3º ENCONTRO NACIONAL DE INVESTIGAÇÃO CLÍNICA & INOVAÇÃO BIOMÉDICA

21 MAIO | ISCTE LISBOA

AICIB
AGÊNCIA DE INVESTIGAÇÃO CLÍNICA E INOVAÇÃO BIOMÉDICA

fct Fundação para a Ciência e a Tecnologia
Infarmed Autoridade Nacional do Medicamento e Produtos de Saúde, I.P.
apifarma Associação Portuguesa da Indústria Farmacêutica
Health Cluster Portugal
PtCRIN Portuguese Clinical Research Infrastructure Network
iscte Instituto Universitário de Lisboa

3º ENCONTRO NACIONAL DE INVESTIGAÇÃO CLÍNICA & INOVAÇÃO BIOMÉDICA

Aplicação ao contexto de resposta de emergência de saúde publica (pandemia COVID19)

A perspectiva do Investigador

Pedro Guimarães Cunha

ULS Alto Ave

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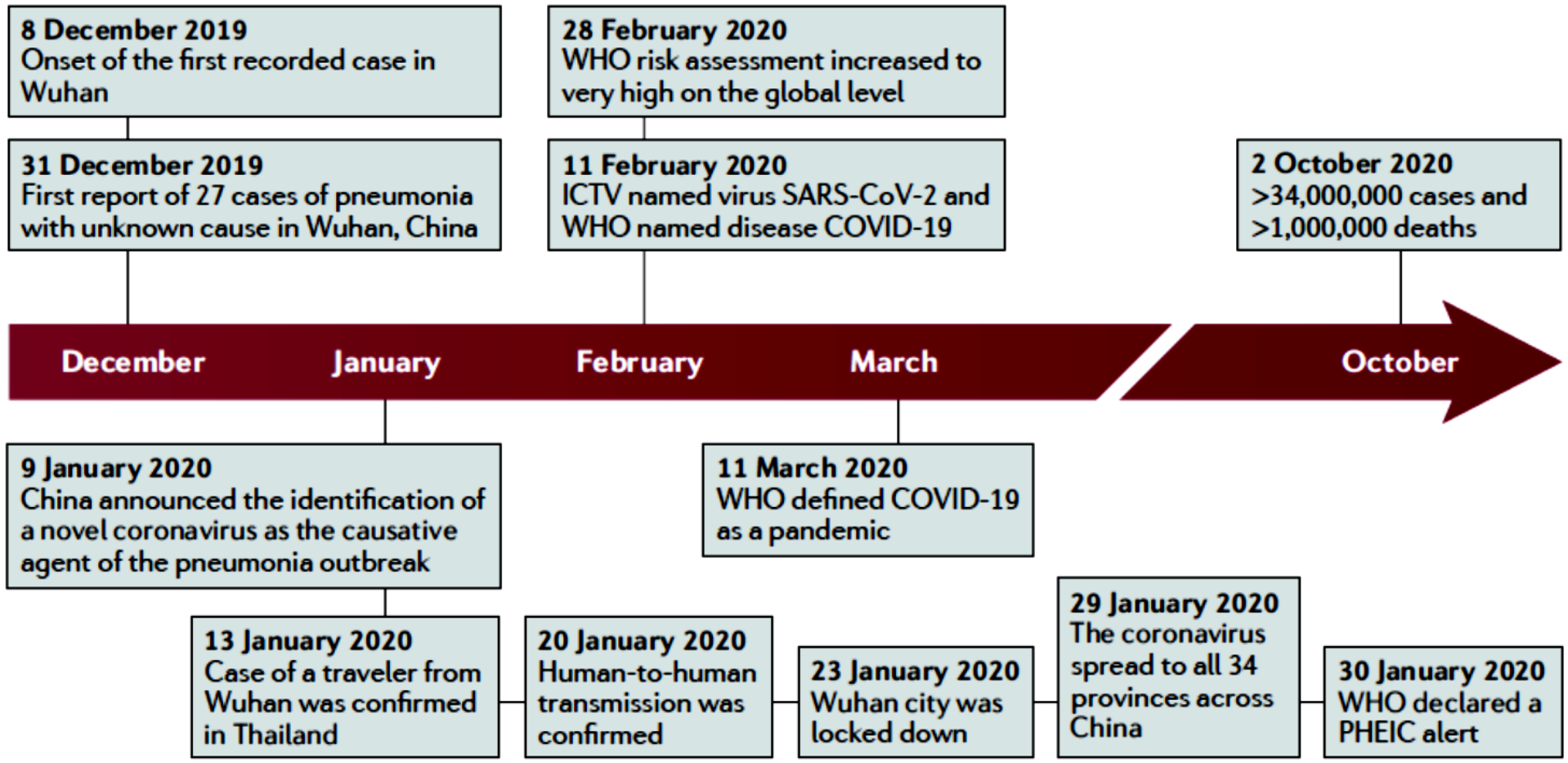
Scholl of Medicine, Minho University
ICVS/3B's - PT Government Associate Laboratory,
Braga/Guimarães, Portugal

Past- President of the Working Group on Hypertension and the Brain of the European Society of Hypertension

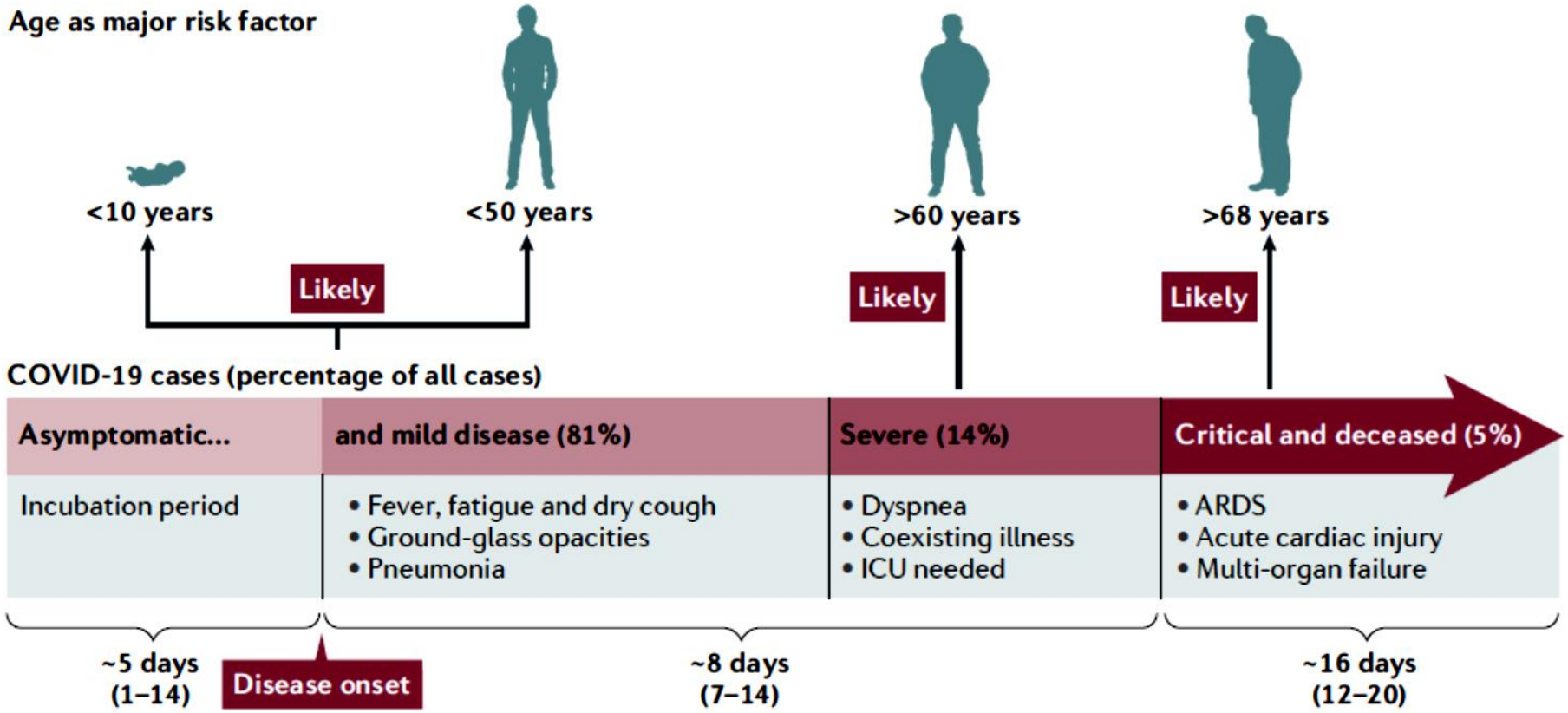
Vice President Executive Committee of the Artery Society

Aplicação ao contexto de resposta de emergência de saúde publica (pandemia COVID19): A perspectiva do Investigador



NATURE REVIEWS | MICROBIOLOGY VOLUME 19 | MARCH 2021 | 141

Aplicação ao contexto de resposta de emergência de saúde publica (pandemia COVID19): A perspectiva do Investigador



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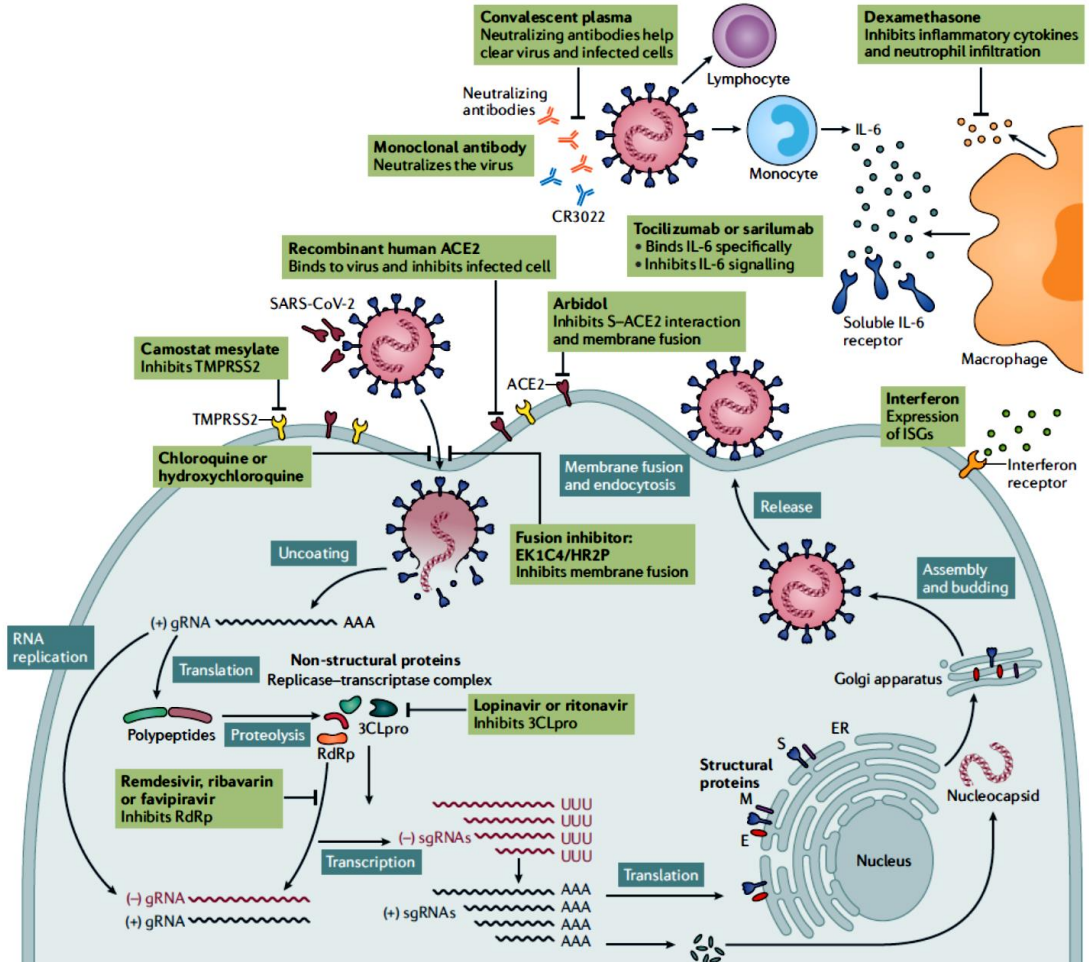


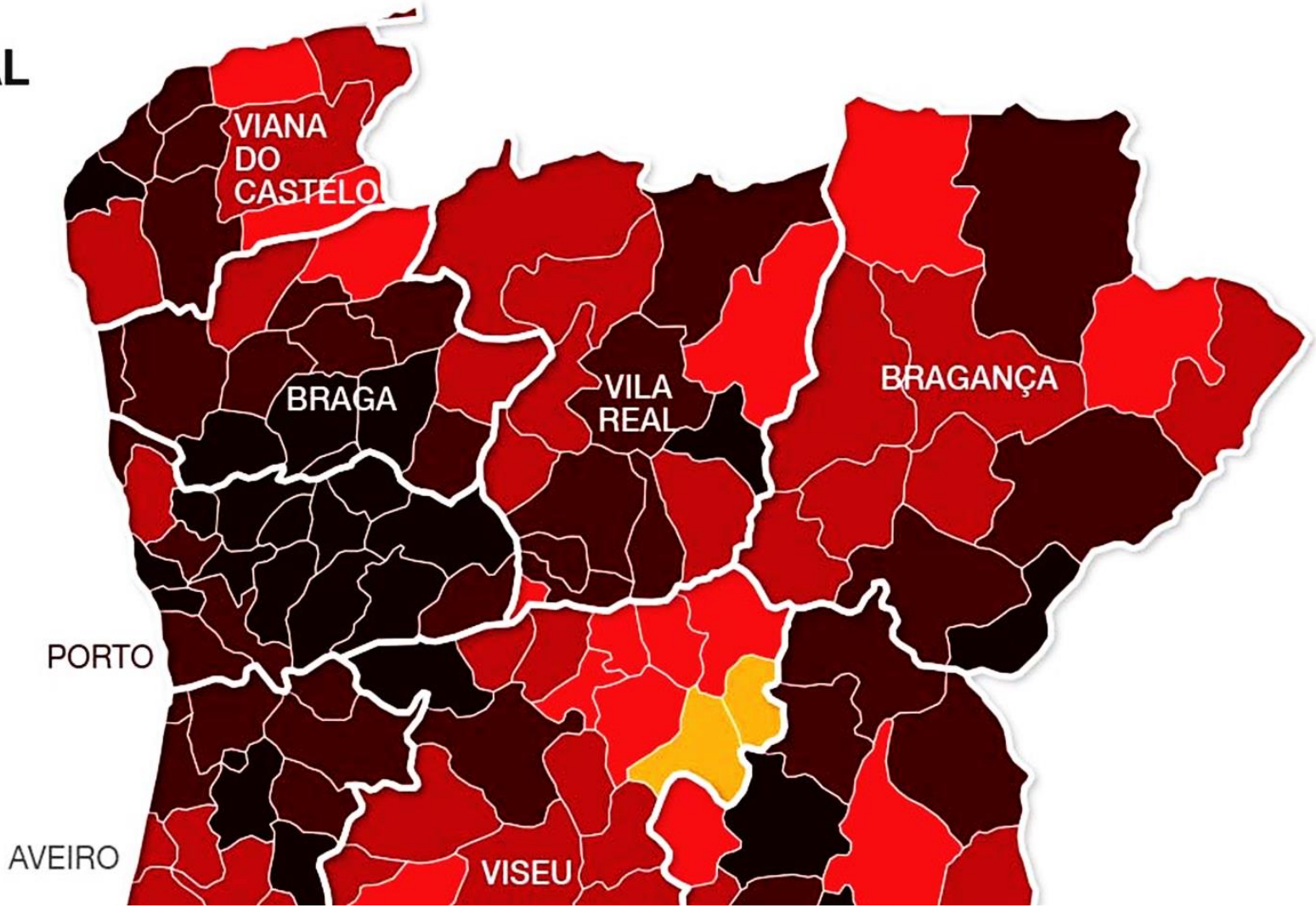
NATURE REVIEWS | MICROBIOLOGY VOLUME 19 | MARCH 2021 | 141

Aplicação ao contexto de resposta de emergência de saúde publica (pandemia COVID19): A perspectiva do Investigador

COVID-19 EM PORTUGAL
INCIDÊNCIA ACUMULATIVA A 14 DIAS POR CONCELHO

(ENTRE 28 DE OUTUBRO E 10 DE NOVEMBRO)

- >960 (4 x acima do patamar de risco mais elevado)
- >480 (2 x acima do patamar de risco mais elevado)
- >240
- >120



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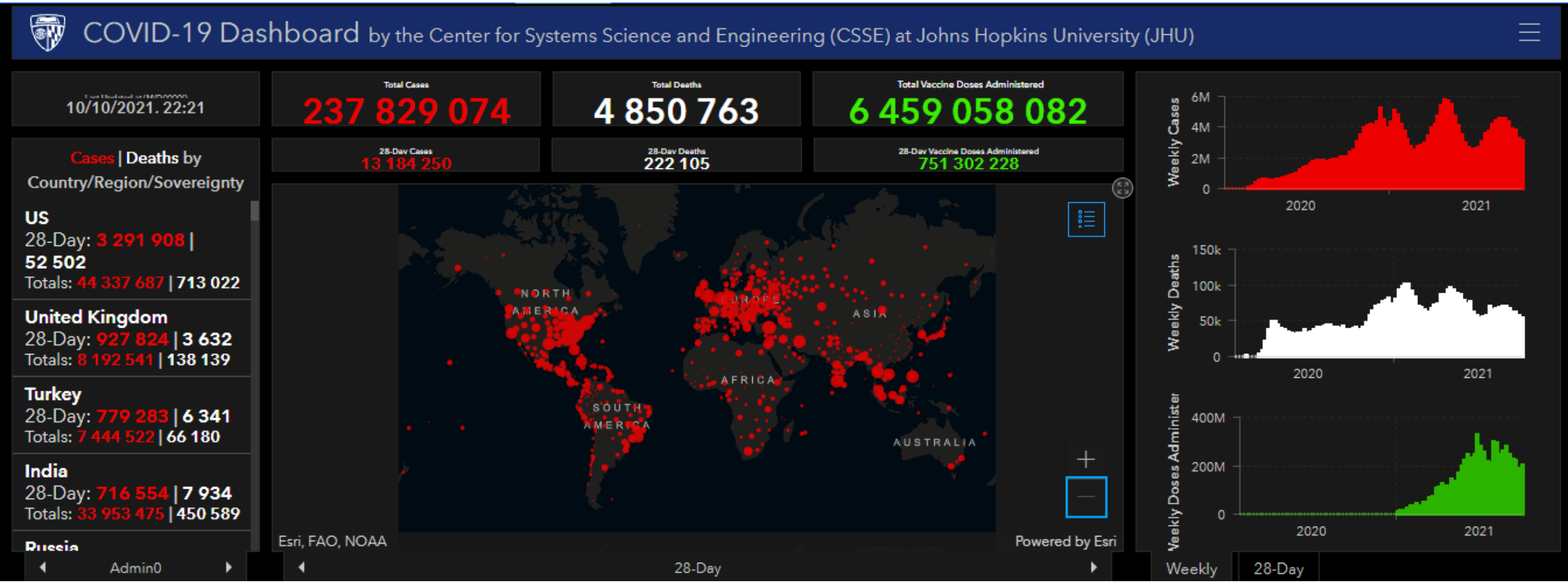
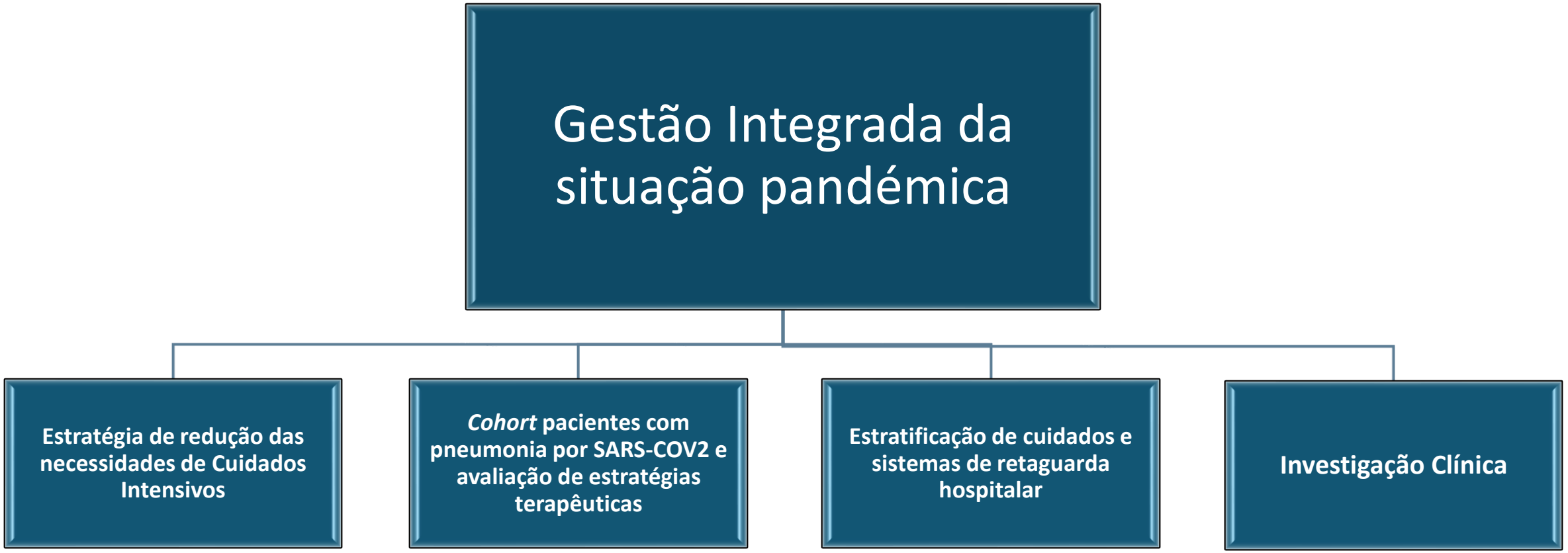
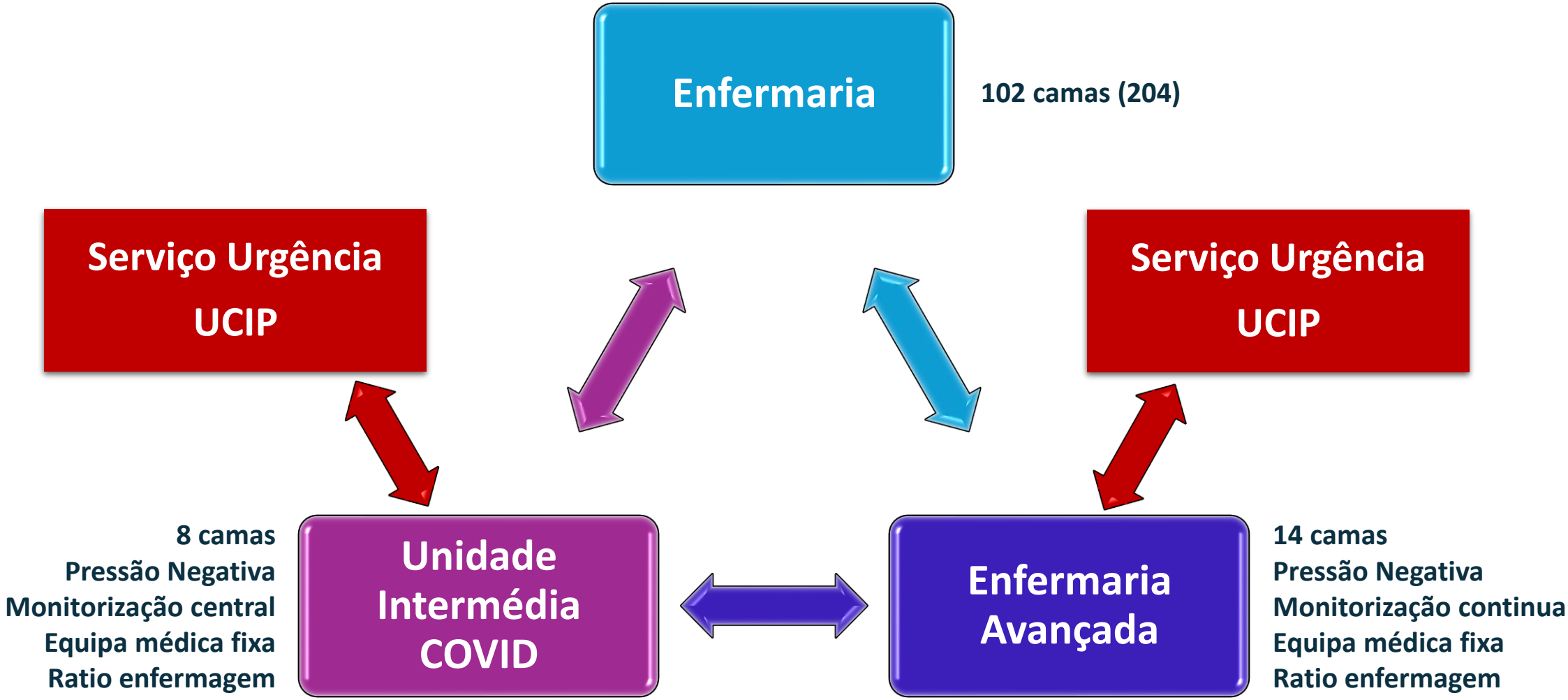


Aplicação ao contexto de resposta de emergência de saúde publica (pandemia COVID19): A perspectiva do Investigador



1. GESTÃO INTEGRADA DE PACIENTES COVID COM INSUFICIÊNCIA RESPIRATÓPRIA GRAVE – UMA ESTRATÉGIA DE REDUÇÃO DA NECESSIDADE DE LEITOS DE CUIDADOS INTENSIVOS



Aplicação ao contexto de resposta de emergência de saúde publica (pandemia COVID19): A perspectiva do Investigador

Unidade Intermédia COVID

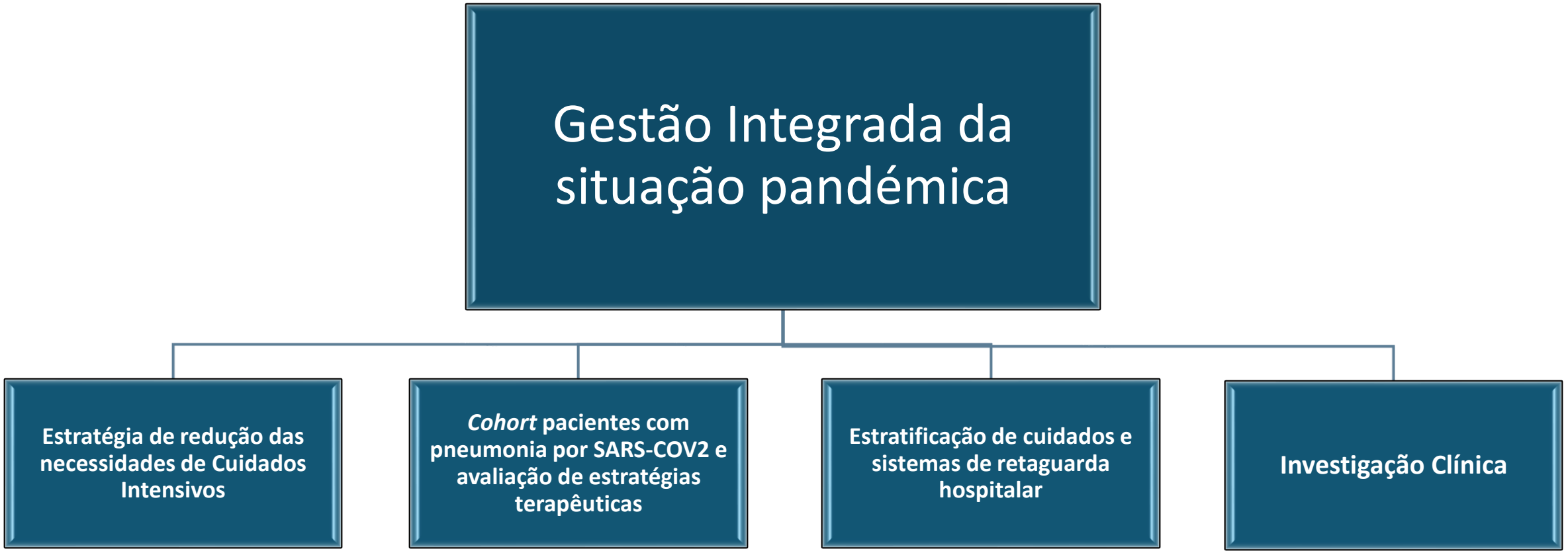
179 pacientes tratados

25% progrediram para UCIP

Demora média 10 dias inferior

Nunca atingimos capacidade lotação UCIP. Não foram necessárias escolhas ética e profissionalmente dolorosas

Aplicação ao contexto de resposta de emergência de saúde publica (pandemia COVID19): A perspectiva do Investigador

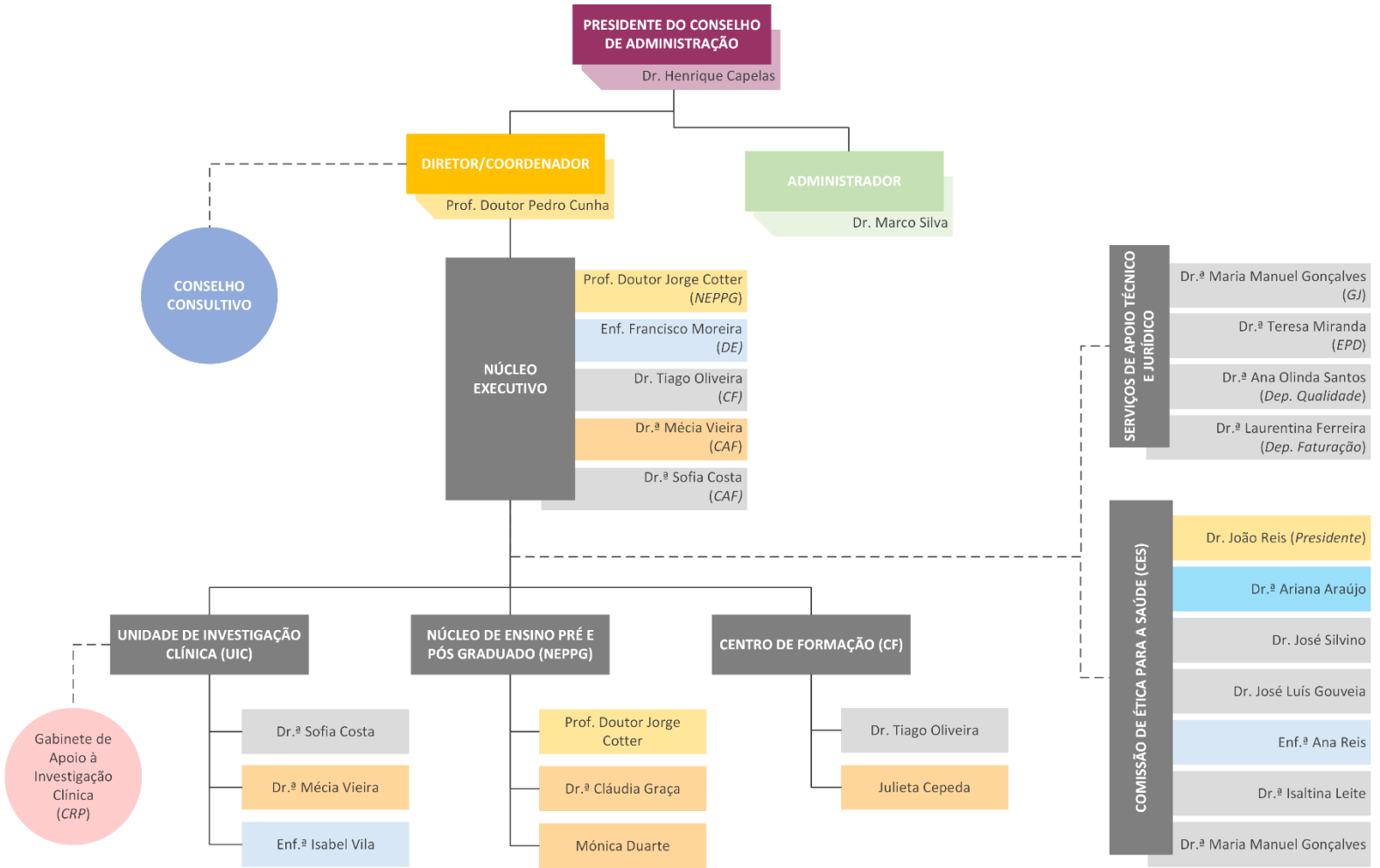


2. Investigação Clínica

AICIB Agência de Investigação Clínica e Inovação Biomédica

FCT
Fundação para a Ciência e a Tecnologia
MINISTÉRIO DA CIÊNCIA, TECNOLOGIA E ENSINO SUPERIOR

CENTRO ACADÉMICO E DE FORMAÇÃO (CAF) - Organograma



CRP: *Clinical Research Partnership*
DE: Direção de Enfermagem
EPD: Encarregado de Proteção de Dados
GJ: Gabinete Jurídico
IC: Investigação Clínica

Aplicação ao contexto de resposta de emergência de saúde publica (pandemia COVID19): A perspectiva do Investigador

RH 90h/Semana

Estrutura complementar

Estratégia oportunidade

Circuitos Processamento

Tratamento dados

Sample Collection protocol and storage

Health Care Workers are at High risk of contracting SARS-COV-2 Infection

The infection rate during amongst health professional during the first wave of the pandemic is not known

The aquisition of circulating antibodies against SARS-COV-2 is not been studied in this setting

Report the rate of infection amongst healthcare workers during the first pandemic wave

To study the immunologic response of these subjects after exposure / infection to the virus

To establish more robust information for prevention

343
HCW

Physiscians
Nurses
Auxiliaries

Revision of all PCR-T positive cases

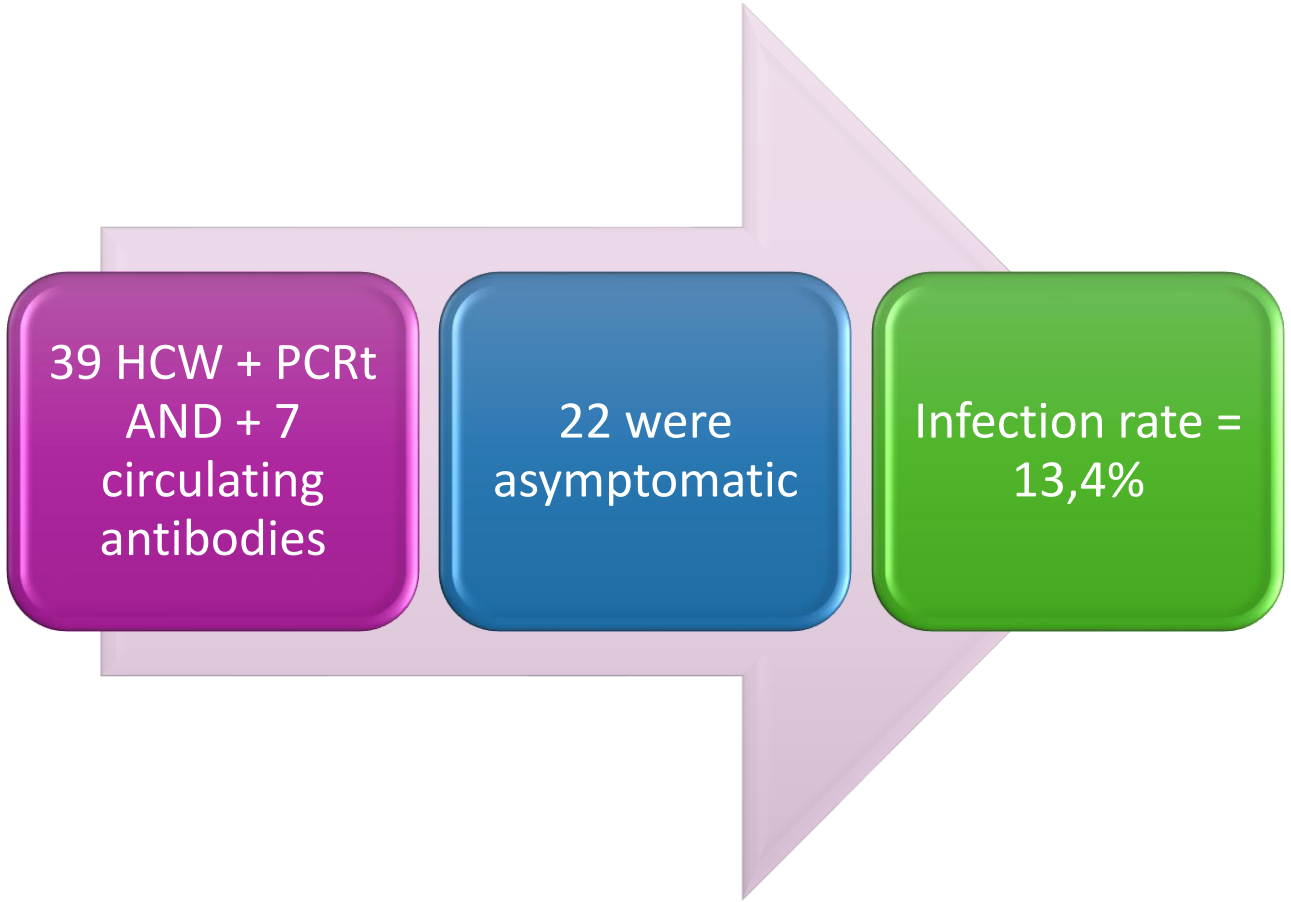
Revision of all Sorologic test

2 Different Methods for sorologic testing

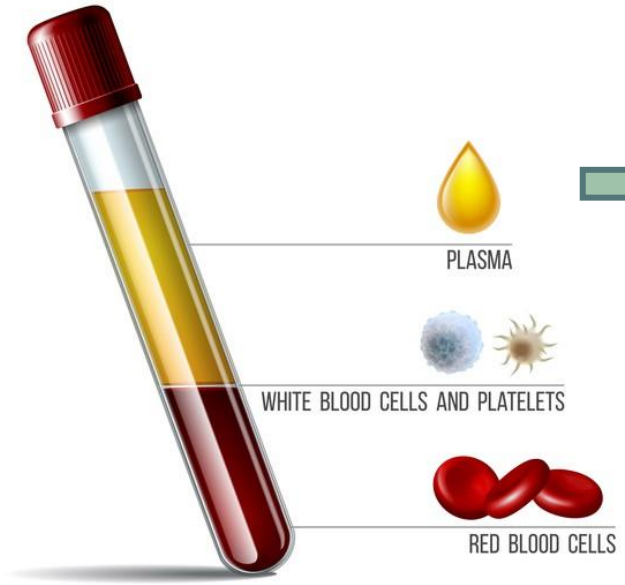
1st patient 16th March 2020

Sorologic Evaluation 4th-8th May 2020

Infection rate



46% of infected HCW were asymptomatic and working during active infection



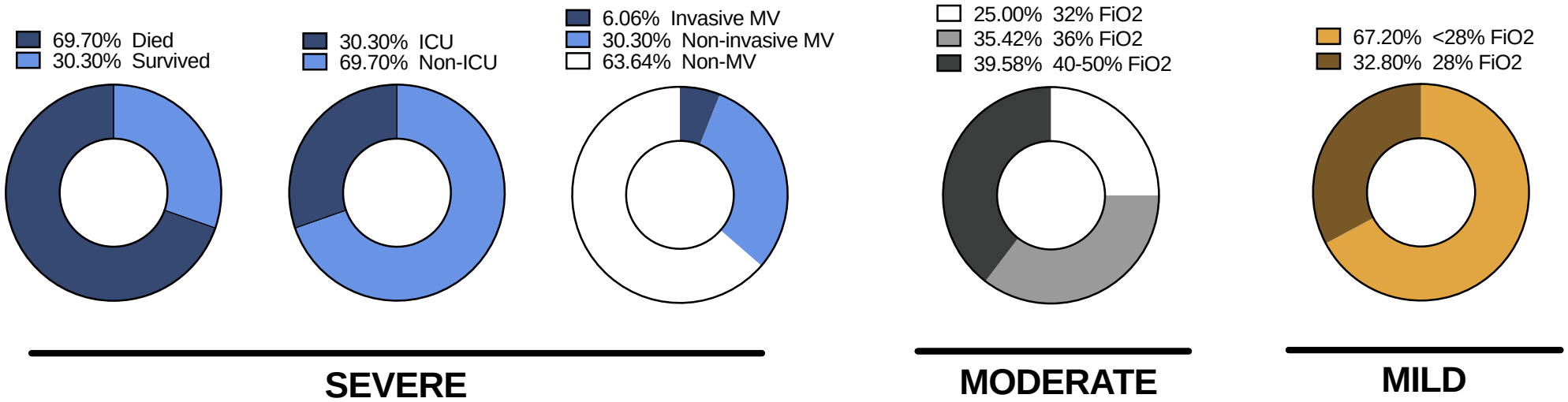
ESTABLISHED A BANK OF SAMPLES

QUANTIFCATION OF SEVERAL INFLAMMATORY MEDIATORS

Bio-Plex Pro Human Cytokine 27-plex Assay

- FGF basic
- Eotaxin
- G-CSF
- GM-CSF
- IFN-γ
- IL-1β
- IL-1ra
- IL-2
- IL-4
- IL-5
- IL-6
- IL-7
- IL-8
- IL-9
- IL-10
- IL-12 (p70)
- IL-13
- IL-15
- IL-17A
- IP-10
- MCP-1 (MCAF)
- MIP-1α
- MIP-1β
- PDGF-BB
- RANTES
- TNF-α
- VEGF

COVID19 hospitalized patients from HSOG



SEVERE

N=33

MODERATE

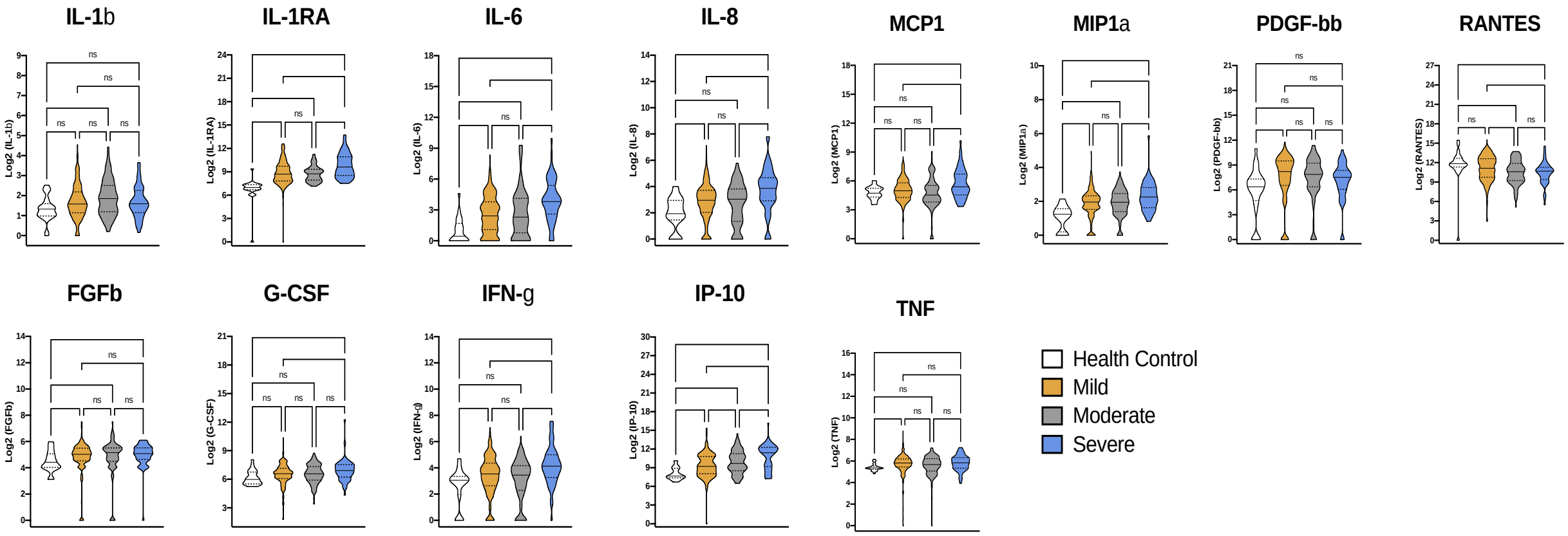
N=48

MILD

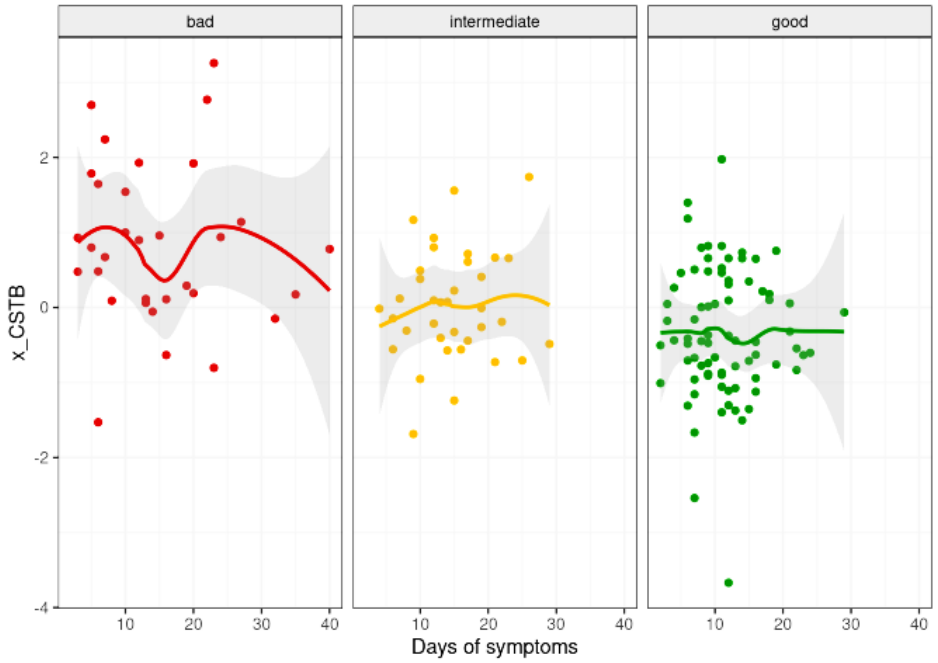
N=125

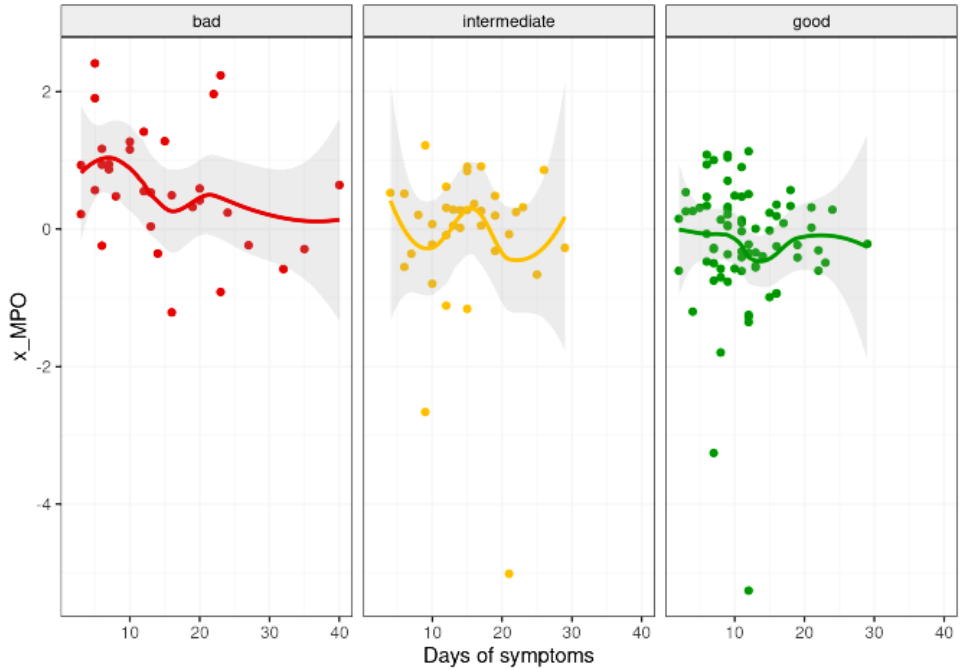
TOTAL SAMPLE SIZE = **206 PATIENTS**

INFLAMMATORY MOLECULES DIFFERENT FROM CONTROLS AND DIFFERENT AMONG DISEASE SEVERITY



ALL SAMPLES – independently of collection timepoint

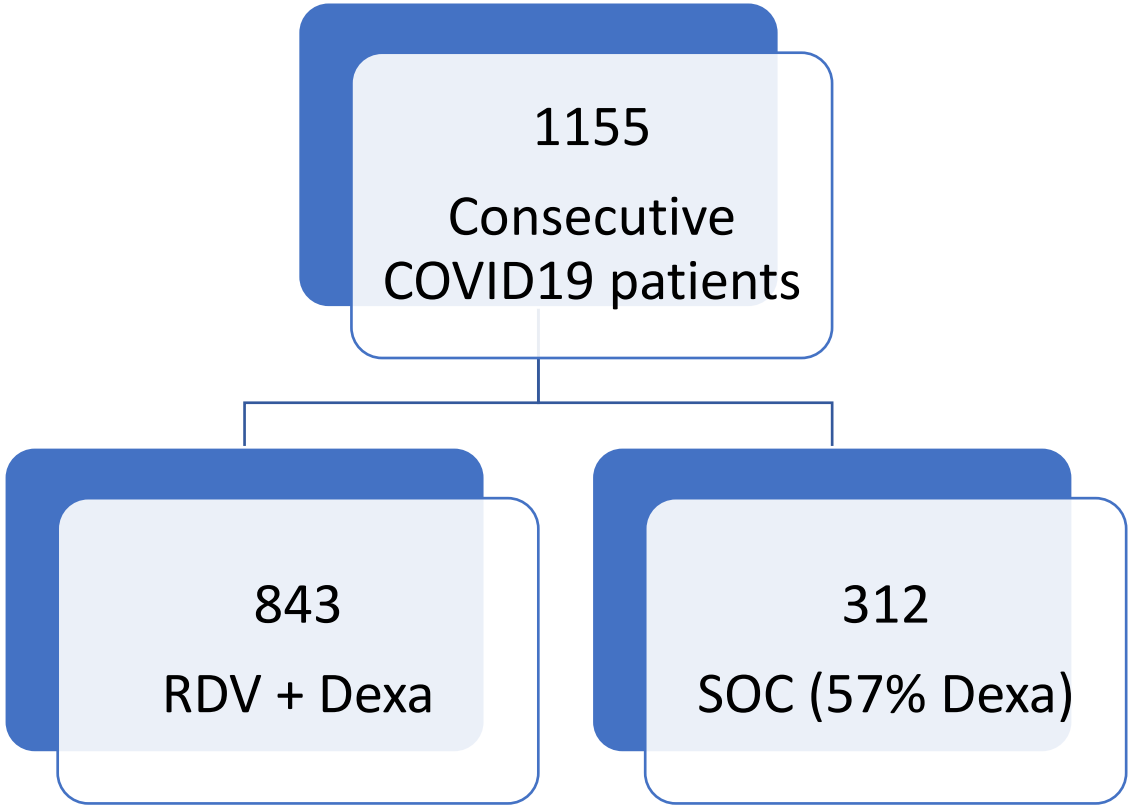


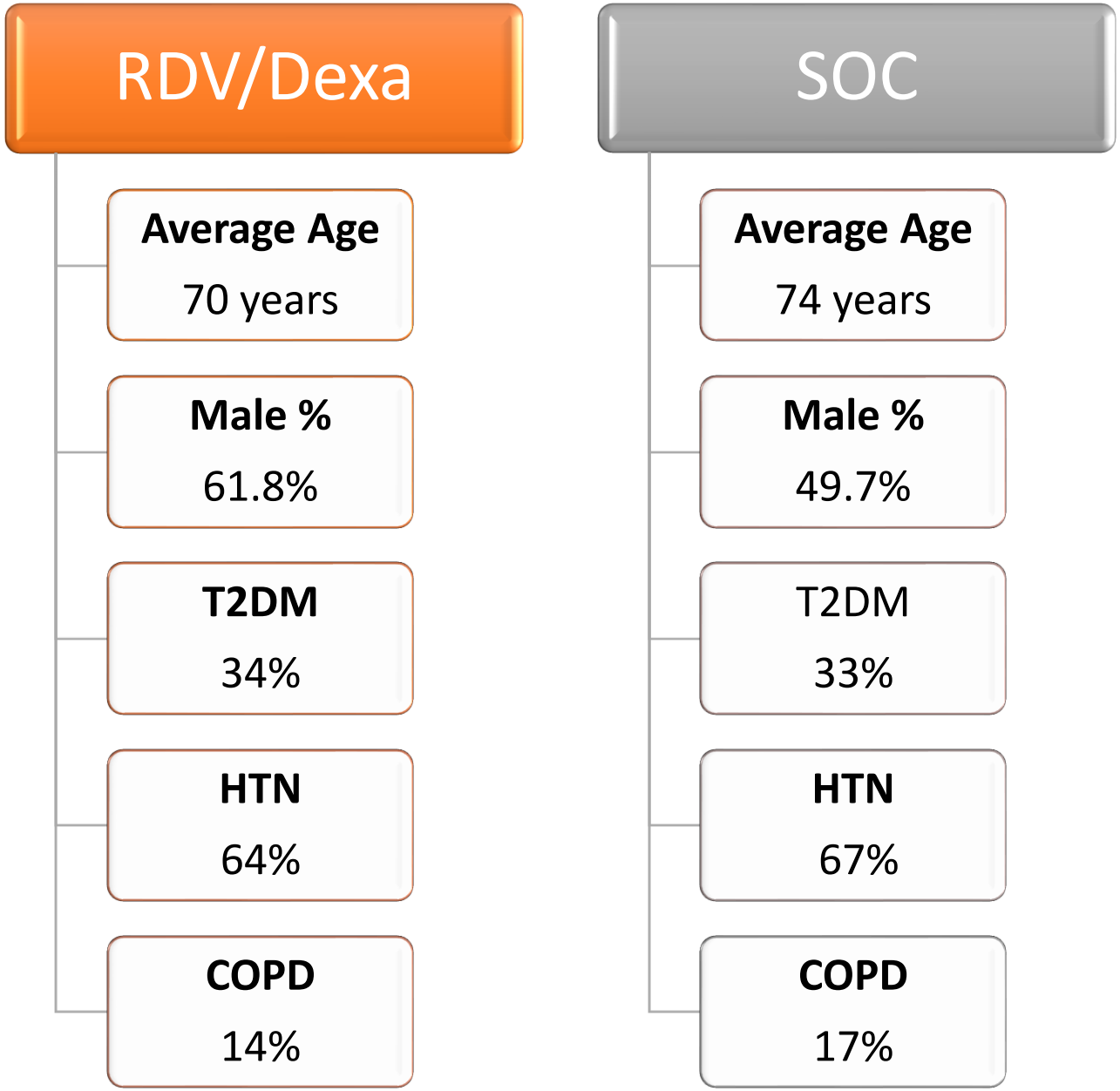


Unpublished data

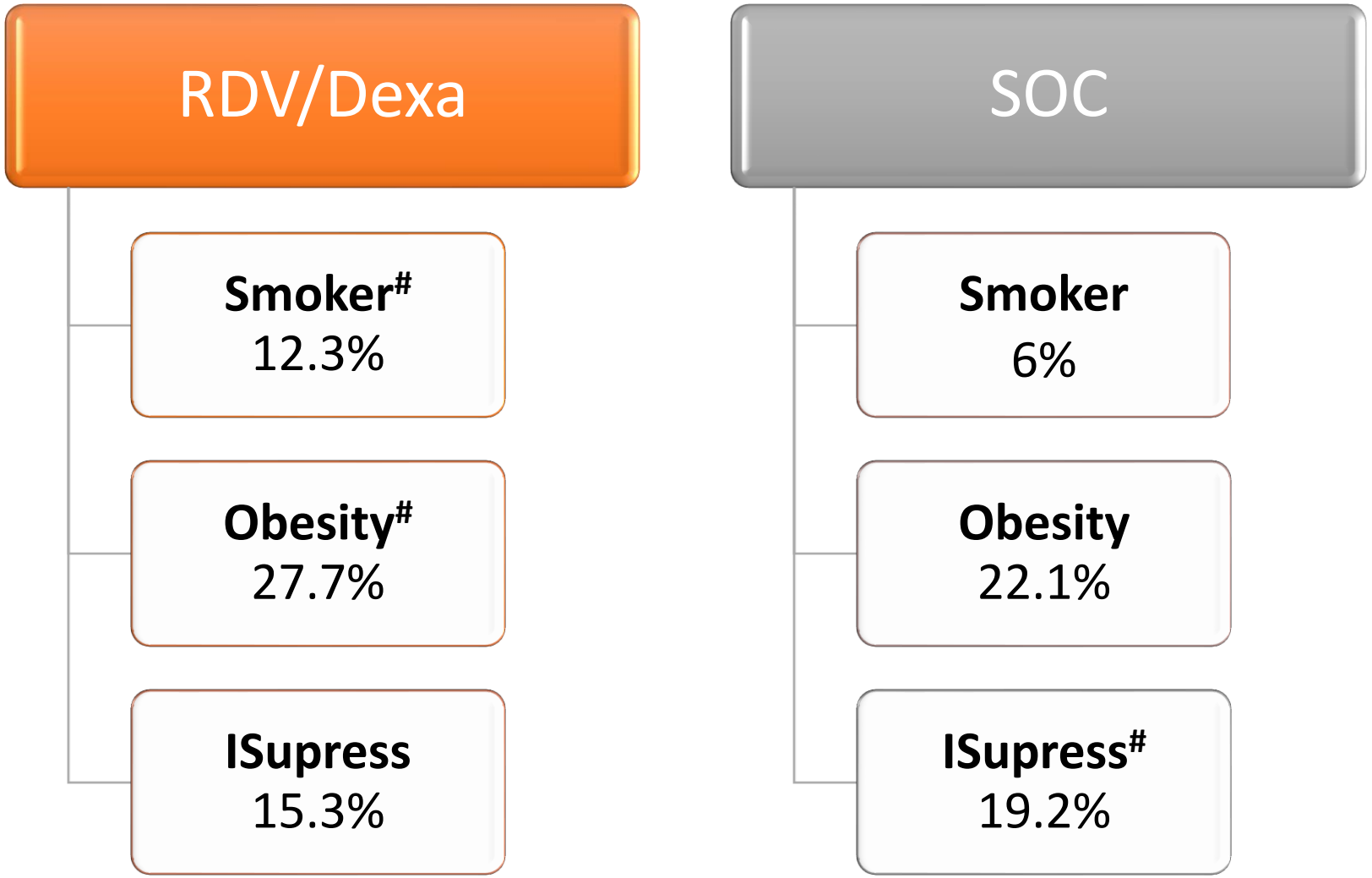
Therapeutic Strategies in hospitalized patients with SarsCov-2 Hypoxemic Pneumonia: Real Life Data on the use of Remdesivir

Pedro Guimarães Cunha[1,2,3,5], Cecília Castro[4], Helena Sarmento[1], Isabel Vila[1,5], Mécia Vieira[5], Ana Sofia Costa[5], Ana Paula Amorim[4], Margarida Correia Neves[2,3], Jorge Cotter[1,2,3]





Cunha et al, ECCMID 2022 poster L0453



Cunha et al, ECCMID 2022 poster L0453

Endpoints

843 RDV/Dex		312 SOC
13.5 days	**Hospital Stay**	17.75 days
15.7%	**Death**	33.3%

4.25 days

OR 0.47

OR Death in RDV group = 0.47 [0.38 – 0.60]

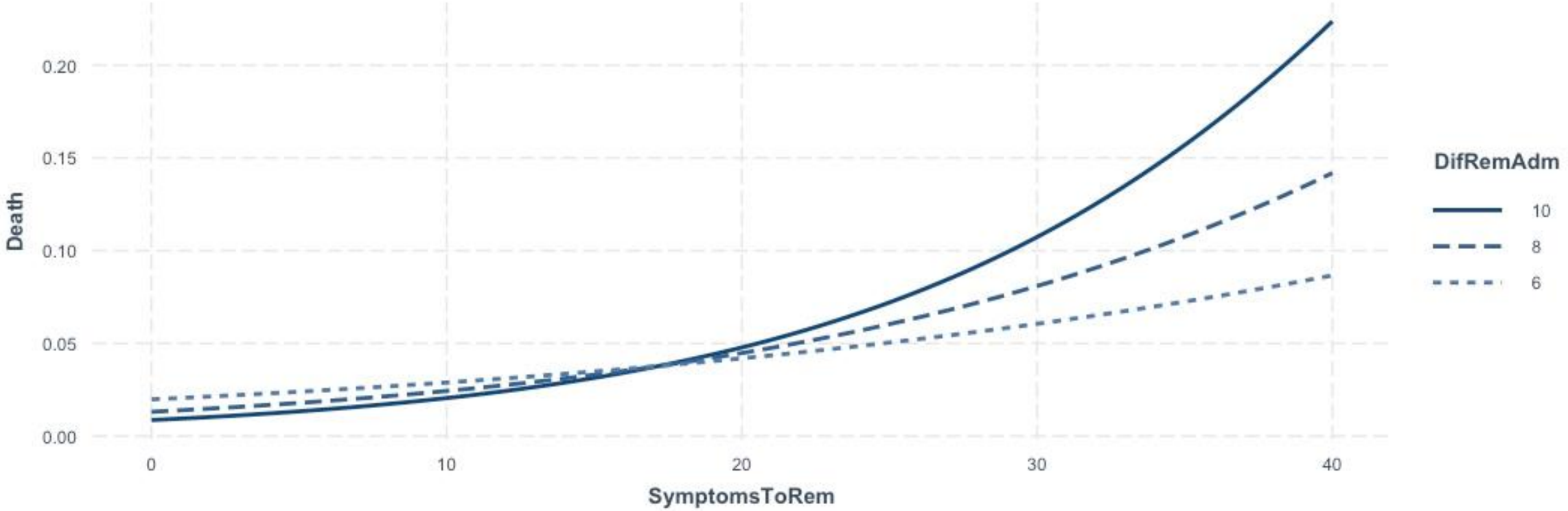
Cunha et al, ECCMID 2022 poster L0453

SORT* → **5 days**

SORT – time from **S**ymptom **O**nset to initiation of **R**emdesivir **T**reatment

Cunha et al, ECCMID 2022 poster L0453

Figure 3. Model and ROC Curve explaining how higher SORT increases death in patients with SARSCOV2 hipoxemic pneumonia



Cunha et al, ECCMID 2022 poster L0453

Figure 3. Model and ROC Curve explaining how higher SORT increases death in patients with SARSCOV2 hipoxemic pneumonia

Parameter	Exp (B)	95% Wald Confidence Interval	Sig.
Age	1.064	1.018 – 1.112	0.006
FiO2 Max (%)	1.064	1.054 – 1.075	0.0001
Hospital days	0.953	0.928 – 0.979	0.0001
SORT (days)	**1.095**	1.018 – 1.17	0.014

Cunha et al, ECCMID 2022 poster L0453

2. Investigação Clínica

WHO SOLIDARITY Trial

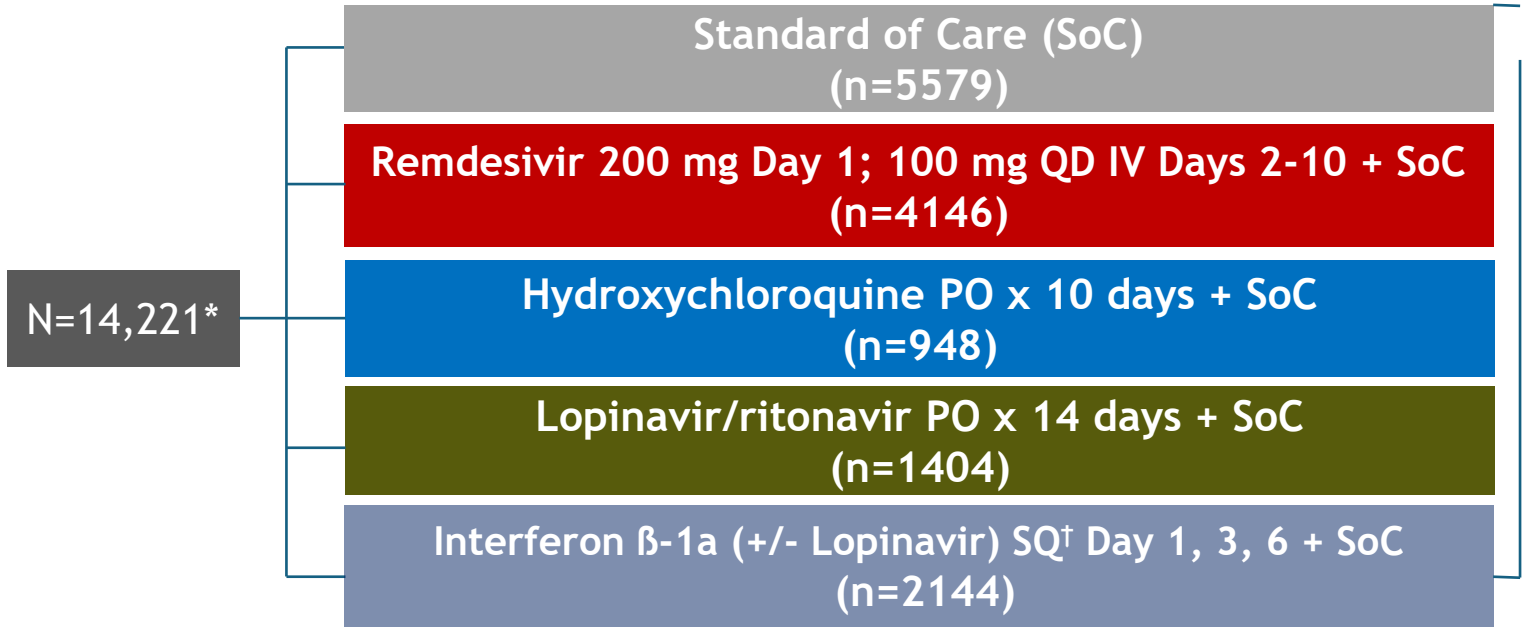
Phase 3 open-label, adaptative, multi-center, randomized trial from 454 hospitals in 35 countries

Key Inclusion Criteria

- Adults ≥18 years old
- Hospitalized with COVID-19
- Not known to have received study drug
- No expected transfer within 72 hours
- No contraindication to study drug

Key Exclusion Criteria

- Study drug contraindication
- Declined to participate in study



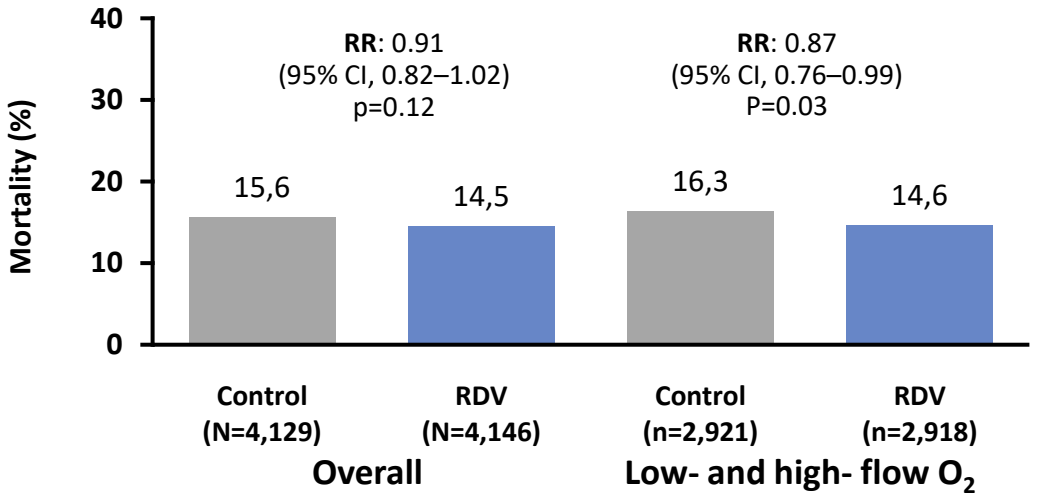
Secondary Endpoints: Progression to ventilation and time to discharge

Data from Mar 2020 – Jan 2021
*14,304 patients enrolled; 14,221 patients left in ITT analysis after no/uncertain consent to follow-up
Participants were randomly assigned in equal proportions to locally available study drug or control (up to 5 options: 4 active and local standard-of-care).
HCQ: 200 mg, 4 tabs PO (hour 0, 6), 2 tabs BID (hour 12 and beyond); LPV/r: 200/50 mg 2 tabs PO BID
†IFN: 44 mcg SQ on day 0, 3, 6 or 10 mcg IV daily for 6 days for patients on high-flow oxygen, ventilators, or ECMO
HCQ, LPV, IFN discontinued on June 18, July 14, Oct 16 respectively

Solidarity: Remdesivir vs standard of care in hospitalised patients with COVID-19 requiring supplemental oxygen

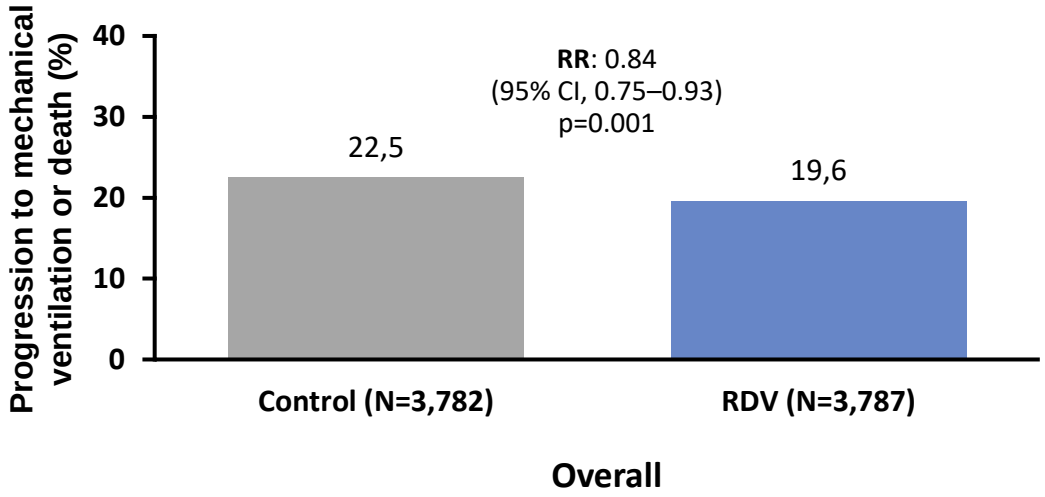
Phase 3, randomised, controlled, open-label trial

Primary endpoint: In-hospital mortality



Remdesivir significantly reduced mortality rates for patients hospitalised on oxygen and not requiring mechanical ventilation compared with SoC. There was no significant difference in the overall population

Composite analyses of ventilation or death in those not ventilated at entry

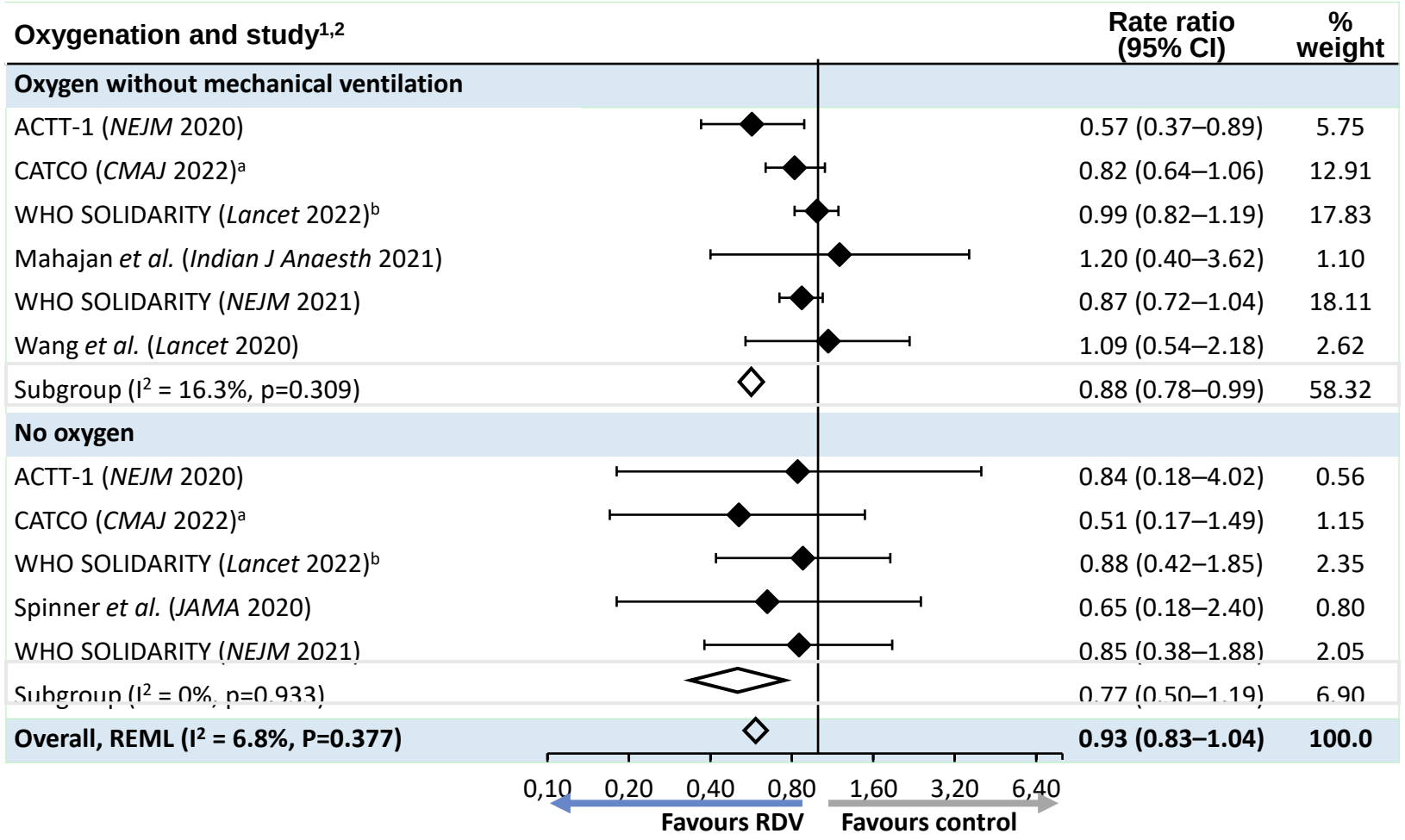


Overall, remdesivir-treated patients had a lower relative risk of progressing to ventilation or death compared with SoC

Meta-analysis of remdesivir treatment in over 10,000 hospitalised patients

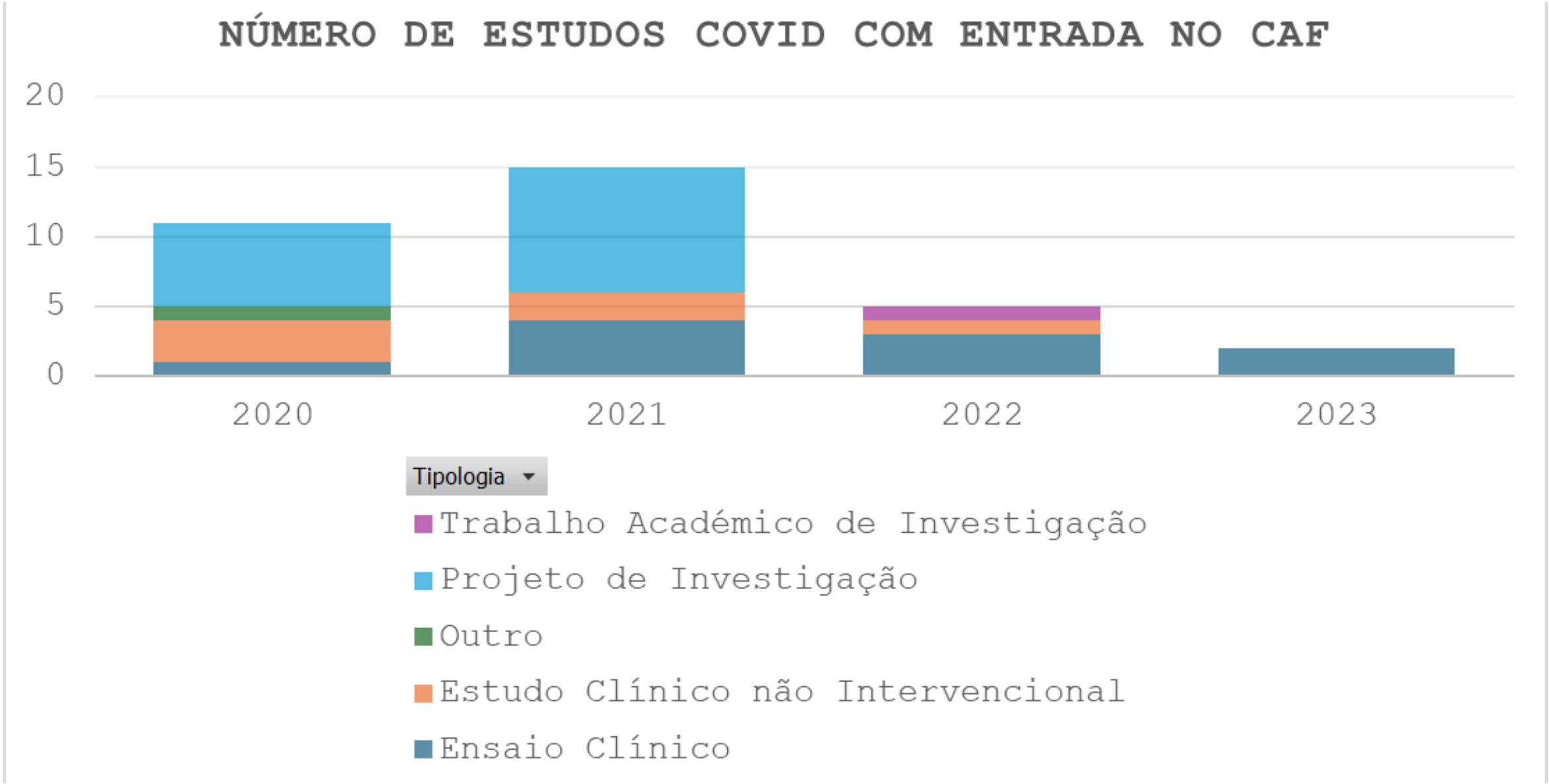
- 8 studies included N=10,751 patients
- Included all hospitalised patients with COVID-19
- Primary outcome was mortality stratified by O_2 use

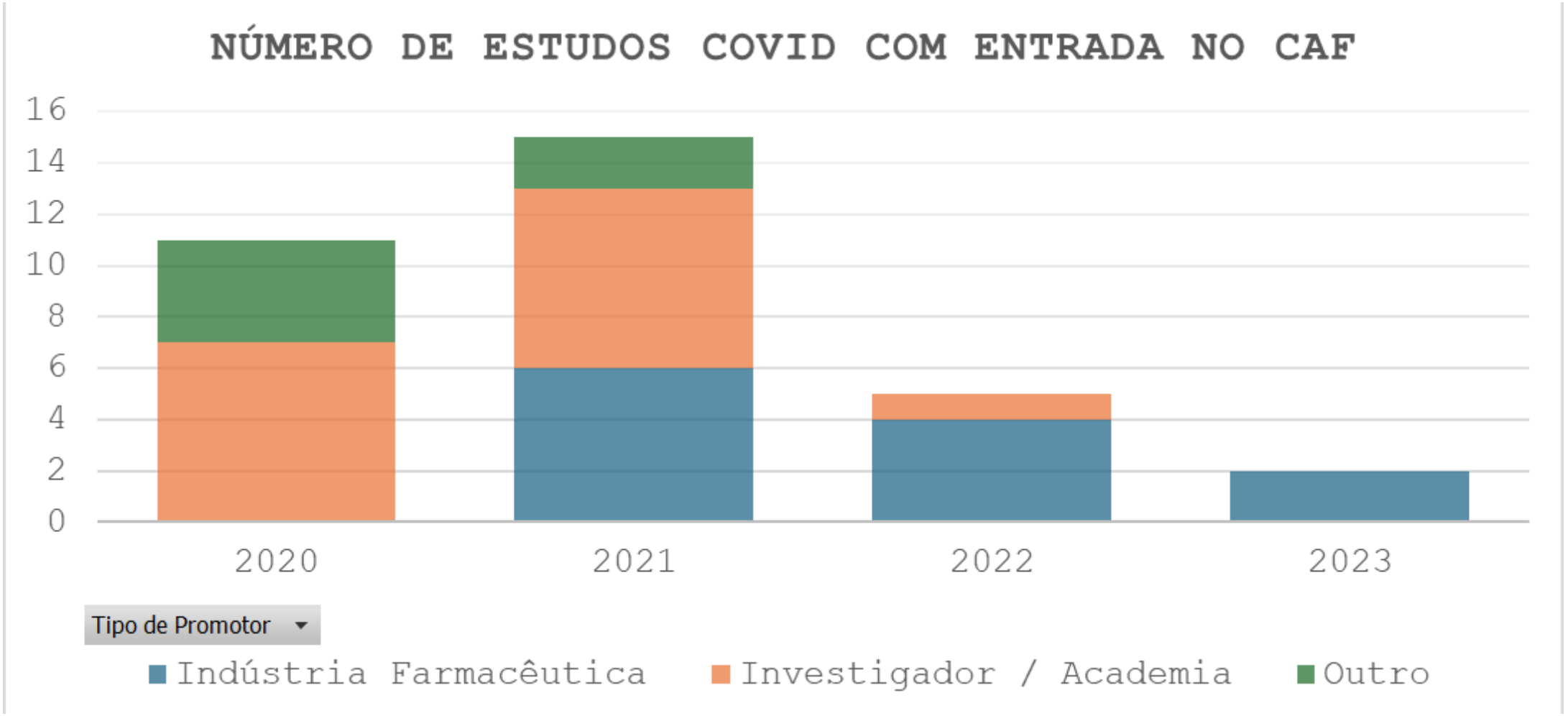
Meta-analysis shows **high probability of mortality reduction for patients on supplemental oxygen (without IMV) treated with remdesivir** vs. PBO or SoC[1]



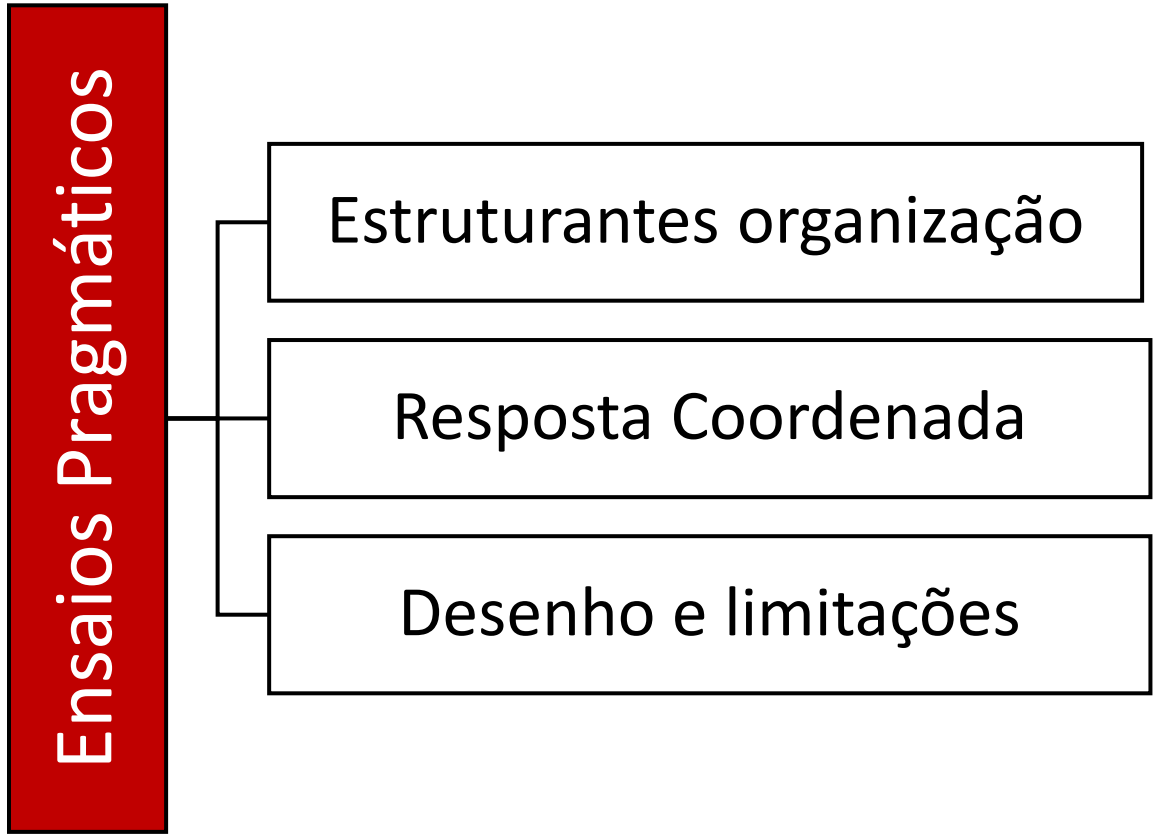
Potential Limitations

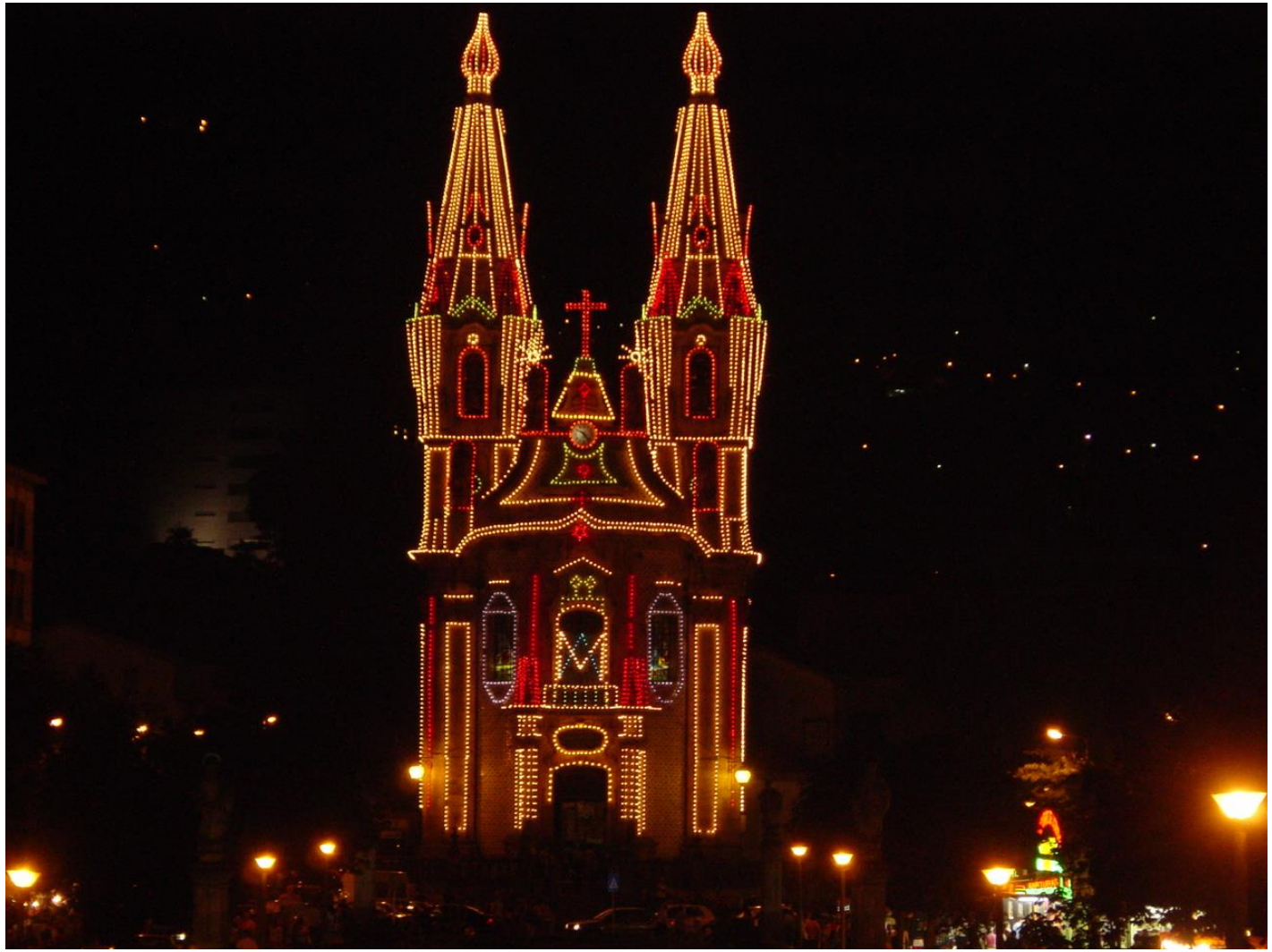
- Open-label pragmatic design
  - Biased allocation, but not unbiased behavior of patients/providers. The open-label nature, especially during a pandemic, would amplify the potential biases of an unblinded study
- No requirement of confirmation of infection
- Unknown time from symptom onset to treatment initiation
- Data reporting was minimal to limit burden on local investigators
  - No on-site data monitoring which ensures accuracy of data
- Trial enrolled primarily in Africa, Asia and Latin America (~69%), where access to healthcare may be limited or delayed and where healthcare practices are heterogeneous and differ across various regions
- COVID-19 inpatients were randomized equally between whichever study drugs were locally available and open control (controls may have been from another study location)


NÚMERO DE ESTUDOS COVID COM ENTRADA NO CAF
20
15
10
5
0
2020
2021
2022
2023
Tipologia
Trabalho Académico de Investigação
Projeto de Investigação
Outro
Estudo Clínico não Intervencional
Ensaio Clínico


NÚMERO DE ESTUDOS COVID COM ENTRADA NO CAF
16
14
12
10
8
6
4
2
0
2020
2021
2022
2023
Tipo de Promotor
Indústria Farmacêutica
Investigador / Academia
Outro

Aplicação ao contexto de resposta de emergência de saúde publica (pandemia COVID19): A perspectiva do Investigador





St. Gualter’s Festivities. **Guimarães, 2004**

Muito obrigado pela vossa atenção.
Thank you for your time.