¿Qué está pasando? ¿Porqué todos los humanos llevan bozal?

Sesión bibliográfica

Medicina Interna

1 de abril de 2022

Alberto Morán

Junta de Castilla y León

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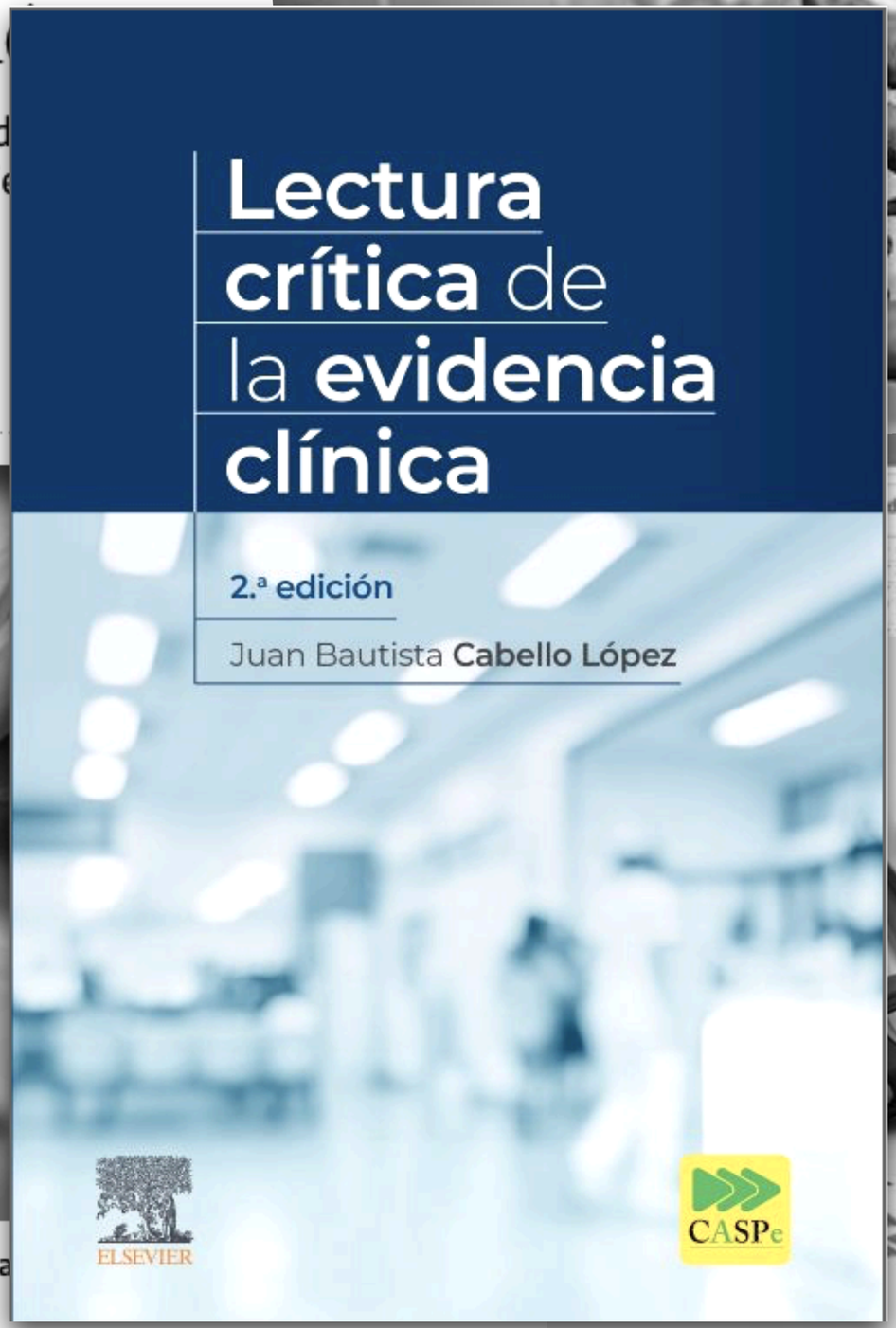
Ciencia ahora y despu

Las iniciativas internacionales en torno a la Covid
claramente la línea a seguir: la de una ciencia abie

La industria farmacéutica estima que no habrá vacuna pa
meses EFE



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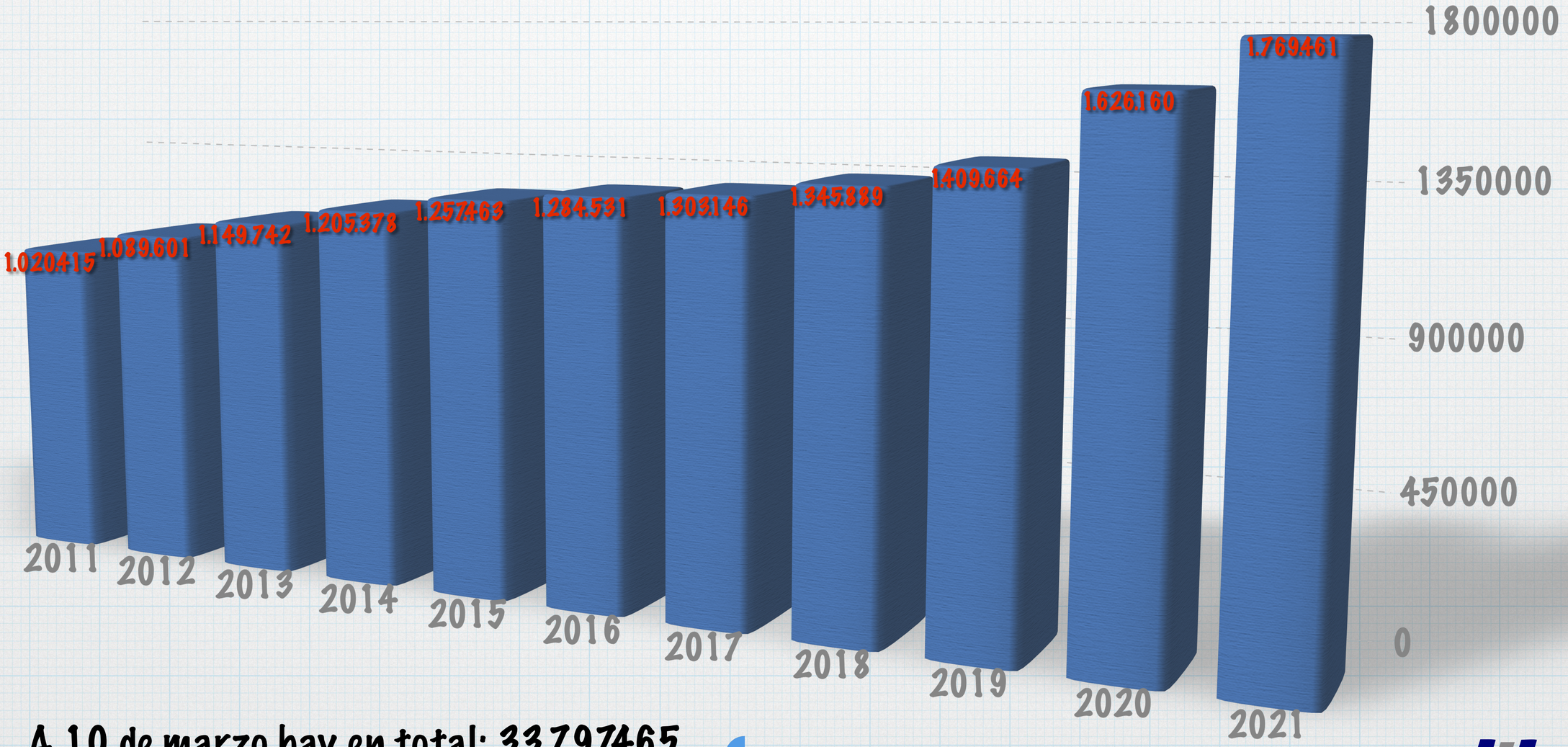

A 10 de marzo hay en total: 33.797.465

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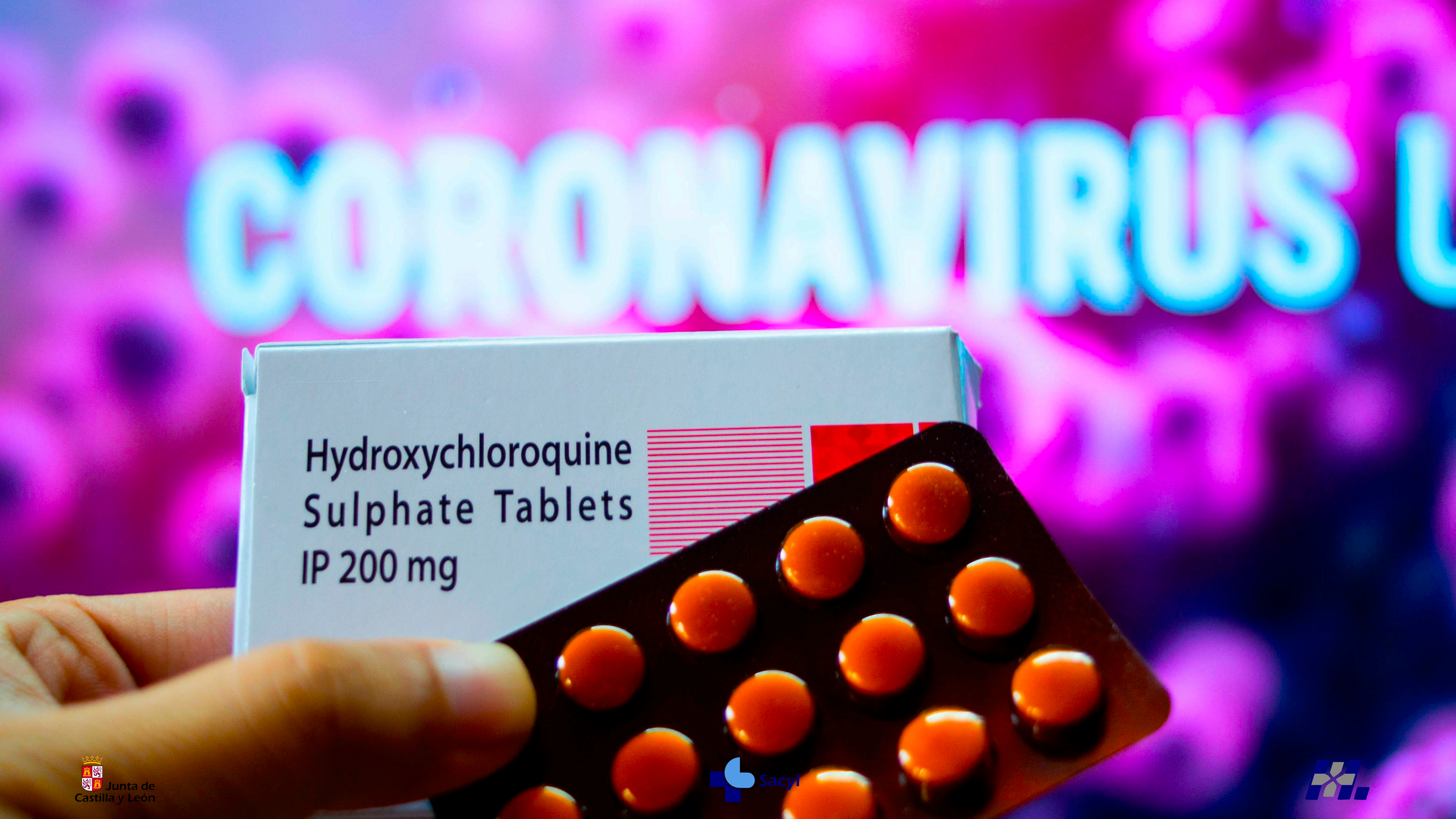

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Virology Journal

BioMed Central

Research

Open Access

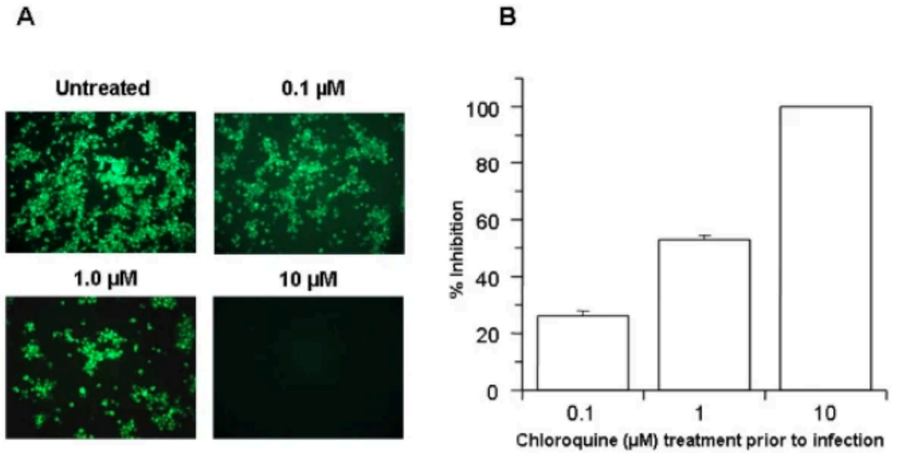
Chloroquine is a potent inhibitor of SARS coronavirus infection and spread

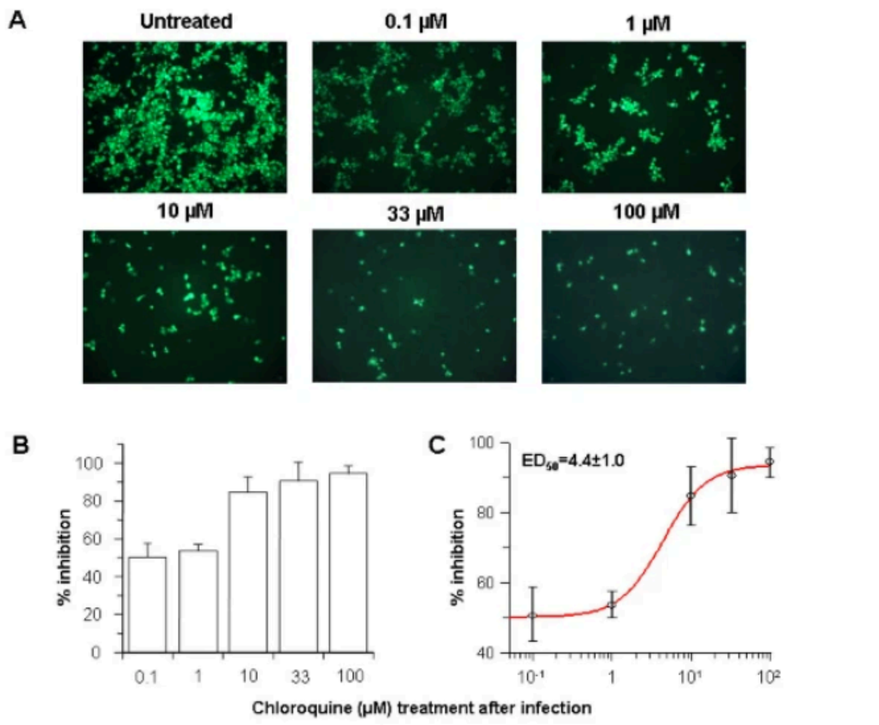
Martin J Vincent[1], Eric Bergeron[2], Suzanne Benjannet[2], Bobbie R Erickson[1], Pierre E Rollin[1], Thomas G Ksiazek[1], Nabil G Seidah[2] and Stuart T Nichol*[1]

Address: [1]Special Pathogens Brach, Division of Viral and Rickettsial Diseases, Centers for Disease Control and Prevention, 1600 Clifton Road, Atlanta, Georgia, 30333, USA and [2]Laboratory of Biochemical Neuroendocrinology, Clinical Research Institute of Montreal, 110 Pine Ave West, Montreal, QCH2W1R7, Canada

Virology Journal 2005, **2**:69

- No sigue la metodología convencional
- Se asumen probables efectos a distintos niveles
- Describen sus resultados:
  - Tto previo a la infección (se pretrataron células Vero E6 con varias concentraciones de cloroquina (0,1-10 µM) durante 20-24 h antes de la infección. Luego, se infectaron con SARS-CoV y los antígenos del virus se visualizaron mediante inmunofluorescencia indirecta.
  - Tto posterior a la infección ...
- Cloruro de amonio!





CONCLUSIONES: ... The fact that the drug has significant inhibitory antiviral effect when the susceptible cells were treated either prior to or after infection suggests a **possible prophylactic and therapeutic use**...

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Llegan los primeros test fiables chinos de coronavirus

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Contents lists available at ScienceDirect

International Journal of Antimicrobial Agents

journal homepage: www.elsevier.com/locate/ijantimicag

Hydroxychloroquine and azithromycin as a treatment of COVID-19: results of an open-label non-randomized clinical trial ☆

Philippe Gautret[a,b,$], Jean-Christophe Lagier[a,c,$], Philippe Parola[a,b], Van Thuan Hoang[a,b,d], Line Meddeb[a], Morgane Mailhe[a], Barbara Doudier[a], Johan Courjon[e,f,g], Valérie Giordanengo[h], Vera Esteves Vieira[a], Hervé Tissot Dupont[a,c], Stéphane Honoré[i,j], Philippe Colson[a,c], Eric Chabrière[a,c], Bernard La Scola[a,c], Jean-Marc Rolain[a,c], Philippe Brouqui[a,c], Didier Raoult[a,c,*]

International Journal of Antimicrobial Agents 56 (2020) 105949

- Criterios inclusión: >12 a y PCR + al ingreso (**índep. de la clínica**)
- Criterios exclusión: alergia a HQ o retinopatia, alarg QT o deficit G6PD. Embarazadas/lactancia
- **Ensayo clínico no randomizado, un brazo, abierto**: HQ: 600 mg/d (200x3, 10d). Los controles fueron los que rechazaron tto + Pac de otros hospitales (**sin enmascaramiento**)
- N=42.
  - 26 (todos neumonía por TAC) HQ (al final 20) y 16 controles. De los 20 con HQ **a 6 se les dio Az** (prevenir sobreinfec bact). Al final **20/16**

28% de perdidas

- Seguimiento 14 d
- Criterio principal: **PCR - al 6ºd**
- Criterios secundarios: PCR - durante el estudio, clínica (Tª, FR, estancia, muerte) y efectos secundarios
- **Análisis por protocolo** (6 perdidas -no finaliz tto-)
- Análisis estadístico: prueba chi-cuadrado de Pearson, la prueba exacta de Fisher, **prueba t de Student**.

Table 1
Characteristics of the study population.

	Age (years)			Male gender		Clinical status				Time between onset of symptoms and inclusion (days)		
	Mean ± SD	t	p-value	n (%)	p-value	Asymptomatic	URTI	LRTI	p-value	Mean ± SD	t	p-value
Hydroxychloroquine treated patients (N=20)	51.2 ± 18.7	-1.95	0.06	9 (45.0)	0.65	2 (10.0)	12 (60.0)	6 (30.0)	0.30	4.1 ± 2.6	-0.15	0.88
Control patients (N=16)	37.3 ± 24.0			6 (37.5)		4 (25.0)	10 (62.5)	2 (12.5)		3.9 ± 2.8		
All patients (36)	45.1 ± 22.0			15 (41.7)		6 (16.7)	22 (61.1)	8 (22.2)		4.0 ± 2.6		

URTI: upper tract respiratory infection, LRTI: lower tract respiratory infection

Figura 1 . Porcentaje de pacientes con muestras nasofaríngeas PCR positivas desde la inclusión hasta el día 6 posterior a la inclusión en pacientes con COVID-19 tratados con hidroxicloroquina y en pacientes control con COVID-19.

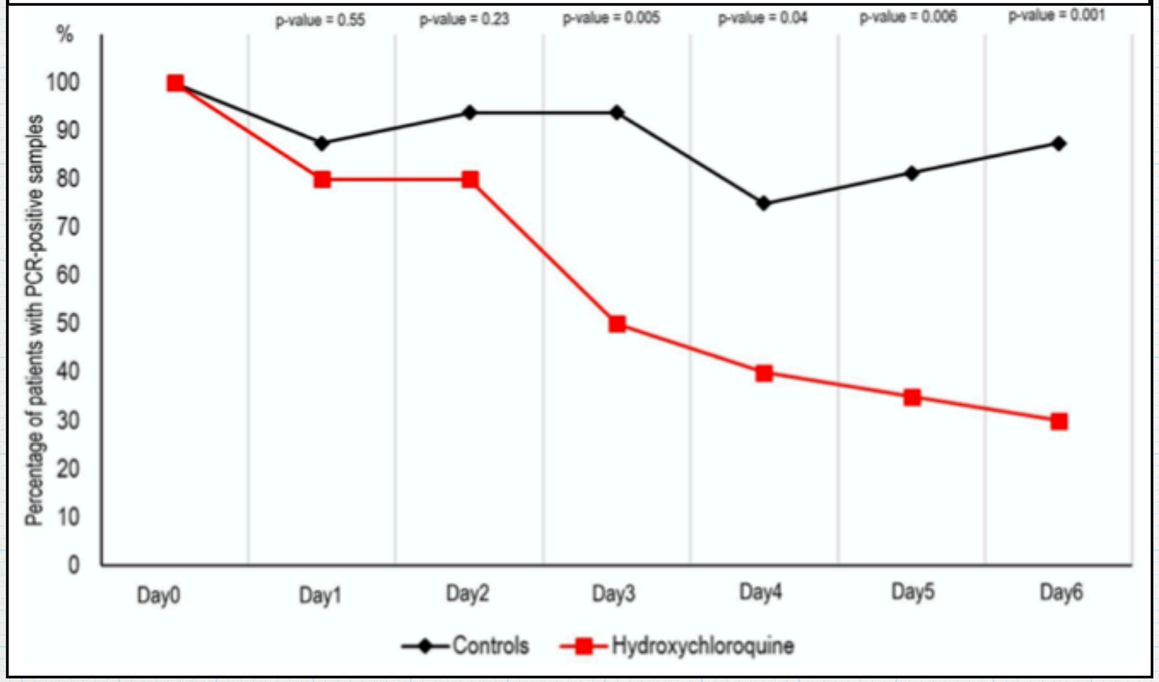
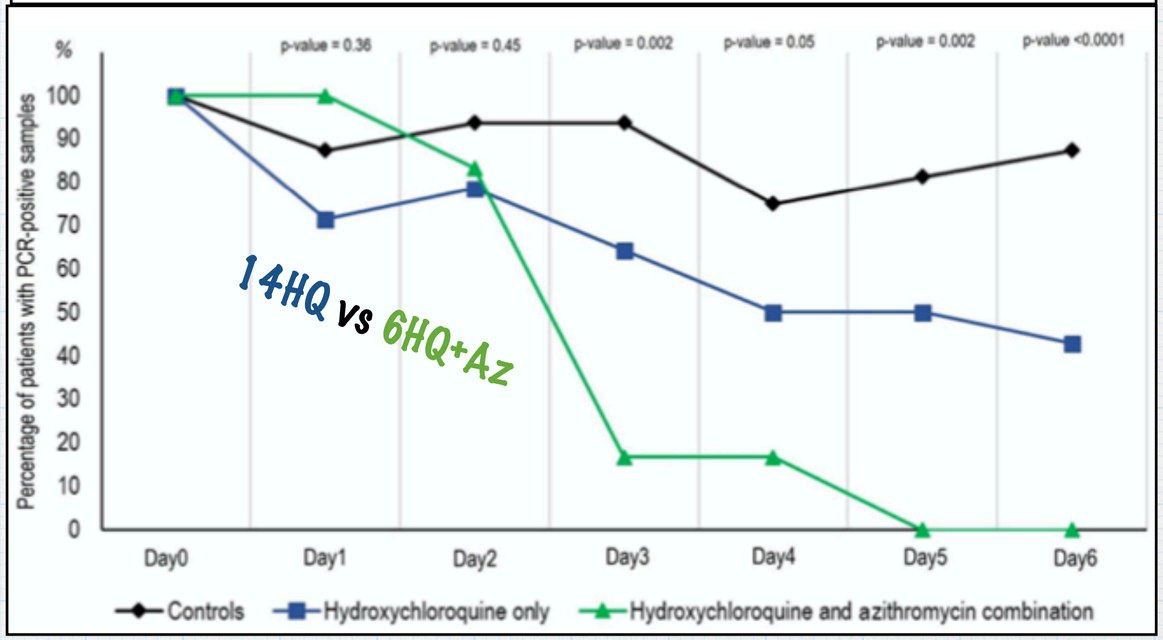


figura 2 Porcentaje de pacientes con muestras nasofaríngeas positivas por PCR desde la inclusión hasta el día 6 posterior a la inclusión en pacientes con COVID-19 tratados solo con hidroxicloroquina, en pacientes con COVID-19 tratados con una combinación de hidroxicloroquina y azitromicina, y en pacientes de control con COVID-19.



ing vaccine development could be also effective, but only in the future. We therefore recommend that COVID-19 patients be treated with hydroxychloroquine and azithromycin to cure their infection and to limit the transmission of the virus to other people in order to curb the spread of COVID-19 in the world. Further works are also warranted to determine if these compounds could be use-

Competing Interests: None declared.

Ethical Approval: French Ethic Committee (CPP Ile de France) (20.02.28.99113).

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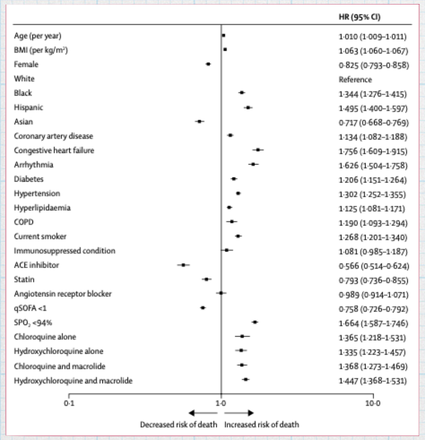
THE LANCET

Publicado: 22 de mayo de 2020

Hospitalizados: 20/12/19 y 14/4/20
671 Hospitales (6 continentes)
Iniciado tto en 1ª 48h a PCR +
N= 96032 (54 a; 46% ♀)
4 grupos tto (14888)
Cl (1868)
Cl+Az (3783)
HQ (3016)
HQ+Az (6221)
Grupo control = 81144
Fallecieron: 10698 (11%)

Resultados:
< supervivencia
> ef. adversos



Hydroxychloroquine or chloroquine with or without a macrolide for treatment of COVID-19: a multinational registry analysis

Mandeep R Mehra, Sapan S Desai, Frank Ruschitzka, Amit N Patel

Summary

Background Hydroxychloroquine or chloroquine, often in combination with a second-generation m…ide, are b… widely used for treatment of COVID-19, despite no conclusive evidence of their benefit. Althoug… …nerally …fe whe… used for approved indications such as autoimmune disease or malaria, the safety and bene… …f th… …treatment regimens are poorly evaluated in COVID-19.

Methods We did a multinational registry analysis of the use of hydroxychloroquine … …oquine with… …thout a macrolide for treatment of COVID-19. The registry comprised data from 671 hosp… …s in s… …ntinents. We included patients hospitalised between Dec 20, 2019, and April 14, 2020, with a positive laboratory … …g for SARS-CoV-2. Patients who received one of the treatments of interest within 48 h of diagn… …e included in … …f four treatment groups (chloroquine alone, chloroquine with a macrolide, hydroxychlor… …ine alone, or hydroxychloroquine with a macrolide), and patients who received none of these treatments formed … control gr… …. Patients for whom one of the treatments of interest was initiated more than 48 h after dia… as well as patients who received remdesivir, were excluded. The… and the occurrence of de-novo ventricular arrhythmias (… ventricular fibrillation).

Findings 96032 patients (mean age 53·8 years, 46·3% women… period and met the inclusion criteria. Of the… …pati… chloroquine, 3783 received chloroquine with… …macro…e, 30… hydroxychloroquine with a macrolide) and … …pati… hospital. After controlling for multiple … …four… …ctors (… cardiovascular disease and its risk fac… …diabetes… …derlying l… and baseline disease severity), wh… …mpared wi… …ortalit… (18·0%; hazard ratio 1·335, 95%… …1·22… …457), hydro…ychloro… chloroquine (16·4%; 1·365, …218–1·531), … …chloroquine with… independently associated… …n an increased … …f in-hospital … hydroxychloroquine (6… …; 2·36… …935–2·900), hydroxychlor… chloroquine (4·3%; …1, …0–4·596), and chloroquine v… independently associat… …an inc… …ed risk of de-novo ver…

Interpreta… We w… …unable… …nfirm a benefit of hydroxyc… a macro… …on in… …spital outcomes for COVID-19. Each of … in-hospita… …vi… …reased frequency of ventricular ar…

Funding William… …vey Distinguished Chair in Advanced Cardio…

Published Online
…22, 2020
https://doi.org/10.1016/S0140-6736(20)31180-6

This online publication has b… corrected. The corrected vers… first appeared at thelancet.co… on May 29, 2020

See Online/Comment
https://doi.org/10.1016/S0140-6736(20)31174-0

Brigham and Women's Hosp… Heart and Vascular Center ar…

RETRACTED

This article has been retracted.

ORIGINAL ARTICLE

Cardiovascular Disease, Drug Therapy, and Mortality in Covid-19

Mandeep R. Mehra, M.D., Sapan S. Desai, M.D., Ph.D., SreyRam Kuy, M.D., M.H.S., Timothy D. Henry, M.D., and Amit N. Patel, M.D.

Article Figures/Media Metrics

June 18, 2020
N Engl J Med 2020; 382:e102
DOI: 10.1056/NEJMoa2007621

22 References 542 Citing Articles

Abstract

BACKGROUND

Coronavirus disease 2019 (Covid-19) may disproportionately affect people with cardiovascular disease. Concern … angiotensin-converting–enzyme … (ARBs) in this clinical context.

METHODS

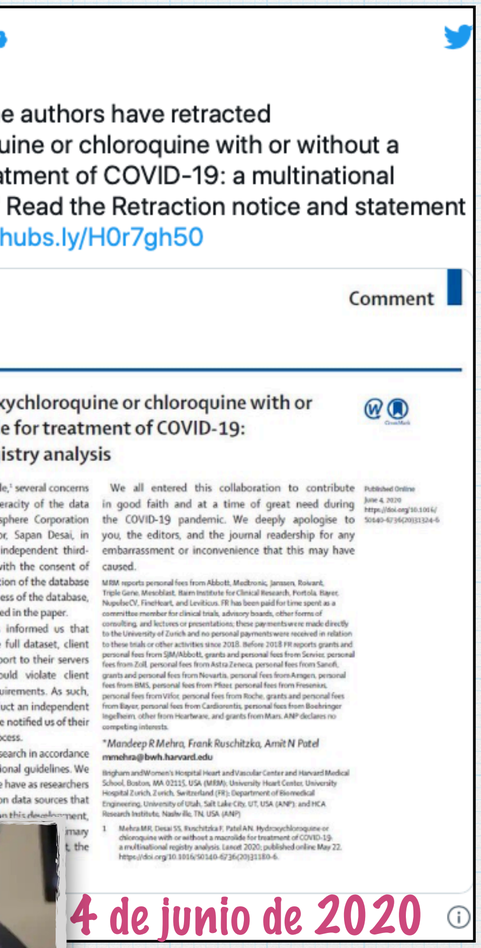
Using an observational database … evaluated the relationship of card… among hospitalized patients wit… and March 15, 2020, and were re… having either died in the hospita…

RESULTS

Of the 8910 patients with Covid-… the analysis, a total of 515 died in… factors we found to be independe… were an age greater than 65 years…

Related Articles

EDITORIAL JUN 18, 2020
Inhibitors of the Renin–Angio… System and Covid-19



4 de junio de 2020

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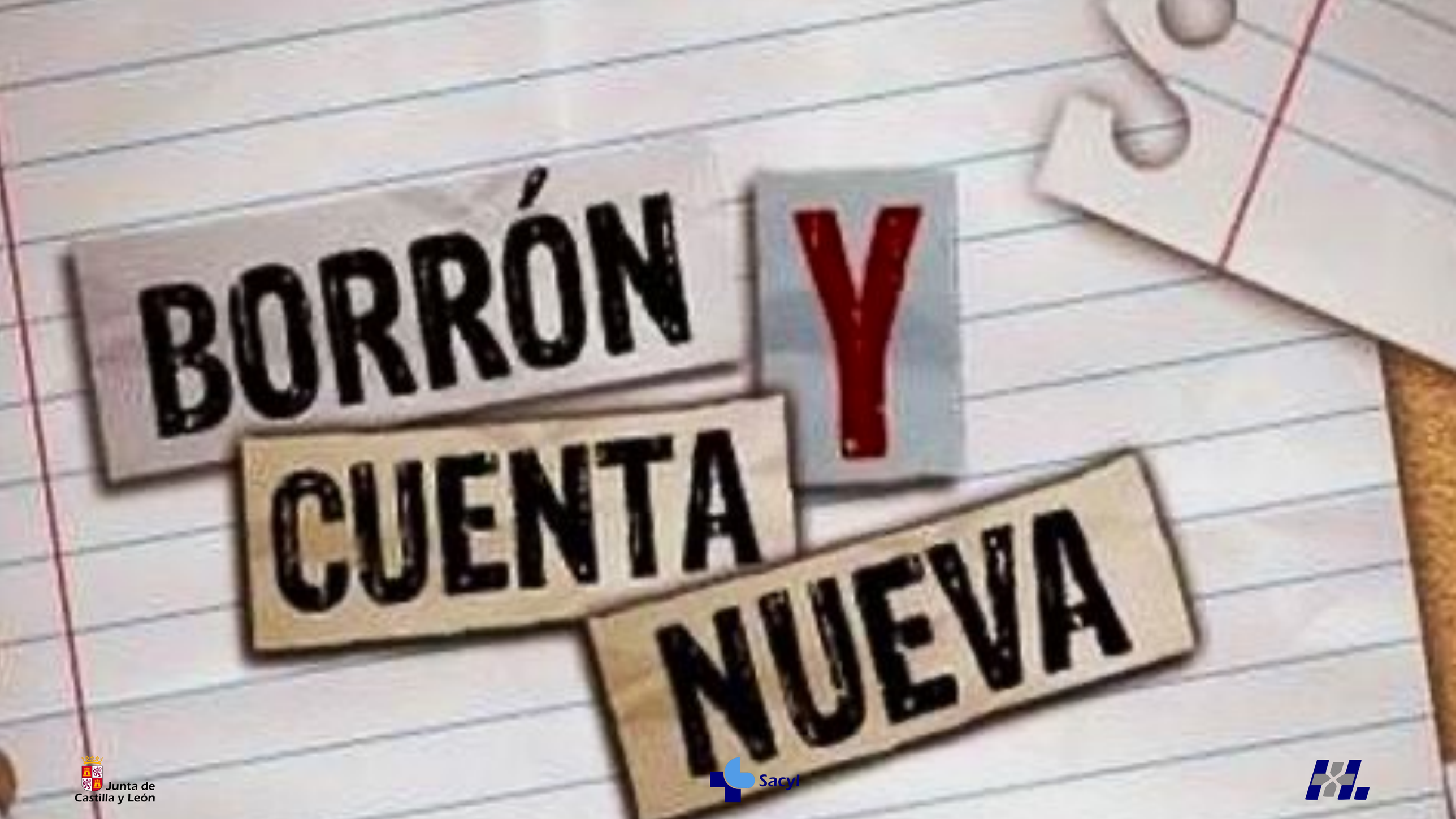

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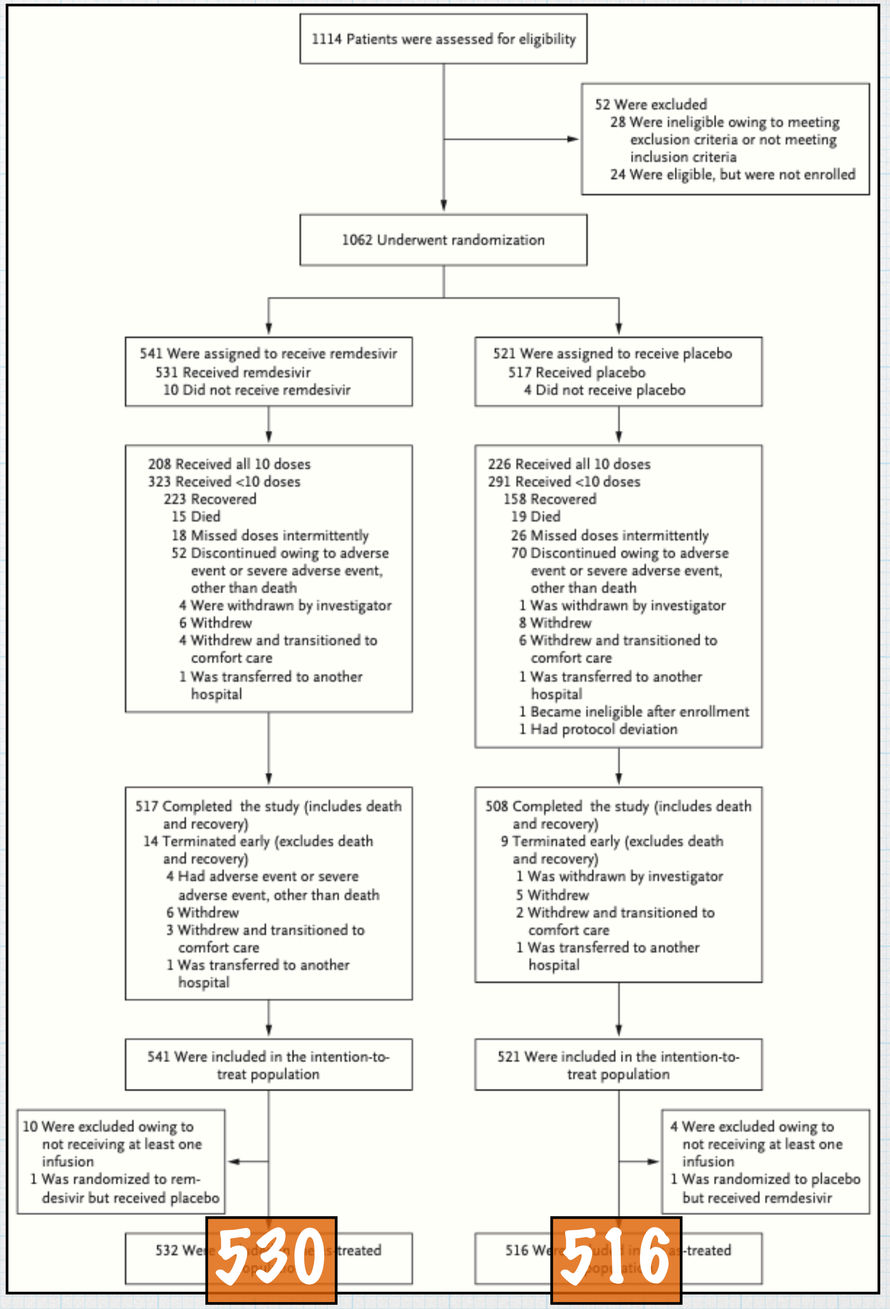
The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 NOVEMBER 5, 2020 VOL. 383 NO. 19

Remdesivir for the Treatment of Covid-19 — Final Report

J.H. Beigel, K.M. Tomashek, L.E. Dodd, A.K. Mehta, B.S. Zingman, A.C. Kalil, E. Hohmann, H.Y. Chu, A. Luetkemeyer, S. Kline, D. Lopez de Castilla, R.W. Finberg, K. Dierberg, V. Tapson, L. Hsieh, T.F. Patterson, R. Paredes, D.A. Sweeney, W.R. Short, G. Touloumi, D.C. Lye, N. Ohmagari, M. Oh, G.M. Ruiz-Palacios, T. Benfield, G. Fätkenheuer, M.G. Kortepeter, R.L. Atmar, C.B. Creech, J. Lundgren, A.G. Babiker, S. Pett, J.D. Neaton, T.H. Burgess, T. Bonnett, M. Green, M. Makowski, A. Osinusi, S. Nayak, and H.C. Lane, for the ACTT-1 Study Group Members*

* Ensayo doble ciego, aleatorizado y controlado con placebo.
* Del 21/2/20 al 19/4/20.
* Multicéntrico: 60 hospitales (80% Norteamericanos; 15% Europeos; 5% Asiáticos).
* N= 1062. 541 a Remdesivir 200 mgx1d + 100 mgx9d vs 521 a placebo x10d. Proporción ni 1/1.
* El estado clínico se evaluó con: 1-Escala ordinal (8 categorías). 2-National Early Warning Score (6 medidas)
* Seguimiento de 29 d.
* Objetivo 1º: tiempo recuperación al día 15 (categorías 1-3). Se cambio el 22/3 por "comparación del tiempo de recuperación para el día 29 "
* Objetivo 2º "clave": estado clínico en el día 15. Y hay muchos más..., el ultimo mortalidad a los 14 y 28 d de hospitalización.
* Análisis por intención de tratar.



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Edad 60

Varones 64%

Blancos 53%

Mediana comienzo sintomas 9

Comorbilidad en 81%

HTA 51%

Table 1. Demographic and Clinical Characteristics of the Patients at Baseline.*

Characteristic	All (N=1062)	Remdesivir (N=541)	Placebo (N=521)
Age — yr	58.9±15.0	58.6±14.6	59.2±15.4
Male sex — no. (%)	684 (64.4)	352 (65.1)	332 (63.7)
Race or ethnic group — no. (%)†			
American Indian or Alaska Native	7 (0.7)	4 (0.7)	3 (0.6)
Asian	135 (12.7)	79 (14.6)	56 (10.7)
Black or African American	226 (21.3)	109 (20.1)	117 (22.5)
White	566 (53.3)	279 (51.6)	287 (55.1)
Hispanic or Latino — no. (%)	250 (23.5)	134 (24.8)	116 (22.3)
Median time (IQR) from symptom onset to randomization — days‡	9 (6–12)	9 (6–12)	9 (7–13)
No. of coexisting conditions — no. /total no. (%)‡			
None	194/1048 (18.5)	97/531 (18.3)	97/517 (18.8)
One	275/1048 (26.2)	138/531 (26.0)	137/517 (26.5)
Two or more	579/1048 (55.2)	296/531 (55.7)	283/517 (54.7)
Coexisting conditions — no./total no. (%)			
Type 2 diabetes	322/1051 (30.6)	164/532 (30.8)	158/519 (30.4)
Hypertension	533/1051 (50.7)	269/532 (50.6)	264/519 (50.9)
Obesity	476/1049 (45.4)	242/531 (45.6)	234/518 (45.2)
Score on ordinal scale — no. (%)			
4. Hospitalized, not requiring supplemental oxygen, requiring ongoing medical care (Covid-19–related or otherwise)	138 (13.0)	75 (13.9)	63 (12.1)
5. Hospitalized, requiring supplemental oxygen	435 (41.0)	232 (42.9)	203 (39.0)
6. Hospitalized, receiving noninvasive ventilation or high-flow oxygen devices	193 (18.2)	95 (17.6)	98 (18.8)
7. Hospitalized, receiving invasive mechanical ventilation or ECMO	285 (26.8)	131 (24.2)	154 (29.6)
Baseline score missing	11 (1.0)	8 (1.5)	3 (0.6)

7% peor ???

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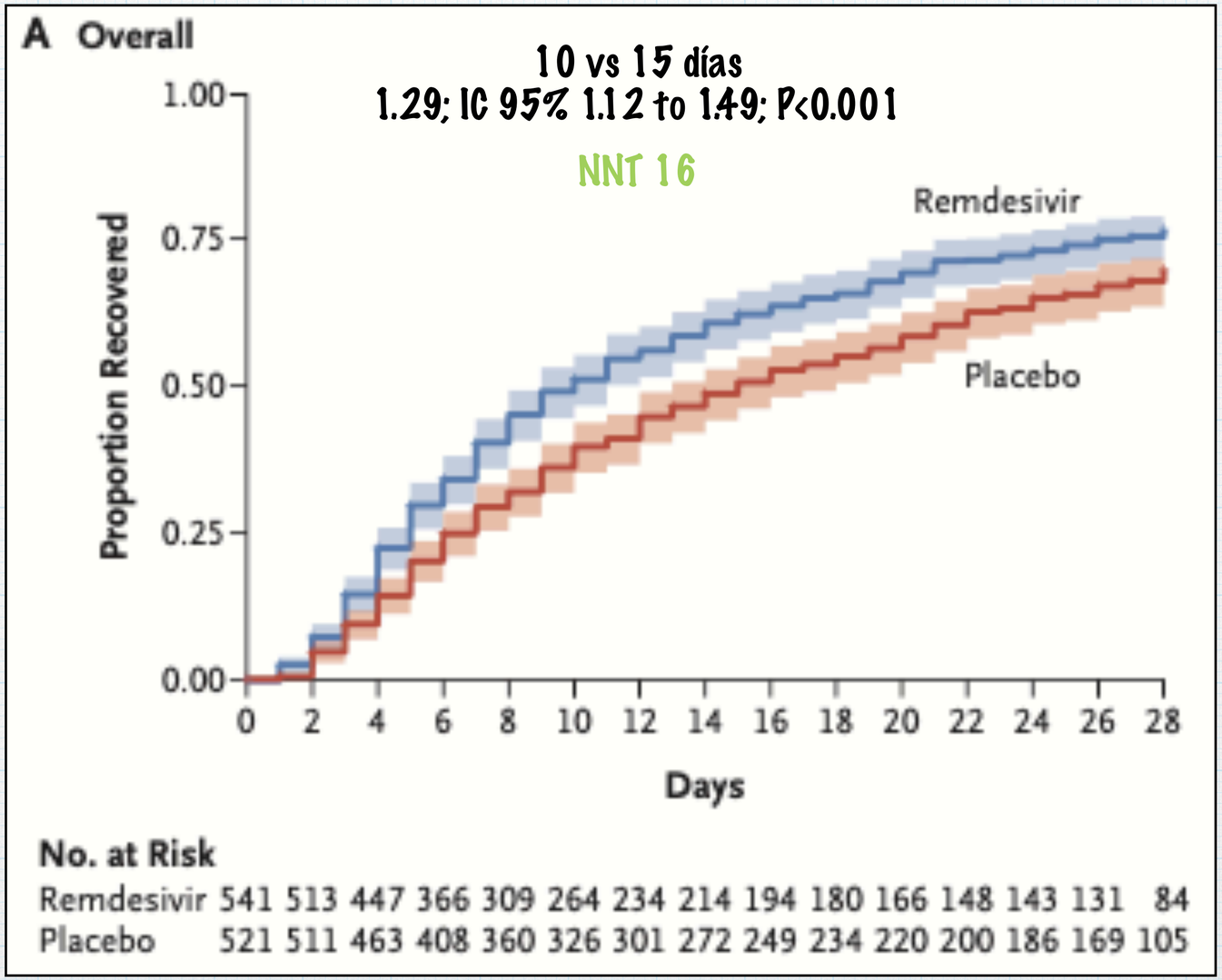
10 vs 15 días

1.29; IC 95% 1.12 to 1.49; P<0.001

NNT 16



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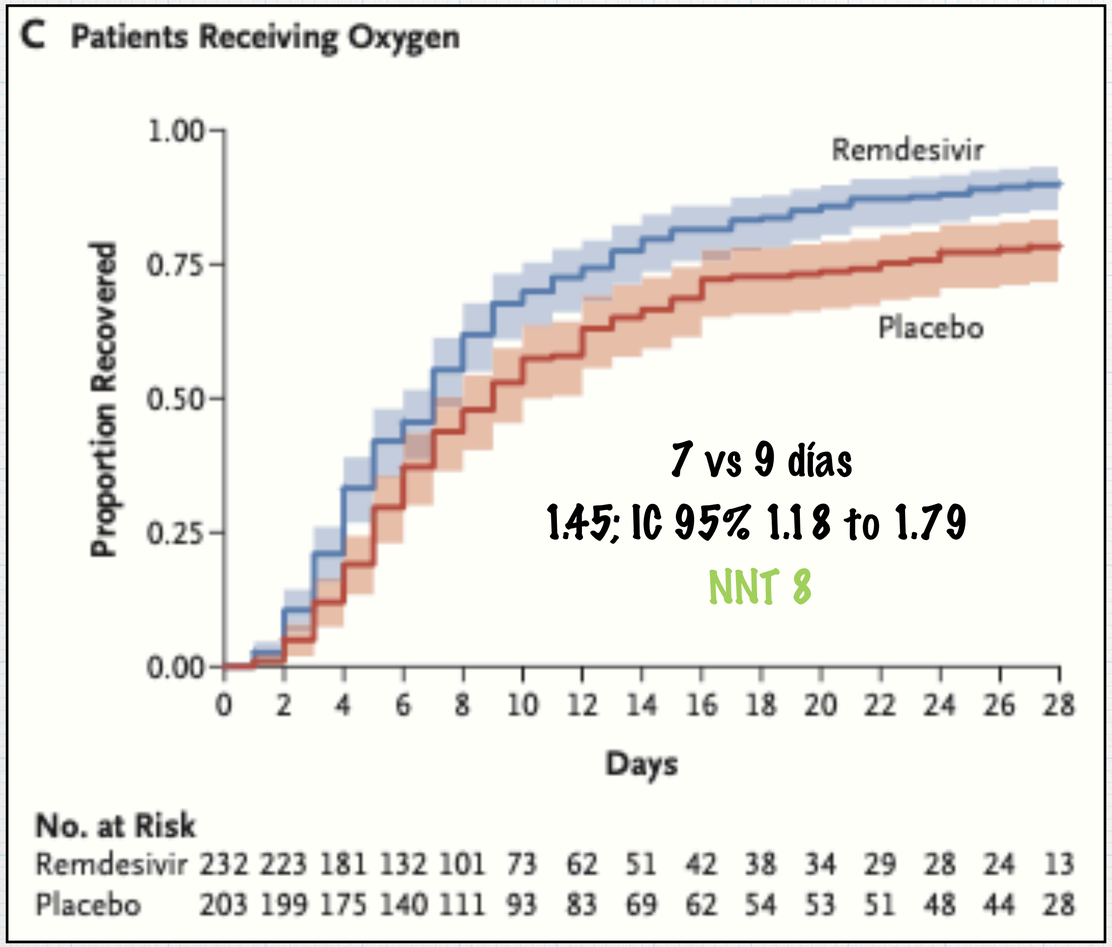

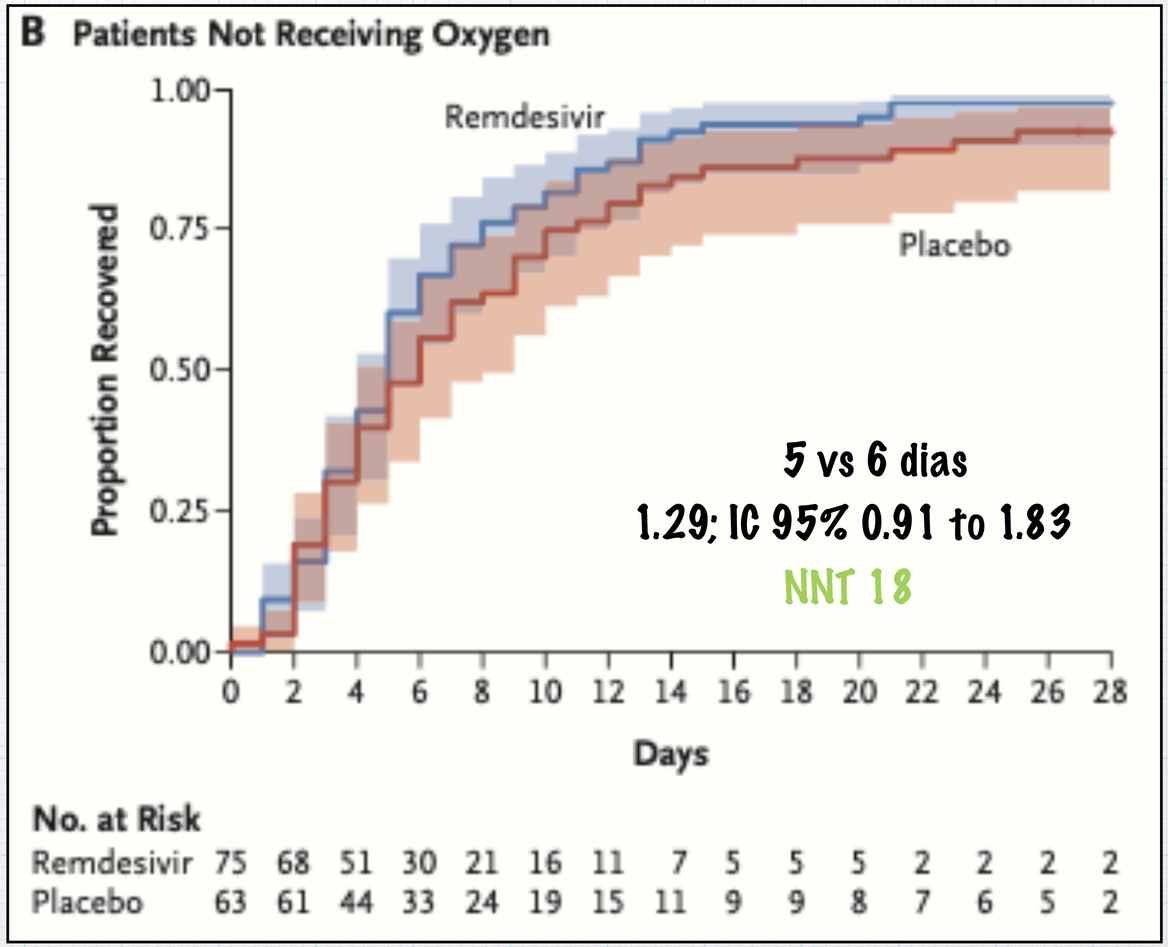

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Table 2. Outcomes Overall and According to Score on the Ordinal Scale in the Intention-to-Treat Population.*

	Overall		Ordinal Score at Baseline							
			4		5		6		7	
	Remdesivir (N=541)	Placebo (N=521)	Remdesivir (N=75)	Placebo (N=63)	Remdesivir (N=232)	Placebo (N=203)	Remdesivir (N=95)	Placebo (N=98)	Remcesivir (N=131)	Placebo (N=154)
Recovery										
No. of recoveries	399	352	73	58	206	156	57	61	63	77
Median time to recovery (95% CI) — days	10 (9–11)	15 (13–18)	5 (4–6)	6 (4–7)	7 (6–8)	9 (7–10)	15 (10– 27)	20 (14– 26)	29 (24–NE)	28 (24–NE)
Rate ratio (95% CI)†	1.29 (1.12–1.49 [P<0.001])		1.29 (0.91–1.83)		1.45 (1.18–1.79)		1.09 (0.76–1.57)		0.98 (0.70–1.36)	
Mortality through day 14‡										
Hazard ratio for data through day 15 (95% CI)	0.55 (0.36–0.83)		0.42 (0.04–4.67)		0.28 (0.12–0.66)		0.82 (0.40–1.69)		0.76 (0.39–1.50)	
No. of deaths by day 15	35	61	1	2	7	21	13	17	14	21
Kaplan–Meier estimate of mortality by day 15 — % (95% CI)	6.7 (4.8–9.2)	11.9 (9.4–15.0)	1.3 (0.2–9.1)	3.2 (0.8–12.1)	3.1 (1.5–6.4)	10.5 (7.0–15.7)	14.2 (8.5–23.2)	17.3 (11.2–26.4)	10.9 (6.6–17.6)	13.8 (9.2–20.4)
Mortality over entire study period‡										
Hazard ratio (95% CI)	0.73 (0.52–1.03)		0.82 (0.17–4.07)		0.30 (0.14–0.64)		1.02 (0.54–1.91)		1.13 (0.67–1.89)	
No. of deaths by day 29	59	77	3	3	9	25	19	20	28	29
Kaplan–Meier estimate of mortality by day 29 — % (95% CI)	11.4 (9.0–14.5)	15.2 (12.3–18.6)	4.1 (1.3– 12.1)	4.8 (1.6–14.3)	4.0 (2.1–7.5)	12.7 (8.8–18.3)	21.2 (14.0–31.2)	20.4 (13.7–29.8)	21.9 (15.7–30.1)	19.3 (13.8–26.5)
Ordinal score at day 15 (±2 days) — no. (%)§										
1	157 (29.0)	115 (22.1)	38 (50.7)	28 (44.4)	90 (38.8)	62 (30.5)	18 (18.9)	14 (14.3)	11 (8.4)	11 (7.1)
2	117 (21.6)	102 (19.6)	20 (26.7)	15 (23.8)	70 (30.2)	58 (28.6)	22 (23.2)	19 (19.4)	5 (3.8)	10 (6.5)
3	14 (2.6)	8 (1.5)	8 (10.7)	4 (6.3)	6 (2.6)	4 (2.0)	0	0	0	0
4	38 (7.0)	33 (6.3)	3 (4.0)	7 (11.1)	17 (7.3)	13 (6.4)	12 (12.6)	4 (4.1)	6 (4.6)	9 (5.8)
5	58 (10.7)	60 (11.5)	3 (4.0)	5 (7.9)	25 (10.8)	18 (8.9)	2 (2.1)	14 (14.3)	28 (21.4)	23 (14.9)
6	28 (5.2)	24 (4.6)	1 (1.3)	0	5 (2.2)	7 (3.4)	12 (12.6)	11 (11.2)	10 (7.6)	6 (3.9)
7	95 (17.6)	121 (23.2)	1 (1.3)	3 (4.8)	13 (5.6)	21 (10.3)	16 (16.8)	20 (20.4)	57 (43.5)	74 (48.1)
8	34 (6.3)	58 (11.1)	1 (1.3)	1 (1.6)	6 (2.6)	20 (9.9)	13 (13.7)	16 (16.3)	14 (10.7)	21 (13.6)
Odds ratio (95% CI)	1.5 (1.2–1.9)		1.5 (0.8–2.7)		1.6 (1.2–2.3)		1.4 (0.9–2.3)		1.2 (0.8–1.9)	

$5\ O_2$

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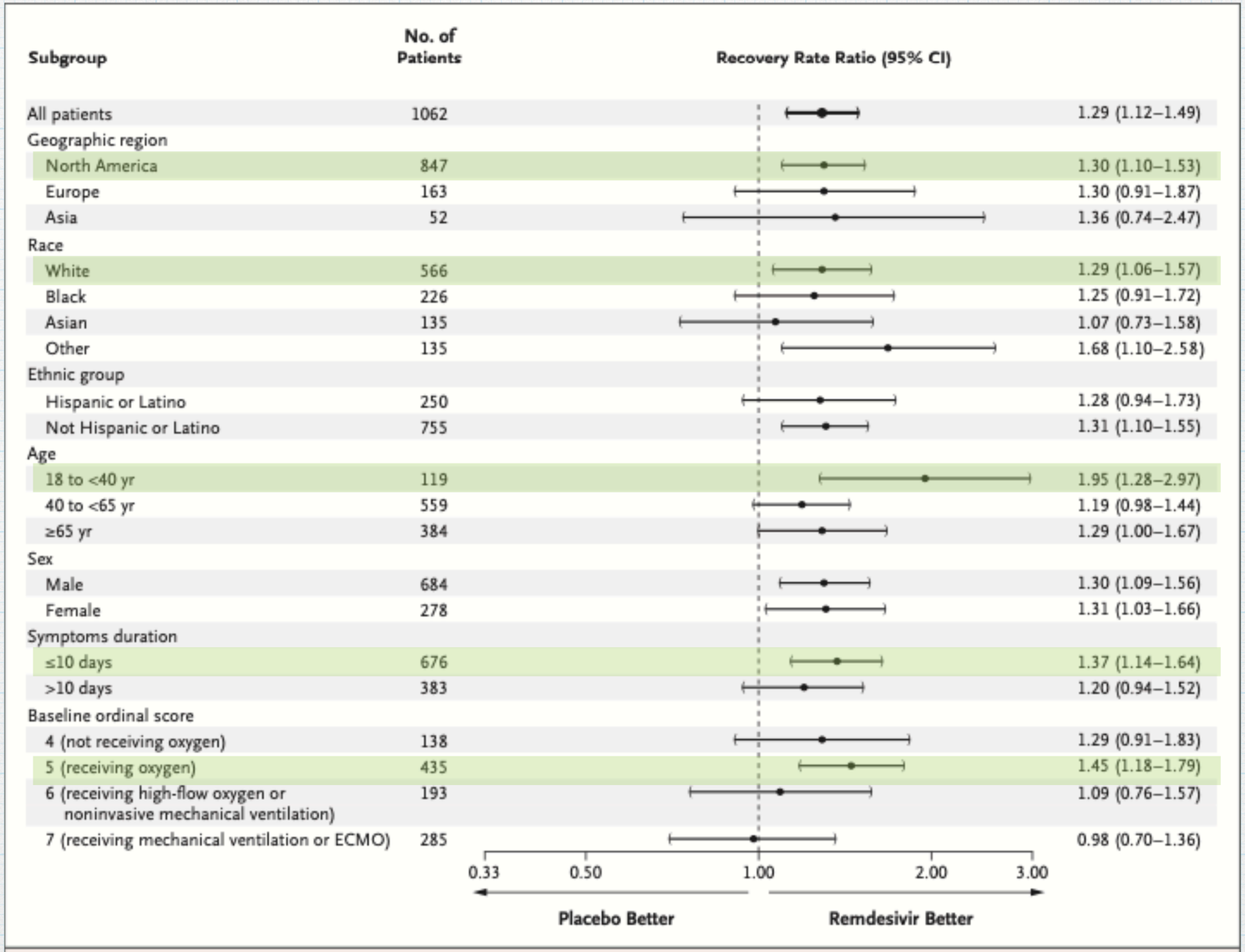

Figure 3. Time to Recovery According to Subgroup.

The widths of the confidence intervals have not been adjusted for multiplicity and therefore cannot be used to infer treatment effects. Race and ethnic group were reported by the patients.

Table 3. Additional Secondary Outcomes.

	Remdesivir (N=541)	Placebo (N=521)	Rate Ratio (95% CI)
Median time to clinical improvement (95% CI) — days			
Improvement of one category on ordinal scale	7.0 (6.0 to 8.0)	9.0 (8.0 to 11.0)	1.23 (1.08 to 1.41)
Improvement of two categories on ordinal scale	11.0 (10.0 to 13.0)	14.0 (13.0 to 15.0)	1.29 (1.12 to 1.48)
Discharge or National Early Warning Score ≤2 for 24 hr*	8.0 (7.0 to 9.0)	12.0 (10.0 to 15.0)	1.27 (1.10 to 1.46)
			Difference (95% CI)
Hospitalization			
Median duration of initial hospitalization (IQR) — days†	12 (6 to 21)	17 (8 to 28)	−5.0 (−7.7 to −2.3)
Median duration of initial hospitalization among those who did not die (IQR) — days	10 (6 to 21)	14 (7 to 27)	−4.0 (−6.0 to −2.0)
Patients rehospitalized — % (95% CI)	5 (3 to 7)	3 (2 to 5)	2 percentage points (0 to 4)
Oxygen			
Median days receiving oxygen if receiving oxygen at baseline (IQR)	10 (5 to 20)	21 (8 to 28)	−8.0 (−11.8 to −4.2)
New use of oxygen			
No. of patients/total no.	75/475	28/63	
Percent of patients (95% CI)	36 (26 to 47)	44 (33 to 57)	−8 (−24 to 8)
Median days receiving oxygen (IQR)	4 (2 to 12)	5.5 (1 to 15)	−1.0 (−7.6 to 5.6)
Noninvasive ventilation or high-flow oxygen			
Median days of noninvasive ventilation, high-flow oxygen use during study if receiving these interventions at baseline (IQR)	6 (3 to 18)	6 (3 to 16)	0 (−2.6 to 2.6)
New use of new noninvasive ventilation, high-flow oxygen use during the study			
No. of patients/total no.	52/307	64/266	
Percent of patients (95% CI)	17 (13 to 22)	24 (19 to 30)	−7 (−14 to −1)
Median days of use during the study (IQR)	3 (1 to 10.5)	4 (2 to 23.5)	−1.0 (−4.0 to 2.0)
Mechanical ventilation or ECMO			
Median days of mechanical ventilation or ECMO during study if receiving these interventions at baseline (IQR)	17 (9 to 28)	20 (8 to 28)	−3.0 (−9.3 to 3.3)
New use of mechanical ventilation or ECMO during study			
No. of patients/total no.	52/402	82/364	
Percent of patients (95% CI)	13 (10 to 17)	23 (19 to 27)	−10 (−15 to −4)
Median days of use during the study (IQR)	21.5 (9 to 28)	23 (12 to 28)	1.0 (−6.0 to 8.0)

Eventos adversos graves en 131/532 pacientes (24.6%) en el grupo de remdesivir y en 163/516 pacientes (31.6%) en el grupo de placebo

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MEJORÍA CLÍNICA

MENOS MORTALIDAD

Conclusiones

* Remdesivir durante 10 días fue superior al placebo en el tratamiento de pacientes hospitalizados con Covid-19.
  * Tiempo de recuperación más corto: 10 vs 15 d 1.29; IC 95%, 1,12 a 1,49. NNT 16 RRA 6.2%.
  * Mejoría en la escala ordinal en el día 15 1,5; IC 95%, 1,2 a 1,9.
* Otros:
  * La mortalidad fue del 11% vs 15% 0,73; IC 95%, 0,52 a 1,03 NNT 26 (RRA 3.9%)
  * **La mortalidad en la categoria 5: 0.30 (0.14-0.64). NNT 12 (RRA 8%)**
  * Mejora de una y dos categorías en escala ordinal.
  * Mas rápida el alta o mejor puntuación en NEWS.
  * Estancia hospitalaria mas corta (mediana, 12 días frente a 17 días).
  * Puede evitar la progresión formas más graves ???

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Comentarios

* Proporción 1/1.
* Solo 208 pacientes completaron los 10 d de tratamiento.
* Escala ordinal ¿validación?
* Cambio objetivo 1º tras iniciar estudio.
* Muchos objetivos 2º.
* ¿ Validez externa ? 80% hospitales americanos. Predominan varones y blancos...

Effect of β-Blocker Withdrawal on Functional Capacity in Heart Failure and Preserved Ejection Fraction

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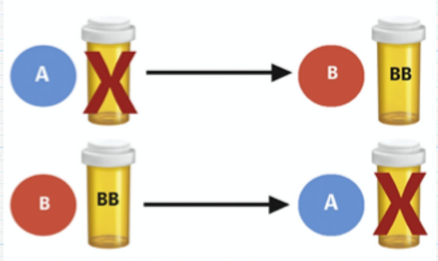
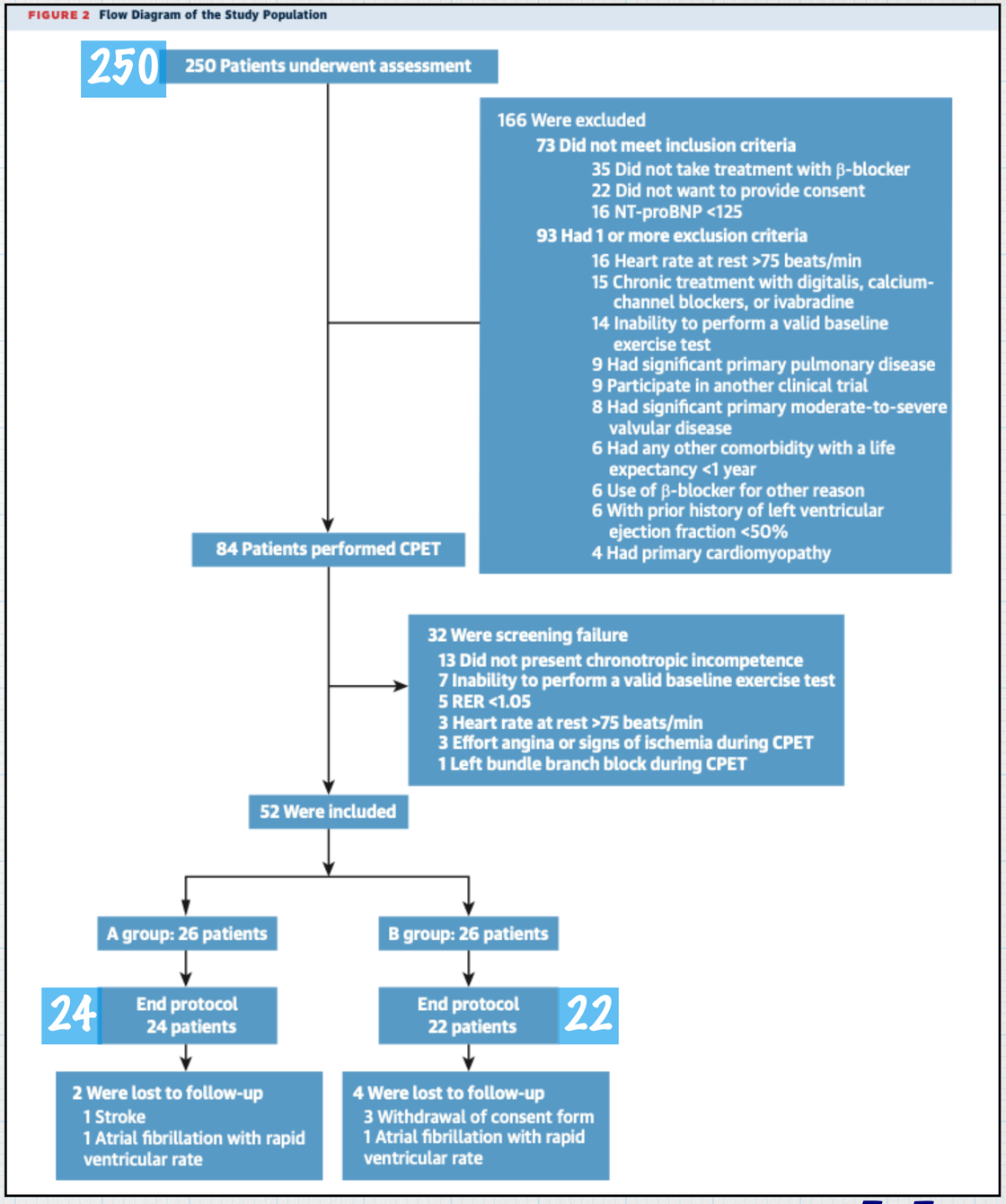
- Ensayo clínico cruzado, multicéntrico, aleatorizado.
- 1 de octubre de 2018 hasta el 31 de diciembre de 2020: 84 → 52
- 1:1
- 2 períodos de tto: 2S separadas por 2 S de lavado
- N= 52 (incluidos finalmente 24 y 22)
- CF NYHA II-III
- IC FEp
- Tto previo con BB
- Incompetencia cronotrópica con Prueba de esfuerzo.
- Seguimiento 60 d
- OP: Consumo de O_2 promedio (CPET incremental y limitado por síntomas)
- OS: función cognitiva, valores ecocardiográficos, calidad de vida, biomarcadores.
- Análisis por intención de tratar modificado.





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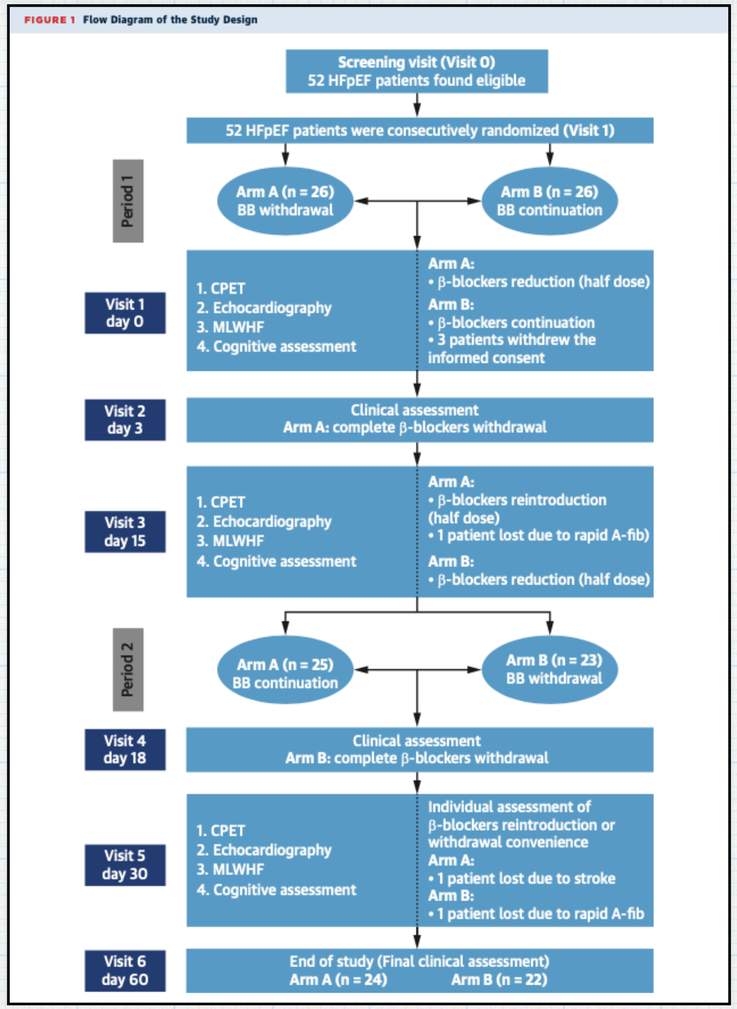
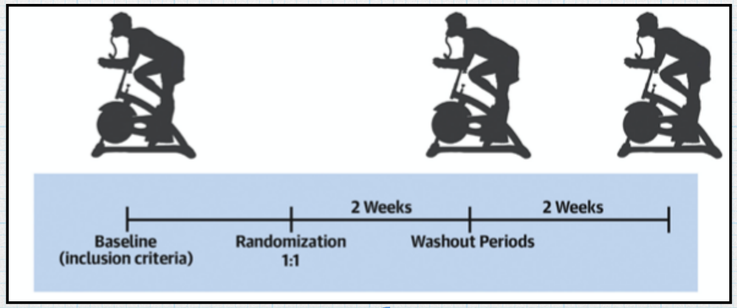
Criterios inclusión

- >18a
- CF NYHA >II
- FE>50%
- ProBNP >126
- Cardiopatia estructural: HVI, AI dilat. o DD
- Ing previo por IC
- BB en ult 3 meses
- Prueba esfuerzo: índice cronotrópico <0.6





Criterios exclusión

- Incapacidad para hacer la prueba de esfuerzo
- Valvulopatia
- Angor/SCA en ult año
- Hacer angor o arritmias en ergometria
- EPOC significativa o HTP
- Tto con digital, ACA o ivabradina
- FC en reposo >75
- Enf. con esperanza de vida <1a

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TABLE 1 Baseline Characteristics of the Patients Stratified by Randomization Arm

	All Patients (N = 52, 100%)	Arm A (n = 26, 50%)	Arm B (n = 26, 50%)	P Value
Demographic and medical history				
Age, y	74.5 (68.5-79.5)	73 (68-77)	76.5 (72-80)	0.101
Women	31 (59.6)	14 (53.9)	17 (65.4)	0.572
BMI, kg/m^2	31.1 ± 4.7	30.9 ± 5.3	31.3 ± 4.0	0.741
Caucasian	52 (100.0)	26 (100.0)	26 (100.0)	1.000
Previous admission for AHF	52 (100.0)	26 (100.0)	26 (100.0)	1.000
Hypertension	46 (88.5)	22 (84.6)	24 (92.3)	0.668
Diabetes mellitus	21 (40.4)	9 (34.6)	12 (46.2)	0.572
Dyslipidemia	37 (71.2)	16 (61.5)	21 (80.8)	0.132
Current smoker	4 (7.7)	4 (15.4)	0 (0.0)	0.110
Prior smoker	12 (23.1)	6 (23.1)	6 (23.1)	1.000
Prior history of IHD	12 (23.1)	7 (26.9)	5 (19.2)	0.743
Prior history of stroke	1 (1.9)	1 (3.9)	0 (0.0)	1.000
Prior history of atrial fibrillation	20 (38.5)	11(42.3)	9 (34.6)	0.776
Prior history of COPD	6 (11.5)	5 (19.2)	1 (3.9)	0.191
NYHA functional class III/IV	18 (34.6)	8 (30.8)	10 (38.5)	0.771
Vital signs at rest				
Heart rate, beats/min	64.8 ± 8.8	64.9 ± 9.2	64.8 ± 8.8	0.531
Systolic blood pressure, mm Hg	123.4 ± 16.8	124.4 ± 16.2	122.4 ± 16.8	0.637
Diastolic blood pressure, mm Hg	65.6 ± 8.4	64.0 ± 8.0	67.1 ± 8.7	0.225
Echocardiographic and electrocardiographic parameters				
Left ventricular ejection fraction	64.7 ± 7.1	63.8 ± 7.1	65.7 ± 7.0	0.338
Left atrial volume index, mL/m^2	39.8 ± 15.1	42.5 ± 16.3	37.1 ± 10.2	0.164
Left ventricular mass index, g/m^2	107.9 ± 32.7	108.1 ± 31.1	107.9 ± 32.7	0.984
Septal E/e' ratio	14.6 (11.8-18.1)	14.3 (11.6-19.1)	15.2 (13.4-18.5)	0.486
Left bundle branch block	5 (9.6)	2 (7.7)	3 (11.5)	0.638
Atrial fibrillation at inclusion	10 (19.2)	7 (26.9)	3 (11.5)	0.291
Laboratory values				
Hemoglobin, g/dL	13.4 ± 1.4	13.4 ± 1.7	13.1 ± 1.1	0.459
eGFR, mL/min/1.73 m^2	64.7 ± 21.2	67.2 ± 23.5	62.2 ± 18.8	0.399
Serum sodium, mEq/L	140.9 ± 3.1	140.5 ± 2.9	141.3 ± 3.3	0.304
NT-proBNP, pg/mL	400.5 (209.5-1,039.5)	424 (234-1,294)	344.5 (204-662)	0.341
CA125, U/mL	10 (7-14.5)	10 (7.7-15)	10 (7-14)	0.653
Cardiopulmonary exercise testing variables				
Peak Vo_2, mL/kg/min	12.4 ± 2.9	12.2 ± 2.9	12.5 ± 2.9	0.687
Peak Vo_2%	72.4 ± 17.8	67.6 ± 17.9	77.2 ± 16.6	0.051
VE/VCO_2 slope	33.7 ± 5.4	34.1 ± 5.7	33.4 ± 5.1	0.644
Respiratory exchange ratio	1.2 (1.1-1.3)	1.1 (1.1-1.3)	1.2 (1.1-1.3)	0.581
Chronotropic index	0.41 ± 0.14	0.40 ± 0.13	0.41 ± 0.16	0.842
Heart rate at exercise peak	97.2 ± 14.7	97.1 ± 15.8	97.3 ± 13.9	0.956
Quality of life and cognitive function variables				
MLHFQ	26 (11-40)	25 (13-35)	27 (11-40)	0.869
MoCA score	20.7 ± 4.6	21.5 ± 4.0	19.8 ± 5.2	0.219
MMSE score	27.5 ± 2.3	28.0 ± 1.7	27.1 ± 2.7	0.173
Medical treatment				
ACE inhibitor or ARB	39 (75)	19 (73.1)	20 (76.9)	0.755
Loop diuretics	44 (84.6)	21 (80.8)	23 (88.5)	0.781
MRA	6 (11.5)	2 (7.7)	4 (15.4)	0.668
Statins	35 (67.3)	18 (69.3)	17 (65.4)	1.000

Values are median (interquartile range), n (%), or mean ± SD.

ACE = angiotensin-converting enzyme; AHF = acute heart failure; ARB = angiotensin receptor blocker; BMI = body mass index; CA125 = serum carbohydrate antigen 125; COPD = chronic obstructive pulmonary disease; E/e' = ratio of mitral peak velocity of early filling (E) to early diastolic mitral annular velocity (e'); eGFR = estimated glomerular filtration rate; IHD = ischemic heart disease; MLHFQ = Minnesota Living With Heart Failure Questionnaire; MMSE = Mini-Mental State Examination; MoCA = Montreal Cognitive Assessment; MRA = mineralocorticoid receptor antagonists; NYHA = New York Heart Association functional class; NT-proBNP = N-terminal pro B-type natriuretic peptide; peak Vo_2 = peak oxygen consumption; peak Vo2% = percentage of predicted peak oxygen consumption; VCO_2 = carbon dioxide production; VE = minute ventilation; VE/VCO_2 slope = ventilatory efficiency.

Grupos iguales

Características basales

* Edad 72,6 ± 13,1 años
* Mujeres 60%
* IMC 31
* HTA 88% DM 40%
* FE 64%
* El 81% están en ritmo sinusal
* Clase funcional III/IV 35%
* FG 65 ml/min/1.73 m^2
* BB 100% (>bisoprolol), IECAs 75%, Diuréticos 85%, ARM 12%, estatinas 67%

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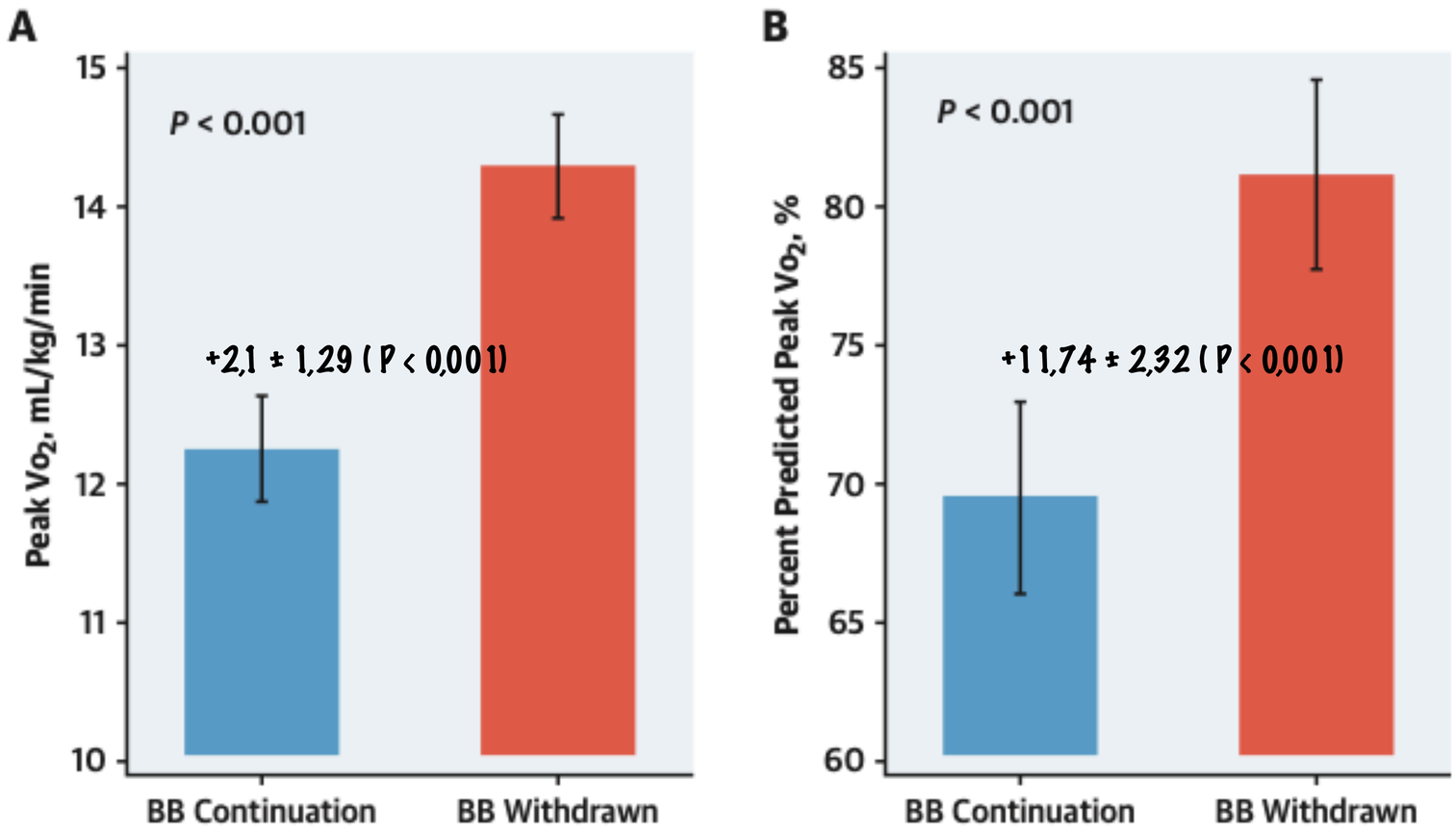
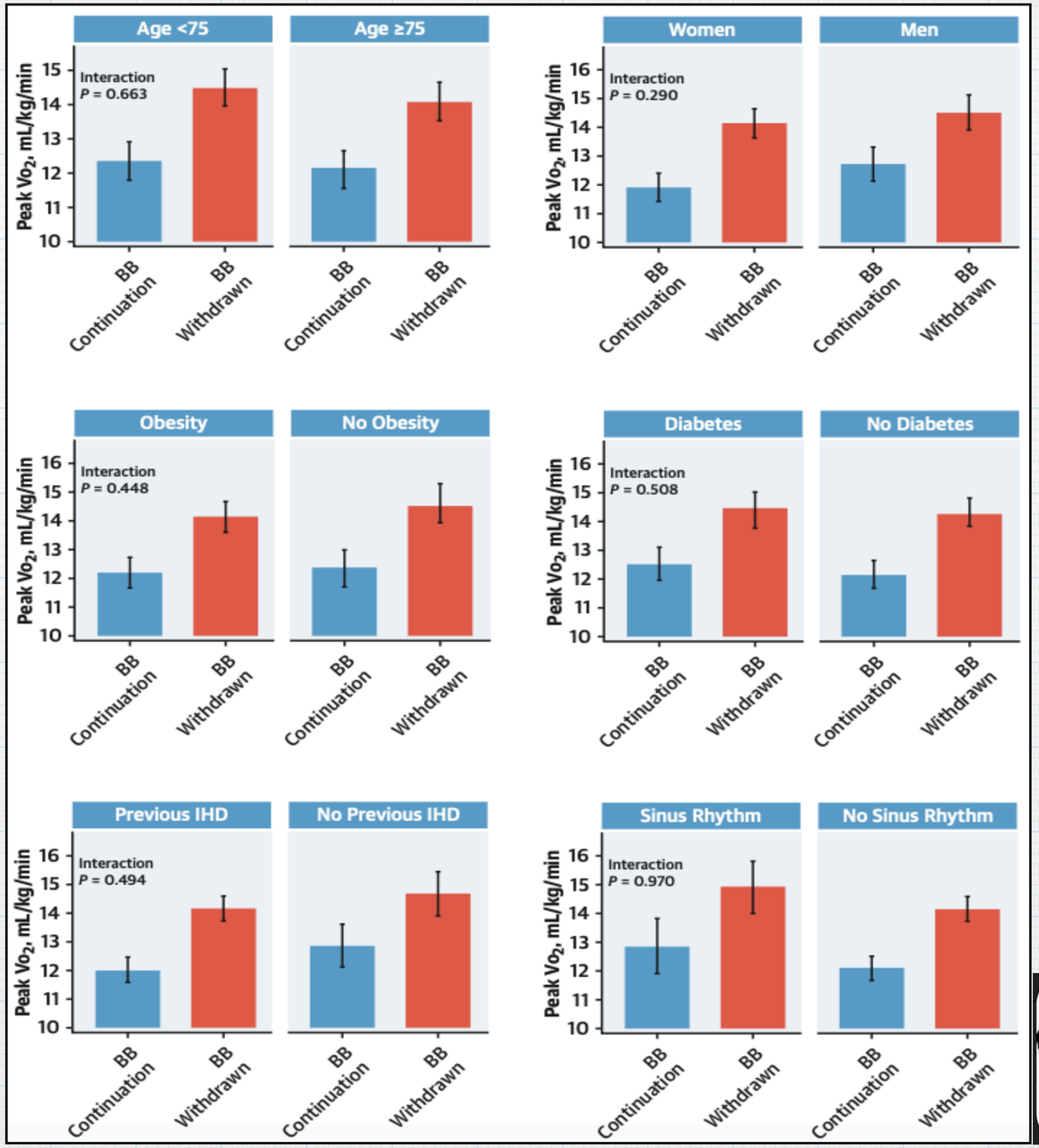
FIGURE 3 Primary Endpoint: Change in Mean Peak VO_2 and Peak VO_2%



(A) The change in peak oxygen consumption (peak Vo_2) after β-blocker (BB) withdrawal was +2.1 ± 1.29 ($P < 0.001$). **(B)** The increase in the percentage of predicted peak oxygen consumption (peak Vo_2%) was +11.74 ± 2.32 ($P < 0.001$).



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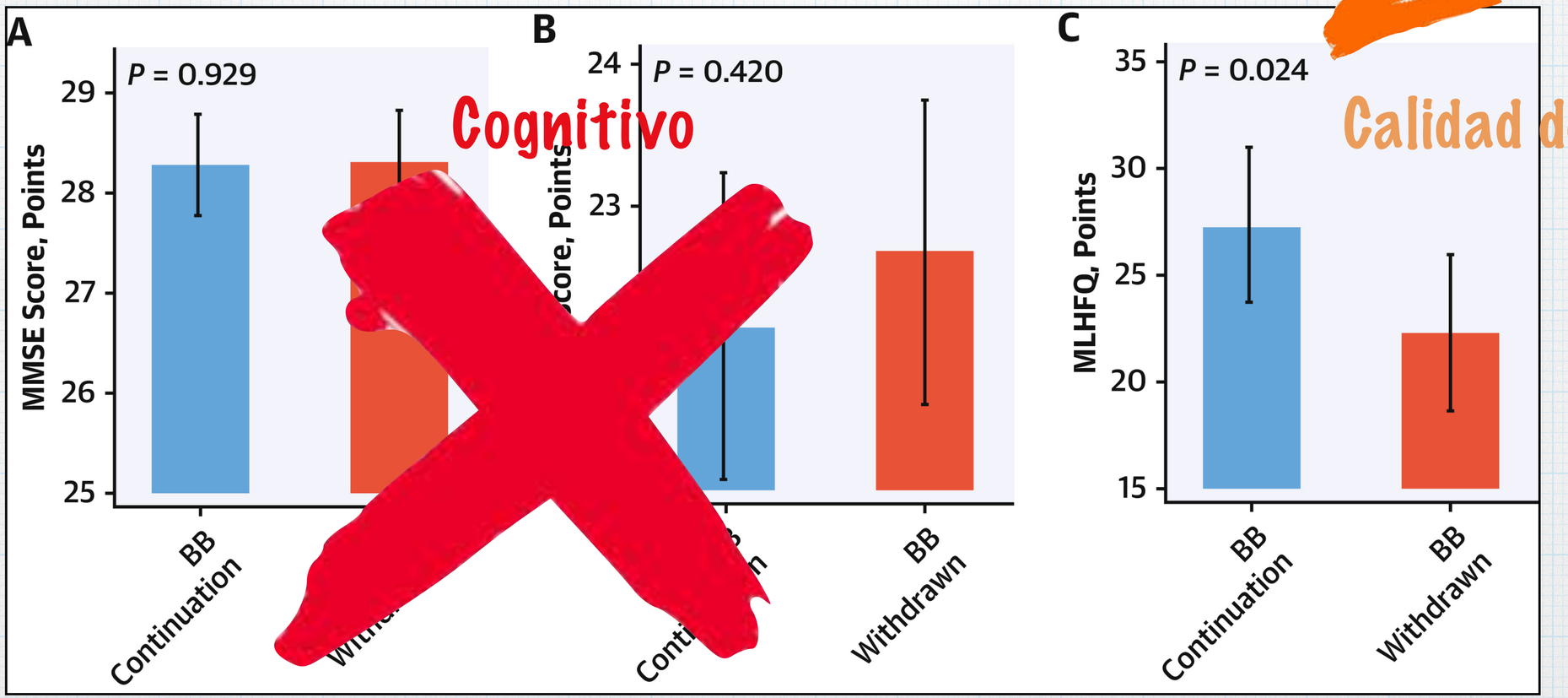

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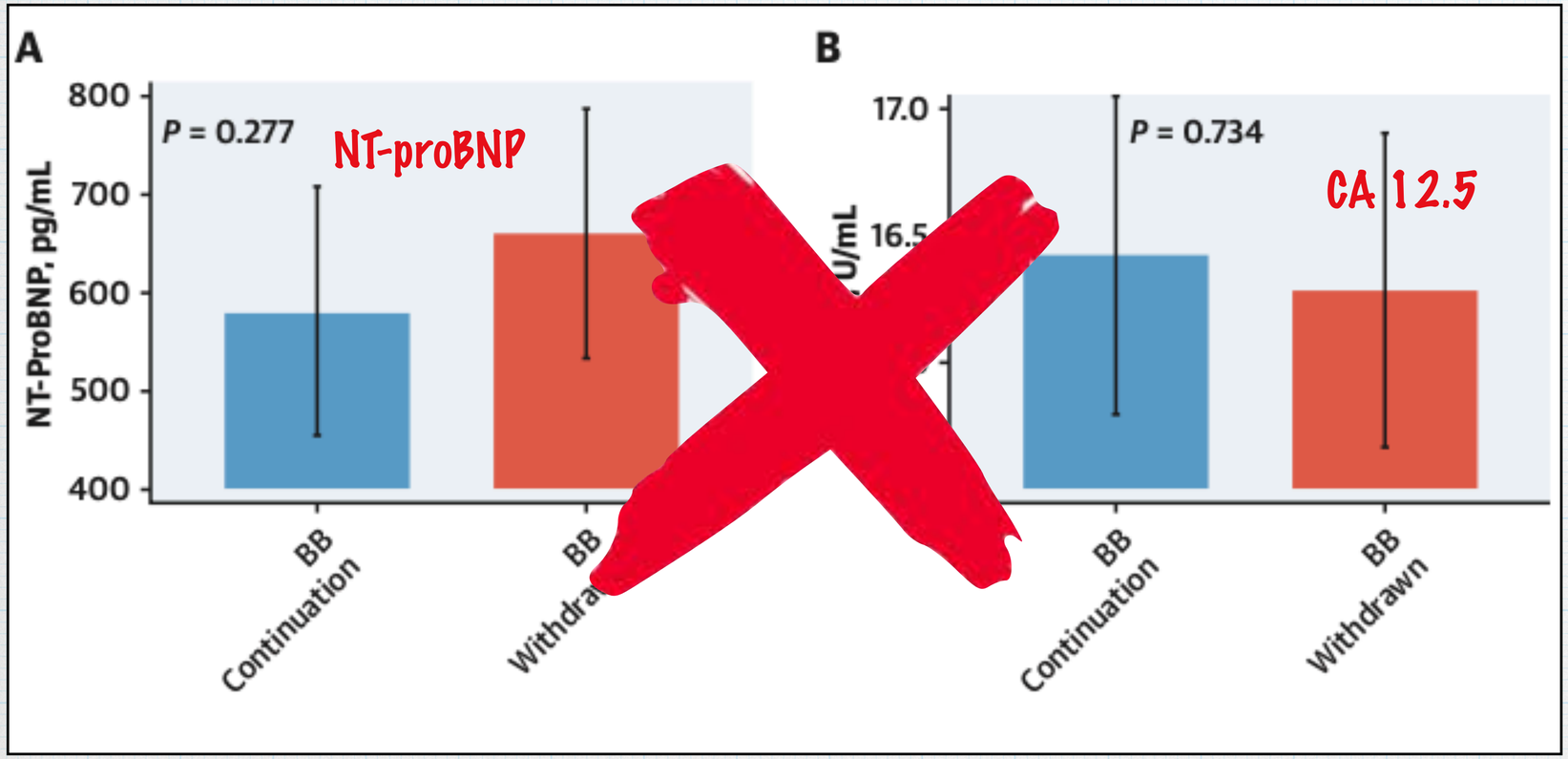

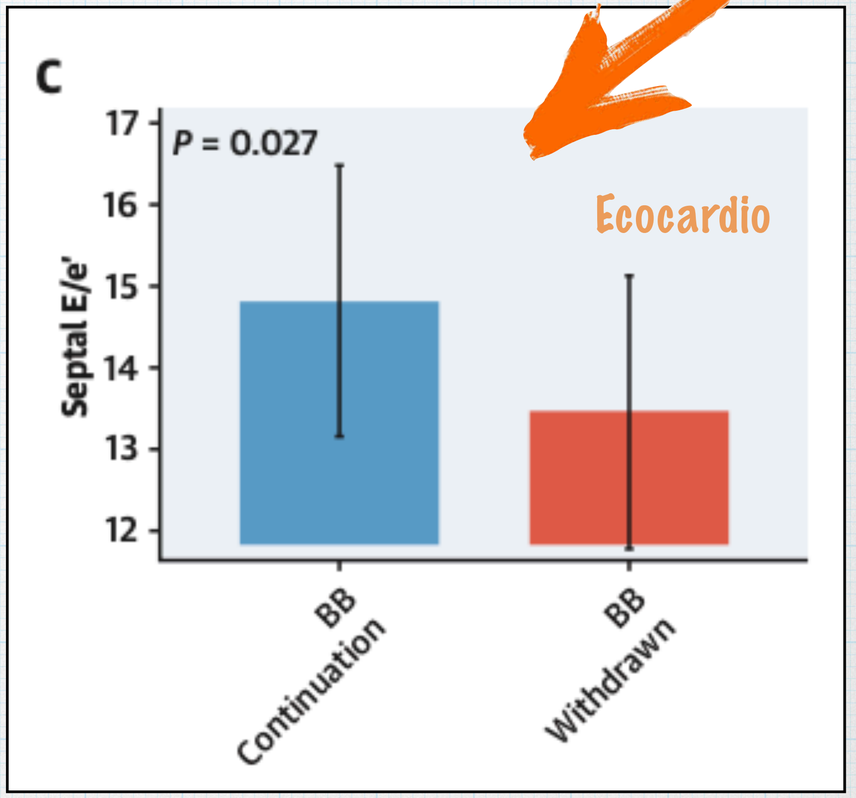

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Conclusiones

En IC con FEp + incompetencia cronotrópica al suspender el BB mejora el VO2 a corto plazo y la calidad de vida.

* Pocos pacientes y "muy bien controlados" y "escogidos"
* No es "ciego"
* Proporción 1:1 (ni a eso llega)
* Mala reproducibilidad en el día a día
* Repercusión clínica y/o funcional a medio-largo plazo


EL GOBIERNO POR FIN
EMPIEZA A HACER CAFÉS MASIVOS
CAFÉS