LAPORAN PENELITIAN

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

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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 e-RASPRO diharapkan dapat merubah pola peresepan antibiotik dengan mengedepankan peresepan antibiotik kategori ACCESS.

Methods: 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 peresepan antibiotik profilaksis, kesesuaian peresepan antibiotik empirik, dan kuantitas peresepan antibiotik kategori WATCH dan ACCESS.

Hasil: Tiga bulan sesudah terapan e-RASPRO di Rumah Sakit A dan B didapatkan peningkatan kuantitas peresepan antibiotik profilaksis Cephazolin masing-masing 89.12% dan 100%. Di Rumah Sakit C tidak tergambar, karena Cephazolin sudah baku digunakan sebelum terapan perangkat e-RASPRO. Kesesuaian peresepan antibiotik empirik dengan panduan penggunaan antimikroba digital perangkat e-RASPRO di Rumah Sakit A, B, dan C masing-masing sebesar 81.59%, 76.77%, dan 24.48%. Pada formulir elektronik perangkat e-RASPRO yang terisi di Rumah Sakit A, B, dan C menunjukkan 90.16%, 83.98%, dan 81.15% pasien pada peresepan antibiotik awal termasuk dalam Stratifikasi Risiko Tipe 1 yang mayoritas pilihan antibiotik empiriknya terkategori ACCESS. 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%, 21.11%, dan 8.59%. Sementara, kuantitas peresepan antibiotik kategori ACCESS di Rumah Sakit A dan B meningkat 12.42% dan 223.17%, di Rumah Sakit C menurun 6.81%.

Kesimpulan: Survei ini belum dapat menggambarkan hubungan sebab-akibat terapan perangkat e-RASPRO dengan kuantitas peresepan antibiotik. Namun, secara umum, terdapat perubahan pola kuantitas peresepan antibiotik profilaksis, serta perubahan kuantitas peresepan antibiotik empirik kategori WATCH dan kategori ACCESS paska terapan perangkat e-RASPRO.

Keywords: Survei, kuantitas, **peresepan, antibiotik**, WATCH, ACCESS, digital, e-RASPRO, Indonesia

Pendahuluan

Pelaksanaan Penatagunaan Antimikroba (PGA) telah dicanangkan secara global dengan tujuan untuk meningkatkan penggunaan antimikroba bijak dan menurunkan risiko munculnya resistensi antimikroba (1). *World Health Organization* (WHO) telah mengkategori antibiotik menjadi ACCESS, WATCH, dan RESERVE (AWARE) (2). Antibiotik kategori ACCESS adalah jenis-jenis antibiotik yang memiliki potensi kejadian resistensi lebih rendah, sementara antibiotik kategori WATCH adalah jenis-jenis antibiotik yang memiliki potensi kejadian resistensi lebih besar, dan antibiotik kategori RESERVE adalah jenis-jenis antibiotik yang hanya digunakan apabila ada tersangka infeksi yang disebabkan oleh bakteri *Multi-Drug Resistant* (MDR), sebaiknya tidak digunakan secara sembarangan, apalagi dalam kuantitas yang besar.

Dalam rangka hal tersebut, RASPRO Indonesia Study Group mencoba membuat suatu sistem, yang disebut sebagai sistem RASPRO yang dapat memandu klinisi dalam peresepan antibiotik berdasarkan panduan lokal (1). Sistem RASPRO dibuat dengan menggunakan stratifikasi risiko pasien yang mengarahkan klinisi dalam peresepan antibiotik empirik awal,

pergantian antibiotik, pemberian antibiotik definitif, sampai dengan keharusan mengisi formulir khusus apabila antibiotik hendak digunakan berkepanjangan (1).

Survei ini merupakan pengembangan dari survei terdahulu, dimana sebuah rumah sakit di Jawa tengah, Indonesia menerapkan sistem RASPRO manual untuk menjalankan PGA. Pada survei sebelum dan sesudah penggunaan sistem manual tersebut selama 3 bulan, diperoleh penurunan peresepan antibiotik dari 64.799 ampul / vial ke 51.661 ampul / vial, dengan prosentase rerata penurunan penggunaan antibiotik selama 3 bulan terapan mencapai 14.44% (1). Sistem RASPRO yang sebelumnya mengunakan formulir-formulir panduan yang bersifat manual tersebut diujicobakan ke dalam bentuk digital berupa elektronik RASPRO (e-RASPRO), sehingga e-RASPRO menjadi perangkat digital di Indonesia yang didesain dalam rangka menjalankan PGA di rumah sakit. Melalui e-RASPRO, panduan antimikroba lokal dibuat secara digital, dengan pengisian formulir-formulir RASPRO yang juga dilakukan secara digital, yang terdiri dari formulir elektronik untuk antibiotik profilaksis, antibiotik empirik, dan antibiotik definitif.

Farmasi klinis juga dapat melakukan verifikasi secara langsung mengenai ketepatan indikasi, pembatasan waktu penggunaan antibiotik, dan kesesuaian penggunaan antibiotik empirik dengan panduan penggunaan antimikroba digital yang berlaku di rumah sakit tempat perangkat e-RASPRO digunakan. Melalui perangkat e-RASPRO ini diharapkan terjadi perubahan pola peresepan antibiotik dengan mengutamakan penggunaan antibiotik kategori ACCESS guna menekan risiko meluasnya resistensi terhadap antibiotik-antibiotik terutama yang berspektrum luas.

Metode

Survei dilakukan pada 3 rumah sakit di Indonesia, Rumah Sakit A, Rumah Sakit B, dan Rumah Sakit C. Sebelumnya dilakukan berbagai sosialisasi terapan penatagunaan antimikroba digital dengan perangkat e-RASPRO, meliputi: sosialisasi peresepan antibiotik profilaksis digital, sosialiasi peresepan antibiotik empirik digital, sosialiasasi peresepan antibiotik definitif digital, sosialisasi penggunaan antibiotik berkepanjangan pada perangkat digital, sosialisasi pengelompokan pasien berdasarkan Stratifikasi Risiko untuk peresepan antibiotik empirik dengan perangkat digital, dan sosialisasi panduan penggunaan antimikroba empirik digital.

Sosialisasi Peresepan Antibiotik Profilaksis Digital pada Perangkat e-RASPRO

Dilakukan sosialisasi terapan penggunaan perangkat e-RASPRO pada ketiga rumah sakit untuk peresepan antibiotik profilaksis. Pada peresepan antibiotik profilaksis, klinisi diminta untuk mengisi formulir digital profilaksis pada e-RASPRO yang kemudian dipandu untuk memilih jenis antibiotik profilaksis sesuai panduan antimikroba digital dalam perangkat tersebut, dengan target penggunaan utama adalah Cephazolin. Kecuali di Rumah Sakit B, berdasarkan kesepakatan Komite Pengendalian Resistensi Antimikroba rumah sakitnya, Cefuroxime juga diputuskan untuk digunakan sebagai antibiotik profilaksis. Pada peresepan antibiotik profilaksis yang tidak sesuai dengan panduan penggunaan antimikroba digital, maka farmasi klinik akan melakukan konfirmasi kepada klinisi dan tim PGA rumah sakit untuk menentukan diijinkan atau tidaknya antibiotik tersebut digunakan. Sosialisasi dilakukan oleh peneliti kepada Komite Pengendalian Resistensi Antimikroba ketiga rumah sakit dan dilanjutkan kepada para klinisi di masing-masing rumah sakit. Sosialisasi dilakukan dengan metode tatap muka dan daring.

Sosialiasi Peresepan Antibiotik Empirik Digital pada Perangkat e-RASPRO

Dilakukan sosialisasi terapan penggunaan perangkat e-RASPRO pada ketiga rumah sakit peresepan antibiotik empirik melalui perangkat e-RASPRO. Pada peresepan antibiotik empirik, klinisi dipandu untuk menentukan stratifikasi risiko pasien yang masuk di rawat inap

berdasarkan status imun pasien, severitas infeksi, dan riwayat medisnya, seperti: riwayat penggunaan antibiotik sebelumnya, riwayat perawatan di rumah sakit sebelumnya, dan riwayat penggunaan instrumen medis sebelumnya.

Dilakukan sosialisasi mengenai panduan dan pengisian formulir eskalasi dan step down antibiotik empirik sesuai dengan panduan penguunaan antimikroba digital pada perangkat e-RASPRO. Pada peresepan antibiotik empirik yang tidak sesuai dengan panduan penggunaan antimikroba digital, maka farmasi klinik akan melakukan konfirmasi kepada klinisi dan tim PGA rumah sakit untuk menentukan diijinkan atau tidaknya antibiotik tersebut digunakan. Sosialisasi dilakukan oleh peneliti kepada Komite Pengendalian Resistensi Antimikroba ketiga rumah sakit dan dilanjutkan kepada para klinisi di masing-masing rumah sakit. Sosialisasi dilakukan dengan metode tatap muka dan daring.

Sosialiasasi Peresepan Antibiotik Definitif pada Perangkat e-RASPRO

Dilakukan sosialisasi terapan penggunaan perangkat e-RASPRO pada ketiga rumah sakit peresepan antibiotik definitif melalui perangkat e-RASPRO. Pada perangkat e-RASPRO terdapat formulir digital pemberian antibiotik definitif yang harus diisi klinisi bila ada peresepan antibiotik definitif sesuai laporan hasil kultur. Sosialisasi dilakukan oleh peneliti kepada Komite Pengendalian Resistensi Antimikroba ketiga rumah sakit dan dilanjutkan kepada para klinisi di masing-masing rumah sakit. Sosialisasi dilakukan dengan metode tatap muka dan daring.

Sosialisasi Penggunaan Antibiotik Berkepanjangan pada Perangkat e-RASPRO

Dilakukan sosialisasi terapan penggunaan perangkat e-RASPRO pada ketiga rumah sakit. Bila terdapat peresepan antibiotik yang berkepanjangan, klinisi wajib menyampaikan indikasi penggunaan antibiotik berkepanjangan tersebut melalui formulir digital pada perangkat e-RASPRO. Hal ini kemudian akan diverifikasi oleh farmasi klinis kepada Tim PGA rumah sakit. Pada pemberian antibiotik berkepanjangan yang tanpa disertai pengisian formulir elektronik antibiotik berkepenjangan yang ada di perangkat e-RASPRO atau tanpa disertai indikasi yang jelas, maka farmasi klinik, sesuai dengan persetujuan Tim PGA rumah sakit dapat melakukan *Automatic Stop Order* (ASO). Sosialisasi dilakukan oleh peneliti kepada Komite Pengendalian Resistensi Antimikroba ketiga rumah sakit dan dilanjutkan kepada para klinisi di masing-masing rumah sakit. Sosialisasi dilakukan dengan metode tatap muka dan daring.

Sosialisasi Pengelompokan Pasien Berdasarkan Stratifikasi Risiko untuk Peresepan Antibiotik Empirik pada Perangkat e-RASPRO

Dilakukan sosialisasi pengelompokan pasien berdasarkan stratifikasi risikonya pada perangkat e-RASPRO. Sosialisasi dilakukan oleh peneliti kepada Komite Pengendalian Resistensi Antimikroba ketiga rumah sakit dan dilanjutkan kepada para klinisi di masing-masing rumah sakit. Sosialisasi dilakukan dengan metode tatap muka dan daring.

Pemberian antibiotik empirik pada pasien rawat inap harus berdasarkan stratifikasi risiko pasien yang dipandu oleh panduan penggunaan antimikroba digital yang ada dalam perangkat e-RASPRO. Perangkat e-RASPRO membagi pasien ke dalam 3 kelompok stratifikasi risiko untuk pemberian antibiotik empirik.

Kelompok Pasien Stratifikasi Risiko Tipe 1 adalah kelompok pasien yang bisa mendapat antibiotik empirik untuk cakupan kuman multi-sensitif. Kelompok ini merupakan kelompok pasien imunokompeten atau bisa juga kelompok imunokompromis dengan severitas infeksi bakteri yang tidak mengancam atau berisiko MDR (1).

Kelompok Pasien Stratifikasi Risiko Tipe 2 adalah kelompok pasien immunokompromis dan / atau diabetes melitus tidak terkontrol, dengan riwayat pemberian antibiotik < 90 hari yang lalu dan / atau riwayat perawatan di fasilitas kesehatan > 48 jam dalam

90 hari yang lalu, dan / atau riwayat penggunaan instrumentasi medis < 90 hari yang lalu. Kelompok ini berisiko untuk kejadian infeksi kuman *Multi Drug Resistant* (MDR) - *Extended Spectrum Beta-Lactamases* (ESBLs) (1,3–8).

Kelompok Pasien Stratifikasi Risiko Tipe 3 adalah kelompok pasien dengan kondisi infeksi mengancam, dan / atau individu imunokompromis dan / atau diabetes melitus tidak terkontrol, dengan riwayat pemberian antibiotik < 30 hari yang lalu dan / atau perawatan di fasilitas kesehatan > 48 jam dalam 30 hari yang lalu, dan / atau riwayat penggunaan instrumentasi medis < 30 hari yang lalu. Kelompok ini merupakan kelompok dengan severitas infeksi tinggi, atau kelompok yang berisiko terinfeksi ESBLs dan mikroorganisme *Multi-Drug Resistant* (MDR) lain termasuk MDR *Pseudomonas sp*. (1,6,9–14). Kelompok pasien dengan *Healthcare Associated Infections* (HAIs) juga masuk dalam kelompok Stratifikasi Risiko Tipe 3. Kelompok terkategori HAIs adalah kelompok dengan periode kejadian infeksi pada > 48 jam perawatan di fasilitas kesehatan, bahkan 90 hari paska pembedahan (15–18).

Sosialisasi Panduan Penggunaan Antimikroba Empirik Digital pada Perangkat e-RASPRO.

Dilakukan sosialisasi terapan perangkat e-RASPRO dengan panduan penggunaan antimikroba digital di dalamnya pada 3 rumah sakit di Indonesia. Sosialisasi dilakukan oleh peneliti kepada Komite Pengendalian Resistensi Antimikroba ketiga rumah sakit dan dilanjutkan kepada para klinisi di masing-masing rumah sakit.

Panduan penggunaan antimikroba digital dibuat dengan memasukkan kategori antibiotik berdasarkan AWARE dari *World Health Organization* (WHO) tahun 2021. Panduan penggunaan antimikroba digital kemudian disepakati bersama oleh manajemen rumah sakit dan Komite Pengendalian Resistensi Antimikroba rumah sakit, yang kemudian dimasukkan ke dalam perangkat e-RASPRO. Ketiga rumah sakit menggunakan panduan penggunaan antimikroba digital yang sejenis yang dibuatkan oleh RASPRO Indonesia Study Group dengan mempertimbangkan pengelompokan AWARE WHO sebagai berikut:

Pilihan Antibiotik Empirik untuk Pasien-pasien dengan Stratifikasi Risiko Tipe 1 pada Panduan Penggunaan Antimikroba Digital Perangkat e-RASPRO.

Mayoritas pilihan antibiotik empirik pada panduan penggunaan antimikroba digital untuk pasien-pasien dengan Stratifikasi Risiko Tipe 1 masuk dalam golongan ACCESS seperti: Ampicillin, Ampicillin Sulbactam, Amoxycillin Clavulanate, Amikacin, dan Gentamycin. Kecuali, di Rumah Sakit B, sesuai dengan pertimbangan kontinuitas ketersediaan obat dan berdasarkan kesepakatan Komite Pengendalian Resistensi Antimikroba, Cefuroxime (Cephalosporin generasi II) dimasukkan ke dalam kelompok antibiotik kategori ACCESS. Jikapun dibutuhkan, pilihan mayoritas antibiotik empirik kategori WATCH Cephalosporin generasi III untuk kelompok pasien Stratifikasi Risiko Tipe 1 adalah Cefotaxime dan Ceftizoxime.

Pilihan Antibiotik Empirik untuk Pasien-pasien dengan Stratifikasi Risiko Tipe 2 pada Panduan Penggunaan Antimikroba Digital Perangkat e-RASPRO.

Untuk kelompok pasien dengan Stratifikasi Risiko Tipe 2 pada perangkat e-RASPRO, pilihan antibiotik empirik yang diberikan adalah antibiotik anti ESBL dengan mayoritas pilihan antibiotik termasuk dalam kategori WATCH pada panduan penggunaan antimiroba digital seperti: Piperacillin Tazobactam atau Ertapenem tunggal.

Pilihan Antibiotik Empirik untuk Pasien-pasien dengan Stratifikasi Risiko Tipe 3 pada Panduan Penggunaan Antimikroba Digital Perangkat e-RASPRO.

Pasien-pasien yang termasuk dalam kelompok Stratifikasi Tipe 3 dalam sistem RASPRO termasuk dalam kelompok pasien yang rawan terjadi sepsis (19). Oleh karenanya, kelompok pasien dengan Stratifikasi Risiko Tipe 3 pada perangkat e-RASPRO, pilihan antibiotik empiriknya adalah antibiotik yang mampu mengeradikasi bakteri-bakteri ESBLs dan bakteri MDR lainnya dengan mayoritas pilihan antibiotik yang tertera pada panduan antimikroba digital termasuk dalam kategori WATCH sampai RESERVE seperti: Meropenem dan Imipenem bisa dengan atau tanpa kombinasi dengan antibiotik kategori ACCESS seperti Amikacin / Gentamycin atau dengan penggunaan Polymixin atau Tygecycline.

Setting dan Jangka Waktu Pengambilan Data Survei

Setting Data Survei

Data yang diambil merupakan data sekunder dari laporan penggunaan antibiotik injeksi di ruang rawat inap di ketiga rumah sakit.

Jangka Waktu Pengambilan Data Survei

Melalui terapan perangkat e-RASPRO, pengambilan data awal dilakukan pada 3 bulan pertama penggunaan perangkat e-RASPRO meliputi: kesesuaian peresepan antibiotik profilaksis, persentase pasien pada masing-masing kelompok stratifikasi risiko dari formulir digital e-RASPRO, serta kesesuaian peresepan antibiotik empirik pada panduan penggunaan antimikroba digital.

Survei dilanjutkan dengan pengumpulan semua data kuantitas peresepan antibiotik empirik dan definitif injeksi pada pasien-pasien rawat inap dalam kurun waktu 9 bulan sebelum dan sesudah penggunaan perangkat e-RASPRO di 2 rumah sakit (Rumah Sakit A dan B) dan 3 bulan sebelum dan sesudah penggunaan perangkat e-RASPRO di 1 rumah sakit (Rumah Sakit C). Pada saat data diambil, Rumah Sakit C baru 3 bulan menggunakan perangkat e-RASPRO. Wawancara dan diskusi dengan Komite Pengendali Resistensi Antimikroba ketiga rumah sakit dilakukan pada saat awal penggunaan perangkat e-RASPRO juga pada saat dilakukan pengambilan data survei.

Pelaporan Data Survei

Setelah pengambilan data survei lengkap, data disampaikan secara deskriptif dan dilihat pola perubahan kuantitas peresepan antibiotik sebelum dan sesudah terapan perangkat e-RASPRO. Data survei dihitung dan disampaikan seorang farmasi klinis pada masing-masing rumah sakit dan telah diverifikasi oleh Komite Pengendalian Resistensi Antimikroba di masing-masing rumah sakit yang disurvei. Data ditampilkan apa adanya sesuai yang disampaikan oleh masing-masing rumah sakit.

Result

Berikut dari survei yang dilakukan 3 bulan pertama terapan perangkat e-RASPRO pada 3 rumah sakit di Indonesia:

Tabel 1. Karakteristik Demografi 3 Rumah Sakit yang Disurvei

Karakteristik Demografi Rumah Sakit	Rumah Sakit A	Rumah Sakit B	Rumah Sakit C
Jumlah Dokter:			
Dokter umum	14	14	25
Dokter gigi	5	15	8
Dokter spesialis	37	98	102
Total	56	127	135
Jumlah farmasis	9	26	39
Jumlah tenaga keperawatan	115	74	368
Jumlah Tempat Tidur:			
Rawat Inap	124	168	259
ICU + HCU + ICCU + NICU + PICU	10	17	26
Total	134	185	285
Rasio jumlah dokter spesialis : tempat tidur	1 : 3.62	1 : 1.89	1 : 2.79
Rasio jumlah farmasis : tempat tidur	1 : 14.89	1 : 7.12	1 : 7.31
Rasio jumlah tenaga keperawatan : tempat tidur	1 : 1.17	1 : 2.50	1 : 0.77
Luas Bangunan	7,247.35	8,120.00	31,099.94

Data: sirs.kemkes.go.id

Data aktual demografi ketiga rumah sakit yang disurvei yang dihimpun dari sirs.kemkes.go.id, Kementerian Kesehatan Republik Indonesia adalah sebagai berikut: Rumah Sakit A, B, dan C masing-masing dengan 134 tempat tidur, 185 tempat tidur, dan 254 tempat tidur dengan rasio dokter spesialis per tempat tidur masing-masing adalah 1 per 3.62 tempat tidur, 1 per 1.89 tempat tidur, dan 1 per 2.79 tempat tidur.

Tabel 2. Kuantitas Peresepan Antibiotik Profilaksis 3 Bulan Sebelum dan Setelah Terapan Perangkat e-RASPRO di Ketiga Rumah Sakit

Antibiotik	Rumah Sakit A 3 Bulan Pre Terapan e-RASPRO Juli - Sept 2021 Ampul / Vial	Rumah Sakit A 3 Bulan Post Terapan e-RASPRO Okt - Des 2021 Ampul / Vial	Kenaikan / Penurunan Ampul / Vial	Rumah Sakit B 3 Bulan Pre Terapan e-RASPRO Sept - Nov 2021 Ampul / Vial	Rumah Sakit B 3 Bulan Post Terapan e-Des 2021 - Feb 2022 Ampul / Vial	Kenaikan / Penurunan Ampul / Vial	Rumah Sakit C 3 Bulan Pre Terapan e-RASPRO Agust - Okt 2022 Ampul / Vial	Rumah Sakit C 3 Bulan Post Terapan e-Nov 2022 - Jan 2023 Ampul / Vial	Kenaikan / Penurunan Ampul / Vial
Cefazolin	294	556	89.12%	-	204	100.00%	568	435	-23.42%
Cefuroxime*	-	-	-	63	84	33.33%	-	-	-
Ceftriaxone	136	70	-48.53%	244	189	-22.54%	-	-	-
Cefotaxime	124	78	-37.10%	7	12	71.43%	-	-	-
Cefoperazone	-	-		-	23	100.00%			
Ceftazidime	-	-	-	23	-	-100.00%	-	-	-
Ceftixozime	-	-	-	72	-	-100.00%	-	-	-
Sulbactam-Ampicillin	-	-	-	11	-	-100.00%	-	-	-

*Berdasarkan kesepakatan Komite Pengendalian Resistensi Antimikroba di Rumah Sakit B, Cefuroxime dimasukkan ke dalam kategori ACCESS dan diputuskan untuk digunakan sebagai antibiotik profilaksis

3 bulan sebelum dan sesudah terapan perangkat e-RASPRO di 3 rumah sakit diperoleh data sebagai berikut: peningkatan kuantitas peresepan antibiotik profilaksis Cephazolin di

Rumah Sakit A dan B masing-masing sebesar 89.12% dan 100%, Terjadi penurunan kuantitas peresepan antibiotik profilaksis Ceftriaxone di Rumah Sakit A dan B masing-masing sebesar 48.53% dan 22.54%. Peresepan antibiotik profilaksis Cefotaxime di Rumah Sakit A juga menurun sebesar 37.10%, namun masih terjadi kenaikan kuantitas peresepan antibiotik profilaksis Cefotaxime di rumah sakit B sebesar 71.43 %, walaupun secara ampul / vial jumlahnya tidak banyak, yaitu hanya sebesar 5 ampul / vial.

Peresepan Cefuroxime sebagai antibiotik profilaksis di rumah sakit B masih terlihat meningkat karena sesuai kesepakatan Komite pengendalian resistensi Antimikroba di Rumah Sakit B, Cefuroxime digunakan sebagai antibiotik profilaksis. Pada Rumah Sakit C tidak dapat dilakukan analisa perbandingan kuantitas peresepan antibiotik profilaksis Cephazolin karena Cephazolin rupanya memang sudah digunakan sebagai antibiotik profilaksis sebelum dan sesudah terapan perangkat e-RASPRO.

Tabel 3. Stratifikasi Risiko Awal Pasien Mendapat Antibiotik yang Terisi pada Formulir Digital 3 Bulan Setelah Terapan Perangkat e-RASPRO di Ketiga Rumah Sakit

Stratifikasi Risiko	A		B		C	
	3 Bulan Okt - Des 2021		3 Bulan Des 2021 - Feb 2022		3 Bulan Nov 2022 - Jan 2023	
	Jumlah	%	Jumlah	%	Jumlah	%
Tipe 1	284	90.16%	692	83.98%	1,472	81.15%
Tipe 2	31	9.84%	15	1.82%	84	4.63%
Tipe 3	-	0.00%	117	14.20%	258	14.22%
Total	315	100.00%	824	100.00%	1,814	100.00%

Pada formulir digital perangkat e-RASPRO yang terisi pada 3 bulan awal penggunaan perangkat e-RASPRO, mayoritas pasien terkategori dalam Stratifikasi Risiko Tipe 1, dengan persentase di Rumah Sakit A, B dan C masing-masing mencapai 90.16%, 83.98%, dan 81.15%.

Tabel 4. Kesesuaian Peresepan Antibiotik Empirik dengan Panduan Penggunaan Antimikroba Digital 3 Bulan Setelah Terapan Perangkat e-RASPRO di Ketiga Rumah Sakit

	Rumah Sakit					
	A 3 Bulan Okt - Des 2021		B 3 Bulan Des 2021 - Feb 2022		C 3 Bulan Nov 2022 - Jan 2023	
	Jumlah	%	Jumlah	%	Jumlah	%
Peresepan Antibiotik Empirik Sesuai Panduan Penggunaan Antimikroba Digital pada Perangkat e-RASPRO	257	81.59%	674	76.77%	444	24.48%
Peresepan Antibiotik Empirik Tidak Sesuai Panduan Penggunaan Antimikroba Digital pada Perangkat e-RASPRO	57	18.10%	204	23.23%	1,022	56.34%
Peresepan Antibiotik Empirik Kesesuaian Tidak Dapat Teridentifikasi pada Perangkat e-RASPRO	1	0.32%	-	0.00%	348	19.18%
Total Pengisian Form	315	100.00%	878	100.00%	1,814	100.00%

Kesesuaian peresepan antibiotik empirik dengan panduan antimikroba digital pada perangkat e-RASPRO yang tercatat di Rumah Sakit A, B, dan C, 3 bulan sebelum dan sesudah

terapan perangkat e-RASPRO masing-masing mencapai 81.59%, 76.77%, dan 24.48%. Peresepan antibiotik empirik dengan kesesuaian yang tidak teridentifikasi yang tercatat pada formulir digital adalah peresepan antibiotik melalui perangkat e-RASPRO yang tidak jelas kesesuaiannya, misalnya antibiotik kombinasi satu jenis sesuai dan satu lagi tidak sesuai dengan panduan antimikroba digital atau kondisi varian lainnya, dimana kesesuaian belum dapat disimpulkan pada saat pengambilan data. Kondisi ini tercatat mencapai 19.18% di rumah sakit C.

Tabel 5. Kuantitas Peresepan Antibiotik Kategori WATCH dan ACCESS 9 Bulan dan 3 Bulan Sebelum dan Sesudah Terapan Perangkat e-RASPRO

Antibiotik	Rumah Sakit A			Rumah Sakit B			Rumah Sakit C		
	9 Bulan			9 Bulan			3 Bulan		
	Pre Terapan e-RASPRO Jan - Sept 2021 Jumlah Pasien = 4,215	Post Terapan e-RASPRO Okt 2021 - Juni 2022 Jumlah Pasien = 4,618	Kenaikan / Penurunan	Pre Terapan e-RASPRO Mar - Nov 2021 Jumlah Pasien = 7,754	Post Terapan e-RASPRO Des 2021 - Agust 2022 Jumlah Pasien = 6,794	Kenaikan / Penurunan	Pre Terapan e-RASPRO Agust - Okt 2022 Jumlah Pasien = 2,805	Post Terapan e-RASPRO Nov 2022 - Jan 2023 Jumlah Pasien = 2,675	Kenaikan / Penurunan
	Ampul / Vial	Ampul / Vial	Ampul / Vial	Ampul / Vial	Ampul / Vial	Ampul / Vial	Ampul / Vial	Ampul / Vial	Ampul / Vial
Ceftriaxone	15,514	5,753	-62.92%	11,602	6,894	-40.58%	4,513	4,014	-11.06%
Cefotaxime 1 g	756	1,023	35.32%	950	4,189	> 100%	1,360	1,237	-9.04%
Cefotaxime 0.5 g	-	-	-	76	145	90.79%	-	-	-
Ceftazidime	-	-	-	866	359	-58.55%	724	774	6.91%
Cefoperazone	-	-	-	232	413	78.02%	-	-	-
Cefoperazone sulbactam	-	-	-	-	-	-	-	146	100.00%
Ceftixozime	-	282	100.00%	527	596	13.09%	129	-	-100.00%
Cefepime	-	-	-	14	6	-57.14%	1,465	1,089	-25.67%
Levofloxacin 750 mg	2,147	741	-65.49%	2,770	2,400	-13.36%	360	854	> 100%
Levofloxacin 500 mg	833	457	-45.14%	3,197	1,124	-64.84%	1,002	238	-76.25%
Ciprofloxacin	-	288	100.00%	136	1,258	> 100%	-	234	100.00%
Moxifloxacin	-	-	-	487	221	-54.62%	-	-	-
Meropenem 1 g	968	568	-41.32%	8,690	7,521	-13.45%	1,619	1,781	10.01%
Meropenem 0.5 g	-	-	-	19	-	-100.00%	550	475	-13.64%
Imipenem + Cilastatin	-	-	-	133	43	-67.67%	-	-	-
Piperacillin tazobactam	-	-	-	45	-	-100.00%	-	-	-
Azithromycin	-	-	-	2,662	179	-93.28%	-	-	-
Vancomycin 0.5 g	-	-	-	207	379	83.09%	356	198	-44.38%
TOTAL WATCH	**20,218**	**9,112**	**-54.93%**	**32,613**	**25,727**	**-21.11%**	**12,078**	**11,040**	**-8.59%**
Ampicillin	-	947	100.00%	-	93	100.00%	-	-	-
Ampicillin Sulbactam 1.5 g	-	-	-	214	484	> 100%	207	466	> 100%
Ampicillin Sulbactam 0.75 g	-	-	-	746	6,291	> 100%	296	164	-44.59%
Amoxycillin-Clavulinic	-	263	100.00%	-	-	-	-	-	-
Gentamycin	969	202	-79.15%	722	1,650	> 100%	-	-	-
Amikacin	-	-	-	428	1,105	> 100%	-	-	-
Metronidazole	1,180	1,004	-14.92%	1,731	2,424	40.03%	1,610	1,339	-16.83%
Cefuroxime*	-	-	-	838	3,074	> 100%	-	-	-
TOTAL ACCESS	**2,149**	**2,416**	**12.42%**	**4,679**	**15,121**	**223.17%**	**2,113**	**1,969**	**-6.81%**

Pada saat data diambil, terapan perangkat e-RASPRO telah berjalan 9 bulan di rumah sakit A dan B, sementara di Rumah Sakit C baru berjalan 3 bulan antara lain dijumpai sebagai berikut:

Kuantitas Peresepan Antibiotik Kategori RESERVE

Tidak dijumpai penggunaan antibiotik kategori RESERVE seperti Polymixin dan Tygecycline pada survei ini.

Kuantitas Peresepan Antibiotik Kategori WATCH

Terdapat penurunan kuantitas peresepan antibiotik Ceftriaxone yang cukup siginifkan di Rumah Sakit A, B, dan C masing-masing sebesar 62.92%, 40.58%, dan 11.06%. Namun terjadi peningkatan sangat signifikan pada peresepan antibiotik Cefotaxime di Rumah Sakit A

dan B dengan peningkatan persentase masing-masing sebesar 35.32 % dan > 100%. **Peningkatan signifikan juga terjadi pada peresepan antibiotik Ciprofloxacin di ketiga rumah sakit. Kuantitas peresepan Levofloxacin 500 mg di Rumah Sakit A, B dan C mengalami penurunan masing-masing sebesar 45.14%, 64.84%, dan 76.25 %. Kuantitas peresepan Levofloxacin 750 mg menurun di rumah sakit A dan B masing-masing sebesar 65.49% dan 13.36 %, namun meningkat signifikan > 100% di Rumah Sakit C.**

Kuantitas peresepan antibiotik Meropenem 1 gram di Rumah Sakit A dan B masing-masing menurun sebesar 41.32% dan 13.45%, namun masih mengalami peningkatan di rumah sakit C sebesar 10.01%. Kuantitas peresepan Azithromycin juga menurun sangat signifikan di Rumah Sakit B, yaitu sebesar 93.28%. Antibiotik Piperacillin Tazobactam tampak sangat jarang digunakan. Penggunaan minimal tercatat di Rumah Sakit B yaitu sebanyak 45 ampul / vial pada 9 bulan sebelum terapan perangkatg e-RASPRO. Secara keseluruhan terjadi penurunan kuantitas peresepan antibiotik kategori WATCH di Rumah Sakit A, B, dan C masing-masing sebesar 54.93%, 21.11%, dan 8.59%.

Kuantitas Peresepan Antibiotik Kategori ACCESS

Kuantitas peresepan antibiotik kategori ACCESS di Rumah Sakit A, B, dan C menunjukkan sebagai berikut: peningkatan sebesar 100% peresepan Ampicillin dan Amoxycillin-Clavulanat di Rumah Sakit A. Sementara peresepan Ampicillin Sulbactam 1.5 g juga mengalami peningkatan > 100% di Rumah Sakit B dan C. **Peresepan antibiotik Ampicillin Sulbactam 0.75 g mengalami peningkatan > 100% di Rumah Sakit B, namun mengalami penurunan 44.59% di Rumah Sakit C.**

Kuantitas peresepan antibiotik Gentamycin mengalami penurunan 79.15% di Rumah Sakit A, namun mengalami peningkatan signifikan hingga sebesar > 100% di Rumah Sakit B. Sementara di Rumah Sakit C Gentamycin belum tercatat digunakan sebelum dan setelah terapan perangkat e-RASPRO. Peningkatan peresepan antibiotik Cefuroxime juga sangat signifikan di Rumah Sakit B, dimana berdasarkan kesepakatan Komite Pengendalian Resistensi Antimikroba dan kontinuitas ketersediaan obat di Rumah Sakit B, Cefuroxime dimasukkan ke dalam kategori ACCESS. Secara keseluruhan, kuantitas peresepan antibiotik kategori ACCESS di Rumah Sakit A dan B meningkat 12.42% dan 223.17%, dan di Rumah Sakit C menurun 6.81%.

Discussion

Survei terpadu terhadap *Antimicrobial Resistance* (AMR) dan *Antimicrobial Use* (AMU) sangat penting untuk dilakukan dalam rangka penilai efektifitas kebijakan, *evidence* dan pelaksanaan PGA (20,21). Survei ini merupakan survei terbatas, dilakukan pada tiga rumah sakit di Indonesia dengan karakter yang berbeda-beda seperti yang terlihat pada tabel 1.

Karakteristik Demografi 3 Rumah Sakit yang Disurvei

Pada Tabel 1 terlihat, Rumah Sakit C merupakan rumah sakit yang memiliki sumber jumlah dokter, jumlah farmasis dan jumlah tenaga keperawatan yang paling besar dibandingkan Rumah Sakit A dan B. Rumah Sakit C juga memiliki luas bangunan sangat besar dibanding kedua rumah sakit lainnya. Banyaknya sumber daya manusia dan luas rumah sakit jadi menyebabkan Rumah Sakit C memiliki tingkat kesulitan tersendiri dalam sosialisasi penatagunaan antimikroba baik secara manual maupun digital. Pada praktek sehari hari, tentunya tingkat sosialisasi yang belum merata bisa berdampak pada tingkat kesesuaian penggunaan antibiotik terhadap panduan penggunaan antimikroba digital yang ada dalam perangkat e-RASPRO.

Kuantitas Peresepan Antibiotik Profilaksis 3 Bulan Sebelum dan Setelah Terapan Perangkat e-RASPRO di Ketiga Rumah Sakit

Pada berbagai kepustakaan, dijelaskan keutamaan penggunaan Cephazolin sebagai antibiotik profilaksis (22,23). Hal ini kemudian juga sesuai dengan regulasi yang dikeluarkan oleh Kementerian Kesehatan Republik Indonesia, yang menjadikan Cephazolin sebagai antibiotik profilaksis (24). Pada tabel 2 terlihat di Rumah Sakit A dan B terjadi kenaikan signifikan kuantitas peresepan Cephazolin sebagai antibiotik profilaksis paska 3 bulan terapan perangkat e-RASPRO. Pada rumah sakit B, Cefuroxime dimasukkan dalam kategori ACCESS dan diputuskan untuk digunakan sebagai antibiotik profilaksis atas kesepakatan panel ahli intra rumah sakit. Hal ini terkait dengan kontinuitas kesediaan obat. Kondisi ini tentunya menjadi sebuah faktor penyebab meningkatnya kuantitas peresepan Cefuroxime sebagai antibiotik profilaksis di Rumah Sakit B.

Peresepan Cephazolin sebagai antibiotik profilaksis sesuai dengan yang tercantum pada panduan antimikroba digital pada perangkat e-RASPRO. Walaupun demikian, memang masih tetap ada peresepan antibiotik Ceftriaxone dan Cefotaxime. Keadaan ini bisa menunjukkan bahwa belum sepenuhnya klinisi dapat taat pada panduan penggunaan anti mikroba digital yang ada pada perangkat e-RASPRO. Pada survei ini memang baru tersaji mengenai ketepatan jenis peresepan antibiotik profilaksis, dan belum dibahas lebih lanjut mengenai ketepatan waktu penggunaan antibiotik profilaksis. Hal ini tentunya memerlukan penelitian dan pembahasan lebih lanjut.

Stratifikasi Risiko Awal Pasien Mendapat Antibiotik yang Terisi pada Formulir Digital 3 Bulan Setelah Terapan Perangkat e-RASPRO di Ketiga Rumah Sakit

Pada tabel 3 terlihat sebagian besar pasien yang akan diresepkan antibiotik empiric awal saat masuk ke rawat inap yang tercatat pada perangkat e-RASPRO jatuh di Stratifikasi Risiko Tipe 1. Kelompok ini merupakan kelompok pasien imunokompeten atau bisa juga kelompok imunokompromis dengan infeksi bakteri yang tidak mengancam atau tidak berisiko terinfeksi kuman MDR (1). Pada pasien-pasien yang mayoritas masuk dalam kelompok Stratifikasi Risiko Tipe 1 tersebut sebisa mungkin dihindari peresepan antibiotik-antibiotik spektrum luas. Hal ini mengingat bahwa penggunaan berbagai antibiotik meningkatkan risiko munculnya kuman-kuman ESBLs dan MDR lainnya (3,6,25). Namun dalam perjalanan penyakit lanjutan, tentunya masih memungkinkan terjadi eskalasi antibiotik empirik sesuai kondisi pasien.

Kesesuaian Peresepan Antibiotik Empirik dengan Panduan Penggunaan Antimikroba Digital 3 Bulan Setelah Terapan Perangkat e-RASPRO di Ketiga Rumah Sakit

Pada tabel 4 tergambarkan kesesuaian peresepan antibiotik empirik dengan panduan antimikroba digital yang tercatat di Rumah Sakit A, B, dan C selama 3 bulan penggunaan perangkat e-RASPRO mencapai 81.59%, 76.77%, dan 24.48%. Terkategori sesuai apabila antibiotik empirik diberikan sesuai dengan panduan penggunaan antimikroba digital pada perangkat e-RASPRO sesuai dengan stratifikasi risiko pasiennya.

Tingginya persentase kelompok pasien yang masuk dalam kelompok Stratifikasi Risiko Tipe 1 dengan capaian kesesuaian peresepan antibiotik empirik yang cukup tinggi dengan panduan penggunaan antimikroba digital pada Rumah Sakit A dan B yang pada 3 bulan awal terapan perangkat e-RASPRO, diharapkan membawa perubahan pola kuantitas peresepan antibiotik dari jenis-jenis antibiotik terkategori WATCH ke jenis-jenis antibiotik terkategori ACCESS.

Di Rumah Sakit C kesesuaian peresepan antibiotik yang tercatat pada formulir digital perangkat e-RASPRO relatif masih rendah. Melalui sebuah diskusi dan wawancara dengan peneliti, diketahui, hal ini kemungkinan disebabkan oleh karena sosialisasi yang belum

menyeluruh kepada klinisi-klinisinya terkait terapan perangkat e-RASPRO atau masih mungkin adanya hambatan lain yang belum teridentifikasi.

Kuantitas Peresepan Antibiotik Kategori RESERVE 9 Bulan dan 3 Bulan Sebelum dan Setelah Terapan Perangkat e-RASPRO di Ketiga Rumah Sakit

Tabel 5 merupakan tabel kuantitas peresepan antibiotik, baik yang diresepkan secara empirik maupun secara definitif melalui perangkat e-RASPRO. Tidak dijumpainya peresepan antibiotik kategori RESERVE pada survei ini kemungkinan disebabkan karena sulitnya penyediaan antibiotik-antibiotik tersebut di ketiga rumah sakit atau memang bisa juga disebabkan karena kasus di ketiga rumah sakit terkait hal ini jumlahnya sangat minim.

Kuantitas Peresepan Antibiotik Kategori WATCH 9 Bulan dan 3 Bulan Sebelum dan Setelah Terapan Perangkat e-RASPRO di Ketiga Rumah Sakit

Tabel 5 menggambarkan kuantitas peresepan antibiotik kategori WATCH selama 9 bulan sebelum dan sesudah terapan perangkat e-RASPRO di Rumah Sakit A dan B serta 3 bulan sebelum dan sesudah terapan perangkat e-RASPRO di Rumah Sakit C. Terdapat penurunan signifikan peresepan antibiotik Ceftriaxone Rumah Sakit A, B, dan C, dikarenakan ketiga rumah sakit tampaknya memiliki upaya untuk menurunkan peresepan Ceftriaxone baik secara empirik maupuin definitif, sehingga pada panduan penggunaan antimikroba digital perangkat e-RASPRO yang digunakan di ketiga rumah sakit, penggunaan Ceftriaxone diminimalkan.

Pada beberapa kelompok pasien dengan Stratifikasi Risiko Tipe 1, jikalau memang dibutuhkan pemberian Cephalosporin Generasi III maka Cefotaxime menjadi pilihan sesuai yang ada pada panduan antimikroba digital ketiga rumah sakit, sehingga walaupun pilihan mayoritas antibiotik empirik pada pasien dengan Stratifikasi Risiko tipe 1 adalah antibiotik kategori ACCESS, namun masih ada fokus-fokus infeksi yang memiliki pilihan antimikroba empirik Cefotaxime. Komite Pengendali Resistensi Antimikroba Rumah Sakit A dan B rupanya juga menambahkan Ceftizoxime sebagai Cephalosporin yang bisa digunakan apabila memang dibutuhkan. Hal ini mungkin yang menjelaskan adanya peningkatan yang cukup signifikan dalam peresepan Cefotaxime dan Ceftizoxime di rumah sakit A dan B. Sementara di Rumah Sakit C Ceftizoxime tidak ditambahkan dalam panduan penggunaan antimikroba digitalnya, sehingga Ceftizoxime tidak lagi digunakan pada 3 bulan paska terapan perangkat e-RASPRO.

Peningkatan peresepan Ciprofloxacin yang signifikan di ketiga rumah sakit masih mungkin disebabkan kurang sesuainya peresepan dengan panduan penggunaan antimikroba digital pada perangkat e-RASPRO. Tetapi, memang, berdasarkan panduan penggunaan antimikroba digital tersebut, Ciprofloxacin dapat digunakan sebagai antibiotik pengganti golongan betalaktam di segala stratifikasi risiko apabila pasien terindikasi alergi Penicillin. Berdasarkan panduan penggunaan antimikroba digital pada perangkat e-RASPRO, Ciprofloxacin juga kerap digunakan sebagai pilihan antibiotik pada penyakit-penyakit infeksi tropis di ketiga rumah sakit , seperti demam tifoid, yang banyak kasusnya dijumpai di Indonesia. Pada infeksi demikia, sesuai panduan penggunaan antimikroba digital pada perangkat e-RASPRO, Ciprofloxacin menjadi salah satu pilihan antibiotiknya. Disamping itu, peningkatan peresepan Cefotaxime dan Ciprofloxacin juga masih bisa dikarenakan klinisi meresepkan antimikroba definitif melalui perangkat e-RASPRO. Peresepan definitif Cefotaxime dapat tersebut juga disebabkan oleh adanya upaya penekanan peresepan antibiotik Ceftriaxone pada pemberian antimikroba definitif di ketiga rumah sakit.

Secara umum, terdapat penurunan signifikan kuantitas peresepan antibiotik Meropenem dan Levofloxacin di rumah sakit A dan B. Hal ini sesuai dengan panduan penggunaan antimikroba digital pada perangkat e-RASPRO di ketiga rumah sakit, yang meminimalisir penggunaan Levofloxacin untuk pasien-pasien dengan Stratifikasi Risiko Tipe

1 yang menjadi kelompok mayoritas di ketiga rumah sakit. Sementara, Meropenem hanya digunakan pada pasien-pasien dengan Stratifikasi Risiko Tipe 3. Penggunaan Meropenem juga tidak terlepas dari adanya kemungkinan eskalasi antibiotik dari antibiotik awal sesuai dengan panduan penggunaan antimikroba digital pada perangkat e-RASPRO. Penggunaan Azithromycin juga menurun sangat tajam di Rumah Sakit B, mengingat Azithromycin juga diminimalisir penggunaannya pada pasien-pasien dengan Stratifikasi Risiko Tipe 1 di ketiga rumah sakit, sesuai dengan panduan antimikroba digital pada perangkat e-RASPRO.

Peningkatan kuantitas peresepan Levofloxacin 750mg dan Meropenem 1g di Rumah Sakit C masih terjadi. Hal ini masih mungkin disebabkan masalah kepatuhan atau ketidaksesuaian dengan panduan penggunaan antimikroba digital. Pada survei 3 bulan pertama di Rumah Sakit C, tingkat kesesuaian peresepan antimikroba dengan panduan penggunaan antimikroba digital masih terbilang rendah, sementara mayoritas pasiennya sebenarnya masuk dalam kelompok Stratifikasi Risiko Tipe 1, dimana seharusnya mayoritas pilihan antibiotik empiriknya adalah termasuk golongan ACCESS. Namun tentunya, masih perlu kajian lebih lanjut terkait situasi di Rumah Sakit C.

Pada survei ini peresepan antimikroba Piperacillin Tazobactam dan Ertapenem untuk pasien-pasien yang termasuk dalam kelompok Stratifikasi Risiko Tipe 2 paska terapan perangkat e-RASPRO juga belum dijumpai. Melalui berbagai diskusi di rumah sakit-rumah sakit tersebut diketahui bahwa antimikroba Piperacillin Tazobactam dan Ertapenem sulit didapatkan, sehingga kerap pemberian antibiotik kategori ACCESS, Ampicillin Sulbactam atau Amoxycillin Clavlulanat dengan atau tanpa kombinasi dengan golongan aminoglkosida sebagai anti ESBLs, kerap menjadi pilihan antibiotik empirik untuk diberikan pada pasien-pasien yang termasuk dalam kelompok Stratifikasi Risiko Tipe 2. Walaupun memang, pada kenyataannya, survei 3 bulan awal penggunaan perangkat e-RASPRO di ketiga rumah sakit menunjukkan jumlah pasien yang masuk dalam kelompok Stratifikasi Risiko Tipe 2 merupakan minoritas. Secara keseluruhan, terlihat adanya penurunan kuantitas peresepan antibiotik kategori WATCH di Rumah Sakit A, B, dan C masing-masing sebesar 54.93% dan 21.11%, dan 8.59% paska terapan perangkat e-RASPRO.

Kuantitas Peresepan Antibiotik Kategori WATCH 9 Bulan dan 3 Bulan Sebelum dan Setelah Terapan Perangkat e-RASPRO di Ketiga Rumah Sakit

Survei selama 9 bulan sebelum dan sesudah penggunaan perangkat e-RASPRO di Rumah Sakit A dan B dan 3 bulan sebelum dan sesudah penggunaan perangkat e-RASPRO di Rumah Sakit C menunjukkan kenaikan signifikan kuantitas peresepan antibiotik Ampicillin, Amoxycillin Clavulanat, dan Ampicillin Sulbactam 1.5g yang merupakan antibiotik-antibiotik kategori ACCESS di ketiga rumah sakit. Pada survei 3 bulan awal penggunaan perangkat e-RASPRO, mayoritas pasien masuk dalam kelompok Stratifikasi Risiko Tipe 1 pada ketiga rumah sakit (Tabel 2), yang memang mayoritas pilihan antibiotik empiriknya adalah antibiotik-antibiotik kategori ACCESS. Namun, tentunya hal ini juga memerlukan survey lebih lanjut pada bulan-bulan berikutnya di Rumah Sakit A dan B.

Peningkatan signifikan peresepan Ampicillin Sulbactam 0.75 g juga masih mungkin terkait kontinuitas ketersediaan Ampicillin Sulbactam 1.5 g di Rumah Sakit B. Beberapa sumber di rumah sakit B, melalui sebuah diskusi dengan peneliti, menyampaikan bahwa ketersediaan Ampicillin Sulbactam 1.5 g di Rumah Sakit B kerap kali mengalami kekosongan. Demikian pula atas alasan ini, maka Komite Pengendalian resistensi Antimikroba Rumah Sakit B memasukkan Cefuroxime ke dalam Kategori ACCESS dalam panduan penggunaan antimikrobanya. Kondisi ini yang menjelaskan adanya peningkatan kuantitas peresepan Cefuroxime, dalam kategori ACCESS di Rumah Sakit B.

Berdasar pada panduan penggunaan antimikroba digital pada perangkat e-RASPRO yang terdapat pada ketiga rumah sakit, sebenarnya golongan aminoglikosida digunakan

sebagai antibiotik kombinasi. Belum diketahui pasti penyebab turunnya peresepan Gentamycin di Rumah Sakit A, sementara di Rumah Sakit C, penggunaan Gentamycin dan Amikacin memang tidak tercatat pada sebelum dan sesudah terapan perangkat e-RASPRO. Peningkatan peresepan Gentamycin dan Amikacin di Rumah Sakit B bisa disebabkan karena pada panduan penggunaan antimirkoba digital di ketiga rumah sakit, Aminoglikosida digunakan sebagai antibiotik empirik kombinasi untuk beberapa fokus infeksi pada pasien dengan Stratifikasi Risiko Tipe 1 dan hampir semua fokus infeksi pada pasien dengan Stratifikasi Risiko Tipe 3. Secara keseluruhan terdapat peningkatan kuantitas peresepan antibiotik kategori ACCESS di Rumah Sakit A dan B masing-masing sebesar 12.42% dan 223.17%. Survei yang dilakukan 3 bulan sebelum dan sesudah terapan perangkat e-RASPRO di Rumah Sakit C menunjukkan penurunan kuantitas peresepan antibiotik kategori ACCESS sebesar 6.81%.

Pada tabel 5 juga terlihat jumlah pasien sebelum dan sesudah terapan perangkat e-RASPRO di ketiga rumah sakit menunjukan jumlah yang tidak terlalu signifikan berbeda. Survei ini belum mengkaitkan kuantitas peresepan dengan lama penggunaan antibiotik dan belum menghitung persentase eskalasi dan *step down* antibiotik empirik. Namun, pada survei ini dapat terlihat adanya penurunan persentase kuantitas peresepan antibiotik kategori WATCH di ketiga rumah sakit, serta peningkatan persentase kuantitas peresepan antibiotik kategori ACCESS di kedua rumah sakit (Rumah Sakit A dan B) paska terapan perangkat e-RASPRO. Terutama di Rumah Sakit B, peningkatan kuantitas peresepan antibiotik kategori ACCESS sangat signifikan.

Perubahan kuantitas peresepan antibiotik kategori WATCH dan ACCESS terutama di Rumah Sakit A dan B masih mungkin dipengaruhi oleh kesesuaian penggunaan antibiotik empirik yang dipandu oleh panduan penggunaan antimikroba digital pada perangkat e-RASPRO. Namun, tentunya hal ini masih memerlukan penelitian-penelitian lanjutan. Karateristik rumah sakit, seperti jumlah tempat tidur, jumlah dokter, dan fasilitas-fasilitas lain yang ada di masing-masing rumah sakit juga masih mungkin memengaruhi pola peresepan antibiotik.

Pada beberapa penelitian disampaikan bahwa penggunaan perangkat digital untuk pelaksanaan PGA mampu menurunkan penggunaan antimikroba dan menurunkan *Defined Daily Dose*-nya (26,27). Namun memang belum dapat disimpulkan jenis intervensi digital seperti apa yang pasti akan menurunkan penggunaan antimikroba (27). Penelitian ini merupakan survei awal penggunaan perangkat e-RASPRO sebagai salah satu model penatagunaan antimikroba digital yang digunakan di Indonesia. Untuk mendapatkan hasil yang baik, tentunya penggunaan perangkat e-RASPRO harus disertai oleh kedisiplinan dan dukungan penuh dari manajemen rumah sakit. Karakteristik demografi rumah sakit juga maasih mungkin memengaruhi efektifitas penggunaan perangkat e-RASPRO. Untuk dapat menjelaskan hal ini, tentunya, dibutuhkan penelitian yang lebih luas dengan dukungan manajerial penuh untuk menganalisa lebih lanjut hubungan sebab akibat penggunaan perangkat e-RASPRO dengan perubahan pola kuantitas peresepan antibiotik.

Kesimpulan

Survei ini belum dapat menggambarkan hubungan sebab-akibat terapan perangkat e-RASPRO dengan kuantitas peresepan antibiotik. Namun, secara umum, terdapat perubahan pola kuantitas peresepan antibiotik profilaksis, serta perubahan kuantitas peresepan antibiotik empirik kategori WATCH dan kategori ACCESS paska terapan perangkat e-RASPRO.

Disclaimer

Survei ini tidak dibiayai oleh perusahaan atau sponsor produk tertentu. Pada saat survei diambil pada ketiga rumah sakit, perangkat e-RASPRO digunakan pada ketiga rumah sakit tersebut

tanpa berbayar. Survei ini bersifat objektif untuk melihat perkembangan penggunaan e-RASPRO di lapangan.

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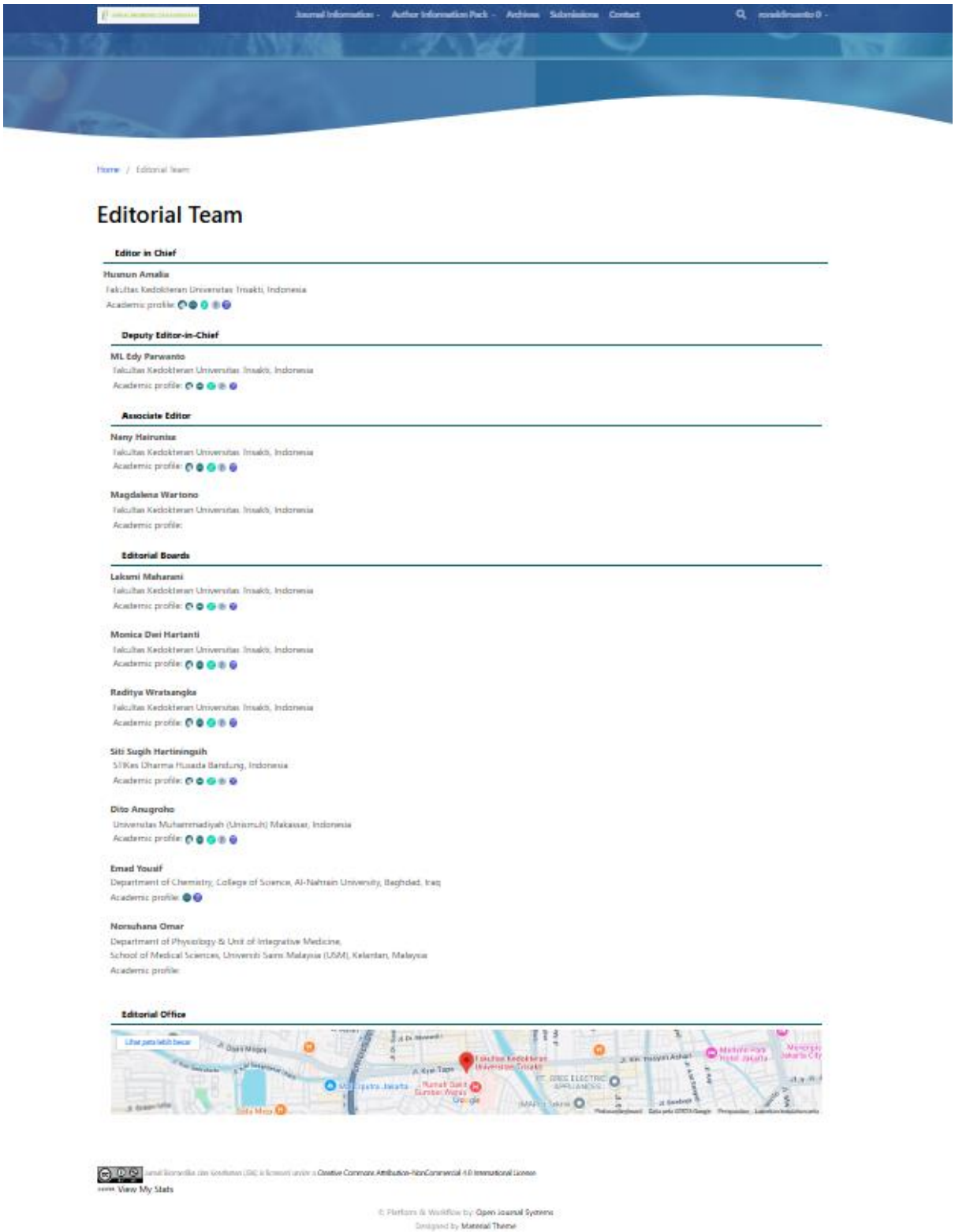

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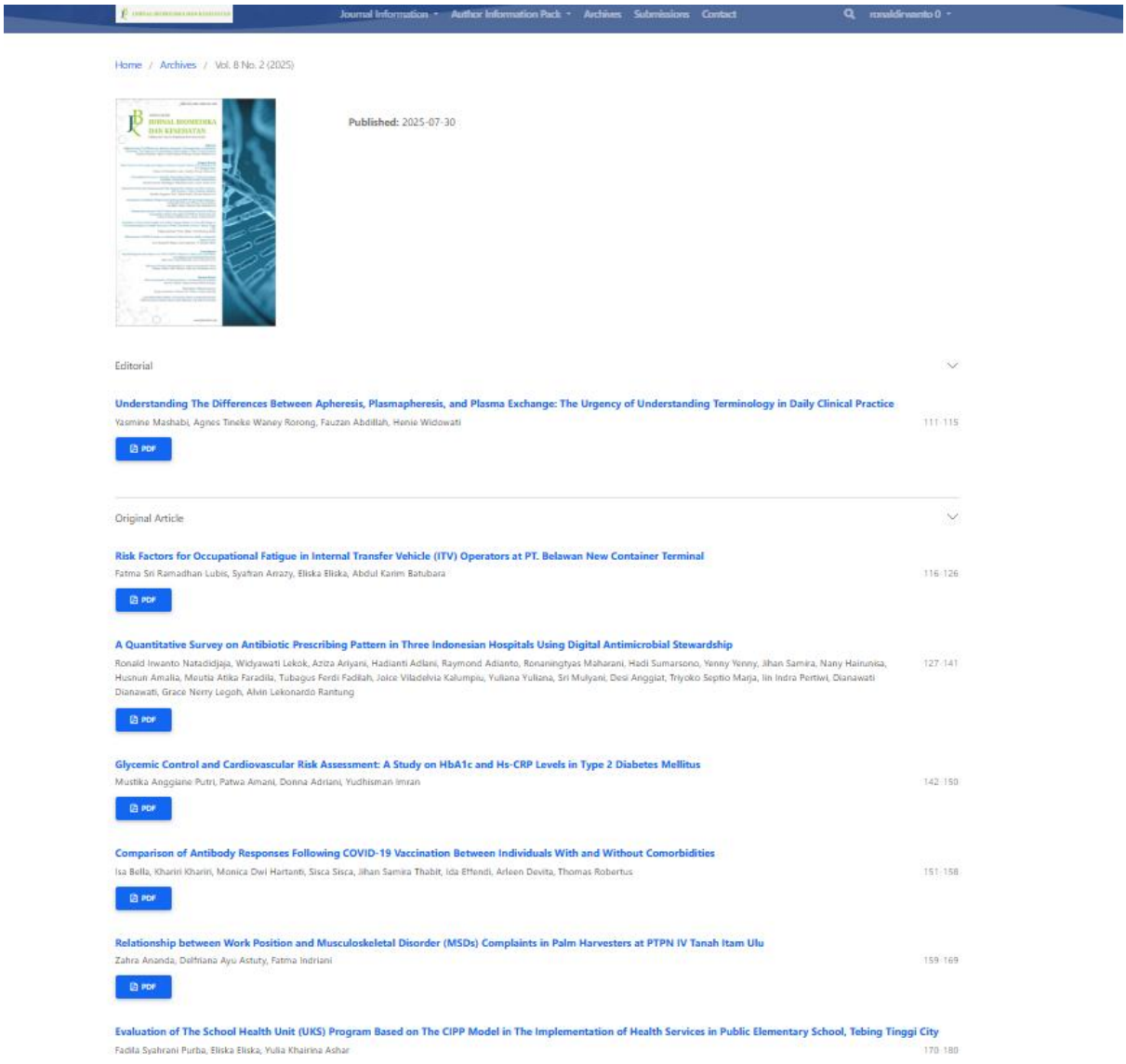

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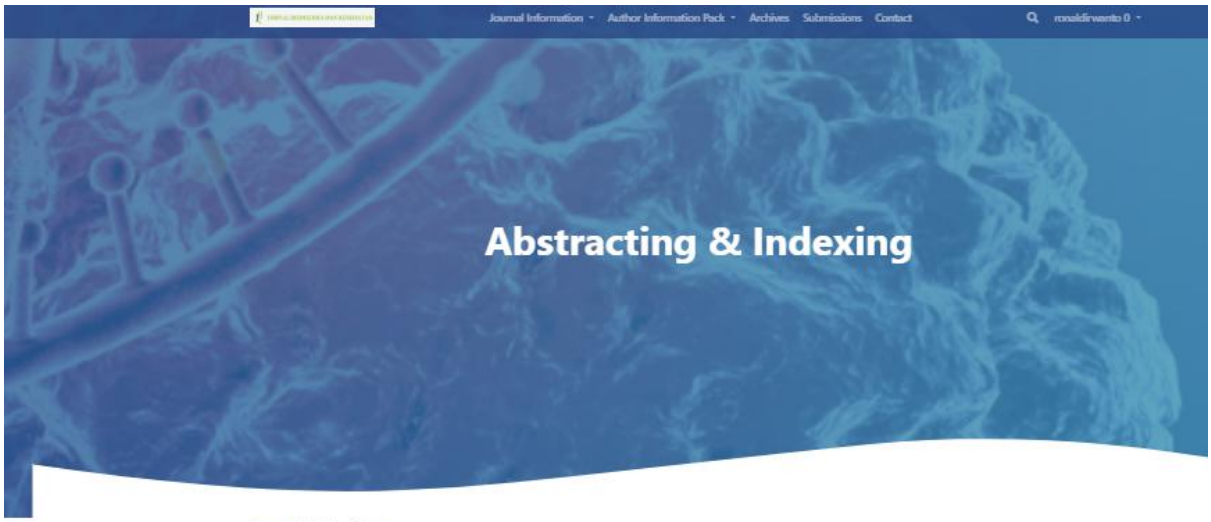

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DS **Dr. dr. Husnun Amalia, Sp.M**
To: me · Tue, Apr 22 at 2:21 PM

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 Jurnal Biomedika dan Kesehatan. With the online journal management system that we are using, you will be able to track its progress through the editorial 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. Husnun Amalia, Sp.M

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[JBK] Editor Decision

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

Our decision is: Revisions Required

Jurnal Biomedika dan Kesehatan

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

1. Drawn logically	√	
ACKNOWLEDGEMENT	√	
AUTHOR CONTRIBUTION	√	
FUNDING STATEMENT	√	
CONFLICT OF INTEREST	√	
REFERENCES		
1. Compliance with journal format (Vancouver style)	√	
2. The minimal number of references should be 20 and 85% of them should be 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	√	
4. The total number of tables and figures not more than 5	√	

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

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 tried to develop a system, which is called as RASPRO system that can guide clinicians in antibiotic 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, Indonesia. 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 antibiotic use within 3 months of implementation reaching 14.44%. 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 antibiotics and definitive antibiotics. Previous survey of e-RASPRO implementation showed a 49.01% decrease of Watch category antibiotics Define Daily Dose (DDD) within 9 months implementation and still showed an increase in Watch category antibiotics DDD by 20.18% within 3 months implementation.[3]

Clinical pharmacies 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 antimicrobial use that is applicable in the hospitals where e-RASPRO has been implemented. By utilizing e-RASPRO, it is expected that there is an altered pattern 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 study is to show the comparison of antibiotic prescription pattern among 9 months and 3 months implementation of e-RASPRO in 3 hospitals.

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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 Java, and were chosen 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 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 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 guideline on the use of antimicrobial agents in e-RASPRO. When empirical antibiotic prescribing

use through a digital form in e-RASPRO.[13] 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.

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

Data: sirs.kemkes.go.id

Table 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 the following: Hospital A, B and C had 134 beds, 185 beds and 254 beds, respectively; with 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

Hospital A	Hospital B	Hospital C

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

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	1	0.32%	-	0.00%	348	19.18%
Total of forms had been filled out	315	100.00%	824	100.00%	1,814	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 81.59%, 76.09% and 24.48%, 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 19.18% in Hospital C.

Metronidazole	1,180	1,004	-14.92%	1,731	2,424	40.03%	1,610	1,339	-16.83%
Cefuroxime	-	-	-	838	3,074	>100%	-	-	-
Total Access	**2,149**	**2,416**	**12.42%**	**4,679**	**15,121**	**223.17%**	**2,113**	**1,969**	**-6.81%**
Total Access / In Patient	**0.5098**	**0.5232**	**2.61%**	**0.6034**	**2.2256**	**268.83%**	**0.7533**	**0.7361**	**-2.29%**

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

Table 4. The use of antibiotic included in Reserve category such as Polymixin and Tygecycline was not found in this survey. There was reduced quantity of Ceftriaxone prescribing significantly in Hospital A, B and C as much as 62.92%, 40.58% and 11.06%, 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 500 mg Levofloxacin prescribing in Hospital A, B and C had some decrease of 45.14%, 64.84% and 76.25%, respectively. The quantity of 750 mg Levofloxacin reduced in Hospital A and B as much as 65.49% and 13.36% 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 10.01%. The quantity of Azithromycin prescribing also decreased very significantly in Hospital B, i.e. 93.28%. Piperacillin Tazobactam seemed to be very rarely used. The minimum use was found in Hospital B i.e.

as many as 45 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 inpatient), 21.11% (-9.97% per inpatient) and 8.59% (-4.15% per inpatient), respectively. The quantity of Access category antibiotic prescribing in Hospital A, B and C was as follows: there was 100% increase of Ampicillin and Amoxycillin-Clavulanate prescribing in

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 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 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 had Type 1 Risk Stratification as documented in e-RASPRO. These patients include a group of immunocompetent patients or immunocompromized patients who had unthreathening 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 caution considering that using various type of antibiotics may increase the risk of developing resistance.[3,6,23] 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 e-RASPRO, which reach 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 patient's risk stratification. There is a high percentage of a group of patients 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 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 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 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), 21.11% (-9.97% per inpatient) and 8.59% (-4.15% 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 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 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 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 in Hospital B, through a discussion with the investigators, suggest that there is often shortage supply of 1.5 Ampicillin Sulbactam 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 B.

Based on the digital guideline on antimicrobial use in e-RASPRO 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 antimicrobial use included in e-RASPRO. 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 systematic review showed a decrease in antimicrobial DDD range from −8.42% to −61.29% related to the digital antimicrobial stewardship tool.[24]

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 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 that will certainly reduce the use of antimicrobial agents.[25] 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 correlation between e-RASPRO using and the antibiotic prescribing pattern. In order to achieve good results, the utilization 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 utilization. In order to provide good explanation on this issue, more extensive studies with full support from managerial team 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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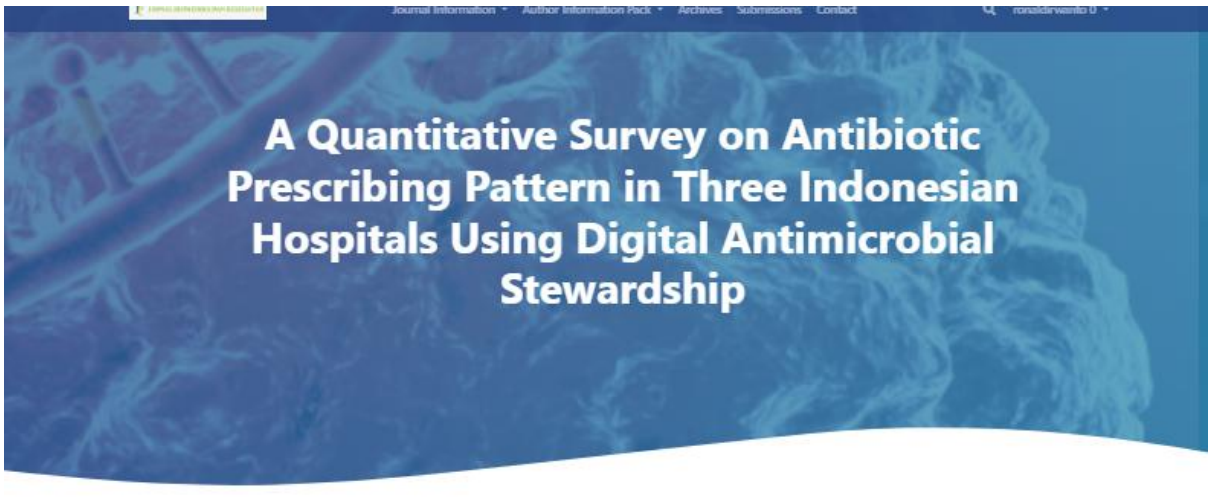

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A Quantitative Survey on Antibiotic Prescribing Pattern in Three Indonesian Hospitals Using Digital Antimicrobial Stewardship

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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

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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.

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 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 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% (+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.[1] The World Health Organization (WHO) has categorized antibiotics into three categories: Access, Watch, and Reserve (AWARE).[2] 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 Group has attempted to develop a system, known as the RASPRO system, that can guide clinicians in antibiotic prescribing based on local guidelines.[2] 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.[1]

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%.[1] 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.[13]

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.[13–8]

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 ≥48 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.*[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 ≥48 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 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.[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.[13] 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 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	B	C
Number of Doctors			
General Physicians	14	14	25
Dentists	5	15	8
Specialist Doctors	37	98	102
Total	56	127	135
Number of Pharmacists	9	26	39
Number of Nurses	115	74	368
Number of Beds			
Wards	124	168	259
ICU + HCU + ICCU + NICU + PICU	10	17	26
Total	134	185	285
Ratio on numbers of specialist doctors : beds	1 : 3.62	1 : 1.89	1 : 2.79
Ratio on numbers of pharmacists : beds	1 : 14.89	1 : 7.12	1 : 7.31
Ratio on numbers of nurses : beds	1 : 1.17	1 : 2.50	1 : 0.77
The extent of the Buildings	7,247.35	8,120.00	31,099.94

Data: sirs.kemkes.go.id

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

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		Hospital B 3 Months Dec 2021 – Feb 2022		Hospital C 3 Months Nov 2022 – Jan 2023	
	Number	%	Number	%	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	1	0.32%	-	0.00%	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 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 Inpatient within 9 Months and 3 Months Before and After Implementing e-RASPRO

Antibiotics	Hospital A			Hospital B			Hospital C		
	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 patients: 4,618	Increase / Decrease	Pre-implementation of e-RASPRO Mar– Nov 2021 Number of patients: 7,754	9 months post implementation of e-RASPRO Dec 2021 – August 2022 Number of patients: 6,794	Increase / Decrease	Pre-implementation of e-RASPRO August – Oct 2022 Number of patients: 2,805	3 months post implementation of e-RASPRO Nov 2022 – Jan 2023 Number of patients: 2,675	Increase / Decrease
	Ampules/vials	Ampules/vials	Ampules/vials	Ampules/vials	Ampules/vials	Ampules/vials	Ampules/vials	Ampules/vials	Ampules/vials
Ceftriaxone	15,514	5,753	-62.92%	11,602	6,894	-40.58%	4,513	4,014	-11.06%
1 g Cefotaxime	756	1,023	35.32%	950	4,189	>100%	1,360	1,237	-9.04%
0.5 g Cefotaxime	-	-	-	76	145	90.79%	-	-	-
Ceftazidime	-	-	-	866	359	-58.55%	724	774	6.91%
Cefoperazone	-	-	-	232	413	78.02%	-	-	-
Cefoperazone Sulbactam	-	-	-	-	-	-	-	146	100.00%
Ceftixozime	-	282	100.00%	527	596	13.09%	129	-	-100.00%
Cefepime	-	-	-	14	6	-57.14%	1,465	1,089	-25.67%
750 mg Levofloxacin	2,147	741	-65.49%	2,770	2,400	-13.36%	360	854	>100%
500 mg Levofloxacin	833	457	-45.14%	3,197	1,124	-64.84%	1,002	238	-76.25%
Ciprofloxacin	-	288	100.00%	136	1,258	>100%	-	234	100.00%
Moxifloxacin	-	-	-	487	221	-54.62%	-	-	-
1 g Meropenem	968	568	-41.32%	8,690	7,521	-13.45%	1,619	1,781	10.01%
0.5 g Meropenem	-	-	-	19	-	-100%	550	475	-13.64%
Imipenem + Cilastatin	-	-	-	133	43	-67.67%	-	-	-

Antibiotics	Hospital A			Hospital B			Hospital C		
	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 patients: 4,618	Increase / Decrease	Pre-implementation of e-RASPRO Mar– Nov 2021 Number of patients: 7,754	9 months post implementation of e-RASPRO Dec 2021 – August 2022 Number of patients: 6,794	Increase / Decrease	Pre-implementation of e-RASPRO August – Oct 2022 Number of patients: 2,805	3 months post implementation of e-RASPRO Nov 2022 – Jan 2023 Number of patients: 2,675	Increase / Decrease
	Ampules/vials	Ampules/vials	Ampules/vials	Ampules/vials	Ampules/vials	Ampules/vials	Ampules/vials	Ampules/vials	Ampules/vials
Piperacillin Tazobactam	-	-	-	45	-	-100%	-	-	-
Azithromycin	-	-	-	2,662	179	-93.28%	-	-	-
0.5 Vancomycin	-	-	-	207	379	83.09%	356	198	-44.38%
Total Watch	20,218	9,112	-54.93%	32,613	25,727	-21.11%	12,078	11,040	-8.59%
Total Watch / In Patient	4.7967	1.9731	-58.86%	4.2060	3.7867	-9.97%	4.3059	4.1271	-4.15%
Ampicillin	-	947	100.00%	-	93	100%	-	-	-
1.5 g Ampicillin Sulbactam	-	-	-	214	484	>100%	207	466	>100%
0.75 g Ampicillin Sulbactam	-	-	-	746	6,291	>100%	296	164	-44.59%
Amoxycillin – Clavulanic	-	263	100.00%	-	-	-	-	-	-
Gentamicin	969	202	-79.15%	722	1,650	>100%	-	-	-
Amikacin	-	-	-	428	1,105	>100%	-	-	-
Metronidazole	1,180	1,004	-14.92%	1,731	2,424	40.03%	1,610	1,339	-16.83%
Cefuroxime	-	-	-	838	3,074	>100%	-	-	-
Total Access	2,149	2,416	12.42%	4,679	15,121	223.17%	2,113	1,969	-6.81%
Total Access / In Patient	0.5098	0.5232	2.61%	0.6034	2.2256	268.83%	0.7533	0.7361	-2.29%

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.[1] 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.[3,6,23] 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 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), 21.11% (-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.[25] 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

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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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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.

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 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 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% (+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.[1] The World Health Organization (WHO) has categorized antibiotics into three categories: Access, Watch, and Reserve (AWARE).[2] 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 Group has attempted to develop a system, known as the RASPRO system, that can guide clinicians in antibiotic prescribing based on local guidelines.[1] 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.[1]

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%.[1] 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.[1,3]

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.[1,3–8]

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 ≥48 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.*[1,6,9–14] 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 ≥48 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 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.[1,3]

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.[1,3] 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.[1,3] 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	B	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	175	74	368
Number of Beds			
Wards	124	168	259
ICU + HCU + ICCU + NICU + PICU	10	17	26
Total	134	185	285
Ratio on numbers of specialist doctors : beds	1 : 3.62	1 : 1.89	1 : 2.79
Ratio on numbers of pharmacists : beds	1 : 14.89	1 : 7.12	1 : 7.31
Ratio on numbers of nurses : beds	1 : 1.17	1 : 2.50	1 : 0.77
The extent of the Buildings	7,247.35	8,120.00	31,099.94

Data: sirs.kemkes.go.id

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

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		Hospital B 3 Months Dec 2021 – Feb 2022		Hospital C 3 Months Nov 2022 – Jan 2023	
	Number	%	Number	%	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	1	0.32%	-	0.00%	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 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 Inpatient within 9 Months and 3 Months Before and After Implementing e-RASPRO

Antibiotics	Hospital A			Hospital B			Hospital C		
	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 patients: 4,618	Increase / Decrease	Pre-implementation of e-RASPRO Mar– Nov 2021 Number of patients: 7,754	9 months post implementation of e-RASPRO Dec 2021 – August 2022 Number of patients: 6,794	Increase / Decrease	Pre-implementation of e-RASPRO August – Oct 2022 Number of patients: 2,805	3 months post implementation of e-RASPRO Nov 2022 – Jan 2023 Number of patients: 2,675	Increase / Decrease
	Ampules/vials	Ampules/vials	Ampules/vials	Ampules/vials	Ampules/vials	Ampules/vials	Ampules/vials	Ampules/vials	Ampules/vials
Ceftriaxone	15,514	5,753	-62.92%	11,602	6,894	-40.58%	4,513	4,014	-11.06%
1 g Cefotaxime	756	1,023	35.32%	950	4,189	>100%	1,360	1,237	-9.04%
0.5 g Cefotaxime	-	-	-	76	145	90.79%	-	-	-
Ceftazidime	-	-	-	866	359	-58.55%	724	774	6.91%
Cefoperazone	-	-	-	232	413	78.02%	-	-	-
Cefoperazone Sulbactam	-	-	-	-	-	-	-	146	100.00%
Ceftixozime	-	282	100.00%	527	596	13.09%	129	-	-100.00%
Cefepime	-	-	-	14	6	-57.14%	1,465	1,089	-25.67%
750 mg Levofloxacin	2,147	741	-65.49%	2,770	2,400	-13.36%	360	854	>100%
500 mg Levofloxacin	833	457	-45.14%	3,197	1,124	-64.84%	1,002	238	-76.25%
Ciprofloxacin	-	288	100.00%	136	1,258	>100%	-	234	100.00%
Moxifloxacin	-	-	-	487	221	-54.62%	-	-	-
1 g Meropenem	968	568	-41.32%	8,690	7,521	-13.45%	1,619	1,781	10.01%
0.5 g Meropenem	-	-	-	19	-	-100%	550	475	-13.64%
Imipenem + Cilastatin	-	-	-	133	43	-67.67%	-	-	-

Antibiotics	Hospital A			Hospital B			Hospital C		
	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 patients: 4,618	Increase / Decrease	Pre-implementation of e-RASPRO Mar– Nov 2021 Number of patients: 7,754	9 months post implementation of e-RASPRO Dec 2021 – August 2022 Number of patients: 6,794	Increase / Decrease	Pre-implementation of e-RASPRO August – Oct 2022 Number of patients: 2,805	3 months post implementation of e-RASPRO Nov 2022 – Jan 2023 Number of patients: 2,675	Increase / Decrease
	Ampules/vials	Ampules/vials	Ampules/vials	Ampules/vials	Ampules/vials	Ampules/vials	Ampules/vials	Ampules/vials	Ampules/vials
Piperacillin Tazobactam	-	-	-	45	-	-100%	-	-	-
Azithromycin	-	-	-	2,662	179	-93.28%	-	-	-
0.5 Vancomycin	-	-	-	207	379	83.09%	356	198	-44.38%
Total Watch	**20,218**	**9,112**	**-54.93%**	**32,613**	**25,727**	**-21.11%**	**12,078**	**11,040**	**-8.59%**
Total Watch / In Patient	**4.7967**	**1.9731**	**-58.86%**	**4.2060**	**3.7867**	**-9.97%**	**4.3059**	**4.1271**	**-4.15%**
Ampicillin	-	947	100.00%	-	93	100%	-	-	-
1.5 g Ampicillin Sulbactam	-	-	-	214	484	>100%	207	466	>100%
0.75 g Ampicillin Sulbactam	-	-	-	746	6,291	>100%	296	164	-44.59%
Amoxycillin – Clavulanic	-	263	100.00%	-	-	-	-	-	-
Gentamicin	969	202	-79.15%	722	1,650	>100%	-	-	-
Amikacin	-	-	-	428	1,105	>100%	-	-	-
Metronidazole	1,180	1,004	-14.92%	1,731	2,424	40.03%	1,610	1,339	-16.83%
Cefuroxime	-	-	-	838	3,074	>100%	-	-	-
Total Access	**2,149**	**2,416**	**12.42%**	**4,679**	**15,121**	**223.17%**	**2,113**	**1,969**	**-6.81%**
Total Access / In Patient	**0.5098**	**0.5232**	**2.61%**	**0.6034**	**2.2256**	**268.83%**	**0.7533**	**0.7361**	**-2.29%**

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.[1] 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.[3,6,23] 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 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% (-38.86% 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 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 in 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.[illegible]% 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.[25] 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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