

# ANTIMICROBIAL STEWARDSHIP YEAR IN REVIEW

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# Faculty/Presenter Disclosure

- Faculty: **Jan DE WAELE**
- Relationships with commercial interests:
  - Grants/Research Support: None
  - Speakers Bureau/Honoraria: MSD, Pfizer, ThermoFisher (fees and honoraria paid to institution)
  - Consulting Fees: None
- Other:
  - Sr. Clinical Researcher, FWO Flanders Research Foundation FWO
  - Surviving Sepsis Campaign Panel Member
  - President-Elect European Society of Intensive Care Medicine



*The Intensive Connection*



# Year in review -

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Focus on clinically relevant research, international guidelines

Pubmed search

Bias inevitable ;-)




# Guidelines

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## GUIDELINES

# Surviving sepsis campaign: international guidelines for management of sepsis and septic shock 2021



Laura Evans<sup>1\*</sup> , Andrew Rhodes<sup>2</sup>, Waleed Alhazzani<sup>3</sup>, Massimo Antonelli<sup>4</sup>, Craig M. Coopersmith<sup>5</sup>, Craig French<sup>6</sup>, Flávia R. Machado<sup>7</sup>, Lauralyn McIntyre<sup>8</sup>, Marlies Ostermann<sup>9</sup>, Hallie C. Prescott<sup>10</sup>, Christa Schorr<sup>11</sup>, Steven Simpson<sup>12</sup>, W. Joost Wiersinga<sup>13</sup>, Fayez Alshamsi<sup>14</sup>, Derek C. Angus<sup>15</sup>, Yaseen Arabi<sup>16</sup>, Luciano Azevedo<sup>17</sup>, Richard Beale<sup>9</sup>, Gregory Beilman<sup>18</sup>, Emilie Belley-Cote<sup>19</sup>, Lisa Burry<sup>20</sup>, Maurizio Cecconi<sup>21,22</sup>, John Centofanti<sup>23</sup>, Angel Coz Yataco<sup>24</sup>, Jan De Waele<sup>25</sup>, R. Phillip Dellinger<sup>11</sup>, Kent Doi<sup>26</sup>, Bin Du<sup>27</sup>,

# Antibiotic Timing

Shock is present

Shock is absent

Sepsis is definite or probable



Administer antimicrobials **immediately**, ideally within 1 hour of recognition

Sepsis is possible



Administer antimicrobials **immediately**, ideally within 1 hour of recognition



Rapid assessment\* of infectious vs noninfectious causes of acute illness



Administer antimicrobials **within 3 hours** if concern for infection persists

\*Rapid assessment includes history and clinical examination, tests for both infectious and non-infectious causes of acute illness and immediate treatment for acute conditions that can mimic sepsis. Whenever possible this should be completed within 3 hours of presentation so that a decision can be made as to the likelihood of an infectious cause of the patient's presentation and timely antimicrobial therapy provided if the likelihood is thought to be high.



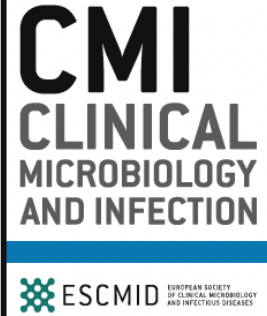


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# Clinical Microbiology and Infection

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## Guidelines

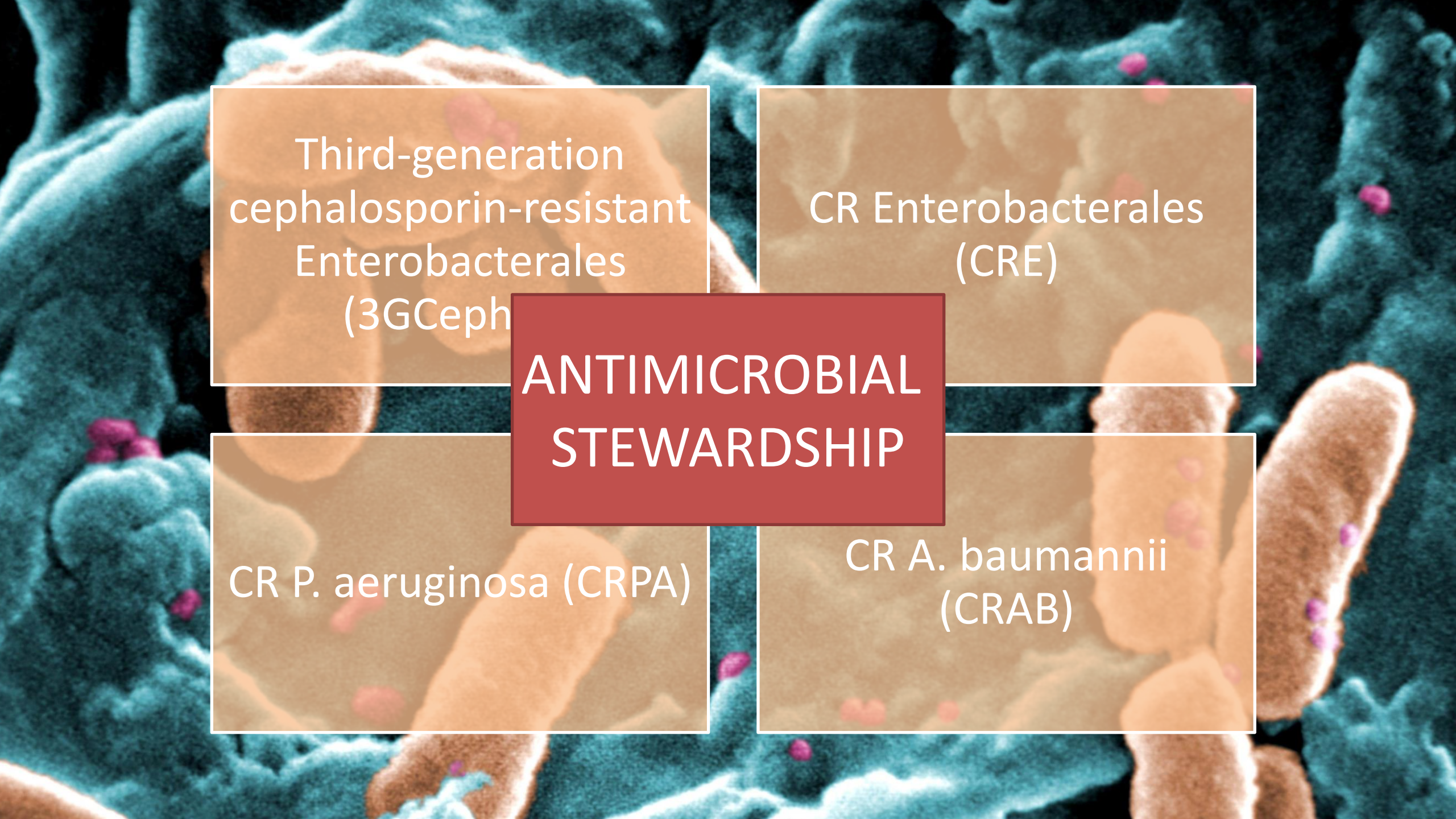
### European Society of Clinical Microbiology and Infectious Diseases (ESCMID) guidelines for the treatment of infections caused by multidrug-resistant Gram-negative bacilli (endorsed by European society of intensive care medicine)

Mical Paul <sup>1, 2, §</sup>, Elena Carrara <sup>3, §</sup>, Pilar Retamar <sup>4, 5</sup>, Thomas Tängdén <sup>6</sup>, Roni Bitterman <sup>1, 2</sup>, Robert A. Bonomo <sup>7, 8, 9</sup>, Jan de Waele <sup>10</sup>, George L. Daikos <sup>11</sup>, Murat Akova <sup>12</sup>, Stephan Harbarth <sup>13</sup>, Celine Pulcini <sup>14, 15</sup>, José Garnacho-Montero <sup>16</sup>, Katja Seme <sup>17</sup>, Mario Tumbarello <sup>18</sup>, Paul Christoffer Lindemann <sup>19</sup>, Sumanth Gandra <sup>20</sup>, Yunsong Yu <sup>21, 22, 23</sup>, Matteo Bassetti <sup>24, 25</sup>, Johan W. Mouton <sup>26, †</sup>, Evelina Tacconelli <sup>3, 27, 28, \*, §</sup>, Jesús Rodríguez-Baño <sup>4, 5, §</sup>

<sup>1</sup>) Infectious Diseases Institute, Rambam Health Care Campus, Haifa, Israel

<sup>2</sup>) Faculty of Medicine, Technion – Israel Institute of Technology, Haifa, Israel

<sup>3</sup>) Division of Infectious Diseases, Department of Diagnostic and Public Health, University of Verona, Verona, Italy

The background is a scanning electron micrograph (SEM) of a bacterial surface, likely a biofilm. It shows a complex, porous structure with various sized pores and channels. The surface is primarily a dark teal color, with some areas appearing more brownish or orange. Several small, bright pink or magenta spots are scattered across the surface, possibly representing specific bacterial cells or structures. Overlaid on this image are four semi-transparent rectangular boxes with white text, and a central dark red box with white text.

Third-generation  
cephalosporin-resistant  
Enterobacterales  
(3GCeph)

CR Enterobacterales  
(CRE)

**ANTIMICROBIAL  
STEWARDSHIP**

CR *P. aeruginosa* (CRPA)

CR *A. baumannii*  
(CRAB)

# Evidence based medicine: what it is and what it isn't

*It's about integrating individual clinical expertise and the best external evidence*

Evidence based medicine, whose philosophical origins extend back to mid-19th century Paris and earlier, remains a hot topic for clinicians, public health practitioners, planners, and the public. There are now frequent conferences in how to practice and teach it (one sponsored by the Royal Society will be held in London on 24 April); undergraduate<sup>1</sup> and postgraduate<sup>2</sup> training programmes are incorporating it<sup>3</sup> (or pondering how to do so); British centres for evidence based practice have been established or planned in adult medicine, child health, surgery, pathology, pharmacotherapy, nursing,

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arrogant to serve cost cutters and suppress clinical freedom. As evidence based medicine continues to evolve and adapt, it is and remains explicit, and decisions about the care of individual patients. The practice of evidence based medicine means integrating individual clinical expertise with the best available external clinical evidence from systematic research. By individual clinical expertise we mean the

what it is not.

Evidence based medicine is the conscientious, explicit, and judicious use of current best evidence in making decisions about the care of individual patients. The practice of evidence based medicine means integrating individual clinical expertise with the best available external clinical evidence from systematic research. By individual clinical expertise we mean the proficiency and judgment that individual clinicians acquire through clinical experience and clinical education. It is not

the mere application of the best available evidence can practice evidence based medicine.

Evidence based medicine is not "cookbook" medicine. Because it requires a bottom up approach that integrates the best external evidence with individual clinical expertise and patients' choice, it cannot result in slavish, cookbook approaches to individual patient care. External clinical evidence can inform, but can never replace, individual clinical expertise, and it is this expertise that decides whether the

# COVID-19

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## WHAT'S NEW IN INTENSIVE CARE

# Antimicrobial stewardship in ICUs during the COVID-19 pandemic: back to the 90s?



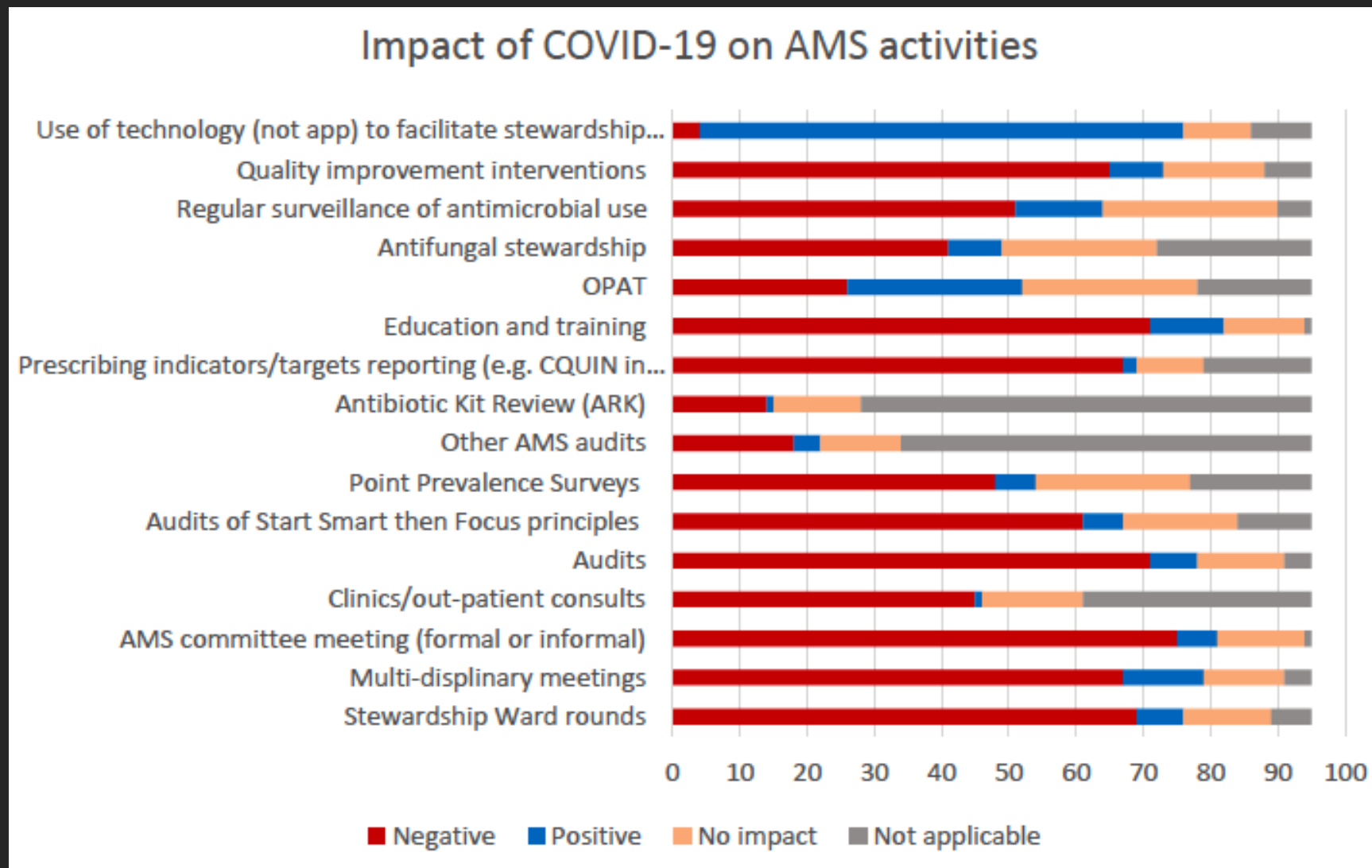
Jan J. De Waele<sup>1\*</sup> , Lennie Derde<sup>2,3</sup>  and Matteo Bassetti<sup>4</sup> 

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SARS-CoV-2 infection has arguably been one of the most significant challenges of health care systems around the world in over a century. The coronavirus disease 2019 (COVID-19) lead to a massive increase in demand for acute care beds in many countries [1]. Here, we focus on one of the unintended side effects of the surge in COVID-















develops, this is typically later in the clinical course, presenting as late-onset ventilator-associated pneumonia [5]. A recent meta-analysis found that only 3.5% of all COVID-19 patients present with co-infection, and 14% develop infections at a later stage; in critically ill patients, an estimated 8% developed infections (including co-infection and

# Antimicrobial stewardship during the pandemic





# Co-infection and ICU-acquired infection in COVID-19 ICU patients: a secondary analysis of the UNITE-COVID data set

Andrew Conway Morris<sup>1,2,3\*†</sup> , Katharina Kohler<sup>1†</sup> , Thomas De Corte<sup>4,5†</sup> , Ari Ercole<sup>1,6</sup> , Harm-Jan De Grooth<sup>7,8</sup> , Paul W. G. Elbers<sup>7</sup> , Pedro Povoá<sup>9,10,11</sup> , Rui Morais<sup>11</sup> , Despoina Koulenti<sup>12,13</sup> , Sameer Jog<sup>14</sup> , Nathan Nielsen<sup>15</sup> , Alasdair Jubb<sup>1,6</sup> , Maurizio Cecconi<sup>16†</sup> , Jan De Waele<sup>4,5†</sup>  and for the ESICM UNITE COVID investigators

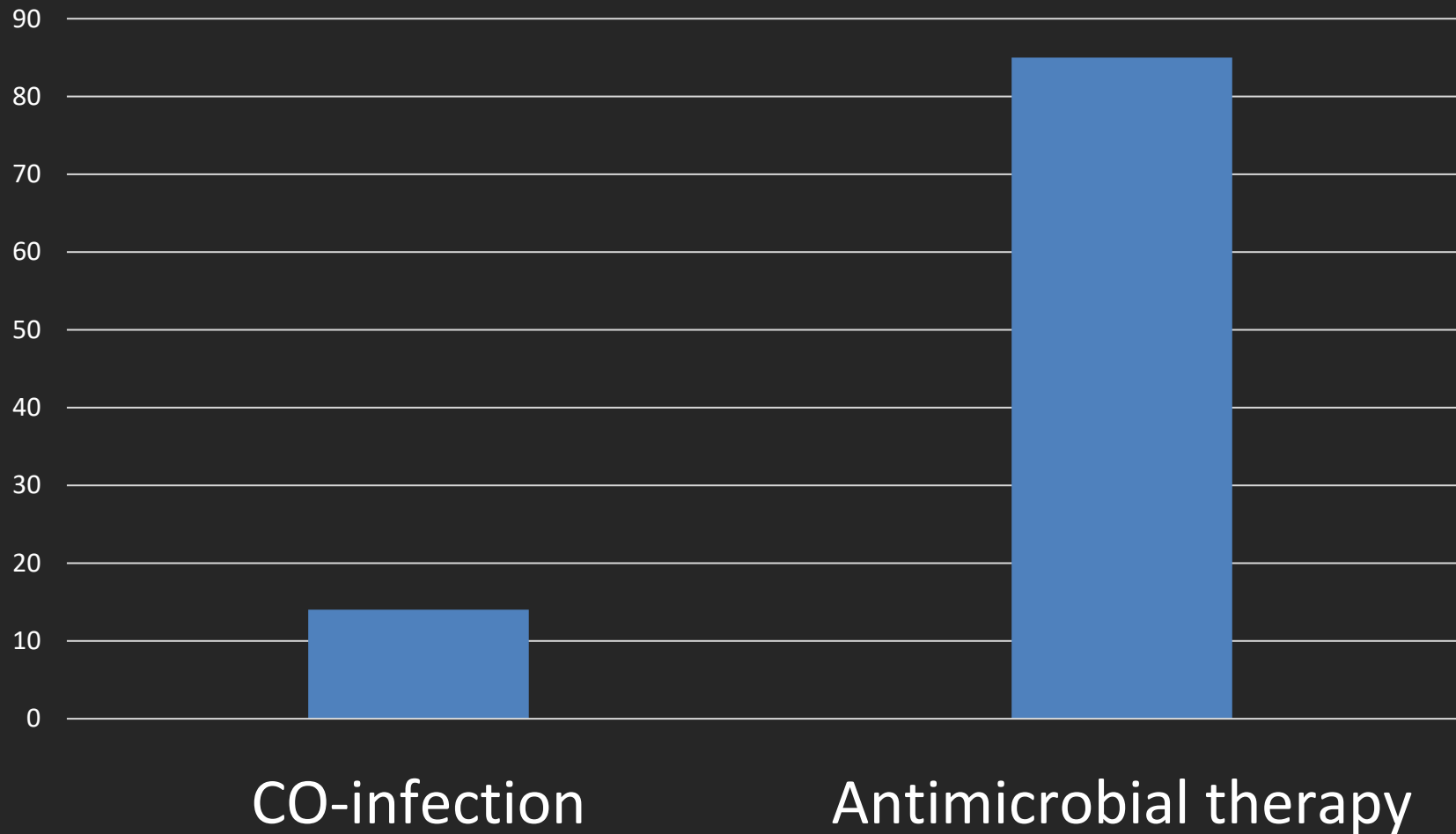
## Abstract

**Background:** The COVID-19 pandemic presented major challenges for critical care facilities worldwide. Infections which develop alongside or subsequent to viral pneumonitis are a challenge under sporadic and pandemic conditions; however, data have suggested that patterns of these differ between COVID-19 and other viral pneumonitides. This secondary analysis aimed to explore patterns of co-infection and intensive care unit-acquired infections (ICU-AI) and the relationship to use of corticosteroids in a large, international cohort of critically ill COVID-19 patients.

**Methods:** This is a multicenter, international, observational study, including adult patients with PCR-confirmed COVID-19 diagnosis admitted to ICUs at the peak of wave one of COVID-19 (February 15th to May 15th, 2020). Data collected included investigator-assessed co-infection at ICU admission, infection acquired in ICU, infection with

# Bacterial co-infection in 5000 COVID patients

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**KEEP  
CALM  
AND  
ACT  
NORMAL**

# ASP impact

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# Narrow-spectrum antibiotics for community-acquired pneumonia in Dutch adults (CAP-PACT): a cross-sectional, stepped-wedge, cluster-randomised, non-inferiority, antimicrobial stewardship intervention trial

Valentijn A Schweitzer\*, Inger van Heijl\*, Wim G Boersma, Wouter Rozemeijer, Kees Verduin, Marco J Grootenboers, Sanjay U C Sankatsing, Akke K van der Bij, Winnie de Bruijn, Heidi S M Ammerlaan, Ilse Overdevest, J M Milena Roorda-van der Vegt, Elske M Engel-Dettmers, Florence E Ayuketah-Ekokobe, Michiel B Haeseker, J Wendelien Dorigo-Zetsma, Paul D van der Linden, C H Edwin Boel, Jan J Oosterheert, Cornelis H van Werkhoven, Marc J M Bonten, on behalf of the CAP-PACT Study Group

## Summary

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See [Comment](#) page 159

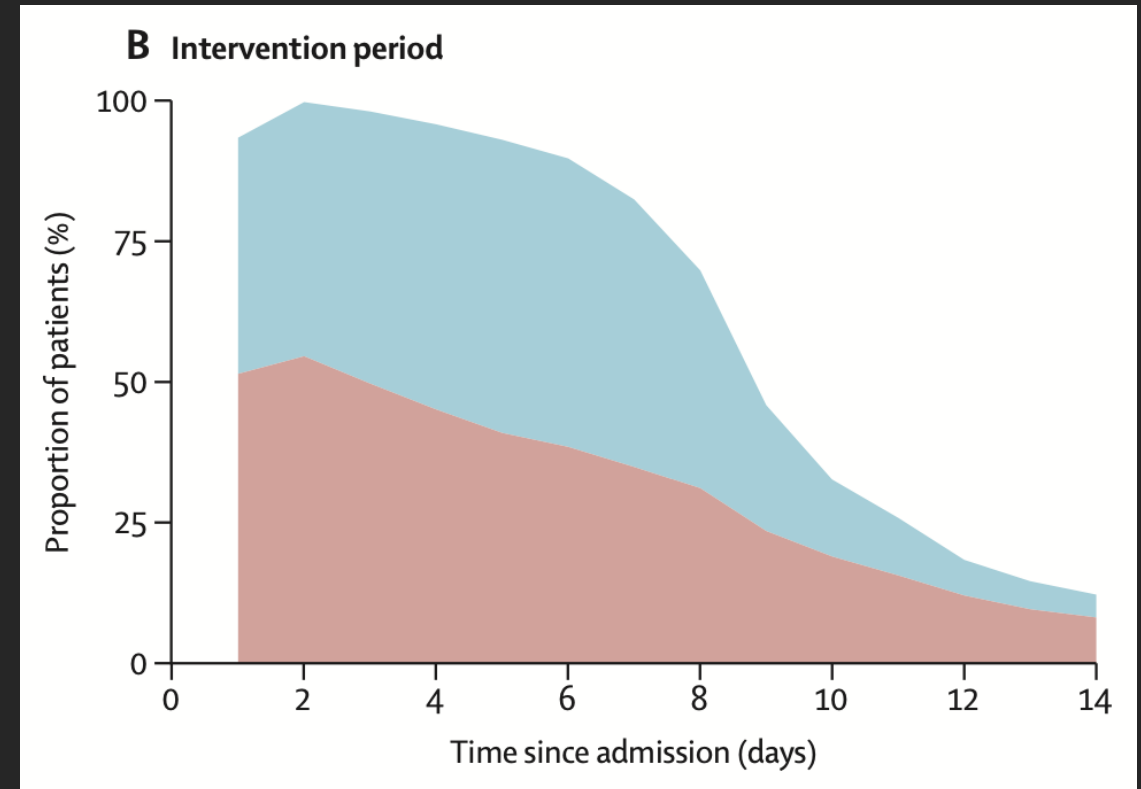
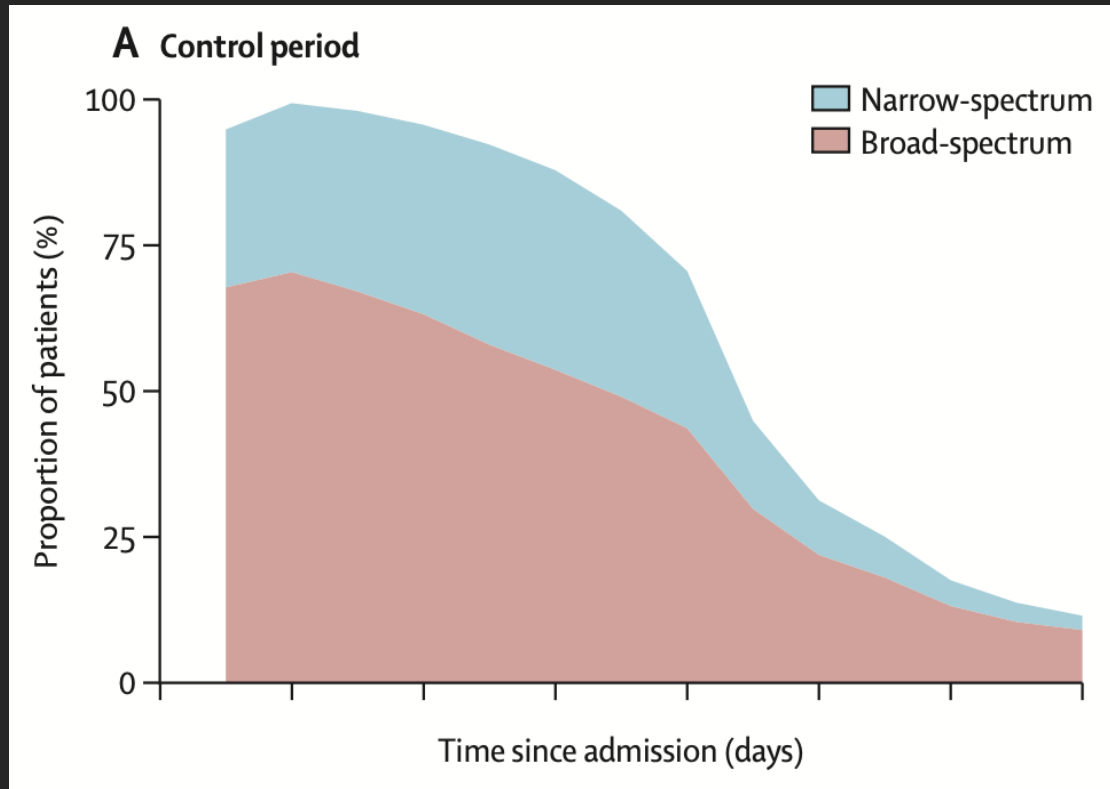
\*Contributed equally

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Microbiology  
(V A Schweitzer MD,  
C H E Boel MD,

**Background** Adults hospitalised to a non-intensive care unit (ICU) ward with moderately severe community-acquired pneumonia are frequently treated with broad-spectrum antibiotics, despite Dutch guidelines recommending narrow-spectrum antibiotics. Therefore, we investigated whether an antibiotic stewardship intervention would reduce the use of broad-spectrum antibiotics in patients with moderately severe community-acquired pneumonia without compromising their safety.

**Methods** In this cross-sectional, stepped-wedge, cluster-randomised, non-inferiority trial (CAP-PACT) done in 12 hospitals in the Netherlands, we enrolled immunocompetent adults ( $\geq 18$  years) who were admitted to a non-ICU ward and had a working diagnosis of moderately severe community-acquired pneumonia. All participating hospitals started in a control period and every 3 months a block of two hospitals transitioned from the control to the intervention period, with all hospitals eventually ending in the intervention period. The unit of randomisation was the hospital

# CAP-PACT



6.5 → 4.8 days

minus 27%



Original Investigation | Critical Care Medicine

# Effect of Gram Stain–Guided Initial Antibiotic Therapy on Clinical Response in Patients With Ventilator-Associated Pneumonia

## The GRACE-VAP Randomized Clinical Trial

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

### Abstract

**IMPORTANCE** Gram staining should provide immediate information for detecting causative pathogens. However, the effect of Gram staining on restricting the initial antibiotic choice has not been investigated in intensive care units (ICUs).

**OBJECTIVE** To compare the clinical response to Gram stain–guided restrictive antibiotic therapy vs guideline-based broad-spectrum antibiotic treatment in patients with ventilator-associated pneumonia (VAP).

**DESIGN, SETTING, AND PARTICIPANTS** This multicenter, open-label, noninferiority randomized clinical trial (Gram Stain–Guided Antibiotics Choice for VAP) was conducted in the ICUs of 12 tertiary referral hospitals in Japan from April 1, 2018, through May 31, 2020. Patients aged 15 years or older with a VAP diagnosis and a modified Clinical Pulmonary Infection Score of 5 or higher were included. The primary analysis was based on the per-protocol analysis population.

**INTERVENTIONS** Patients were randomized to Gram stain–guided antibiotic therapy or guideline-based antibiotic therapy (based on the 2016 Infectious Disease Society of America and American

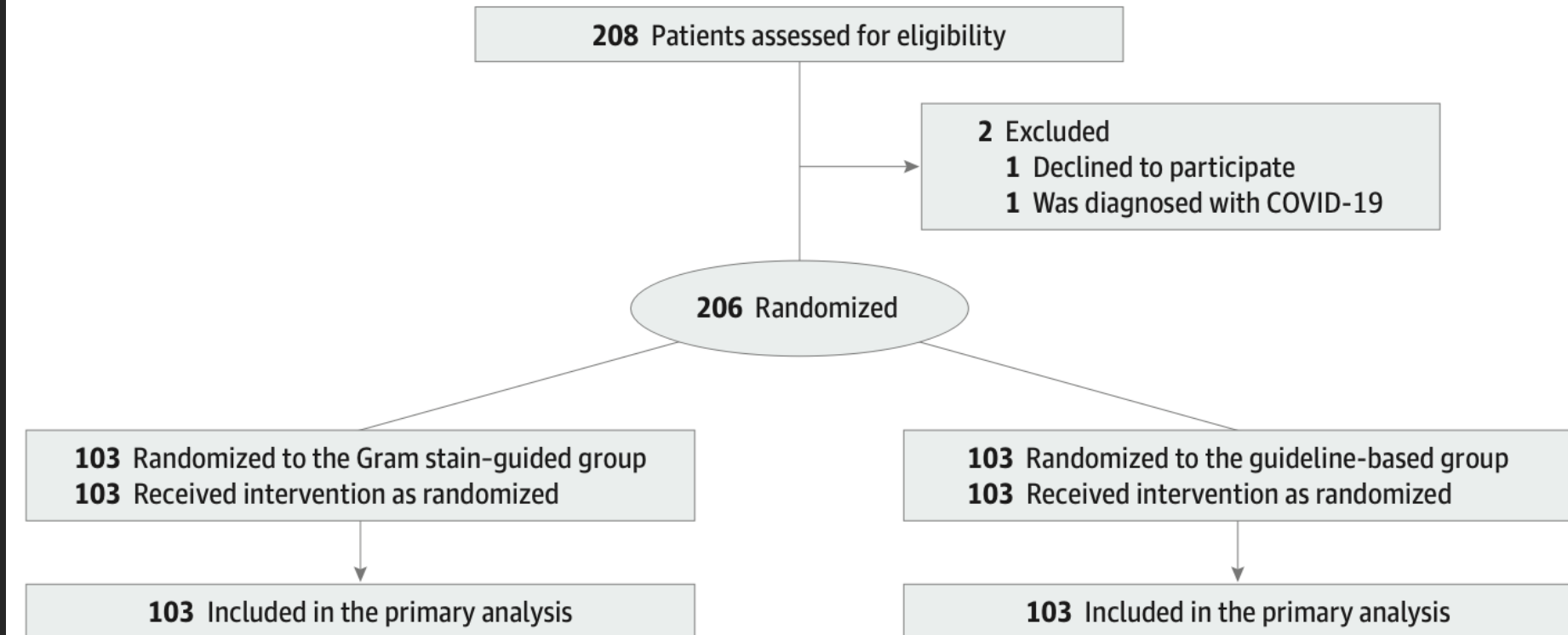
### Key Points

**Question** Does Gram stain–guided antibiotic therapy restrict the administration of broad-spectrum antibiotic agents for ventilator-associated pneumonia without detrimental effects on patient outcomes?

**Findings** In this randomized clinical trial that included 206 patients with ventilator-associated pneumonia in the intensive care unit, the clinical response to Gram stain–guided antibiotic therapy was noninferior to that of guideline-based antibiotic therapy (76.7% vs 71.8%). Gram stain–guided antibiotic therapy reduced the use of

# Study flow diagram

Figure 1. Study Flow Diagram



**Table 2. Primary and Secondary Outcomes**

Outcome	No. (%)		P value
	Gram stain-guided group (n = 103)	Guideline-based group (n = 103)	
Primary outcome			
Clinical response rate	79 (76.7)	74 (71.8)	<.001 <sup>a</sup>
Completion of antibiotic therapy within 14 d <sup>b</sup>	98 (95.1)	94 (91.3)	NA
Improvement or lack of progression of baseline radiographic findings <sup>b</sup>	85 (82.5)	78 (75.7)	NA
Resolution of signs and symptoms of pneumonia <sup>b</sup>	87 (84.5)	85 (82.5)	NA
Lack of antibiotic agent readministration <sup>b</sup>	85 (82.5)	85 (82.5)	NA
Secondary outcomes			
28-d mortality	14 (13.6)	18 (17.5)	.44
28-d ventilator-free days, median (IQR)	22 (15-24)	22 (18-25)	.21
28-d ICU-free days, median (IQR)	19 (15-22)	20 (16-23)	.42
Administration of antibiotic therapy			
Antipseudomonal agents	72 (69.9)	103 (100)	<.001
Anti-MRSA agents	63 (61.2)	103 (100)	<.001
Coverage rate of initial antibiotic therapy	89 (86.4)	95 (92.2)	.18
Escalation <sup>b</sup>	7 (6.8)	1 (1.0)	.03
De-escalation	67 (65.0)	79 (76.7)	.07
Antibiotic therapy days until de-escalation, median (IQR)	3 (2-4)	3 (2-4)	.22
Antibiotic therapy days, median (IQR)	8 (7-11)	8 (7-11)	.09







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## Research note

# Effect of discontinuation of an antimicrobial stewardship programme on the antibiotic usage pattern

Wooyoung Jang<sup>1, †</sup>, Hyeonjun Hwang<sup>2, †</sup>, Hyun-uk Jo<sup>3, 4</sup>, Yong-Han Cha<sup>5</sup>,  
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<sup>6</sup> Department of Internal Medicine, Hanyang University College of Medicine, Seoul, South Korea

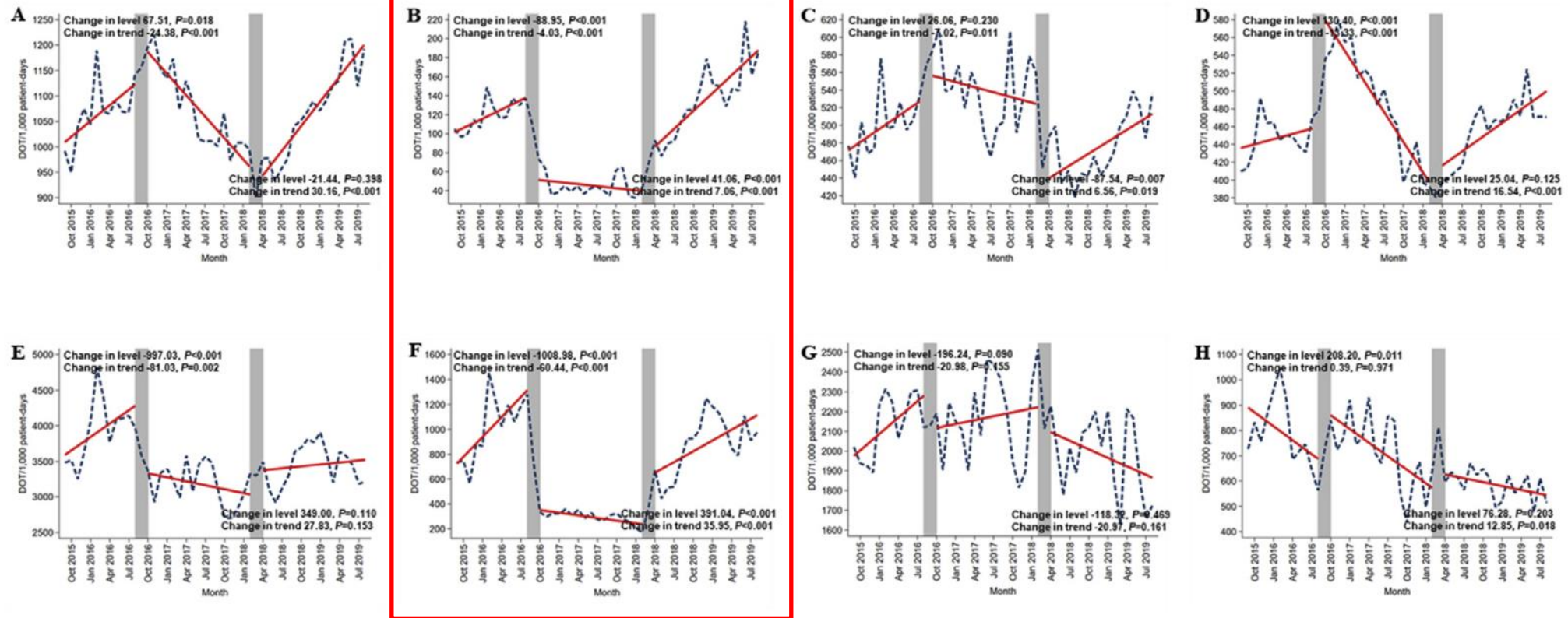
## ARTICLE INFO

Article history:

## ABSTRACT

**Objectives:** This study aimed to analyse the effect of discontinuation of antimicrobial stewardship pro

# Trends after ASP discontinuation



**Fig. 1.** Changing trends in antibiotic use over time. (A) Total antibiotics in the general ward. (B) Restrictive antibiotics in the general ward. (C) Broad-spectrum antibiotics in the general ward. (D) Non-broad-spectrum antibiotics in the general ward. (E) Total antibiotics in the intensive care unit (ICU). (F) Restrictive antibiotics in the ICU. (G) Broad-spectrum antibiotics in the ICU. (H) Non-broad-spectrum antibiotics in the ICU.

# Impact of Antibiotic Stewardship Rounds in the Intensive Care Setting: A Prospective Cluster-Randomized Crossover Study

Jessica L. Seidelman,<sup>1,2</sup> Nicholas A. Turner,<sup>1,2</sup> Rebekah H. Wrenn,<sup>1,2</sup> Christina Sarubbi,<sup>3</sup> Deverick J. Anderson,<sup>1,2</sup> Daniel J. Sexton,<sup>1,2</sup> and Rebekah W. Moehring<sup>1,2</sup>

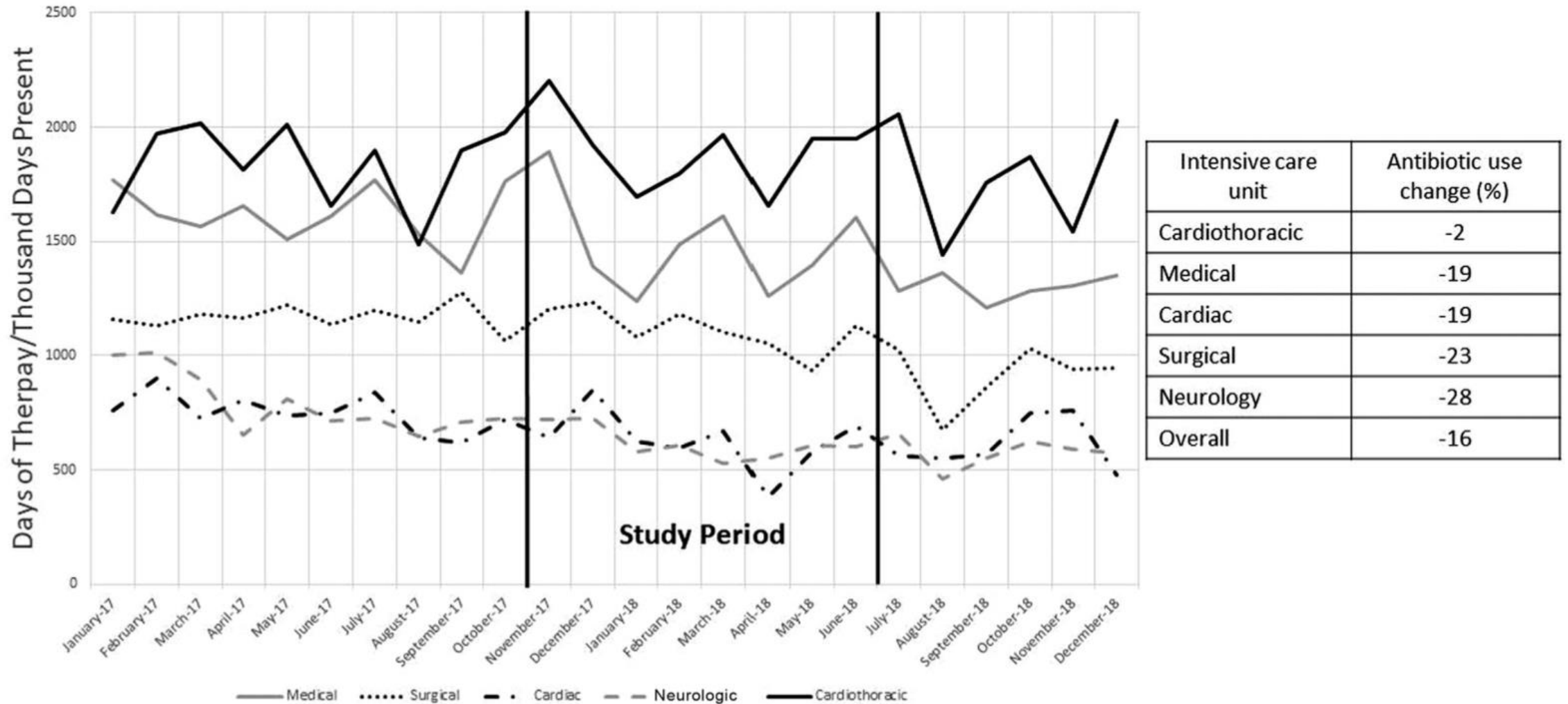
<sup>1</sup>Division of Infectious Diseases, Department of Medicine, Duke University Medical Center, Durham, North Carolina, USA; <sup>2</sup>Duke Center for Antimicrobial Stewardship and Infection Prevention, Durham, North Carolina, USA; and <sup>3</sup>UNC Rex Healthcare, Raleigh, North Carolina, USA

**Background.** Few groups have formally studied the effect of dedicated antibiotic stewardship rounds (ASRs) on antibiotic use (AU) in intensive care units (ICUs).

**Methods.** We implemented weekly ASRs using a 2-arm, cluster-randomized, crossover study in 5 ICUs at Duke University Hospital from November 2017 to June 2018. We excluded patients without an active antibiotic order, or if they had a marker of high complexity including an existing infectious disease consult, transplantation, ventricular assist device, or extracorporeal membrane oxygenation. AU during and following ICU stay for patients with ASRs was compared to the controls. We recorded the number of reviews, recommendations delivered, and responses. We evaluated change in ICU-specific AU during and after the study.

**Results.** Our analysis included 4683 patients: 2330 intervention and 2353 controls. Teams performed 761 reviews during ASRs, which excluded 1569 patients: 60% of patients off antibiotics, and 8% complex patients. Exclusions affected 88% of cardiothoracic ICU (CTICU) patients. The AU rate ratio (RR) was 0.97 (95% confidence interval [CI], .91–1.04). When CTICU was removed, the RR was 0.93 (95% CI, .89–.98). AU in the poststudy period decreased by 16% (95% CI, 11%–24%) compared to AU in the baseline period. Change in AU was differential among units: largest in the neurology ICU (–28%) and smallest in the CTICU (–2%).

Antibiotic Use by Unit from 1/2017 to 12/2018



**Figure 2.** Antibiotic use measured in days of therapy (DOT) per 1000 days present prior to, during, and after the study period in the 5 study intensive care units.

# Antibiotic optimisation

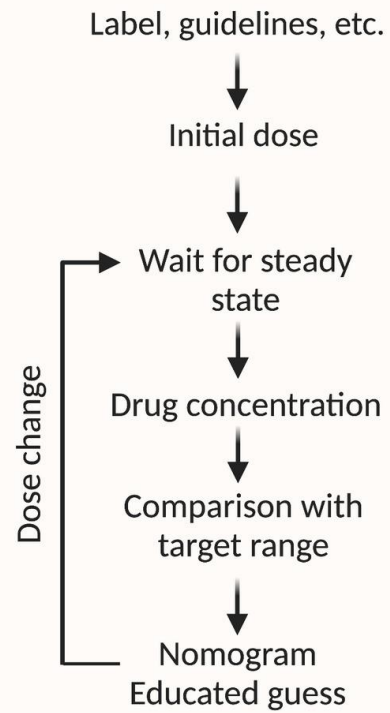
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# From Therapeutic Drug Monitoring to Model-Informed Precision Dosing for Antibiotics

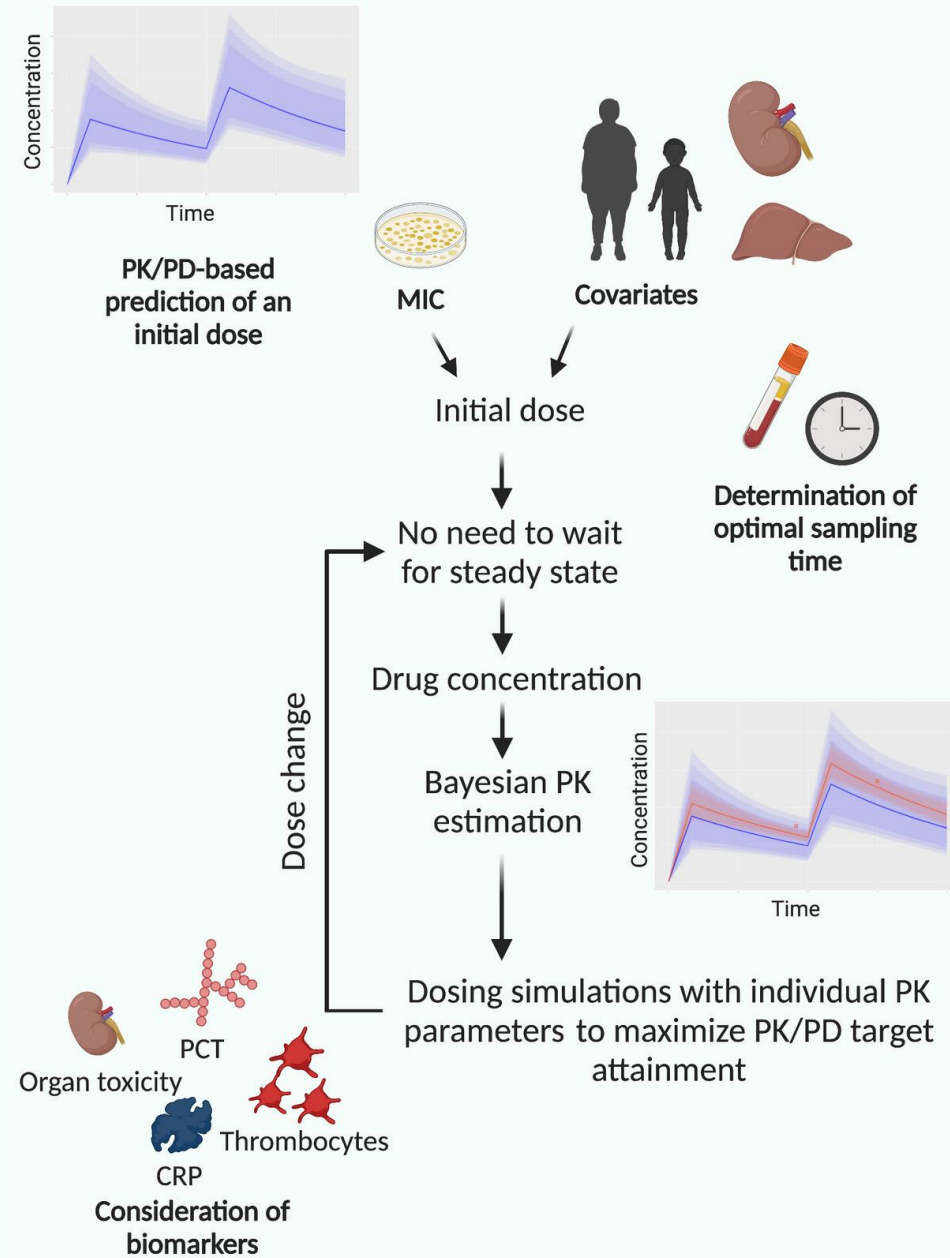
Sebastian G. Wicha<sup>1,\*</sup>, Anne-Grete Märtson<sup>2</sup>, Elisabet I. Nielsen<sup>3</sup>, Birgit C.P. Koch<sup>4</sup>, Lena E. Friberg<sup>3</sup>, Jan-Willem Alffenaar<sup>5,6,7</sup> and Iris K. Minichmayr<sup>3</sup> on behalf of the International Society of Anti-Infective Pharmacology (ISAP), the PK/PD study group of the European Society of Clinical Microbiology, Infectious Diseases (EPASG)

Therapeutic drug monitoring (TDM) and model-informed precision dosing (MIPD) have evolved as important tools to inform rational dosing of antibiotics in individual patients with infections. In particular, critically ill patients display altered, highly variable pharmacokinetics and often suffer from infections caused by less susceptible bacteria. Consequently, TDM has been used to individualize dosing in this patient group for many years. More recently, there has been increasing research on the use of MIPD software to streamline the TDM process, which can increase the flexibility and precision of dose individualization but also requires adequate model validation and re-evaluation of existing workflows. In parallel, new minimally invasive and noninvasive technologies such as microneedle-based sensors are being developed, which—together with MIPD software—have the potential to revolutionize how patients are dosed with antibiotics. Nonetheless, carefully designed clinical trials to evaluate the benefit of TDM and MIPD approaches are still sparse, but are critically needed to justify the implementation of TDM and MIPD in clinical

## Conventional TDM




## MIPD



ORIGINAL

# Effect of therapeutic drug monitoring-based dose optimization of piperacillin/tazobactam on sepsis-related organ dysfunction in patients with sepsis: a randomized controlled trial



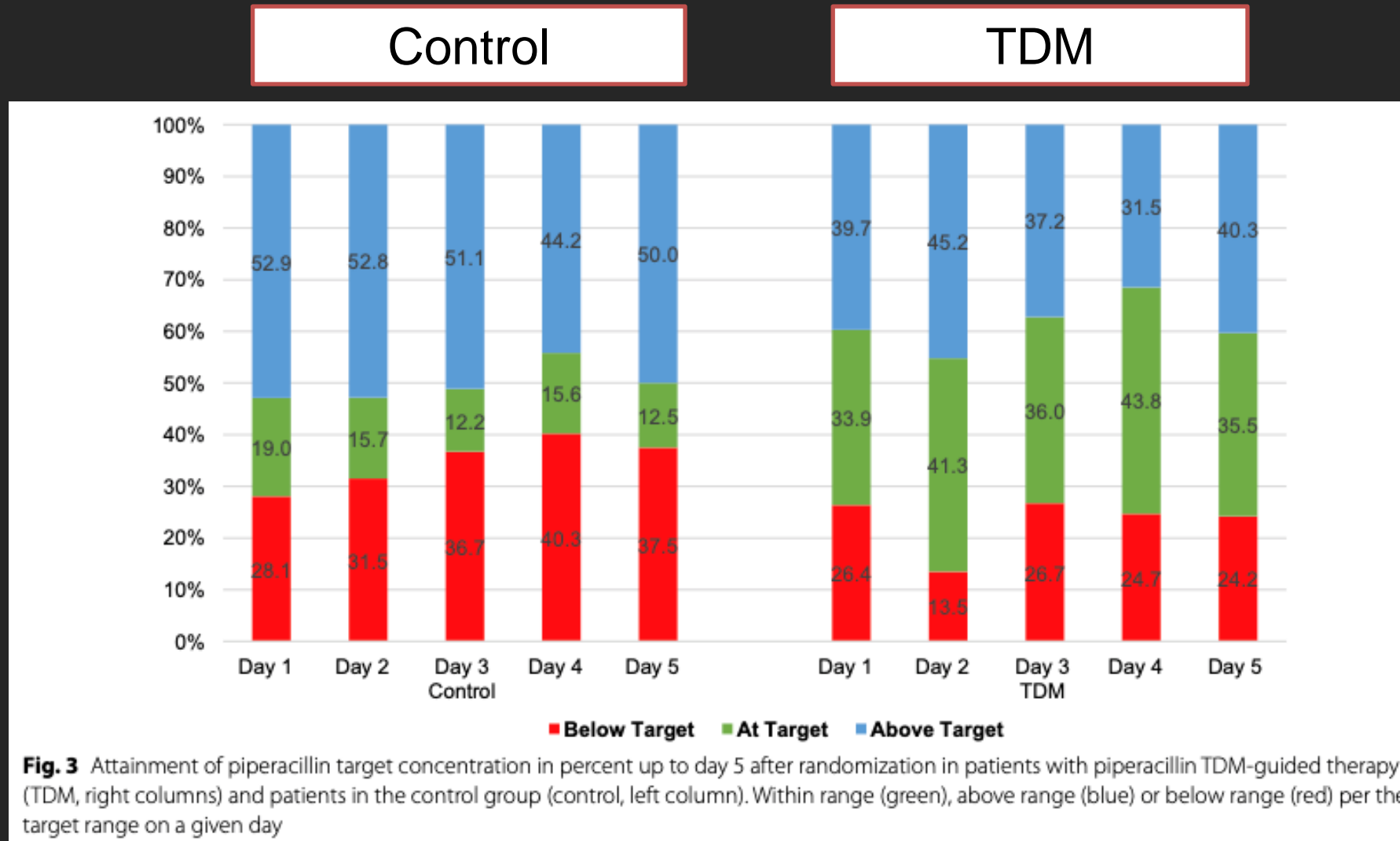
Stefan Hagel<sup>1,2\*</sup> , Friedhelm Bach<sup>3</sup>, Thorsten Brenner<sup>4,5</sup>, Hendrik Bracht<sup>6</sup>, Alexander Brinkmann<sup>7</sup>, Thorsten Annecke<sup>8,9</sup>, Andreas Hohn<sup>8,10</sup>, Markus Weigand<sup>5</sup>, Guido Michels<sup>11</sup>, Stefan Kluge<sup>12</sup>, Axel Nierhaus<sup>12</sup>, Dominik Jarczak<sup>12</sup>, Christina König<sup>12</sup>, Dirk Weismann<sup>13</sup>, Otto Frey<sup>14</sup>, Dominic Witzke<sup>3</sup>, Carsten Müller<sup>15</sup>, Michael Bauer<sup>16</sup>, Michael Kiehntopf<sup>17</sup>, Sophie Neugebauer<sup>2,17</sup>, Thomas Lehmann<sup>18</sup>, Jason A. Roberts<sup>19,20,21</sup> and Mathias W. Pletz<sup>1,2</sup> on behalf of the TARGET Trial Investigators



**Table 1 Demographics and baseline characteristics**

Characteristic	TDM (n = 125)	No-TDM (n = 124)
Age, mean (SD), years	67.2 (13.9)	65.3 (13.5)
Male sex, no. (%)	80 (63.5)	92 (72.4)
Body mass index, mean (SD) <sup>a</sup>	28.3 (7.9)	27.4 (7.4)
APACHE II score, mean (SD) <sup>b</sup>	23.2 (6.7)	22.4 (5.7)
SOFA score, mean (SD) <sup>c</sup>	12.1 (2.8)	12.2 (2.6)
SAPS II score, mean (SD) <sup>b</sup>	44.6 (12.4)	43.9 (12.2)
Charlson comorbidity index score, median (IQR)	2 (1–3)	2 (1–3)
Septic shock, no. (%)	96 (76.2)	92 (72.4)
Required mechanical ventilation, no. (%)	100 (79.3)	92 (72.4)
Laboratory values, median (IQR)		
White blood cell count, cells/ $\mu$ L	17.0 (11.7–22.2)	13.6 (10–23.5)
Plasma procalcitonin, ng/mL	4.3 (0.9–13.4)	4.2 (1.0–14.5)
Plasma lactate, mg/dL	2.2 (1.5–3.5)	2.2 (1.4–3.6)
Plasma creatinine, mg/dL	1.3 (0.84–2)	1.4 (0.9–2.3)
Creatinine clearance, mL/min	55.6 (34.5–90.3)	53 (32.7–95)
Plasma albumin, g/dL	2.5 (2.2–2.9)	2.4 (2–3)
Source of infection, no. (%) <sup>d</sup>		
Pneumonia	74 (62.7)	81 (65.8)
Intra-abdominal infection	25 (21.2)	24 (19.5)
Urinary tract	15 (12.7)	17 (13.8)
Bone or soft tissue	11 (9.3)	15 (6.2)
Surgical site infection	5 (4.2)	4 (3.3)
Other	20 (16.9)	17 (13.8)
Unknown	8 (6.3)	4 (3.1)
Acquisition, no. (%)		
Health care-associated	71 (56.3)	72 (56.7)
Community-associated	55 (43.7)	55 (43.3)
Time between onset of sepsis and randomization, mean (SD), h	15.0 $\pm$ 6.4	15.1 $\pm$ 6.9

# TARGET study




**Table 2 Study outcomes**

Outcome	TDM (n = 125)	No-TDM (n = 124)	p value <sup>a</sup>
SOFA score, mean (95% CI)	7.9 (7.1–8.7)	8.2 (7.5–9)	0.39
28-Day mortality, no. (%)	27 (21.6)	32 (25.8)	0.44
ΔSOFA, mean score day 1–10 (or 24 points if death within 10 days) minus score at baseline	2.1 (-0.2–4.3)	2.6 (0.3–4.9)	0.59
ΔSOFA, score at day 10 (or 24 points if death within 10 days) minus score at baseline	1.6 (-1–4.2)	2.9 (0.2–5.6)	0.26
SOFA subscore, median (IQR)			
Cardiovascular	2 (1–3)	2 (1.2–3.2)	0.81
Respiratory	2.5 (2–3)	2.5 (2–2.9)	0.45
Coagulation	0.1 (0–1)	0 (0–0.8)	0.54
Renal	0.5 (0–1.5)	0.8 (0–2)	0.4
Hepatic	3.2 (2.6–4)	3.3 (2.8–4)	0.68
Central nervous system	0.1 (0–1.2)	0.3 (0–1.3)	0.31
Length of stay (days), median (IQR)			
In ICU	9 (4–15)	11 (7–17)	0.24
In hospital	24 (15–28)	25 (15–28)	0.52
Intervention-free days, median (IQR)			
Ventilator <sup>b</sup>	20 (5–27)	18.5 (1–25)	0.06
Renal replacement therapy <sup>b</sup>	28 (21–28)	28 (10–28)	0.33
Antibiotic <sup>c</sup>	8 (6–12)	8 (5–11)	0.19
Vasopressor <sup>c</sup>	11 (2–13)	9 (2–12)	0.14
Clinical cure, EOT <sup>d</sup>	21/59 (35.6)	12/69 (17.4)	
Microbiological cure, EOT <sup>e</sup>	27/48 (56.3)	23/50 (46)	
Total daily dose (grams) of piperacillin/tazobactam, mean (SD)	10.3 ± 5.6	9.8 ± 2.5	0.12



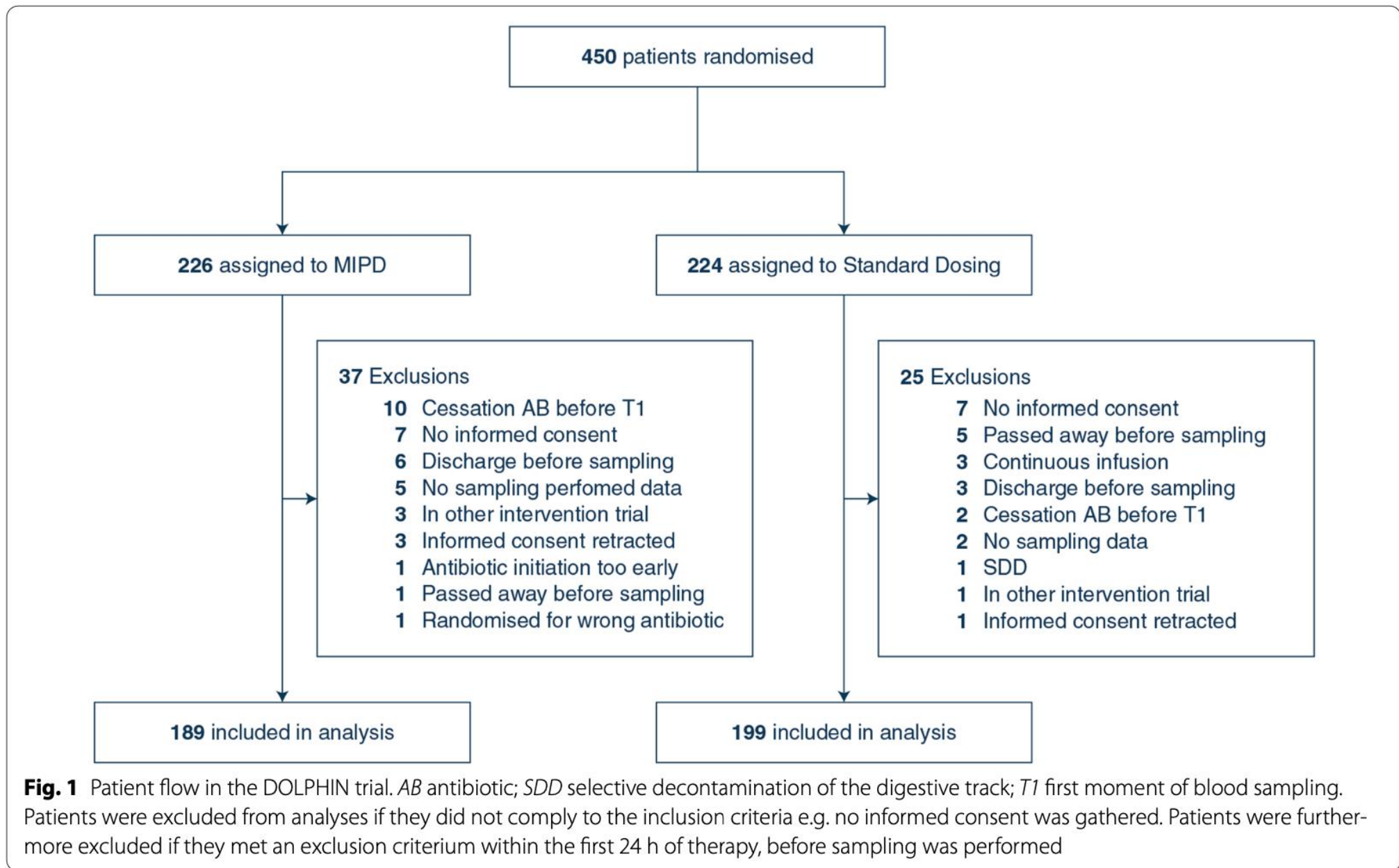
# Model-informed precision dosing of beta-lactam antibiotics and ciprofloxacin in critically ill patients: a multicentre randomised clinical trial

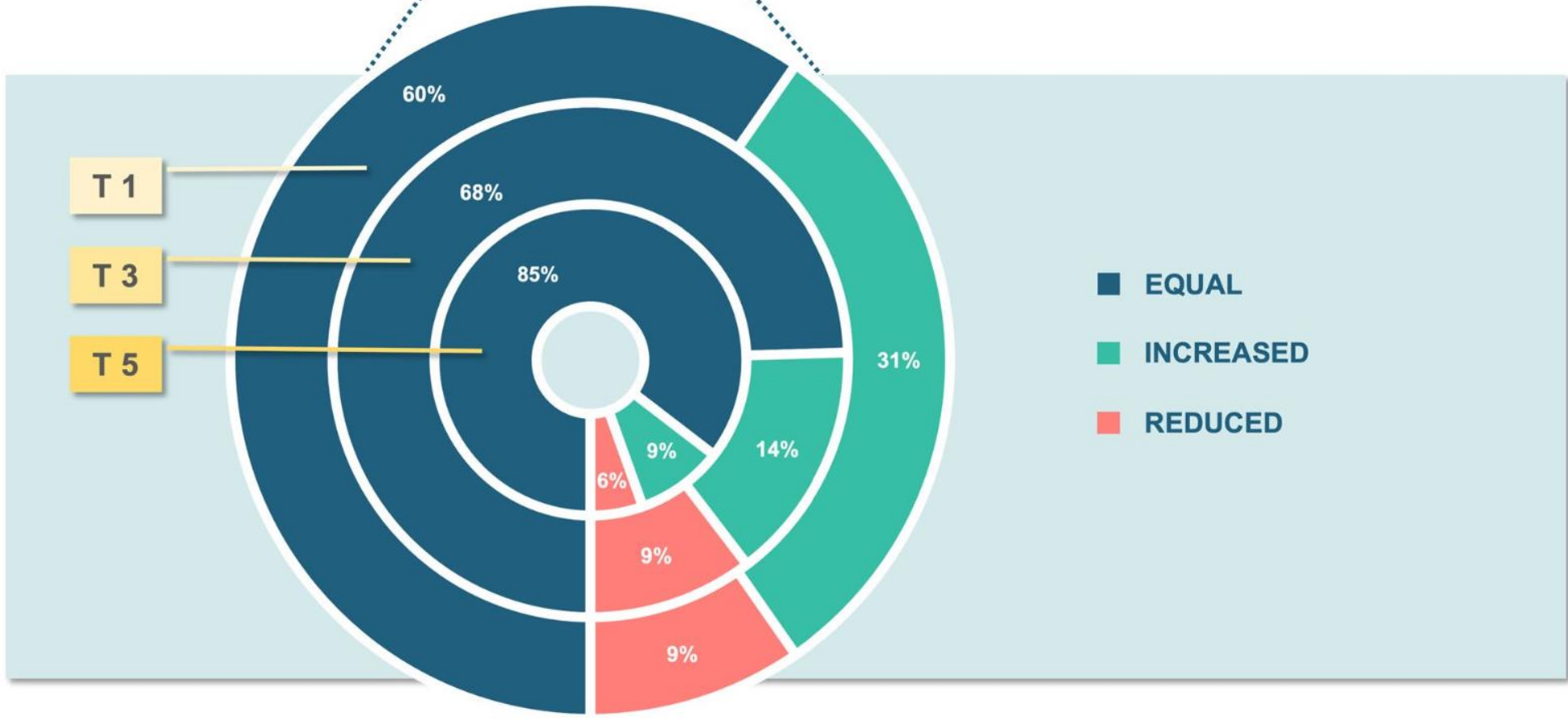
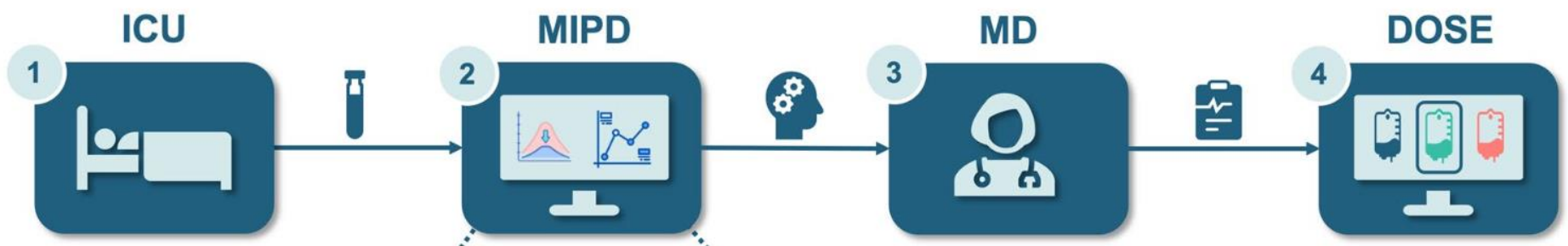
Tim M. J. Ewoldt<sup>1,2,3\*</sup> , Alan Abdulla<sup>2,3</sup>, Wim J. R. Rietdijk<sup>2</sup>, Anouk E. Muller<sup>3,4,5</sup>, Brenda C. M. de Winter<sup>2,3</sup>, Nicole G. M. Hunfeld<sup>1,2</sup>, Ilse M. Purmer<sup>6</sup>, Peter van Vliet<sup>7</sup>, Evert-Jan Wils<sup>1,8</sup>, Jasper Haringman<sup>9</sup>, Annelies Draisma<sup>10</sup>, Tom A. Rijpstra<sup>11</sup>, Attila Karakus<sup>12</sup>, Diederik Gommers<sup>1</sup>, Henrik Endeman<sup>1</sup> and Birgit C. P. Koch<sup>2,3</sup>

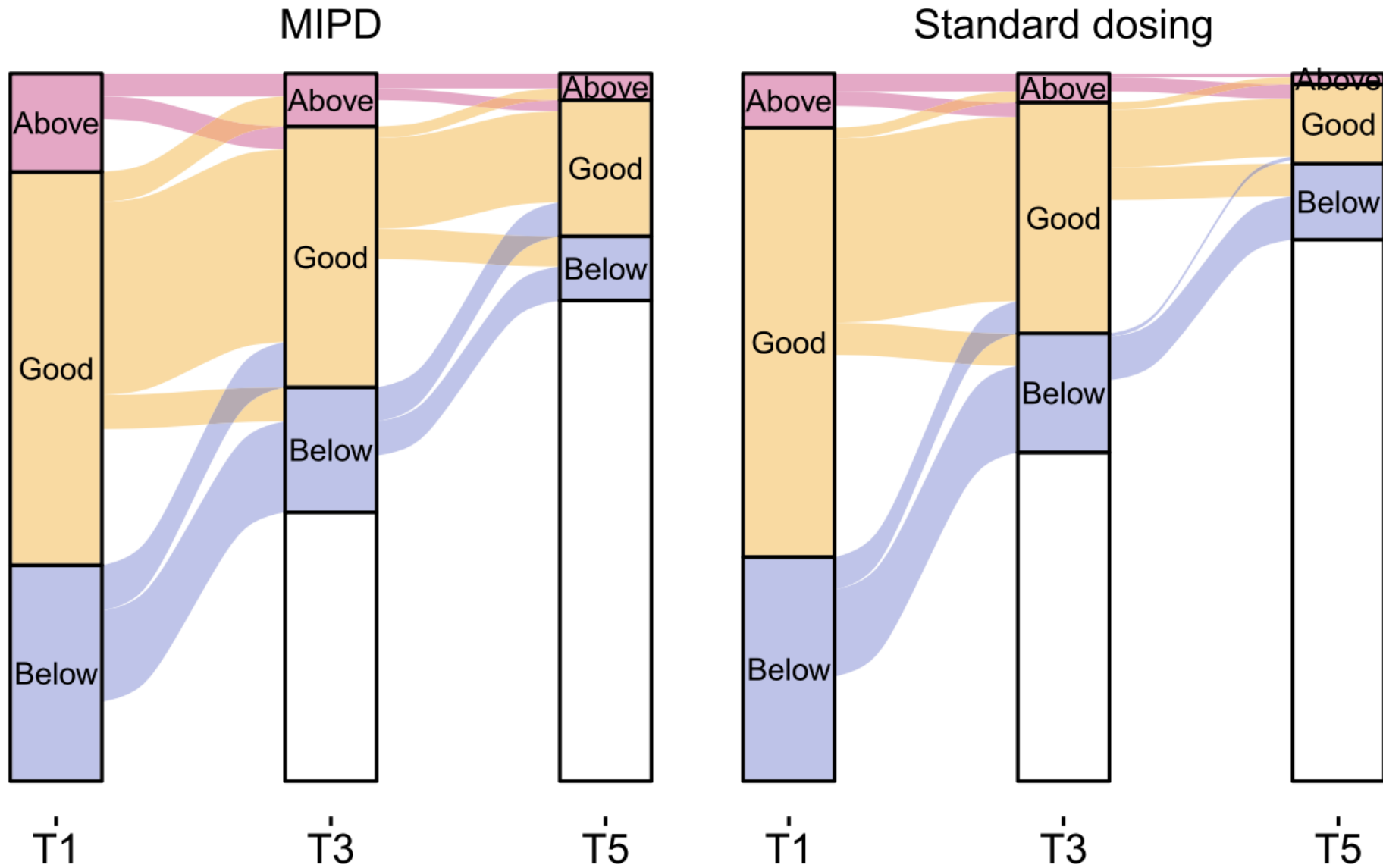
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## Abstract

**Purpose:** Individualising drug dosing using model-informed precision dosing (MIPD) of beta-lactam antibiotics and ciprofloxacin has been proposed as an alternative to standard dosing to optimise antibiotic efficacy in critically ill







**Fig. 3** Alluvial plot of target attainment over time. T1, first moment of antibiotic sampling, 1 day after initiation of antibiotic; T3, second moment of sampling, 48 h after T1; T5, third moment of sampling, 48 h after T3

**Table 2 Study outcomes**

Outcome	MIPD	Standard therapy	Crude effect (95% CI)	Adjusted Effect (95% CI)	P-value	P-value adjusted
ICU LOS, median (IQR)	10 (5–20)	8 (3–19)	1.12 (0.92–1.36) <sup>b</sup>	1.16 (0.96–1.41) <sup>b</sup>	0.27	0.13
ICU LOS after T0, median (IQR)	7 (3–13)	6 (3–14)	1.09 (0.9–1.31) <sup>b</sup>	1.11 (0.92–1.34) <sup>b</sup>	0.4	0.27
ICU-free days alive, median (IQR) <sup>a</sup>	16 (0–23)	18 (0–25)			0.21 <sup>h</sup>	
ICU mortality, No. (%)	41 (21.7)	36 (18.1)	1.25 (0.76–2.07) <sup>c</sup>	1.21 (0.74–2.02) <sup>c</sup>	0.37	0.44
28-day mortality, no. (%)	50 (26.5)	49 (24.6)	1.1 (0.7–1.74) <sup>c</sup>	1.04 (0.65–1.66) <sup>c</sup>	0.68	0.87
Hospital mortality, no. (%)	53 (28)	51 (25.6)	1.13 (0.72–1.77) <sup>c</sup>	1.07 (0.68–1.7) <sup>c</sup>	0.59	0.76
6 month mortality, no. (%)	69 (36.5)	64 (32.2)	1.21 (0.8–1.85) <sup>c</sup>	1.14 (0.74–1.76) <sup>c</sup>	0.37	0.57
SOFA score at T5, median (IQR)	3 (0–6)	1.5 (0–7)			0.11 <sup>h</sup>	
Delta-SOFA score at T5, median (IQR)	4 (1–7)	4 (1–7)	– 0.03 (– 0.92 to 0.87) <sup>d</sup>	– 0.1 (– 0.99 to 0.79) <sup>d</sup>	0.95	0.82
CRP at T5, median (IQR)	79 (41–162)	84 (42–180)			0.68 <sup>h</sup>	
Delta-CRP score at T5, median (IQR)	61 (9–160)	75 (17–190)	– 12.2 (– 49.1 to 24.6) <sup>d</sup>	– 14.2 (– 51.1 to 22.8) <sup>d</sup>	0.52	0.45
WBC at T5, median (IQR)	13.5 (9.5–18.7)	12.9 (9.8–17.1)			0.51 <sup>h</sup>	
Delta-WBC score at T5, median (IQR)	0.02 (– 6.7 to 4.7)	0.7 (– 4.9 to 4.9)	– 0.7 (– 3.2 to 1.8) <sup>d</sup>	– 0.8 (– 3.3 to 1.7) <sup>d</sup>	0.59	0.55
Target attainment at T1, no. (%)	105 (55.6)	120 (60.9)	0.8 (0.53–1.2) <sup>c</sup>	0.78 (0.52–1.18) <sup>c</sup>	0.29	0.24
Above target at T1, no. (%)	26 (13.8)	15 (7.6)	1.93 (1–3.86) <sup>c</sup>	1.84 (0.94–3.7) <sup>c</sup>	0.05	0.08
Target attainment at T3, No. (%) <sup>e</sup>	69 (59.5)	64 (60.4)	0.96 (0.56–1.64) <sup>c</sup>	0.95 (0.55–1.63) <sup>c</sup>	0.89	0.84
Above target at T3, No. (%) <sup>e</sup>	14 (12.1)	8 (7.5)	1.68 (0.69–4.37) <sup>c</sup>	1.62 (0.65–4.25) <sup>c</sup>	0.26	0.31
Target attainment at T5, no. (%) <sup>f</sup>	36 (60)	24 (50)	1.5 (0.7–3.25) <sup>c</sup>	1.52 (0.7–3.33) <sup>c</sup>	0.3	0.29
Above target at T5, no. (%) <sup>f</sup>	7 (11.7)	3 (6.3)	1.98 (0.52–9.6) <sup>c</sup>	1.87 (0.48–9.13) <sup>c</sup>	0.34	0.39
Target attainment at T7, No. (%) <sup>g</sup>	15 (71.4)	15 (57.7)	1.83 (0.55–6.54) <sup>c</sup>	1.71 (0.5–6.27) <sup>c</sup>	0.33	0.4
Above target at T7, no. (%) <sup>g</sup>	2 (9.5)	0 (0)	∞ (0–∞) <sup>c</sup>	∞ (0–∞) <sup>c</sup>	1	1
Quality of Life VAS at 6 months, median (IQR)	70 (50–80)	65 (55–75)	– 0.8 (– 6.26 to 4.66) <sup>d</sup>	– 0.75 (– 6.26 to 4.76) <sup>d</sup>	0.775	0.79
QALY at 6 months, median (IQR)	0.78 (0.57–0.89)	0.72 (0.51–0.85)	– 0.03 (– 0.12 to 0.06) <sup>d</sup>	– 0.03 (– 0.12 to 0.06) <sup>d</sup>	0.55	0.49



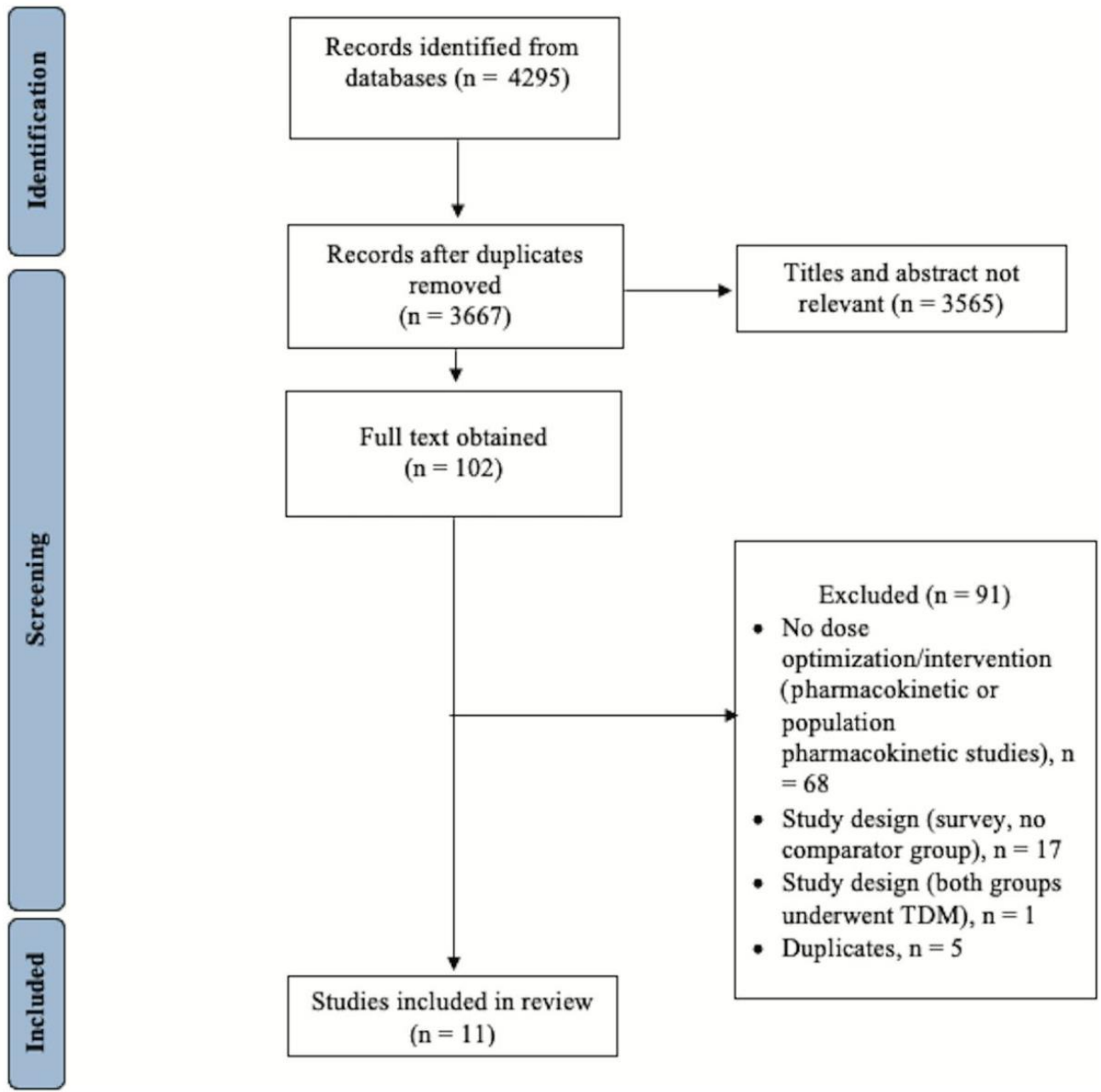
# Beta-Lactam Antibiotic Therapeutic Drug Monitoring in Critically Ill Patients: A Systematic Review and Meta-Analysis

Rekha Pai Mangalore,<sup>1,2,✉</sup> Aadith Ashok,<sup>1</sup> Sue J. Lee,<sup>1,2</sup> Lorena Romero,<sup>3</sup> Trisha N. Peel,<sup>1,2</sup> Andrew A. Udy,<sup>4,5</sup> and Anton Y. Peleg<sup>1,2,6</sup>

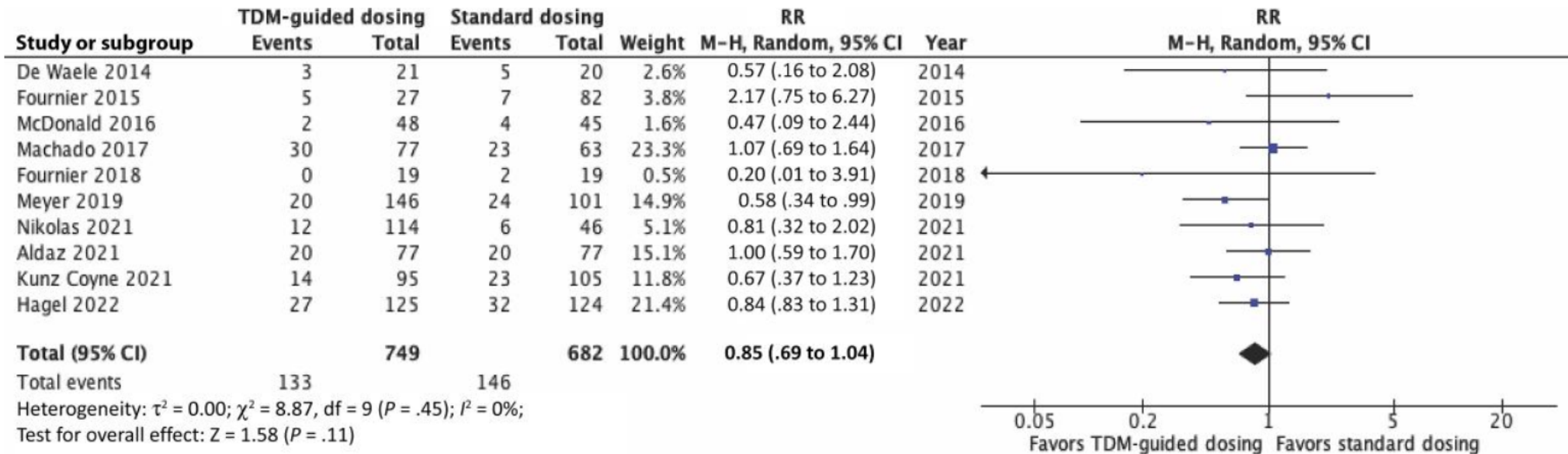
<sup>1</sup>Department of Infectious Diseases, Alfred Hospital, Alfred Health, Melbourne, Victoria, Australia; <sup>2</sup>Central Clinical School, Monash University, Melbourne, Victoria, Australia; <sup>3</sup>Ian Potter Library, Alfred Hospital, Melbourne, Victoria, Australia; <sup>4</sup>Department of Intensive Care and Hyperbaric Medicine, Alfred Hospital, Alfred Health, Melbourne, Victoria, Australia; <sup>5</sup>School of Public Health and Preventative Medicine Australia, Monash University, Melbourne, Victoria, Australia; and <sup>6</sup>Monash Biomedicine Discovery Institute, Department of Microbiology, Monash University, Melbourne, Victoria, Australia

Therapeutic drug monitoring (TDM) of beta-lactam antibiotics is recommended to address the variability in exposure observed in critical illness. However, the impact of TDM-guided dosing on clinical outcomes remains unknown. We conducted a systematic review and meta-analysis on TDM-guided dosing and clinical outcomes (all-cause mortality, clinical cure, microbiological cure, treatment failure, hospital and intensive care unit length of stay, target attainment, antibiotic-related adverse events, and emergence of resistance) in critically ill patients with suspected or proven sepsis. Eleven studies (n = 1463 participants) were included. TDM-guided dosing was associated with improved clinical cure (relative risk, 1.17; 95% confidence interval [CI], 1.04 to 1.31), microbiological cure (RR, 1.14; 95% CI, 1.03 to 1.27), treatment failure (RR, 0.79; 95% CI, .66 to .94), and target attainment (RR, 1.85; 95% CI, 1.08 to 3.16). No associations with mortality and length of stay were found. TDM-guided dosing improved clinical and microbiological cure and treatment response. Larger, prospective, randomized trials are required to better assess the utility of beta-lactam TDM in critically ill patients.

**Keywords.** antibacterial agents; pharmacokinetics; pharmacodynamics; drug concentration; critical illness.



# Systematic review TDM



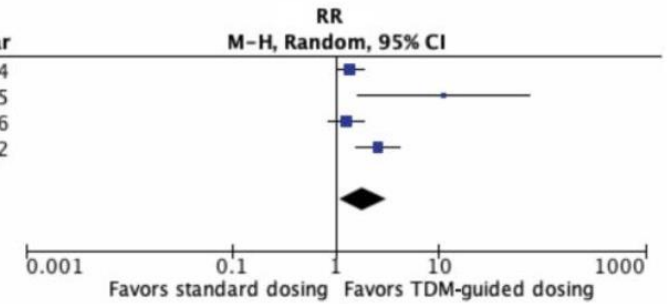
**Figure 2.** Forest plot showing the risk of mortality with TDM-guided beta-lactam dosing compared with standard dosing. The blue squares represent the effect estimates from individual studies; the size of the square is proportional to the weight of the study. The horizontal lines represent the 95% CI of the study estimate. The black diamond represents the pooled effect size. Abbreviation: CI, confidence interval; df, degrees of freedom; M-H, Mantel-Haenszel Test; RR, risk ratio; TDM, therapeutic drug monitoring.

Target attainment

A

Study or subgroup	TDM-guided dosing		Standard dosing		Weight	RR		Year
	Events	Total	Events	Total		M-H, Random, 95% CI		
De Waele 2014	18	19	13	19	33.4%	1.38 (1.00 to 1.91)		2014
Sime 2015	11	15	1	15	6.5%	11.00 (1.62 to 74.88)		2015
2016	27	48	20	45	31.1%	1.27 (.84 to 1.91)		2016
2022	47	125	18	124	29.1%	2.59 (1.60 to 4.20)		2022
<b>Total (95% CI)</b>		<b>207</b>		<b>203</b>	<b>100.0%</b>	<b>1.85 (1.08 to 3.16)</b>		
Total events	103		52					

Heterogeneity:  $\tau^2 = 0.20$ ;  $\chi^2 = 12.75$ ,  $df = 3$  ( $P = .005$ );  $I^2 = 76\%$   
 Test for overall effect:  $Z = 2.24$  ( $P = .03$ )

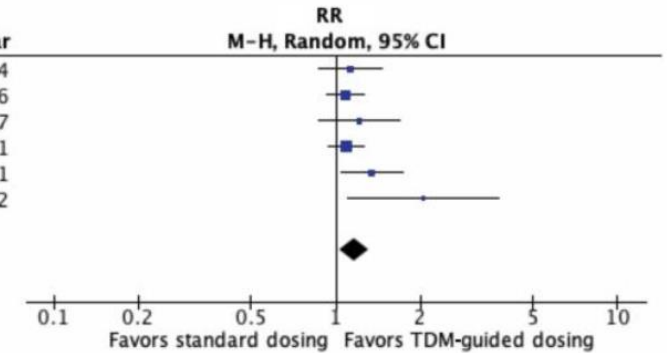


Clinical cure

B

Study or subgroup	TDM-guided dosing		Standard dosing		Weight	RR		Year
	Events	Total	Events	Total		M-H, Random, 95% CI		
De Waele 2014	19	21	16	20	14.6%	1.13 (.87 to 1.47)		2014
McDonald 2016	44	48	38	45	27.8%	1.09 (.93 to 1.26)		2016
2017	43	77	29	63	9.9%	1.21 (.87 to 1.69)		2017
2021	78	95	79	105	29.1%	1.09 (0.94 to 1.26)		2021
2021	55	77	41	77	15.2%	1.34 (1.04 to 1.73)		2021
2022	21	59	12	69	3.3%	2.05 (1.10 to 3.80)		2022
<b>Total (95% CI)</b>		<b>377</b>		<b>379</b>	<b>100.0%</b>	<b>1.17 (1.04 to 1.31)</b>		
Total events	260		215					

Heterogeneity:  $\tau^2 = 0.01$ ;  $\chi^2 = 7.53$ ,  $df = 5$  ( $P = .18$ );  $I^2 = 34\%$   
 Test for overall effect:  $Z = 2.59$  ( $P = .010$ )

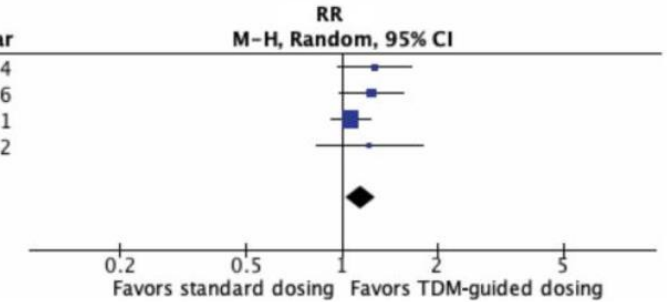


Microbiological cure

C

Study or subgroup	TDM-guided dosing		Standard dosing		Weight	RR		Year
	Events	Total	Events	Total		M-H, Random, 95% CI		
2014	20	21	15	20	15.5%	1.27 (.97 to 1.66)		2014
2016	41	48	31	45	21.7%	1.24 (.99 to 1.56)		2016
2021	66	77	62	77	55.5%	1.06 (.92 to 1.23)		2021
2022	27	48	23	50	7.4%	1.22 (0.83 to 1.81)		2022
<b>Total (95% CI)</b>		<b>194</b>		<b>192</b>	<b>100.0%</b>	<b>1.14 (1.03 to 1.27)</b>		
Total events	154		131					

Heterogeneity:  $\tau^2 = 0.00$ ;  $\chi^2 = 2.20$ ,  $df = 3$  ( $P = .53$ );  $I^2 = 0\%$   
 Test for overall effect:  $Z = 2.45$  ( $P = .01$ )



# Preventing HAI

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JAMA | [Original Investigation](#) | CARING FOR THE CRITICALLY ILL PATIENT

# Effect of Selective Decontamination of the Digestive Tract on Hospital Mortality in Critically Ill Patients Receiving Mechanical Ventilation

## A Randomized Clinical Trial

The SuDDICU Investigators for the Australian and New Zealand Intensive Care Society Clinical Trials Group

**IMPORTANCE** Whether selective decontamination of the digestive tract (SDD) reduces mortality in critically ill patients remains uncertain.

**OBJECTIVE** To determine whether SDD reduces in-hospital mortality in critically ill adults.

**DESIGN, SETTING, AND PARTICIPANTS** A cluster, crossover, randomized clinical trial that recruited 5982 mechanically ventilated adults from 19 intensive care units (ICUs) in Australia between April 2018 and May 2021 (final follow-up, August 2021). A contemporaneous ecological assessment recruited 8599 patients from participating ICUs between May 2017 and August 2021.

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## POPULATION



3780 Men 2202 Women

Adults receiving mechanical ventilation in an intensive care unit

Mean age: 58 years

## LOCATIONS

19 Intensive care units in Australia



## INTERVENTION



5982 Patients randomized

2791

### SDD

6-Hourly oral paste and gastric suspension of colistin, tobramycin, and nystatin, plus 4-day IV antibiotic course

3191

### Standard care

Standard care without SDD

## PRIMARY OUTCOME

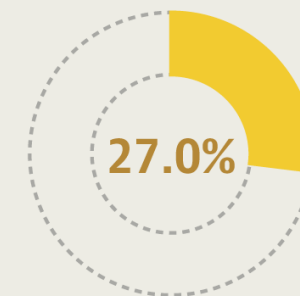
90-Day in-hospital mortality

## FINDINGS

### In-hospital deaths

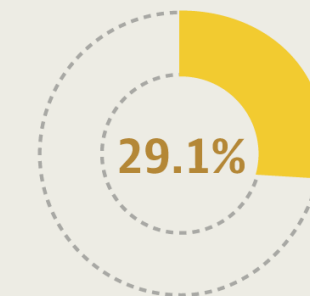
#### SDD

753 of 2791 patients



#### Standard care

928 of 3191 patients

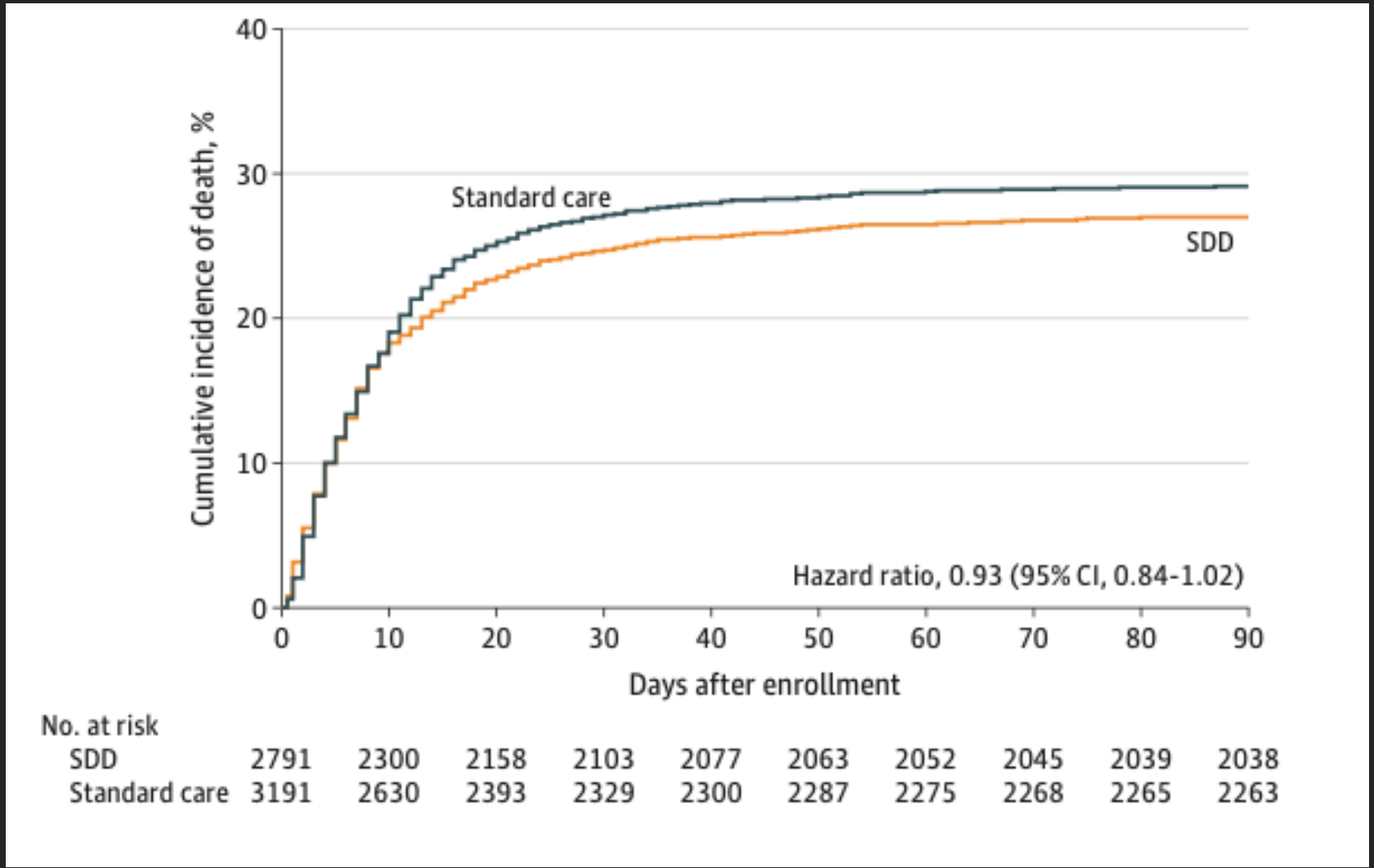


SDD did not significantly reduce in-hospital mortality:

Mean difference, **-1.7%** (95% CI, -4.8% to 1.3%)

Odds ratio, **0.91** (95% CI, 0.82-1.02);  $P = .12$

# Probability of in-hospital death within 90 days





JAMA | **Original Investigation**

# Association Between Selective Decontamination of the Digestive Tract and In-Hospital Mortality in Intensive Care Unit Patients Receiving Mechanical Ventilation

## A Systematic Review and Meta-analysis

Naomi E. Hammond, RN, PhD; John Myburgh, MD, PhD; Ian Seppelt, MD; Tessa Garside, MBBS, PhD; Ruan Vlok, MBBS; Sajeev Mahendran, MD; Derick Adigbli, MD, PhD; Simon Finfer, MD; Ya Gao, MM; Fiona Goodman, BN; Gordon Guyatt, MD, PhD; Joseph Alvin Santos, PhD; Balasubramanian Venkatesh, MD; Liang Yao, MM; Gian Luca Di Tanna, PhD; Anthony Delaney, MBBS, PhD

**IMPORTANCE** The effectiveness of selective decontamination of the digestive tract (SDD) in critically ill adults receiving mechanical ventilation is uncertain.

**OBJECTIVE** To determine whether SDD is associated with reduced risk of death in adults receiving mechanical ventilation in intensive care units (ICUs) compared with standard care.

**DATA SOURCES** The primary search was conducted using MEDLINE, EMBASE, and CENTRAL databases until September 2022.

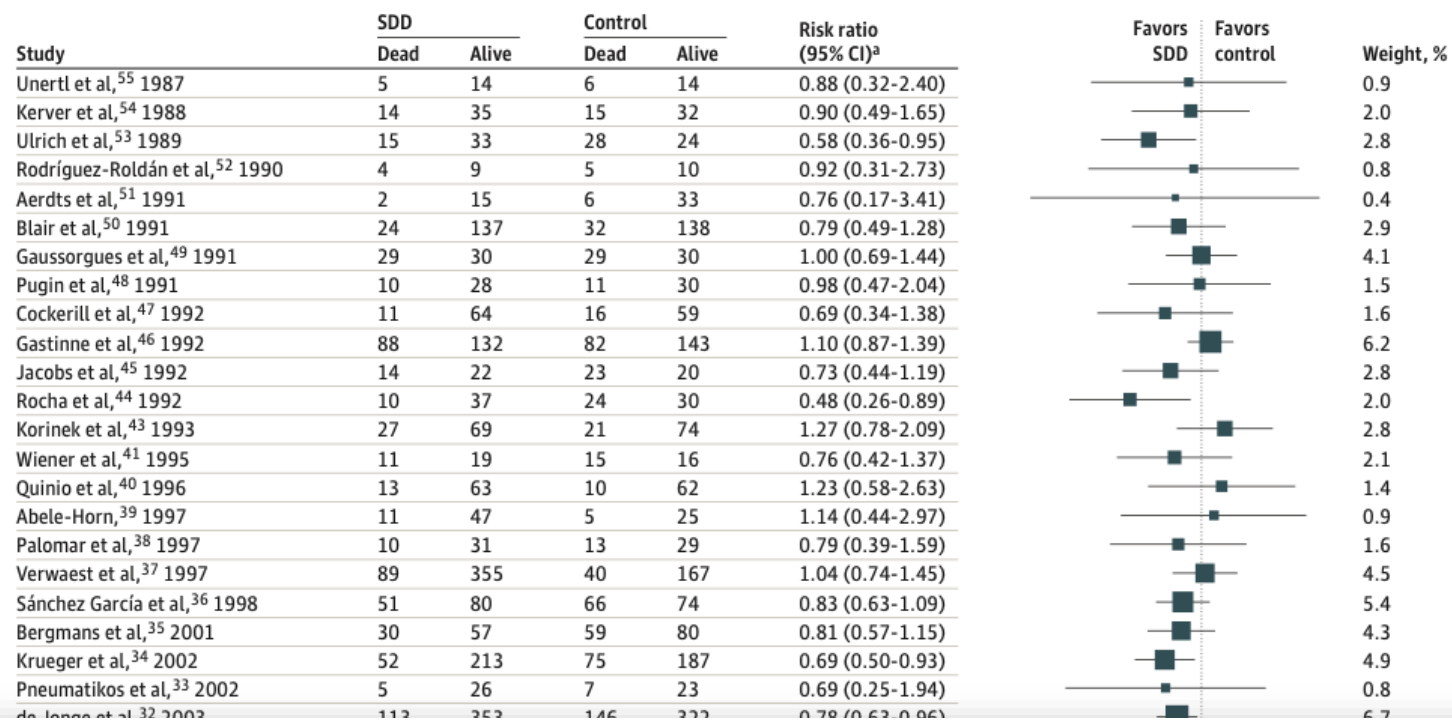
**STUDY SELECTION** Randomized clinical trials including adults receiving mechanical ventilation in the ICU comparing SDD vs standard care or placebo.

**DATA EXTRACTION AND SYNTHESIS** Data extraction and risk of bias assessments were performed in duplicate. The primary analysis was conducted using a Bayesian framework

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Figure 2. Forest Plot for Hospital Mortality for the Comparison Between Selective Decontamination of the Digestive Tract (SDD) Compared With Standard Care



Bayesian

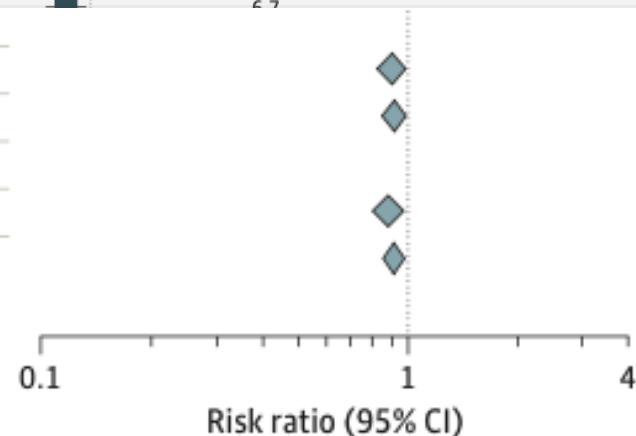
Vague priors 0.91 (0.82-0.99)

Semi-informative priors 0.92 (0.85-0.99)

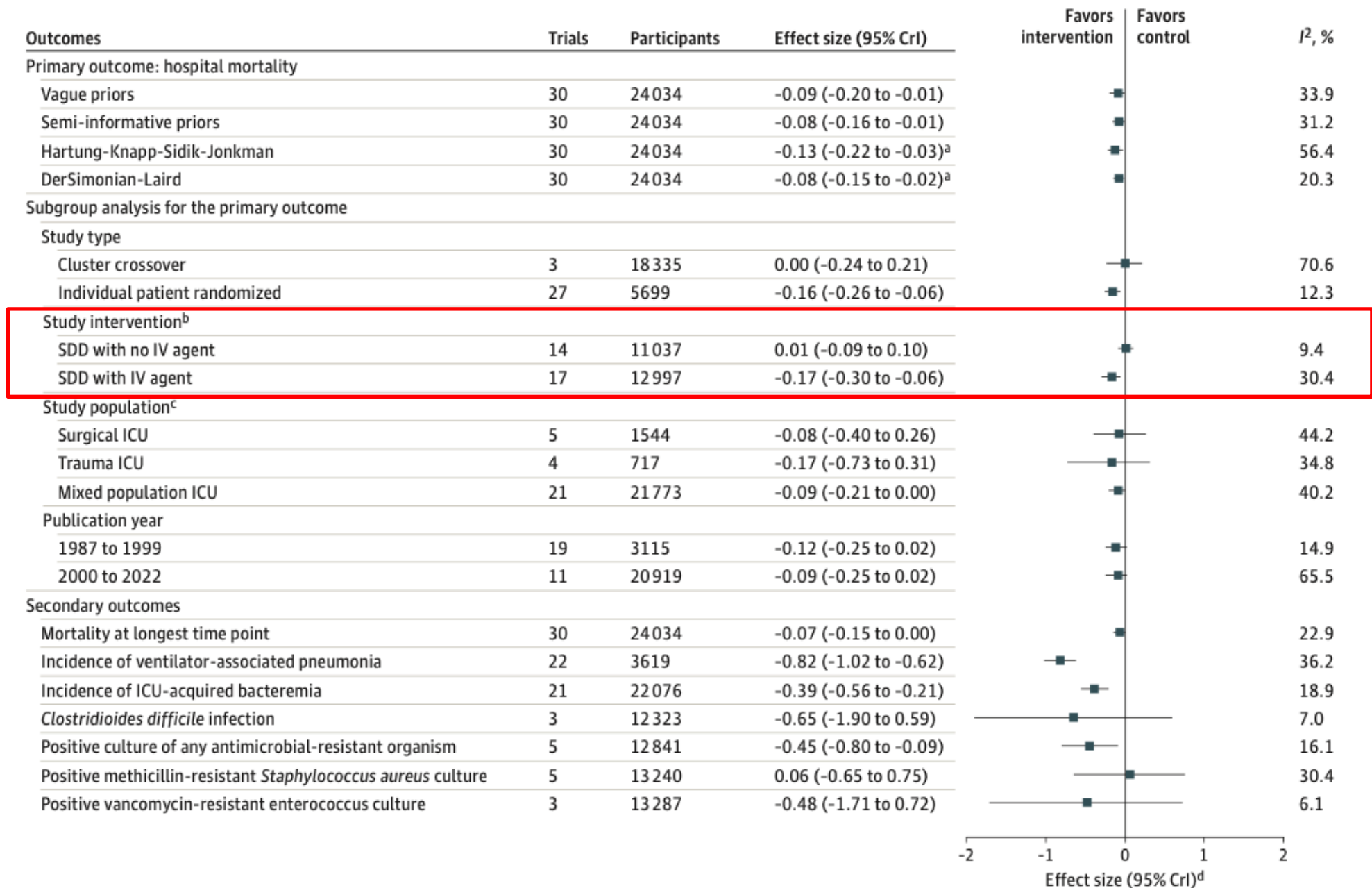
Frequentist

Sidik-Jonkman 0.88 (0.80-0.97)

DerSimonian-Laird 0.92 (0.86-0.98)



Risk ratio (95% CI)



# Organisational aspects of ASP


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RESEARCH

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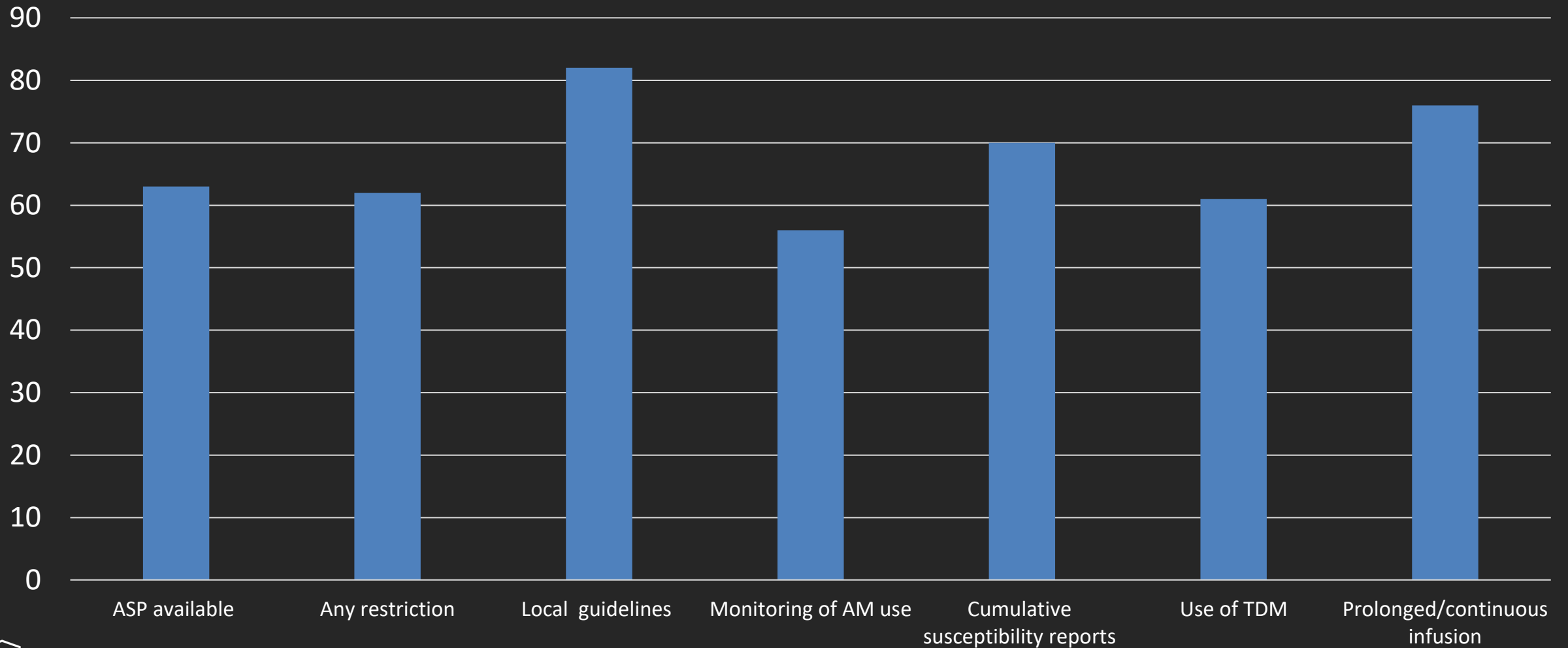
# Antimicrobial stewardship, therapeutic drug monitoring and infection management in the ICU: results from the international A-TEAMICU survey

Christian Lanckohr<sup>1</sup>, Christian Boeing<sup>1</sup>, Jan J. De Waele<sup>2</sup>, Dylan W. de Lange<sup>3</sup>, Jeroen Schouten<sup>4</sup>, Menno Prins<sup>5</sup>, Maarten Nijsten<sup>6</sup>, Pedro Pova<sup>7</sup>, Andrew Conway Morris<sup>8</sup> and Hendrik Bracht<sup>9\*</sup> 

## Abstract

**Background:** Severe infections and multidrug-resistant pathogens are common in critically ill patients. Antimicrobial stewardship (AMS) and therapeutic drug monitoring (TDM) are contemporary tools to optimize the use of anti-

# ASP components in ICUs



## **White Paper: Bridging the gap between human and animal surveillance data, antibiotic policy and stewardship in the hospital sector—practical guidance from the JPIAMR ARCH and COMBACTE-MAGNET EPI-Net networks**

**Maria Diletta Pezzani<sup>1†</sup>, Elena Carrara<sup>1†</sup>, Marcella Sibani <sup>1\*</sup>, Elisabeth Prestler<sup>2,3,4</sup>, Petra Gastmeier<sup>5,6</sup>, Hanna Renk<sup>7</sup>, Souha S. Kanj<sup>8</sup>, Thirumalaisamy P. Velavan<sup>9,10,11</sup>, Le Huu Song<sup>10,12</sup>, Leonard Leibovici<sup>13</sup>, Didem Torumkuney<sup>14</sup>, Tomislav Kostyanev<sup>15</sup>, Marc Mendelson<sup>16‡</sup> and Evelina Tacconelli<sup>1,17,18‡</sup> on behalf of the ARCH working group§**

<sup>1</sup>*Infectious Diseases Section, Department of Diagnostics and Public Health, University of Verona, Verona, Italy;* <sup>2</sup>*European Committee on Infection Control, Basel, Switzerland;* <sup>3</sup>*ESCMID Study group for nosocomial infections, Basel, Switzerland;* <sup>4</sup>*Department of Infection Control and Hospital Epidemiology, Medical University of Vienna, Vienna, Austria;* <sup>5</sup>*German Centre for Infection Research Association (DZIF), Braunschweig, Germany;* <sup>6</sup>*Institute for Hygiene and Environmental Medicine, Charité - Universitätsmedizin Berlin, Germany, corporate member of Freie Universität Berlin, Humboldt-Universität zu Berlin, and Berlin Institute of Health, Berlin, Germany;* <sup>7</sup>*University Children's Hospital Tübingen, Department of Paediatric Cardiology, Pulmology and Intensive Care Medicine, Tübingen,*

**Table 4.** Leadership commitment, accountability and antimicrobial stewardship team

---

**Participants in the antimicrobial stewardship team**

---

1.1. Essential

All hospitals should establish a multidisciplinary antimicrobial stewardship team. The core members should always include an antibiotic prescriber and a pharmacist trained in infection management, antimicrobial usage and antimicrobial resistance or another professional with a similar role.

---

1.2. Desirable

The antimicrobial stewardship team should have core members comprising an infectious disease specialist and/or a clinical microbiologist, and an infection control professional trained in antimicrobial usage and resistance.

---

1.3. Desirable

Include additional figures in the core group according to the setting, resources and type of intervention (i.e. other specialists from target wards, infection control nurses, clinical psychologists and IT experts).

---

**Institutional support for organization and management of antimicrobial stewardship programmes: legal framework**

---

1.4. Essential

Regulate and promote antimicrobial stewardship activities at every level of the healthcare organization with well-defined roles and responsibilities and a clear governance structure.

---

**Institutional support for the organization and management of antimicrobial stewardship programmes: staffing personnel**

---

1.5. Essential

Include dedicated time and specific salary support for antimicrobial stewardship activities as part of antimicrobial stewardship programmes.

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1.6. Essential

Allocate full-time equivalents according to national requirements for the different settings and level of intervention, where available.

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# Opportunities in ASP

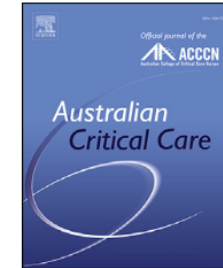
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Research paper

## Nursing experiences in antimicrobial optimisation in the intensive care unit: A convergent analysis of a national survey

Junel Padigos, MHSc (Hons), RN <sup>a, b, \*</sup>, Simon Reid, PhD <sup>b</sup>, Emma Kirby, PhD <sup>c</sup>, Chris Anstey, MSc FANZCA FCICM <sup>d, f</sup>, Jennifer Broom, PhD FRACP <sup>e, f</sup>

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### A B S T R A C T

**Background:** Recent evidence highlights the need for an interdisciplinary approach to antimicrobial stewardship (AMS). Nursing involvement in optimising antimicrobials in the intensive care unit (ICU) remains understudied.

**Objective:** The objective of this study was to explore nurses' perceptions and experiences of antimicrobial optimisation or stewardship in ICUs in Australia.

**Methods:** An anonymous web-based survey was deployed nationally in early 2021 through two ICU nursing networks. Associations between survey responses were analysed descriptively and by using



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# Australian Critical Care

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Research paper  
data were integrated.

**Results:** A total of 226 ICU nurses completed the survey. The majority (197/226; 87%) responded that **lack of education** limits engagement in AMS. Only 13% (30/226) reported the presence of AMS education and training for nurses in their ICUs. Only about half (108/226; 48%) of the nurses **were confident to question prescribers when they considered that the antimicrobial prescribed was unnecessary**, with nurses in senior roles more likely to do so than nurses providing bedside care ( $p < 0.05$ ). Gaps in education (including unfamiliarity with AMS roles), **noninclusive antimicrobial discussions**, moral distress, and **potential workload burden** were seen as potential barriers/challenges to engagement.

**Conclusion:** The multifactorial barriers identified that inhibit nurses from performing AMS tasks could be addressed by strengthening interprofessional education at all levels and by applying practical AMS in-

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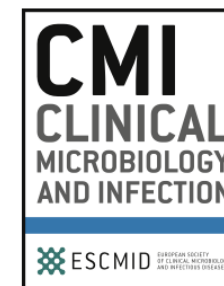
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# Clinical Microbiology and Infection

journal homepage: [www.clinicalmicrobiologyandinfection.com](http://www.clinicalmicrobiologyandinfection.com)



Narrative review

## Indications for medical antibiotic prophylaxis and potential targets for antimicrobial stewardship intervention: a narrative review

Petros Ioannou<sup>1</sup>, Stamatis Karakonstantis<sup>1</sup>, Jeroen Schouten<sup>2</sup>, Tomislav Kostyanov<sup>3</sup>, Esmita Charani<sup>4</sup>, Vera Vlahovic-Palcevski<sup>5</sup>, Diamantis P. Kofteridis<sup>1,\*</sup>, supported by the ESCMID Study Group for Antimicrobial Stewardship (ESGAP)

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<sup>4</sup> Health Protection Research Unit in Healthcare Associated Infections and Antimicrobial Resistance, Imperial College London, UK

<sup>5</sup> Department of Clinical Pharmacology, University Hospital Rijeka / Medical Faculty and Faculty of Health Studies, University of Rijeka, Rijeka, Croatia

### ARTICLE INFO

*Article history:*

### ABSTRACT



*Background:* Most of the antimicrobial stewardship (AMS) literature has focused on antimicrobial con-

# Potential targets for AMS interventions

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- Reducing unnecessary prophylaxis beyond recommended indications
- Reducing the use of prophylaxis with a broader spectrum than necessary
- reducing the use of prophylaxis for longer than the recommended duration

## **Why we prescribe antibiotics for too long in the hospital setting: a systematic scoping review**

**Robin M. E. Janssen** <sup>1,2,3\*</sup>, **Anke J. M. Oerlemans**<sup>2</sup>, **Johannes G. Van Der Hoeven**<sup>1</sup>, **Jaap Ten Oever** <sup>3,4</sup>,  
**Jeroen A. Schouten**<sup>1,2,3</sup> and **Marlies E. J. L. Hulscher**<sup>2,3</sup>

<sup>1</sup>Department of Intensive Care Medicine, Radboud Institute for Health Sciences, Radboud University Medical Center, Nijmegen, The Netherlands; <sup>2</sup>Scientific Center for Quality of Healthcare (IQ healthcare), Radboud Institute for Health Sciences, Radboud University Medical Center, Nijmegen, The Netherlands; <sup>3</sup>Radboud Center for Infectious Diseases (RCI), Radboud University Medical Center, Nijmegen, The Netherlands; <sup>4</sup>Department of Internal Medicine, Radboud Institute for Health Sciences, Radboud University Medical Center, Nijmegen, The Netherlands

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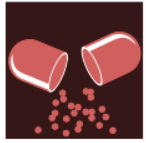
**Background:** In daily hospital practice, antibiotic therapy is commonly prescribed for longer than recommended in guidelines. Understanding the key drivers of prescribing behaviour is crucial to generate meaningful interventions to bridge this evidence-to-practice gap.

**Objectives:** To identify behavioural determinants that might prevent or enable improvements in duration of

**Table 2.** Determinants describing group differences in antibiotic therapy duration

Category	Determinants
1. Pathogen factors	Resistant (+) versus non-resistant pathogens <sup>42</sup>
2. Disease factors	Type of infection (either + or -) <sup>35</sup> Type of infection in palliative patient/end-of-life patient (either + or -) <sup>28</sup> Severity of infection (either + or -) <sup>35</sup> Clinical infectious disease not meeting certified diagnostic criteria (+) (e.g. VAP criteria) <sup>31</sup>
3. Patient factors	<i>Type of surgery [emergency (+) versus elective surgery]</i> <sup>30</sup> Age of patient (+) <sup>31</sup> End-of-life vignette (either + or -) <sup>28</sup> <i>Age of patient (-)</i> <sup>30</sup>
4. Professional factors	<i>Being a consultant (-) versus other occupations</i> <sup>38</sup> Prescriber personality traits [extraversion, more likely to choose to continue antibiotics (+); agreeableness, less likely to continue antibiotics (-)] <sup>38</sup> <i>Profession of healthcare provider [nurse (+) versus aesthetic technician]</i> <sup>34</sup> <i>Academic career [orthopaedic surgeon (+) versus (associate) professor]</i> <sup>26</sup> <i>Number of arthroplasties per month [1-10 (+) versus &gt;10]</i> <sup>26</sup>
5. Hospital department factors	<i>Type of medical specialty [surgical (+) versus general medical]</i> <sup>25</sup> <i>Type of surgical (sub)specialty/surgical procedure [orthopaedic, neurological, urological and gastroenterology (+)]</i> <sup>27</sup> <i>Patient care department [orthopaedic surgery (+) versus obstetrics &amp; gynaecology]</i> <sup>34</sup>

(+), longer duration of antibiotic treatment; (-), shorter duration of antibiotic treatment. Text in Roman type denotes antibiotic therapy studies; text in italic type denotes antibiotic prophylaxis studies.



*Article*

# Instant Gratification and Overtreating to Be Safe: Perceptions of U.S. Intensive Care Unit Pharmacists and Residents on Antimicrobial Stewardship

Katharina Rynkiewich <sup>1,\*</sup> , Kruthika Uttla <sup>2</sup> and Leila Hojat <sup>3,4</sup> 

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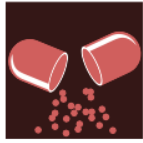
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**Abstract:** Antimicrobial stewardship programs have been associated with numerous impacts on





## Article

# Instant Gratification and Overtreating to Be Safe: Perceptions of

standings of the value of antimicrobial stewardship among medical practitioners vary. Additionally, non-physician practitioners are regularly left out of antimicrobial stewardship interventions targeting antimicrobial decision-making. Here, we contribute the **perspective from resident physicians and specialists in pharmacy** regarding their involvement in antimicrobial prescribing. Notably, our semi-structured interviews with 10 residents and pharmacy specialists described their **limited autonomy in the clinical setting**. However, the participants regularly worked alongside primary antimicrobial decision-makers and described **feeling pressure to overtreat to be safe**. The clear rationales and motivations associated with antimicrobial prescribing have a **noticeable impact on physicians in training and non-physician practitioners**, and as such, we argue that antimicrobial stewardship interventions targeting primary antimicrobial decision-makers are missing an opportunity to address the breadth

OH 44106, USA

\* Correspondence: [krynkievich@fau.edu](mailto:krynkievich@fau.edu)

**Abstract:** Antimicrobial stewardship programs have been associated with numerous impacts on

## RESEARCH ARTICLE

# Use of stewardship smartphone applications by physicians and prescribing of antimicrobials in hospitals: A systematic review

R. I. Helou<sup>1</sup>, D. E. Foudraine<sup>1</sup>, G. Catho<sup>2</sup>, A. Peyravi Latif<sup>3</sup>, N. J. Verkaik<sup>1</sup>,  
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## Abstract

### Background

Antimicrobial stewardship (AMS) programs promote appropriate use of antimicrobials and reduce antimicrobial resistance. Technological developments have resulted in smartphone

### OPEN ACCESS

**Citation:** Helou RI, Foudraine DE, Catho G, Peyravi Latif A, Verkaik NJ, Verbon A (2020) Use of

## Results

Thirteen studies met the eligibility criteria. None was a randomized controlled trial. Methodological study quality was considered low to moderate in all but three qualitative studies. The primary outcomes were process indicators, adherence to guidelines and user experience. Guidelines were more frequently accessed by app (53.0% - 89.6%) than by desktop in three studies. Adherence to guidelines increased (6.5% - 74.0%) significantly for several indications after app implementation in four studies. Most users considered app use easy (77.4%—>90.0%) and useful (71.0%—>90%) in three studies and preferred it over guideline access by web viewer or booklet in two studies. However, some physicians regarded app use adjacent to colleagues or patients unprofessional in three qualitative studies. Susceptibility to several antimicrobials changed significantly post-intervention (from 5%

## Abstract

### Background

Antimicrobial stewardship (AMS) programs promote appropriate use of antimicrobials and reduce antimicrobial resistance. Technological developments have resulted in smartphone

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REVIEW

Open Access



# Artificial Intelligence in Infection Management in the ICU

Thomas De Corte<sup>1,2\*</sup>, Sofie Van Hoecke<sup>3</sup> and Jan De Waele<sup>1,2</sup>

## Abstract

This article is one of ten reviews selected from the Annual Update in Intensive Care and Emergency Medicine 2022. Other selected articles can be found online at <https://www.biomedcentral.com/collections/annualupdate2022>. Further information about the Annual Update in Intensive Care and Emergency Medicine is available from <https://link.springer.com/bookseries/8901>.

## Introduction

Research and development of data-driven artificial intelligence (AI), so-called machine learning, in the intensive care unit (ICU) is at an all-time high. Data scientists and physicians are exploring the potential of machine learning in a vast range of domains, including infection man-

important progress has been made in the infection management field as well [2–4]. In this chapter, we provide an overview of the current stance of AI/machine learning research in different areas of antimicrobial infection management, the barriers that hinder clinical adaptation, and pitfalls for bedside use.

# Surgeons, Infectious Diseases, and Twitter Hit a Home Run for Antibiotic Stewardship

Debra A. Goff,<sup>1</sup> John Alverdy,<sup>2</sup> Anthony T. Gerlach,<sup>1</sup> Julio Mayol,<sup>3</sup> and Benedict Nwomeh<sup>4</sup>

<sup>1</sup>Department of Pharmacy, Ohio State University Wexner Medical Center, Ohio State University College of Pharmacy, Columbus, Ohio, USA; <sup>2</sup>Department of Surgery, University of Chicago, Chicago, Illinois, USA; <sup>3</sup>Hospital Clínico San Carlos, Instituto de Investigación Sanitaria San Carlos, Universidad Complutense de Madrid, Madrid, Spain; and <sup>4</sup>Department of Pediatric Surgery, Nationwide Children's Hospital, Columbus, Ohio, USA

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Many infectious diseases (ID) clinicians join Twitter to follow other ID colleagues or “like” people. While there is great value in engaging with people who have similar interests, there is equal value in engaging with “unlike” or non-ID people. Here, we describe how Twitter connected an ID pharmacist with a pediatric surgeon, a vice chair of surgery, a surgeon chief medical officer from Spain, and a surgical intensive care unit pharmacist. This Twitter collaboration resulted in several scholarly activities related to antibiotic resistance and antibiotic stewardship and served as a conduit for global collaboration.

**Keywords.** social media; Twitter; antibiotic stewardship; antibiotic resistance; surgeons.

The coronavirus disease 2019 (COVID-19) global pandemic required antibiotic stewardship programs (ASPs) to pause from providing daily antibiotic prospective audit and feedback of antibiotics to developing COVID-19 guidelines, managing drug shortages, completing emergency use authorization forms, and

the authors of this viewpoint confirmed that 63% of 173 responding ID clinicians and surgeons initially followed people within their specialty. While there is great value in engaging with people and organizations with similar interests, there is equal value in engaging with “unlike” or non-ID people and organizations. ID clinicians and

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