SepsEast
Central and Eastern European Sepsis Forum

Results of the SEARCH registry

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SEARCH-COVID-19

- SepsEAst Registry to define the CHaracteristics in COronaVIrus Disease 2019

Aim of the study

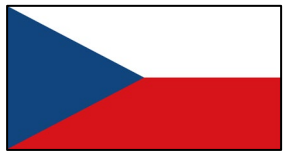
- to collect structured data from ICUs within the SepsEast community during the COVID-19 pandemic

Methods

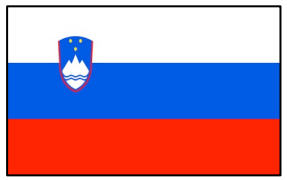
Study design and setting

- originally the study was designed to be a prospective registry
- due to overwhelming workload and staff shortages during the actual COVID-19 waves it was impossible to prospectively enrol patients and collect data
- data were collected retrospectively within the time period of 01.03.2020 - 28.02.2021, encompassing the first surge in Spring and second wave in Autumn 2020
- participating centres were all related to the major SepsEast collaborators within Central and Eastern Europe
- 11 centers in 6 countries









Country – Centre
CROATIA
University Hospital Rijeka
CZECHIA
University Hospital Plzen
HUNGARY
Flór Ferenc Hospital County Pest
University of Pécs, School of Medicine
POLAND
Poznań Medical University Hospital
Central Clinical Hospital of the Ministry of Interior and Administration, Warsaw
SLOVAKIA
University Hospital Nitra
University Hospital Nové Zámky
University Hospital Banska Bystrica
SLOVENIA
General Hospital Celje
General Hospital Murska Sobota

Patients

- All consecutive adult patients admitted to the ICU due to COVID-19 pneumonia within the dedicated time period were found eligible
- Patients admitted with severe acute respiratory failure due to other reasons than coronavirus 2 (SARS-CoV-2), but in whom SARS-CoV-2 screening proved positive on hospital or ICU admission, were excluded

Main outcome

- **all-cause in-hospital mortality** (understood as case fatality)
  - defined as a death during ICU stay or death occurring after transfer from ICU to the ward during the same hospitalization

- there was no censoring nor missing data of the main (primary) outcome
- the most probable cause of death was identified by using the methodology of a study by Contou et al. (Causes and timing of death in critically ill COVID-19 patients. Crit Care. 2021;25:79)
- orders to either withhold or withdraw treatment were also screened

Other collected data

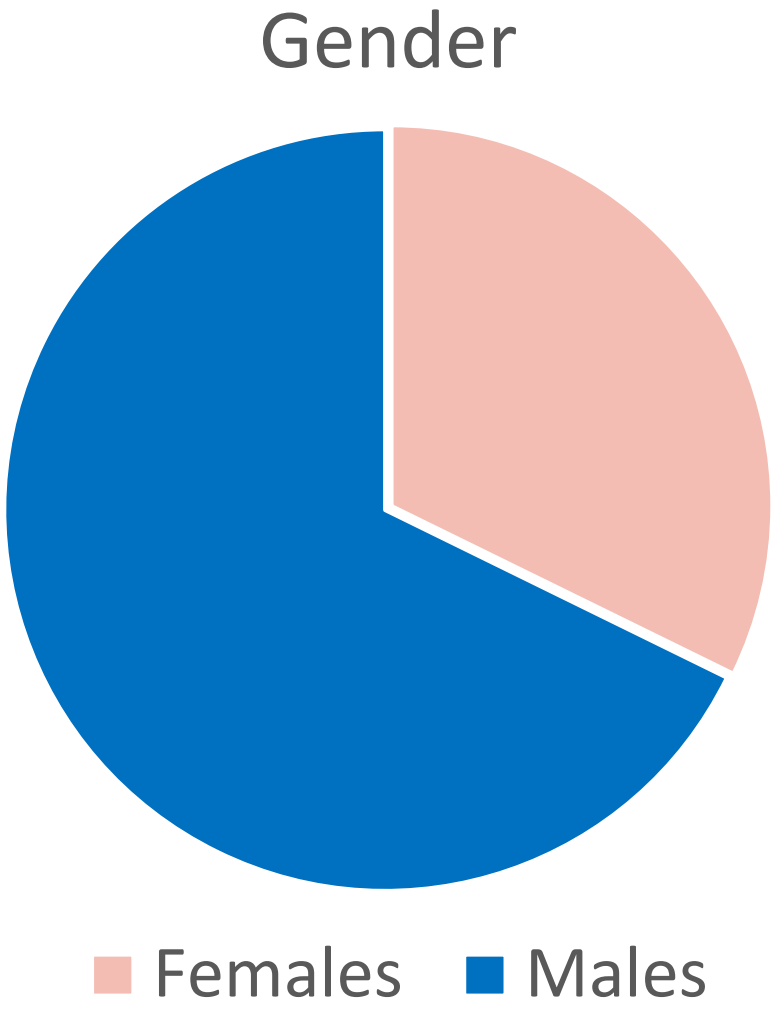
- baseline demographic parameters and comorbidities
- time describing parameters (i.e. symptom onset, date of first proved SARS-CoV-2 positivity, admission and discharge/death dates)
- parameters of **organ support** (i.e. mode and length of ventilator support, other vital organ supports such as vasoconstrictors, inotropes, RRT)
- **treatment** (corticosteroids, anti-viral and disease modifying drugs, anticoagulation)
- ICU stay related **complications** (i.e. deep-vein thrombosis, pulmonary embolism, barotrauma)
- laboratory parameters on ICU admission (i.e. leukocyte, lymphocyte count, C-reactive protein, procalcitonin level, PaO_2/FiO_2 ratio)

Results

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%**

Demographics

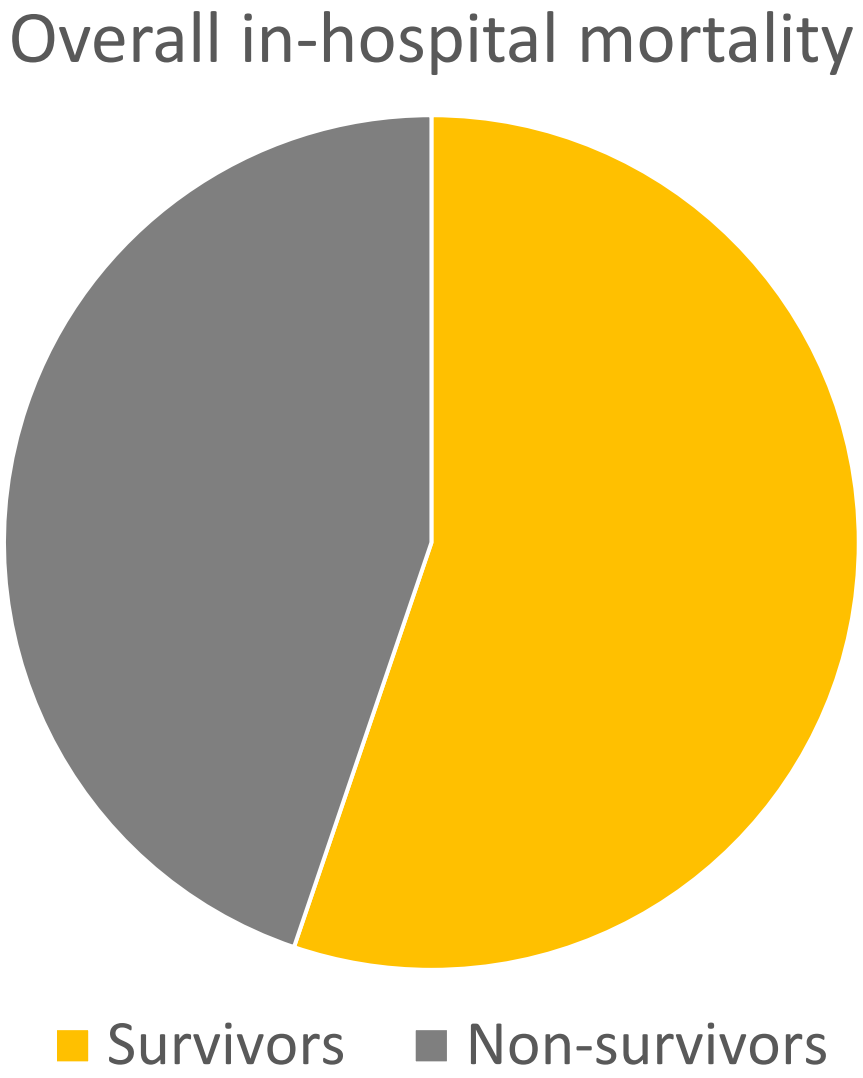
- **2139 patients**
- Female: 33% (690)
- Age: median 68 years (IQR 60-75)



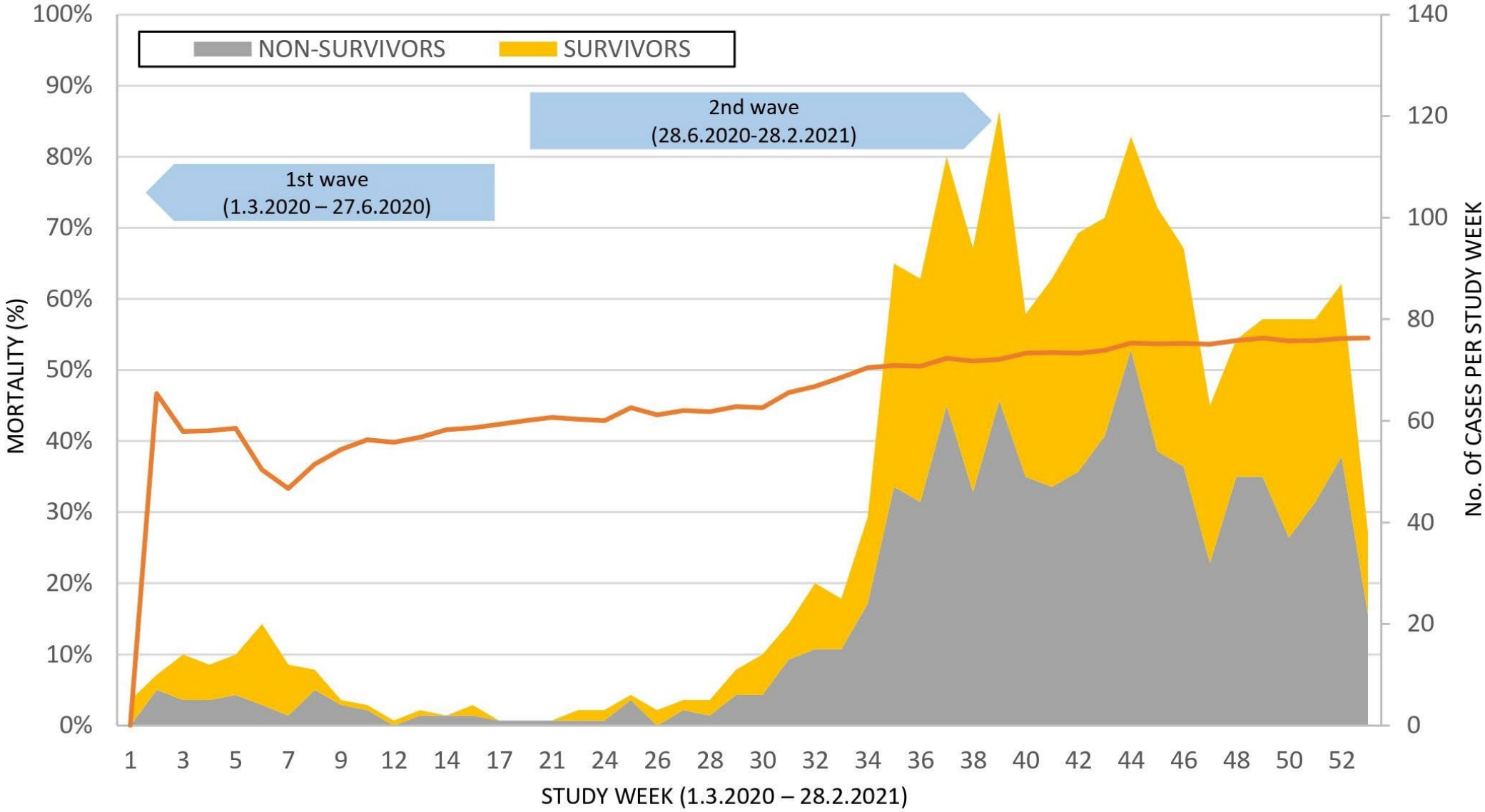
Mortality

- **55%** (1181 patients)
- only 53 patients (4%) died outside ICU
  - Median time to death 6 days (IQR 3-14)

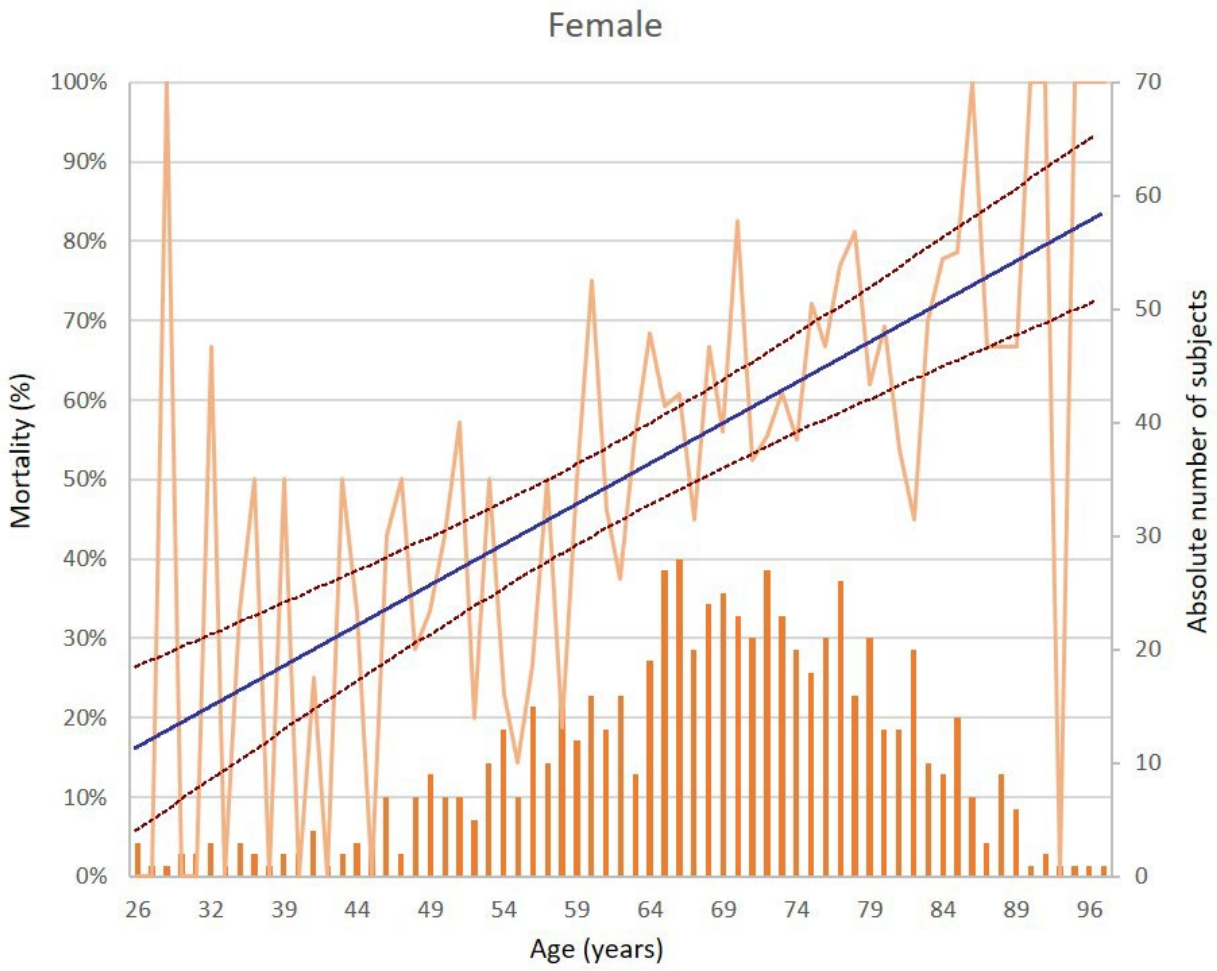
- any form of treatment limitation in 35% of non-survivors
  - withholding: 8%
  - withdrawing: 7%

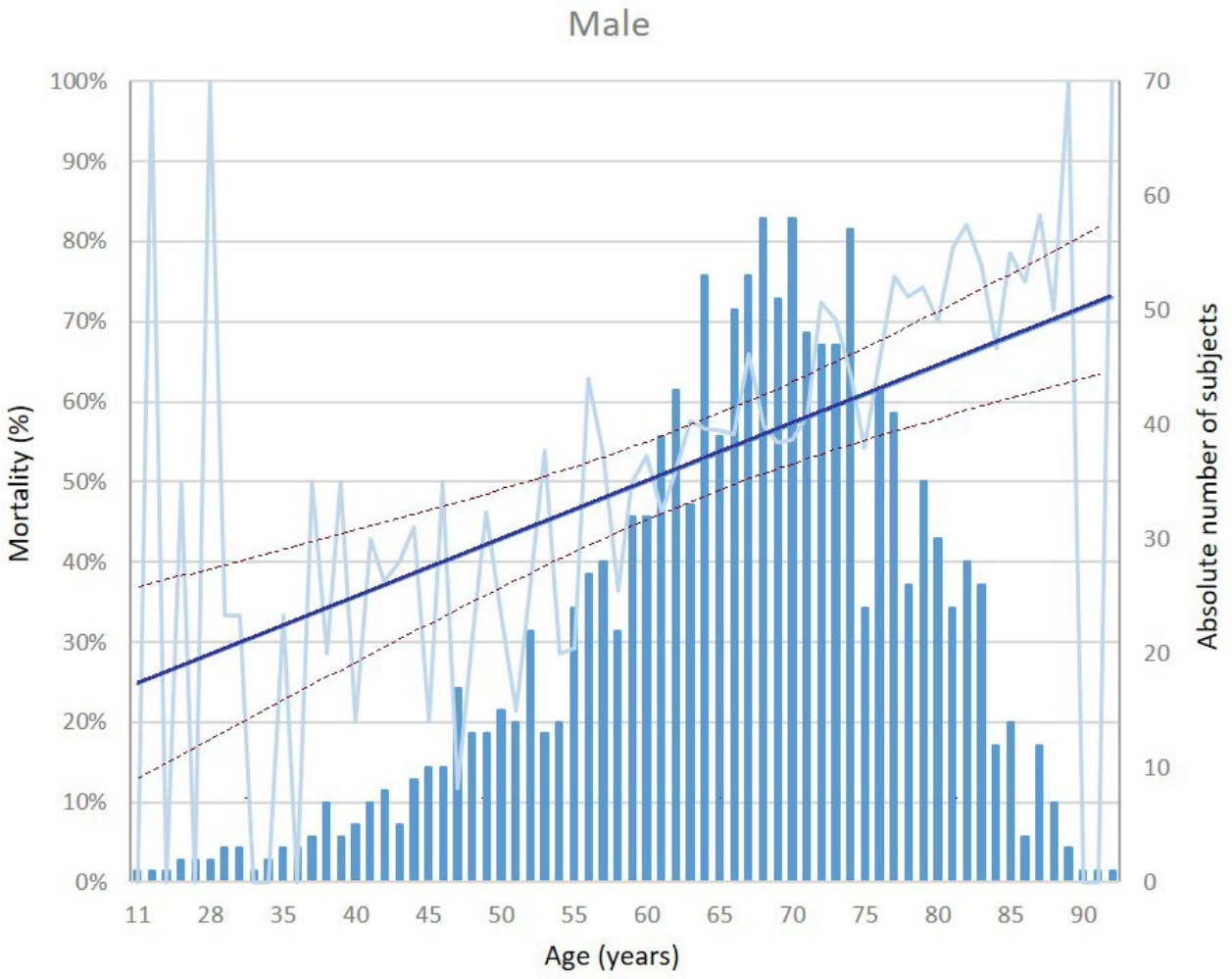


Time course of enrollment and mortality

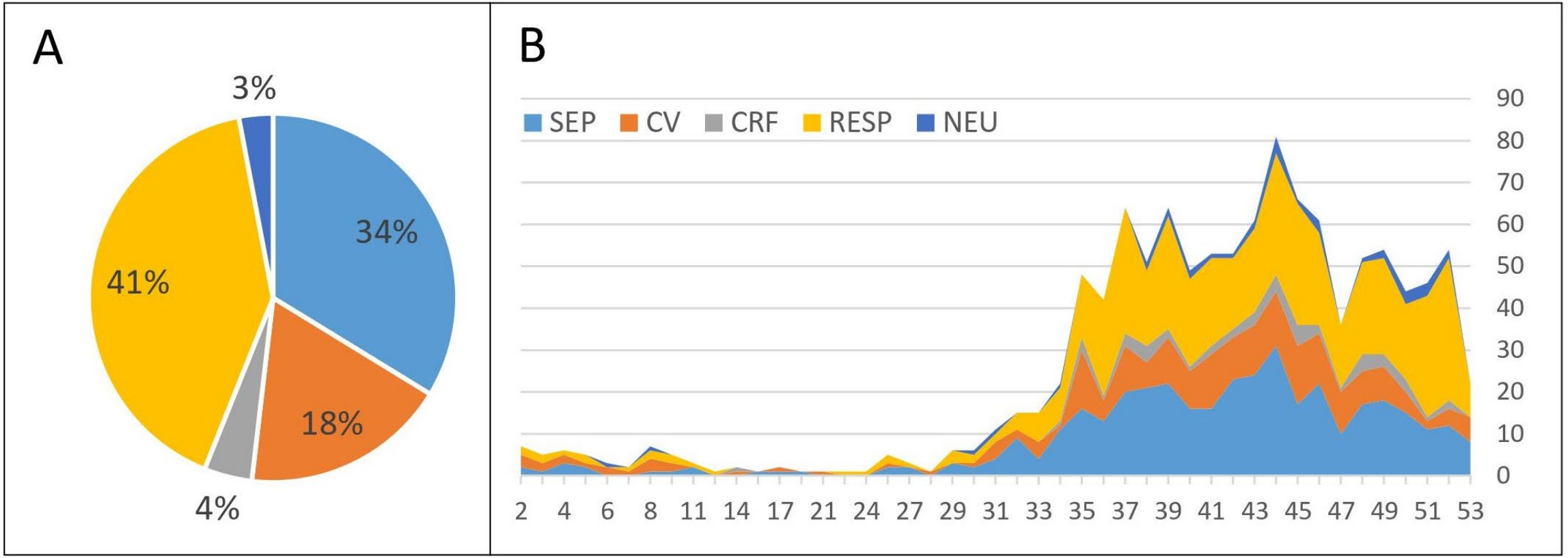


Patient distribution and mortality by gender and age groups





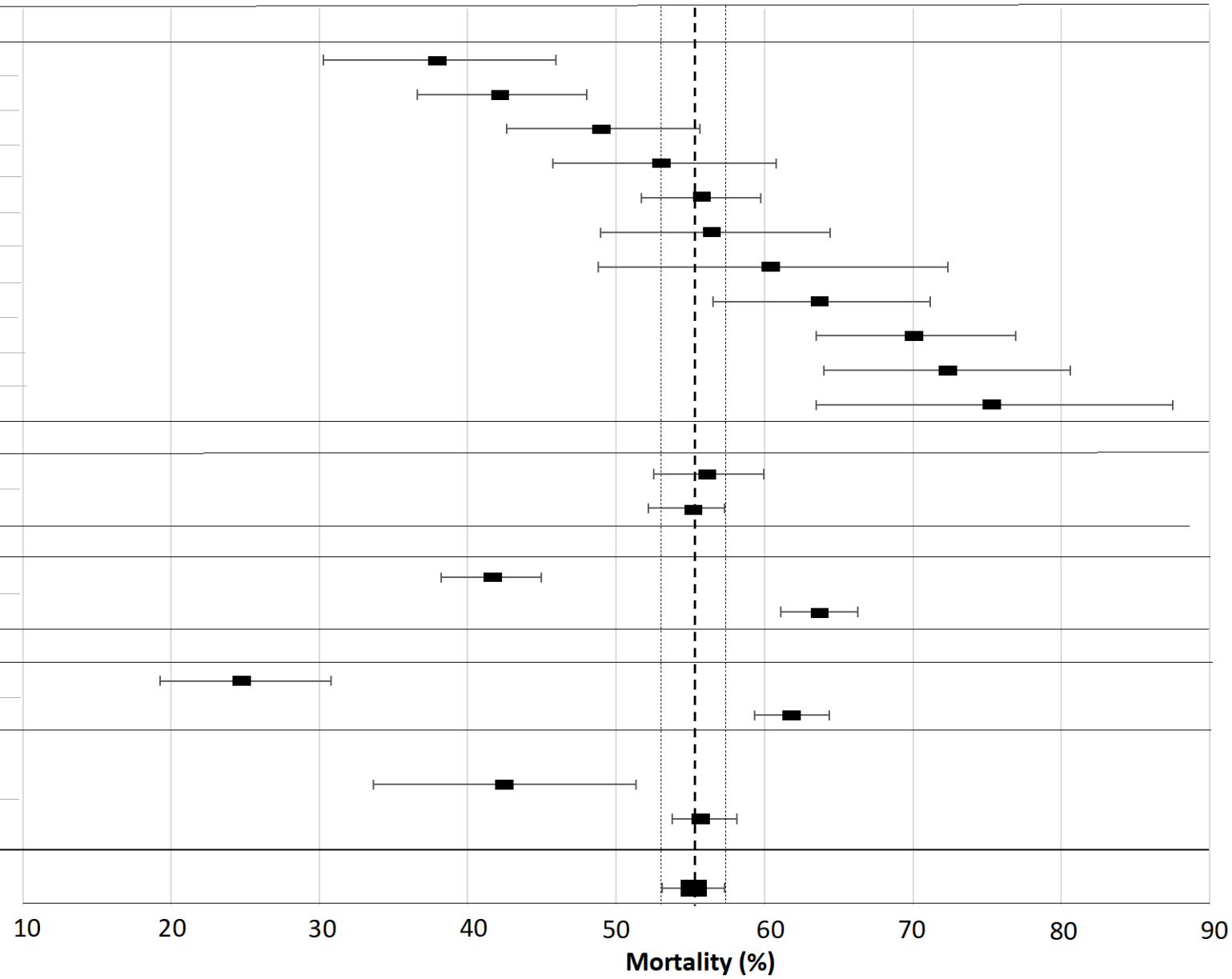
Causes of death



RESP – respiratory, CV – cardiovascular, CRF – cardiorespiratory failure, SEP – sepsis, NEU - neurological

Determinants of mortality?

	No of patients deceased/total	Mortality % (95%CI)
CENTRE		
1	56/147	38.1 (30.2-45.9)
2	12/286	42.3 (36.6-48.0)
3	111/226	49.1 (42.6-55.6)
4	90/169	53.3 (45.7-60.8)
5	325/583	55.7 (51.7-59.8)
6	89/157	56.7 (48.9-64.4)
7	40/66	60.6 (48.8-72.4)
8	106/166	63.9 (56.5-71.2)
9	125/178	70.2 (63.5-76.9)
10	81/112	72.3 (64.0-80.6)
11	37/49	75.9 (63.5-87.6)
GENDER		
Female	388/690	56.3 (52.5-59.9)
Male	793/1449	54.7 (52.2-57.3)
AGE GROUP		
<65 years	341/820	41.6 (38.2-45.0)
≥65 years	840/1319	63.7 (61.1-66.3)
CHRONIC MORBIDITY		
NO	54/216	25.0 (19.2-30.8)
ANY	900/1319	61.9 (59.4-64.4)
PANDEMIC WAVE		
1st	51/120	42.5 (33.7-51.3)
2nd	1130/2019	56.0 (53.8-51.8)
TOTAL	1181/2139	55.2 (53.1-57.3)



Survivors vs. non-survivors: demographic and time describing parameters

	Overall N=2139	Survivors N=958	Non-survivors N=1181	p-value
Age	68 (60-75)	65 (55-72)	***70 (64-77)***	< 0.0001
Female	690 (33 %)	302 (34 %)	388 (33 %)	NS
BMI	30.1 (27.0-34.7)	30.7 (27.3-34.9)	30.0 (26.8-34.6)	NS
Onset of symptoms before ICU admission (days)	6 (2-9)	***6 (3-9)***	5 (2-8)	<0.0001
ICU pre-admission hospital length of stay (days)	1 (0-4)	***2 (0-4)***	1 (1-5)	0.023
ICU length of stay (days)	9 (5-16)	***10.5 (6-18)***	8 (4-15)	< 0.0001
Organ support free total length of stay (days)	1 (0-4)	***3 (1-7)***	1 (0-3)	< 0.0001

Survivors vs. non-survivors: **comorbidities**

	Overall N=1656	Survivors N=475	Non-survivors N=1181	p-value
Without comorbidities	230 (12 %)	***162 (23 %)***	68 (6 %)	<0.0001
Diabetes mellitus	626 (38 %)	165 (35 %)	461 (39 %)	NS
Arterial hypertension	1201 (73%)	475 (64 %)	895 (74 %)	NS
Chronic heart disease	575 (35 %)	114 (24 %)	461 (39 %)	NS
Chronic respiratory disease	297 (18 %)	80 (17 %)	217 (18 %)	NS
Immunocompromised (including dialysis, malignancy)	450 (27 %)	91 (19 %)	359 (30 %)	NS
CPR before ICU admission	32 (2 %)	7 (1 %)	25 (2 %)	NS

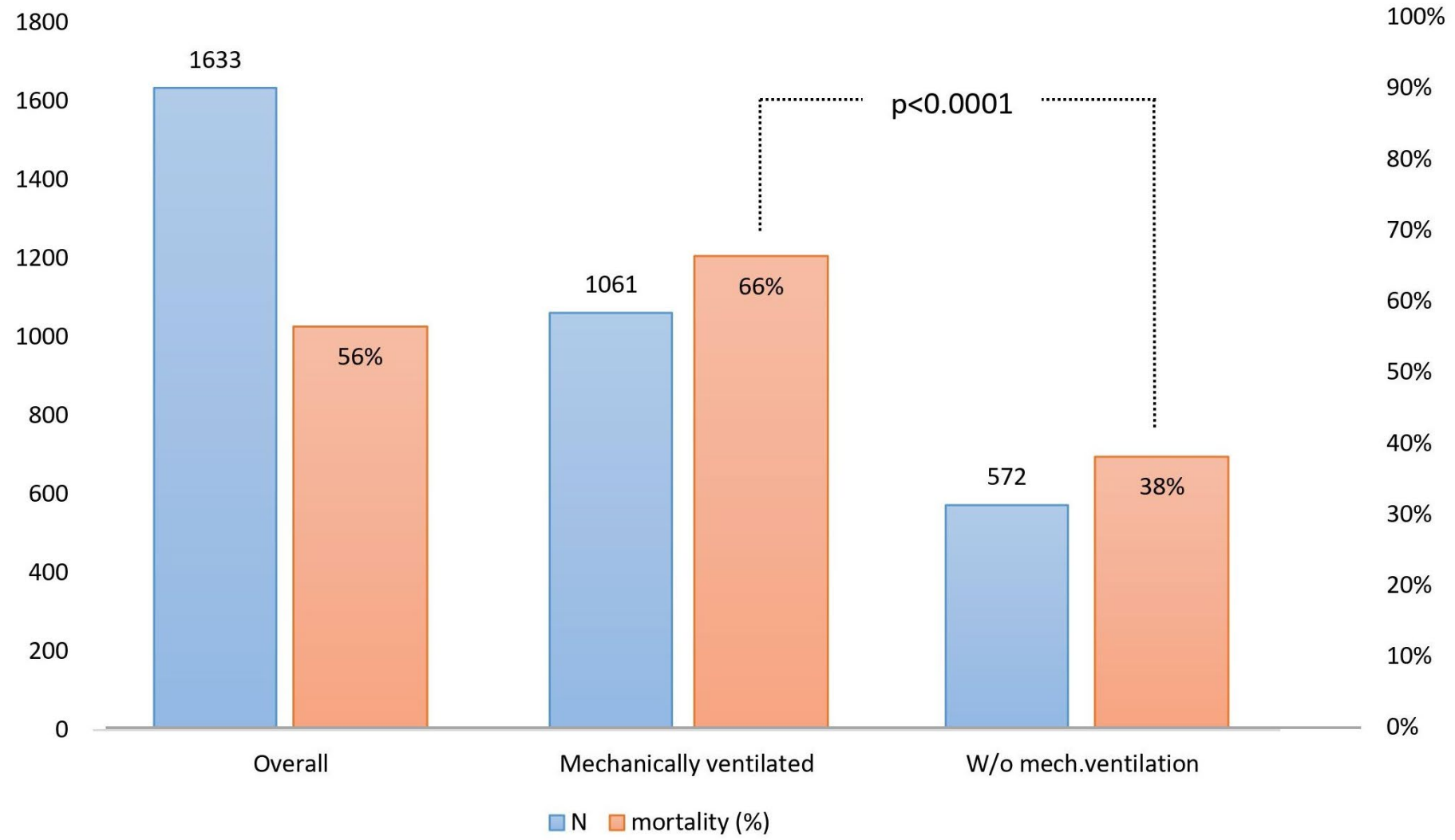
Survivors vs. non-survivors: ICU complications

	Overall N=1656	Survivors N=475	Non-survivors N=1181	p-value
Pulmonary embolism	106 (6 %)	27 (6 %)	79 (7 %)	NS
HAP/VAP	444 (27 %)	148 (31 %)	296 (25 %)	NS
Barotrauma	32 (2 %)	5 (1 %)	27 (2 %)	NS
CPR	255 (15 %)	7 (1 %)	248 (21 %)	NS

Survivors vs. non-survivors: **organ support**

	Overall N=1687	Survivors N=733	Non-Survivors N=954	p-value
Only HFNC	317 (19 %)	***192 (26 %)***	125 (13 %)	<0.0001
Only NIV	129 (8 %)	64 (9 %)	65 (7 %)	NS
Invasive ventilation w/o ECMO	1061 (63 %)	357 (49 %)	***704 (74 %)***	<0.0001
ECMO	54 (3 %)	22 (3 %)	32 (3 %)	NS
Vasopressor therapy	1093 (65 %)	365 (50 %)	***728 (76 %)***	<0.0001
Inotropic support	200 (12 %)	38 (5 %)	***162 (17 %)***	<0.0001
RRT	205 (12 %)	54 (7 %)	***151 (16 %)***	<0.0001

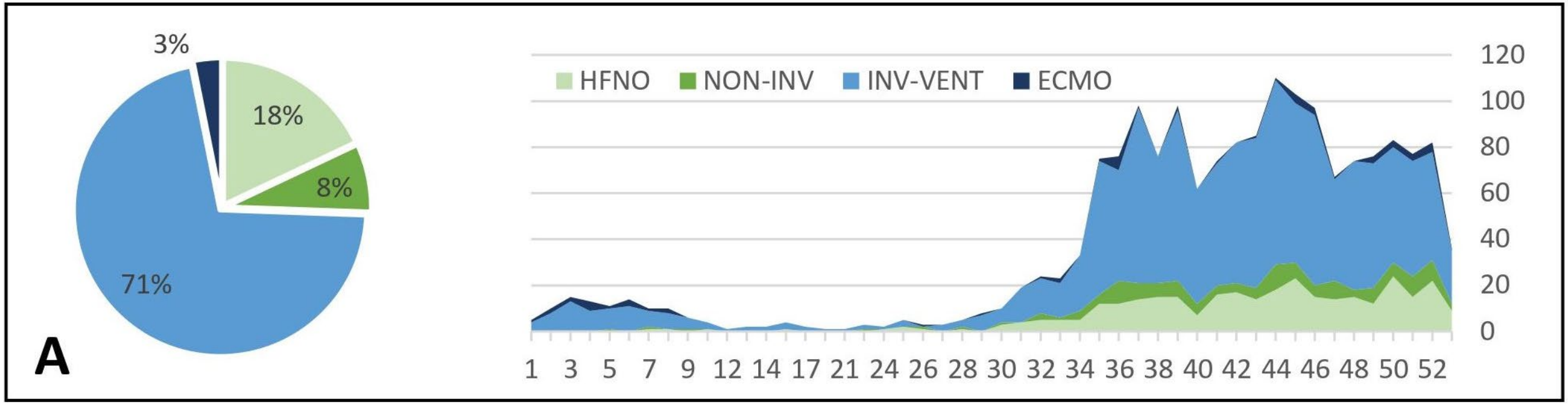
Invasive mechanical ventilation & mortality



Respiratory support initial use

- HFNO: 913 pts (54.1%)
  - sufficient in 317 (35%) of pts
- NON-INV: 405 pts (24.0%)
  - escalated to INV-VENT in 276 pts (68%)
- INV-VENT from admission in 434 pts (25.7%)
  - mortality 70%
  - 109 pts (25%) died during first 24 hrs

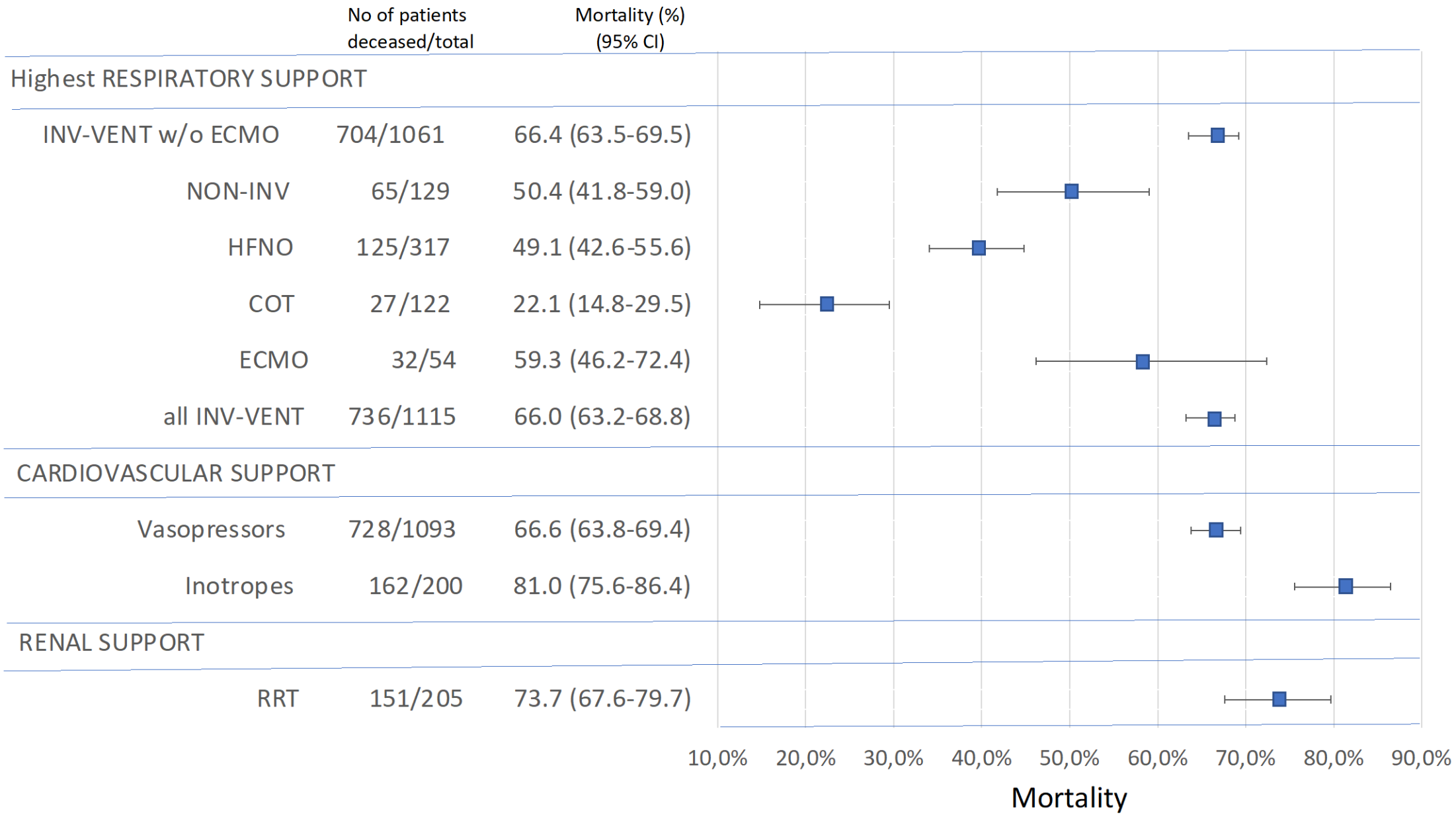
Treatment:
the highest form of **respiratory support**



HFNO - high-flow nasal oxygen; NON-INV - non-invasive ventilation
INV-VENT - invasive mechanical ventilation; ECMO - extracorporeal oxygenation

Conventional oxygen therapy (COT) excluded from the analysis

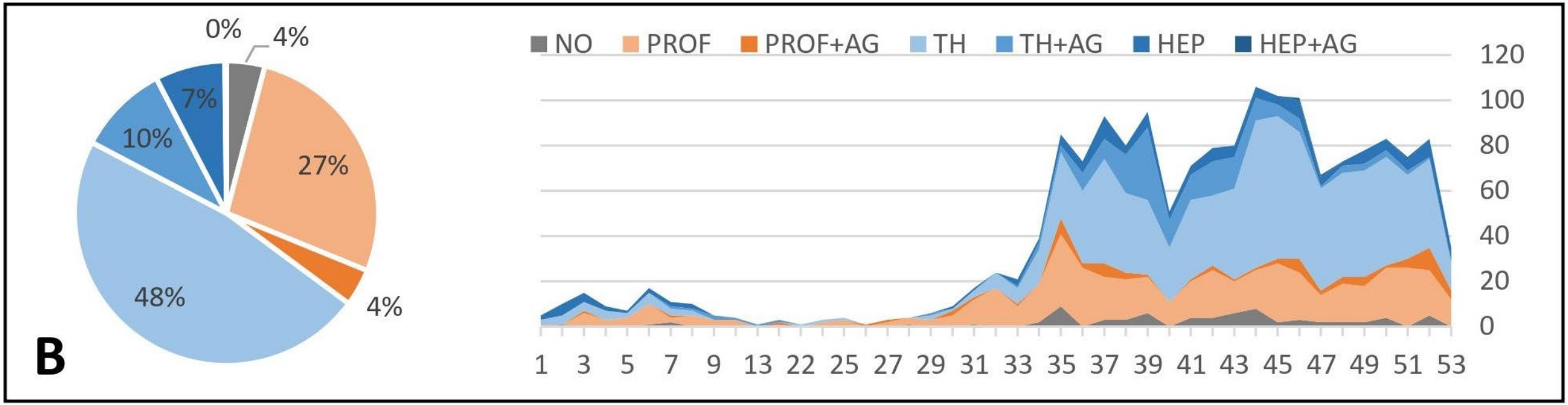
Organ support & mortality



Survivors vs. non-survivors: **treatment**

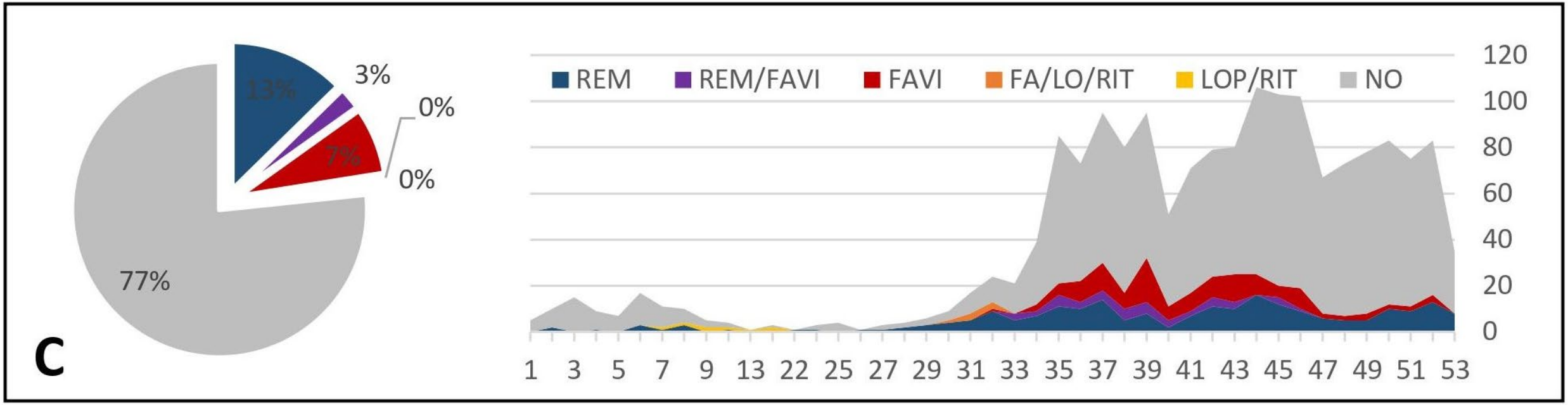
Specific treatments	Overall N=1744	Survivors N=721	Non-survivors N=1023	
Corticosteroids (any dose)	1520 (87 %)	626 (87 %)	894 (84 %)	NS
Standard dose	1017 (58 %)	424 (59 %)	593 (58 %)	NS
Higher dose	503 (29 %)	202 (28 %)	301 (29 %)	NS
DVT prophylaxis	540 (31 %)	218 (30 %)	322 (31 %)	NS
Anticoagulation (heparin or high-dose LMWH)	1128 (65 %)	486 (67 %)	642 (63 %)	NS
Anti-platelets (chronic or new medication)	240 (14 %)	93 (13 %)	146 (14 %)	NS
Antivirals (any of the following)	407 (23 %)	196 (27 %)	211 (21 %)	NS
Remdesivir	264 (15 %)	145 (20 %)	119 (12 %)	NS
Lopinavir/ritornavir	15 (1 %)	8 (1 %)	7 (1 %)	NS
Favirapivir	178 (10 %)	68 (9 %)	110 (11 %)	NS

Treatment: **antithrombotics**



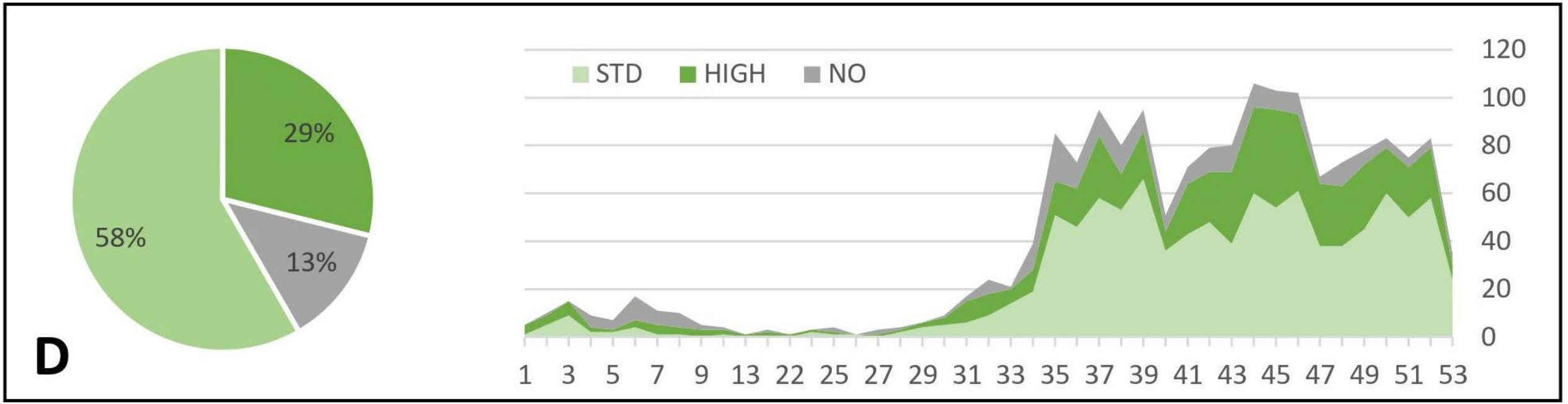
NO - no anti-thrombotics; PROF - prophylactic low-molecular weight;
PROF+AG - prophylactic low-molecular weight heparin + anti-aggregants;
TH - therapeutic low-molecular weight heparin;
TH+AG - therapeutic low-molecular weight heparin + anti-aggregants;
HEP - heparin anticoagulation; HEP+AG - heparin anticoagulation + anti-aggregants

Treatment: **antivirals**



NO - no antivirals; REM – remdesivir; FAVI - favirapivir; LOP/RIT - lopinavir-ritornavir combination

Treatment: **corticosteroids**



NO - without steroids; STD - standard dose of dexamethasone 6-8mg/day equivalents; HIGH - any higher dose

Survivors vs non-survivors: baseline SOFA, APACHE II, PaO_2/FiO_2 & laboratory parameters

	Overall		Survivors		Non-survivors		p-value
	N	Median (IQR)	N	Median (IQR)	N	Median (IQR)	
SOFA	515	7 (4-10)	156	4 (2-8)	359	**8 (5-11)**	<0.0001
APACHE II	551	17 (12-25)	187	13 (10-19)	364	**21 (14-27)**	<0.0001
PaO_2/FiO_2 (mmHg)	1352	97 (66-150)	527	123 (80-200)	825	**84 (62-124)**	<0.0001
Lymphocyte count (10^9/L)	1286	0.46 (0.16-0.95)	424	0.70 (0.46-1.86)	862	**0.32 (0.07-0.75)**	<0.0001
CRP (mg/L)	1711	118 (62-190)	706	104 (54-173)	1005	**128 (70-205)**	<0.0001
PCT (ng/mL)	1490	0.39 (0.18-1.14)	501	0.30 (0.12-1.00)	989	**0.41 (0.20-1.31)**	<0.0001
IL-6 (pg/mL)	448	68 (23-144)	155	45 (15-106)	293	**88 (28-191)**	<0.0001
Ferritin (µg/L)	939	1081 (580-2000)	351	797 (418-1542)	588	**1311 (741-2030)**	< 0.0001
D-dimers (mg/L)	1226	2.65 (1.22-9.00)	373	2.12 (1.13-7.32)	853	**3.06 (1.26-10.19)**	0.0083
Serum lactate (mmol/L)	1308	1.8 (1.3-2.9)	400	1.3 (1.0-1.8)	908	**2.2 (1.5-3.5)**	<0.0001

How we compare to others?

American Journal of Respiratory and Critical Care Medicine Volume 203 Number 1 | January 1 2021

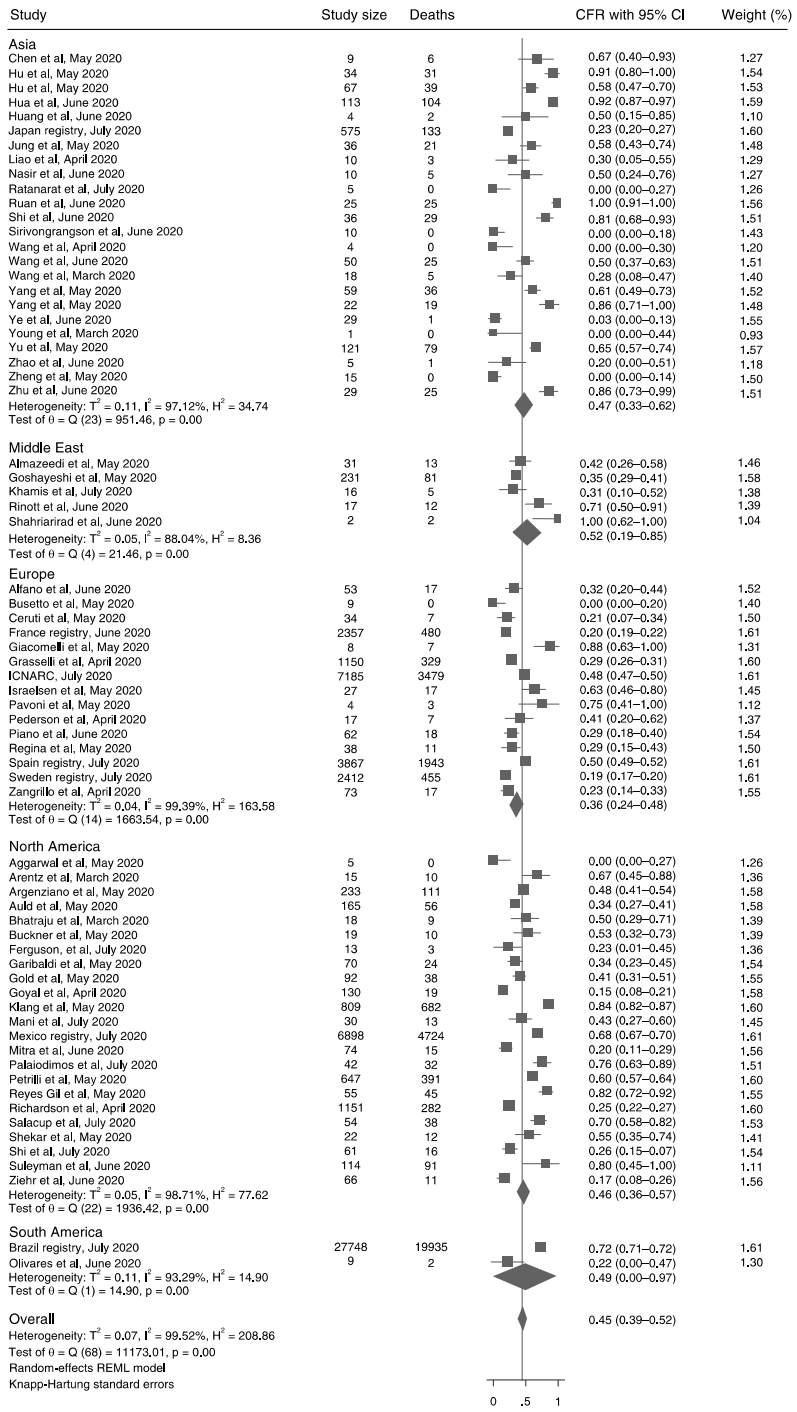
COVID-19 1st wave

Case Fatality Rate (CFR)

- January 1, 2020 – June 8, 2020
- 57 420 adults requiring INV-VENT
- **CFR 45% (95%CI: 35%-52%)**
- *Heterogeneity (I^2 >90%)*

- **Europe 36% (95%CI: 24%-48%)**
  - **ICNARC 48% (95%CI: 47%-50%)**

- Asia 47% (95%CI: 33%-62%)
- Middle East 52% (95%CI: 19%-85%)
- North America 46% (95%CI: 36%-57%)
- South America 49% (95%CI: 0%-87%)
  - Brazil registry 72% (95%CI: 71%-72%)



American Journal of Respiratory and Critical Care Medicine Volume 203 Number 1 | January 1 2021

Mortality in other studies of ICU patients

- **Italy**: ICU mortality in Lombardy **25%** (Graselli et al., JAMA 2020) and **37%** in invasively ventilated pts from COVID-19 Italian ICU Network (Zanella et al. Intensive Care Med. 2021)
- **UK** (ICNARC): overall mortality **50.2%** (1st wave) and **35.2%** (2nd wave)
- **Germany**: slightly >**50%** in invasively ventilated pts during 1st and 2nd wave (Karagiannidis et al. Lancet Respir Med. 2021)
- SEMICYUC Working Group (**Andora, Ireland and Spain**, n= 3795): overall mortality **31.7%** (1st wave) and **28.8%** (2nd wave) (Carbonell et al.. Lancet Reg Health Eur. 2021)
- The Euroregio Meuse-Rhine (7 ICUs, n= 551): overall mortality **22%** in **Belgium**, **42%** in **The Netherlands** and **44%** in **Germany** during 1st wave (Mesotten et al. Crit Care Med 2022)
- ***Poland**: small cohort (n=32) from Tychy: overall mortality **67%** (Kokoszka-Bargiel et. al. Med Sci Monitor 2021); bigger cohort (n=286) from Wrocław: overall mortality **68%** (Czapla et. al. Nutrients 2021)*
- ***Croatia**: small cohort (n=30) from Zagreb: invasively ventilated pts mortality **67%** (Gjurasin et. al. Wien Clin Wochenschr 2021)*
- ***Russia** (n=1522): overall mortality **65.4%** (Moiseev et al. Anaesthesia 2021 [letter])*

EJA

Eur J Anaesthesiol 2023; **40:**4–12

ORIGINAL ARTICLE

Clinical characteristics and factors associated with ICU mortality during the first year of the SARS-Cov-2 pandemic in Romania

A prospective, cohort, multicentre study of 9000 patients

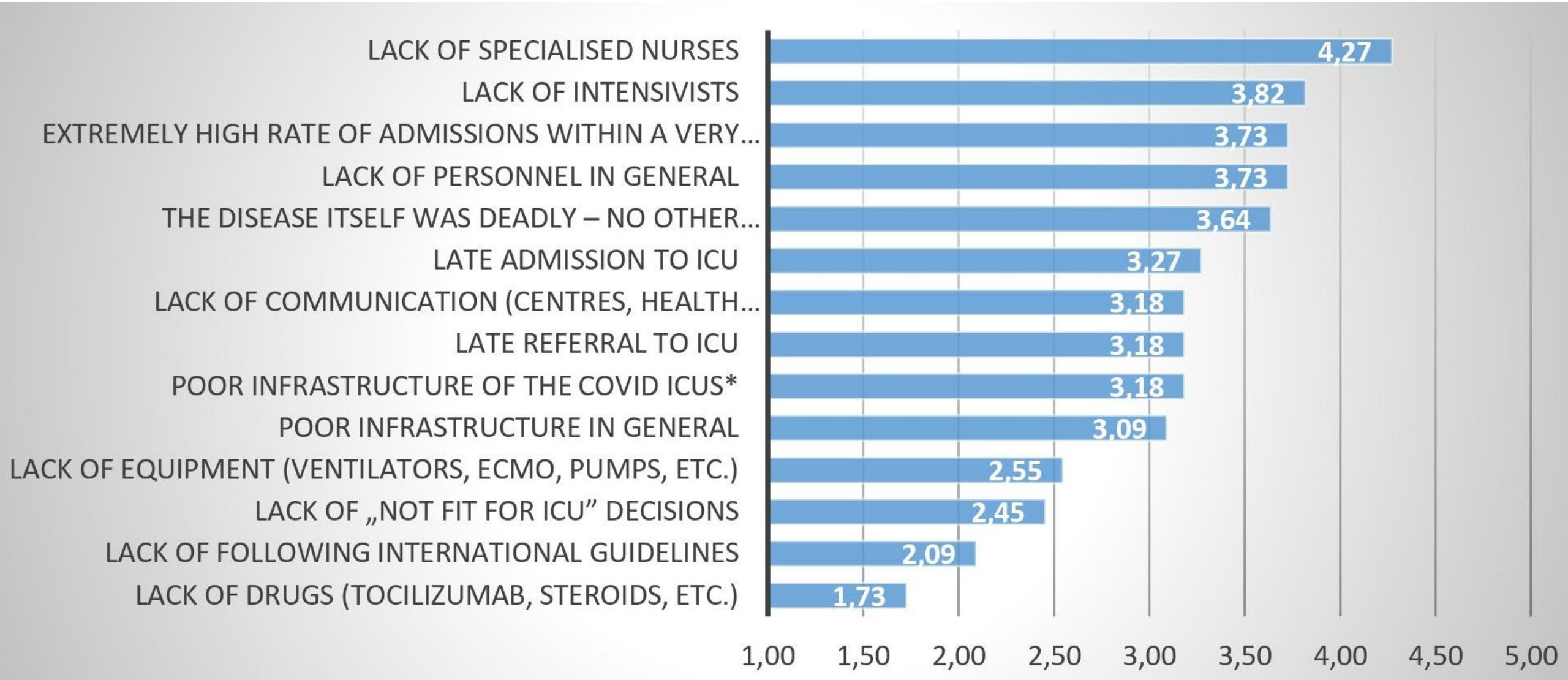
Şerban-Ion Bubenek-Turconi*, Stefan Andrei*, Liana Văleanu*, Mihai-Gabriel Ştefan*, Ioana Grigoraş, Sanda Copotoiu, Constantin Bodolea, Dana Tomescu, Mihai Popescu, Daniela Filipescu, Horatiu Moldovan, Alexandru-Florin Rogobete, Cosmin Bălan, Bianca Moroşanu, Dorel Săndesc and Raed Arafat, COVATI-RO Collaborative†

KEY POINTS

- This study analysed data from a large national European cohort, which to our knowledge, is the largest published Eastern European cohort of critically ill patients.
- Older age, male gender, neoplasia, chronic kidney disease, diabetes, chronic heart failure, clinical severity on ICU admission, the necessity for noninvasive or invasive ventilation were the factors associated with higher ICU mortality.
- Treatment with tocilizumab and hydroxychloroquine were associated with improved survival.

- Overall mortality 62%
- Maximal SOFA 6 (median)
- Mechanical ventilation in 49% of pts
  - 9.6% of survivors and 73.3% of non-survivors

Factors subjectively associated with unfavourable outcome



Conclusions

- We present comprehensive COVID-19 dataset from Central-Eastern European ICUs suggesting the potential high mortality rate observed especially in those receiving invasive mechanical ventilation.

- There is still a plausible difference in quality of health care and research output between the East and West that has not changed for almost two decades since our joining the European Union.

- Our results render the need of a paradigm change in Central-Eastern Europe to establish high quality, structured data collection and to improve research facilities and output, all contributing to better patient outcomes in Central-Eastern Europe.

scientific reports

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OPEN

SepsEast Registry indicates high mortality associated with COVID-19 caused acute respiratory failure in Central-Eastern European intensive care units

Jan Benes[1,2,3,23], Miłosz Jankowski[4,5,23], Konstanty Szułdrzynski[4,5], Roman Zahorec[6], Mitja Lainscak[7,8], Zoltán Ruszkai[9], Matej Podbregar[8,10], Jan Zatloukal[1,2], Jakub Kletecka[1,2], Krzysztof Kusza[11], Jakub Szrama[11], Estera Ramic[12], Katarina Galkova[13], Stefan Krbila[14], Josef Valky[15], Jaka Ivanic[16], Marko Kumik[10], Angéla Mikó[9], Tamás Kiss[17], Barbara Hetényi[17], Peter Hegyi[18,19,20], Alan Sustic[12,21]✉ & Zsolt Molnar[11,19,22]✉

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