



Translational Medicine

Changing paradigm in Eastern Europe

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Background



Exodus



<http://www.eekh.hu/>

	Specialised in anaesthesia&crit. care	Still in medical practice
2007	55	36

What could be the reasons?

2011	78	26
Total	341	182

- We've lost 261 anaesthetist/intensivist over 5 years
- Planning to work in the West 2012:
 - Out of 175 doctors: 55% trainees, 53% specialist

Courtesy of Dr. Dóra Varga



System failure



- Limited number of devoted specialists
- Authorocratic rule of heads of departments
- Residency **Key to future** whether being trained and working
- Missing or inadequate **MOTIVATION**



Situation in 2010



My survey as a RAE in 2010



SZEGEDI TUDOMÁNYEGYETEM
Szent-Györgyi Albert Klinikai Központ
Aneszteziológiai és Intenzív Terápiás Intézet
Intézetvezető: Prof. Dr. Molnár Zsolt
Cím: 6725 Szeged, Semmelweis u. 6.
Telefón: 62 - 545 168, Fax: 62 - 545 593



Specialists

II. A szakképzést nehezítő legalapvetőbb hiányosságok (Szeged nélkül):

1. Hiányzik minimum 24 szakorvos – amíg ezt a kórházak nem rendezik, a képzés, továbbképzés, oktatás feltételei magától értetődően, nem teljesülhetnek
2. Hiányzik minimum 84 szakápoló – bár az létezik a kórházban, a szakképzés feltételeihez, de elfogadhatatlan, hogy a kórház hiányosságokat fogadjanak el szakmai standardnak, ami nem tükrözi a hazai és nemzetközi szakmai minimumfeltételeket, ráadásul bizonyítottan rontja a betegek

Nurses

8/10 hospitals unsuitable for proper training

ismertetésével kérésre mellékelem.)



Lack of specialists



Bogár L, és mtsai. *Aneszt Intenzív Terápia* 2012; 42: 69-76

5. táblázat. Az egyszerre két műtőben vagy műtőben és intenzív osztályon is dolgozó aneszteziológussal ellátott műtők százalékos aránya

	n	Műtők	Egyszerre 2 műtőben dolgozó	Egyszerre 2 műtőben dolgozó aneszt. orvosokkal ellátott műtők aránya	Egyszerre két feladattal: műtővel és intenzív osztályon
Összes					
Városi kórházak	1	100,0	0	0%	0%
Megyei kórházak	1	100,0	0	0%	0%
Egyetemi klinikák	4	100,0	0	0%	1%
Országos int.	4	21,0	0	0%	0%
Észak-Mo.	13	61,0	4,4 (18)	14,4%	17,6%
Észak-Alföld	11	97,5	2,0 (8)	4,1%	10,3%
Dél-Alföld	11	75,5	4,0 (16)	10,6%	13,9%
Dél-Dunántúl	10	65,0	0,5 (2)	1,5%	6,9%
Nyugat-Dunántúl	8	47,0	3,5 (14)	14,9%	21,3%
Közép-Dunántúl	7	46,5	3,0 (12)	12,9%	19,4%
Közép-Mo.	11	71,0	7,5 (30)	21,1%	23,9%

**1 anaesthetist in 2 ORs:
11 (0-26)%**

**Same doctor for ICU+OR:
15 (0-35)%**



Thrown into deep water...



Bogár L, és mtsai. *Aneszt Intenzív Terápia* 2012; 42: 69-76

1. táblázat. A szakmai kapacitásadatok és a rezidens- illetve szakorvosképzési jellegzetességek intézményi átlagai

	n	A műtők átlagszáma	Az ITO átl. napi beteg-	Első önálló aneszt.	Rezidenseknek szervezett elméleti képzés (alk./év)	Rezidensi számonkérés (alk./26 hó)	Közp. ITO-n munka	Központi gyakorlat (alk./év)
Összes	71				11,6			
Városi kórházak								
Megyei kórházak								
Egyetemi klinikák								
Országos int.					7,0			
Észak-Mo.	13	5,1		5,5	16,9	10,2	10,8	23,2
Észak-Alföld	11	8,9	9,6	4,4	16,6	2,7	10,2	20,0
Dél-Alföld	11	6,9	7,4	5,6	4,9	1,8	9,2	18,2
Dél-Dunántúl	10	6,5	6,8	6,0	10,5	5,0	19,3	21,3
Nyugat-Dunántúl	8	5,9	7,2	4,6	5,3	2,3	12,6	5,5

**1st anaesthesia
on your own after
univ:
6 (2-7) months**

**On ICU/5 years
of training:
11 (9-19) months**

>20 years after The Wall came down...



We need to talk!



SepsEast  2012
1st Central and Eastern European Sepsis Forum

SepsEast  2014
2nd Central and Eastern European Sepsis Forum

SepsEast  2016
3rd Central and Eastern European Sepsis Forum



ELSEVIER

Contents lists available at [ScienceDirect](#)

Journal of Critical Care

journal homepage: www.jccjournal.org





Shared legacy in Eastern Europe



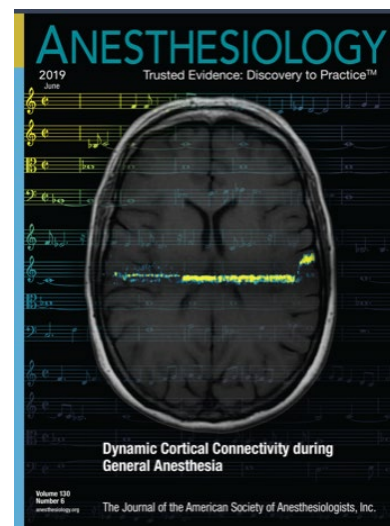
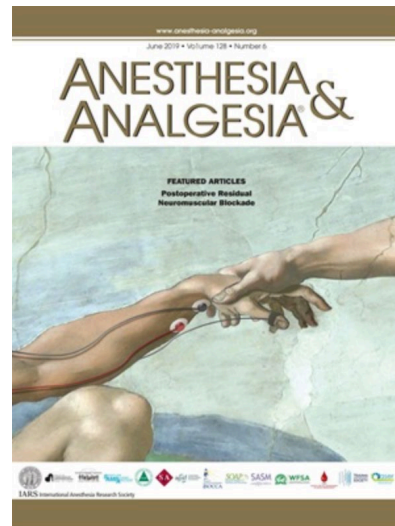
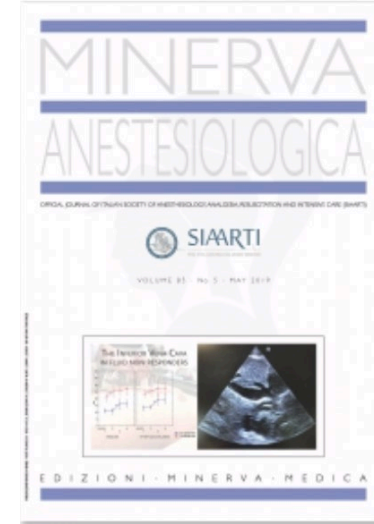
- Patient care
 - Same drugs, same equipments – same price
 - Problems with funding
 - Quality varies from hospital-to-hospital
- Human resources
 - Exodus of doctors & nurses
 - Income?
- Training, teaching
 - Not structured: „by chance”
 - Intensive care is combined with anaesthesiology – priority?
- Research
 - PhD training
 - Structured clinical research - no
 - Not enough grants – centralized to the Hungarian Academy



Research output from Eastern Europe



















Publications: West vs. East





May 2018-June 2019











Journal	No of articles/year	From Eastern Europe
EJA 	180	2: (letter)  
Acta Anaesth Scand 	233	1: 
ICM 	438	-
Minerva Anaesth 	211	3: 2 -  1 - 
A&A 	420	1: 
Anesthesiol 	460	-
JCC 	273	1: 
CCM 	643	1: 
	2858	9/6



ClicalTrials.gov



Country (Population, M)	Registered (ongoing)	Original
 (10)	541	40
 (38)	978	223
 (10)	660	162
 (20)	273	45
		
		
 (11)	1665	850
 (8)	1317	717
(46)	5608	3033 (54%)

High quality research is not solely the question of money – but mentality and will



Scientific mirror

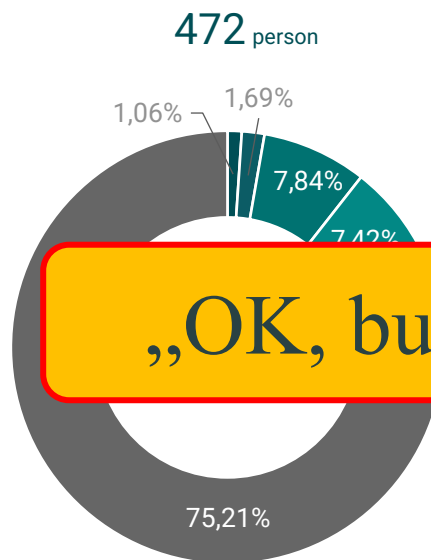


Scientific activity

Analysis of one of the Hungarian universities

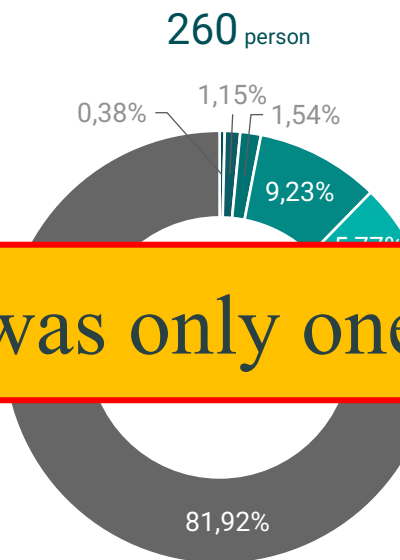
2011 – first or last authorships

ACADEMIC - LECTURER FL IF



■ 20-50 ■ 10-20 ■ 5-10 ■ 2,5-5 ■ 0-2,5 ■ 0
5 pers. 8 pers. 37 pers. 35 pers. 32 pers. 355 pers.

ACADEMIC - SCIENTISTS FL IF



■ 20-50 ■ 10-20 ■ 5-10 ■ 2,5-5 ■ 0-2,5 ■ 0
1 pers. 3 pers. 4 pers. 24 pers. 15 pers. 213 pers.

MEDICAL ONLY FL IF



■ 20-50 ■ 10-20 ■ 5-10 ■ 2,5-5 ■ 0-2,5 ■ 0
0 pers. 1 pers. 4 pers. 8 pers. 9 pers. 606 pers.

„OK, but this was only one specific year...”



Scientific mirror

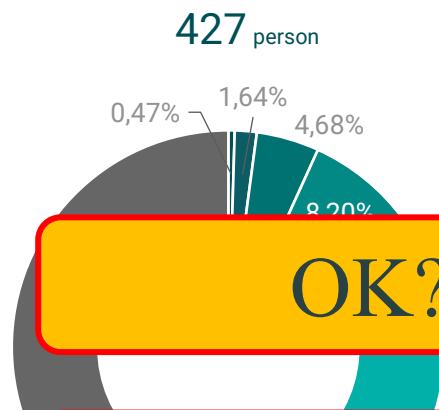


Scientific activity

Analysis of one of the Hungarian universities

2008-2011 (4 year period) – first or last authorships

ACADEMIC - LECTURER FL IF



ACADEMIC - SCIENTISTS FL IF

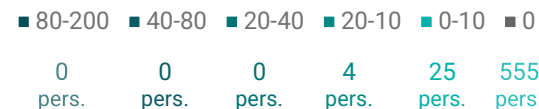
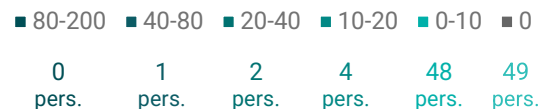
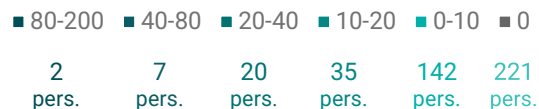


MEDICAL ONLY FL IF



OK? But this was a long time ago!

(Then fasten your seatbelts and watch out...)





Is there a way out?



Pécs, 2016 – TM was founded



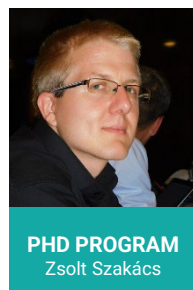
STRATEGY
Péter Hegyi



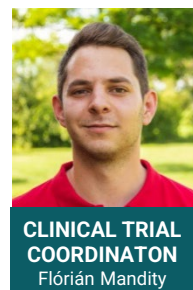
OPERATION
Andrea Szentesi



MEDICAL GROUP
Bálint Eröss



PHD PROGRAM
Zsolt Szakács



**CLINICAL TRIAL
COORDINATOR**
Flórián Mandity



**CLINICAL TRIAL
COORDINATION**
Katalin Márta



**CLINICAL TRIAL
COORDINATION**
Noémi Zádory



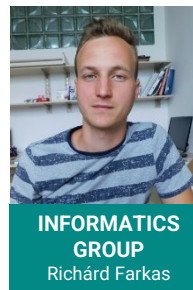
**METAANALYSIS
COORDINATION**
Szabolcs Kiss



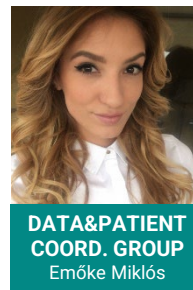
**PATIENT REGIST.
COORDINATION**
Vivien Vass



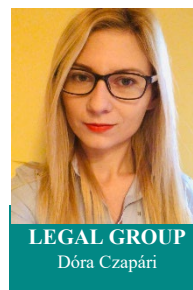
**BIostatISTICS
GROUP**
Nelli Farkas



**INFORMATICS
GROUP**
Richárd Farkas



**DATA&PATIENT
COORD. GROUP**
Emőke Miklós



LEGAL GROUP
Dóra Czapári



**COMMUNICATION
GROUP**
Dalma Dobszai



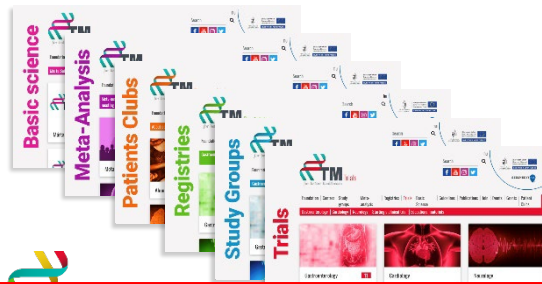
**HR&FINANCIAL
GROUP**
Margit Solymár



**HEALTH
ECONOMICS G.**
Antal Zemplényi

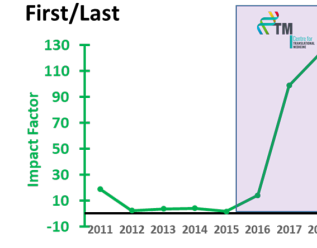
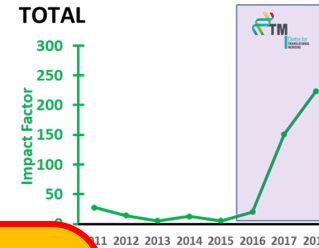
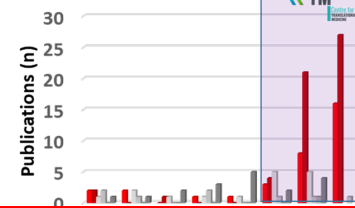
Results over 4 years

Broad range of scientific activity



Institute for Translational Medicine

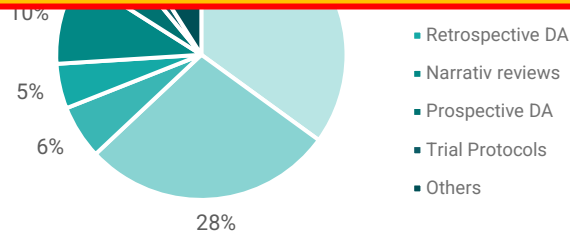
n=4:7:7/15:40:56



Year	2014	2015	2016	2017	2018
Percentage	22%	29%	70%	65,3%	20%

20% of all PTE output in 2020

Why do we need this?
Do we need this at all?



150
articles

01.01.2016 – 30.06.2019

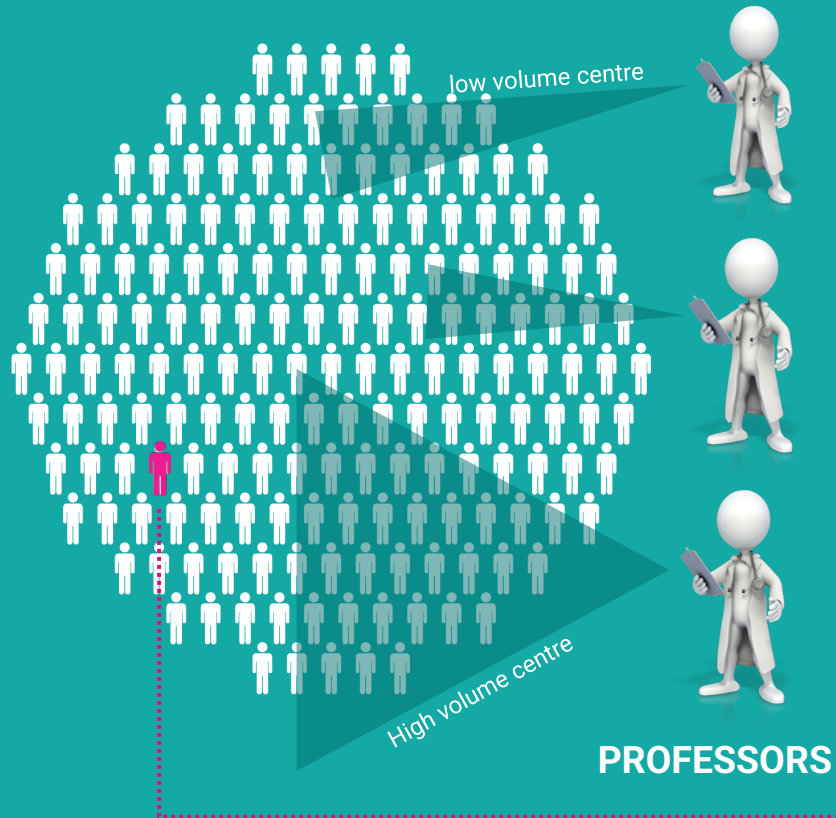
10 articles (above IF: 10.0)
21 articles (above IF: 5.0)
Average: 4.188

EXCELLENCE IS A MUST

Medicine before 2000

Individual experience

EMINENCE BASED MEDICINE

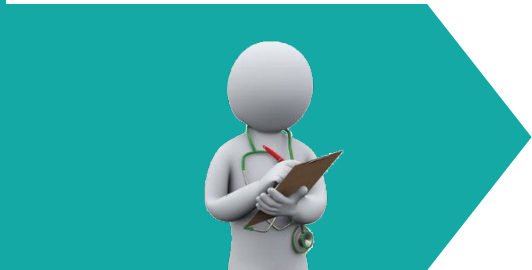


They think differently

They teach differently

They choose treatments differently

Before 2000



RESIDENTS
Need to learn
who likes what



UNLUCKY



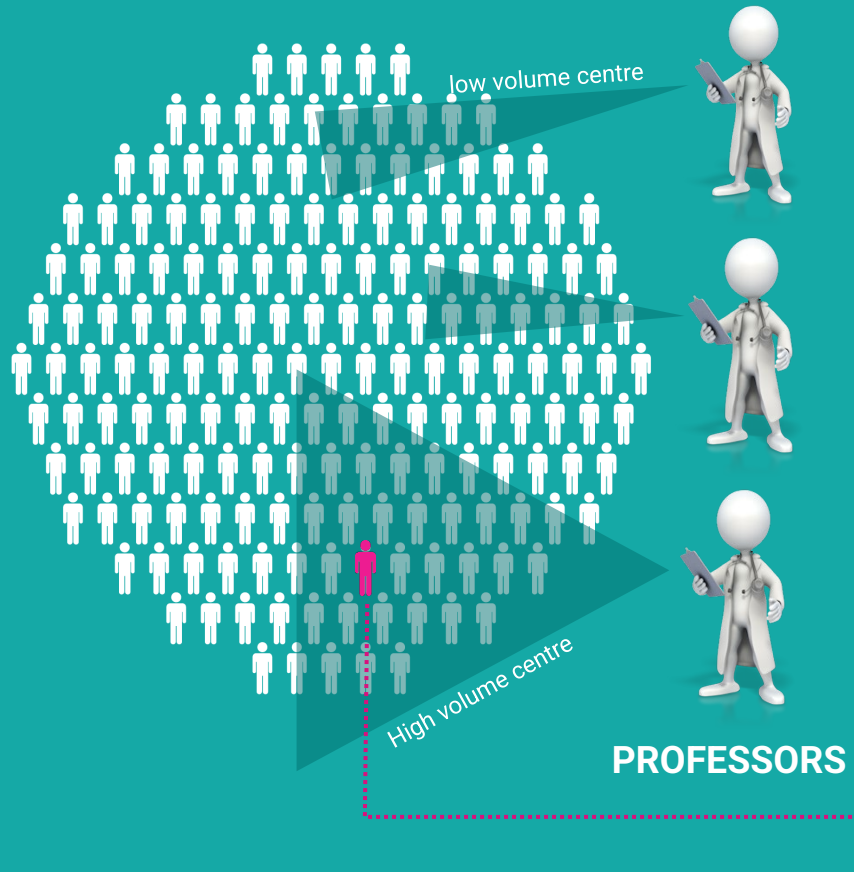


Medicine before 2000



Individual experience

EMINENCE BASED MEDICINE



They think differently

They teach differently

They choose treatments differently

Before 2000



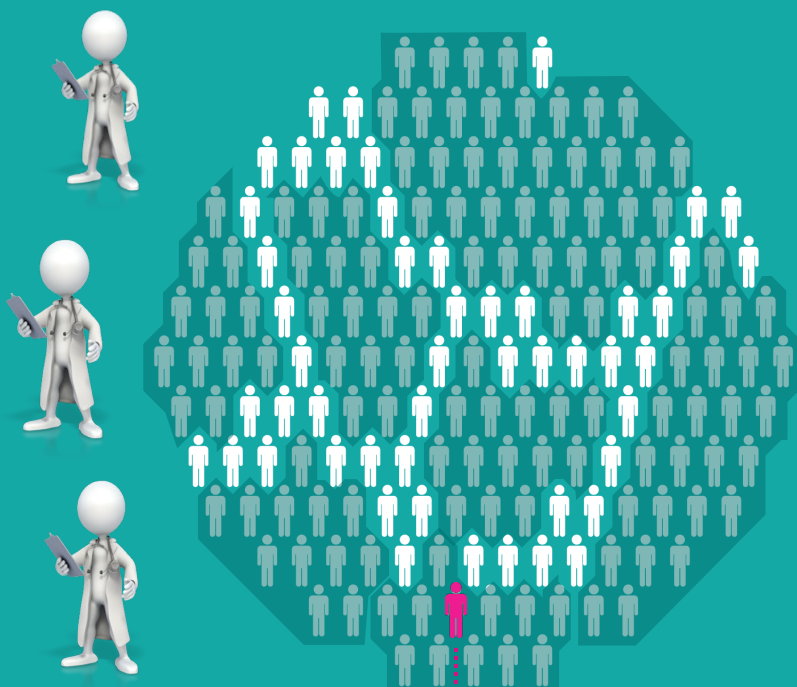
RESIDENTS
Need to learn
who likes what



LUCKY

Scientific evidence

EVIDENCE BASED MEDICINE



PROFESSORS
Generate evidences

They think the same way
They teach the same way
They treat the same way

2000 after



RESIDENTS
Need to learn
the evidences



LUCKY

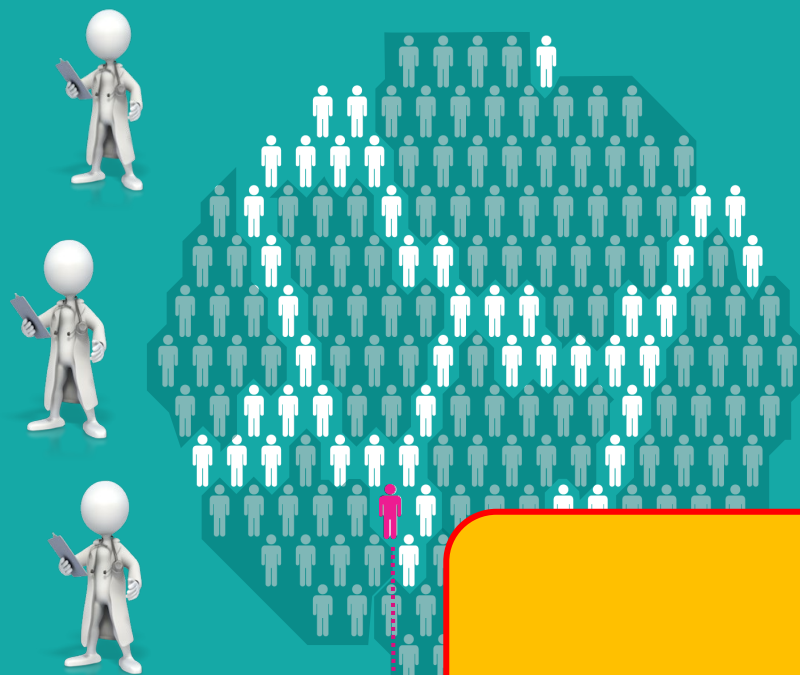


Medicine after 2000



Scientific evidence

EVIDENCE BASED MEDICINE



PROFESSORS
Generate evidences

2000 after

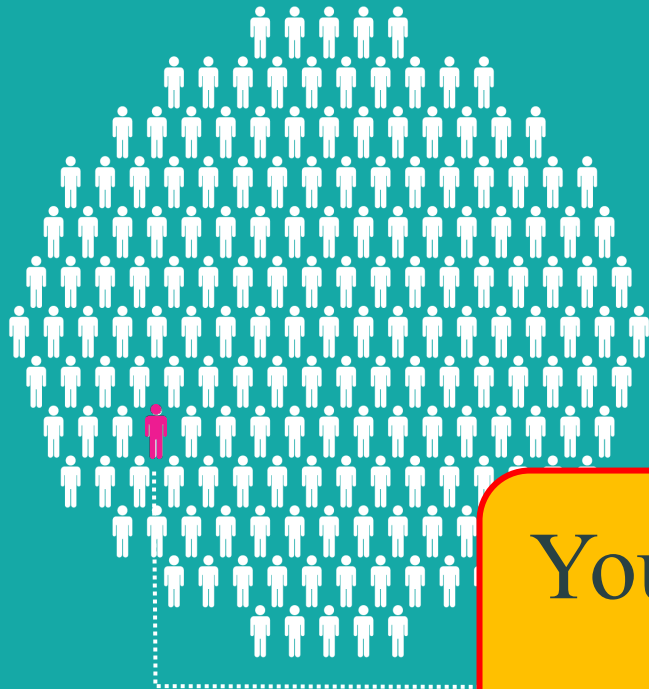
They think the same way
They teach the same way
They treat the same way



**What we need:
Science AT THE BEDSIDE**

Personalized medicine by 2040

Scientific evidence
PERSONALISED MEDICINE



Each patient handled differently



By 2040

Based on patients' genetics and conditions



You don't treat a population, but the individual



On the international scene

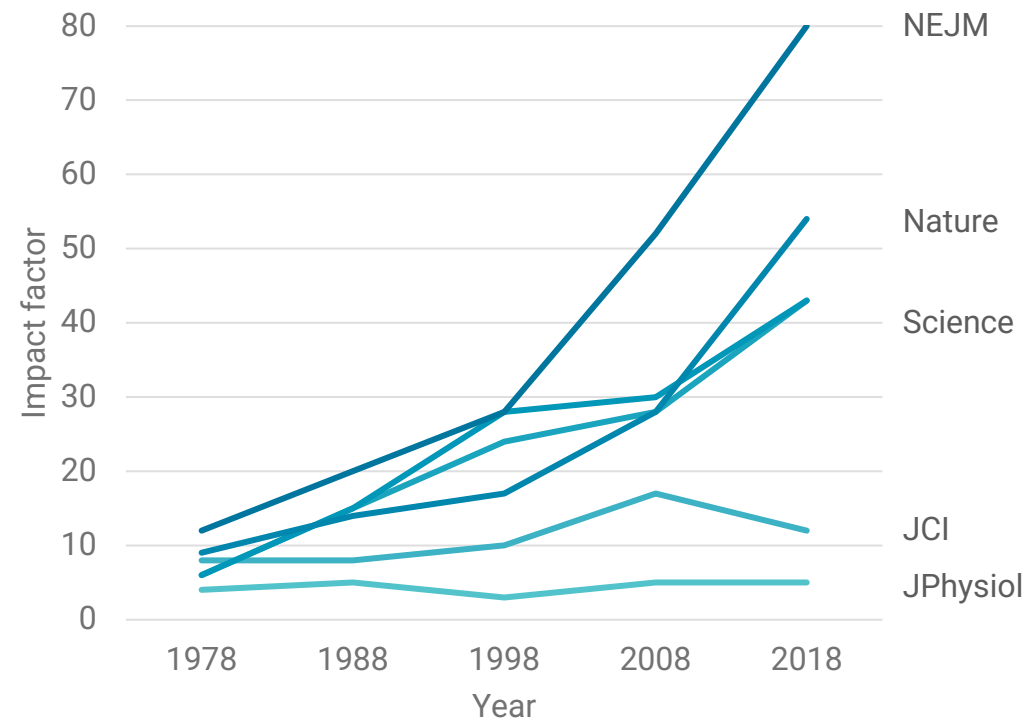


Distribution of Scientists



2-3x

Clinical journals' impact factor





In Hungary

Doctoral schools

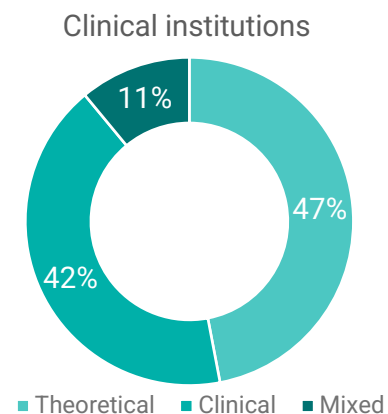
Analysis of one of the Hungarian universities

2013-2018



PhD
188

Institution	No	Subject	No
Clinical	99	theoretical	46
		clinical	42
		mixed	11

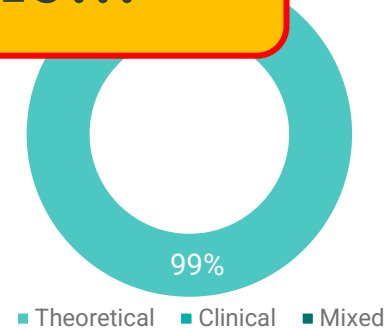


Paradigm shift is yet to come...



Clinical science
articles
133

Mixed	9	theoretical	9
SUM	188		





Research worldwide in COVID-19



Unprecedented times in medicine



250 papers per day in 2020-2021:
Unprecedented in the history of science!

Contribution of Eastern Europe is
weightless

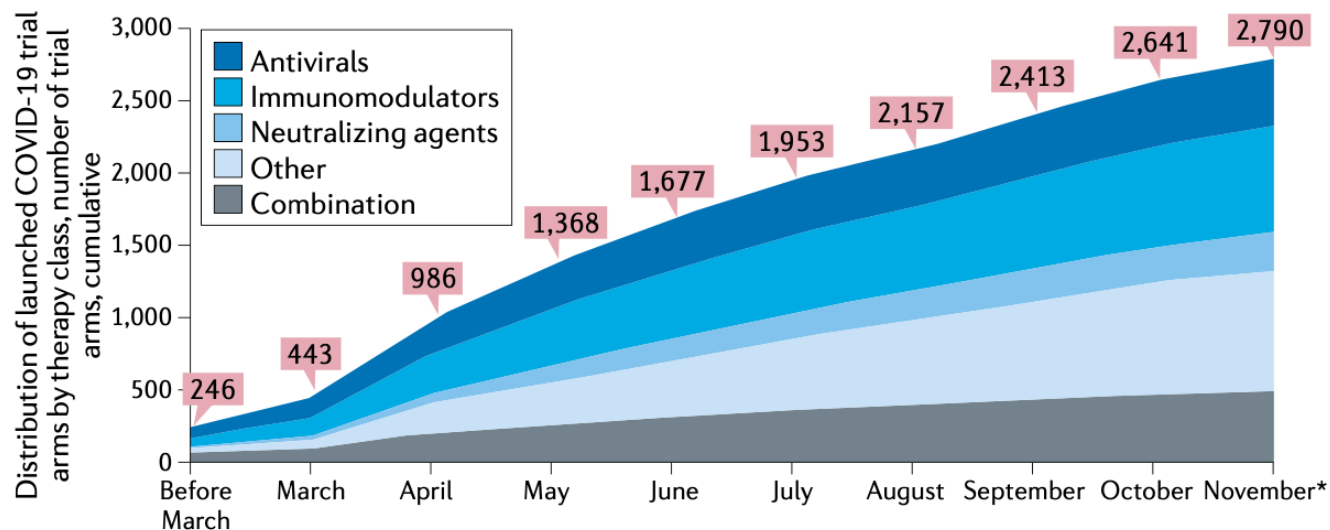


Trends in COVID-19 therapeutic clinical trials

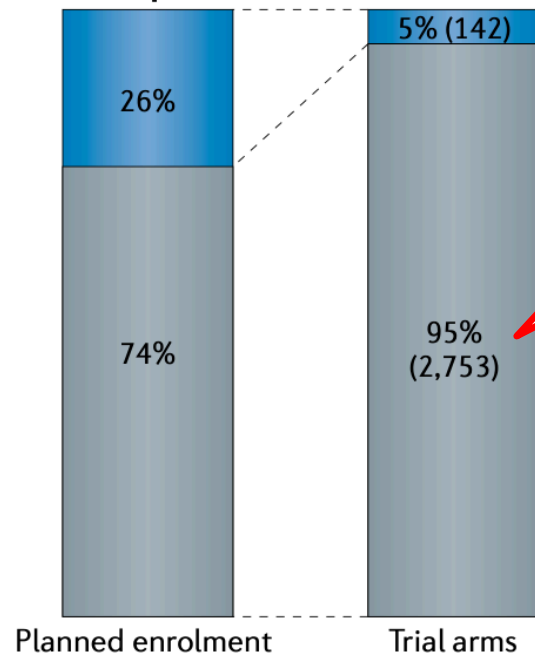
Kevin Bugin and Janet Woodcock
US Food and Drug Administration, Silver Spring,

NATURE REVIEWS | DRUG DISCOVERY

VOLUME 20 | APRIL 2021 | 255



530,692 patients 2,895 arms



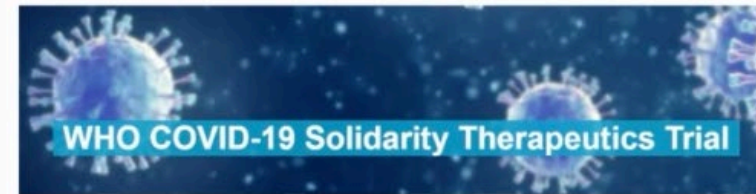
Randomized, adequately powered
All other trial arms



COVID-19: Platform trials



47,272 participants, 194 active sites



~12,000 patients, ~500 active sites



**Randomised, Eembedded, Multifactorial,
Aadaptive Platform trial**

11,077 patients, 359 active sites

RECOVERY Collaborative Group - Sample size

10 trials, patients admitted to hospital with COVID-19, primary endpoint: 28-day mortality

	Total number of patients	Usual care	Usual care + Trial drug	Survival benefit
Dexamethasone	6,425	4,321	2,104	Yes
Tocilizumab	4,116	2,094	2,022	Yes
Baricitinib	8,156	4,008	4,148	Yes
Casirivimab+Imdevimab	9,785	4,946	4,839	Yes
Aspirin	14,892	7,351	7,541	No
Hydroxychloroquine	4,716	3,155	1,561	No
Lopinavir/ritonavir	5,040	3,424	1,616	No
Azithromycin	7,763	5,181	2,582	No
Colchicine	11,340	5,730	5,610	No
Convalescent plasma	11,588	5,763	5,795	No

<https://www.recoverytrial.net/results>



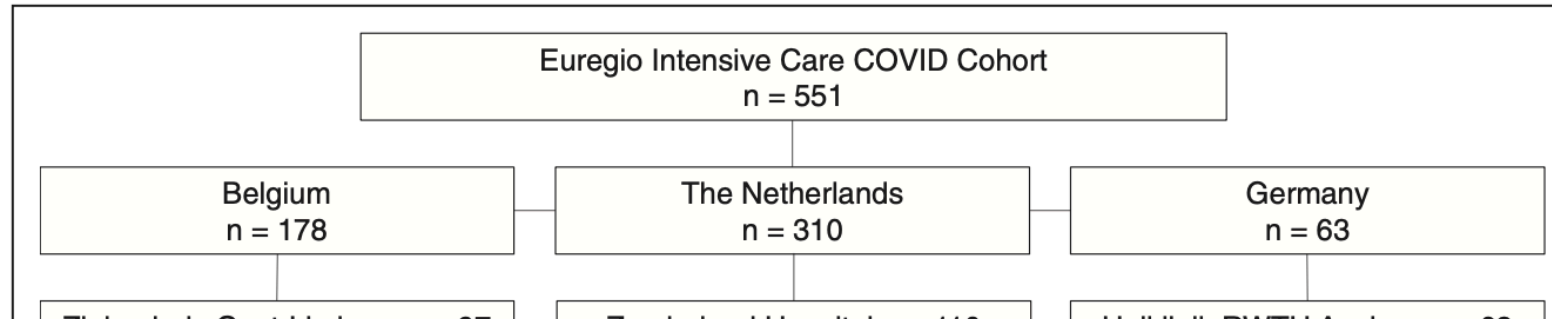


Comment on COVID-19 in Eastern Europe



Differences and Similarities Among COVID-19 Patients Treated in Seven ICUs in Three Countries Within One Region: An Observational Cohort Study*

Mesotten et al *Critical Care Medicine* April 2022 • Volume 50 • Number 4



Variables	Full Cohort (n = 551)	Belgian Part (n = 178)	Dutch Part (n = 310)	German Part (n = 63)	p
ICU outcome					
ICU mortality, %	36	22	42	44	< 0.001
Length of ICU stay, d, median (interquartile range)	15 (6–30)	10 (5–27)	14 (7–24)	33 (20–57)	< 0.001

variables	full cohort N = 434	Belgian part N = 94	Dutch part N = 277	German part N = 63	p-value
ICU mortality, %	42	29	45	44	0.018



Results of the SepsEast Registry to define the Characteristics in Coronavirus Disease in Central-Eastern Europe between March 2020-February 2021: an international, multicentre retrospective study of the SEARCH-COVID-19 Study Group

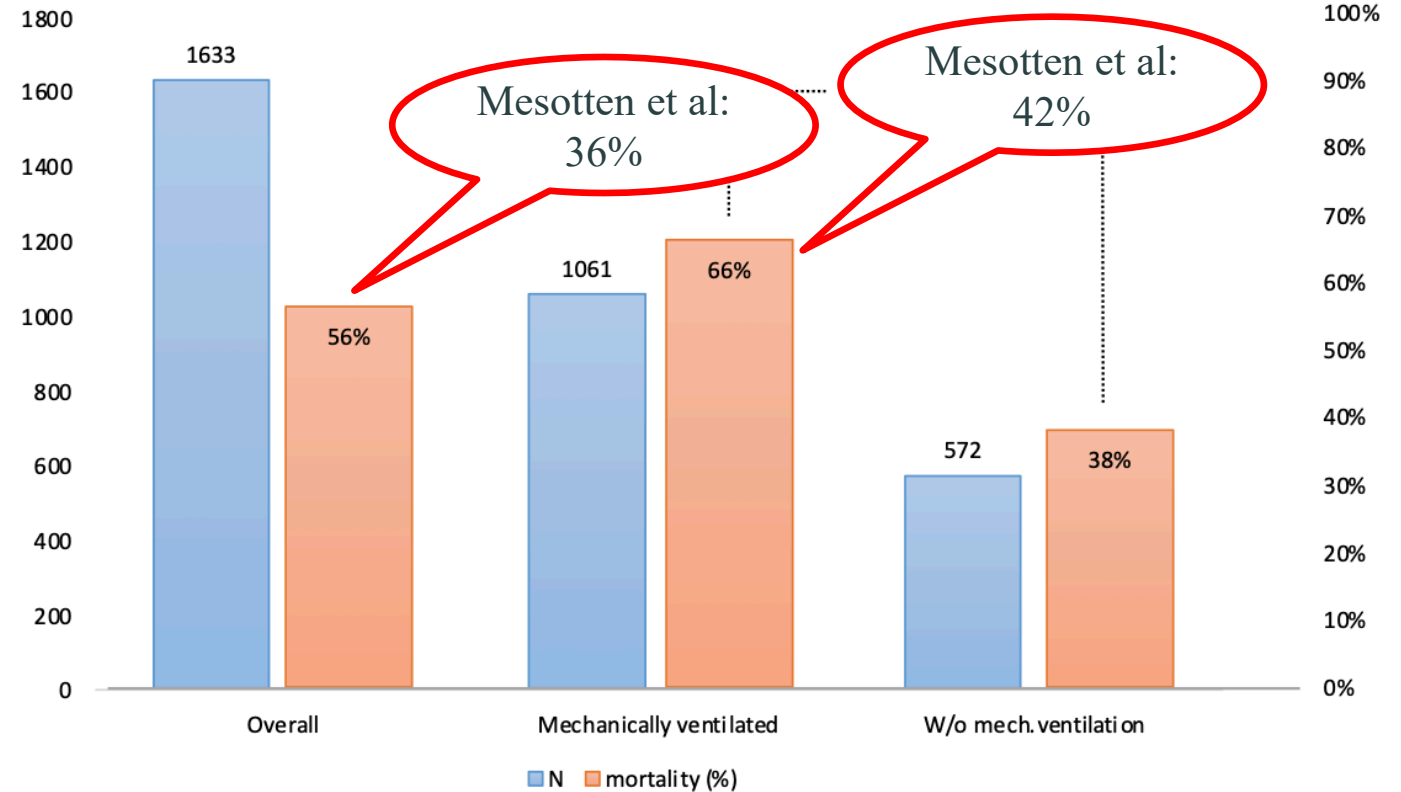


DOI: 10.21203/rs.3.rs-1339000/v1

> Jan Benes, Miłosz Jankowski, Konstanty Szuldrzynski, Roman Zahorec, Mitja Lainscak, Zoltán Ruskai, Matej Podbregar, Jan Zatloukal, Jakub Kletecka, Krzysztof Kusza, Jakub Szrama, Estera Ramic, Katarina Galkova, Stefan Krbila, Josef Valky, Jaka Ivanic, Marko Kurnik, Angéla Mikó, Tamás Kiss, Barbara Hetényi, Peter Hegyi, Alan Sustic, Zsolt Molnar

Country – Centre	No of ICU patients	Percentage of the dataset
CROATIA	286	13%
University Hospital Rijeka	286	13%
CZECHIA	583	27%
University Hospital Plzen	583	27%
HUNGARY	269	13%
Flór Ferenc Hospital County Pest	112	5%
University of Pécs, School of Medicine	157	7%
POLAND	115	5%
Poznań Medical University Hospital	66	3%
Central Clinical Hospital of the Ministry of Interior and Administration, Warsaw	49	2%
SLOVAKIA	491	23%
University Hospital Nitra	178	8%
University Hospital Nové Zámky	166	8%
University Hospital Banska Bystrica	147	7%
SLOVENIA	395	18%
General Hospital Celje	226	11%
General Hospital Murska Sobota	169	8%
Overall	2139	100%

Supplementary Figure S2. Patient distribution based on ventilator support.





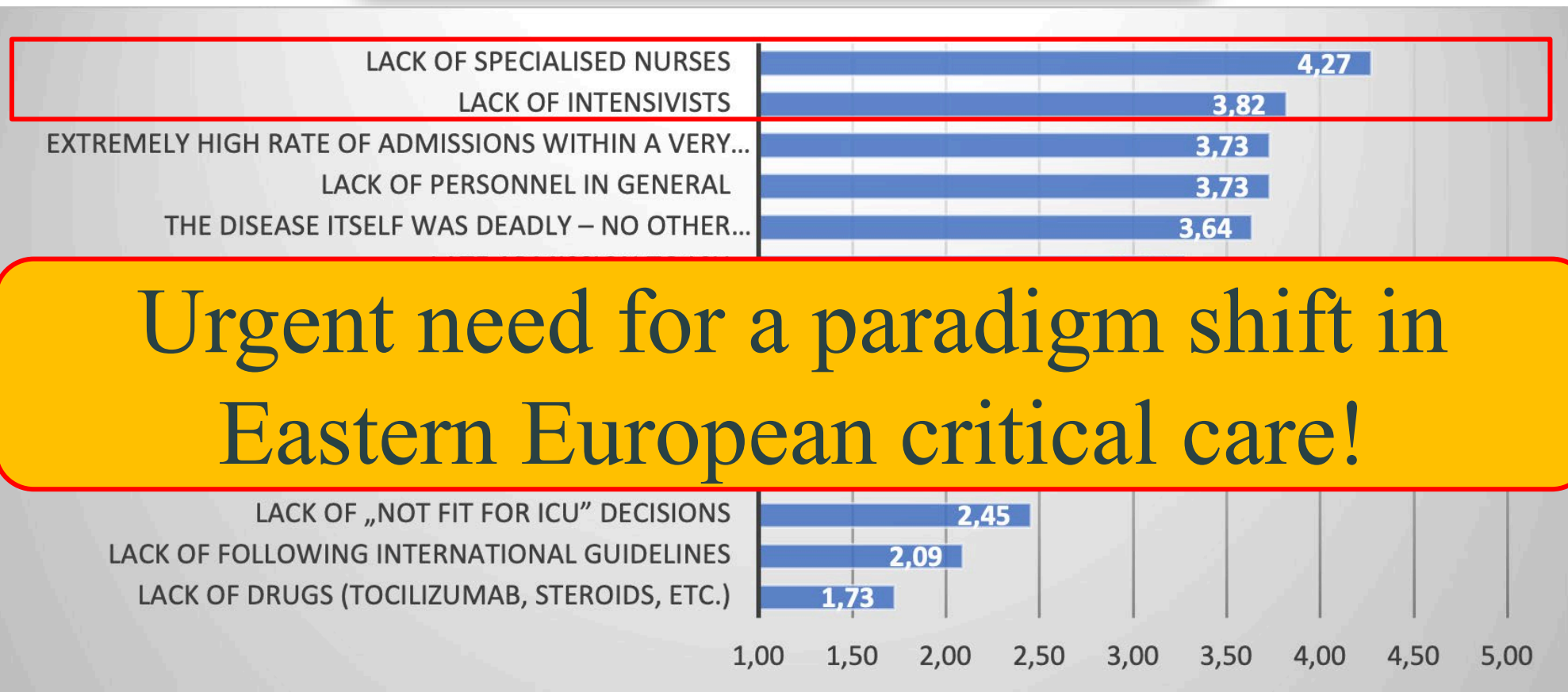
RESEARCH ARTICLE

Results of the SepsEast Registry to define the Characteristics in Coronavirus Disease in Central-Eastern Europe between March 2020-February 2021: an international, multicentre retrospective study of the SEARCH-COVID-19 Study Group

> Jan Benes, Miłosz Jankowski, Konstanty Szuldrzynski, Roman Zahorec, Mitja Lainscak, Zoltán Ruzskai, Matej Podbregar, Jan Zatloukal, Jakub Kletecka, Krzysztof Kusza, Jakub Szrama, Estera Ramic, Katarina Galkova, Stefan Krbila, Josef Valky, Jaka Ivanic, Marko Kurnik, Angéla Mikó, Tamás Kiss, Barbara Hetényi, Peter Hegyi, Alan Sustic, Zsolt Molnar



DOI: [10.21203/rs.3.rs-1339000/v1](https://doi.org/10.21203/rs.3.rs-1339000/v1)



Urgent need for a paradigm shift in Eastern European critical care!



Is there a chance?



CTM at Semmelweis University



Students

Knowledge in clinics
Dedicated time
Knowledge in methods



STUDENTS

Clinicians/Experts

Knowledge in clinics
Dedicated time
Knowledge in methods



CLINICIANS



METHODOLOGY
EXPERTS

Methodology Experts

Knowledge in clinics
Dedicated time
Knowledge in methods

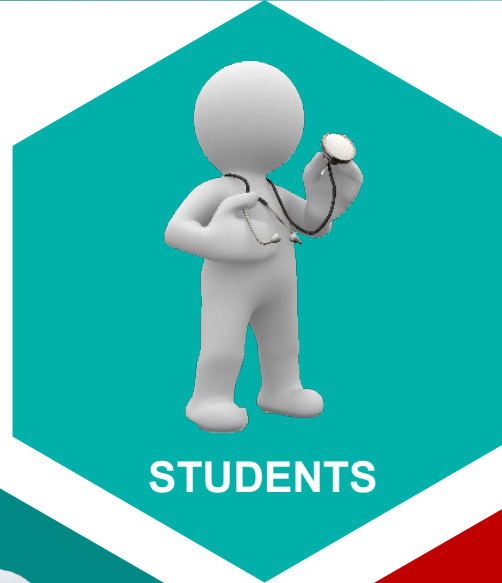


CTM at Semmelweis University



Students

Knowledge in clinics
Dedicated time
Knowledge in methods



STUDENTS

Clinicians/Experts

Knowledge in clinics
Dedicated time
Knowledge in methods



CLINICIANS



METHODOLOGY
EXPERTS

Methodology Experts

Knowledge in clinics
Dedicated time
Knowledge in methods



CTM at Semmelweis University



Workload:
4+1 day

Meetings:
2.5h/week/group
0.5h/week/project



IT COORDINATORS

META-ANALYSIS COORDINATORS

REGISTER COORDINATORS

CLINICAL TRIAL COORDINATORS

COMMUNICATIONS AND EDUCATIONS

DATA AND PATIENTS MANAGEMENT

EXPERT STATISTICIANS (BME, OE, ÁOTE)



Training of research



GENERAL OVERVIEW OF META-ANALYSES

I. The role of meta-analysis in Translational Medicine

- What is the role of translational medicine in modern science?
- What are systematic reviews and meta-analyses?
- Why are meta-analyses important in evidence-based medicine?

II. Main steps of the workflow: How to be transparent and reproducible?

- What are the main steps of conducting a systematic review or meta-analysis?

III. Questions of meta-analysis

- What kind questions can be answered by a meta-analysis?
- What are the characteristics of a good scientific question?

IV. How to gather information from electronic databases systematically?

- What does systematic data collection mean?

V. First impression of forest plots - introduction to meta-analytical statistics

- How to avoid false conclusions by judging a forest plot at first sight?
- How to appraise forest plots critically?

VI. Bias - The truth is beyond

- What does bias mean?
- Why is it important to integrate the results of the risk of bias assessment into your results?

VII. Should we trust in meta-analyses?

- What are the strengths and limitations of meta-analyses?
- How to appraise meta-analyses critically?

STATISTICS COURSE

OPEN LECTURES
Objective and brief summary

The aim of this course is to make the participants familiar with the basics of statistical methods used in the medical/biological sciences. Furthermore, to help the participants to interpret the results of statistical analysis more easily and to recognize possible biases in scientific literature. The course introduces the most commonly used statistical methods, thus the participants get acquainted with the most important elements of descriptive statistics, basic principles of hypothesis testing, parametric and non-parametric statistical methods and risks of decision errors. Furthermore, topics such as survival analysis, adaptation of questionnaires, sensitivity and specificity of diagnostic tests, and Receiver Operating Characteristic (ROC) Curve analysis will also be covered during the course. Participants also have the opportunity to practice on examples and to get acquainted with the use of SPSS program.



PATIENT REGISTRY COURSE

OPEN LECTURES AND PRACTICE
Objective and brief summary

Course participation provides insight into the world of patient registries. The course aims to introduce patient registries with their role in science, focusing on practical questions. Topics will embrace the entire process from planning a registry to publication. The general built of a registry, the role of the patient registry coordinator and the contributors in the phase of registry development will be discussed. The course will include presentations on the IT background, details on how to develop an electronic case report form, data management, ethical approval, and other roles, such as biostatisticians and clinical research administrators. At the end of the course, participants will learn the main points of setting up a patient registry.



CLINICAL TRIALS COURSE

PRACTICE
Objective and brief summary

Course participation provides an insight into the world of clinical trials. The course aims to overview the main features of both observational (DAY 1) and experimental (DAY 2) study designs and their role in science, focusing on practical questions. Topics will embrace the entire process from study planning to conclusions from result. Questions will cover key topics, such as the identification of study designs, the role of randomization, the effects of bias, and the judgement of cause-effect relationships. At the end of the course, participants will learn how to read and understand reports from clinical studies and the main points of setting up clinical research.



CLINICAL PHARMACOLOGY COURSE

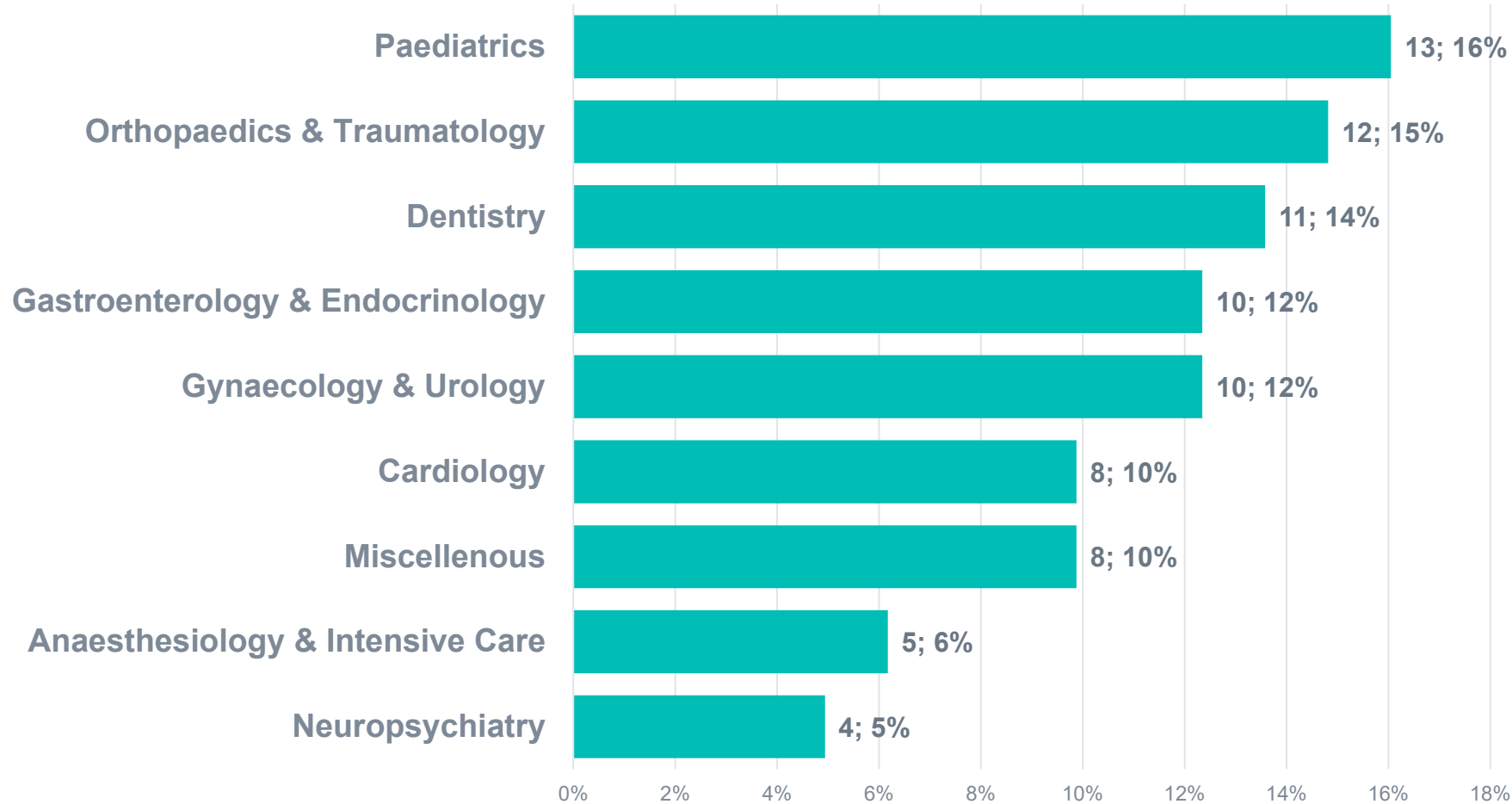
OPEN LECTURES
Objective and brief summary

This course covers the fundamentals of clinical pharmacology as a translational scientific discipline focused on rational drug development and utilization in therapeutics. The course focuses on the following core principles of pharmacology: pharmacokinetics, drug metabolism and transport; drug therapy in special populations; assessment of drug effects; drug discovery and development, pharmacogenomics, and pharmacotherapy. The course will provide an in-depth look at drug absorption, distribution, metabolism, and excretion. It will describe the impact of age, pregnancy, disease on pharmacokinetics, the basic principles in assessing drug effects, the process of drug discovery, and the phases of drug development and the development of trial protocols. It will provide an overview of clinical pharmacotherapy and medication safety. This course intends to complement the other courses of the translational research teaching program so that participants will have a broad and in-depth overview of the mainstream methodologies of clinical research.





PhD students in September 2021



148 applicants
81 accepted
9 plus



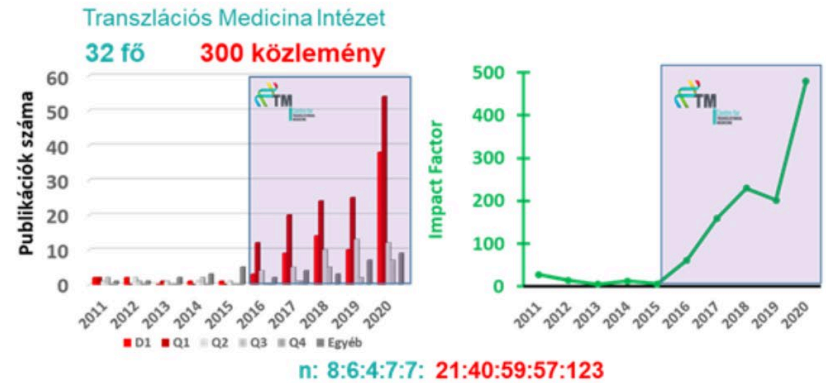
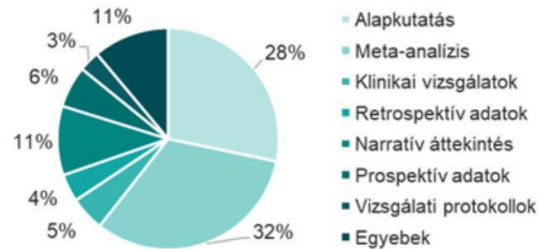
National TM Program (Proposal)



NEMZETI TRANZLÁCIÓS MEDICINA PROGRAM 2021



Ország: **51**
Város: **204**
Intézet: **542**
Kutató: **1286**



300
közlemény

2016.01.01. – 2021.01.01.

15 cikk 10 IF felett
35 cikk 5.0 IF felett
Átlag IF: 4.207

5 év

8. ábra: A TM hatása a tudományos aktivitásra. A PTE Transzlációs Medicina Intézetének 51 ország, 204 város 542 intézetének 1286 kutatójával készült közös publikációja. A TM megalakulása előtti 5 évben 32 míg utána 300 közlemény került publikálásra.





SepsEast 2012

1st Central and Eastern European Sepsis Forum



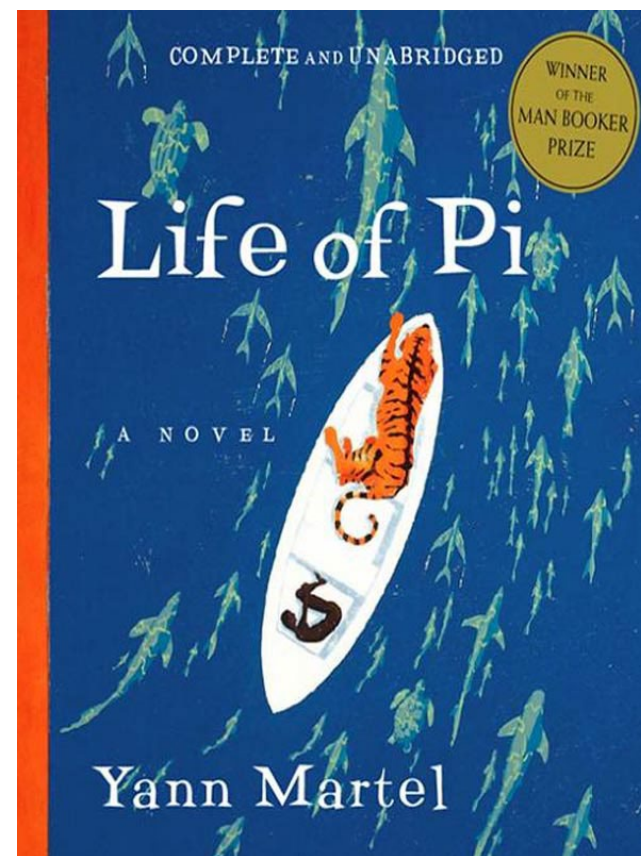
***50 invited lecturers
From 20 countries!***

United we win, divided we're slow!

Thank you!

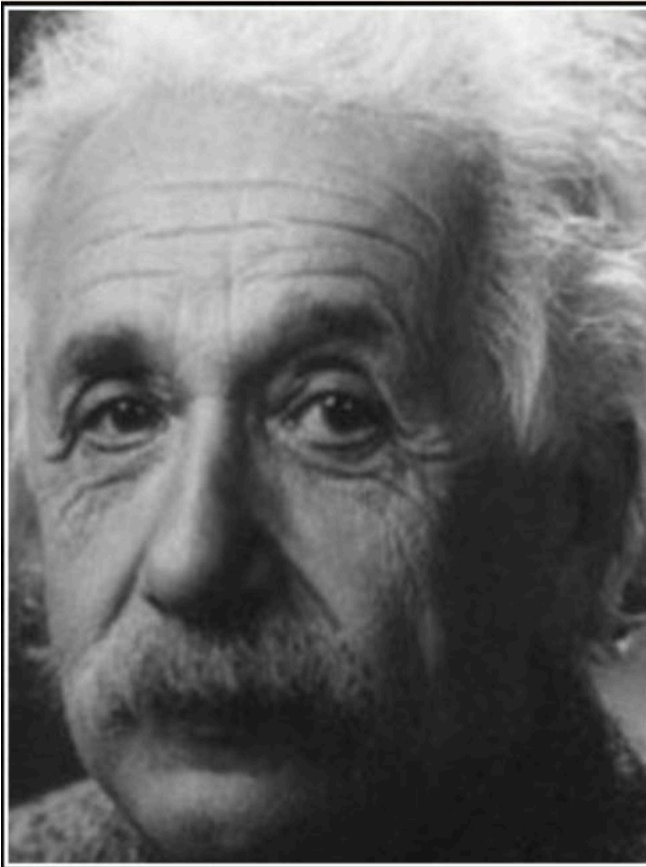
Is it possible?

„The biggest mistake of a shipwreck is that he hopes too much and does little.”





Final thought



Everyone knew it was impossible,
until a fool who didn't know came
along and did it.

— *Albert Einstein* —

AZ QUOTES