



**ΕΘΝΙΚΟ ΚΑΙ ΚΑΠΟΔΙΣΤΡΙΑΚΟ ΠΑΝΕΠΙΣΤΗΜΙΟ ΑΘΗΝΩΝ**  
**ΣΧΟΛΗ ΕΠΙΣΤΗΜΩΝ ΥΓΕΙΑΣ**  
**ΙΑΤΡΙΚΗ ΣΧΟΛΗ**

**ΠΡΟΓΡΑΜΜΑ ΜΕΤΑΠΤΥΧΙΑΚΩΝ ΣΠΟΥΔΩΝ «ΛΟΙΜΩΞΙΟΛΟΓΙΑ» 2021-2022**

**ΔΙΑΜΟΡΦΩΣΗ ΕΡΕΥΝΗΤΙΚΗΣ  
ΔΗΜΟΣΙΕΥΣΗΣ: ΕΠΟΠΤΙΚΟ ΥΛΙΚΟ**

*Ευδοξία Κυριαζοπούλου*  
*Παθολόγος, Επιμελήτρια Β*  
*ΠΓΝ ΑΤΤΙΚΟΝ*

# ΕΙΔΗ ΕΡΕΥΝΗΤΙΚΩΝ ΣΗΜΟΣΙΕΥΣΕΩΝ

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## ORIGINAL ARTICLE

### Urinary Leukotriene E<sub>4</sub> and Prostaglandin D<sub>2</sub> Metabolites Increase in Adult and Childhood Severe Asthma Characterized by Type 2 Inflammation

A Clinical Observational Study

Johan Kolmert<sup>1,2,3</sup>, Cristina Gómez<sup>1,2,3</sup>, David Balgoma<sup>1,2,3</sup>, Marcus Sjödin<sup>1,2,3</sup>, Johan Bood<sup>1,3,4</sup>, Jon R. Konradsen<sup>1,5,6</sup>, Magnus Ericsson<sup>7</sup>, John-Olof Thörnigren<sup>7</sup>, Anna James<sup>1,3</sup>, Maria Mikus<sup>1,3</sup>, Ana R. Sousa<sup>8</sup>, John H. Riley<sup>8</sup>, Stewart Bates<sup>8</sup>, Per S. Bakke<sup>9</sup>, Ioannis Pantis<sup>10</sup>, Massimo Caruso<sup>11,12</sup>, Pascal Chanez<sup>10</sup>, Stephen J. Fowler<sup>14</sup>, Thomas Geiser<sup>15</sup>, Peter Howarth<sup>16</sup>, Ildikó Horváth<sup>17</sup>, Norbert Krug<sup>18</sup>, Paolo Montuschi<sup>19</sup>, Marek Sarak<sup>20</sup>, Annelie Behndig<sup>21</sup>, Dominick E. Sharr<sup>22</sup>, Richard G. Knowles<sup>23</sup>, Cécile T. J. Holweg<sup>24</sup>, Åsa M. Wheelock<sup>25</sup>, Barbro Dahlén<sup>24</sup>, Björn Nordlund<sup>26</sup>, Kjell Ålving<sup>26</sup>, Gunilla Hedlin<sup>1,5,6</sup>, Kian Fan Chung<sup>10</sup>, Ian M. Adcock<sup>10</sup>, Peter J. Sterk<sup>27</sup>, Ratko Djukanovic<sup>18</sup>, Sven-Erik Dahlén<sup>1,5,6</sup>, and Craig E. Wheelock<sup>2,3,4</sup>, on behalf of the U-BIOPRED Study Group

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## ORIGINAL ARTICLE

### Case Fatality Rates for Patients with COVID-19 Requiring Invasive Mechanical Ventilation

A Meta-analysis

Zheng Jie Lim<sup>1\*</sup>, Ashwin Subramaniam<sup>2,3\*</sup>, Mallikarjuna Ponnappa Reddy<sup>2,4</sup>, Gabriel Blecher<sup>5,6</sup>, Umesh Kadam<sup>7,8</sup>, Afsana Atroz<sup>9,10</sup>, Baki Billah<sup>9</sup>, Sushma Ashwin<sup>11</sup>, Mark Kubicki<sup>1</sup>, Federico Bilotta<sup>12</sup>, J. Randall Curtis<sup>13,14</sup>, and Francesca Rubulotta<sup>15</sup>

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## What Sepsis Researchers Can Learn from COVID-19

To the Editor:

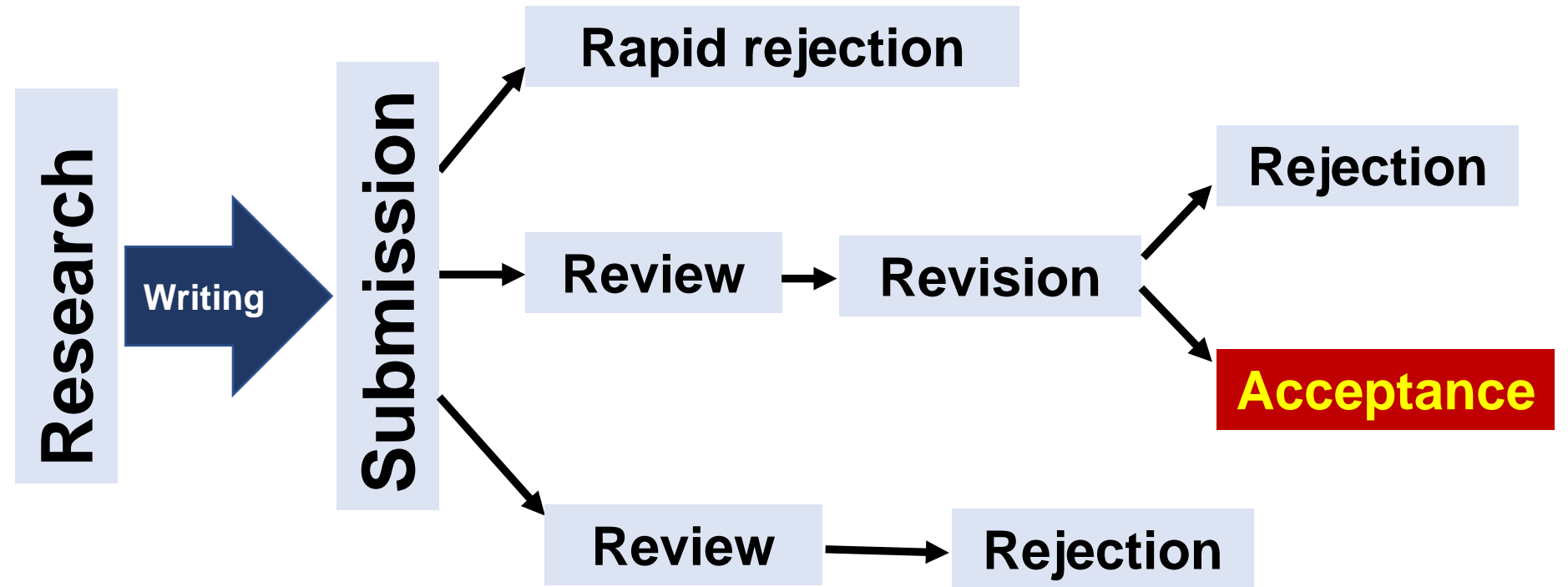
Despite intensive research efforts, the search for new therapeutic options for sepsis has yielded no result (1). However, the ongoing coronavirus disease (COVID-19) pandemic shows that effective therapeutic options for the distinct subgroup of viral sepsis due to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection can be found within months (2). What can sepsis researchers learn from the way COVID-19 is studied?

Original  
research

Review  
Systematic  
(± Meta-analysis)  
or  
Narrative

Other  
Opinion letters  
Editorials  
Case reports  
etc

# ΠΟΡΕΙΑ ΕΡΕΥΝΗΤΙΚΩΝ ΔΗΜΟΣΙΕΥΣΕΩΝ





Tip 10 - Choice of journal: define a list of target journals!

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Ανάλογα με γνωστικό αντικείμενο

Ανάλογα με σκοπό/ προφίλ περιοδικού

Ανάλογα με συντελεστή απήχησης

# ΕΠΙΛΟΓΗ ΠΕΡΙΟΔΙΚΟΥ: ΠΡΟΦΙΛ ΠΕΡΙΟΔΙΚΟΥ



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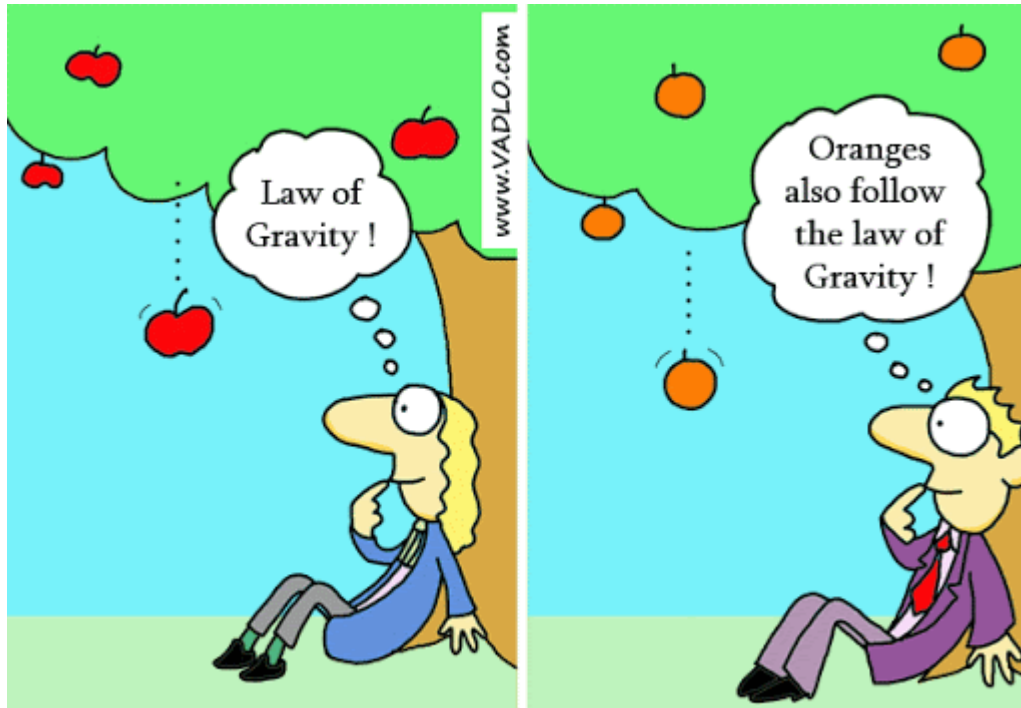
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SJR

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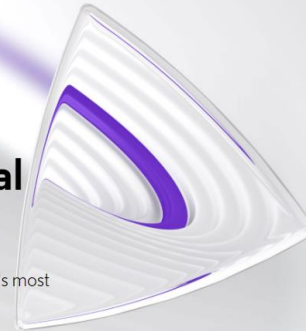
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Cover letter



Manuscript



Figures/ Tables



Supplement



Checklist of reporting guidelines



COI etc



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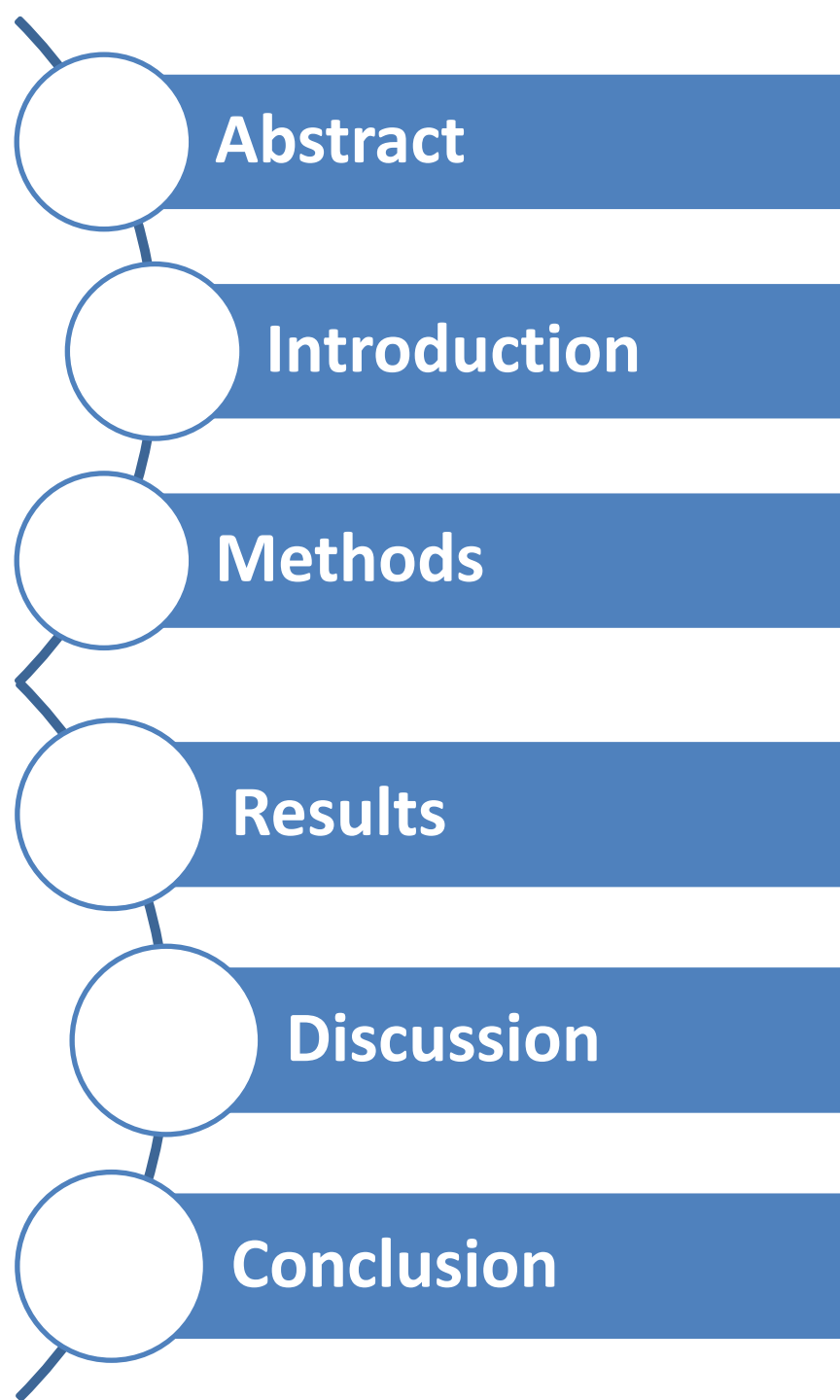
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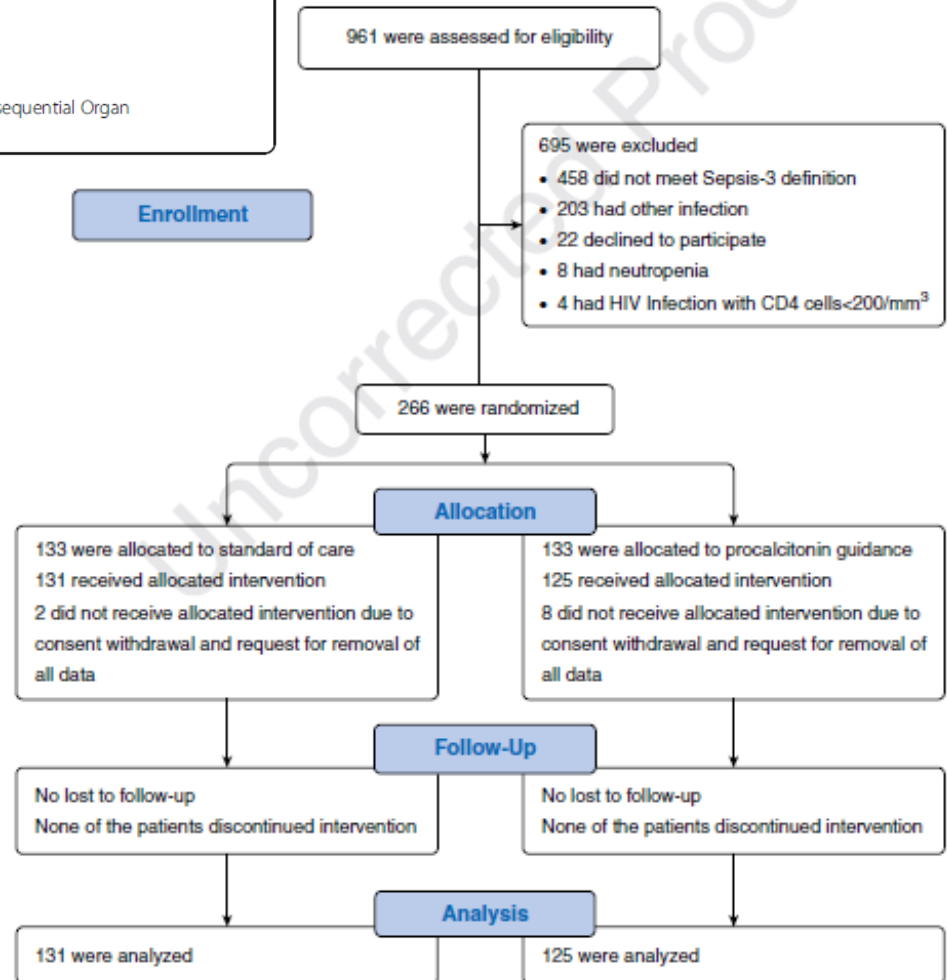
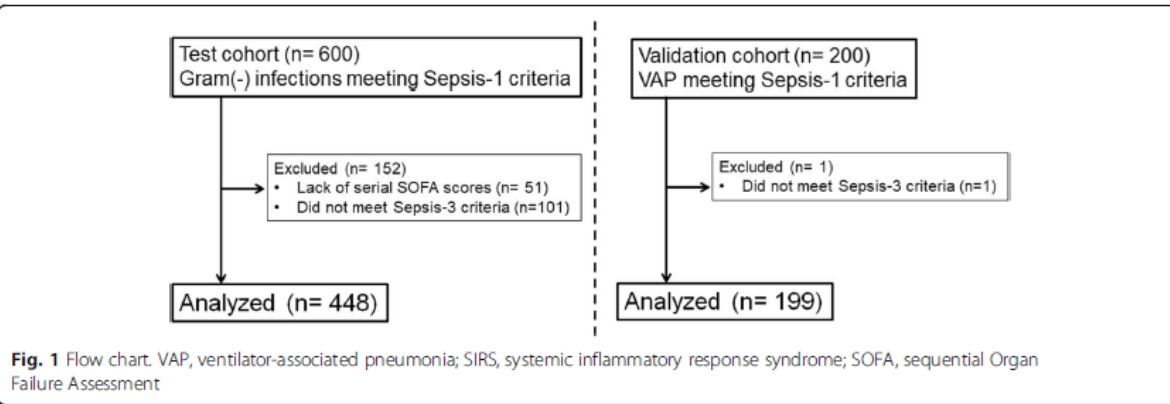
# Manuscript



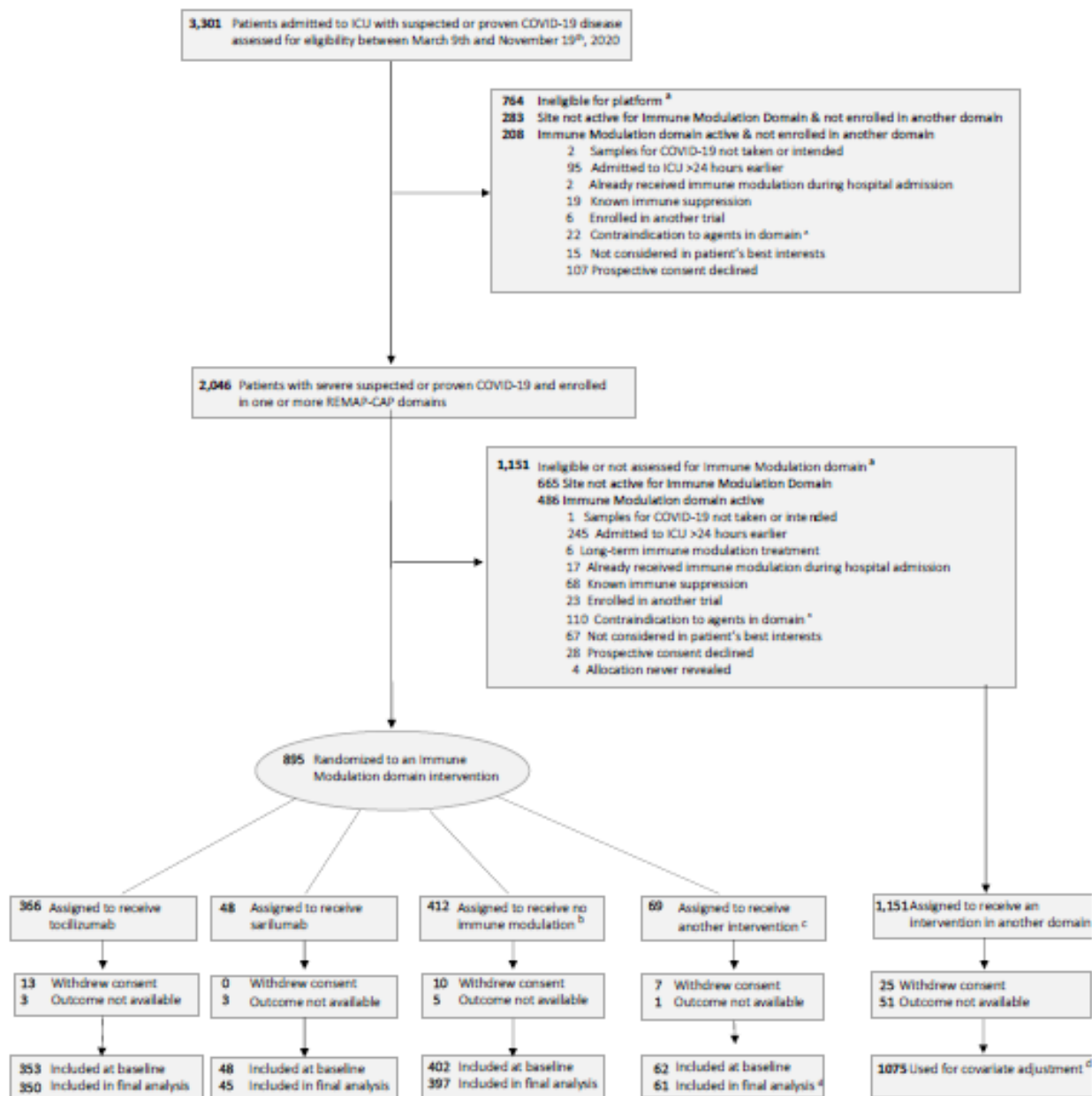
# Methods and Results: Figures and Tables

- Το Α και το Ω μιας δημοσίευσης
- Πρέπει να μπορούν να «στέκονται» αυτόνομα – να περιέχουν μια ολοκληρωμένη πληροφορία
- Απαραίτητο να φαίνεται ανάμεσα σε ποιες ομάδες γίνεται η σύγκριση και ο αριθμός των ασθενών/πειραματοζώων κλπ ανά ομάδα καθώς και η τιμή του στατιστικού κριτηρίου σύγκρισης
- Η παρουσίαση πρέπει να είναι ευκρινής και ελκυστική

# Study flow chart I



# Study flow chart II



# Table of baseline demographics I

**Table 1.** Baseline Characteristics of Enrolled Patients

	Standard of Care (n = 131)	PCT Guidance (n = 125)	All Patients (N = 256)
Age, mean (SD), yr	78.0 (13.1)	79.6 (9.8)	78.6 (11.6)
Sex, M, n (%)	62 (45.8)	52 (40.8)	114 (44.5)
Charlson's comorbidity index, mean (SD)	6.0 (2.4)	5.6 (1.9)	5.8 (2.2)
Septic shock, n (%)	9 (6.9)	9 (7.2)	18 (7.0)
APACHE II score, mean (SD)	13.3 (4.7)	13.0 (4.6)	13.2 (4.7)
SOFA score, mean (SD)	4.1 (2.2)	4.1 (2.1)	4.1 (2.2)
Procalcitonin, median (Q1–Q3), µg per liter	0.53 (0.15–5.03)	0.86 (0.17–5.95)	0.65 (0.17–5.77)
Meeting stopping rule on Day 5, n (%)			
≥80% decrease of initial serum PCT	32 (24.4)	35 (28.0)	67 (26.2)
Serum PCT <0.5 µg per liter	74 (56.5)	71 (56.8)	145 (56.6)
Combined criteria	92 (70.2)	89 (71.2)	181 (70.7)
Meeting stopping rule after Day 5*, n (%)	N/A	20 (16.0)	N/A
Noncompliance with PCT stopping rule because of medical instability, n (%)	N/A	13 (10.4)	N/A
Overall compliance with PCT stopping rule, n (%)	N/A	96 (76.8)	N/A
Type of infection, n (%)			
Community-acquired pneumonia	57 (43.5)	55 (44.0)	112 (43.8)
Healthcare-associated pneumonia	27 (20.6)	16 (12.8)	43 (16.8)
Acute pyelonephritis	44 (33.6)	51 (40.8)	95 (37.1)
Primary bloodstream infection	1 (0.8)	2 (1.6)	3 (1.2)
Hospital-acquired pneumonia	2 (1.5)	1 (0.8)	3 (1.2)
Microbiological documentation, n (%)			
<i>E. coli</i>	22 (16.7)	24 (19.2)	46 (18.0)
<i>K. pneumoniae</i>	7 (5.3)	5 (4.0)	12 (4.7)
<i>P. aeruginosa</i>	2 (1.5)	1 (0.8)	3 (1.2)
<i>S. pneumoniae</i>	8 (6.1)	4 (3.2)	12 (4.7)
<i>H. influenzae</i>	8 (6.7)	6 (5.0)	14 (5.5)
<i>S. aureus</i>	3 (2.3)	3 (2.4)	6 (2.3)
<i>C. difficile</i>	0 (0.0)	0 (0.0)	0 (0.0)
Other	6 (4.6)	9 (7.2)	15 (5.9)
Multidrug-resistant pathogen	6 (4.6)	4 (3.2)	10 (3.9)
Extensively drug-resistant	0 (0.0)	0 (0.0)	0 (0.0)
Pandrug-resistant	0 (0.0)	0 (0.0)	0 (0.0)
Positive blood culture, n (%)	23 (17.6)	19 (15.2)	42 (16.4)
Empiric treatment according to ESCMID guidelines, n (%) <sup>†</sup>	112 (85.5)	103 (82.4)	215 (84.0)

# Table of baseline demographics II

**Table 1** Comparative baseline demographics of the two cohorts

	Derivation cohort (n= 448)	Validation cohort (n= 199)	p value
Male gender, n (%)	213 (47.5)	147 (73.9)	<0.001
Age (years, mean ± SD)	71.7 ± 16.6	58.4 ± 19.1	<0.001
SOFA score (mean ± SD)	6.1 ± 4.1	7.8 ± 3.4	<0.001
APACHE II score (mean ± SD)	15.1 ± 7.4	17.1 ± 5.7	0.001
CCI (mean ± SD)	4.1 ± 2.5	2.6 ± 1.7	<0.001
PaO <sub>2</sub> /FIO <sub>2</sub> ratio (mean ± SD)	298.8 ± 112.6	218.5 ± 98.0	<0.001
Mechanical ventilation, n (%)	90 (20.1)	199 (100)	<0.001
Characteristics of MV population			
Tidal volume (ml/kg, mean ± SD)	6.6 ± 0.9	6.5 ± 0.9	0.179
PEEP level (mmHg, mean ± SD)	5.7 ± 0.9	6 ± 0.9	0.011
PaO <sub>2</sub> /FIO <sub>2</sub> ratio (mean ± SD)	252.7 ± 113.7	218.5 ± 98.0	0.020
Duration of MV (days, mean ± SD)	14.5 ± 13.8	14.7 ± 10.4	0.346
Underlying infection, n (%)			
Acute pyelonephritis	207 (46.2)	0 (0)	NA
Acute intra-abdominal infection	162 (36.2)	0 (0.0)	NA
Primary Gram-negative bacteremia	71 (15.8)	0 (0.0)	NA
Secondary Gram-negative bacteremia (other than urinary or intra-abdominal)	8 (1.8)	0 (0.0)	0.107
Ventilator-associated pneumonia	0 (0)	199 (100.0)	NA
Early (<7 days of MV)		84 (42.2)	
Late (>7 days of MV)		115 (57.8)	
Septic shock, n (%)	88 (19.6)	85 (42.7)	<0.001
ARDS, n (%)	136 (30.4)	150 (75.4)	<0.001
ICU admission, n (%)	90 (20.1)	198 (99.5)	<0.001
ICU LOS (days, mean ± SD)	45.3 ± 94.3	36.9 ± 34.4	0.317
Hospital LOS (days, mean ± SD)	20.0 ± 47.6	51.7 ± 47.5	<0.001
For ICU-admitted population	49.6 ± 98.9	51.7 ± 47.5	0.006
For non-ICU-admitted population	12.6 ± 0.9	NA	
ICU mortality, n (%)	49 (54.4)	89 (44.9)	0.162
Hospital mortality, n (%)	123 (27.5)	110 (55.3)	<0.001
28-day mortality, n (%)	102 (22.8)	59 (29.6)	0.075
90-day mortality, n (%)	118 (26.3)	153 (76.9)	<0.001

Abbreviations: ARDS: Acute Respiratory Distress Syndrome, SD: standard deviation, SOFA: Sequential Organ Failure Assessment, APACHE: Acute Physiology and Chronic Health Evaluation, CCI: Charlson's comorbidity index, ICU: Intensive Care Unit, LOS: Length of Stay, MV: mechanical ventilation, NA: not applicable

# Other Tables and Figures

- Σε μια κλινική μελέτη είμαστε υποχρεωμένοι να δώσουμε σε πίνακα αναλυτικά τα δεδομένα για **primary and secondary outcomes**
- Σε μια κλινική μελέτη είμαστε υποχρεωμένοι να δώσουμε σε πίνακα αναλυτικά τα δεδομένα για **AE/SAE**
- Βασικό Figure συνήθως αποτελεί το **primary outcome** ή το **καίριο στοιχείο της έρευνας**



# Methods and Results I

- Συνήθως γράφονται μαζί καθώς το ένα κομμάτι απαντά στο άλλο
- Στις μεθόδους είμαστε όσο πιο αναλυτικοί μπορούμε, εξηγούμε τι ακριβώς πράξαμε υπό ποιες συνθήκες και πότε. Ορίζουμε με ακρίβεια νόσους και συνθήκες και εξηγούμε πιθανές παραδοχές.
- Αν πρόκειται για κλινική μελέτη ή μελέτη με ζώα απαραίτητο στα methods να δίνονται οι απαραίτητοι αριθμοί πρωτοκόλλου των **εγκρίσεων**. Ειδικά για κλινική μελέτη απαραίτητος και ο **αριθμός καταγραφής** σε μια έγκυρη βάση καταγραφής κλινικών μελετών (πχ [clinicaltrials.gov](http://clinicaltrials.gov))

# Methods and Results II

- Σειρά methods και results κατά προτίμηση πρέπει να είναι ίδια
- Συχνές οι υποκεφαλίδες για μεγαλύτερη σαφήνεια

## 2. Patients and methods

### 2.1. Study design

This was a retrospective analysis of prospectively collected clinical data of patients with infections and SIRS who were admitted to the 65 clinical sites that participate in HSSG. The study protocol was approved by the hospital ethics committees. All methods were performed in accordance with the relevant guidelines and regulations. Patients were enrolled after written informed consent was provided by themselves or their first-degree relatives in cases where patients were unable to consent themselves. The approved protocol and the informed consent form (ICF) allowed the analysis of clinical data and treatment modalities of patients in relation to final outcome. As a consequence, no new protocol submission for approval was needed and no new ICF was col-

### 2.2. Pre-defined analysis plan

Only patients with CAP and sepsis classified according to the new Sepsis-3 criteria were analysed. Patients treated with cef-tazidime were excluded. Four treatment groups were formed:

- clarithromycin group, comprising all available patients treated with a combination of clarithromycin and one  $\beta$ -lactam;
- azithromycin group, comprising patients treated with a combination of azithromycin and one  $\beta$ -lactam;
- respiratory fluoroquinolone group, comprising patients treated with moxifloxacin or levofloxacin alone; and

### 2.3. Study endpoints

The primary study endpoint was comparative 28-day mortality between the clarithromycin group and the  $\beta$ -lactam group.

The secondary study endpoints were: (a) impact of clarithromycin intake on 28-day mortality in comparison with the other groups; (b) time to development of new organ dysfunction between the clarithromycin group and the  $\beta$ -lactam group; and (c) impact of clarithromycin intake on resolution of CAP in comparison with the other groups. Resolution of CAP was defined as resolution of the signs of SIRS and the symptoms compatible with CAP (cough, sputum production, dyspnoea, auscultatory rales) at the completion of 7 days of treatment.

### 2.4. Statistical analysis

The baseline characteristics of the four treatment groups were compared. Dichotomous variables were analysed using the Chi-squared test and quantitative variables were analysed by

# Introduction and Discussion

Συχνά γράφονται μαζί καθώς το ένα φυσική συνέχεια του άλλου

## Introduction

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**1 σελίδα A4**

**3-4 παράγραφοι το πολύ**

We aimed to show that.....

Our aim was to investigate if...

We conducted the.... trial to show that....

1<sup>η</sup> παράγραφος = μια γενικότητα



2-3<sup>η</sup> παράγραφος = εστίαση περισσότερο στο θέμα



Τέλος = ξεκάθαρη αναφορά στο σκοπό μας

# Discussion, τέχνη και εμπειρία...

Η πρώτη παράγραφος έρχεται ως απάντηση στο ερώτημα που θέσαμε στην τελευταία παράγραφο του Introduction και είναι σύνοψη των κύριων ευρημάτων

Long-term use of antibiotics causes substantial damage to the gut flora, increasing the risk of infections caused by *C. difficile* and MDROs in critically ill patients, which are associated with poor clinical outcomes (14, 15). We conducted the PROGRESS (Procalcitonin-guided Antimicrobial Therapy to Reduce Long-Term Sequelae of Infections) trial to investigate whether the PCT-guided early discontinuation of antibiotic therapy would reduce the incidence of adverse events associated with these long-term infection sequelae in patients with sepsis that are driven by the prolonged use of antibiotics. These include death by MDROs and acquisition of infections by *C. difficile* and MDROs.

## Discussion

In this multicenter randomized trial, we found that early discontinuation of antimicrobial therapy guided by a PCT measurement below  $<0.5 \mu\text{g}$  per liter or a reduction of at least 80% from the baseline at Day 5 or later significantly reduced the rate of infection-associated adverse events. Following the PCT-guidance approach, the length of antibiotic therapy was reduced and there were survival benefits in terms of reduction in both in-hospital and 28-day mortality reflecting a direct impact on all baseline infections.

In the PROGRESS trial, we demonstrate for the first time that PCT-guided early discontinuation of antimicrobials in patients with sepsis prevents infection caused by MDROs and/or *C. difficile*. Two important

# Discussion

- 2-3 σελίδες
- Συζήτηση κύριων και δευτερευόντων ευρημάτων στο πλαίσιο ως τώρα υπαρχόντων στοιχείων
- 10-20 βιβλιογραφικές παραπομπές το πολύ
- Οχι «θέσφατα» χωρίς βιβλιογραφική στήριξη
- Added value of the study vs Limitations (όσο το δυνατόν μεγαλύτερη ειλικρίνεια)

## Conclusion

- Η τελευταία παράγραφος
- Σύνοψη του κύριου μηνύματος
- Όσο πιο catchy γίνεται
- Να αφήνει νέο παράθυρο για μετέπειτα έρευνα

## Conclusions

The use of PCT guidance for early discontinuation of antimicrobials in medically stable and afebrile patients with sepsis demonstrated significant clinical benefits. The PCT-guidance approach was associated with lower infection-associated adverse events, lower 28-day mortality, shorter LOT, early hospital discharge, and decreased costs of hospitalization. These benefits may have substantial impact on public health, particularly for countries with high antimicrobial consumption. ■

# Abstract-Keywords



Tip 2 - Title and abstract: sell your paper!

- Γράφεται στο τέλος
- Σχεδόν όλα τα περιοδικά με περιορισμό λέξεων
- Σχεδόν όλα τα περιοδικά ζητούν structured abstract
- Introduction, Methods, Results, Conclusion

- Μικρογραφία του manuscript
- Τα αποτελέσματα όσο πιο αναλυτικά γίνεται (με νούμερα!!!)





Tip 12 - Responding to reviewers: don't get frustrated!