

# RECOVER Closing Conference

REMAP-CAP  
*Lennie Derde*

6-7 June 2023

Esplanade Hotel, Zagreb, Croatia



*This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 101003589.*

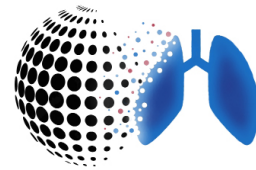
2009

H1N1

2014



2018



Randomized, Embedded,  
Multifactorial Adaptive Platform  
trial for Community-Acquired  
Pneumonia

1st patient

2020

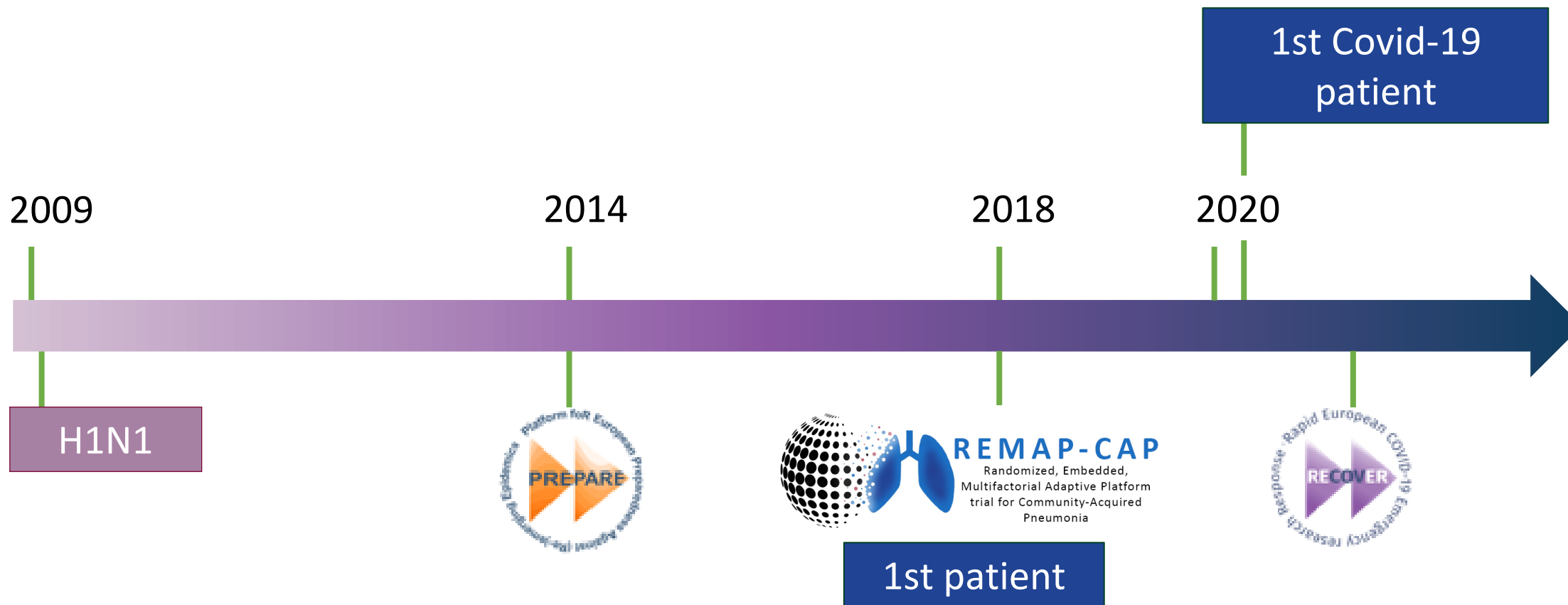












# Objectives



New COVID-19 treatments

Translate research findings into measures

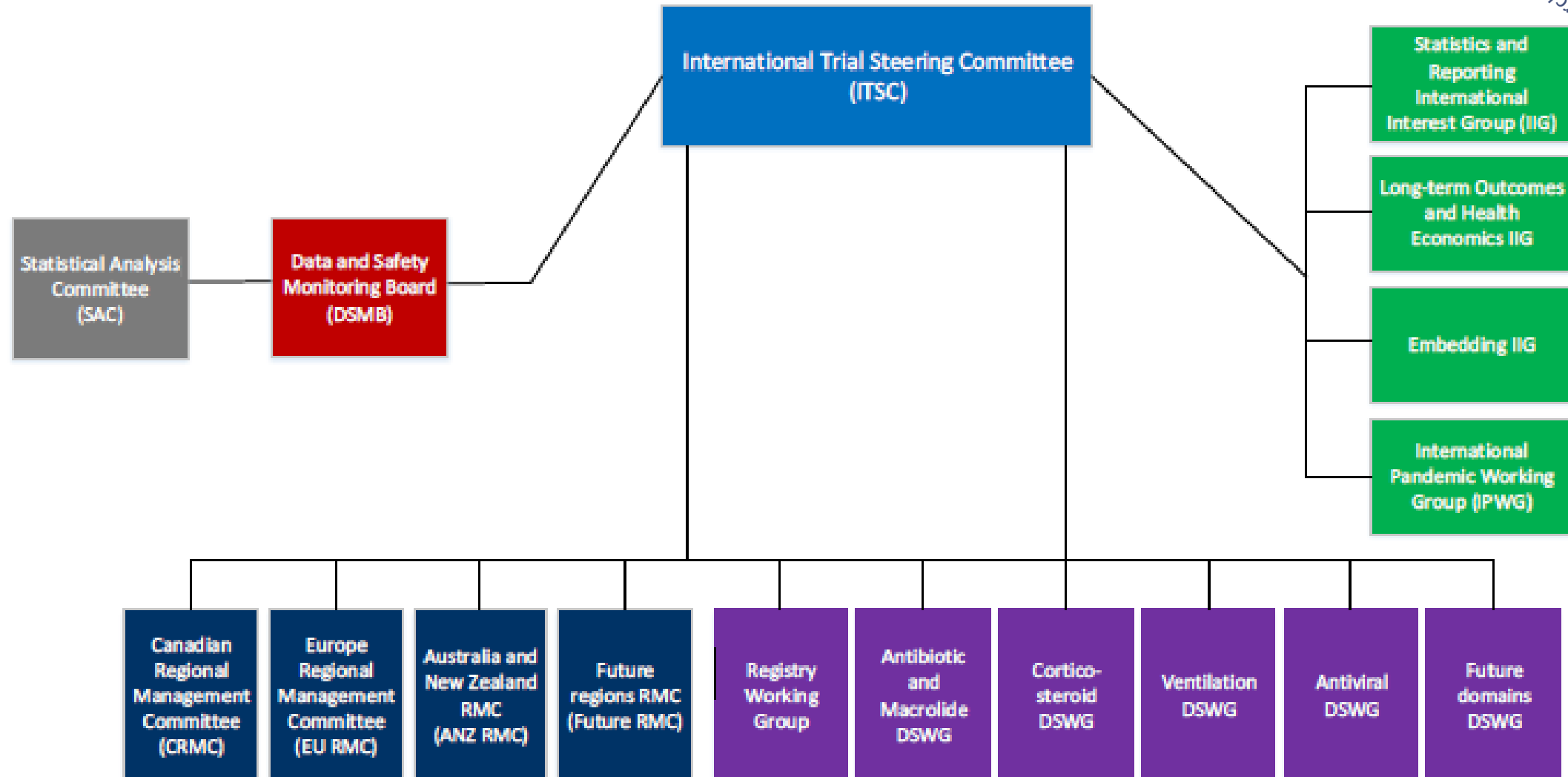
Strengthen Europe's pandemic (research) preparedness

Determine mechanisms of disease

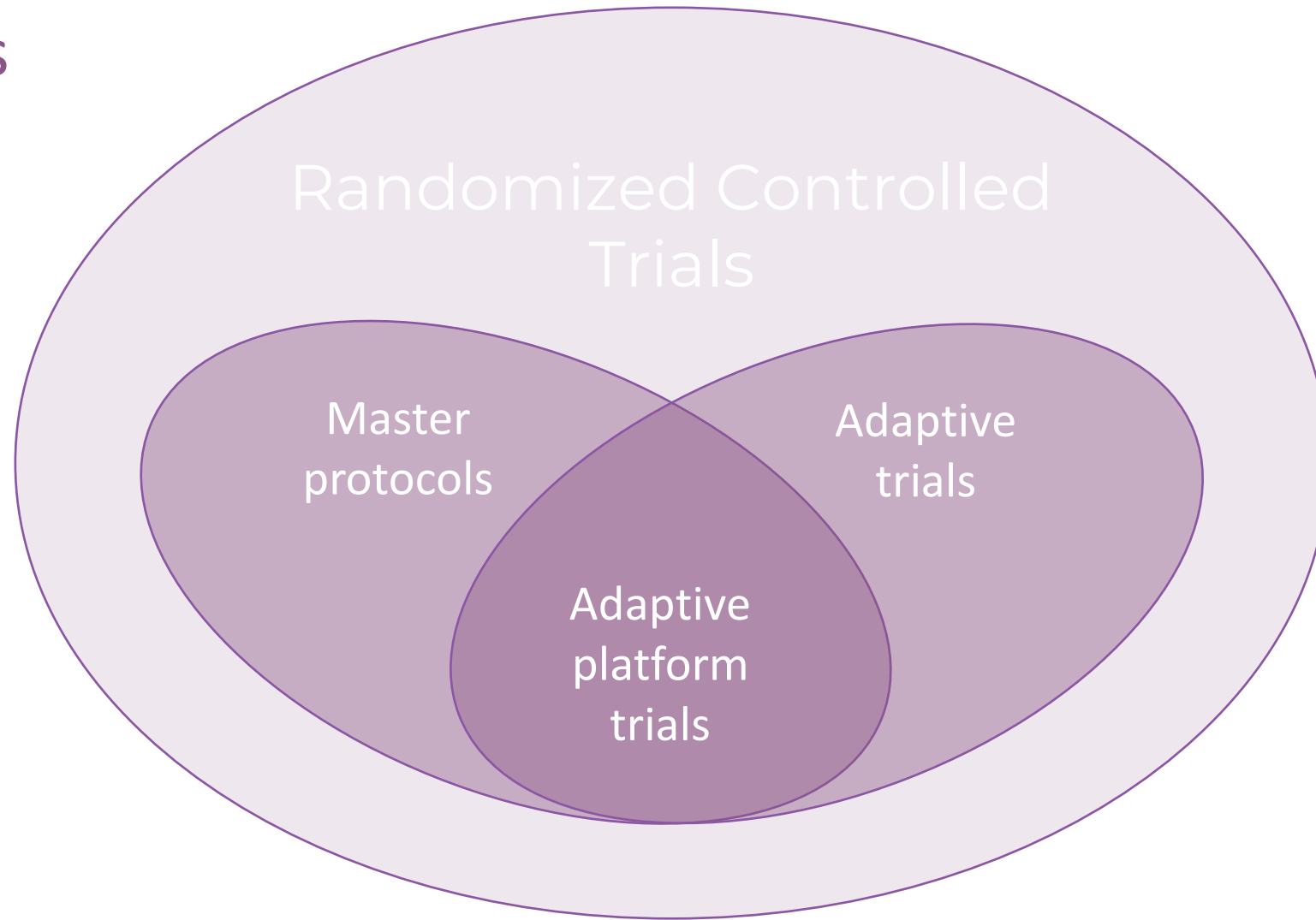


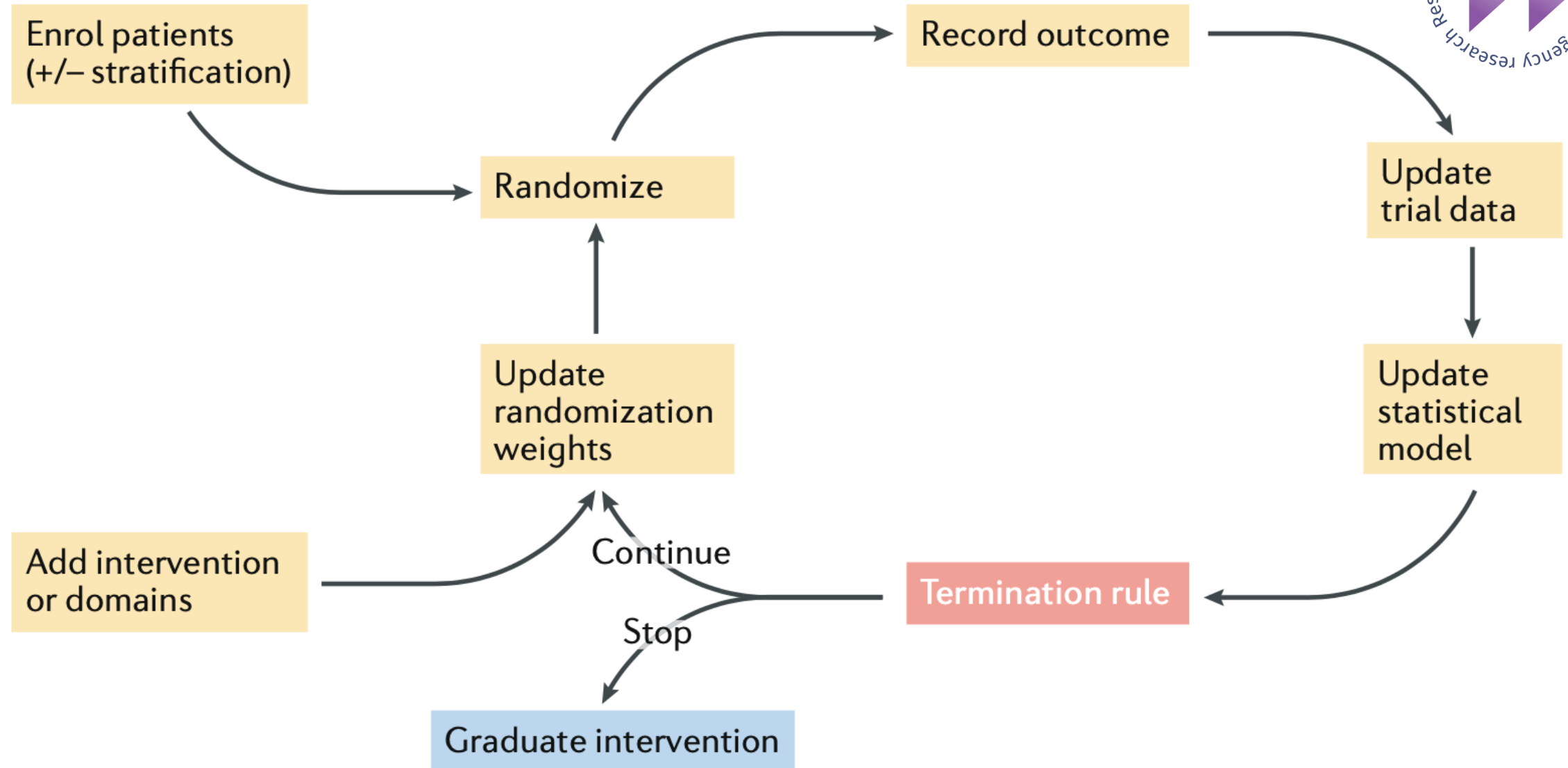


Figure 2: REMAP-CAP Organization Chart

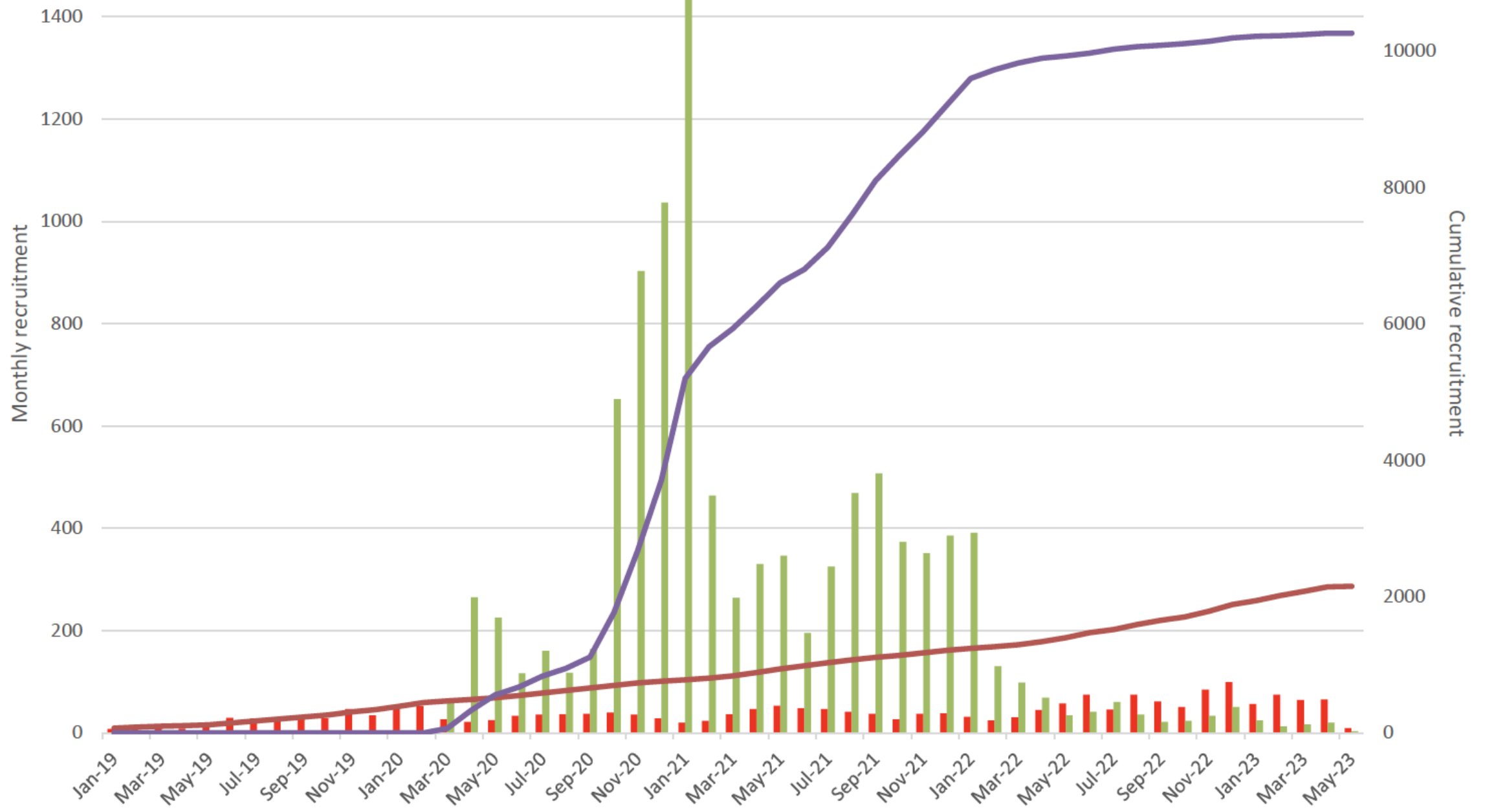


# Methods











REMAP-CAP Latest JAMA Publication - ACE2RAS - [Click here to read.](#)

13,950

Patient  
randomisation  
s

12,983

Patient  
randomisation  
s with  
suspected or  
proven COVID-  
19

28

Available  
interventions  
in 10 domains

7,362

Total patients

6,812

Patients with  
suspected or  
proven COVID-  
19

207

Active sites in  
Europe

# REMAP-CAP

A **R**andomised, **E**Embedded, **M**Multi-factorial,  
**A**Adaptive **P**Platform trial for  
**C**Community-**A**Acquired **P**Pneumonia

[Learn more](#)



Belgium  
Czech republic  
Germany  
Estonia  
Finland  
France  
Ireland  
Italy  
Netherlands  
Portugal  
Serbia  
Slovenia  
Spain  
Switzerland  
UK



Mar Apr May Jun Jul Aug Sep Oct Nov Dec Jan Feb Mar

1st Covid-19  
patient

#  
steroids

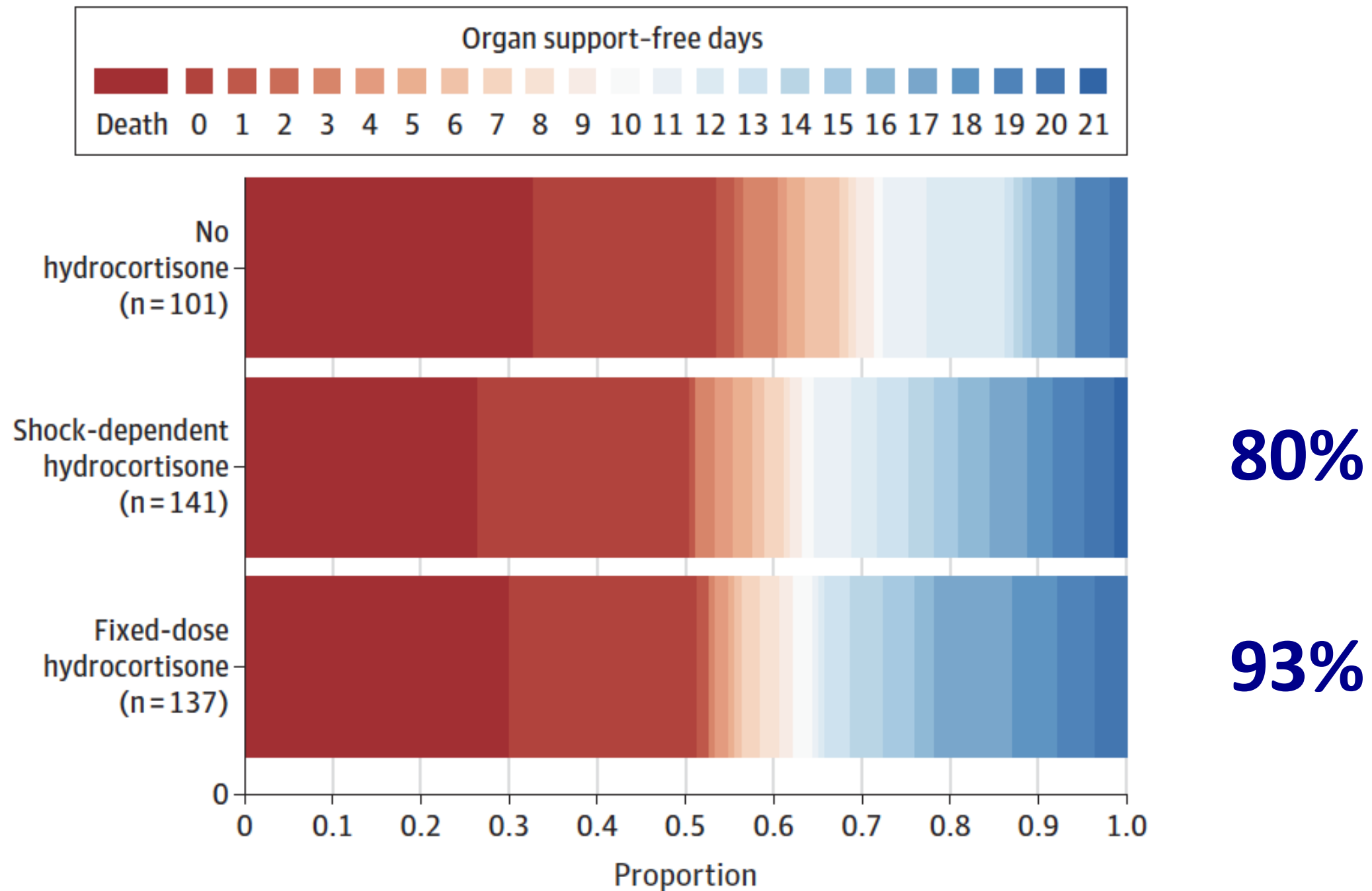
# HCQ  
#HCQ +  
L/r

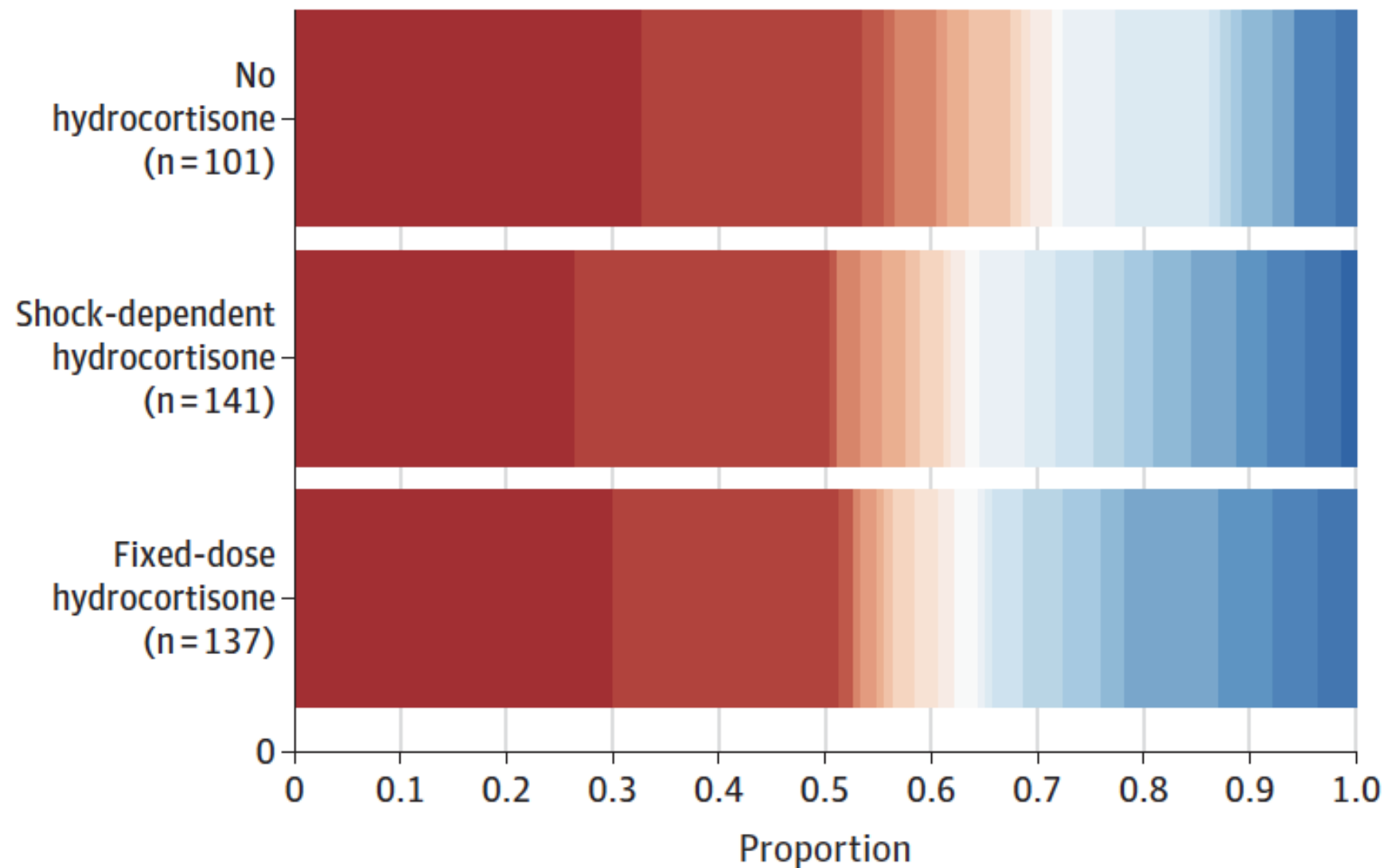
publication

pMA

2020

2021



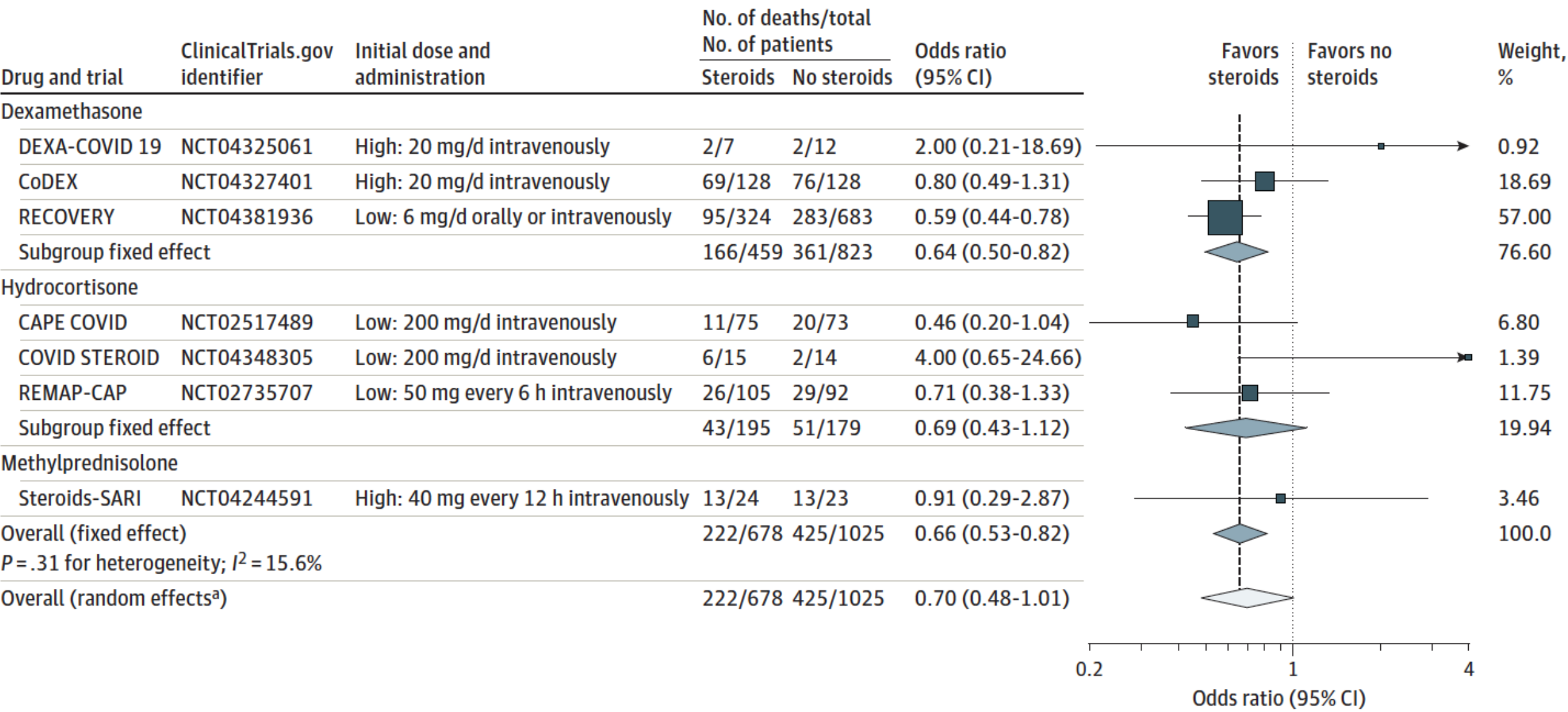


62%

54%

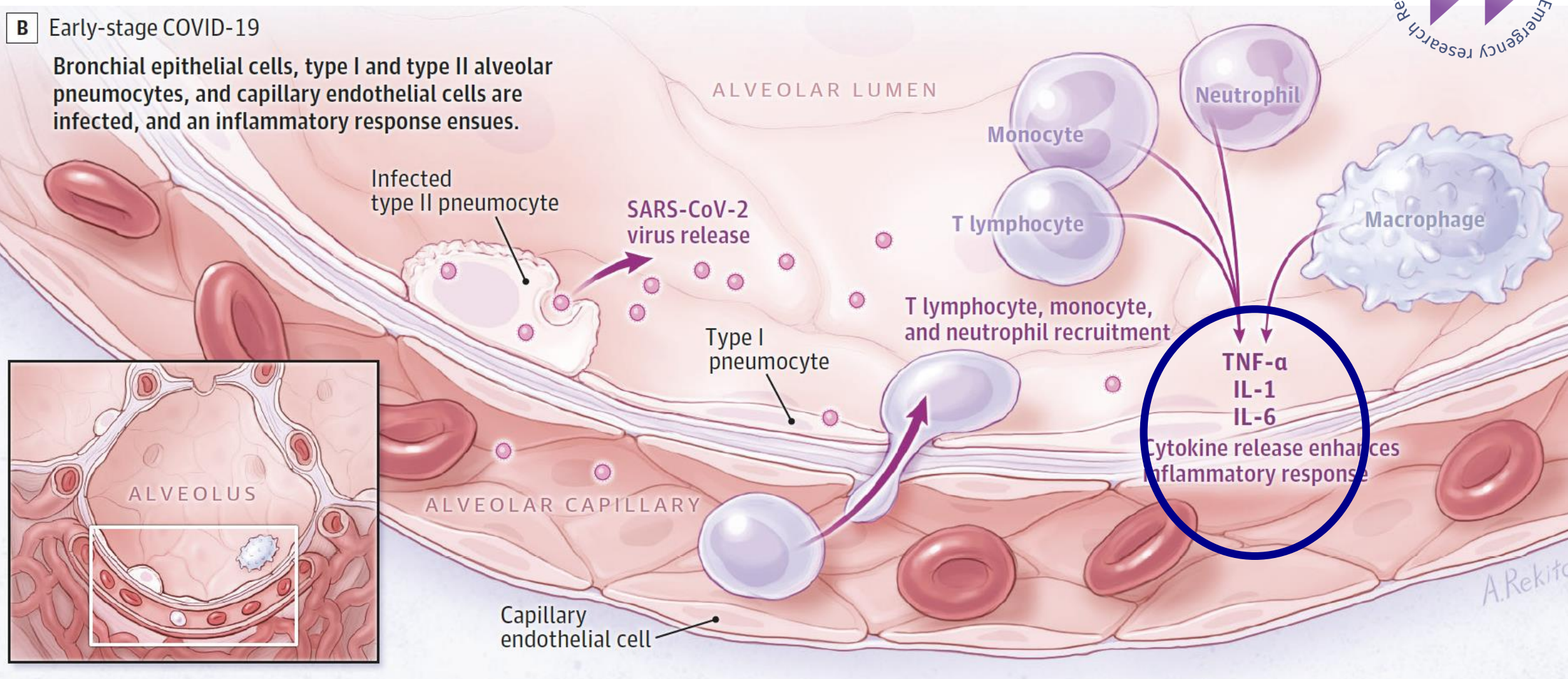


Figure 2. Association Between Corticosteroids and 28-Day All-Cause Mortality in Each Trial, Overall, and According to Corticosteroid Drug



**B** Early-stage COVID-19

Bronchial epithelial cells, type I and type II alveolar pneumocytes, and capillary endothelial cells are infected, and an inflammatory response ensues.



Mar Apr May Jun Jul Aug Sep Oct Nov Dec Jan Feb Mar

1st Covid-19  
patient

#  
steroids

# HCQ  
#HCQ +  
L/r

publication

pMA

tocilizum  
ab

preprint

publication

2020

2021

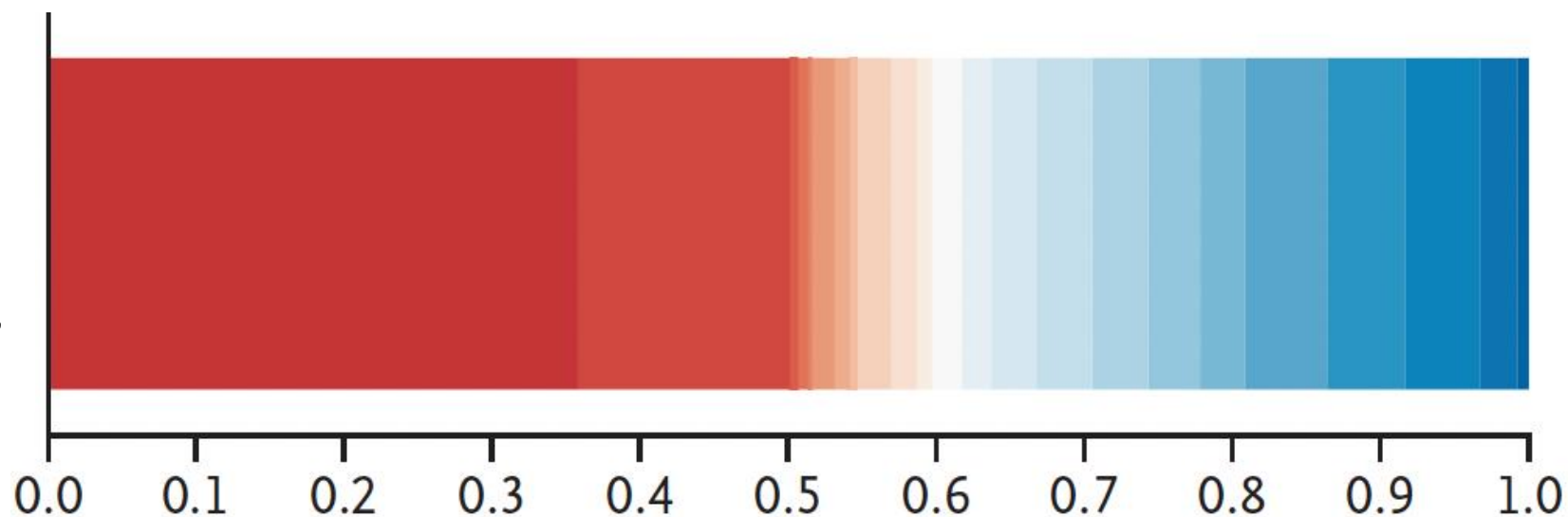


**toci/sari**

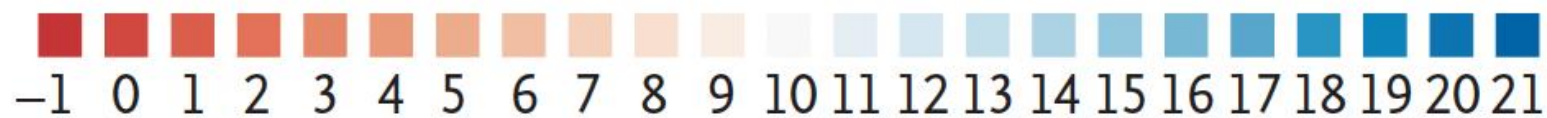
n=395

**standard**

n=397

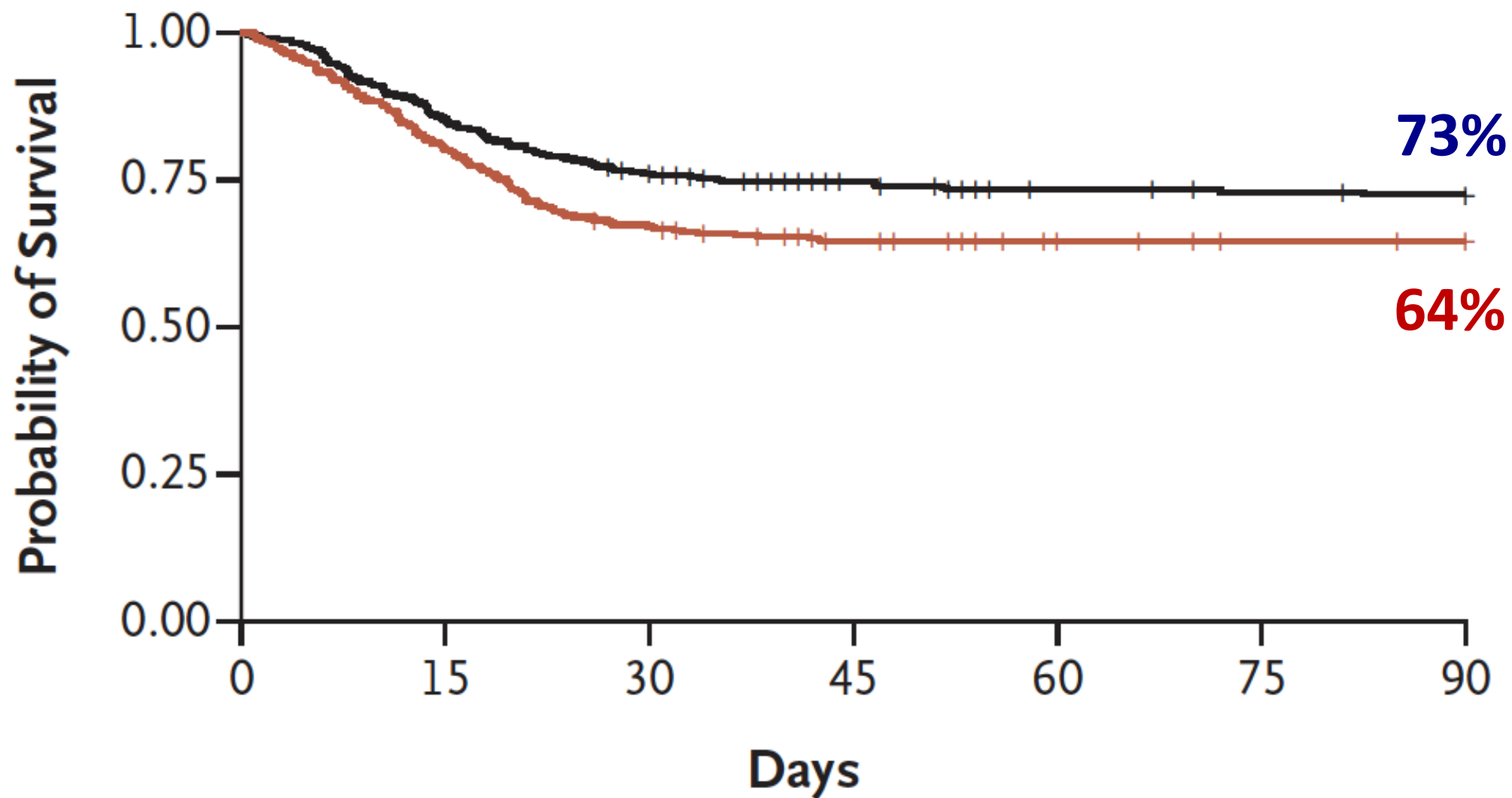


Proportion

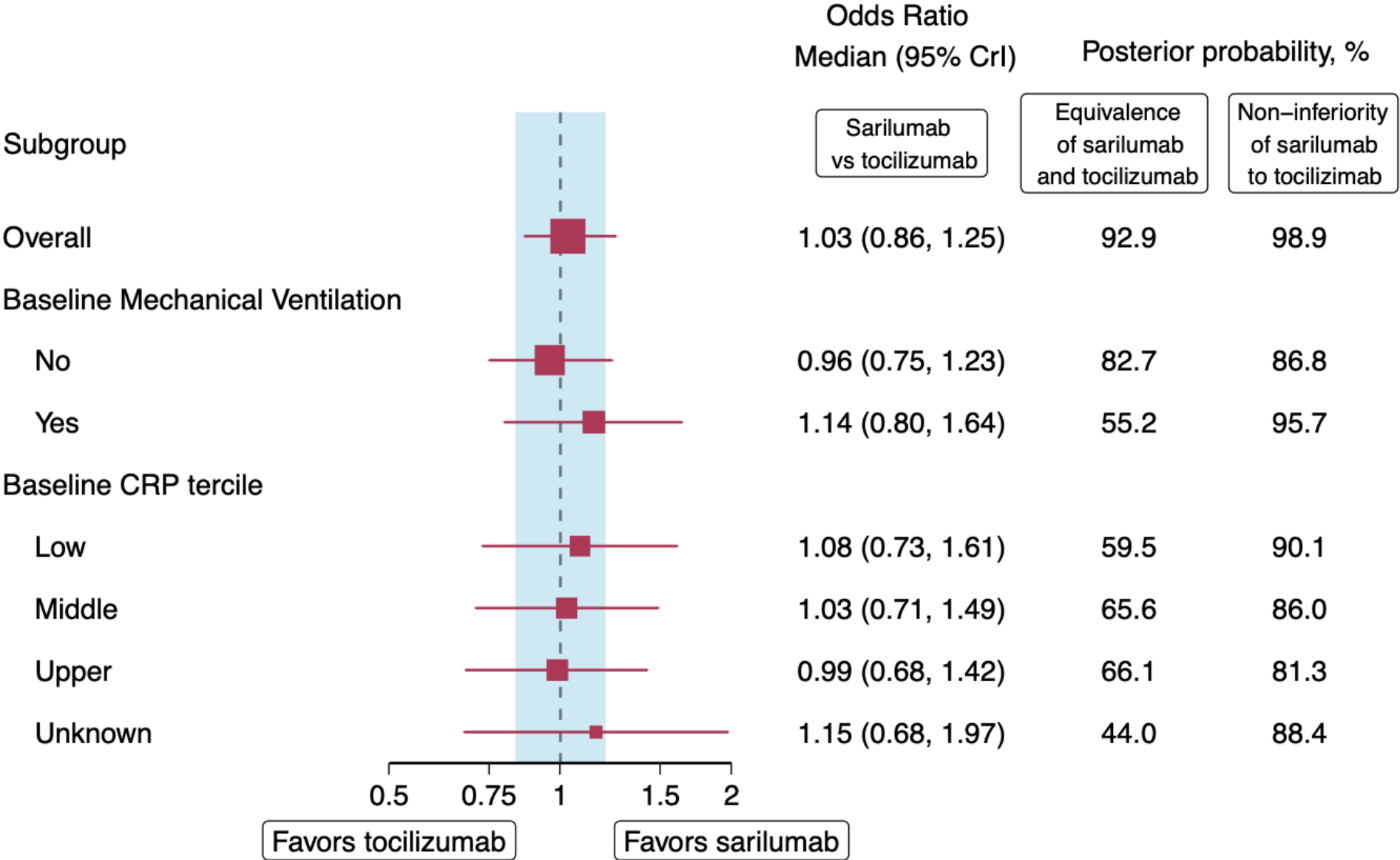


Organ Support-free Days





**Figure S2. Forest Plot of Organ Support Free days for sarilumab compared to tocilizumab**



NEWS › UK

# Boris Johnson struggles to pronounce new Covid drug tocilizumab at Downing Street press briefing

 [VIEW COMMENTS](#)



# THE TIMES

£2.20 ~~£1.10~~ to subscribers  
(based on 7 Day Print Pack)

## patients

### as NHS starts to be overwhelmed

is mobilising  
sibly can" but  
t be enough  
missions was

on the trial of  
ough on their  
of Imperial  
the study, said  
diate implica-  
patients with  
a time when  
deaths from  
the UK, it's  
ntify effective  
p to turn the

as quickly as possible. That is a small  
number of patients to treat to save a  
life," Professor Gordon said.

The findings are from the Remap-  
Cap study, which is led by Imperial and  
the Intensive Care National Audit &  
Research Centre (ICNARC) in the UK  
and the University Medical Centre  
Utrecht in Europe. The researchers  
looked at tocilizumab and a very similar  
drug called sarilumab.

Of the patients who got the treat-  
ment within a day of receiving assist-  
ance for breathing in an intensive care  
unit, 27.3 per cent died compared with  
35.8 per cent for a control group. This

Continued on page 2, col 3



9 771742 498059

## COVID-19 Therapeutic Alert

CEM/CMO/2021/001

8 January 2021

Interleukin-6 inhibitors (tocilizumab or sarilumab) for patients admitted to ICU with COVID-19 pneumonia (adults)

### Summary

The REMAP-CAP trial has reported a finding of survival and time to recovery benefits for tocilizumab or sarilumab, over and above current standard of care (including corticosteroids), in the immune modulation therapy domain of the REMAP-CAP platform trial. Mortality was reported as 35.8% in the placebo group, compared to 27% in the treatment group, an overall reduction in the risk of death of 24%. The treatment also reduced the time patients spent in the intensive care unit (ICU) by more than a week on average. The published UK wide Interim Position Statement has therefore been revised to support access to either tocilizumab or sarilumab (when available), administered intravenously, for eligible COVID-19 positive patients in the intensive care setting.

## Therapeutics and COVID-19

LIVING GUIDELINE  
31 MARCH 2021



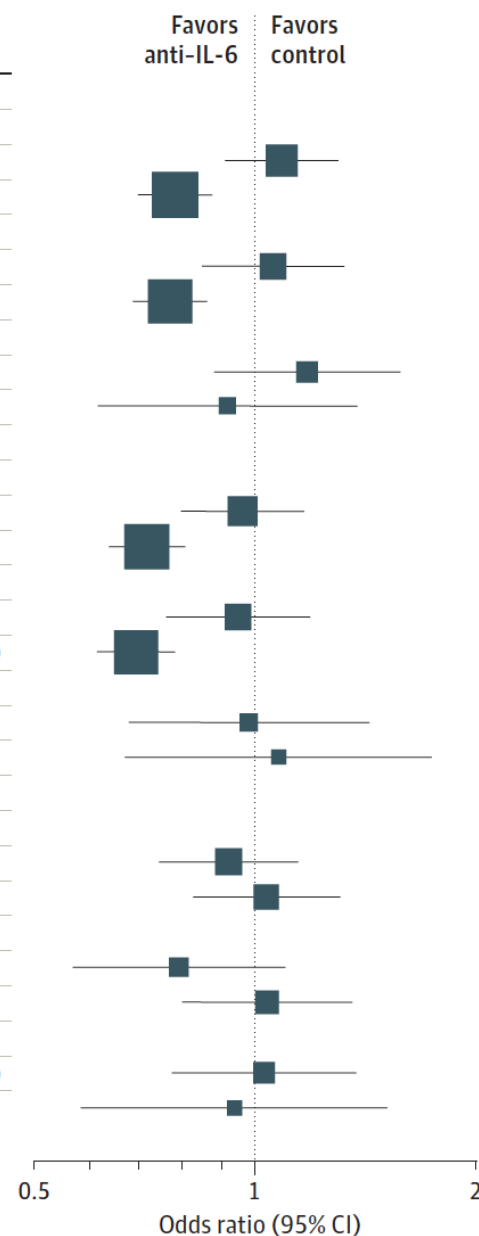
>3800 trials [...]

RECOVERY, WHO SOLIDARITY, DISCOVERY, REMAP-CAP and ACTIV

Publication of the RECOVERY and REMAP-CAP trials [...] triggered this recommendation



Outcome and treatment	<i>I</i> <sup>2</sup> , %	No. of events/total patients		Odds ratio (95% CI)
		Control	Anti-IL-6	
28-d mortality				
All anti-IL-6				
No corticosteroid use	0	293/1280	537/2357	1.09 (0.91-1.30)
Corticosteroid use	0	838/2848	827/3468	0.78 (0.69-0.88)
Tocilizumab				
No corticosteroid use	0	211/898	254/1192	1.06 (0.85-1.33)
Corticosteroid use	0	793/2585	693/2815	0.77 (0.68-0.87)
Sarilumab				
No corticosteroid use	0	83/384	283/1134	1.18 (0.88-1.58)
Corticosteroid use	0	48/281	124/607	0.92 (0.61-1.38)
Progression to IMV, ECMO, or death at 28 d				
All anti-IL-6				
No corticosteroid use	0	308/1004	399/1541	0.96 (0.79-1.17)
Corticosteroid use	0	893/2496	822/2986	0.71 (0.63-0.80)
Tocilizumab				
No corticosteroid use	0	250/791	266/1016	0.95 (0.76-1.20)
Corticosteroid use	0	859/2283	729/2518	0.69 (0.61-0.78)
Sarilumab				
No corticosteroid use	0	59/214	126/498	0.98 (0.67-1.44)
Corticosteroid use	0	38/227	75/423	1.08 (0.67-1.75)
28-d secondary infections <sup>a</sup>				
All anti-IL-6				
No corticosteroid use	3	165/758	434/1820	0.92 (0.74-1.15)
Corticosteroid use	1	160/798	310/1378	1.04 (0.82-1.31)
Tocilizumab				
No corticosteroid use	0	86/385	146/659	0.79 (0.57-1.10)
Corticosteroid use	16	132/573	210/772	1.04 (0.80-1.36)
Sarilumab				
No corticosteroid use	8	79/373	285/1130	1.03 (0.77-1.38)
Corticosteroid use	0	28/225	92/560	0.94 (0.58-1.52)



July 6, 2021  
pMA  
invited by WHO

Dec Jan Feb Mar Apr May Jun Jul Aug Sept Oct Nov Dec Jan

publication

heparin

(C)

conv

plasma

heparin

**2021**(M)

2

publications

CP

publication

**2022**



*The NEW ENGLAND JOURNAL of MEDICINE*

ORIGINAL ARTICLE

## Therapeutic Anticoagulation with Heparin in Noncritically Ill Patients with Covid-19

The ATTACC, ACTIV-4a, and REMAP-CAP Investigators\*

*The* **NEW ENGLAND**  
**JOURNAL** *of* **MEDICINE**

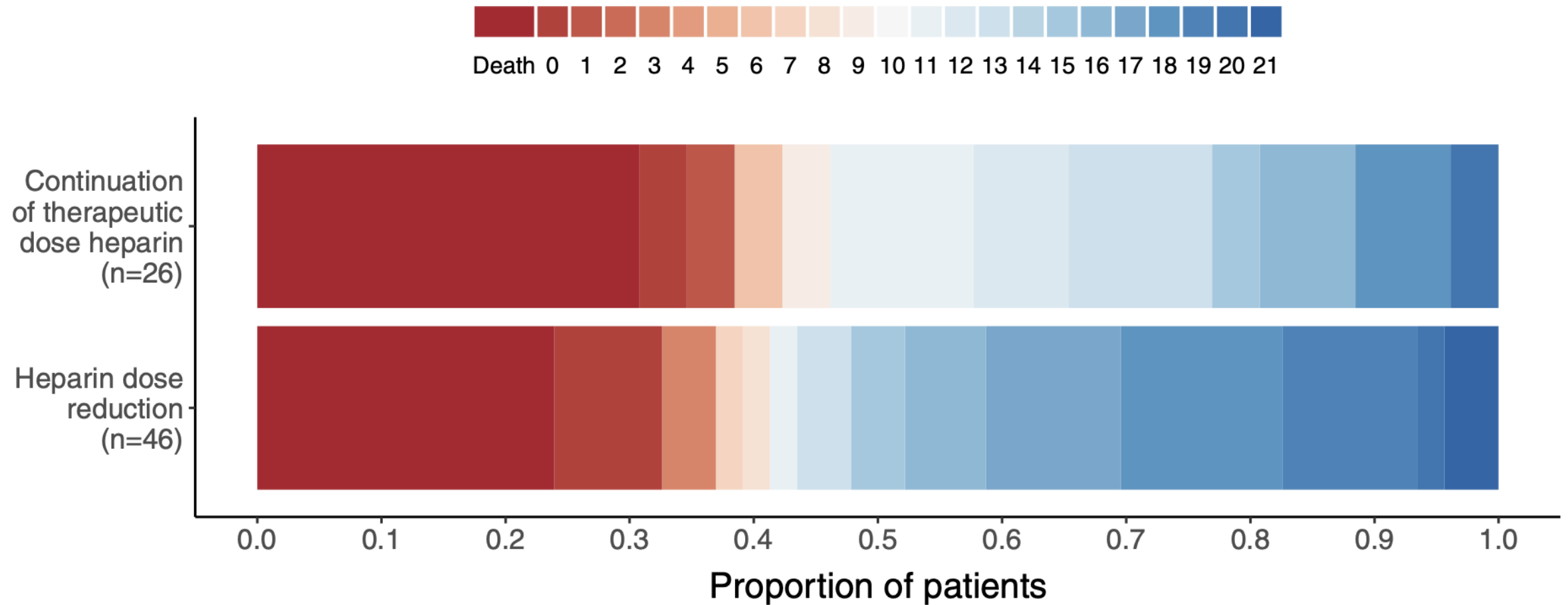
ESTABLISHED IN 1812

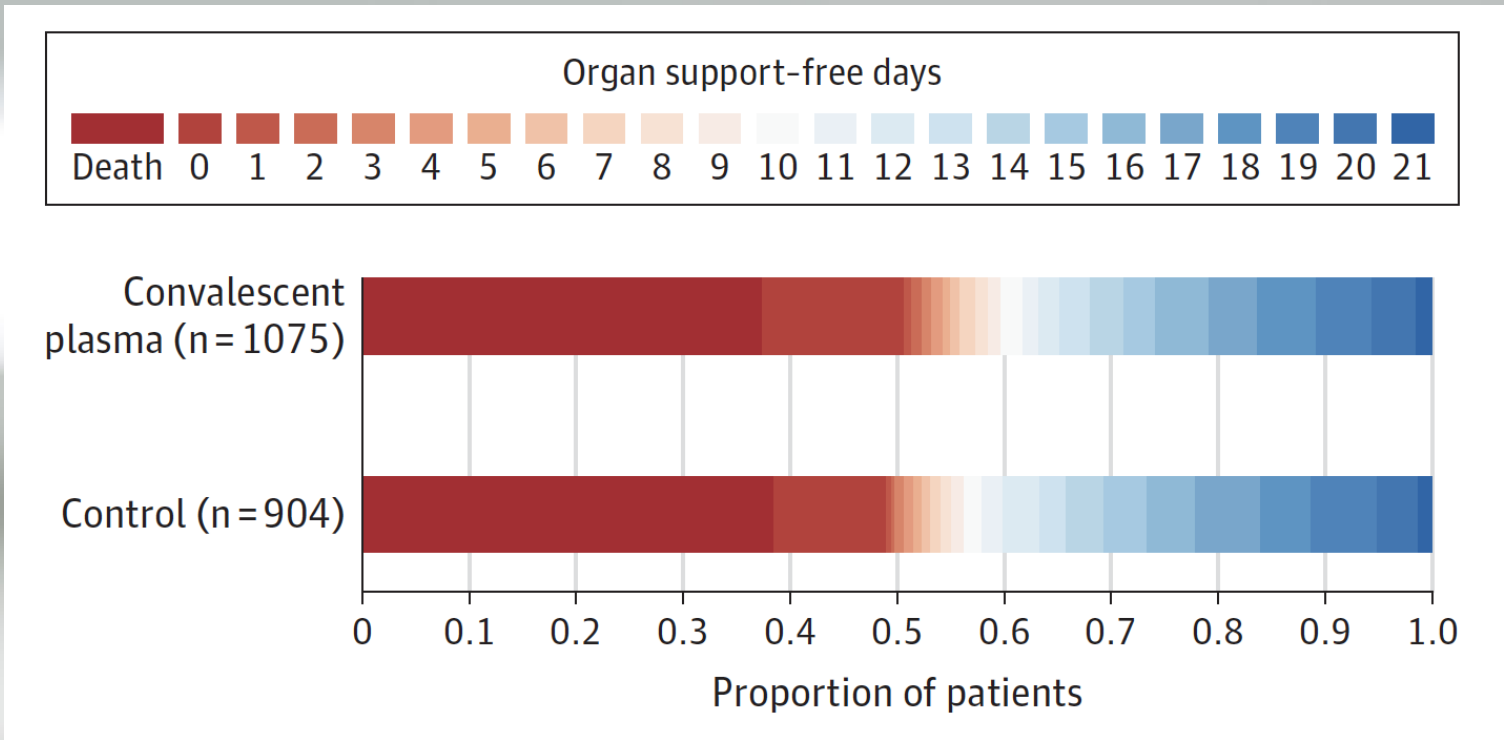
AUGUST 26, 2021

VOL. 385 NO. 9

## Therapeutic Anticoagulation with Heparin in Critically Ill Patients with Covid-19

The REMAP-CAP, ACTIV-4a, and ATTACC Investigators\*

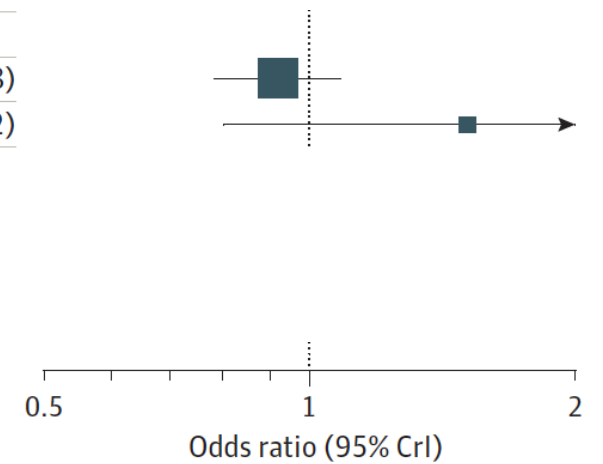


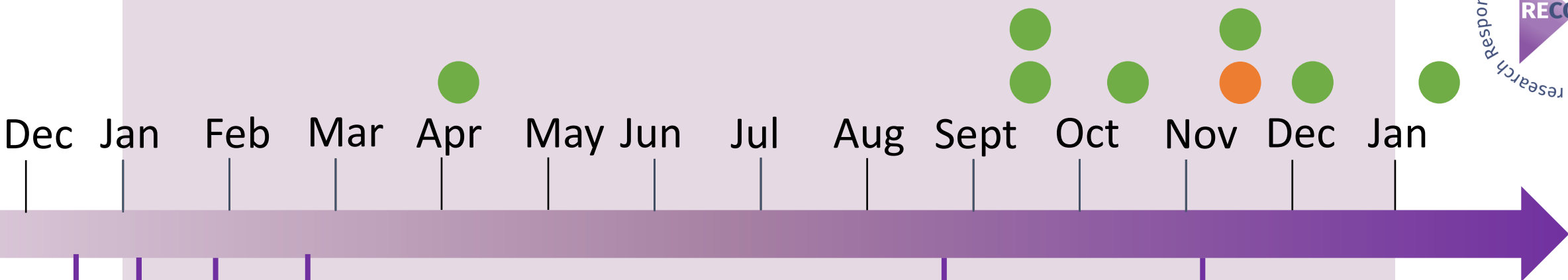




Convalescent plasma		Control		Odds ratio (95% CrI) <sup>b</sup>	Favors control : Favors convalescent plasma
No. of patients	Median (IQR)	No. of patients	Median (IQR)		

Immunodeficiency <sup>d</sup>					
No	994	0 (-1 to 16)	840	5 (-1 to 16)	0.92 (0.78 to 1.08)
Yes	66	0 (-1 to 13)	60	-1 (-1 to 3)	1.51 (0.80 to 2.92)





publication

heparin

conv  
plasma

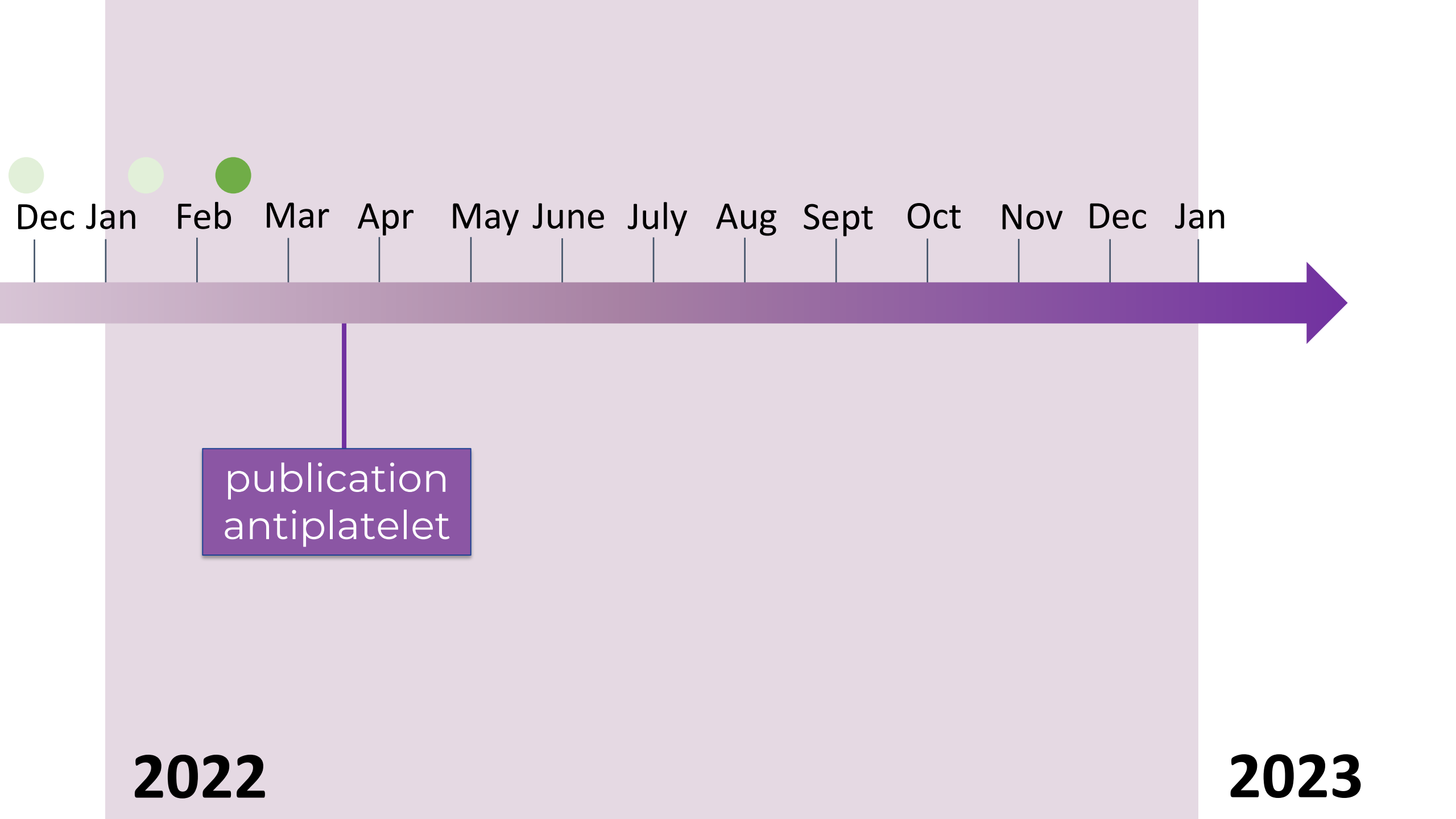
heparin

2  
publications

CP  
publication

2021(M)

2022

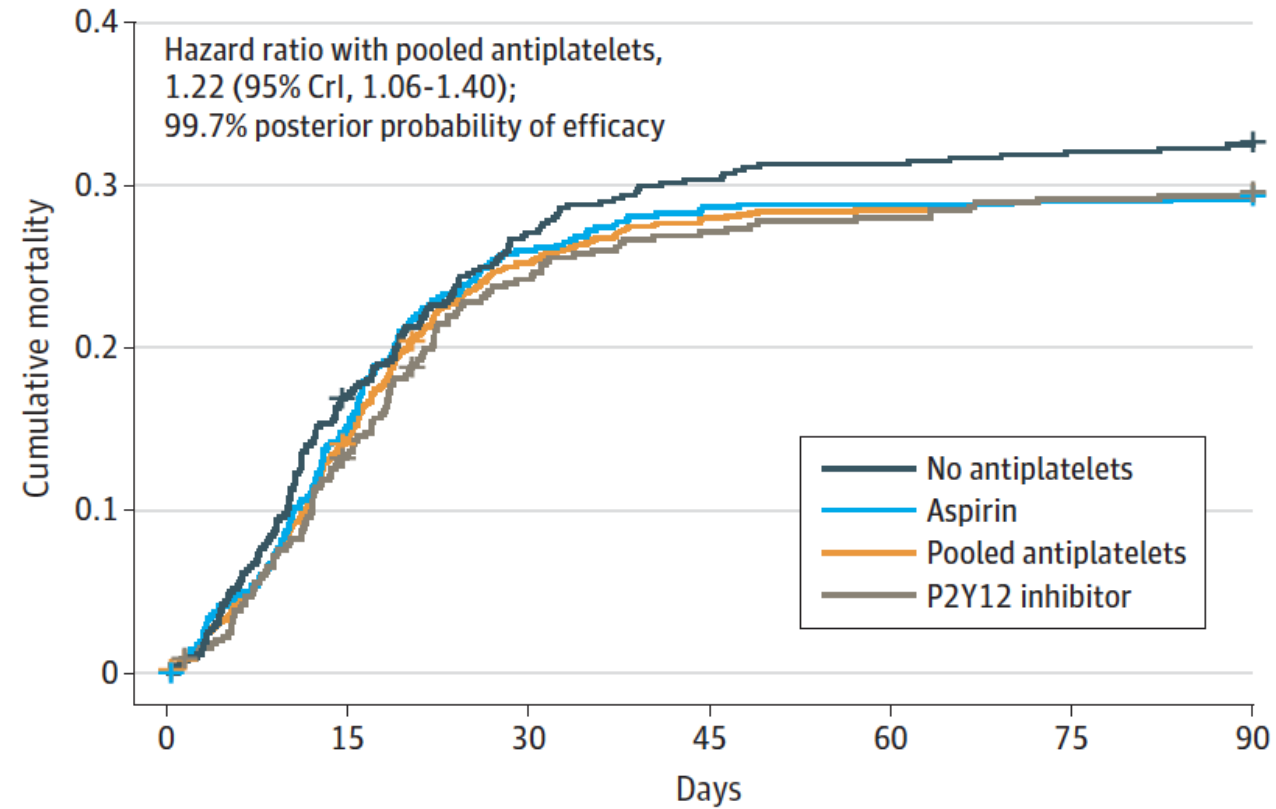


2022

2023

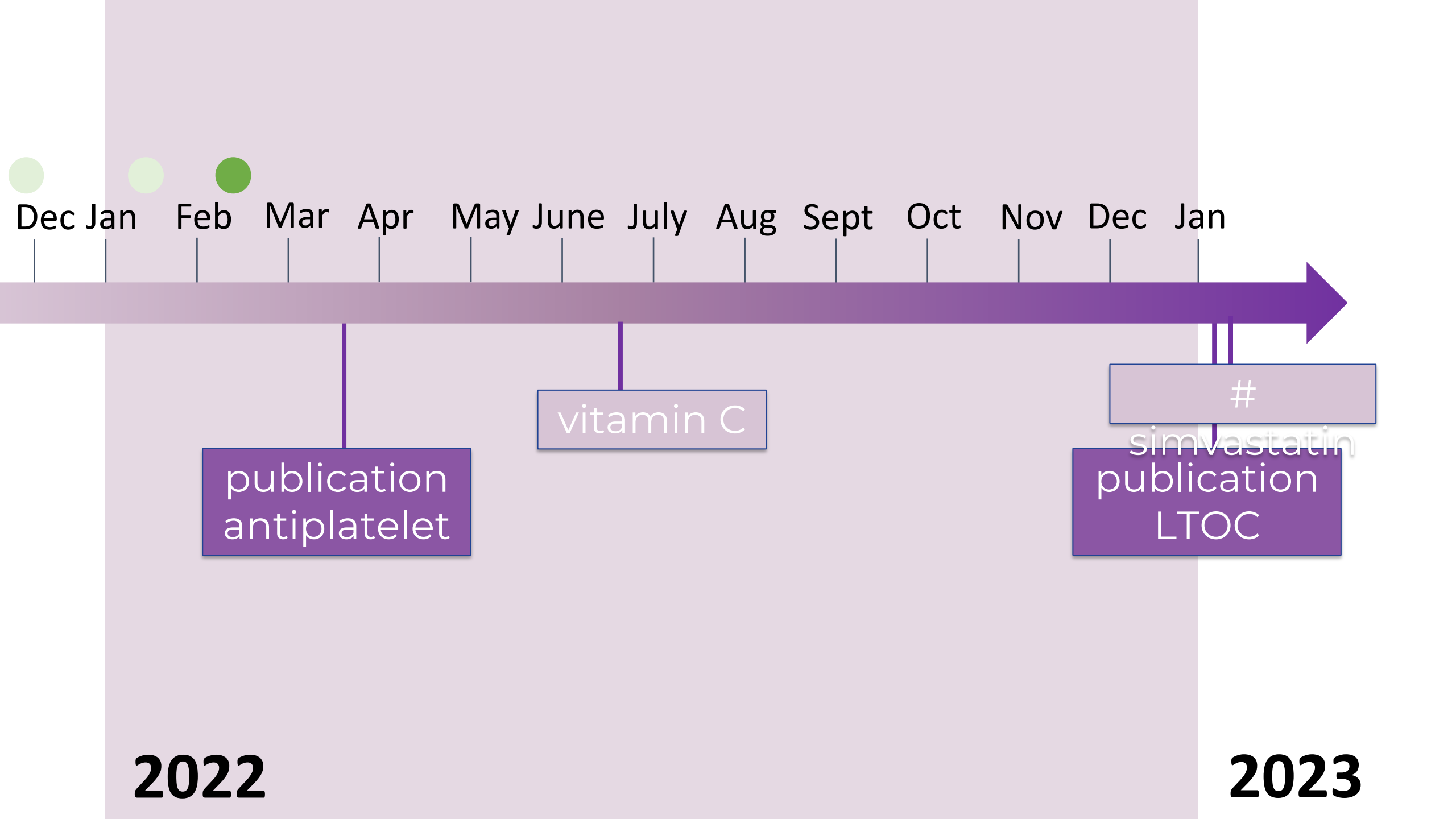
publication  
antiplatelet

Figure 3. Survival Through 90 Days in Critically Ill Patients



No. at risk

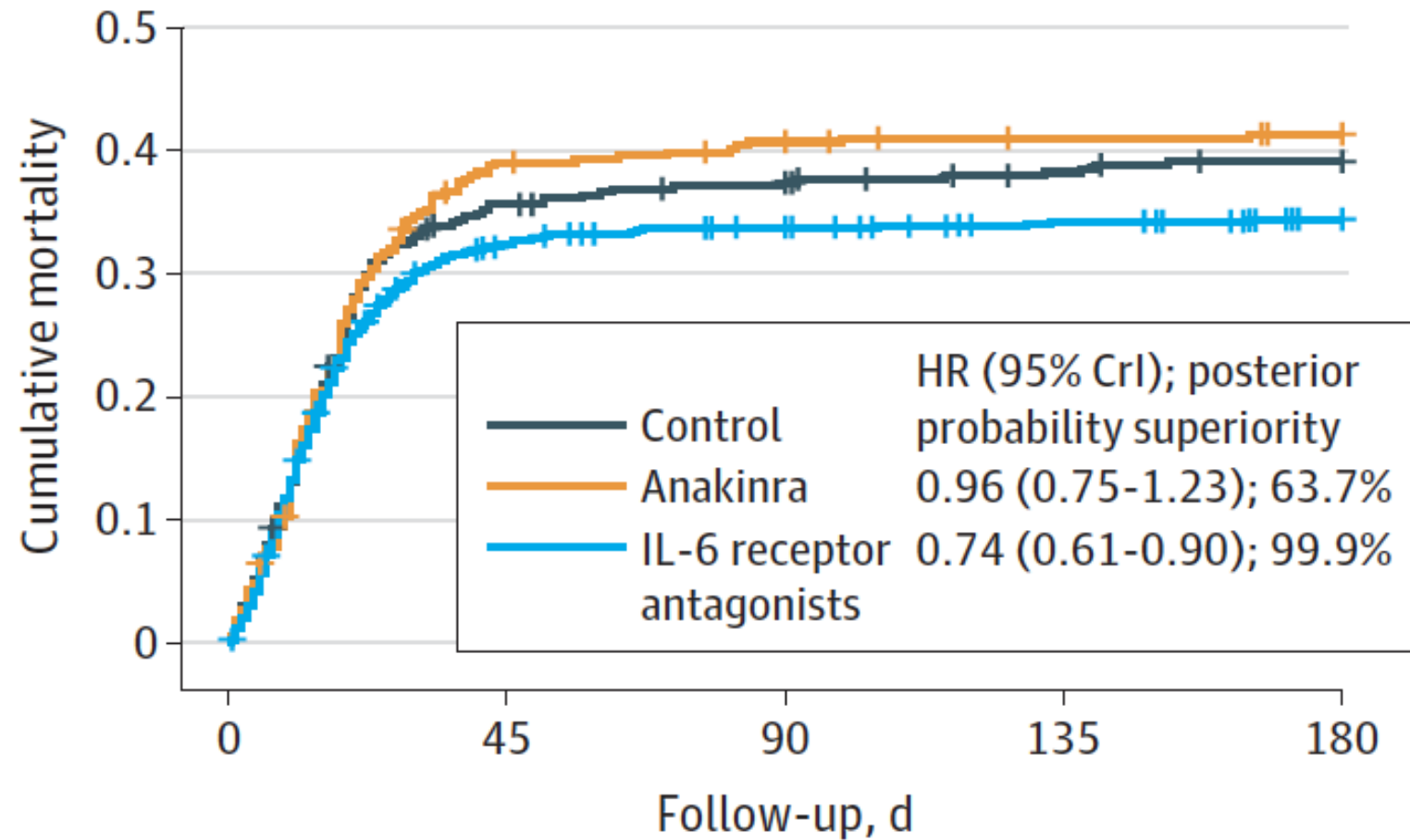
No antiplatelets	521	431	379	362	357	353	351
Aspirin	563	477	416	401	400	399	398
Pooled antiplatelets	1011	863	753	725	720	714	712
P2Y12 inhibitor	448	386	337	324	320	315	314



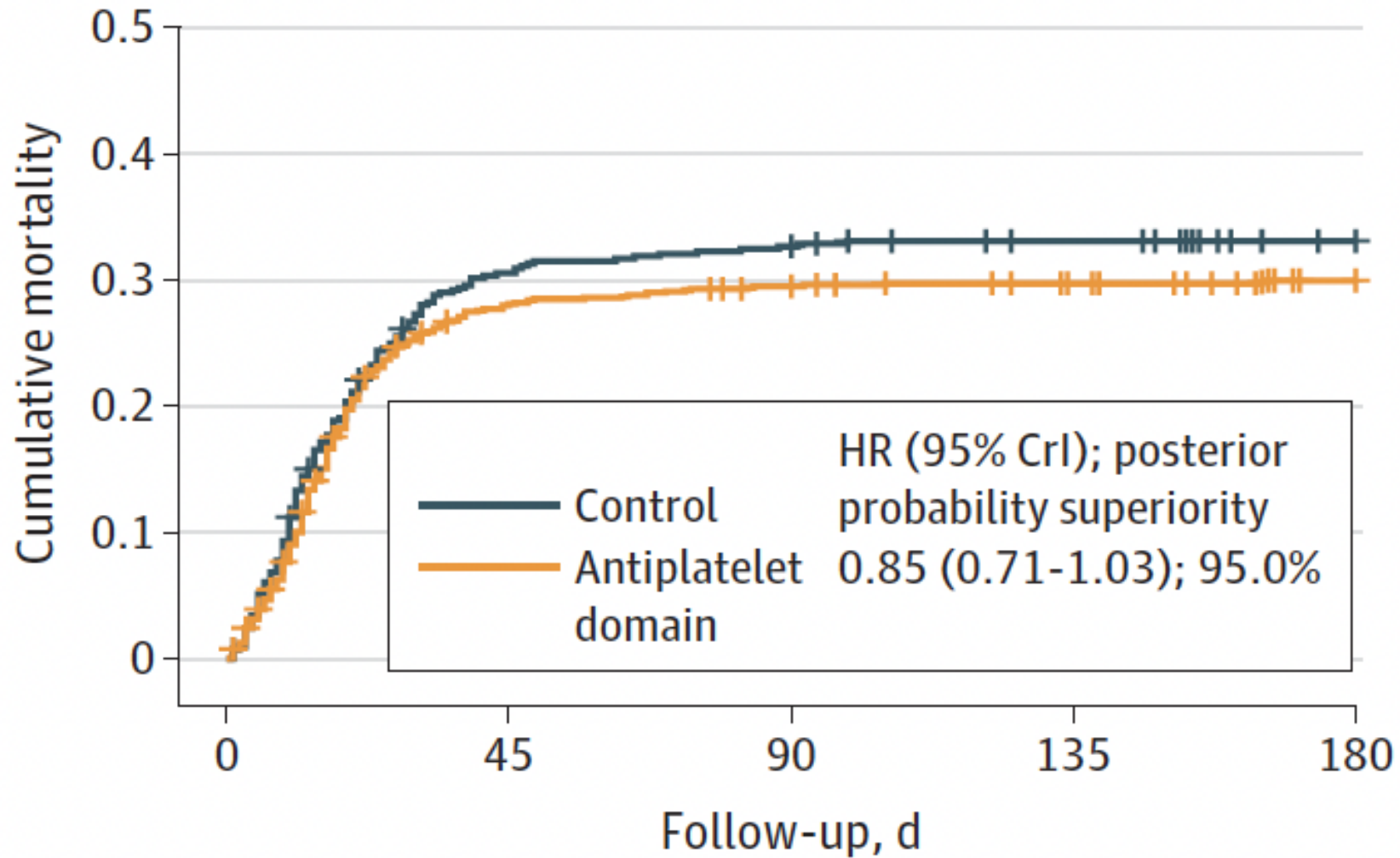


# Long term outcomes

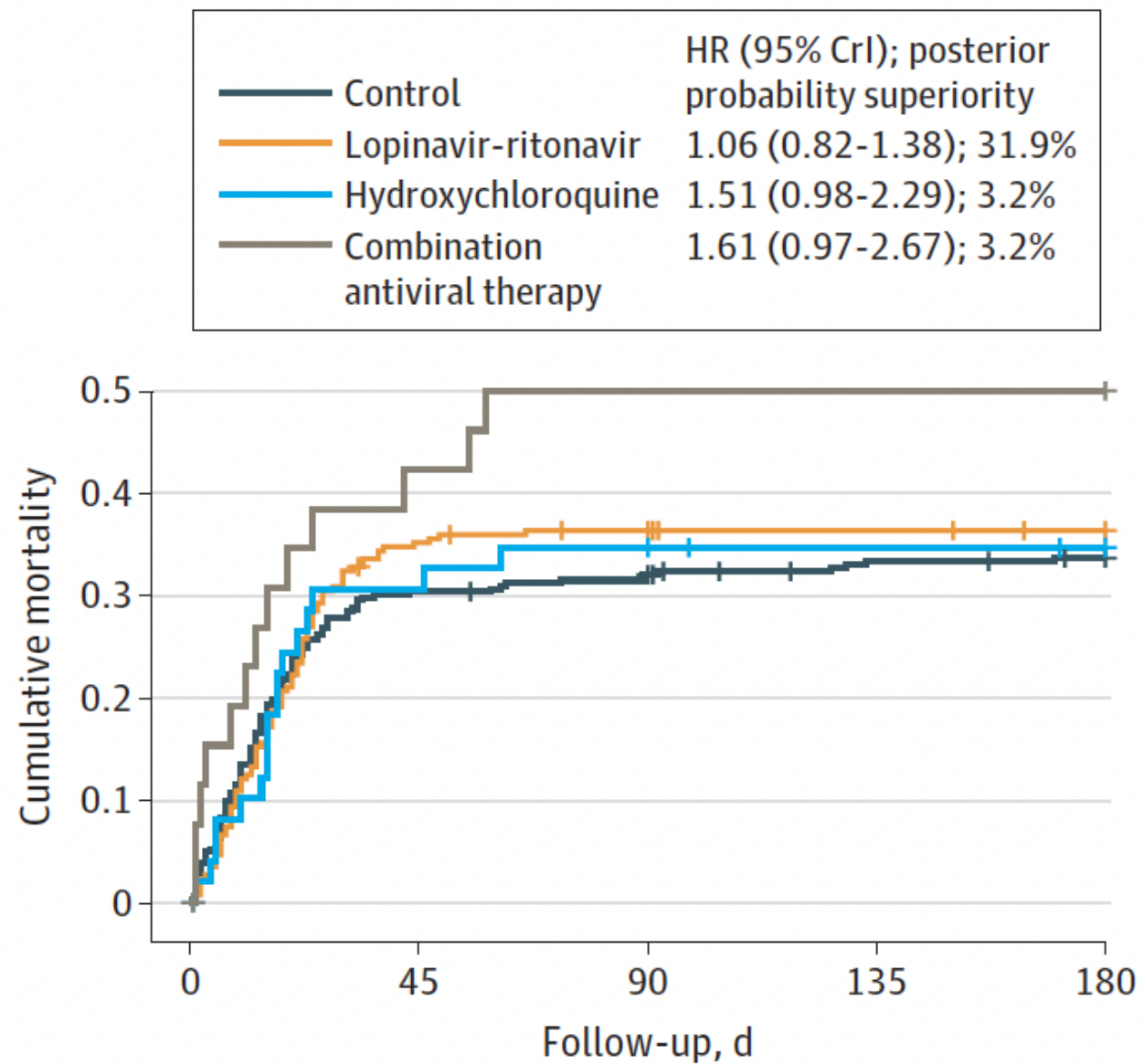
## A Immune modulation domain

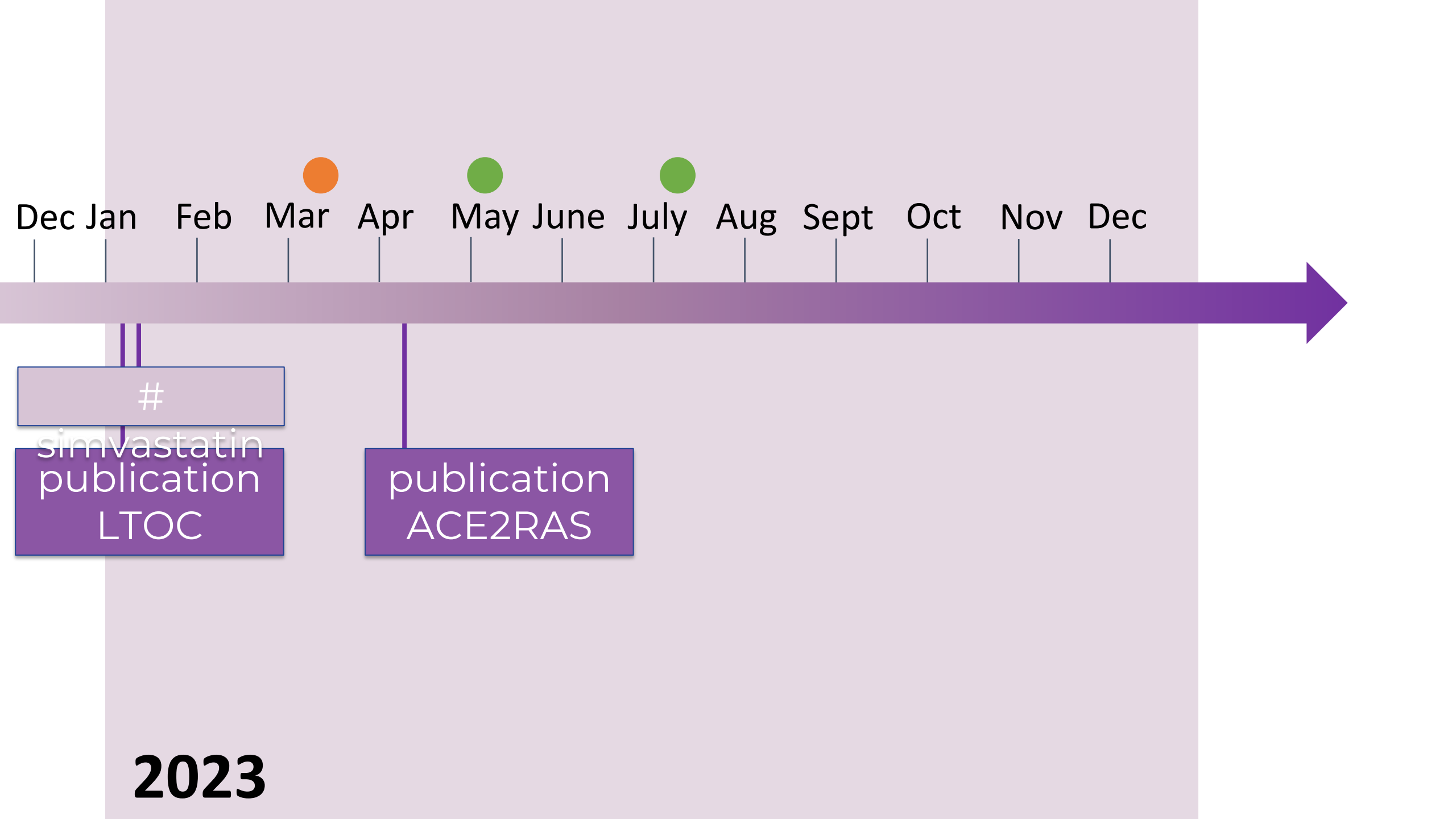


**C** Antiplatelet domain



**E** Antiviral domain





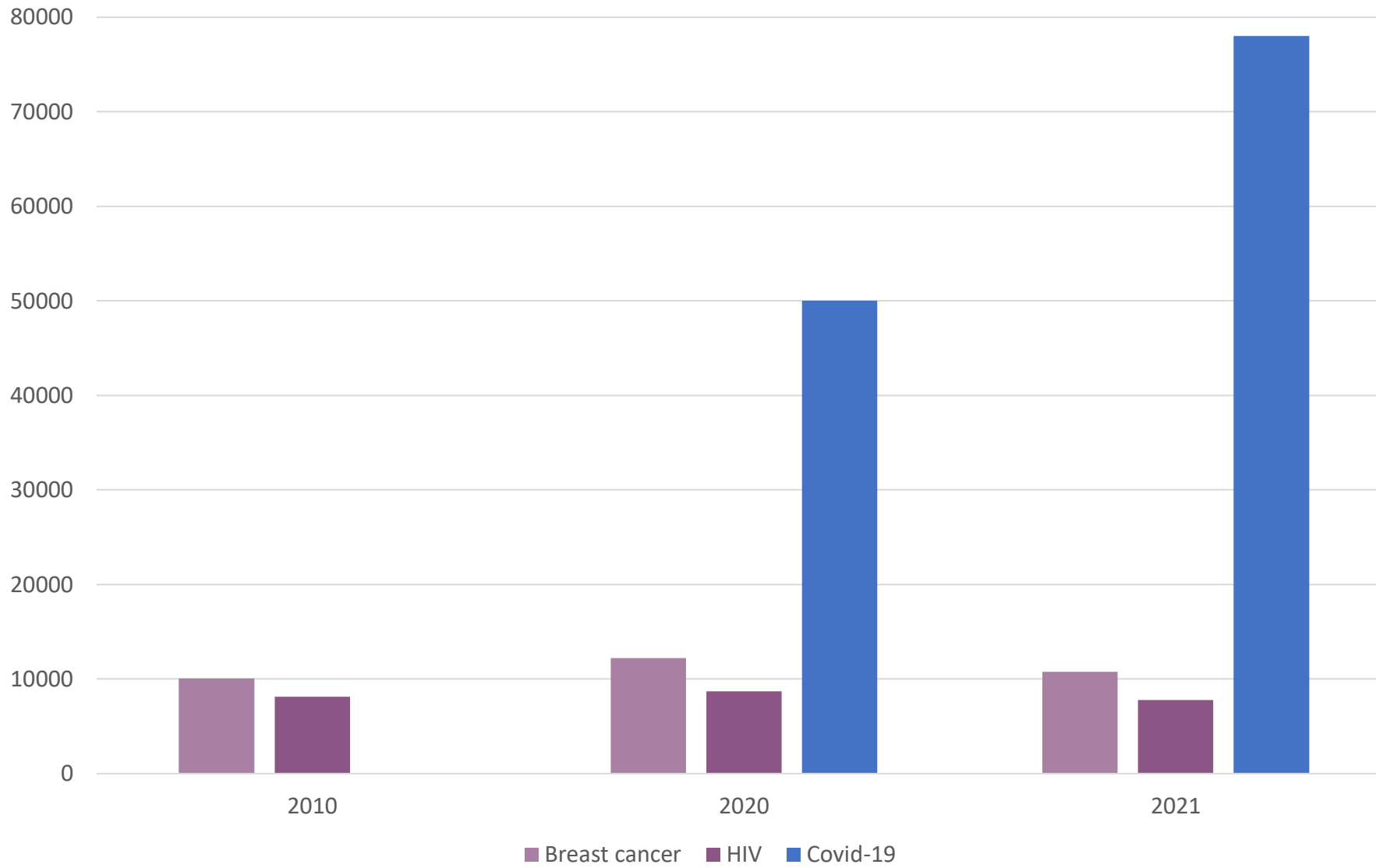


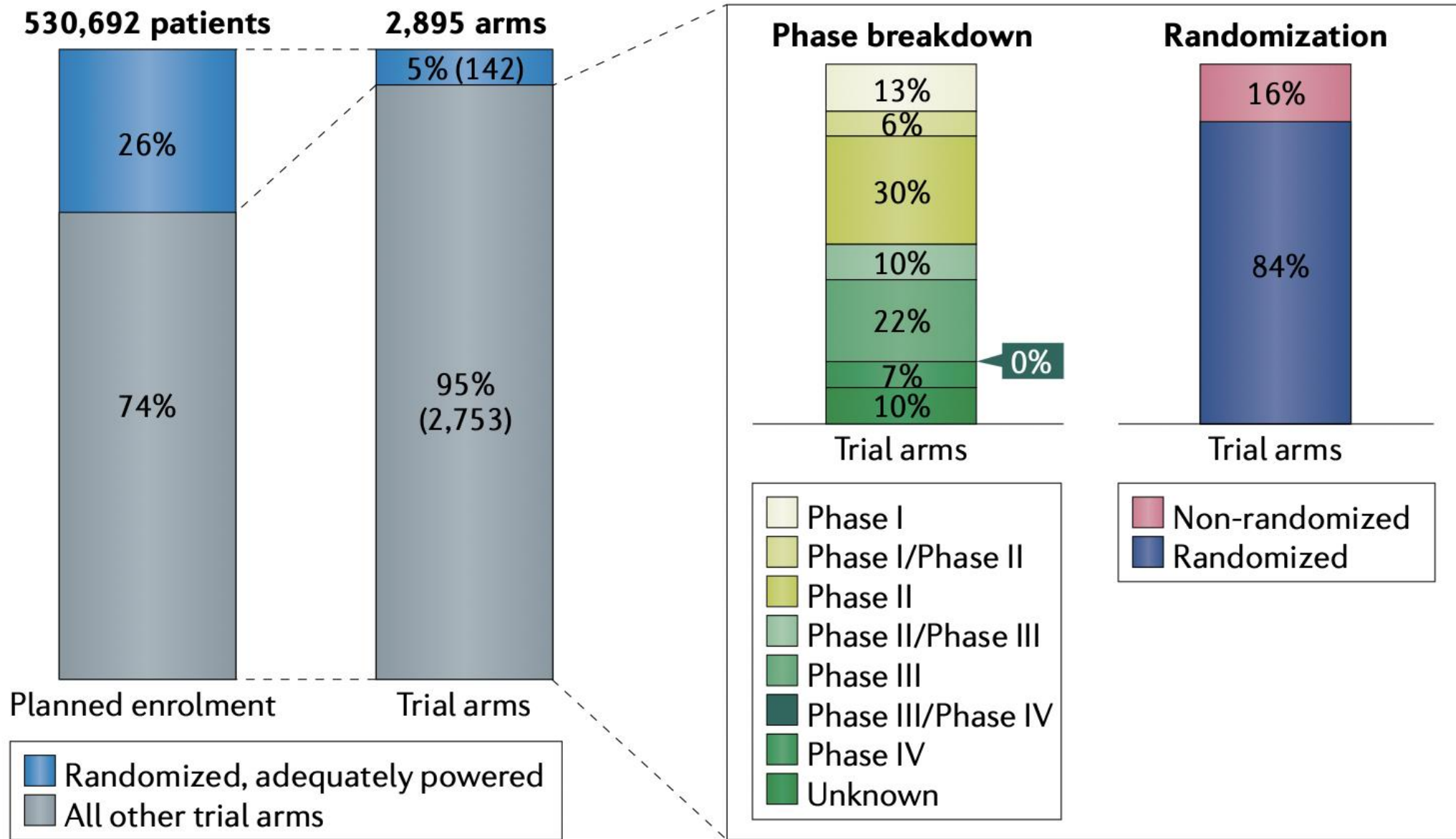
Conclusion	Result	Publications
Corticosteroids	Benefit	JAMA 2020;324(13):1317-1329
Lopinavir/ritonavir Hydroxychloroquine	Likely harm Harm	ICM 2021 Aug;47(8):867-886
Tocilizumab Sarilumab Anakinra Interferon beta-1a	Benefit Benefit Futile Operationally futile	NEJM 2021;384(16):1491-1502
Heparin – moderate	Benefit	NEJM 2021;385(9):790-802
Heparin – severe	Futile	NEJM 2021;385(9):777-789
Convalescent plasma	Futile	JAMA 2021;326(17):1690-1702
Aspirin	Futile	JAMA 2022;327(13):1247–1259
ACEi and ARB	Likely harm	JAMA 2023;329(14):1183–1196
Long term outcomes	Consistent	JAMA 2023;329(1):39-51
continued TAC - severe	Likely harm	ICM 2023 May 31 doi: 10.1007/s00134-023-07095-8

**impact**



## Research Publications











# Impact



14 conclusions directly impacting patient care  
learning while doing

immediate uptake in (inter-)national guidelines  
modes of collaboration: pMA, mpRCT  
educating the community



@remap\_cap



@REMAPCAP



REMAP-CAP



REM-AP-CAP  
PODCAST

## Lessons learned



PREPARE seed funding crucial

Trust versus control

A pandemic is different from peacetime

F2F

Inspections

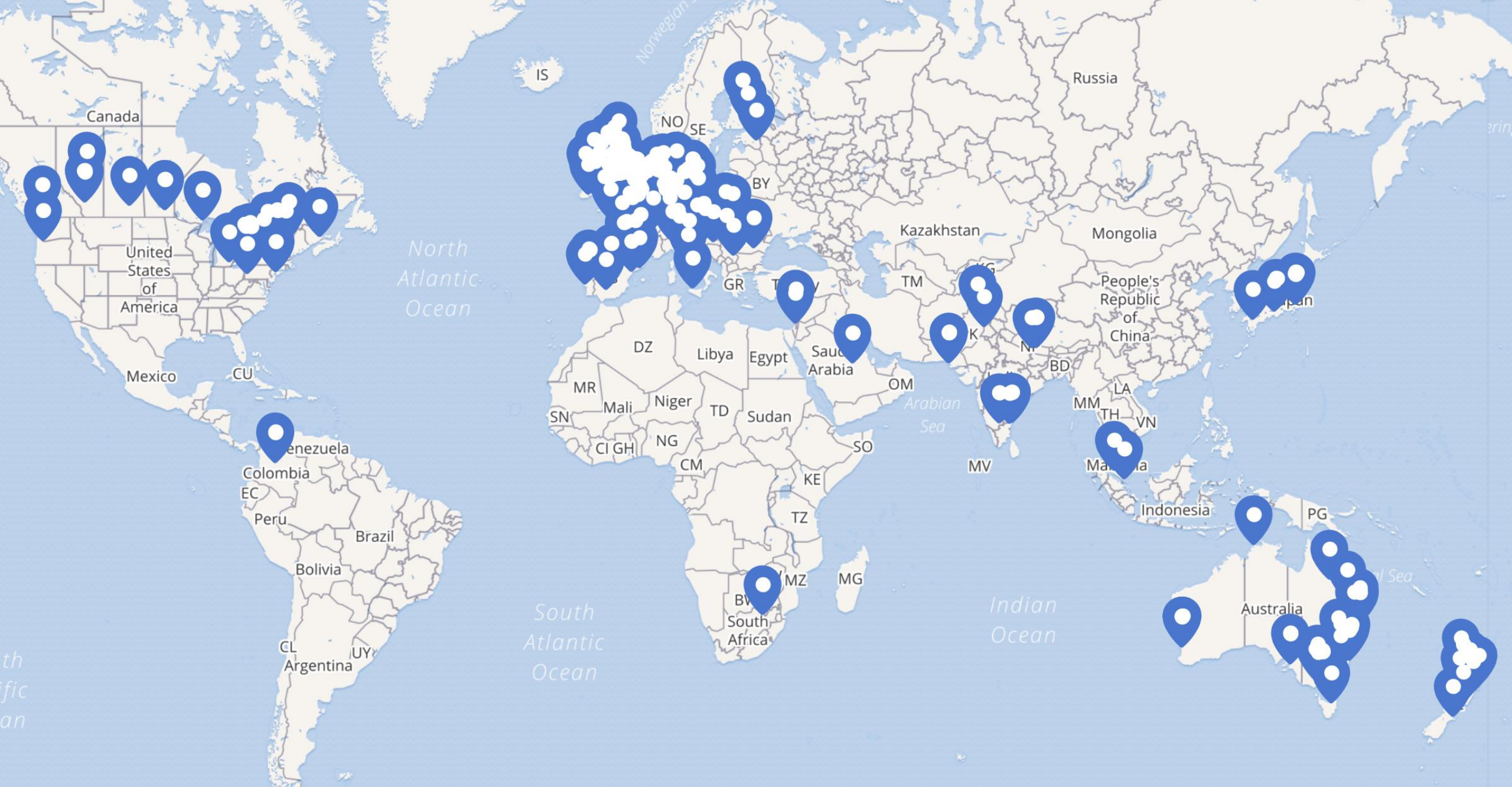
Prioritization (all levels) needed

National vs international needs

Embedding (staff shortages)

Lab infrastructure

Work needed on different intervention types in APTs



# Recommendations for scientists, healthcare workers and policy makers



Collaboration

Strong leadership – prioritization

Pandemic **Research** Preparedness

Funding – we need to remain active

The world of clinical trials is changing...



A low-angle, close-up photograph of several sprinters at the starting line of a race. The focus is on their hands and forearms as they are positioned in their starting blocks on a red running track. The track has white lane markings and yellow starting line indicators. The background is blurred, showing more athletes further down the track. The lighting is bright, suggesting a sunny day.

**ready**  
for the next pandemic