-RASPRO. Analisis hubungan antara penggunaan perangkat PGA digital dengan hasil yang ada masih membutuhkan penelitian lebih lanjut.

Kata Kunci: Access; Penatagunaan Antimikroba Digital; Kuantitas; Survei; Watch.

INTRODUCTION

The implementation of the Antimicrobial gewardship Program (ASP) has been planned globally with the aim of promoting the prudent use of antimicrobial agent ind reducing the risk of antimicrobial resistance development. The World Health Organization (WHO) has categorized antibiotics into three categories: Access, Watch, and Reserve (AWARE). Antibiotics included in Access category are antibiotics that have potency of lower incidence on resistance; while those in 20 access category are types of antibiotics that have greater potency on resistance and antibiotics in Reserve category are types of antibiotics that are used only when there is an infection caused by suspected Multi-Drug Resistant (MDR) bacteria; these antibiotics should not be used carelessly, particularly in large quantity.



In this case, the RASPRO Indonesia Study Group has attempted to develop a system, known as the RASPRO system, that can guide clinicians in antibiotic prescribing based on local guidelines. The RASPRO system was made by using risk stratification of patients, and it directs clinicians in initial prescribing of empirical antibiotics, as well as a guideline in changing antibiotics and providing definitive antibiotic treatment, including filling out compulsory specialized forms when there is any prolonged use of antibiotics.

Our survey is a continuation of a previous survey conducted in a hospital in Central Java, Indonesia. The hospital has implemented a manual RASPRO system to carry out the ASP. The survey, conducted before and after the manual system had been implemented for three months, revealed a decrease in antibiotic prescribing from 64,799 ampules/vials to 51,661 ampules/vials, with a reduced mean percentage of antibiotic use within three months of implementation reaching 14.44%. The previous RASPRO system, which used manual guideline forms, was then converted into an electronic form of RASPRO (e-RASPRO); therefore, e-RASPRO has become a digital tool in Indonesia designed to facilitate ASP in hospitals. Through e-RASPRO, a local antimicrobial guideline is developed digitally by completing RASPRO forms, which are also created digitally and comprise electronic forms for empirical antibiotics and definitive antibiotics. A previous survey of e-RASPRO implementation showed a 49.01% decrease in that category antibiotics DDD by 20.18% within 3 months of implementation.

Clinical pharmacies can also perform direct verification on the appropriateness of indications, time limitations of antibiotic use, and the appropriateness of using empirical antibiotics by utilizing the digital guidelines on antimicrobial use that are applicable in hospitals where e-RASPRO has been implemented. By utilizing e-RASPRO, it is expected that there will be an altered pattern of antibiotic prescribing, i.e., prioritizing the use of Access category antibiotics to suppress the instance of widespread antibiotic resistance, particularly against wide-spectrum antibiotics. The aim of this study is to show the comparison of antibiotic prescription patterns among 9 months and 3 months of implementation of e-RASPRO in 3 hospitals.

METHODS

A survey was conducted at three hospitals in Indonesia: Hospital A, Hospital B, and Hospital C. All hospitals are located in West Java and were selected based on their service level category. One of them is a primary hospital (Hospital A), and the other two hospitals are secondary hospitals (Hospital B and C). Previously, various socialization on implementing digital antimicrobial stewardship program using e-RASPRO has been performed that includes socialization on digital prescribing of empirical antibiotics as well as definitive antibiotics, socialization on patient grouping based on the Risk Stratification in order to perform empirical antibiotics prescribing using digital tool and socialization on the digital guideline on using empirical antimicrobial agents, and socialization on prolonged antibiotic use in digital tools.

Socialization on Digital Prescribing of Empirical Antibiotics in e-RASPRO

Socialization was conducted on the implementation of e-RASPRO in three host itals to guide the prescription of empirical antibiotics. When prescribing empirical antibiotics, pinicians were advised to determine the risk stratification of hospitalized patients based on their immune status, severity of infection, and medical history, such as previous antibiotic use, prior hospitalizations, and history of medical instrument usage.

Socialization also covered the guidelines and procedures for filling out forms for escalating and stepping down empirical antibiotics, aligning with the digital guideline on antimicrobial agent use in e-RASPRO. When empirical antibiotic prescribing did not follow the digital guideline, clinical

pharmacy would confirm with clinicians and the ASP team in the hospital to decide if the antibiotic could be used. The socialization was conducted by the investigators for the Antimicrobial Resistance Control Program Committee of the three hospitals and continued for clinicians at each hospital. It was held both online and offline.

Socialization on Patient Grouping based on Risk Stratification for Empirical Antibiotics Prescribing in e-RASPRO

Socialization was conducted on patient grouping based on their risk stratification in e-RASPRO. The socialization was carried out by the investigators for the Antimicrobial Resistance Control Program Committee of the three hospitals and was continued with the clinicians at each hospital. The socialization was performed both online and offline.

The administration of initial empirical antibior is in hospitalized patients should be based on patients' risk stratification, as recommended by the digital guideline on the use of antimicrobial agents, which has been incorporated into e-RASPRO. The e-RASPRO categorized patients into three groups for risk stratification in initial empirical antibiotic treatment.

The Group of Patients with Type 1 Risk Stratification was a group of patients who could receive empirical antibiotics covering multidrug-resistant microorganisms. This group included immunocompetent patients and immunocompromised patients with a non-threatening severity of bacterial infection or without a risk of MDR, as classified by Non-Type 2 and/or Type 3 Risk Stratification.

The group of Patients with Type 2 Risk Stratification was a group of (immunocompromised patients and/or uncontrolled diabetes melitus with unthreatening severity of bacterial infection) US (a history of receiving antibiotic treatment within 90 days ago (31-90 days in the system) and/or a history of having treatment at a healthcare facility of ×48 days within 90 days ago (31-90 days in the system), and/or a history of using medical instruction within 90 days ago (31-90 days in the system)). This group was at risk of having a multidrug-resistant (MDR) Extended-Spectrum Beta-Lactamase (ESBL) infection. 19-8

The Group of Patients with Type 3 Risk Stratification was a group of (patients with threatening infection, and/or immunocompromised individuals and/or individuals with uncontrolled diabetes mellitus) PLUS (a history of receiving antibiotic treatment within 30 days ago and/or having treatment at a healthcare facility 248 hours within 30 days ago, and/or a history of using medical instrument within 30 days ago). This group was a group with high everity of infection or a group that was at risk of having ESBL infection and infection caused by other Multi-Drug Resistant (MDR) microorganisms, including MDR Pseudomonas sp. 16.9-14 A group of patients with Healthcare-Associated Infections (HAIs) was also included in the group with Type 3 Risk Stratification. The group with the HAI category was a group with a period of infection of 248 hours of treatment at a healthcare facility, even within 90 days following a surgery, 15-18

Socialization on the Digital Guideline of Using Empirical Antimicrobial Agents in e-RASPRO

Socialization was conducted on the implementation of e-RASPRO, which included the digital guideline on the use of antimicrobial agents in three Indonesian hospitals. The socialization was carried out by the investigators for the Antimicrobial Resistance Control Program Committee of each hospital and was continued for clinicians at each facility.

A digital guideline on the use of antimicrobial ages is was developed, incorporating antibiotic categories based on the AWARE category proposed by the World Health Organization (WHO) in 2021. The guideline was then mutually agreed upon by the hospital management and the Antimicrobial Resistance Control Program Committee, which was subsequently incorporated into

e-RASPRO. The tiglee hospitals used similar digital guidelines on using antimicrobial agents, which were developed by the RASPRO Indonesia Study Group by considering the WHO AWARE category as follows:

Impirical Antibiotic Choice for Patients with Type 1 Risk Stratification in e-RASPRO Digital Guidelines on the Use of Antimicrobial Agents

Most of empirical antibiotic choice included in the digital guideline on antimicrobial use for patients with type-1 risk stratification were the Access category antibiotics such as: Ampicillin, Ampicillin Sulbactam, Amoxycillin Clavulanate, Amikacin and Gentamicin; with the exception of Hospital B, in accordance with and on consideration of the continuity of drug availability as well as based on the agreement made by the Antimicrobial Resistance Control Program Committee, Cefuroxime (second generation of Cephalosporin) was included as the Access category antibiotic. Whenever necessary, most empirical antibiotic choices for the Type 1 Risk Stratification patient group could include antibiotics in the Watch category, i.e., third-generation cephalosporins such as Cefotaxime and Ceftizoxime.

Impirical Antibiotic Choice for Patients with Type 2 Risk Stratification in e-RASPRO Digital Guidelines on the Use of Antimicrobial Agents

For the group of patients with Type 2 Risk Stratification in e-RASPRO, the empirical antibiotic options included anti-ESBL antibiotics. Most of the antibiotic choices fell into either the Access category, such as Ampicillin-Sulbactam / Amoxici Clavulanate combined with Amikacin / Gentamicin, or the Watch category, as outlined in the digital guidelines for antimicrobial use, which include Piperacillin-Tazobactam or the single use of Ertapenem.

impirical Antibiotic Choice for Patients with Type 3 Risk Stratification in e-RASPRO Digital Guidelines on the Use of Antimicrobial Agents

Patients included in the Type 3 Risk Stratification group of the e-RASPRO system were a group of patients at risk of having sepsis. Therefore, for this group, the inpirical antibiotic choice was an antibiotic capable of eradicating ESBL-producing bacteria and other MDR bacteria, with the majority of antibiotic selection following the digital guidelines on antimicrobial agents. These guidelines include categories such as Watch to Reserve, which encompasses antibiotics like Meropenem and Imipenem, with or without combination with Access category antibiotics, including Amikacin or Gentamicin, or with the use of Polymyxin or Tigecycline.

The e-RASPRO system with digital guidelines also guide clinicians if they need to step down or escalate the antibiotic empirically while the culture result still in progress, 13

Socialization on Prescribing Definitive Antibiotics in e-RASPRO

Socialization was performed by implementing e-RASPRO in three hospitals to prescribe definitive antibiotics. In e-RASPRO, a digital form was used to administer definitive antibiotics, which clinicians were required to fill out when prescribing antibiotics in accordance with culture findings. The socialization was conducted by the investigators for the Antimicrobial Resistance Control Program Committee of the three hospitals, and it was subsequently continued for clinicians at each hospital. The socialization was performed online and offline.

Socialization on Prolonged Antibiotic Use in e-RASPRO

Socialization was performed by implementing e-RASPRO in three hospitals. When there is a prolonged antibiotic prescribing, a clinician must describe the indication for prolonged antibiotic use through a digital form in e-RASPRO.¹³ It would then be verified by the clinical pharmacy, and the results would be reported to the ASP team in the hospital.

When prolonged antibiotic use occurred without a completed electronic form in e-RASPRO regarding the concerned issue or without clear indication, the clinical pharmacy, in accordance with the consent issued by the Hospital ASP team, could perform an Automatic Stop Order (ASO). Socialization was conducted by the investigators for the Antimicrobial Resistance Control Program Committee of the three hospitals, and it was also continued for clinicians at each hospital. The socialization was performed online and offline.

Survey Setting and Time Period of Data Collection

The retrieved data were secondary, univariate analyses obtained from reports on the use of injected antibiotics in the hospital wards of the three hospitals. Data was taken from January 2021 – June 2022 in Hospital A, March 2021 – August 2022 in Hospital B and August 2021 – January 2022 in Hospital C. Through implementation of eRASPRO, initial data collection was performed within the first three-month, which included percentage of patients in each risk stratification group based on the digital e-RASPRO forms as well as appropriateness of initial empirical antibiotic prescribing with the digital guidelines on the use of antimicrobial agents.

The survey was followed by collecting all quantitative data on empirical ptibiotic prescribing, as well as definitive antibiotic prescribing, for hospitalized patients within 9 months before and after the implementation of e-RASPRO in two hospitals (Hospital A and B), and within 3 months before and after utilizing e-RASPRO in another hospital (Hospital C). When the data was retrieved, Hospital C had just implemented e-RASPRO for 3 months. Interviews and discussions with the Antimicrobial Resistance Control Program Committee of the three hospitals were conducted during the initial implementation of e-RASPRO, as well as when the survey data were retrieved.

RESULTS

The following was data obtained from the survey conducted within the first 3 months of implementing e-RASPRO at 3 hospitals in Indonesia:

Table 1. Demographic Characteristics of 3 Surveyed Hospitals

Demographic Characteristics of Hospitals		Hospital	
	A	В	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	117-31
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 1. Actual demographic data of the three surveyed hospitals, which was collected from sirs.kemkes.go.id, Ministry of Health, Republic of Indonesia, was as follows: Hospital A, B, and C had 134 beds, 185 beds, and 254 beds, respectively; with a ratio of specialist doctors per bed of each hospital was 1 per 3.62 beds, 1 per 1.89 beds, and 1 per 2.79 beds.

Table 2. 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	3 Mo	ital A onths lec 2021	3 Mo	ital B enths - Feb 2022	3 Mc	ital C inths - Jan 2023
100000000000000000000000000000000000000	Number	×	Number	1	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	16.22%
Total	315	100.00%	824	100.00%	1,814	100.003

Table 2. In the digital e-RASPRO form, which was completed within 3 months during the initial utilization of e-RASPRO, the majority of patients were in the Type 1 Risk Stratification category, with percentages of 90.16%, 83.98%, and 81.15% in Hospitals A, B, and C, respectively.

Table 3. Appropriateness of Initial Empirical Antibiotic Prescribing with the Digital Guideline on the Use of Antimicrobial Agents within 3 Months Following the Implementation of e-RASPRO in Three Hospitals

	3 M	oital A onths Dec 2021	3 M	oital B onths - Feb 2022	3 Me	oital C onths - Jan 2023
	Number	1	Number	x	Number	×
Empirical antibiotic prescribing is consistent with the digital guideline of antimicrobial use in e-RASPRO	257	81.59%	627	76.09%	444	24.48%
Empirical antibiotic prescribing is not consistent with the digital guideline of antimicrobial use in e-RASPRO	57	18.09%	197	23.91%	1,022	56.34%
Empirical antibiotic prescribing has unidentified consistency in e- RASPRO		0.32%		200.0	348	19.18%
Total of forms had been filled out	315	100.00%	824	100.00%	1,814	100.00%

Table 3. The appropriateness of empirical antibiotic prescribing, as documented in Hospitals A, B, and C, using the digital guideline on the use of an incrobial agents contained in e-RASPRO, reached 81.59%, 76.09%, and 24.48%, respectively, within 3 months before and after the implementation of e-RASPRO. Empirical antibiotic prescribing with non-identified appropriateness, which was documented in the digital forms, was defined as antibiotic prescribing using e-RASPRO with vague appropriateness, for example combined antibiotics prescribing in which one of the antibiotic was appropriate; while the other was not consistent with the digital guideline of antimicrobial agents or other variant condition, in which the appropriateness could not be concluded during data collection. Such a condition was documented in as many as 19.18% of cases at Hospital C.

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Table 4. The Quantity of Intravenous Watch and Access Category Antibiotic Prescribing for Inpatient within 9 Months and 3 Months Before and After Implementing e-RASPRO

Antibiotics	Hospital A			Hospital B			HospitalC		
	Pre- implementation of e-RASPRO Jan - Sept 2021 Number of patients 4,215	9 months post implementation of e-RASPRO Oct 2021 - June 2022 Number of	Decrease /	Pre- implementation of e-RASPRO Mar-Nov 2021	The second secon	Decrease / Decrease	Pre- implementation of e-RASPRO August - Oct 2022 Number of		Decrease / Decrease
	Amoulesivials	Amoules/vials	Amoulesivials	patients: 7,754 Ampules/Mals	Amoulesivials	Ampules/vials	Ampuleskials	patients: 2,675 Amoules/vials	Amoules/vials
Ceftriaxone	15,514	573	-62.92X	11,602	6,894	40.58%		4,014	-11.06X
1g Cefotaxime	756	1,023	35-312	950	4,189	>100%	1,360	1237	-9.04X
0.5 g Cefotaxime				76	145	90.79%			
Ceftazidime			+	866	359	-58,55%	724	77.4	6.91%
Cefoperazone			4	232	413	78.02%			
Cefoperaz one Sulbactam								146	100.001
Ceftivozime	V	282	100,001	527	286	13.09%	129	v	-100,00%
Cefepime		55	6	4	9	-57.14%	1,465	1,089	-25.67%
750 mg Levofloxacin	2,147	741	-65-49E	2,770	2,400	13,362	360	854	>100%
500 mg Levofloxacin	833	427	45.148	3,197	4124	-64.84%	1,002	23.6	-76.25%
Ciprofloxadin	8	288	100.001	136	85th	>100%		234	100.00%
Moxifloxadin				487	122	·54.62%			
18 Meropenem	968	568	41.32%	8,690	7,521	13.45%	619'1	1,781	X10.01
0.5 g Meropenem	,	1.7	4	19	4	-100%	250	475	-13.64%
Imipenem + Glastatin			4	133	43	.67.67%			a

Artibiotics	HOSpitalA			H-DODGE B			HOSEGAIC		
	Pre- implementation of eRASPRO an - Sept som Number of preferes 4.25	9 morehs peak implementation of e-1AGFRO 2023 2023 Number of patients 4618	Decrease /	Pre- implementation of eAASPBO Mar-Norami Number of patients 3,354	9 months post implementation of eAASPRO Dec. 2021 - August 2022 Number of patterns 6,794	Decrease /	Pre- inspirmmentation of eAASPRO August - Oct 1011 Number of Number of patients 1,805	3 months post implementation of eAASHID Nov 2022 - Jan 2023 Number of potentic 1473	Decrease
	Arrendes/938	Arrestedrings	Ampuleshigh	Ampadeschiats	Ampadeschiels	Ampuleshiels	Ampulestyles	Ampades/visits	Armgoole schools
Pperacilin Tazobactam	0.000	+	1	45		1001			
Adthomyon				1,662	60	49.081			
15 (ancompc)s				107	6	1 tota	376	19.8	44.38
Fotal Watch	30,316	\$rd	-54-85	33,613	18,713	-dang	12,075	11,040	-8.99X
Total Watch / In Patient	4-7967	16231	1979	43069	32867	100	6506*	LETT.	157
pidlin	31	240	100.001	4	66	TOOL	+		12
S g Ampicilin Subsessm	*		,	334	191	31000	300	464	30000
0.75 g Ampolin Subscrien				更	1679	3)100(38	ā	# 3# #
Amonydilin - Canalanic		163	100.001		7			15	v i
Gentamistn	696	100	なが	733	1650	recet	150	17	
Amhacin				418	7105	Heat		- Carrier	Photogram
Metroridacole	1,180	toos	1441	5	3/03/	Read	1,610	1339	16.855
Cefuronine				838	34074	10011			
Fetal Access	3,149	1446	1240	6/9/9	15,121	myer	1/03	6963	4.817
Total Access!	86050	4,513.1	2.60	1609'0	111196	268.835	6,7533	6.7944	The s

When the data was collected, e-RASPRO had been implemented for 9 months in Hospitals A and B, but it had only been implemented for 3 months in Hospital C; the results were as follows:

Table 4. The use of antibiotics included in the Reserve category, such as Polymixin and Tetracycline, e was not found in this survey. There was a significant reduction in the quantity of Ceftriaxone prescribed in Hospitals A, B, and C, by 62.92%, 40.58%, and 11.06%, respectively. Nevertheless, there was a significant increase in Cefotaxime prescribing in Hospitals A and B, with increases of 35.32% and more than 100%, respectively. A significant increase also occurred for Ciprofloxacin prescribing in three hospitals. The quantity of 500 mg Levofloxacin prescribed in Hospitals A, B, and C decreased by 45.14%, 64.84%, and 76.25%, respectively. The quantity of 750 mg Levofloxacin was reduced in Hospitals A and B by 65.49% and 13.36%, respectively; however, it increased significantly by more than 100% in Hospital C. The quantity of prescribing 1 gram of Meropenem in Hospitals A and B decreased by 41.32% and 13.45%, respectively; however, it increased in Hospital C by 10.01%. The quantity of azithromycin prescribed also decreased significantly in Hospital B, by 93.28%. Piperacillin-Tazobactam seemed to be used very rarely. The minimum use was found in Hospital B i.e.

as many as 45 ampules/vials within 9 9-month period before the e-RASPRO tool was implemented. In general, the quantity of antibiotic use included in the Watch category at Hospitals A, B, and C was reduced by 54.93% (-58.86% per inpatient), 21.11% (-9.97% per inpatient), and 8.59% (-4.15% per inpatient), as spectively. The quantity of Access category antibiotic prescribing in Hospitals A, B, and C was as follows: there was a 100% increase in Ampicillin and Amoxicillin-Clavulanate prescribing in Hospital A. While the prescribing of 1.5 g Ampicillin Sulbactam had also increased by>100% in Hospitals B and C.

Antibiotic prescribing of 0.75 g ampicillin-sulbactam increased by more than 100% in Hospital B; however, there was a decrease of 44.59% in Hospital C. The quantity of Gentamycin prescribing had a reduction of 79.15% in Hospital A; nevertheless, there was a significant pcrease up to >100% in Hospital B. Meanwhile, in Hospital C, Gentamycin had not been used before and after the implementation of e-RASPRO. Increased Cetroxime prescribing was also found very significant in Hospital B, based on the agreement made by the Antimicrobial Resistance Control Program Committee, as well as continuity of drug availability in Hospital B, Cefuroxime was included in the Access category. In general, the quantity of Access category antibiotic prescribing in Hospitals A and B increased by 12.42% (+2.61 % per inpatient) and 223.17% (+268.83% per inpatient), respectively. Meanwhile, in Hospital C, it decreased by 6.81% (-2.29% per inpatient)

DISCUSSION

An integrated survey on Antimicrobial Resistance (AMR) and Antimicrobial Use (AMU) is very essential, and it should be carried out in order to evaluate the effectiveness of policy, evidence and the implementation of ASP."1-23 This survey is a limited survey conducted at three hospitals in Indonesia, which have different characteristics as shown in Table 1.

In Table 1, it is evident that Hospital C has the greatest resources in terms of the number of physicians, pharmacists, and nurses compared to Hospitals A and B. It also has the largest building compared to the other two hospitals. The various human resources in the hospital, along with its large size, presented their own challenges in implementing the antimicrobial stewardship program, whether using manual or digital methods. In daily practice, unevery distributed levels of socialization may affect the level of appropriateness of antibiotic use with the digital guideline on the use of antimicrobial agents contained in e-RASPRO.

In Table 2, we can see that most patients who would receive early empirical antibiotic prescribing at hospital admission are those who have a Type 1 Risk Stratification, as documented in e-RASPRO. These patients include a group of immunocompetent patients or

immunocompromised patients who had unthreatening bacterial infection or those who are not at risk of having infection caused by MDR microorganisms. Prescribing wide-spectrum antibiotics should be avoided as much as possible in patients who were mostly included in the group with Type 1 Risk Stratification. It should be taken into consideration that using various types of antibiotics may increase the risk of developing resistance. 3623 As the disease progresses, empirical antibiotic treatment certainly can be escalated in accordance with the patient's condition.

Table 3 describes the appropriateness of initial empirical antibiotic prescribing using the digital antimicrobial guideline as documented in Hospitals A, B, and C within 3 months of implementing e-RASPRO, which achieved rates of 81.59%, 76.09%, and 24.48%. It is categorized as "appropriate prescribing" when the empirical antibiotic is given in accordance with the digital guideline of antimicrobial use included in e-RASPRO that is compliant with the patient's risk stratification. There is a high percentage of patients in a group with Type 1 Risk Stratification. This result is expected to bring some damages in the quantitative pattern of antibiotic prescribing from the type of antibiotics included in the Watch category to those in the Access category.

The appropriateness of antibiotic prescribing in Hospital C, which is documented in digital e-RASPRO forms, is still relatively low. Through discussions and interviews with the investigators, it may be caused by the socialization associated with e-RASPRO implementation that has not been thoroughly conducted for the clinicians, or there might be other unidentified obstacles.

Table 4 is a table describing the quantity of antibiotic prescribing, both empirical and definitive antibiotics prescribed using e-RASPRO. The absence of Reserve category antibiotic prescribing in our survey may be ducted difficulties in supplying those antibiotics in the three hospitals, or it may also be attributed to the extremely small number of cases associated with this issue in the three hospitals.

Table 4 describes the quantity of Watch category antibiotic prescribing within 9 months before and after implementing e-RASPRO in Hospital A and 8 as well as within 3 months before and after implementing the tool in Hospital C. There was a significant decrease of Ceftriaxone prescribing in Hospital A, 8 and C since those three hospitals had carried out some pforts to lower Ceftriaxone prescribing either as empirical or definitive antibiotics; therefore, in the digital guidelines on the antimicrobial use in e-RASPRO of the three hospitals, the use of Ceftriaxone could be minimged.

In some group of patients with Type 1 Risk Stratification when the Third Ceneration of Cephalosporins struid be administered, Cefotaxime becomes the appropriate choice as recommended by the digital antimicrobial guidelines in the three hospitals; therefore, although in most cases the empirical antibiotics used in patients with Type 1 Risk Stratification are those in the Access category, but there are some focal infection that can be treated with Cefotaxime as the empirical antimicrobial agent of choice. The Antimicrobial Resistance Control Program Committee of Hospitals A and B has obviously included Ceftizoxime as the Cephalosporin that has been commonly used, and it can be administered when necessary. This might explain the relatively significant increase in Cefotaxime and Ceftizoxime prescribing in Hospital A and B. Meanwhile, in Hospital C. Ceftizoxime had not been included in the digital antimicrobial guideline; therefore, Ceftizoxime had not been used within 1 months following the implementation of e-RASPRO.

The significant increase in Ciprofloxacin prescribing in three hospitals may occur because the prescribing was less consistent with the recommendation included in the digital antimicrobial guideline of e-RASPRO. Nevertheless, the guideline recommends that Ciprofloxacin may serve as a β-lactam antibiotic, which is optional for all types of risk stratifications when patients have a Penicillin allergy. Based on the digital guidelines for antimicrobial use in e-RASPRO, Ciprofloxacin has also been used as the antibiotic of choice for tropical infectious diseases in the three hospitals, such as typhoid fever, and many cases have been reported in Indonesia. For such

infections, according to the digital guideline of antimicrobial use in e-RASPRO, Ciprofloxacin is recommended as one of the antibiotics of choice. Moreover, increased prescribing of Cefotaxime and Ciprofloxacin may also be caused by clinicians who have prescribed definitive antimicrobial treatments using e-RASPRO. However, we still require additional data to confirm this event.

In general, there is a significant decrease in the quantity of Meropenem and Levofloxacin prescribing in hospitals A and B. This is consistent with the digital guideline on antimicrobial use included in e-RASPRO of the three hospitals, which minimizes the use of Levofloxacin for patients with Type 1 Risk Stratification, who are the majority in the three hospitals. Meanwhile, Meropenem can only be administered to patients with Type 3 Risk Stratification. The use of peropenem cannot be separated from the possibility of escalating antibiotic treatment, which is in accordance with the digital guideline on antimicrobial use included in e-RASPRO.

The increased prescribing quantity of 750 mg Levofloxacin and 1 g Meropenem in Hospital C still persists. It is probably caused by a compliance issue or inconsistency with the digital guideline on antimicrobial use. In the first 3 months of survey conducted in Hospital C, the appropriateness level of antimicrobial prescribing with the digital guideline on the use of antimicrobial agents is still considered to be low; while the majority of patients actually are included in the Type 1 Risk Stratification group, in which most of their empirical antibiotic choices are those included in the Access category. Nevertheless, further review should be conducted to assess the situation that has occurred at Hospital C.

This survey has not found antimicrobial prescribing of Piperacillin-Tazobactam and Ertapenem for patients included in the Type 2 Risk Stratification group following the implementation of e-RASPRO. Through various discussions with those hospitals, we identified that it is difficult to provide antimicrobial agents of Piperacillin Tazobactam and Ertapenem; therefor antibiotics of Access category such as Ampicillin Sulbactam or Amoxycillin Clavulanate with or without combination of Aminoglycosides as the anti-ESBLs often serve as empirical antibiotic of choice to be given for patients who are included in the Type 2 Risk Stratification. Nevertheless, in reality, the initial 3-month survey on the implementation of e-RASPRO in three hospitals has shown that the number of patients included in the Type 2 Risk Stratification group was a minority. Overall, there is a reduction in the quantity of antibiotic prescribing in the Watch category at Hospitals A, B, and C, by 54.93% (-8.86% per inpatient), 21.11% (-9.97% per inpatient), and 8.59% (-4.15% per inpatient), respectively, following the implementation of e-RASPRO.

In Table 4 a survey and ucted for 9 months before and after the utilization of e-RASPRO in Hospital A and B and 3 months before and after implementing e-RASPRO in Hospital C has demonstrated a significant increase in the quantity of antibiotic prescribing of Ampicillin, Amoxycillin Clavulanate and 1.5 g Ampicillin Sulbactam, which are antibiotics included in Access category in the three hospitals. The survey condexted within the first 3 months of e-RASPRO utilization has demonstrated that the majority of patients are included in the Type 1 Risk Stratification group 1 those three hospitals (Table 2), in which the majority of empirical antibiotic choices are indeed antibiotics included in the Access category. Nevertheless, further surveys are certainly required to be carried out in Hospitals A and B in the following months.

The significant increase of 0.75 g Ampicillin Sulbactam prescribing may also still be associated with the continuity of 1.5 g Ampicillin Sulbactam availability in Hospital B. Some sources at Hospital B, through discussions with investigators, suggest that there is often a shortage of 1.5 Ampicillin-Sulbactam in the hospital. Therefore, considering this reasoning, the Antimicrobial Resistance Control Program Committee in Hospital B has included Cefuroxime in the Access category of its guideline on antimicrobial use. This condition explains the presence of an increased quantity of Cefuroxime prescribing, which is included in the Access category in Hospital B.

Based on the digital guideline on antimicrobial use in e-RASPRO of the three hospitals, Aminoglycosides have actually been used as combined antibiotics. It has not been identified clearly about the cause of reduced Gentamycin prescribing is in Hospital A, while in Hospital C, the use of Gentamycin and Amikacin has not been documented either before or after the implementation of e-RASPRO. Increased Gentamycin and Amikacin prescribing in Hospital B could occur because the digital guideline on antimicrobial use for those three hospitals recommends using aminoglycosides as combined empirical antibiotics for some focal infections in patients with Type 1 risk stratification and almost of focal infections in patients with Type 3 Risk Stratification. Overall, there is increased quantity of Access category antibiotic prescribing in Hospital A and B of 12.423 (+2.435 per inpatient) and 223.173 (+268.833 per inpatient), respectively. A survey conducted within 3 months before and after the implementation of e-RASPRO in Hospital C demonstrated a reduction in Access category antibiotic prescribing of 6.813 (-2.293 per inpatient). In Table 4, regarding the number of patients before and after the implementation of e-

In Table 4, regarding the number of patients before and after the implementation of e-RASPRO in those three hospitals, it can also be seen that the numbers were not significantly different. This survey has not correlated the quantity of prescribing with the duration of antibiotic use; furthermore, it has not calculated the percentage of escalating and stepping down empirical antibiotic treatment. However, in this survey, we observed a reduced percentage of Watch category antibiotic prescribing in three hospitals, as well as an increased percentage of Access category antibiotic prescribing in two hospitals (Hospital A and B) following the implementation of e-RASPRO. The increased quantity of Access category antibiotic prescribing, particularly in Hospital B, is extremely significant.

The altered quantity of Watch and Access category antibiotics prescribed, particularly in Hospitals A and B, is likely still influenced by the appropriateness of empirical antibiotic use, which is guided by the digital guideline on antimicrobial use included in e-RASPRO. However, it certainly requires further studies. Hospital characteristics, such as the number of hospital beds, the number of physicians, and of er facilities, may also affect the pattern of antibiotic prescribing. A systematic leview showed a decrease in the antimicrobial DDD range from -8.42% to -61.29% related to the use of a digital antimicrobial stewardship tool. **

Some studies have demonstrated that the utilization of digital tools to implement ASP can reduce the use of antimicrobial agents and also decrease the DDD. ASP in other previous study the duration of digital antimicrobial stewardship implementation may show a different antibiotic DDD result. However, we still cannot conclude what type of digital intervention will certainly reduce the use of antimicrobial agents. Our study is an initial survey on the utilization of e-RASPRO, one of the digital antimicrobial stewardship programs used in Indonesia. This study is a survey only and cannot yet describe the correlation between e-RASPRO use and antibiotic prescribing patterns. To achieve good results, the utilization of e-RASPRO should be carried out in conjunction with compulsory disciplines and with full support from the hospital management team. Demographic characteristics of the hospitals can also affect the effectiveness of e-RASPRO utilization. To provide a comprehensive explanation of this issue, more extensive studies with full support from the managerial team are required to further analyze the causal correlation between the utilization of e-RASPRO and the abered quantitative pattern in antibiotic prescribing.

CONCLUSION

The survey has not been able to describe the causal-effect correlation between e-RASPRO implementation and the quantity of antibiotic prescribing. However, in general, there is an altered quantitative pattern in the quantity of empirical antibiotic prescribing, particularly for those included in the Watch and Access categories, following the implementation of e-RASPRO. We

suggest a broader scope of research on digital antimicrobial stewardship tools to evaluate their effectiveness in implementing antimicrobial stewardship programs.

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AUTHORS CONTRIBUTION

The authors confirm their contribution to the paper as follows: studing proception and design: RIN; data collection: WIL, RA, RM, HS, SM, DA, TSM, IIP, DD, GNL, ALR; analysis and interpretation of research. RIN, WIL, AA, HA; draft manuscript preparation: RIN, WIL, YY, 35, NH, HA, MAF, TFF, JVK, YY. At authors reviewed the results and approved the final version of the manuscript.

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CONFLICT OF INTEREST

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