

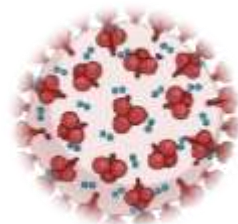
República de Cuba
Ministerio de Salud Pública
Universidad de Ciencias Médicas de La Habana



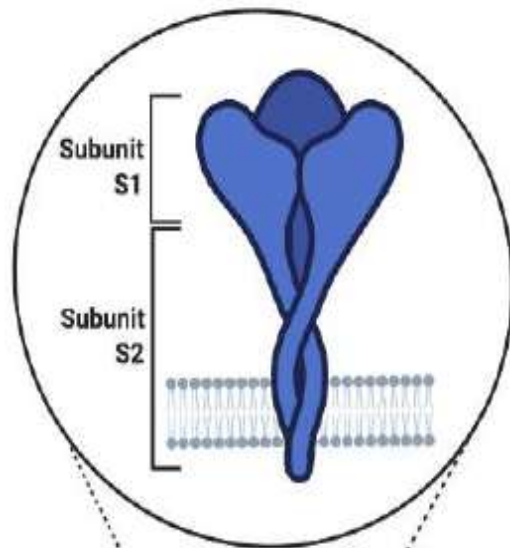
Tratamiento para la COVID-19: Actualización basada en la evidencia

Autores: Dr. C. Frank Daniel Martos Benítez,
HDCQ "Hermanos Ameijeiras"
fdmartos@infomed.sld.cu

La Habana, 2022

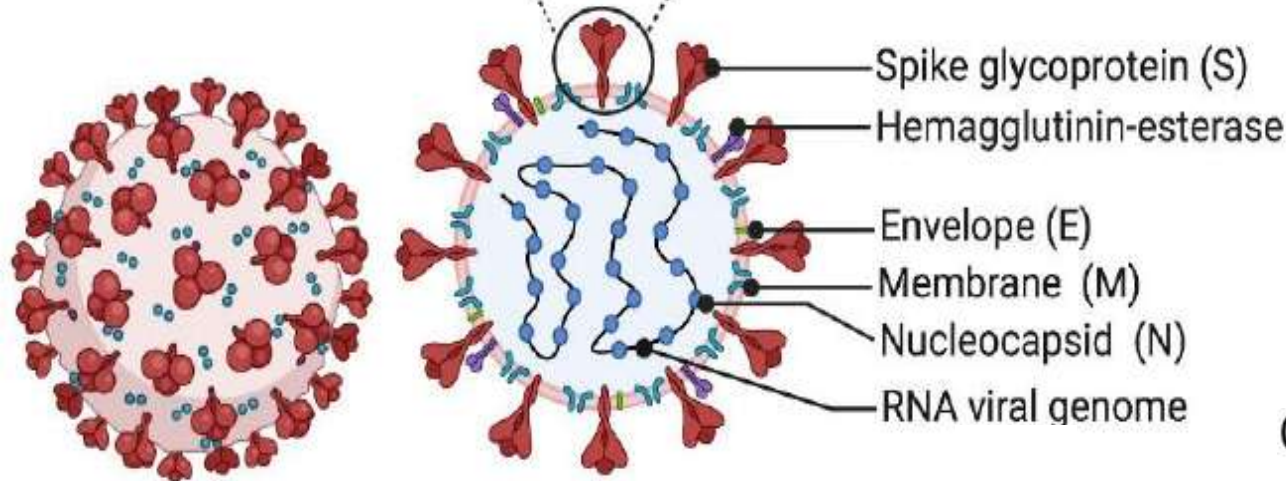
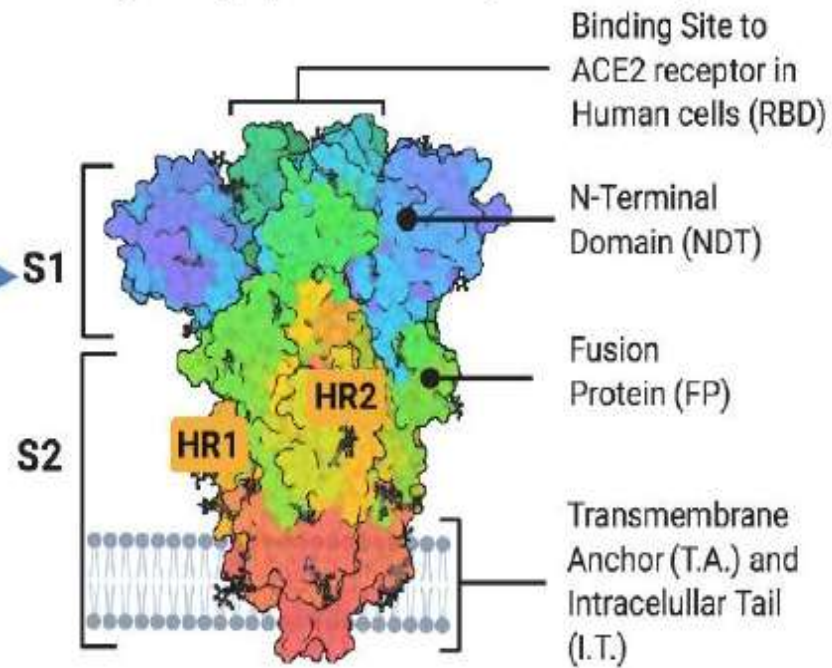


SARS-CoV-2 Spike glycoprotein



SARS-CoV-2 Spike glycoprotein

Crystallographic structure (PDB ID: 6VXX)



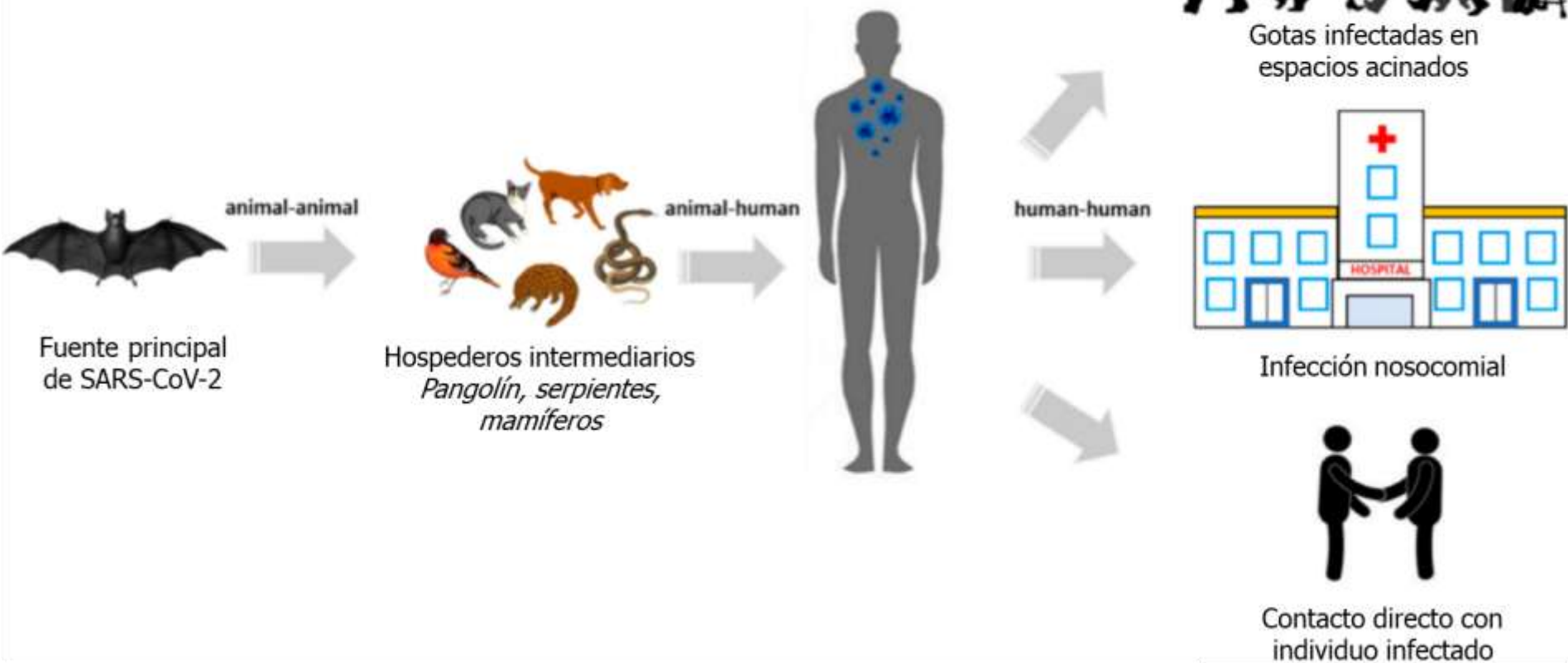
SARS-CoV-2 Virus structure

COVID-19: Characteristics and Therapeutics



Cells 2021, 10, 206.

Rameswari Chilamakuri and Saurabh Agarwal

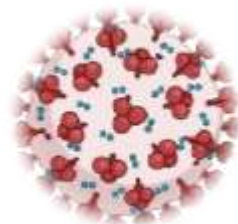
TRANSMISIÓN DEL SARS-CoV-2



COVID-19: A Review on the Novel Coronavirus Disease Evolution, Transmission, Detection, Control and Prevention

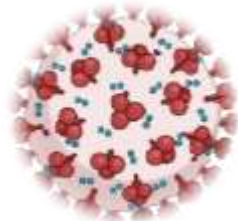
Anshika Sharma ^{1,†}, Isra Ahmad Farouk ^{1,†}  and Sunil Kumar Lal ^{1,2,*} 

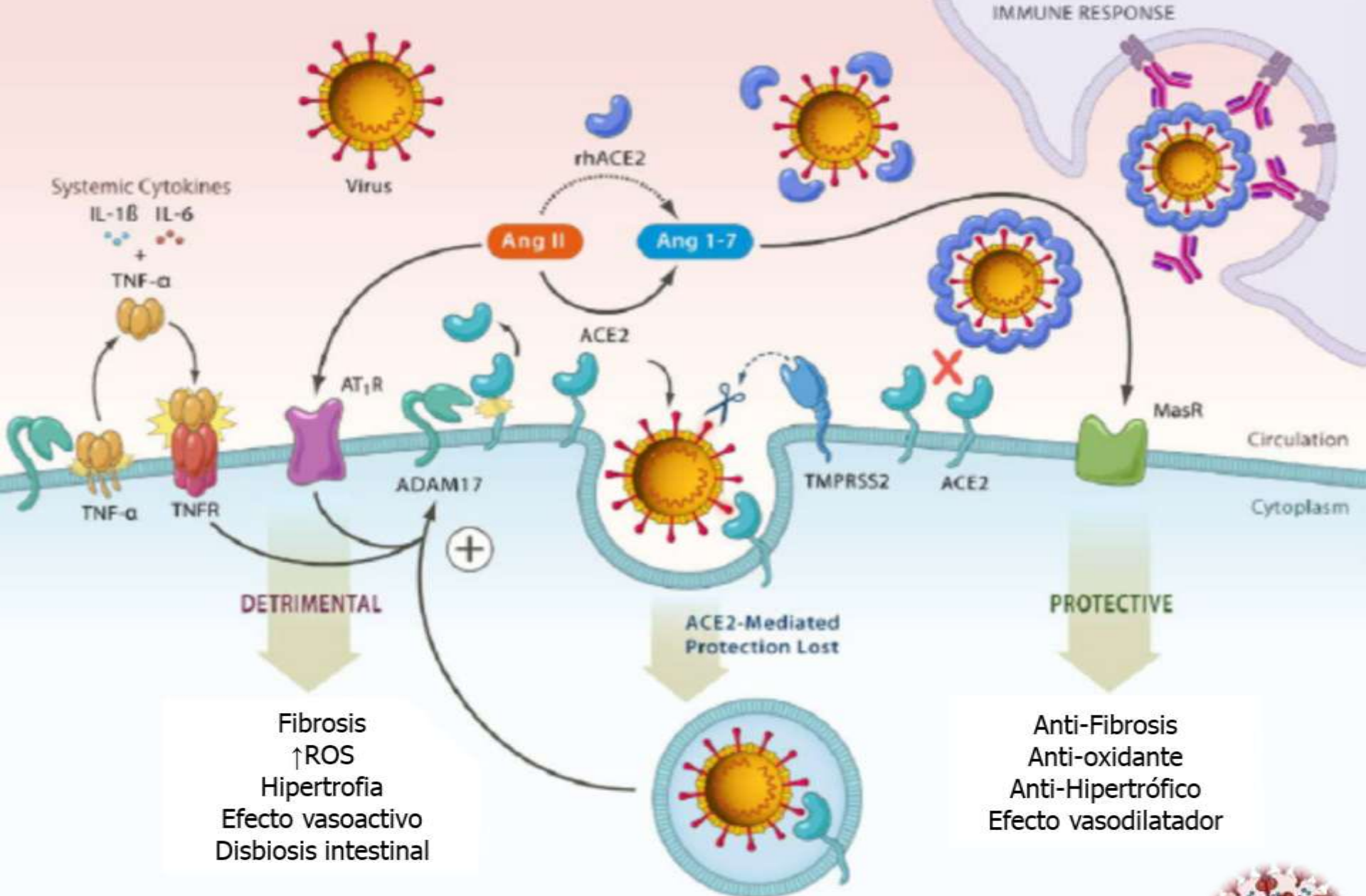
Viruses 2021, 13, 202.





Día 09 de mayo del 2022

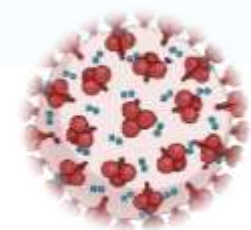


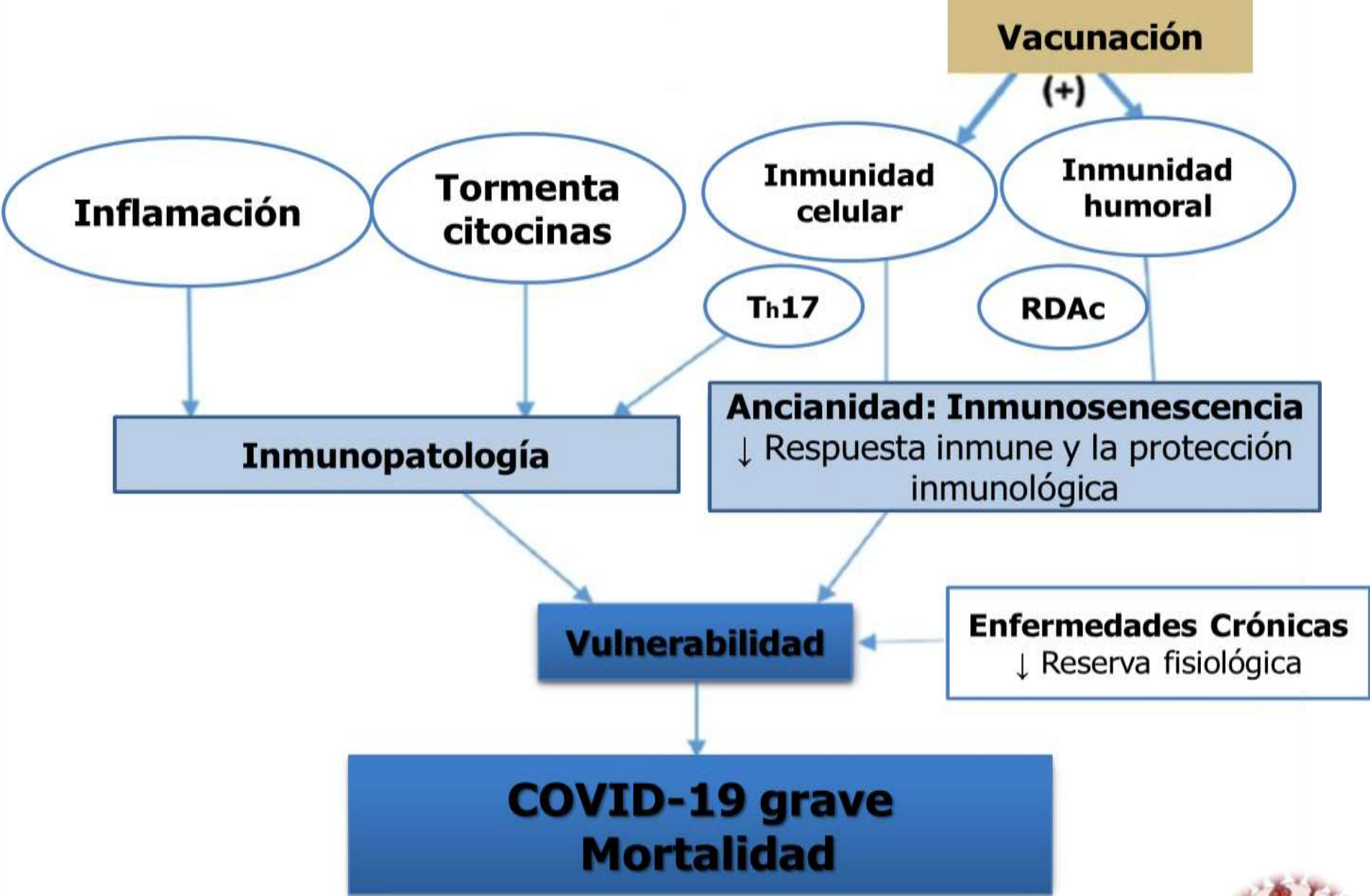


Aging in COVID-19: Vulnerability, immunity and intervention

Ageing Research Reviews 65 (2021) 101205

Yiyin Chen^a, Sabra L. Klein^b, Brian T. Garibaldi^c, Huifen Li^d, Cunjin Wu^{a,e}, Nicole M. Osevala^f, Taisheng Li^g, Joseph B. Margolick^b, Graham Pawelec^{h,i}, Sean X. Leng^{b,d,*}





Aging in COVID-19: Vulnerability, immunity and intervention

Ageing Research Reviews 65 (2021) 101205

Yiyin Chen ^a, Sabra L. Klein ^b, Brian T. Garibaldi ^c, Huifen Li ^d, Cunjin Wu ^{a,e}, Nicole M. Osevala ^f, Taisheng Li ^g, Joseph B. Margolick ^b, Graham Pawelec ^{h,i}, Sean X. Leng ^{b,d,*}

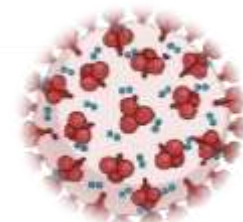
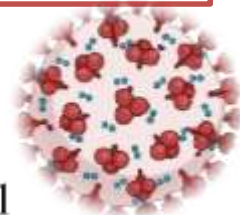


Table 3 Multivariate logistic regression analyses of factors associated with adverse clinical outcomes in the SARS-CoV-2 positive patients

Chronic comorbidities	Hospital admission OR (99% CI)	Pneumonia OR (99% CI)	ICU admission OR (99% CI)	Endotracheal intubation OR (99% CI)	Mortality OR (99% CI)
Age, years					
≤ 20	Ref.	Ref.	Ref.	Ref.	Ref.
21–40	1.06 (0.84–1.34)	1.32 (1.00–1.74)	0.59 (0.32–1.11)	0.83 (0.38–1.81)	1.57 (0.75–3.28)
41–60	2.75 (2.19–3.46)**	3.01 (2.28–3.97)**	1.59 (0.86–2.92)	2.43 (1.14–5.20)*	5.97 (2.90–12.33)**
61–80	6.13 (4.84–7.77)**	5.50 (4.14–7.30)**	2.74 (1.47–5.07)**	4.78 (2.23–10.27)**	13.47 (6.51–27.85)**
> 80	7.18 (5.32–9.70)**	7.09 (5.09–9.88)**	3.05 (1.53–6.11)**	4.47 (1.94–10.27)**	20.44 (9.66–43.26)**
Sex, male	1.71 (1.61–1.82)**	1.58 (1.48–1.68)**	1.64 (1.41–1.91)**	1.76 (1.51–2.06)**	1.70 (1.54–1.88)**
Smoking habit	0.97 (0.87–1.08)	1.05 (0.94–1.17)	0.87 (0.68–1.12)	1.01 (0.79–1.27)	0.89 (0.76–1.05)
Time from symptoms onset to medical contact, days					
0–3	Ref.	Ref.	Ref.	Ref.	Ref.
4–7	1.14 (1.07–1.22)**	1.47 (1.38–1.58)**	1.47 (1.26–1.71)**	1.46 (1.25–1.70)**	1.14 (1.03–1.26)*
≥ 8	1.16 (1.06–1.27)**	1.54 (1.40–1.69)**	1.39 (1.13–1.72)**	1.36 (1.10–1.68)**	0.95 (0.82–1.09)
COPD	1.70 (1.35–2.05)**	1.29 (1.07–1.56)*	1.18 (0.83–1.68)	1.18 (0.84–1.67)	1.50 (1.21–1.87)**
Bronchial asthma	0.71 (0.59–0.85)**	0.78 (0.64–0.94)*	1.00 (0.65–1.54)	0.54 (0.31–0.95)*	0.86 (0.64–1.16)
High blood pressure	1.27 (1.18–1.37)**	1.22 (1.13–1.32)**	1.20 (1.02–1.41)*	1.13 (0.96–1.33)	1.33 (1.20–1.48)**
Cardiovascular disease	1.08 (0.90–1.30)	1.03 (0.86–1.22)	1.02 (0.72–1.43)	1.03 (0.74–1.44)	1.04 (0.84–1.30)
Diabetes mellitus	2.11 (1.94–2.28)**	1.80 (1.66–1.95)**	1.43 (1.21–1.68)**	1.46 (1.25–1.72)**	1.68 (1.52–1.87)**
Obesity	1.35 (1.25–1.45)**	1.38 (1.28–1.49)**	1.49 (1.28–1.75)**	1.58 (1.35–1.85)**	1.53 (1.38–1.71)**
Chronic kidney disease	2.58 (2.08–3.20)**	1.66 (1.38–2.00)**	1.09 (0.76–1.57)	1.32 (0.94–1.85)	2.18 (1.77–2.69)**
Other comorbidities	1.30 (1.11–1.52)**	1.14 (0.97–1.35)	1.19 (0.85–1.68)	0.75 (0.49–1.12)	1.29 (1.04–1.61)*

Edad > 40 años (> 60 años), sexo masculino, demora en atención médica > 3 días, enfermedades crónicas (EPOC, HTA, DM, obesidad, ERC) se relacionaron significativamente con malos resultados clínicos

Chronic comorbidities and clinical outcomes in patients with and without COVID-19: a large population-based study using national administrative healthcare open data of Mexico Internal and Emergency Medicine



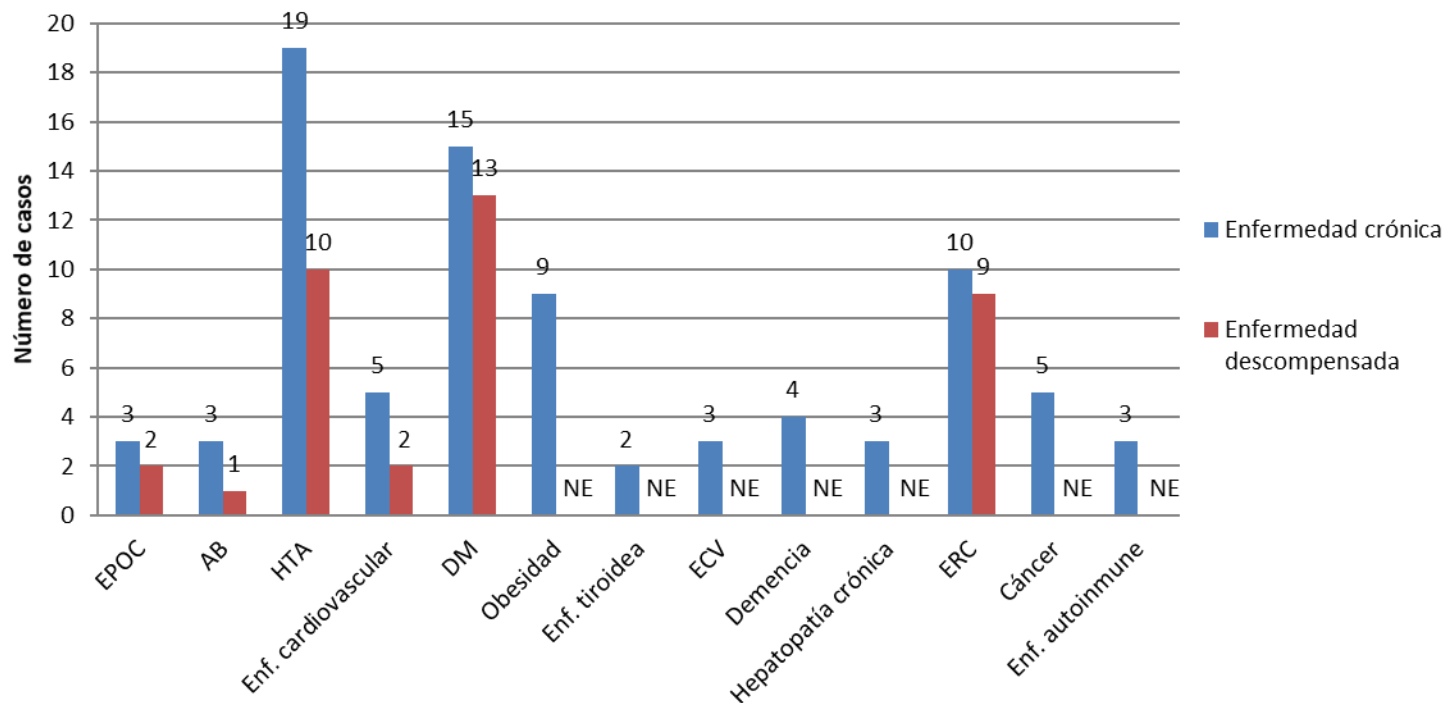
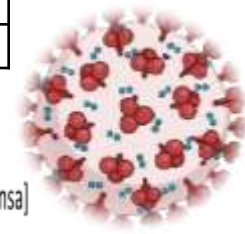


Tabla 3. Relación entre las enfermedades crónicas descompensadas y los resultados clínicos.


Variables	Enfermedad crónica descompensada		χ^2 o <i>t</i> -Student	p
	No (n = 15)	Sí (n = 17)		
Mortalidad en UCI, n (%)	2 (13,3)	12 (70,0)	5,349	0,021
Estadía en UCI, días (media y DE)	10,5 (4,2)	10,2 (3,4)	0,264	0,793
Agravamiento, n (%)	4 (30,8)	15 (78,9)	5,565	0,018
Cambio de VNI a VMI, n (%)	3 (23,1)	7 (36,8)	NP	0,467
Tiempo de VMI, días (media y DE)	11,9 (3,7)	9,1 (3,5)	1,711	0,102
Necesidad de aminas vasopresoras, n (%)	4 (26,7)	8 (47,1)	NP	0,267
Terapia de remplazo renal, n (%)	1 (6,7)	3 (17,6)	NP	0,629

DE: desviación estándar; NP: no procede.; UCI: unidad de cuidados intensivos; VMI: ventilación mecánica invasiva; VNI: ventilación no invasiva.



Pulmonary embolism in patients with COVID-19 and value of D-dimer assessment: a meta-analysis

European Radiology (2021) 31:8168–8186

Robert M. Kwee¹  • Hugo J. A. Adams² • Thomas C. Kwee³

Studies	Estimate (95% C.I.)	COVID-19 patients with PE/total number of COVID-19 patients
Alharthy et al. [23]	0.880 (0.753, 1.000)	22/25
Bellmunt–Montoya et al. [27]	0.421 (0.264, 0.578)	16/38
Benito et al. [28]	0.385 (0.120, 0.649)	5/13
Bompard et al. [30]	0.500 (0.300, 0.700)	12/24
Brüggemann et al. [31]	0.769 (0.540, 0.998)	10/13
Contou et al. [35]	0.615 (0.428, 0.802)	16/26
Fang et al. [39]	0.650 (0.441, 0.859)	13/20
Grillet et al. [45]	0.500 (0.321, 0.679)	15/30
Helms et al. [48]	0.253 (0.167, 0.338)	25/99
Mak et al. [61]	0.353 (0.222, 0.484)	18/51
Mirsadraee et al. [68]	0.472 (0.357, 0.588)	34/72
Mouhat et al. [71]	0.426 (0.309, 0.544)	29/68
Mueller–Peltzer et al. [72]	0.562 (0.319, 0.806)	9/16
Parzy et al. [75]	0.231 (0.002, 0.460)	3/13
Patel et al. [76]	0.385 (0.232, 0.537)	15/39
Poissy et al. [79]	0.647 (0.486, 0.808)	22/34
Schiaffino et al. [83]	0.600 (0.457, 0.743)	27/45
Taccone et al. [86]	0.325 (0.180, 0.470)	13/40
Thomas et al. [87]	0.455 (0.160, 0.749)	5/11
Whyte et al. [11]	0.462 (0.351, 0.572)	36/78
Zhang et al. [91]	0.279 (0.145, 0.413)	12/43
Zotzmann et al. [92]	0.600 (0.385, 0.815)	12/20
Overall (I²=80% , P< 0.001)	0.486 (0.410, 0.561)	369/818

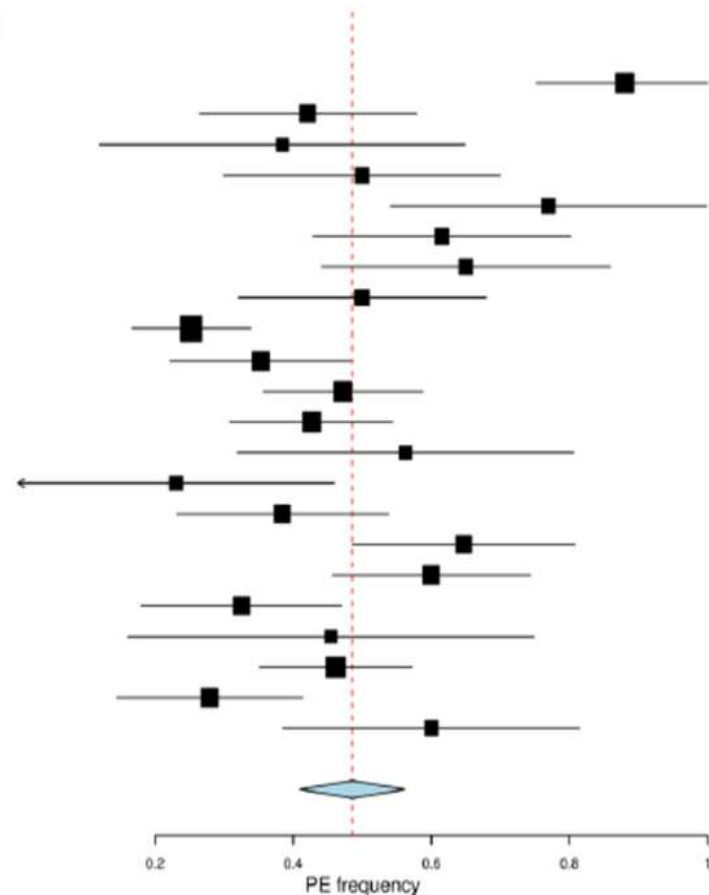
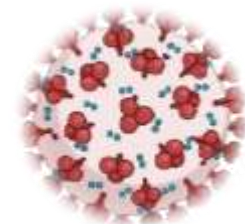


Fig. 4 Frequency of PE in patients with COVID-19 who had been admitted to the ICU

Incidencia de embolismo pulmonar en UCI: 49%

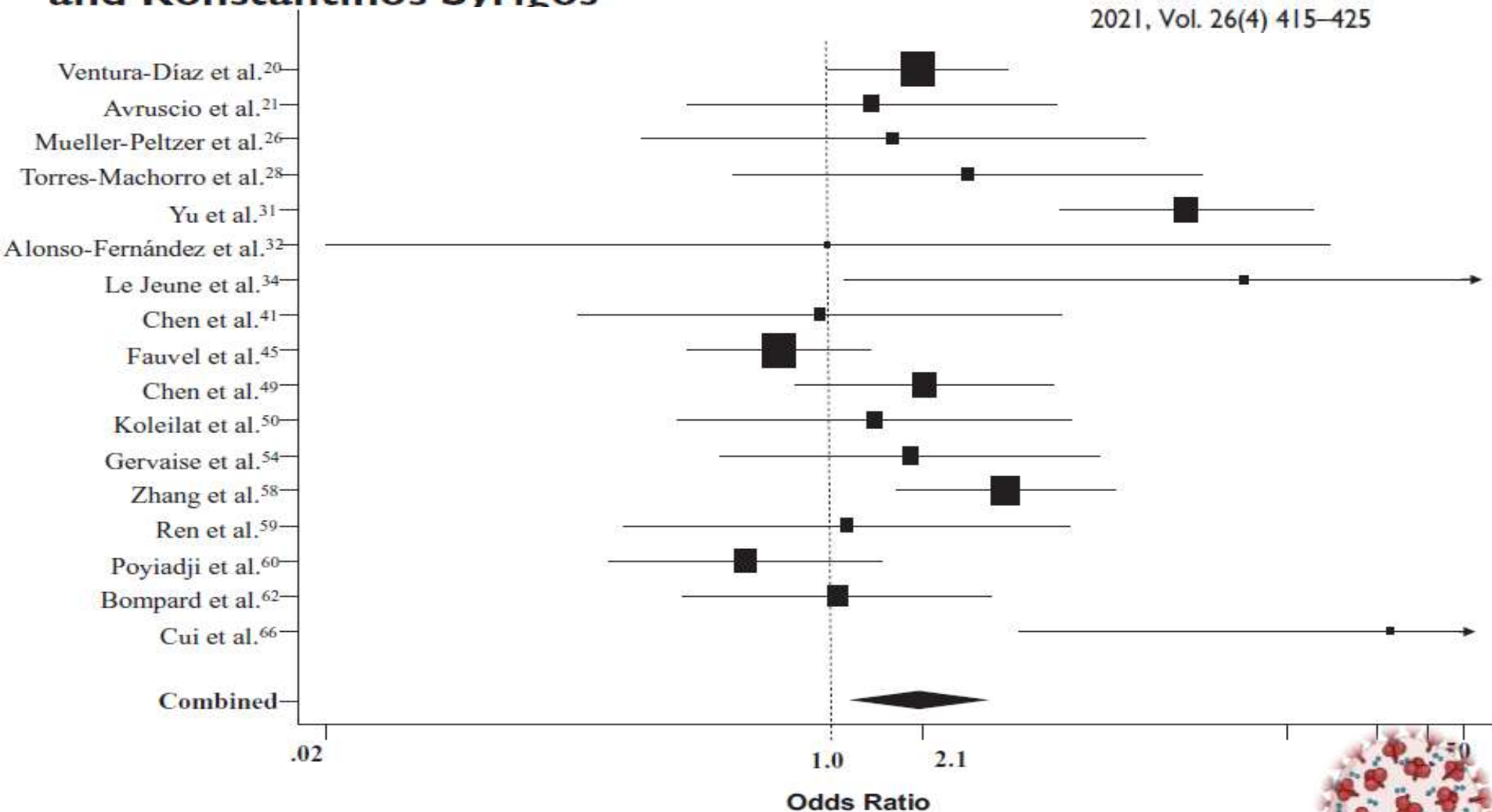


Venous thromboembolism in COVID-19:

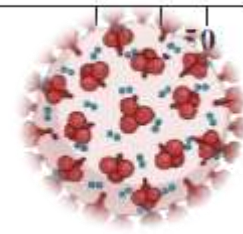
A systematic review and meta-analysis

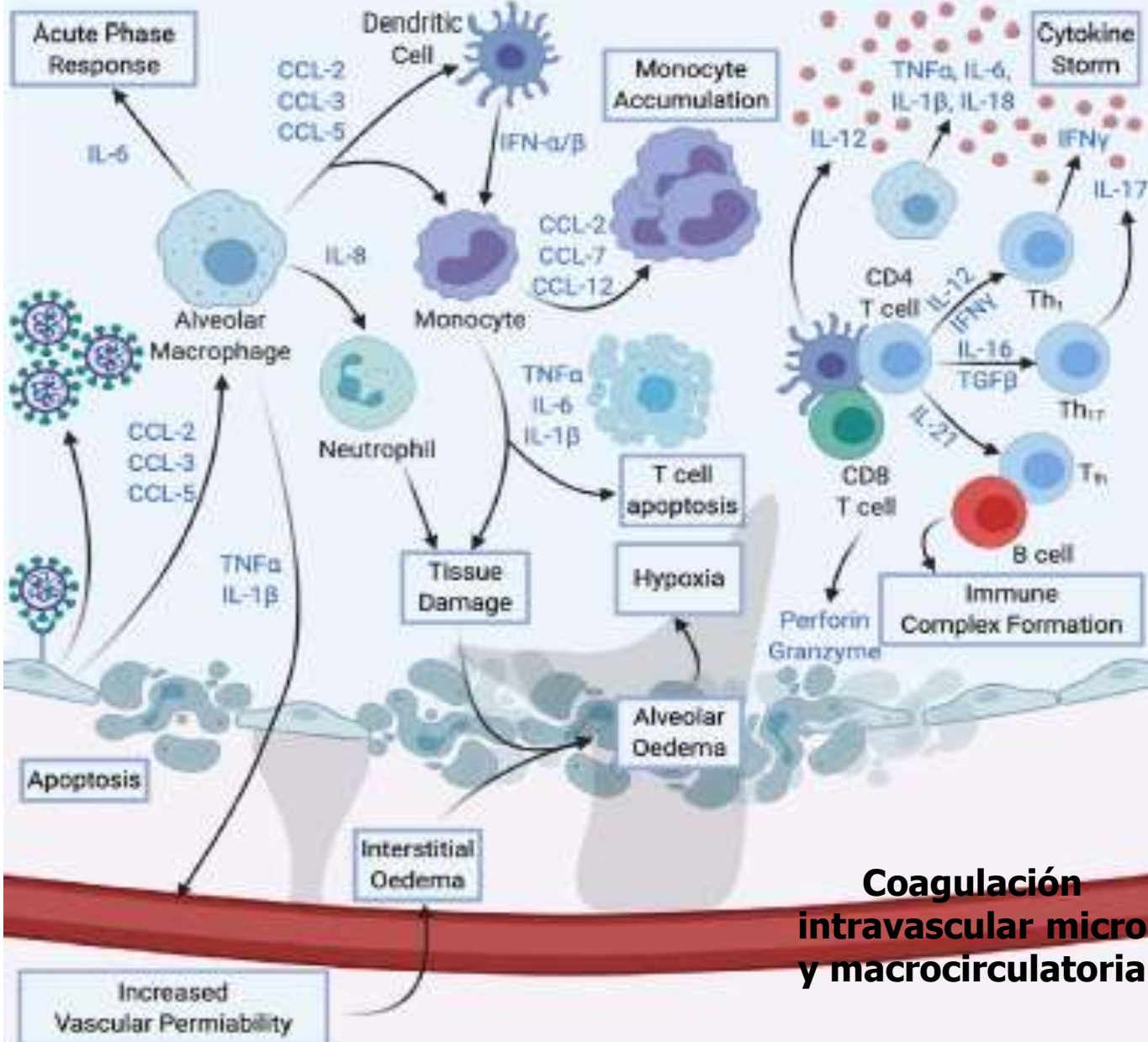
Anastasios Kollias^{1*} , Konstantinos G Kyriakoulis^{1*},
Styliani Lagou¹, Evangelos Kontopantelis^{2,3}, George S Stergiou¹
and Konstantinos Syrigos¹

Vascular Medicine
2021, Vol. 26(4) 415–425



El tromboembolismo venoso incrementa significativamente el riesgo de muerte en los pacientes con COVID-19



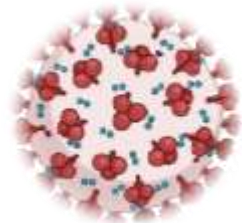


Trastornos fisiopatológicos cardinales de la COVID-19

Lesión tisular directa
Hiperinflamación
Hipercoagulabilidad

Coagulación intravascular micro y macrocirculatoria

Coronavirus disease 2019 (COVID-19): An overview of the immunopathology, serological diagnosis and management





Tratamiento



Principios del tratamiento en la COVID-19



Reducir carga viral



Reducir respuesta inflamatoria



Reducir estado trombofílico

Mejora de resultados clínico a corto plazo



Neumonía



UCI



Ventilación

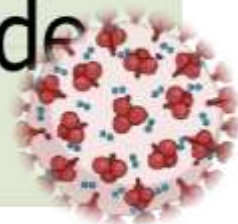


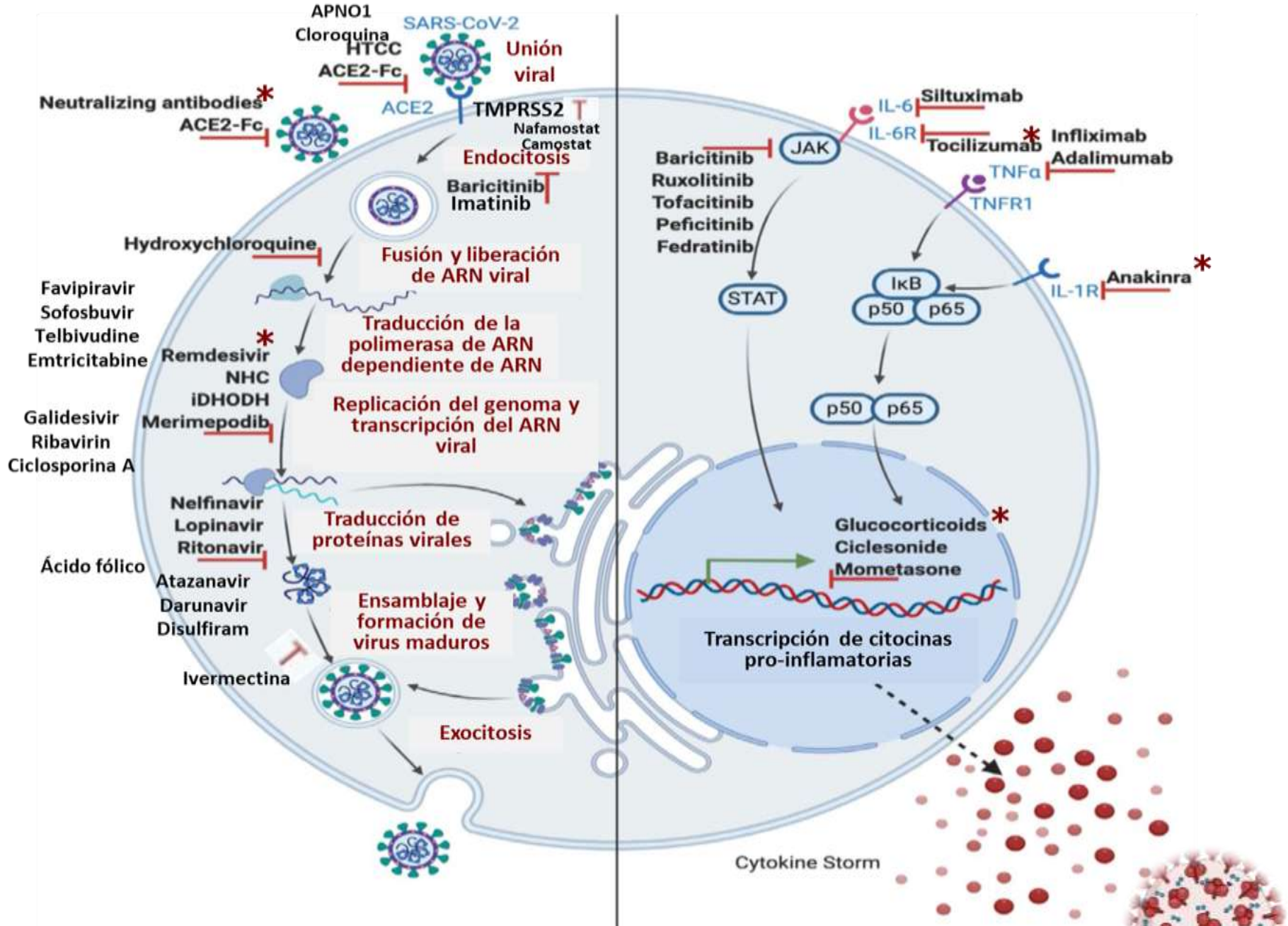
Mortalidad

COVID-19 prolongado

Secuelas

Calidad de vida





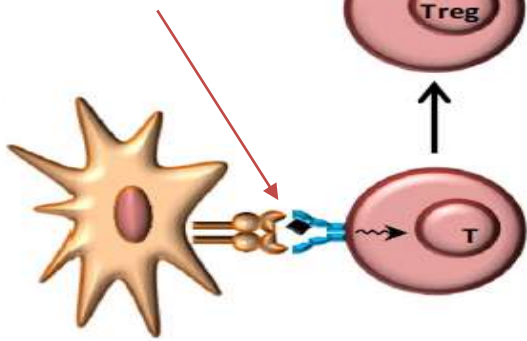
Coronavirus disease 2019 (COVID-19): An overview of the immunopathology, serological diagnosis and management

COVID-19: Characteristics and Therapeutics

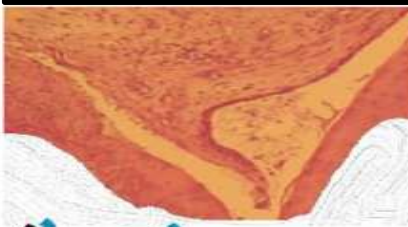
Abubakar Umar Anka¹, Mohammed Ibrahim Tahir¹, Scand J Immunol. 2020;00:e12998.
 SharaBadeen Daidra Abubakar^{1,2}, Mohamed Alsaibgh³, Zineb Zian⁴,
 Moleb, HassanUfou^{5,6}, A. A. Saad, Saad^{5,7}, Ehab, Hassan, A. A. Saad^{5,7}

Cells 2021, 10, 206.
 Rameswari Chilamakuri and Saurabh Agarwal

Juzvinsa

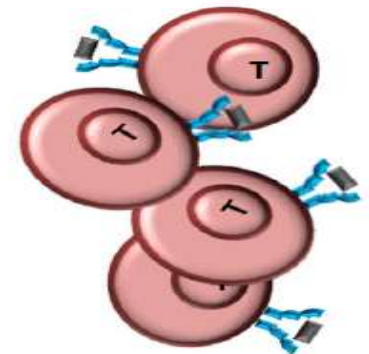


Tejido inflamado

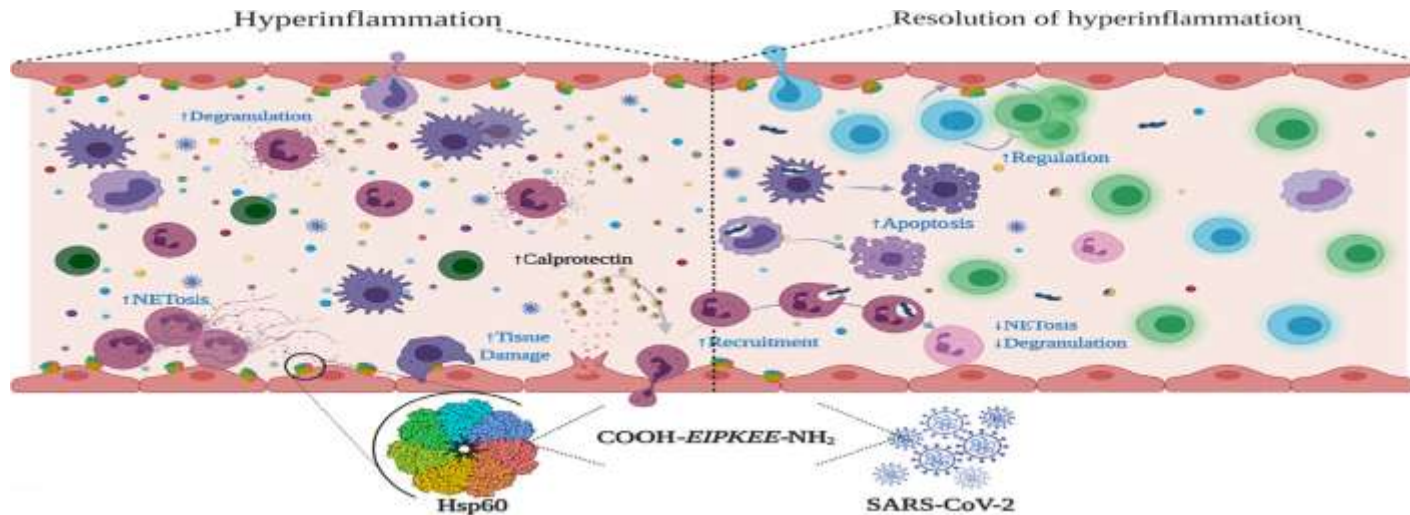


↑ ■ Wild-type peptide

Supresión



↓ Citocinas proinflamatorias



CIGB-258, a peptide derived from human heat-shock protein 60, decreases hyperinflammation in COVID-19 patients

Cell Stress and Chaperones (2021) 26:515–525

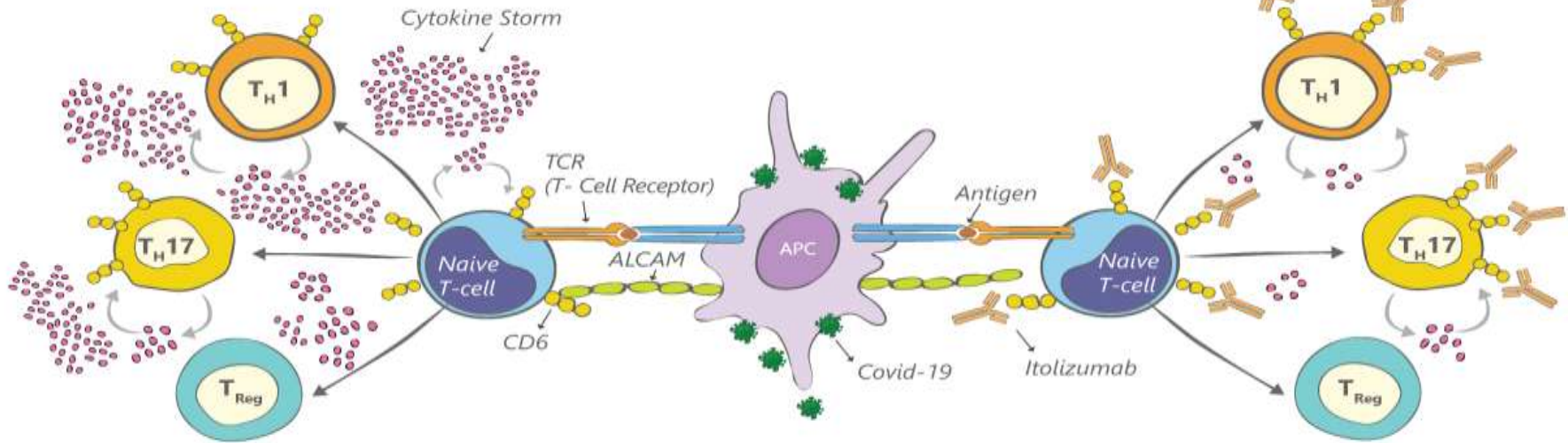
M. Hernandez-Cedeño¹ · R. Venegas-Rodriguez² · R. Peña-Ruiz² · M. Bequet-Romero¹ · R. Santana-Sanchez² · E. Penton-Arias¹ · G. Martinez-Donato¹ · G. Guillén-Nieto¹ · María del Carmen Dominguez-Horta¹

Biodistribution and pharmacokinetic profiles of an altered peptide ligand derived from heat-shock proteins 60 in Lewis rat

Cell Stress and Chaperones (2020) 25:133–140

María del Carmen Dominguez¹ · Ania Cabrales¹ · Norailys Lorenzo² · Gabriel Padrón¹ · L. J. Gonzalez¹





Without Itolizumab

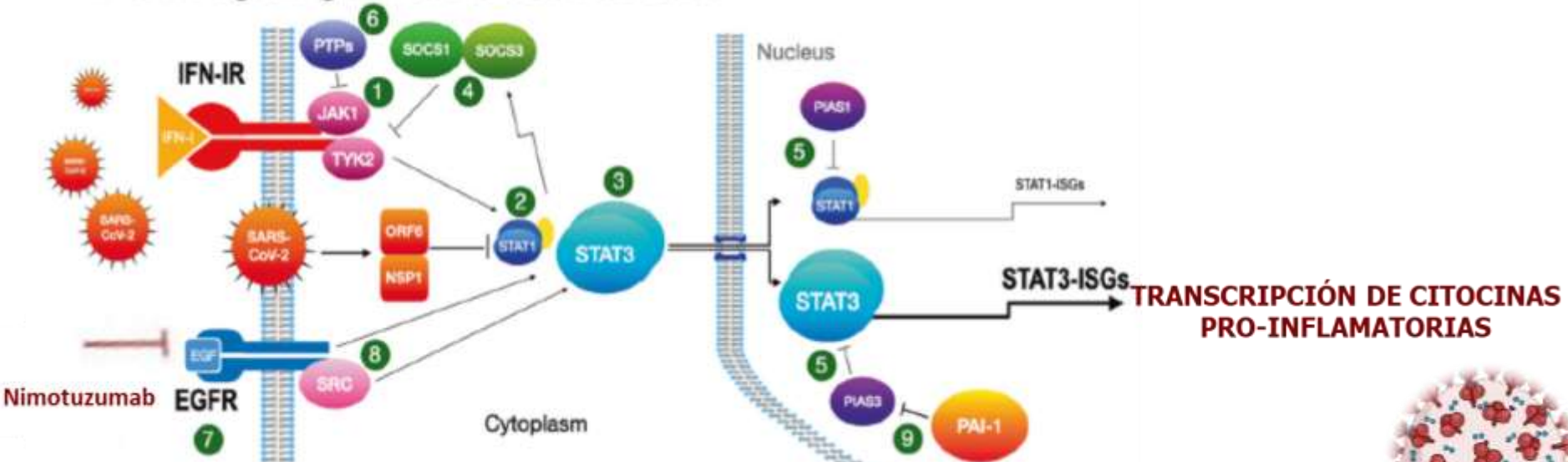
With Itolizumab

A two-arm, randomized, controlled, multi-centric, open-label Phase-2 study to evaluate the efficacy and safety of Itolizumab in moderate to severe ARDS patients due to COVID-19

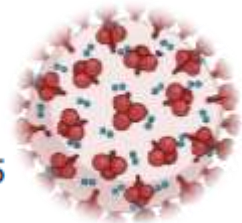
medRxiv preprint doi: <https://doi.org/10.1101/2020.12.01.20239574>

Suresh Kumar,¹ Rosemarie de Souza,² Milind Nadkar,³ Randeep Guleria,⁴ Anjan Trikha,⁴ Shashank R. Joshi,⁵ Subramanian Loganathan,⁶ Sivakumar Vaidyanathan,⁶ Ashwani Marwaha,⁶ Sandeep N. Athlye⁶

B. IFN-I signaling with SARS-CoV-2 infection



TRANSCRIPCIÓN DE CITOCINAS PRO-INFLAMATORIAS



An aberrant STAT pathway is central to COVID-19

Cell Death & Differentiation (2020) 27:3209–3225

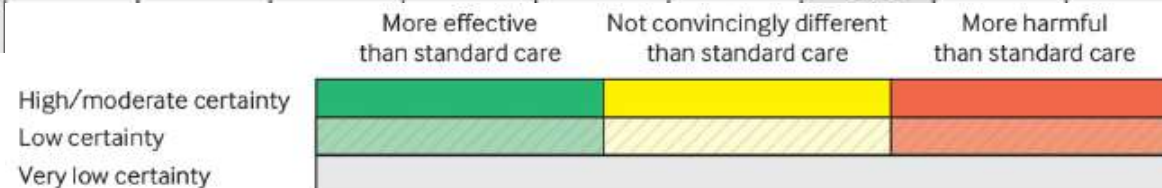
Toshifumi Matsuyama¹ · Shawn P. Kubli² · Steven K. Yoshinaga³ · Klaus Pfeffer⁴ · Tak W. Mak^{2,5,6}

Antibody and cellular therapies for treatment of covid-19: a living systematic review and network meta-analysis

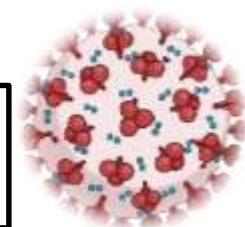
BMJ 2021;374:n2231

Reed AC Siemieniuk, ^{1,2,*} Jessica J Bartoszko, ^{1,*} Juan Pablo Díaz Martínez, ^{1,*} Elena Kum, ^{1,*} Anila Qasim, ^{1,*}

	Mortality	Mechanical ventilation	Admission to hospital	Viral clearance at 7 days	Adverse events*	Infusion reactions*	TRALI*	TACO*	Duration of hospitalisation	Time to symptom resolution	Time to viral clearance	Ventilator free days	ICU length of stay
Non severe disease													
Standard care†	3 per 1000	6 per 1000	60 per 1000	160 per 1000					14 days	9 days	24 days		
Bamlanivimab	-2 (-3 to 82)‡		-41 (-57 to -6)	2 (-113 to 216)						-1 (-3 to 3)	4 (-15 to 43)		
Bamlanivimab, etesevimab	-3 (-3 to 0)‡		-38 (-54 to -9)	57 (-100 to 319)						-1 (-3 to 1)	1 (-16 to 35)		
Casirivimab, imdevimab	-1 (-3 to 1)‡	-4 (-6 to 2)	-42 (-50 to -30)							-2 (-4 to -1)			
Convalescent plasma	-1 (-2 to 2)‡	-1 (-5 to 4)		132 (-15 to 348)					-4 (-10 to 1)				
CT-P59 monoclonal antibody	-2 (-3 to 90)‡	4 (-7 to 231)‡	-24 (-52 to 37)	94 (-72 to 352)						-3 (-5 to 0)	3 (-16 to 40)		
Sotrovimab	-2 (-3 to 29)‡	-6 (-6 to -4)‡	-48 (-58 to -25)										
Severe or critical disease													
Standard care†	220 per 1000	300 per 1000							12 days			14 days	4 days
Casirivimab, imdevimab	-7 (-79 to 82)												
Control plasma	118 (-41 to 307)												
Convalescent plasma	-14 (-56 to 20)	-14 (-135 to 115)							-1 (-2 to 1)			-1 (-2 to 0)	1 (-2 to 0)‡
Intravenous immunoglobulin	-53 (-119 to 29)	-70 (-190 to 80)											



Los Ac neutralizantes anti-SARS-CoV-2 reducen el riesgo de hospitalización y el tiempo para la resolución de los síntomas en pacientes con COVID-19 no grave

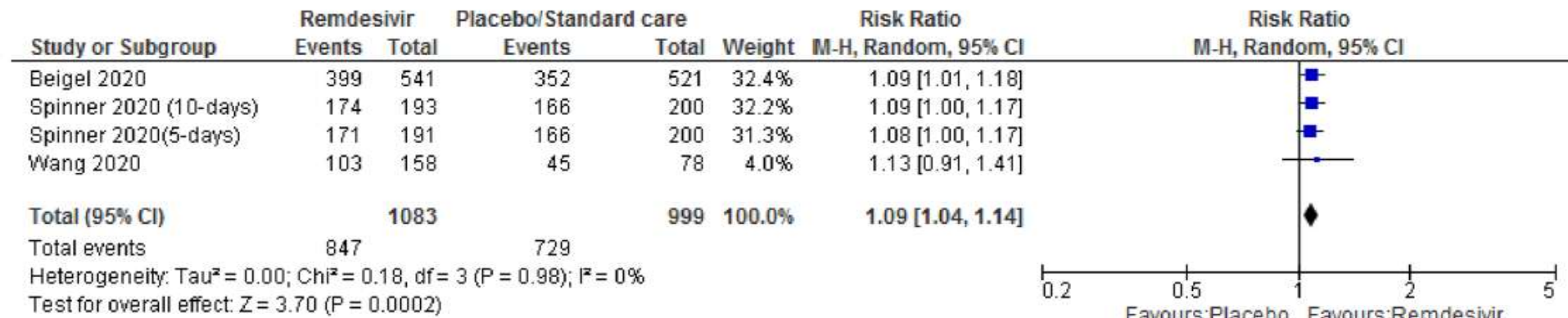


Efficacy and safety of remdesivir in hospitalised COVID-19 patients: a systematic review and meta-analysis

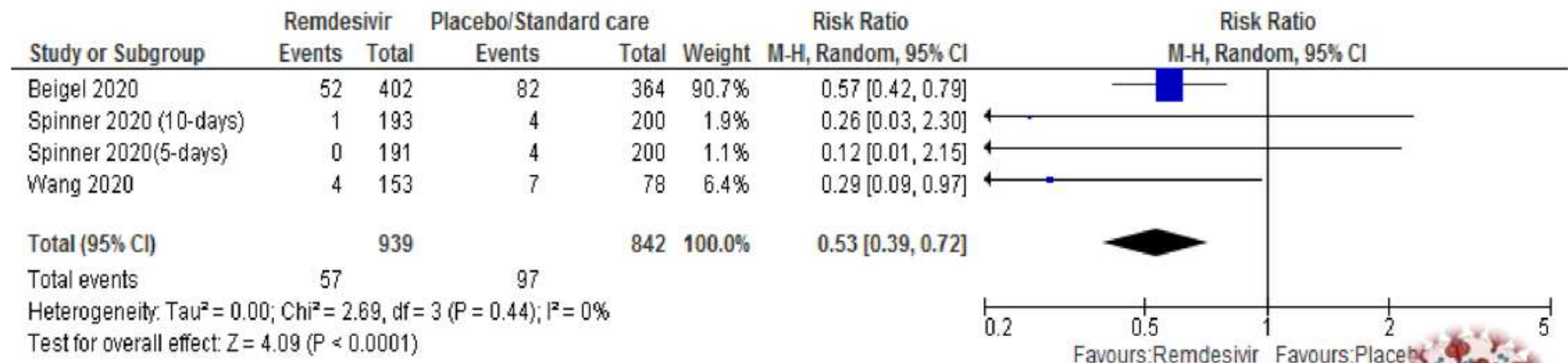
Infection (2022) 50:27–41

Mulugeta T. Angamo¹ · Mohammed A. Mohammed² · Gregory M. Peterson¹

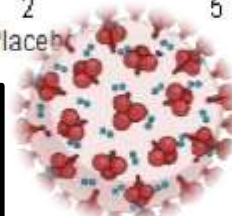
Number of patients with clinical recovery on day 28



Number of patients requiring mechanical ventilation or ECMO



El Remdesevir se asocia con mejoría clínica y menor necesidad de oxígeno, ventilación y ECMO en pacientes con neumonía por COVID-19

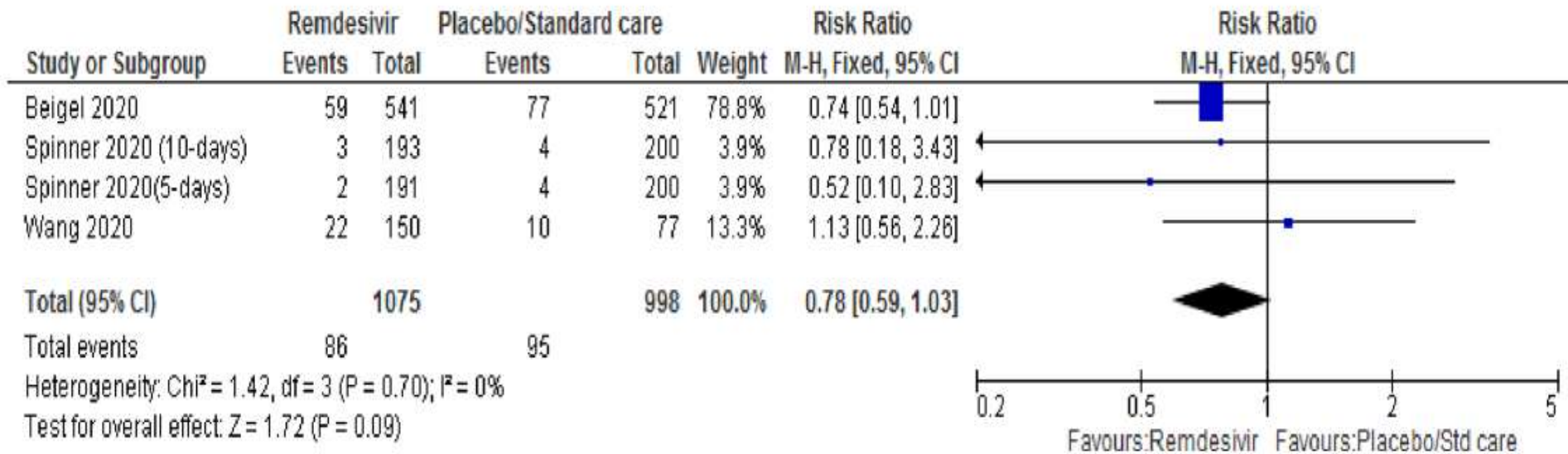


Efficacy and safety of remdesivir in hospitalised COVID-19 patients: a systematic review and meta-analysis

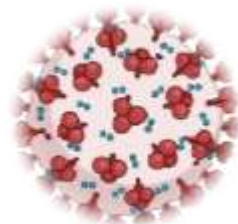
Infection (2022) 50:27–41

Mulugeta T. Angamo¹ · Mohammed A. Mohammed² · Gregory M. Peterson¹

All-cause mortality on day 28



El Remdesevir no se asocia con reducción significativa de la mortalidad en pacientes con neumonía por COVID-19

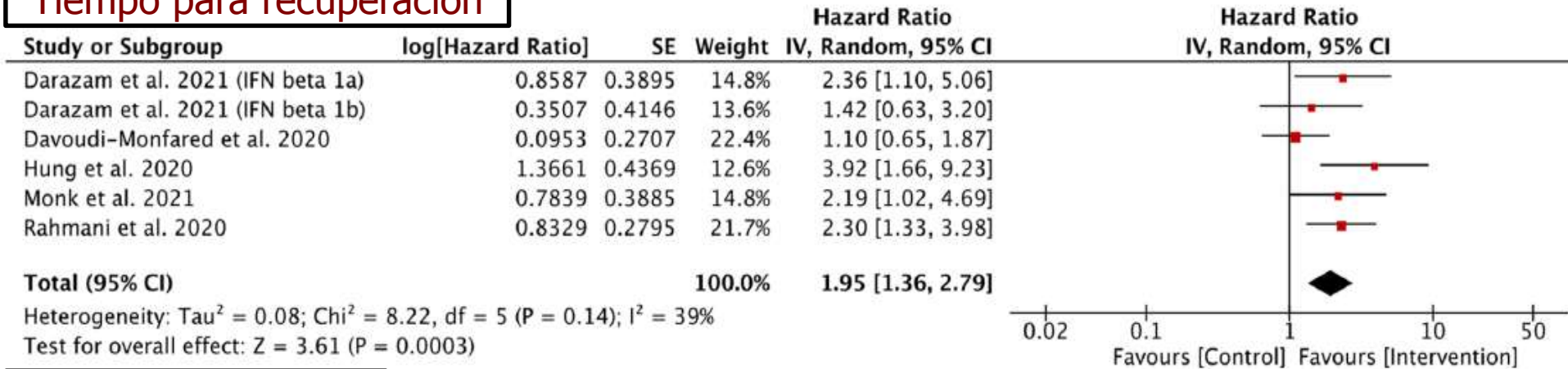


Efficacy of Interferon- β in Moderate-to-Severe Hospitalised Cases of COVID-19: A Systematic Review and Meta-analysis

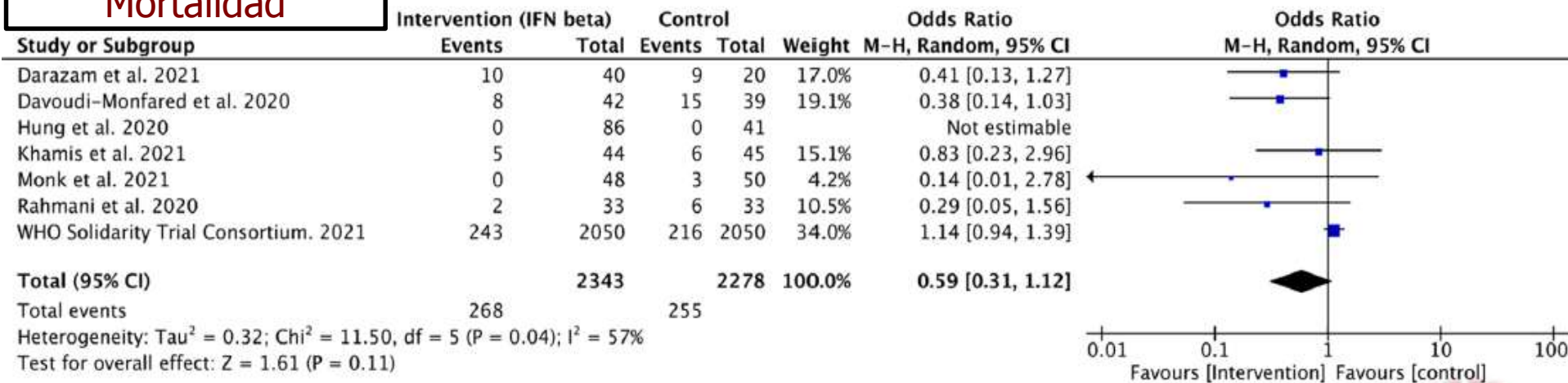
Subodh Kumar¹ · Manoj Kumar Saurabh¹ · Venkata Lakshmi Narasimha¹ · Vikas Maharshi¹

Clinical Drug Investigation (2021) 41:1037–1046

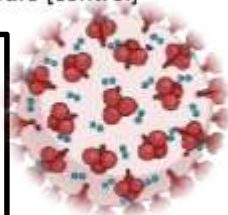
Tiempo para recuperación



Mortalidad



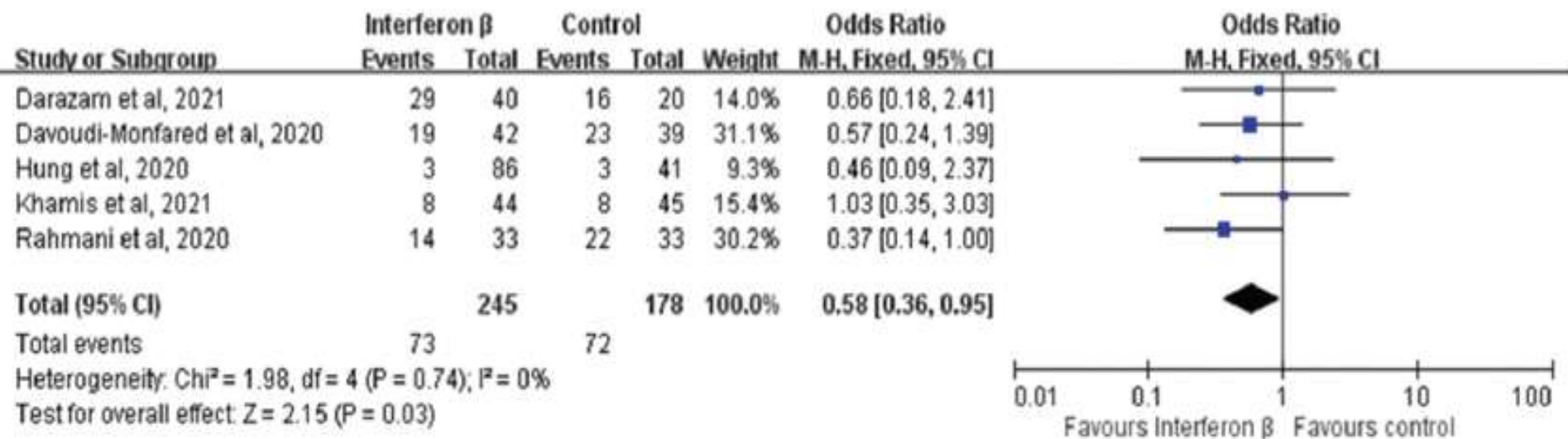
El interferón se asocia con reducción significativa del tiempo para la recuperación; pero no de la mortalidad en pacientes con COVID-19 moderada y grave



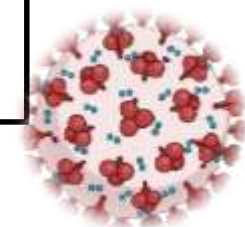
Clinical efficacy and safety of interferon- β -containing regimens in the treatment of patients with COVID-19: a systematic review and meta-analysis of randomized controlled trials

EXPERT REVIEW OF ANTI-INFECTIVE THERAPY Accepted 28 October 2021

Wang-Chun Chen^{a,b}, Chi-Kuei Hsu^{c,d,e}, Ching-Yi Chen^{c,d}, Chih-Cheng Lai^f, Shun-Hsing Hung^g and Wei-Ting Lin^h



El interferón se asocia con reducción significativa de la necesidad de ingreso en la UCI de pacientes con COVID-19 leve-moderado



Comparative efficacy and safety of pharmacological interventions for the treatment of COVID-19: A systematic review and network meta-analysis

. PLoS Med 17(12): e1003501.

Min Seo Kim^{1,2}✉✉*, Min Ho An^{3,4}✉, Won Jun Kim^{1,5}, Tae-Ho Hwang^{6,7}✉✉*

B Mortality for moderate-severe COVID-19 patients – all studies

Contrast to control

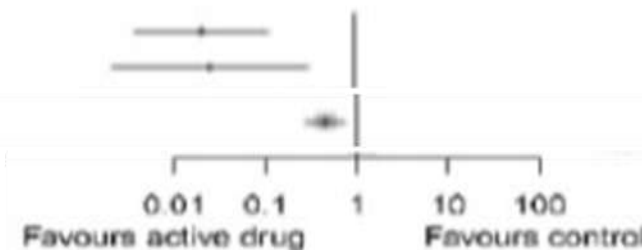
High dose corticosteroid plus tocilizumab
Interferon- α 2b
Remdesivir

Random effect model

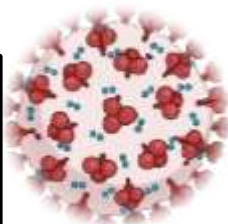
OR

95%-CI

0.04 [0.01; 0.17]
0.05 [0.01; 0.39]
0.52 [0.34; 0.80]



El interferón- α 2b y el remdesivir se asociaron con una reducción significativa de la mortalidad en pacientes con COVID-19 moderado y grave

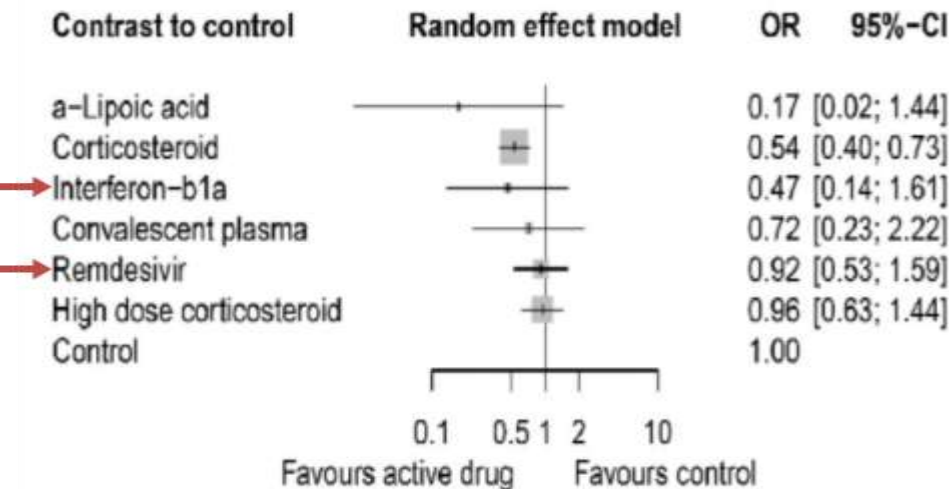


Comparative efficacy and safety of pharmacological interventions for the treatment of COVID-19: A systematic review and network meta-analysis

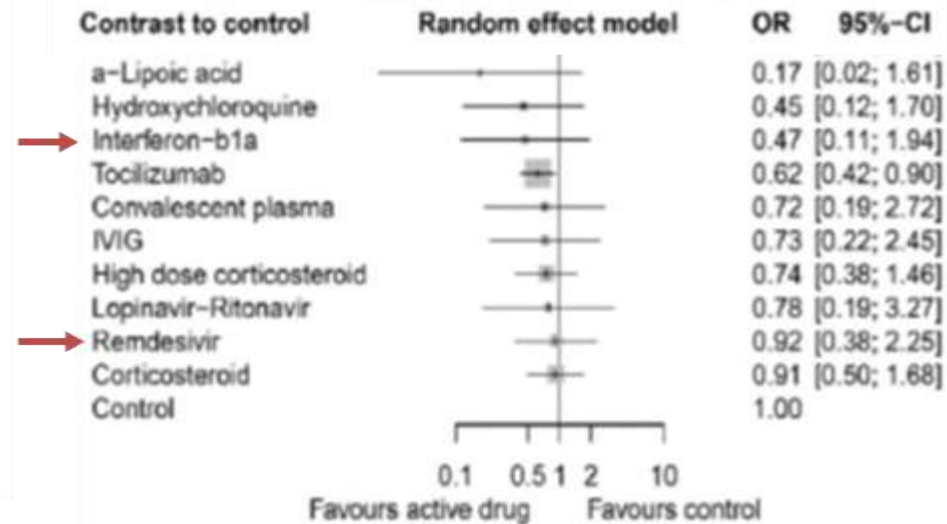
. PLoS Med 17(12): e1003501.

Min Seo Kim^{1,2}✉, Min Ho An^{3,4}✉, Won Jun Kim^{1,5}, Tae-Ho Hwang^{6,7}✉

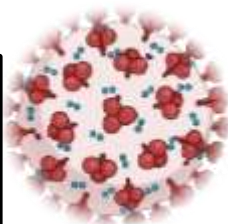
C Mortality for critically ill patients – RCTs only



D Mortality for critically ill patients – all studies



El interferón y el remdesivir no reducen la mortalidad en pacientes críticos por COVID-19





Revisiting Pleiotropic Effects of Type I Interferons: Rationale for Its Prophylactic and Therapeutic Use Against SARS-CoV-2

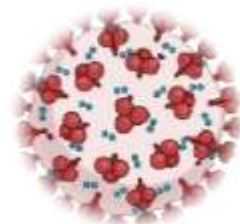
Diana Garcia-del-Barco^{1*}, *Daniela Risco-Acevedo*¹, *Jorge Berlanga-Acosta*²,
*Frank Daniel Martos-Benítez*³ and *Gerardo Guillén-Nieto*⁴

¹ Neuroprotection Project, Center for Genetic Engineering and Biotechnology, Pharmaceutical Division, Havana, Cuba,

² Cytoprotection Project, Center for Genetic Engineering and Biotechnology, Pharmaceutical Division, Havana, Cuba,

³ Intensive Care Unit 8B, Hermanos Ameijeiras Hospital, Havana, Cuba, ⁴ Biomedical Research Direction, Center for Genetic Engineering and Biotechnology, Havana, Cuba

OPEN ACCESS



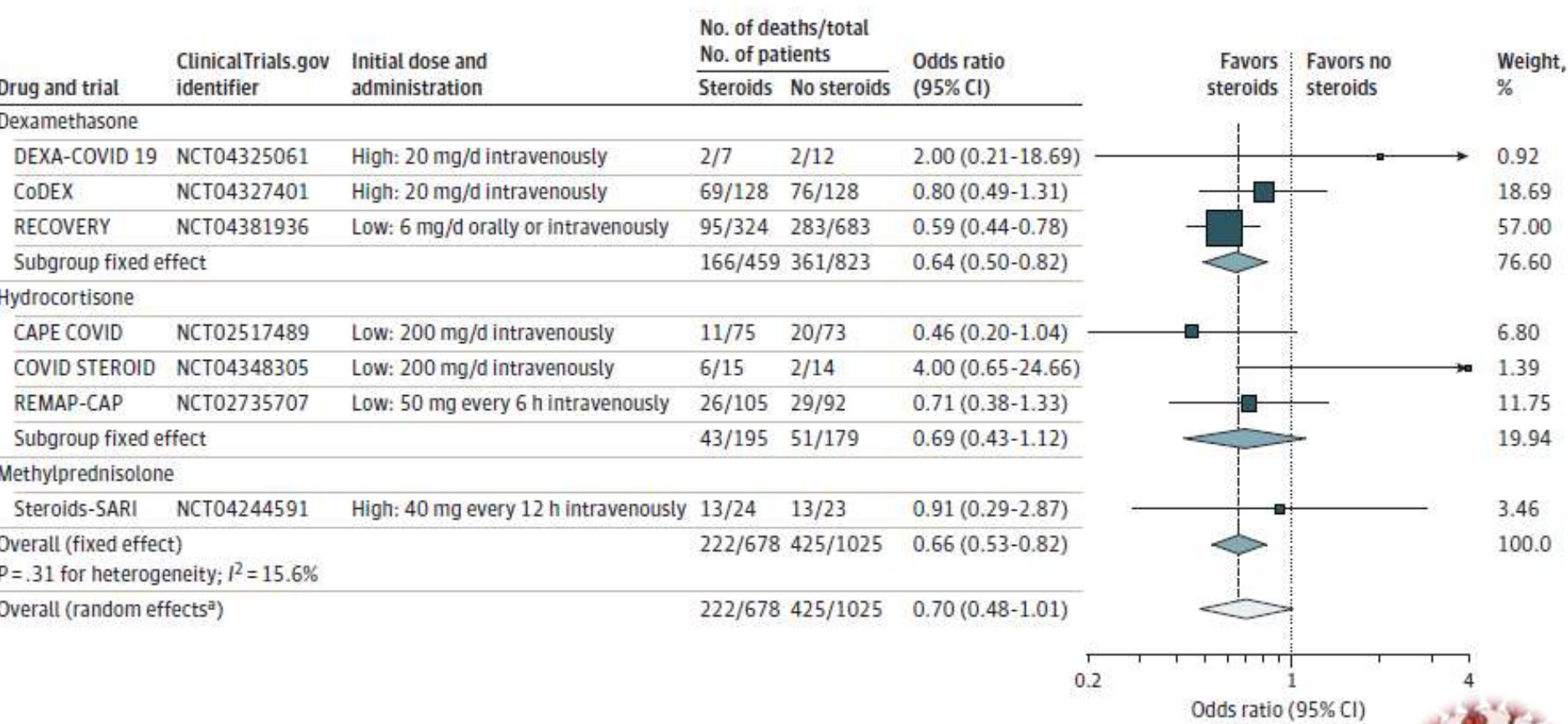
Association Between Administration of Systemic Corticosteroids and Mortality Among Critically Ill Patients With COVID-19

A Meta-analysis

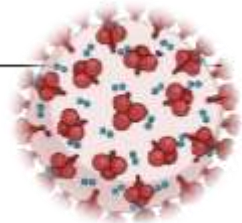
JAMA. doi:10.1001/jama.2020.17023
 Published online September 2, 2020.

The WHO Rapid Evidence Appraisal for COVID-19 Therapies (REACT) Working Group

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



Dexametasona > Metilprednisolona > Hidrocortisona



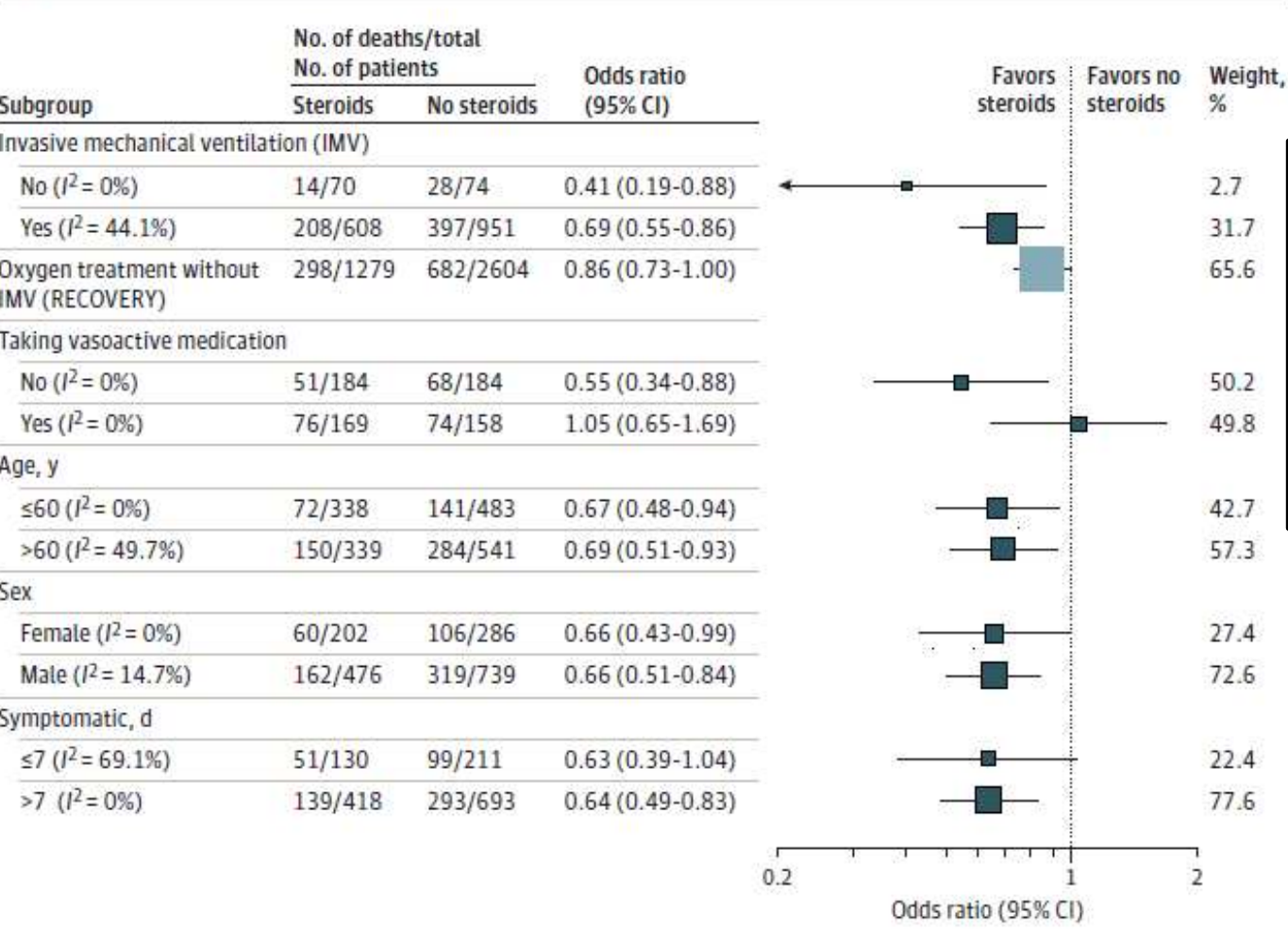
Association Between Administration of Systemic Corticosteroids and Mortality Among Critically Ill Patients With COVID-19

A Meta-analysis

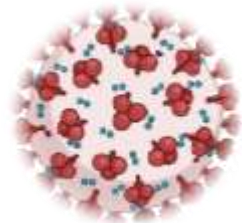
JAMA. doi:10.1001/jama.2020.17023
 Published online September 2, 2020.

The WHO Rapid Evidence Appraisal for COVID-19 Therapies (REACT) Working Group

Figure 3. Association Between Corticosteroids and 28-Day All-Cause Mortality Within Subgroups Defined by Patient Characteristics at the Time of Randomization



Los esteroides mejoran los resultados clínico en todos los subgrupos de pacientes críticos



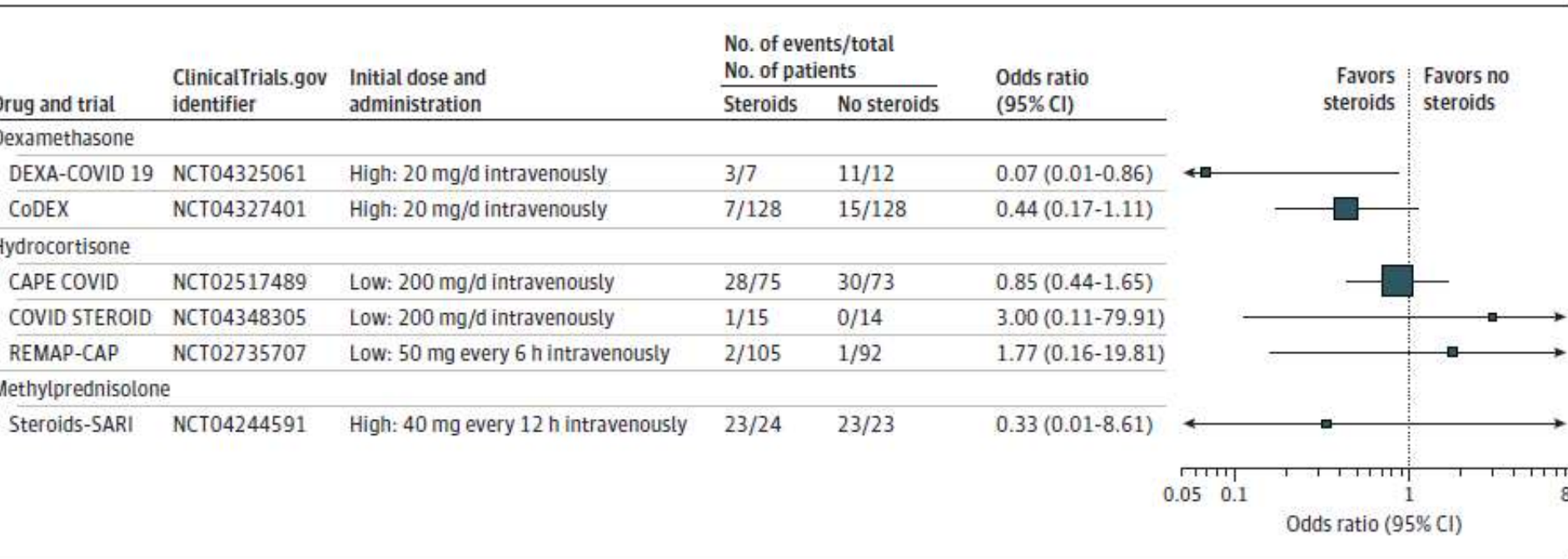
Association Between Administration of Systemic Corticosteroids and Mortality Among Critically Ill Patients With COVID-19

A Meta-analysis

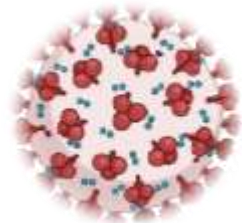
JAMA. doi:10.1001/jama.2020.17023
 Published online September 2, 2020.

The WHO Rapid Evidence Appraisal for COVID-19 Therapies (REACT) Working Group

Figure 4. Association Between Corticosteroids and Serious Adverse Events in Each Trial



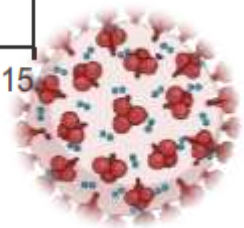
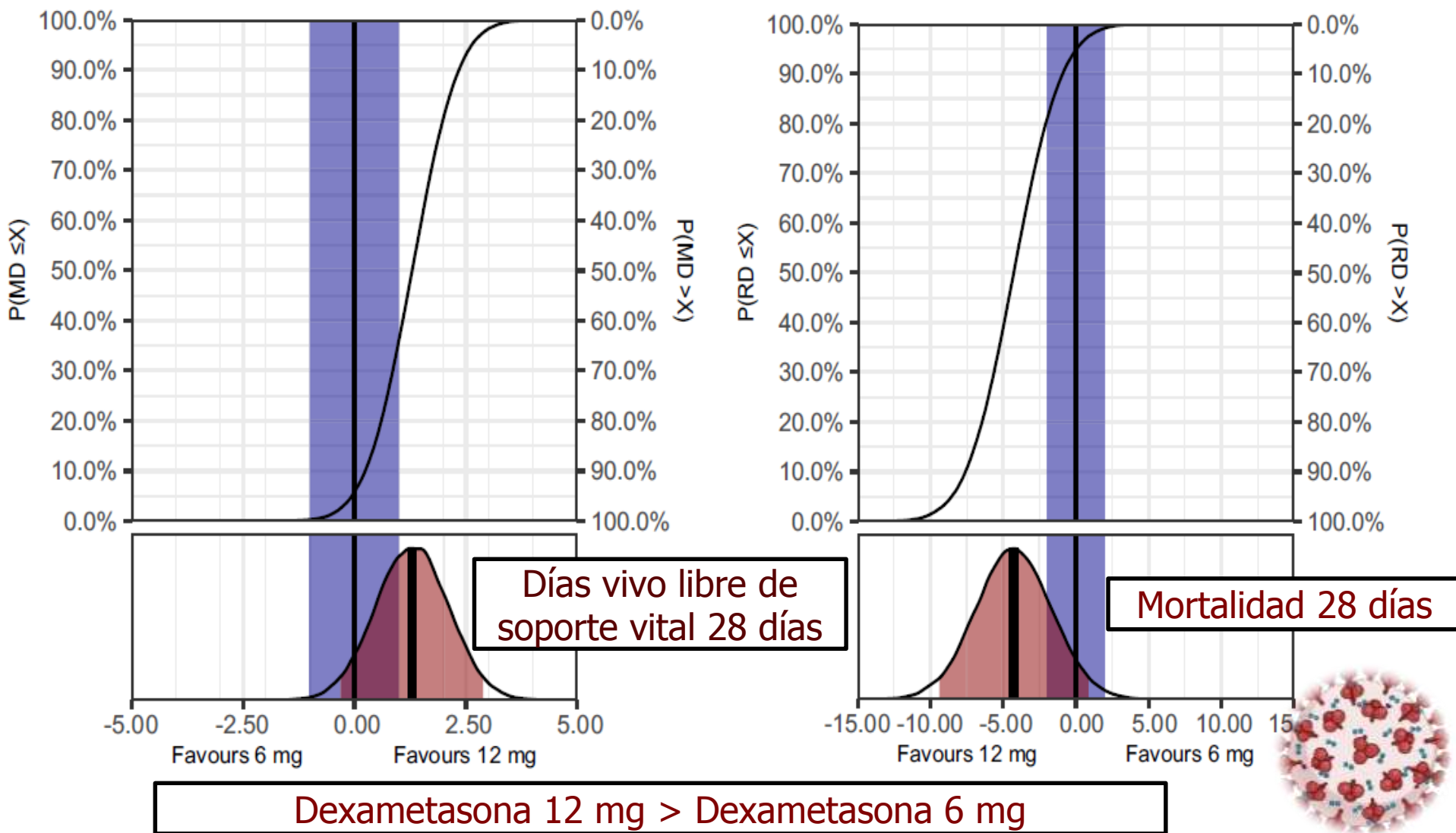
El tratamiento con esteroides es seguro



Dexamethasone 12 mg versus 6 mg for patients with COVID-19 and severe hypoxaemia: a pre-planned, secondary Bayesian analysis of the COVID STEROID 2 trial

Anders Granholm^{1,2*}, Marie Warrer Munch^{1,2}, Sheila Nainan Myatra³,

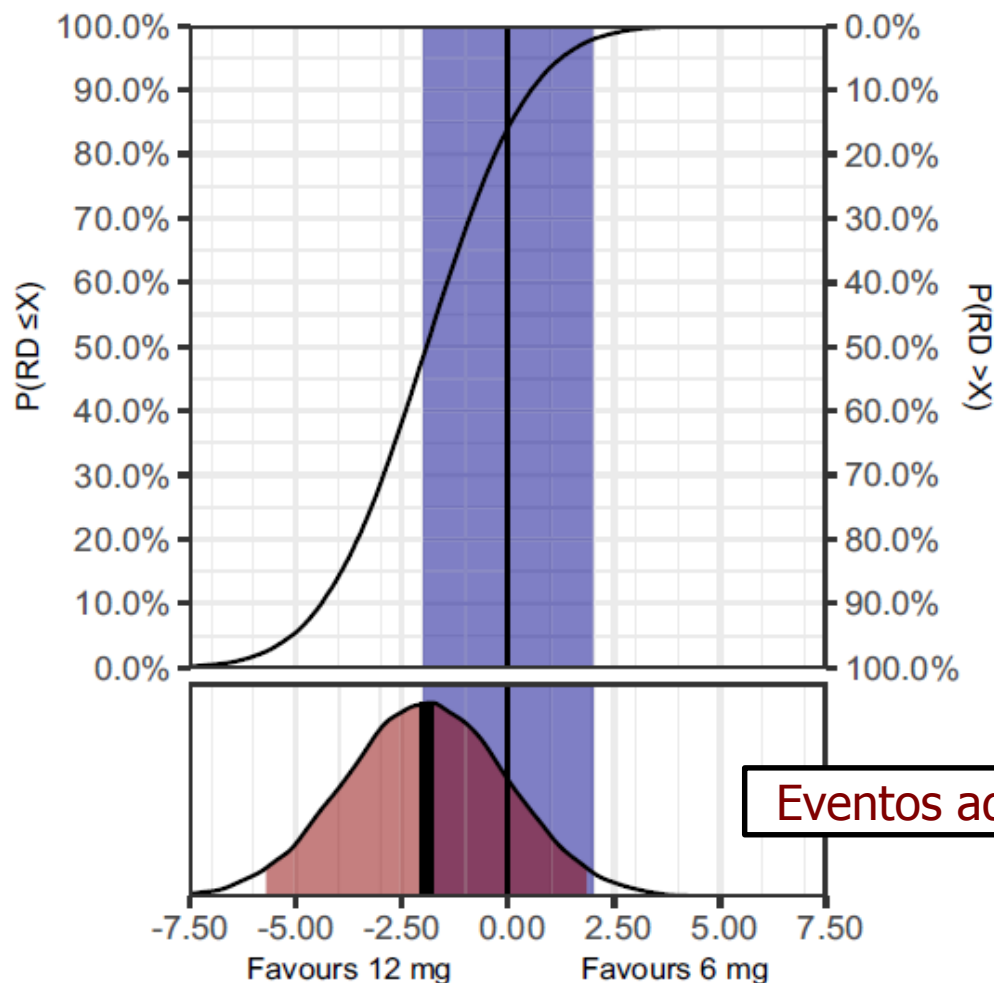
Intensive Care Med 2021



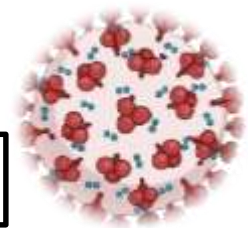
Dexamethasone 12 mg versus 6 mg for patients with COVID-19 and severe hypoxaemia: a pre-planned, secondary Bayesian analysis of the COVID STEROID 2 trial

Anders Granholm^{1,2*}, Marie Warrer Munch^{1,2}, Sheila Nainan Myatra³,

Intensive Care Med 2021



Seguridad de Dexamentasona 12 mg = Seguridad de Dexametasona 6 mg

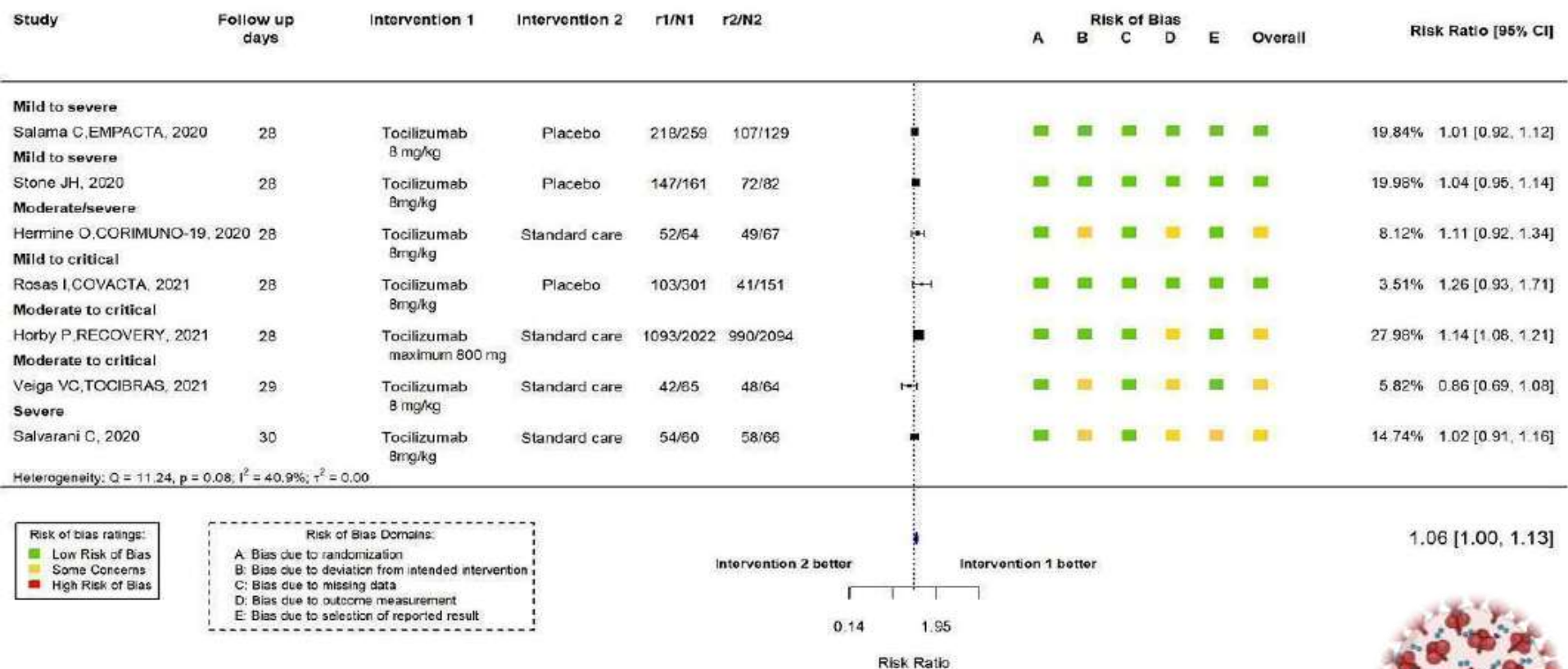


Interleukin-6 blocking agents for treating COVID-19: a living systematic review (Review)

Ghosh L, Chaimani A, Evrenoglou T, Davidson M, Graña C, Schmucker C, Bollig C, Henschke N, Sguassero Y, Nejstgaard CH, Menon S, Nguyen TV, Ferrand G, Kapp P, Riveros C, Ávila C, Devane D, Meerpohl JJ, Rada G, Hróbjartsson A, Grasselli G, Tovey D, Ravaud P, Boutron I

Cochrane Database of Systematic Reviews 2021, Issue 3. Art. No.: CD013881.

Figure 2. Tocilizumab compared to standard care/placebo for mild/moderate/severe/critical COVID-19: Clinical improvement D28



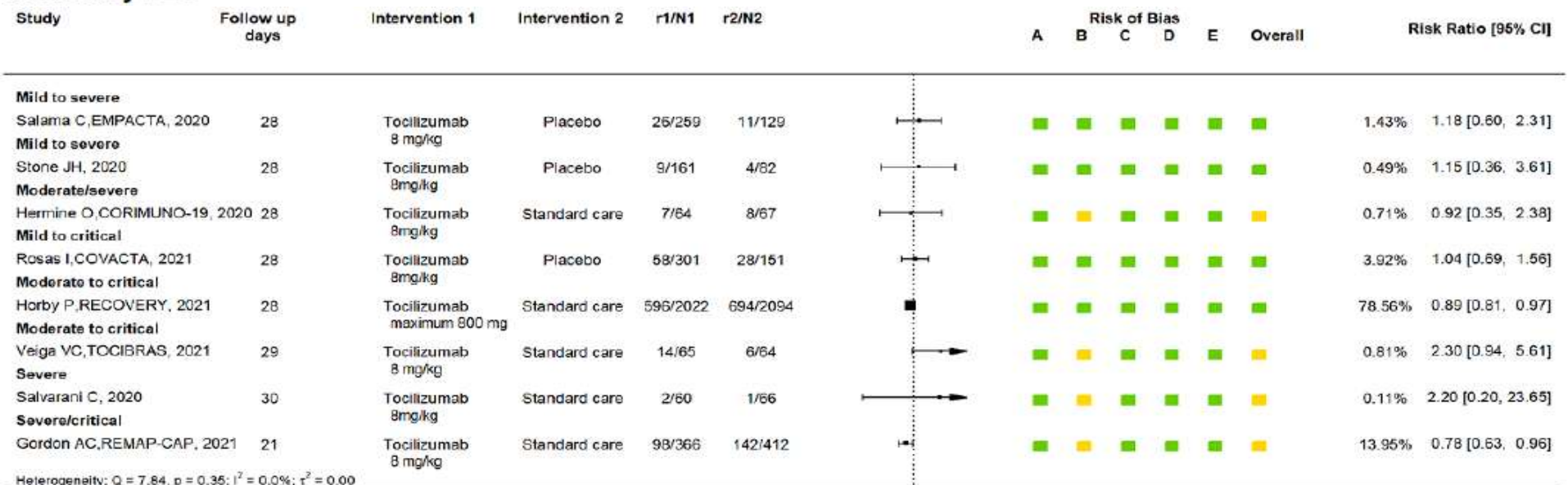
Tocilizumab se asocia con mejoría clínica, principalmente en pacientes con COVID-19 severa y crítica

Interleukin-6 blocking agents for treating COVID-19: a living systematic review (Review)

Ghosh L, Chaimani A, Evrenoglou T, Davidson M, Graña C, Schmucker C, Bollig C, Henschke N, Sguassero Y, Nejstgaard CH, Menon S, Nguyen TV, Ferrand G, Kapp P, Riveros C, Ávila C, Devane D, Meerpohl JJ, Rada G, Hróbjartsson A, Grasselli G, Tovey D, Ravaud P, Boutron I

Cochrane Database of Systematic Reviews 2021, Issue 3. Art. No.: CD013881.

Figure 4. Tocilizumab compared to standard care/placebo for mild/moderate/severe/critical COVID-19: All-cause mortality D28



Risk of bias ratings:

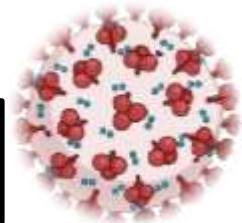
- Low Risk of Bias
- Some Concerns
- High Risk of Bias

Risk of Bias Domains:

- A: Bias due to randomization
- B: Bias due to deviation from intended intervention
- C: Bias due to missing data
- D: Bias due to outcome measurement
- E: Bias due to selection of reported result



Tocilizumab reduce la mortalidad a corto plazo, principalmente en pacientes con COVID-19 moderada-grave-crítica

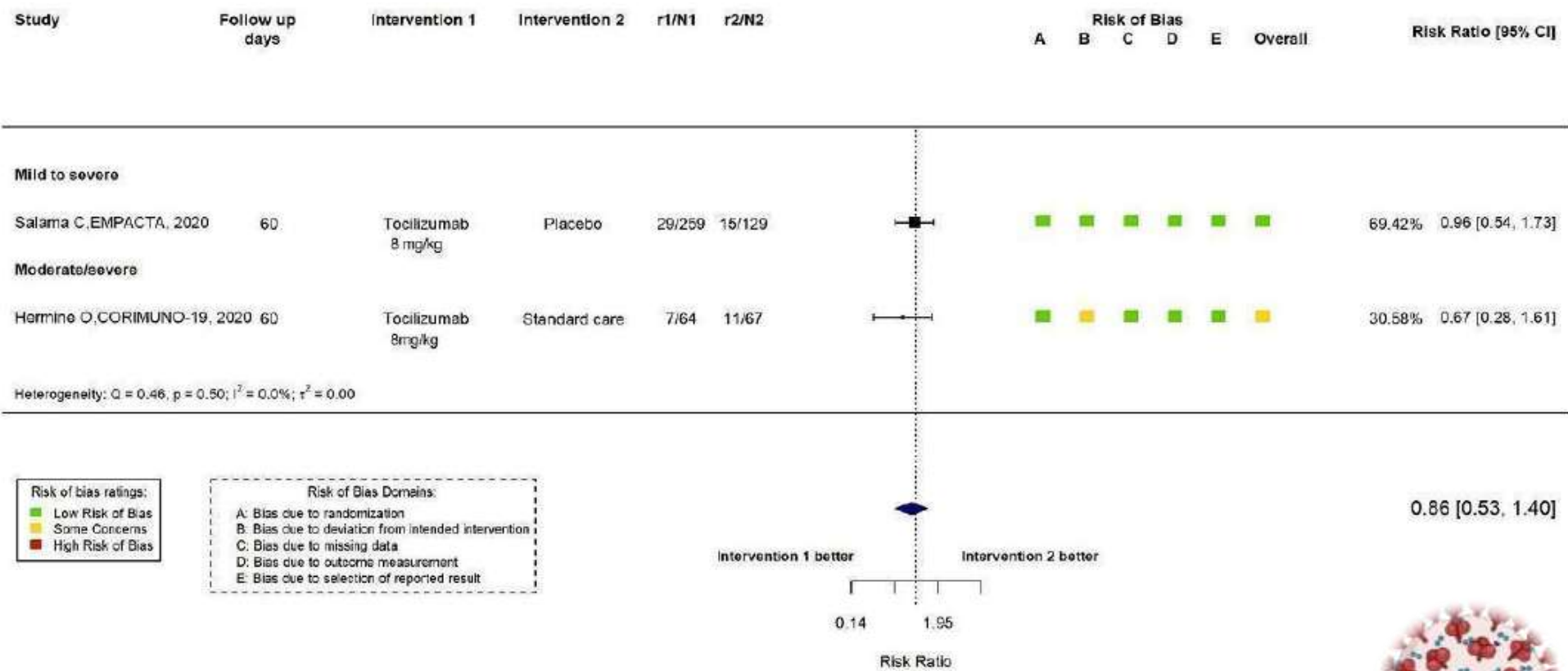


Interleukin-6 blocking agents for treating COVID-19: a living systematic review (Review)

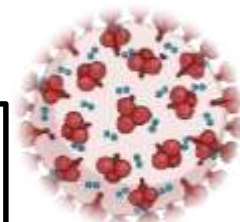
Ghosh L, Chaimani A, Evrenoglou T, Davidson M, Graña C, Schmucker C, Bollig C, Henschke N, Sguassero Y, Nejstgaard CH, Menon S, Nguyen TV, Ferrand G, Kapp P, Riveros C, Ávila C, Devane D, Meerpohl JJ, Rada G, Hróbjartsson A, Grasselli G, Tovey D, Ravaud P, Boutron I

Cochrane Database of Systematic Reviews 2021, Issue 3. Art. No.: CD013881.

Figure 5. Tocilizumab compared to standard care/placebo for mild/moderate/severe/critical COVID-19: All-cause mortality D60 or above



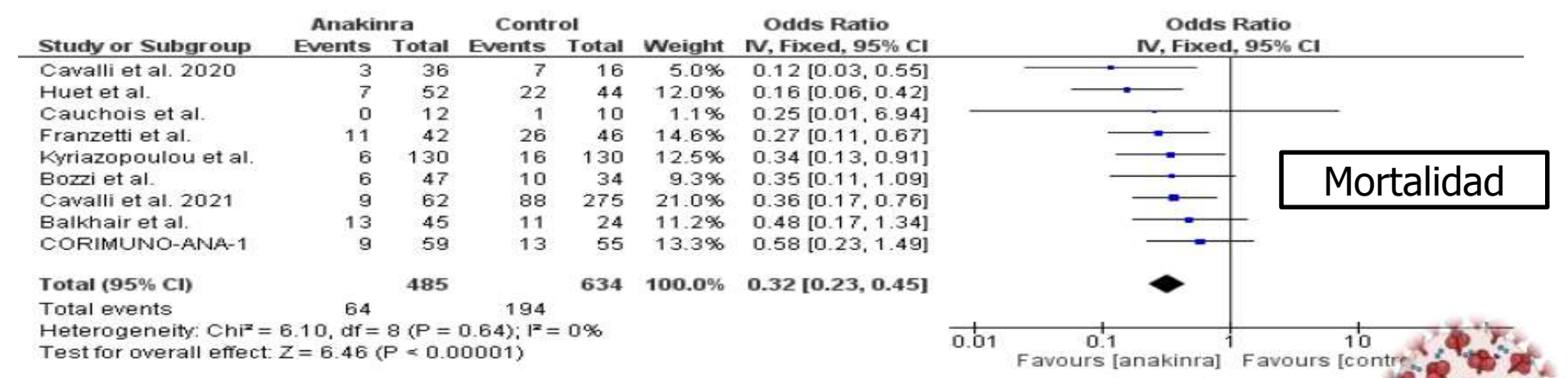
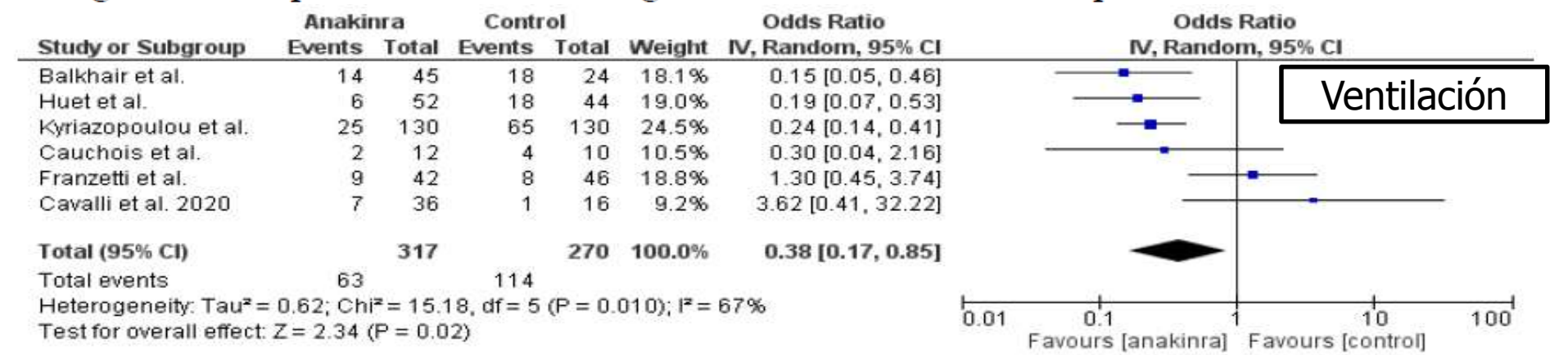
Tocilizumab no reduce la mortalidad a mediano y largo plazo



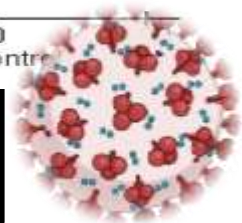
Anakinra in hospitalized non-intubated patients with coronavirus disease 2019: a systematic review and meta-analysis

Rheumatology 2021

Fotios Barkas, MD, MSc, PhD, Sebastian Filippas Ntekouan, MD, Maria Kosmidou, MD, PhD, Evangelos Liberopoulos, MD, PhD, Angelos Lontos, MD, Haralampos Milionis, MD, PhD*



Anakinra reduce el riesgo de ventilación mecánica y la mortalidad en pacientes con COVID-19 moderada y grave

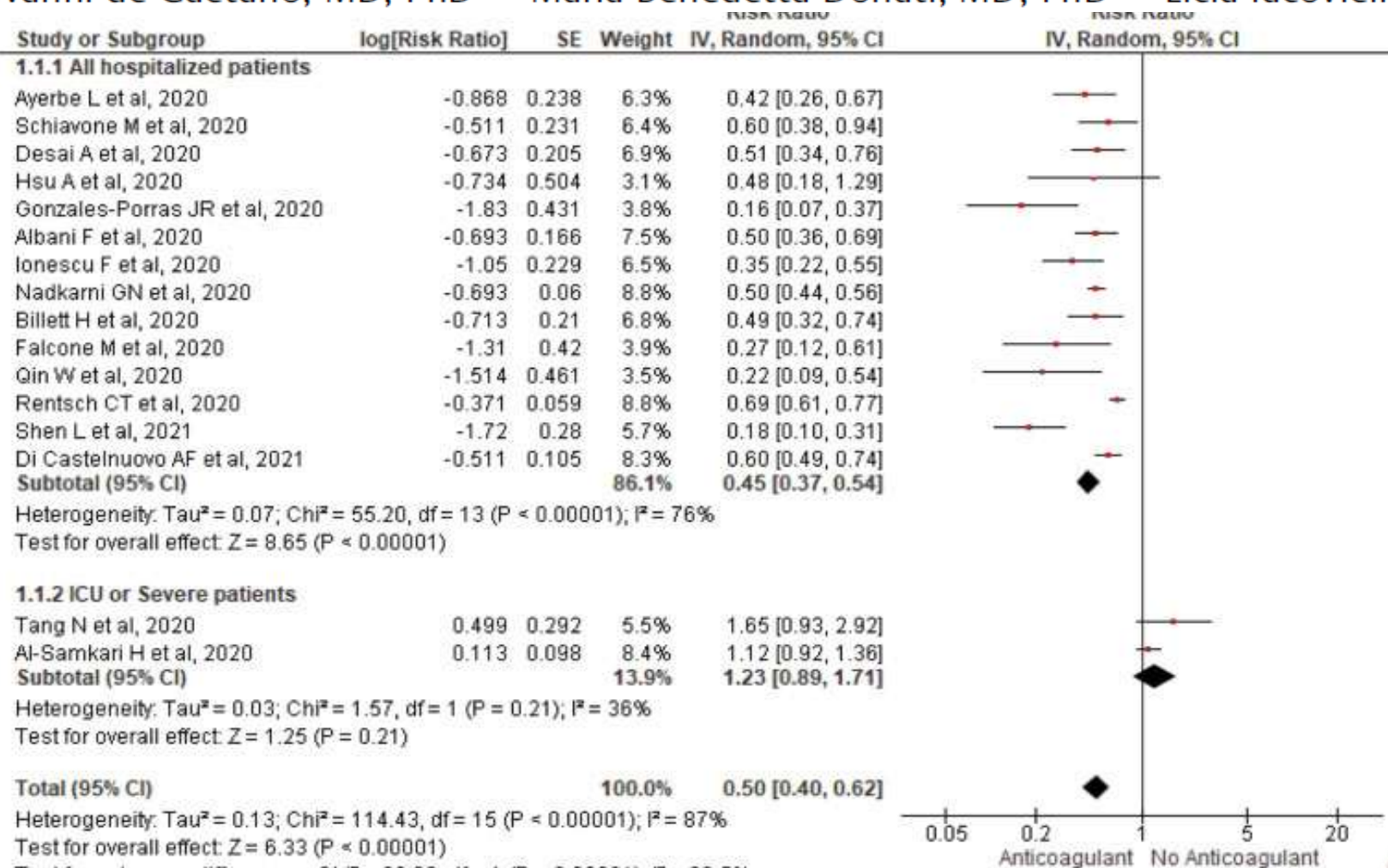


Different Anticoagulant Regimens, Mortality, and Bleeding in Hospitalized Patients with COVID-19: A Systematic Review and an Updated Meta-Analysis

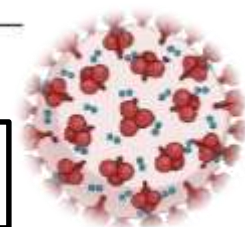
Semin Thromb Hemost 2021;47:372–391.

Roberta Parisi, MSc¹ Simona Costanzo, PhD¹ Augusto Di Castelnuovo, PhD²

Giovanni de Gaetano, MD, PhD¹ Maria Benedetta Donati, MD, PhD¹ Licia Iacoviello, MD, PhD



Anticoagulación reduce mortalidad en pacientes con neumonía COVID-19

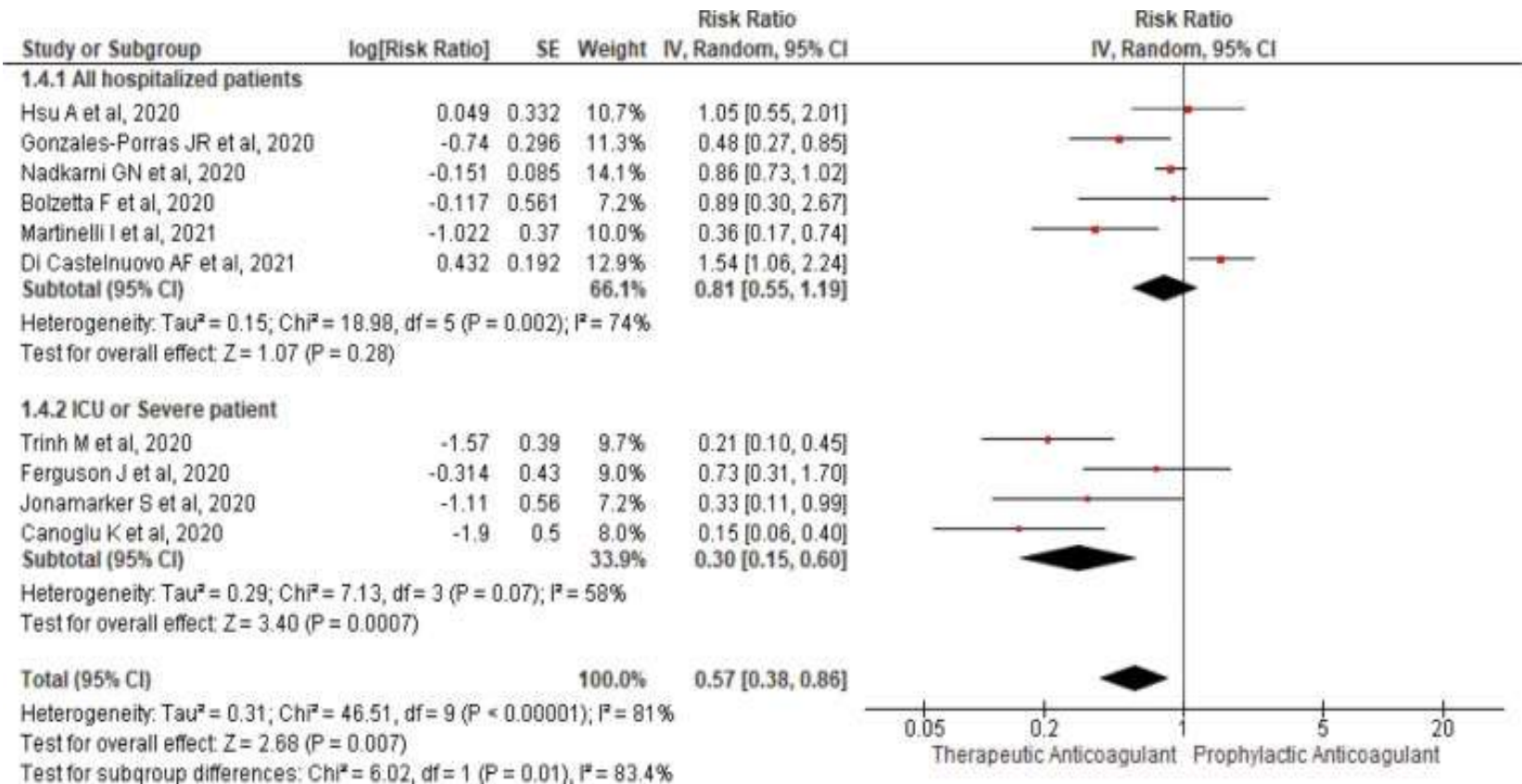


Different Anticoagulant Regimens, Mortality, and Bleeding in Hospitalized Patients with COVID-19: A Systematic Review and an Updated Meta-Analysis

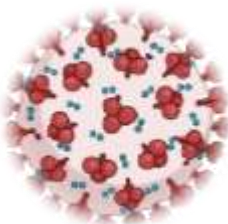
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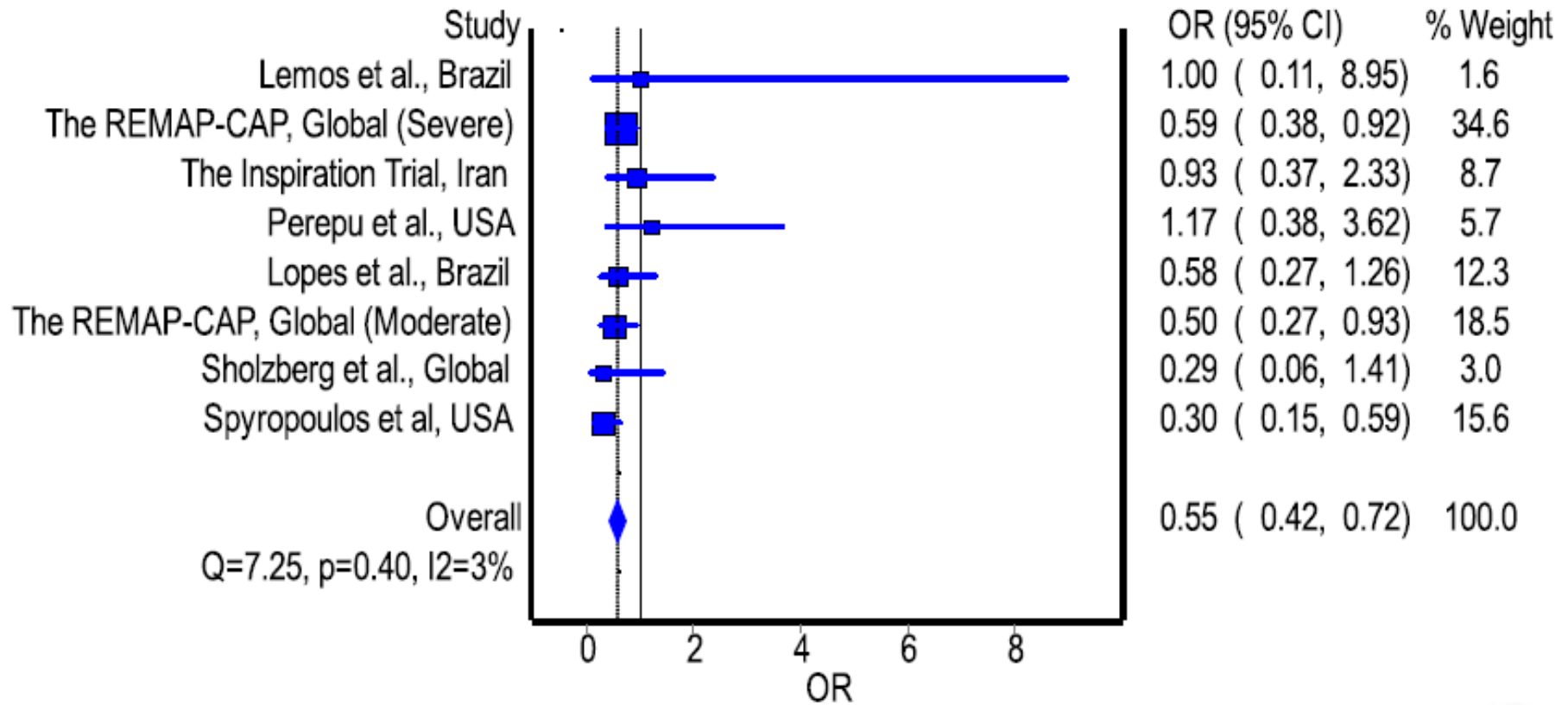
Anticoagulación terapéutica > Anticoagulación profiláctica para reducir mortalidad en pacientes con neumonía COVID-19



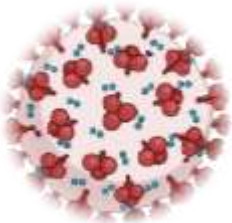
The effect of higher-intensity dosing of anticoagulation on the clinical outcomes in hospitalized patients with COVID-19: A meta-analysis of randomized controlled trials

Journal of Infection and Chemotherapy 28 (2022) 257–265

Chia Siang Kow^{a,b,*}, Dinesh Sangarran Ramachandram^b, Syed Shahzad Hasan



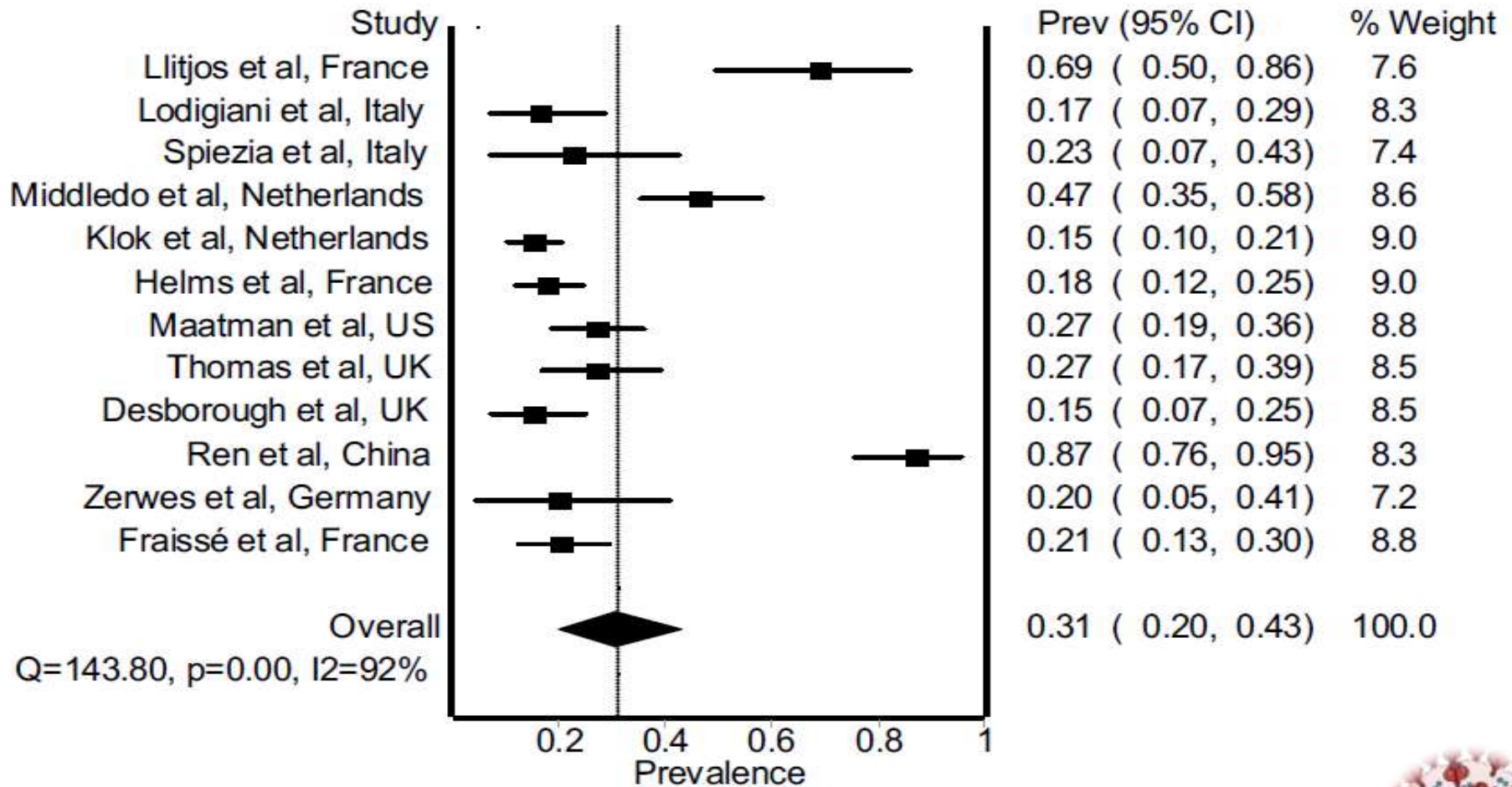
Anticoagulación intermedia/terapéutica > Anticoagulación profiláctica para reducir eventos trombóticos en pacientes con neumonía COVID-19



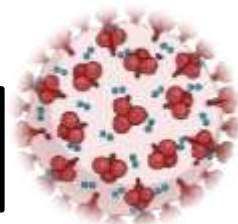
Venous thromboembolism in critically ill COVID-19 patients receiving prophylactic or therapeutic anticoagulation: a systematic review and meta-analysis

Journal of Thrombosis and Thrombolysis (2020) 50:814–821

Syed Shahzad Hasan¹  · Sam Radford^{2,3} · Chia Siang Kow⁴ · Syed Tabish Razi Zaidi^{5,6}



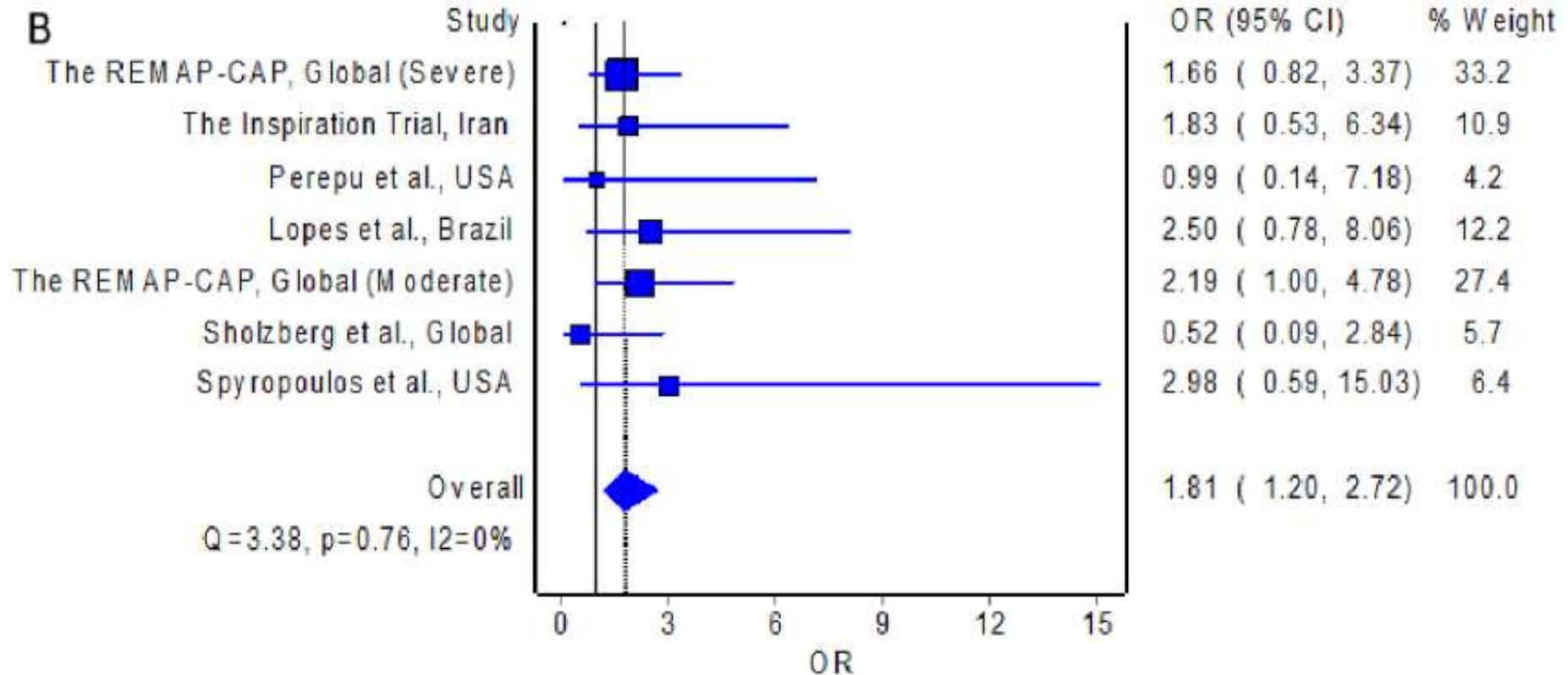
Alta prevalencia de TEP en pacientes graves y críticos con anticoagulación terapéutica



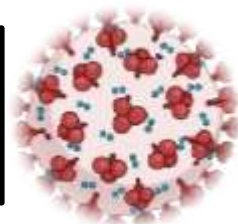
The effect of higher-intensity dosing of anticoagulation on the clinical outcomes in hospitalized patients with COVID-19: A meta-analysis of randomized controlled trials

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Chia Siang Kow^{a,b,*}, Dinesh Sangarran Ramachandram^b, Syed Shahzad Hasan



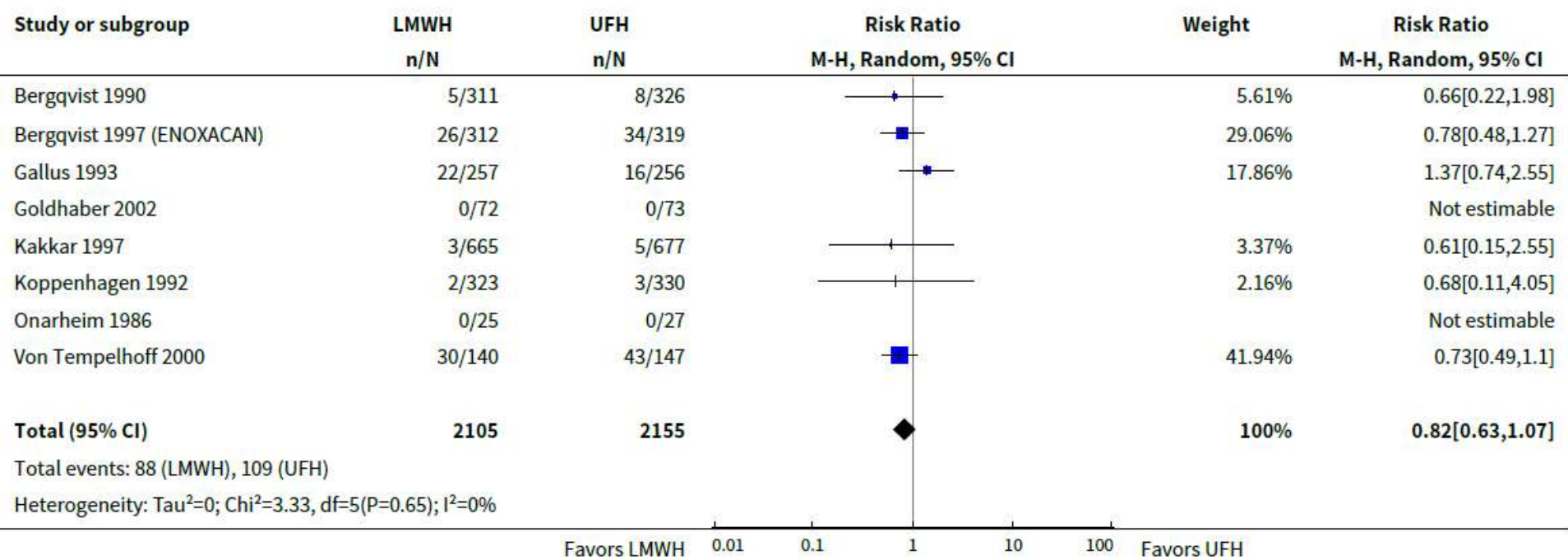
Anticoagulación intermedia/terapéutica incrementa riesgo de sangrado comparado con Anticoagulación profiláctica en pacientes con neumonía COVID-19 → **Tratamiento personalizado basado en el diagnóstico**



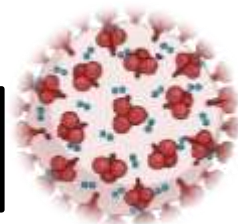
Anticoagulation for perioperative thromboprophylaxis in people with cancer (Review)

Matar CF, Kahale LA, Hakoum MB, Tsolakian IG, Etxeandia-Ikobaltzeta I, Yosucio VED, Terrenato I, Sperati F, Barba M, Schünemann H, Akl EA *Cochrane Database of Systematic Reviews* 2018, Issue 7. Art. No.: CD009447.

Analysis 1.1. Comparison 1 Low-molecular weight heparin (LMWH) versus unfractionated heparin (UFH), Outcome 1 All-cause mortality.



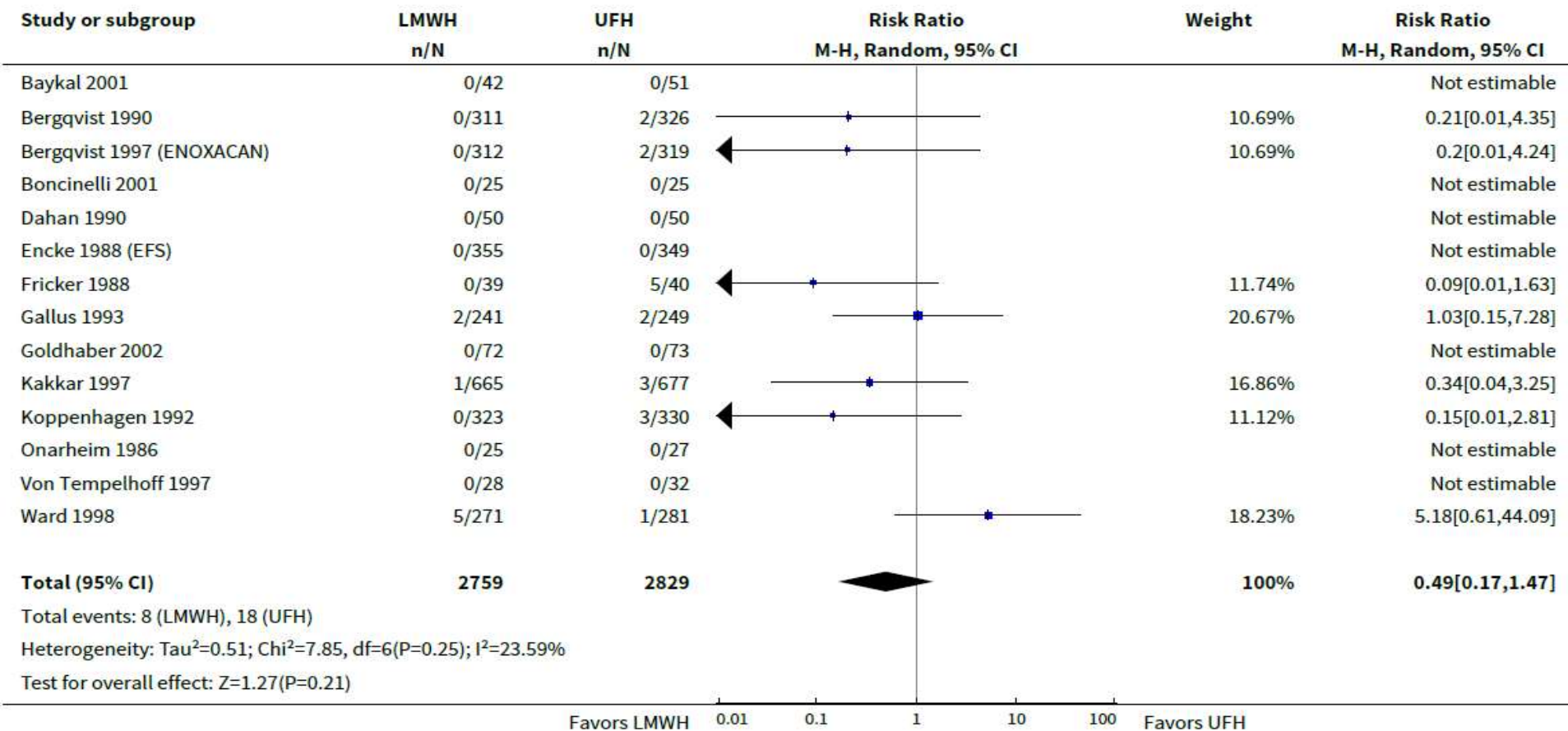
HBPM > Heparina no fraccionada: **Menor mortalidad**



Anticoagulation for perioperative thromboprophylaxis in people with cancer (Review)

Matar CF, Kahale LA, Hakoum MB, Tsolakian IG, Etxeandia-Ikobaltzeta I, Yosucio VED, Terrenato I, Sperati F, Barba M, Schünemann H, Akl EA *Cochrane Database of Systematic Reviews* 2018, Issue 7. Art. No.: CD009447.

Analysis 1.2. Comparison 1 Low-molecular weight heparin (LMWH) versus unfractionated heparin (UFH), Outcome 2 Pulmonary embolism (PE).



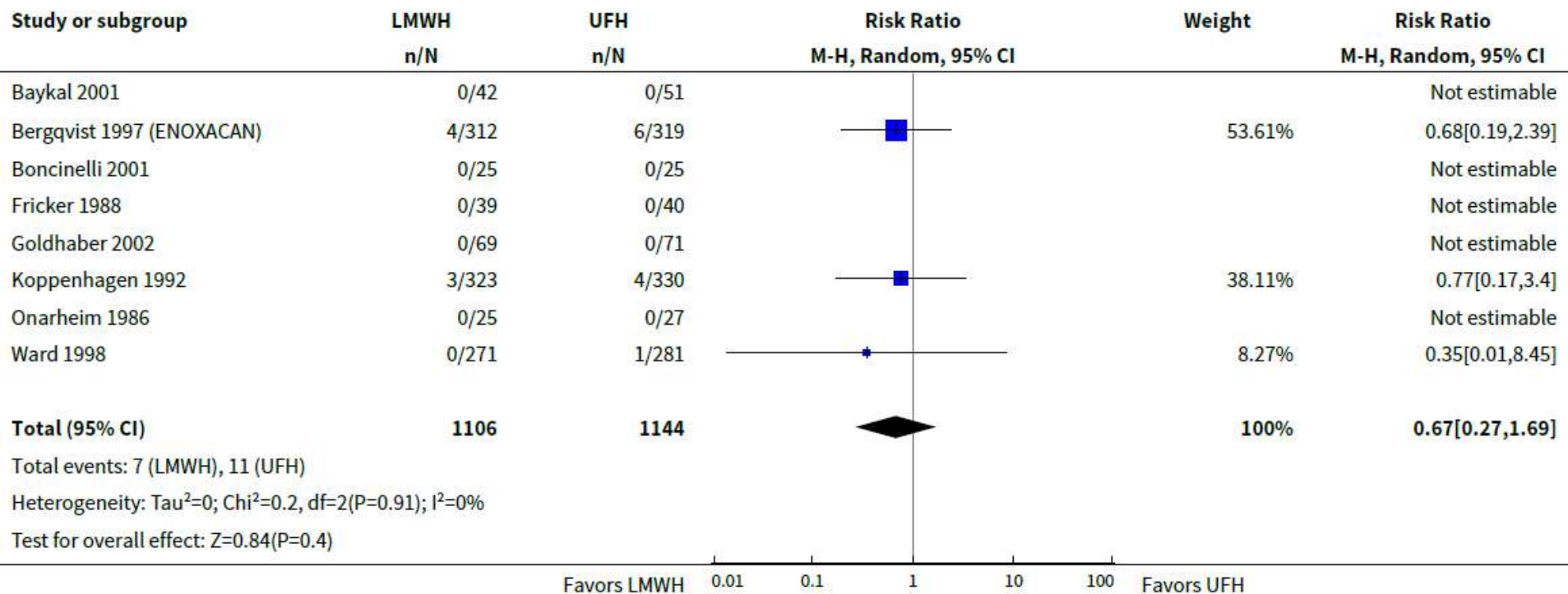
HBPM > Heparina no fraccionada: **Menor TEP**



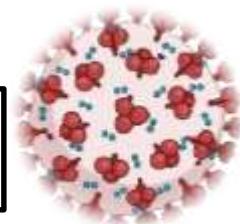
Anticoagulation for perioperative thromboprophylaxis in people with cancer (Review)

Matar CF, Kahale LA, Hakoum MB, Tsolakian IG, Etxeandia-Ikobaltzeta I, Yosucio VED, Terrenato I, Sperati F, Barba M, Schünemann H, Akl EA *Cochrane Database of Systematic Reviews* 2018, Issue 7. Art. No.: CD009447.

Analysis 1.3. Comparison 1 Low-molecular weight heparin (LMWH) versus unfractionated heparin (UFH), Outcome 3 Symptomatic deep venous thrombosis (DVT).



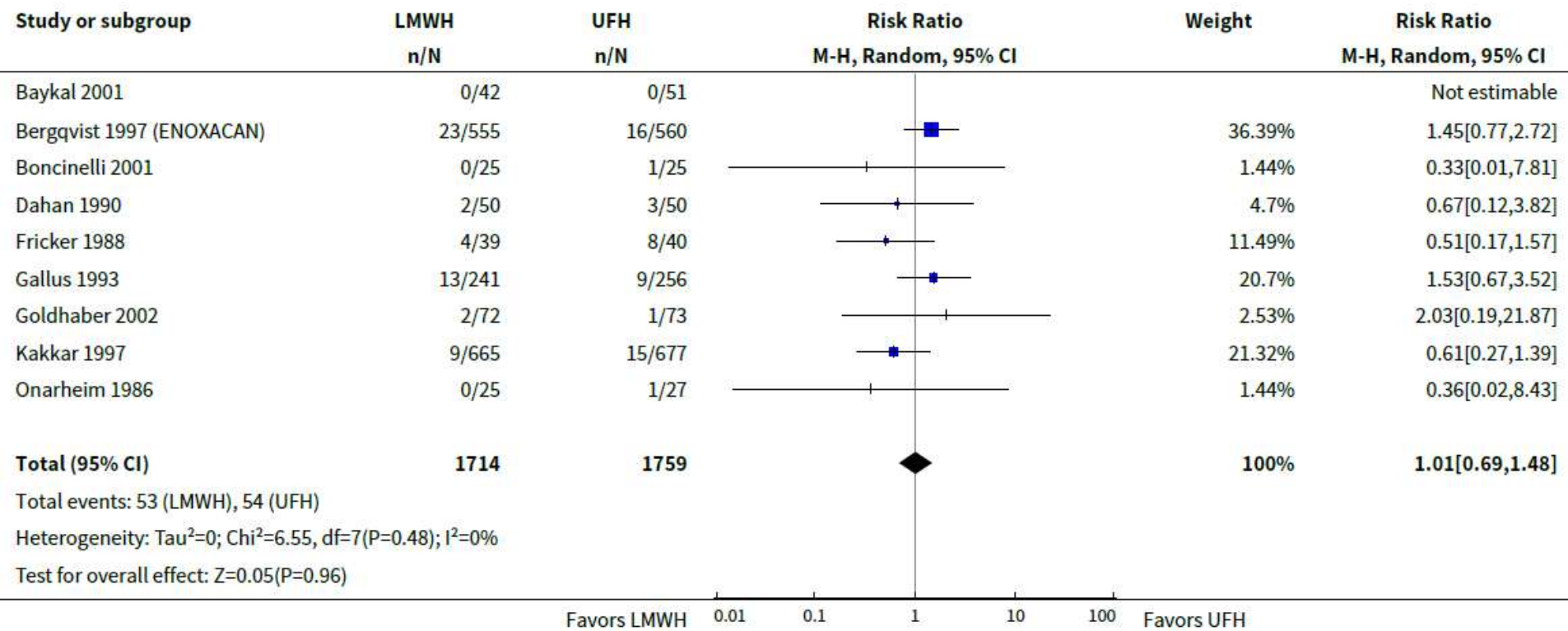
HBPM > Heparina no fraccionada: **Menor TVP**



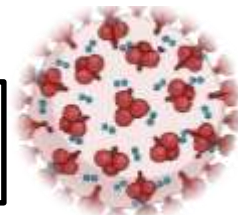
Anticoagulation for perioperative thromboprophylaxis in people with cancer (Review)

Matar CF, Kahale LA, Hakoum MB, Tsolakian IG, Etxeandia-Ikobaltzeta I, Yosucio VED, Terrenato I, Sperati F, Barba M, Schünemann H, Akl EA *Cochrane Database of Systematic Reviews* 2018, Issue 7. Art. No.: CD009447.

Analysis 1.5. Comparison 1 Low-molecular weight heparin (LMWH) versus unfractionated heparin (UFH), Outcome 5 Major bleeding.



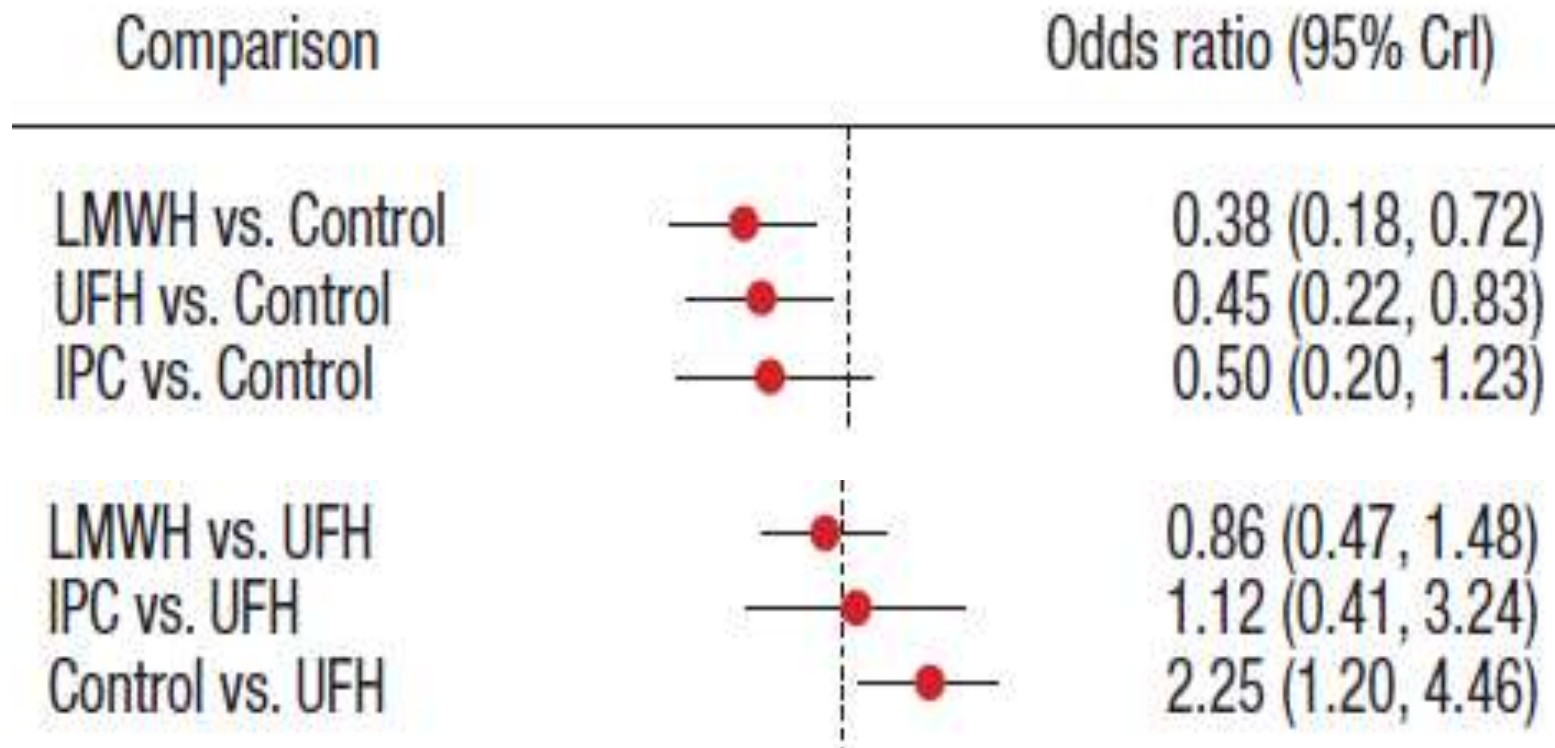
HBPM > Heparina no fraccionada: **Igual riesgo de sangrado**



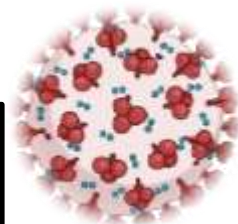
Pharmacological and Mechanical Thromboprophylaxis in Critically Ill Patients: a Network Meta-Analysis of 12 Trials

Jonghane Park,^{1*} Joo Myung Lee,^{2*}
Jeong Seok Lee,³ and Young-Jae Cho⁴

J Korean Med Sci 2016; 31: 1828-1837



HBPM > Heparina no fraccionada como tromboprolifaxis en el pacientes críticos



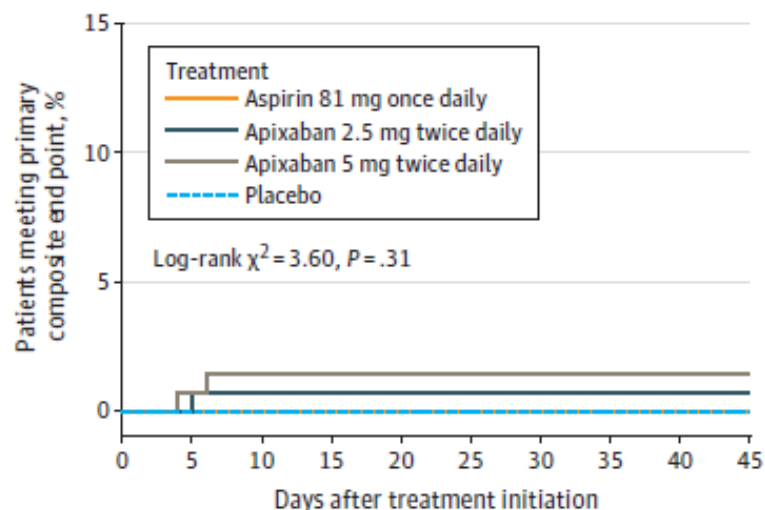
Effect of Antithrombotic Therapy on Clinical Outcomes in Outpatients With Clinically Stable Symptomatic COVID-19

The ACTIV-4B Randomized Clinical Trial

JAMA November 2, 2021 Volume 326, Number 17

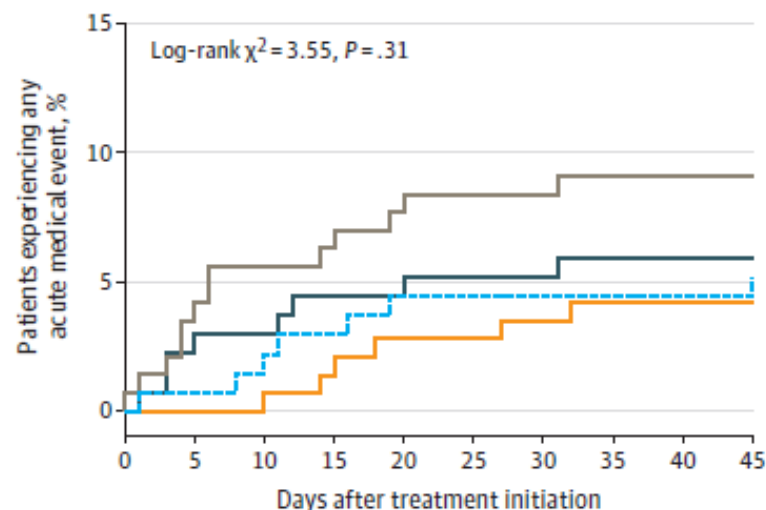
Jean M. Connors, MD; Maria M. Brooks, PhD; Frank C. Sciurba, MD; Jerry A. Krishnan, MD; Joseph R. Bledsoe, MD; Andrei Kindzelski, MD;

A Cumulative incidence of adjudicated primary end point



No. at risk	0	5	10	15	20	25	30	35	40	45
Aspirin 81 mg	144	144	144	144	144	144	144	144	143	140
Apixaban 2.5 mg	135	135	134	134	134	134	134	134	133	132
Apixaban 5.0 mg	143	142	141	141	141	141	140	140	140	137
Placebo	136	136	136	136	136	136	136	136	135	132

B Cumulative incidence of any acute medical event

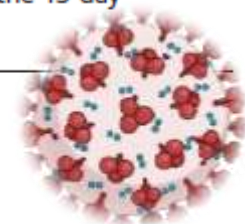


No. at risk	0	5	10	15	20	25	30	35	40	45
Aspirin 81 mg	144	144	144	142	140	140	139	138	137	134
Apixaban 2.5 mg	135	132	131	129	129	128	128	127	126	125
Apixaban 5.0 mg	143	138	135	134	132	131	130	129	129	126
Placebo	136	135	134	132	130	130	130	130	129	126

The primary end point is defined as the composite of all-cause mortality, symptomatic venous or arterial thromboembolism, myocardial infarction, stroke, or hospitalization for cardiovascular or pulmonary cause. The end point

of any acute medical event is inclusive of all emergency department visits, all acute outpatient clinic visits, and all hospitalizations during the 45-day follow-up period, regardless of etiology.

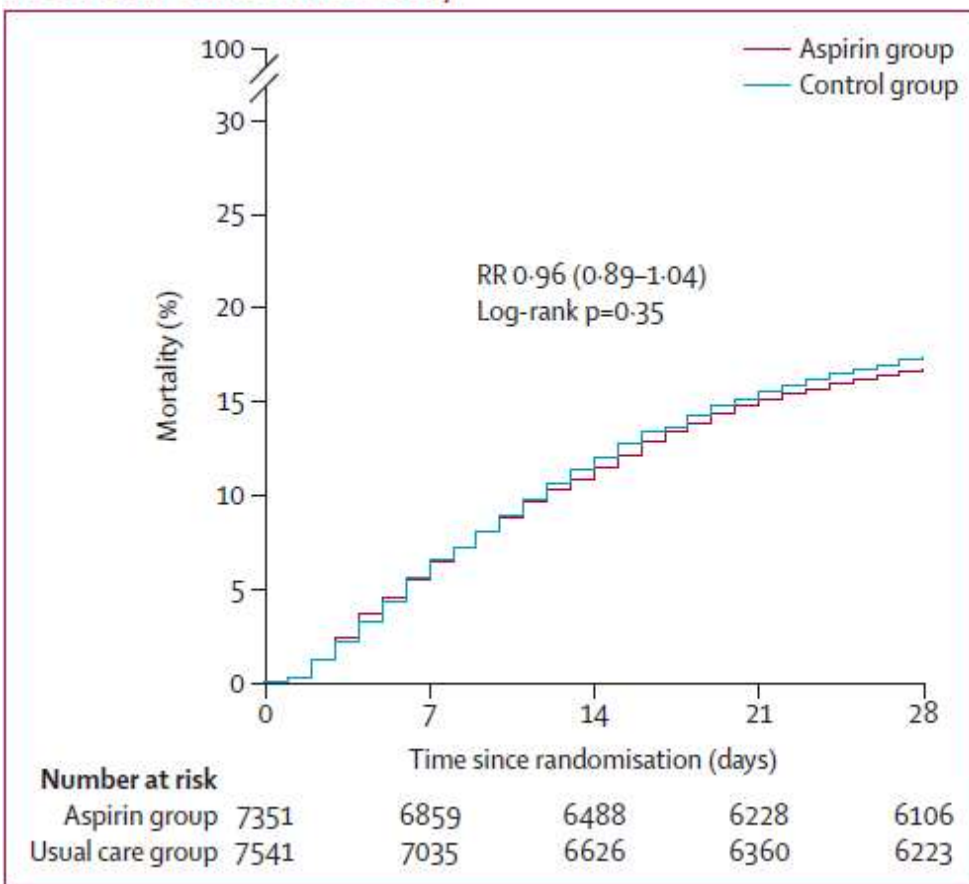
La aspirina y los NACO no son eficaces en pacientes con COVID-19 atendidos en la comunidad



Aspirin in patients admitted to hospital with COVID-19 (RECOVERY): a randomised, controlled, open-label, platform trial

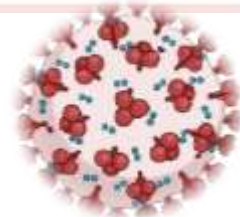
www.thelancet.com Published online November 17, 2021

RECOVERY Collaborative Group*

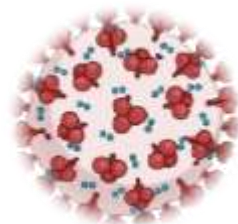


	Treatment allocation		RR (95% CI)	p value
	Aspirin (n=7351)	Usual care (n=7541)		
Primary outcome				
28 day mortality	1222 (17%)	1299 (17%)	0.96 (0.89-1.04)	0.35
Secondary outcomes				
Median time to being discharged alive (IQR), days	8 (5 to >28)	9 (5 to >28)
Discharged from hospital within 28 days	5496 (75%)	5548 (74%)	1.06 (1.02-1.10)	0.0062
Receipt of invasive mechanical ventilation or death*	1473/6993 (21%)	1569/7169 (22%)	0.96 (0.90-1.03)	0.23
Invasive mechanical ventilation	772/6993 (11%)	829/7169 (12%)	0.95 (0.87-1.05)	0.32
Death	1076/6993 (15%)	1141/7169 (16%)	0.97 (0.90-1.04)	0.39
Subsidiary clinical outcomes				
Use of ventilation	1131/4936 (23%)	1198/5036 (24%)	0.96 (0.90-1.03)	0.30
Non-invasive ventilation	1101/4936 (22%)	1162/5036 (23%)	0.97 (0.90-1.04)	0.36
Invasive mechanical ventilation	296/4936 (6%)	325/5036 (6%)	0.93 (0.80-1.08)	0.35
Successful cessation of invasive mechanical ventilation	135/358 (38%)	135/372 (36%)	1.08 (0.85-1.37)	0.54
Renal replacement therapy	273/7291 (4%)	282/7480 (4%)	0.99 (0.84-1.17)	0.93

La aspirina no es eficaz en pacientes hospitalizados por COVID-19



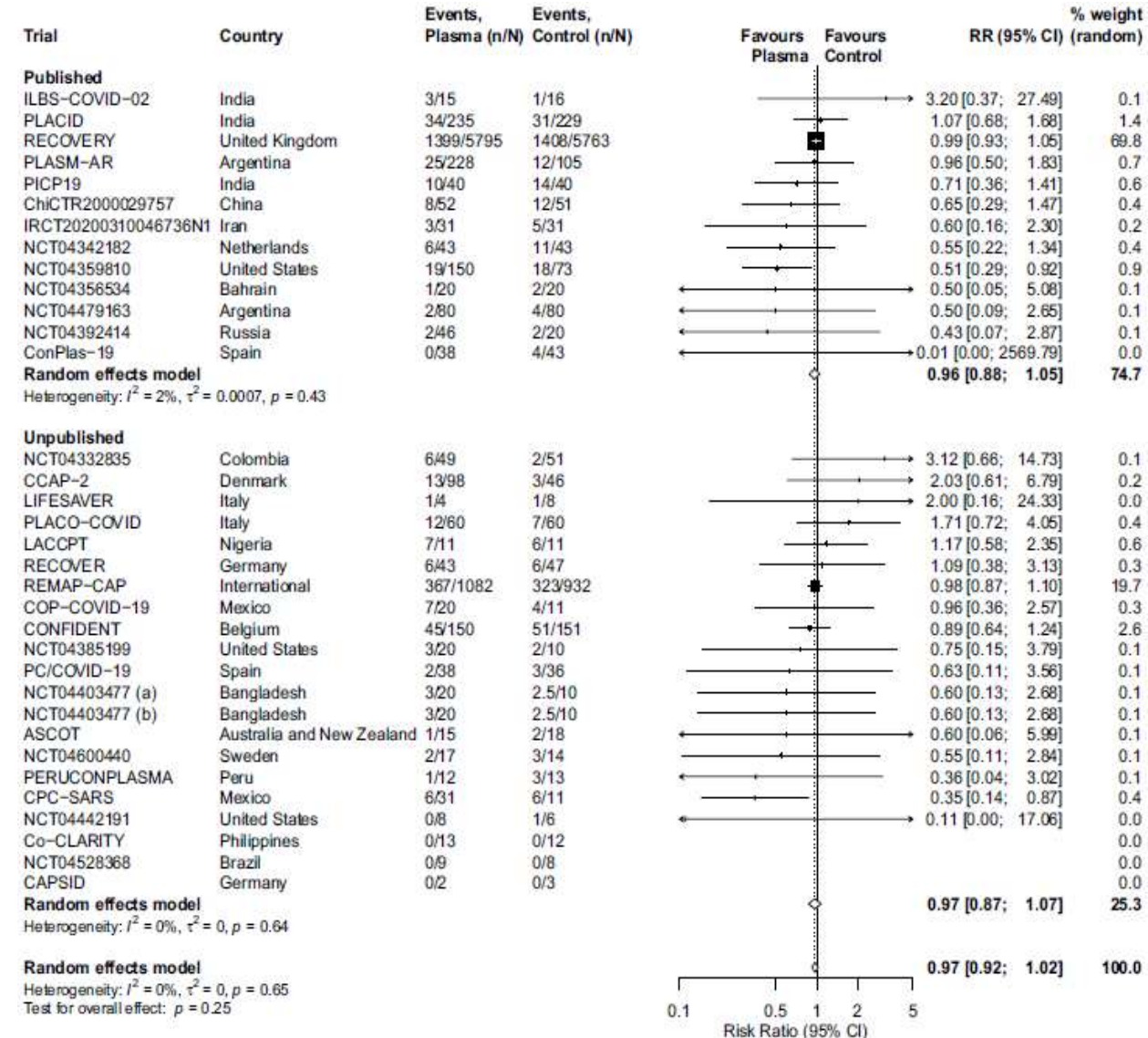
PLASMA DE CONVALECIENTES



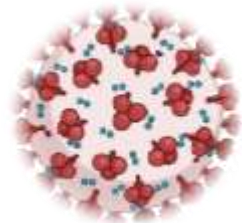
Association between convalescent plasma treatment and mortality in COVID-19: a collaborative systematic review and meta-analysis of randomized clinical trials

BMC Infectious Diseases (2021) 21:1

Cathrine Axfors^{1,2}, Perrine Janiaud^{3†}, Andreas M. Schmitt^{3,4}, Janneke van't Hooft⁵, Emily R. Smith⁶,



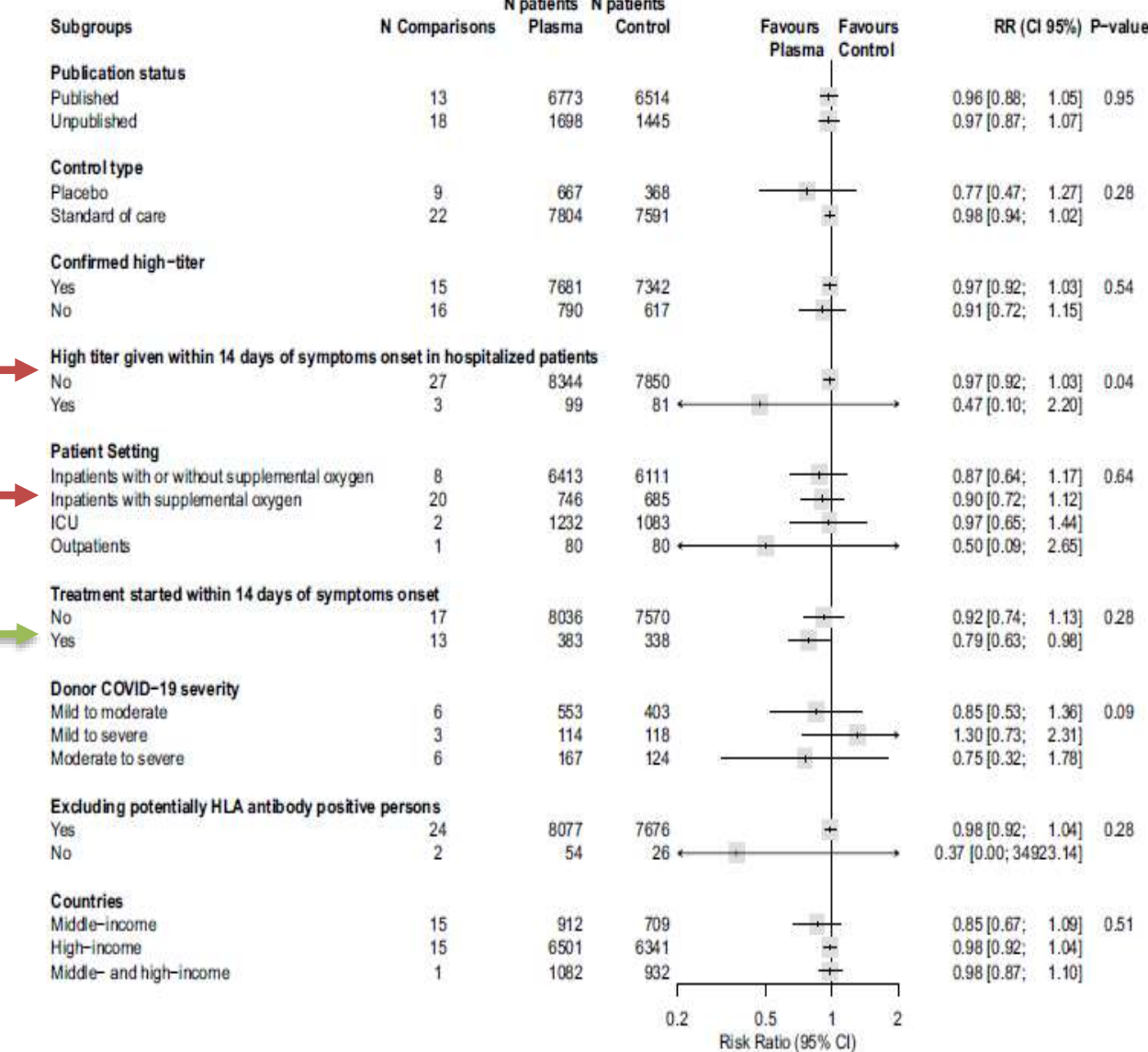
El tratamiento con plasma de convalecientes no reduce la mortalidad en pacientes con COVID-19



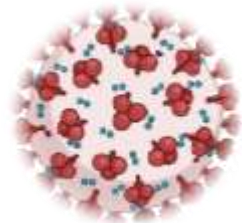
Association between convalescent plasma treatment and mortality in COVID-19: a collaborative systematic review and meta-analysis of randomized clinical trials

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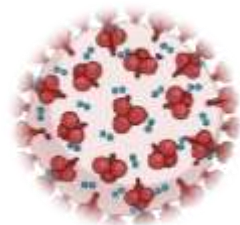
Cathrine Axfors^{1,2}, Perrine Janiaud^{3,4}, Andreas M. Schmitt^{3,4}, Janneke van't Hooft⁵, Emily R. Smith⁶,



El efecto poco beneficioso del plasma de convalecientes se mantiene en todos los subgrupos de pacientes con COVID-19



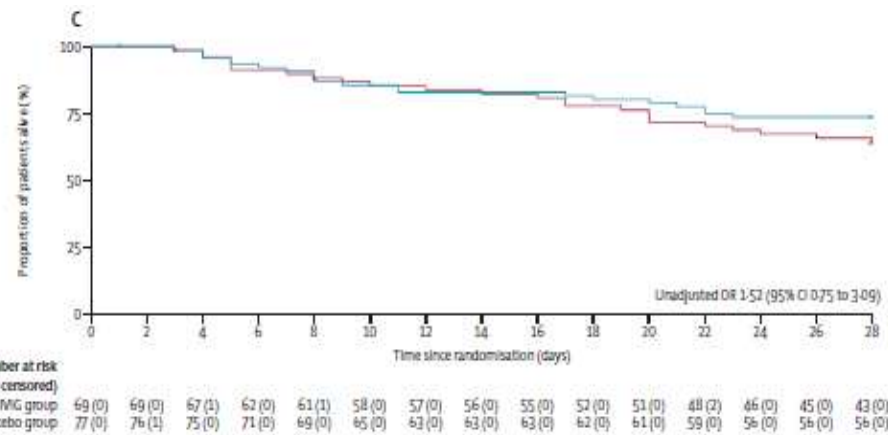
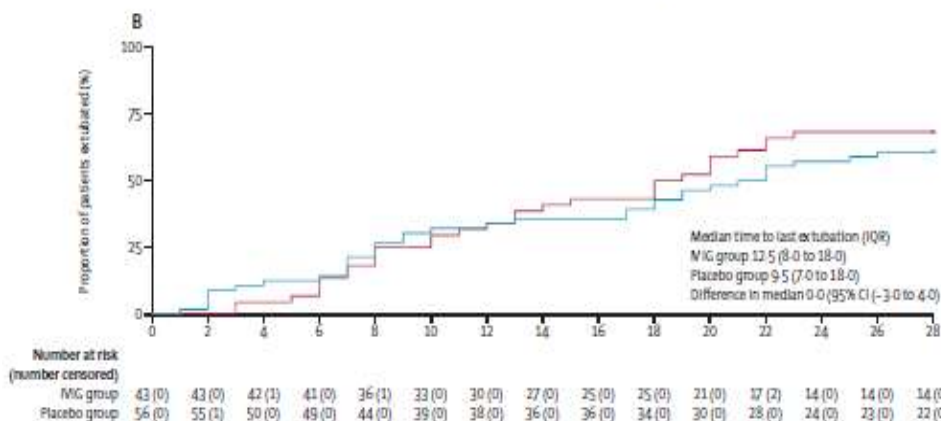
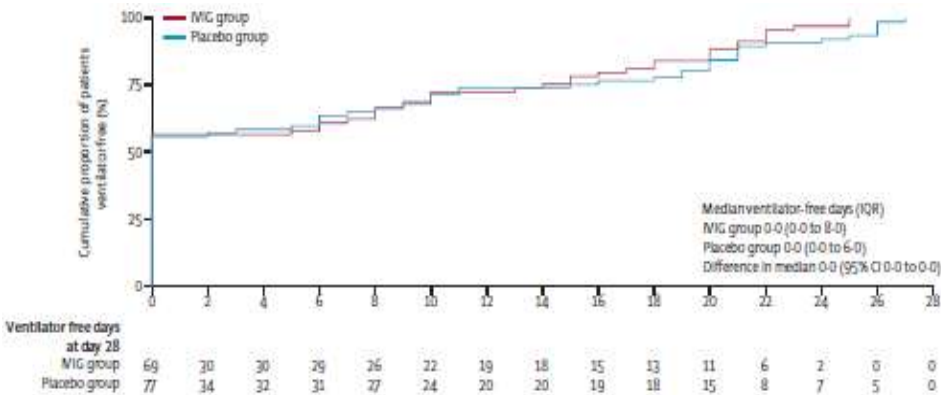
INMUNOGLOBULINA ENDOVENOSA



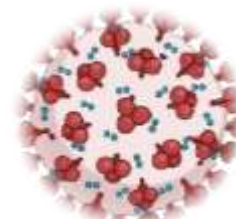
Intravenous immunoglobulins in patients with COVID-19-associated moderate-to-severe acute respiratory distress syndrome (ICAR): multicentre, double-blind, placebo-controlled, phase 3 trial

Lancet Respir Med 2021

Aurélien Mazeraud, Matthieu Jamme*, Rossella Letizia Mancusi*, Claire Latroche*, Bruno Megarbane, Shidasp Siami, Jonathan Zarka,

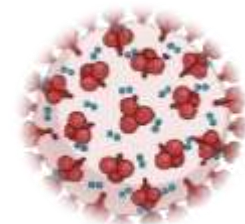


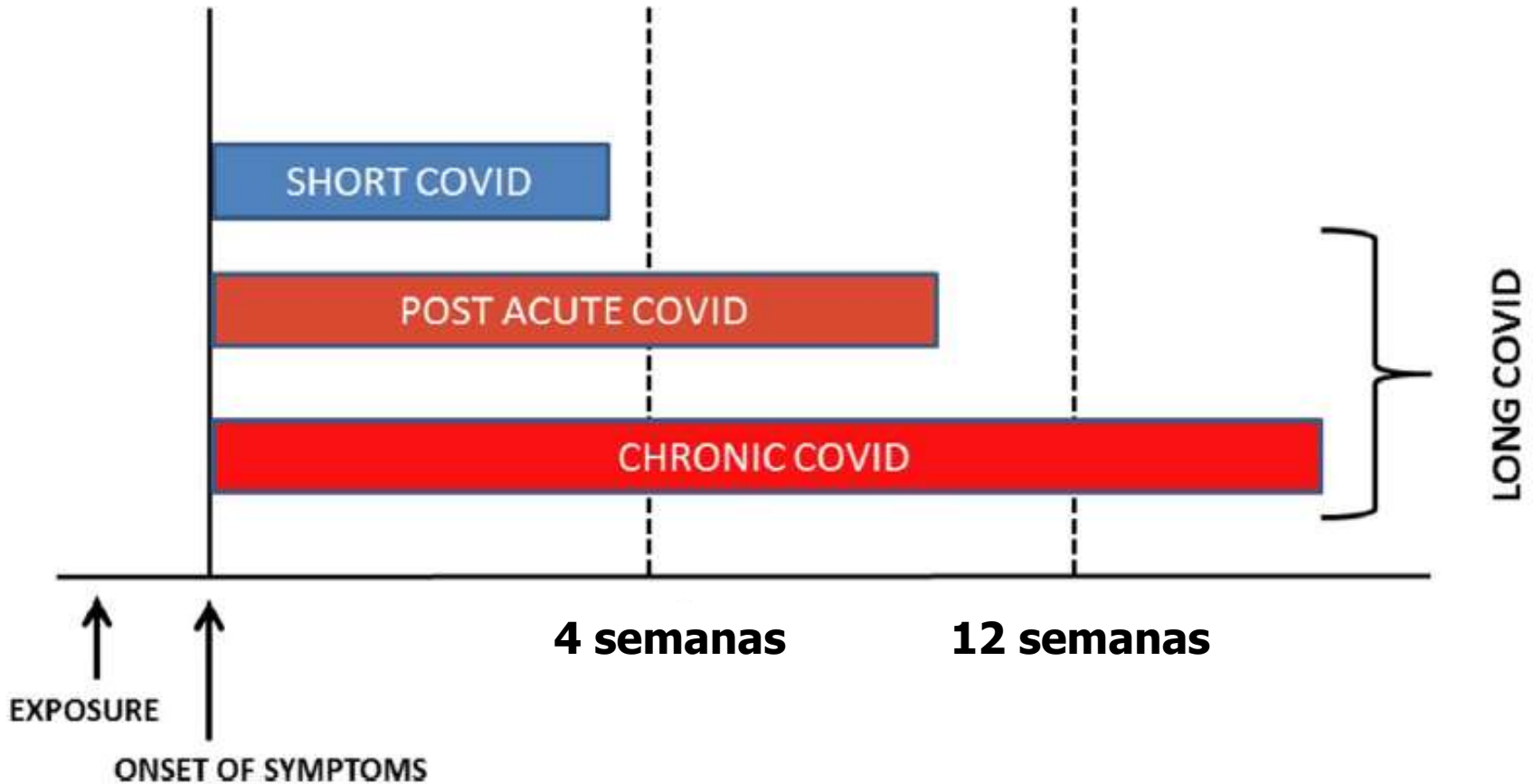
La Ig IV no es eficaz en pacientes críticos por COVID-19 y puede asociarse a eventos adversos





SÍNDROME DE COVID-19 PROLONGADO

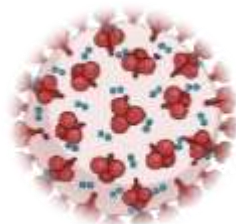


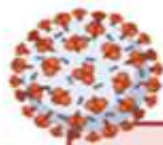


Long COVID: An overview

Diabetes & Metabolic Syndrome: Clinical Research & Reviews 15 (2021) 869–875

A.V. Raveendran ^{a, b, *}, Rajeev Jayadevan ^c, S. Sashidharan





POST-COVID-19 SYNDROME

Estimated time to resolution

6-12 weeks

8-12 weeks

¿?

PSYCHOLOGICAL

- Depression and anxiety
- Post-traumatic stress

NEUROLOGICAL

- Cognitive impairment
- Headache
- Taste and smell alterations
- Post-traumatic stress
- Sleep disturbances
- Peripheral neuropathy
- Dizziness
- Delirium

CARDIOVASCULAR

- Chest tightness
- Palpitations
- Orthostatic hypotension
- Syncope
- Dysautonomia

RESPIRATORY

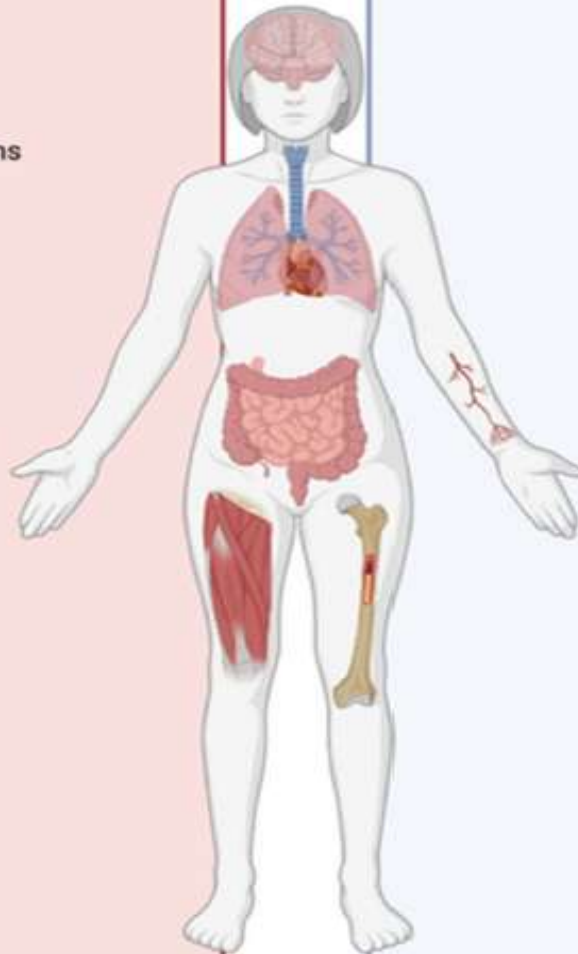
- Dyspnea
- Chest pain
- Cough

MUSCULOSKELETAL

- Fatigue
- Weakness
- Osteoarticular pain
- Muscular pain

OTHERS

- Abdominal pain
- Nausea
- Diarrhoea
- Anorexia



POTENTIAL BENEFITS OF EXERCISE

PSYCHOLOGICAL

- Modulates pain
- ↑ Well-being and mood state
- ↓ Stress

NEUROLOGICAL

- Stimulates brain plasticity
- ↑ Neurocognitive abilities
- ↓ Cognitive dysfunction
- ↓ Allostatic overload
- ↑ Sleep quality

CARDIOVASCULAR

- ↑ Mitochondrial biogenesis
- ↑ Vasculature
- ↑ Cardiovascular function
- ↓ Blood pressure
- Normalizes dysautonomia

RESPIRATORY

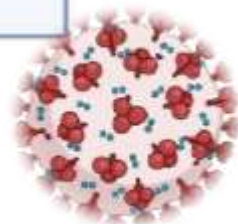
- ↓ Dyspnea
- ↑ Oxygen uptake
- ↑ Pulmonary function
- ↑ Oxidative stress

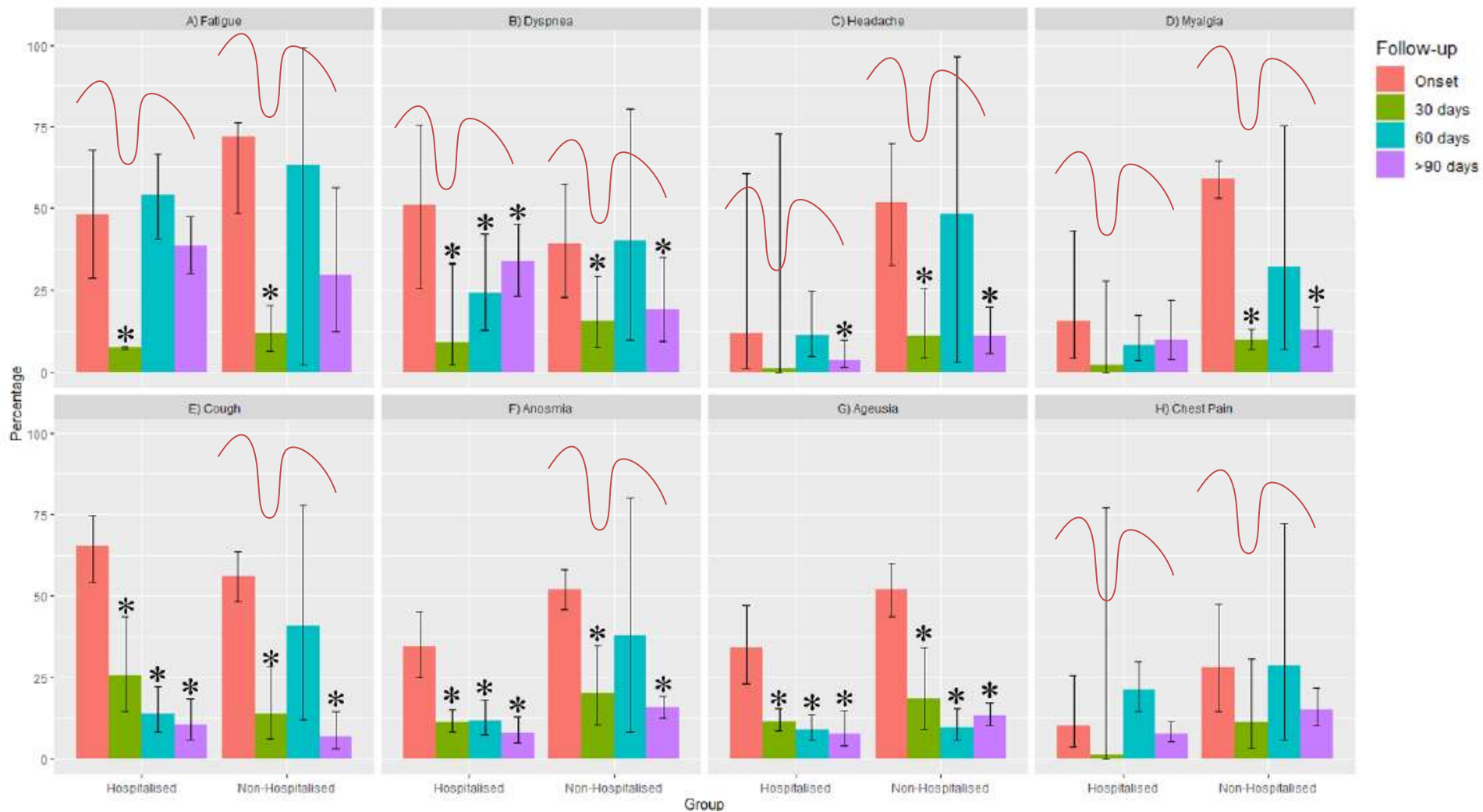
MUSCULOSKELETAL

- ↑ Muscle mass
- ↑ Muscle strength
- ↑ Intermuscular coordination
- ↑ Tolerance to exercise

IMMUNE SYSTEM

- ↑ Immune function
- ↑ Anti-inflammatory cytokines
- ↓ Pro-inflammatory cytokines
- ↓ Immunosenescence

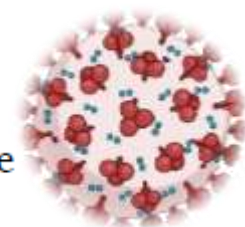




Prevalence of post-COVID-19 symptoms in hospitalized and non-hospitalized COVID-19 survivors: A systematic review and meta-analysis

European Journal of Internal Medicine 92 (2021) 55–70

César Fernández-de-las-Peñas^{a,*}, Domingo Palacios-Ceña^a, Víctor Gómez-Mayordomo^b, Lidiane L Florencio^a, María L. Cuadrado^{b,c}, Gustavo Plaza-Manzano^{d,e}, Marcos Navarro-Santana^d



Tipo 1

- Síntomas con un tiempo de recuperación y rehabilitación variable, relacionados con la severidad de la infección, el daño de órganos y la condición médica pre-existente al momento de ocurrencia de la infección

Tipo 2

- Síntomas persistentes \geq 4-6 semanas desde el inicio de la infección

Tipo 3

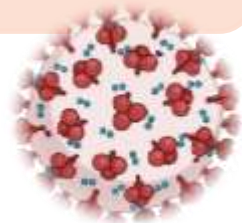
- Período de quiescencia o recuperación casi completa seguido de reaparición de síntomas que persisten \geq 3 meses (3A) o \geq 6 meses (3B)

Tipo 4

- Asintomático al momento del diagnóstico de COVID-19; pero aparición de síntomas después de 1-3 meses (4A) o \geq 3 meses (4B), de duración variable

Tipo 5

- Asintomático o enfermedad leve al momento del diagnóstico de COVID-19; pero muerte súbita dentro de los siguientes 12 meses



CATEGORÍAS DE SÍNDROMES DE COVID PROLONGADO

Síndrome de fatiga crónica

Síndrome cardio-respiratorio

Síndrome neuro-psiquiátrico

Síndrome gastrointestinal

Síndrome hepato-biliar

Síndrome músculo-esquelético

Síndrome tromboembólico

Síndrome de inflamación multisistémica/ Síndrome autoinmune

Síndrome renal/ genito-urinario

Síndrome dermatológico

**Requiere
como mínimo**

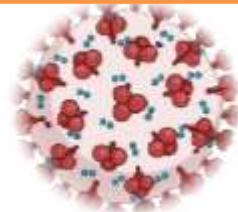
8

**especialidades
médicas**

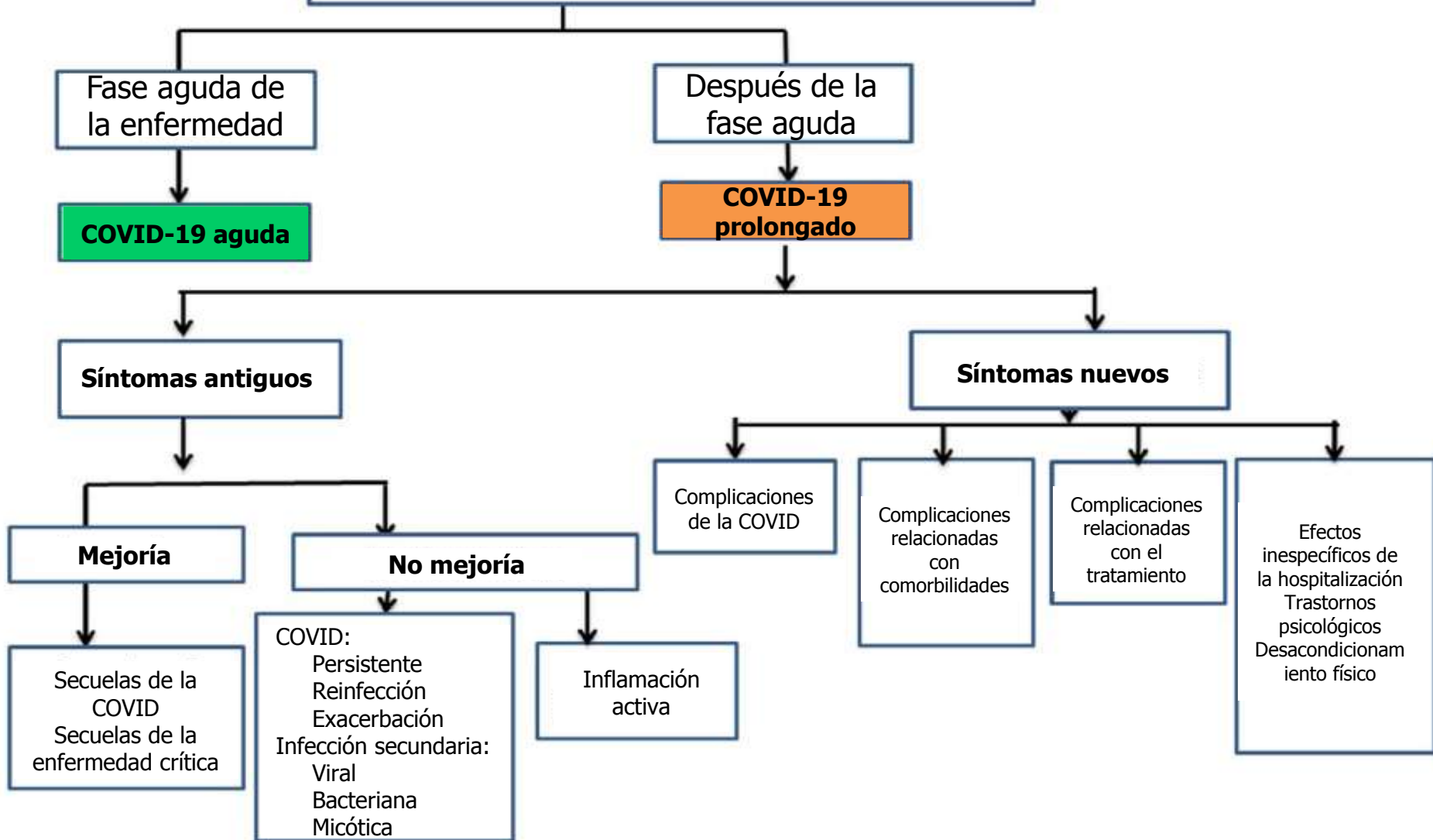
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SÍNTOMAS EN PACIENTES CON COVID-19



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