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Corticosteroids in the Acute Respiratory Distress Syndrome

Dr. Hamidreza Jamaati

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Corticosteroids in the Acute Respiratory Distress Syndrome

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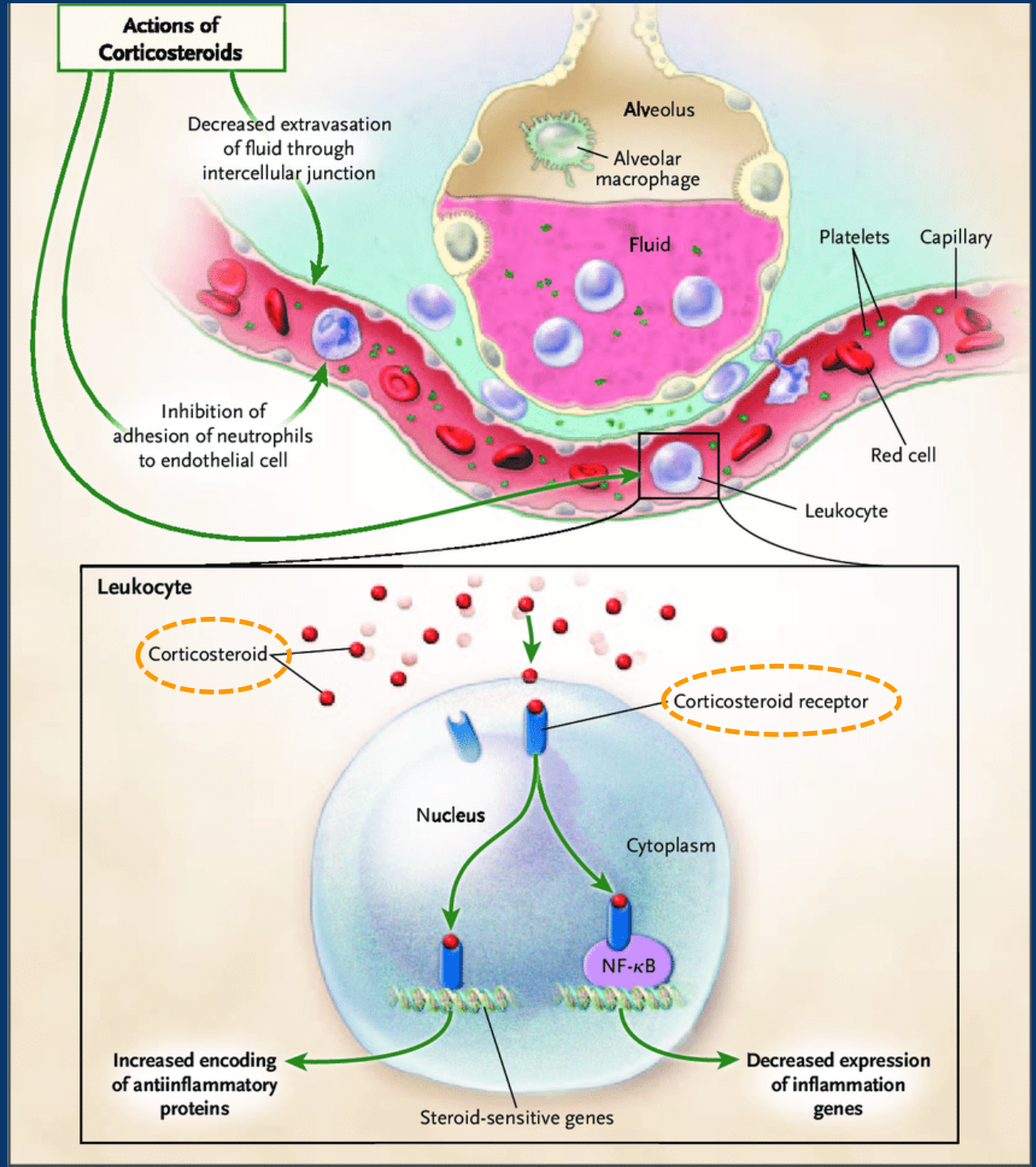
Essences From
ERS Congress 2021

Lung inflammation in ARDS – Friend or foe?



Peter M. Suter
NEJM 2006, 354:1739-42

Corticosteroids can decrease the signs and symptoms of inflammation

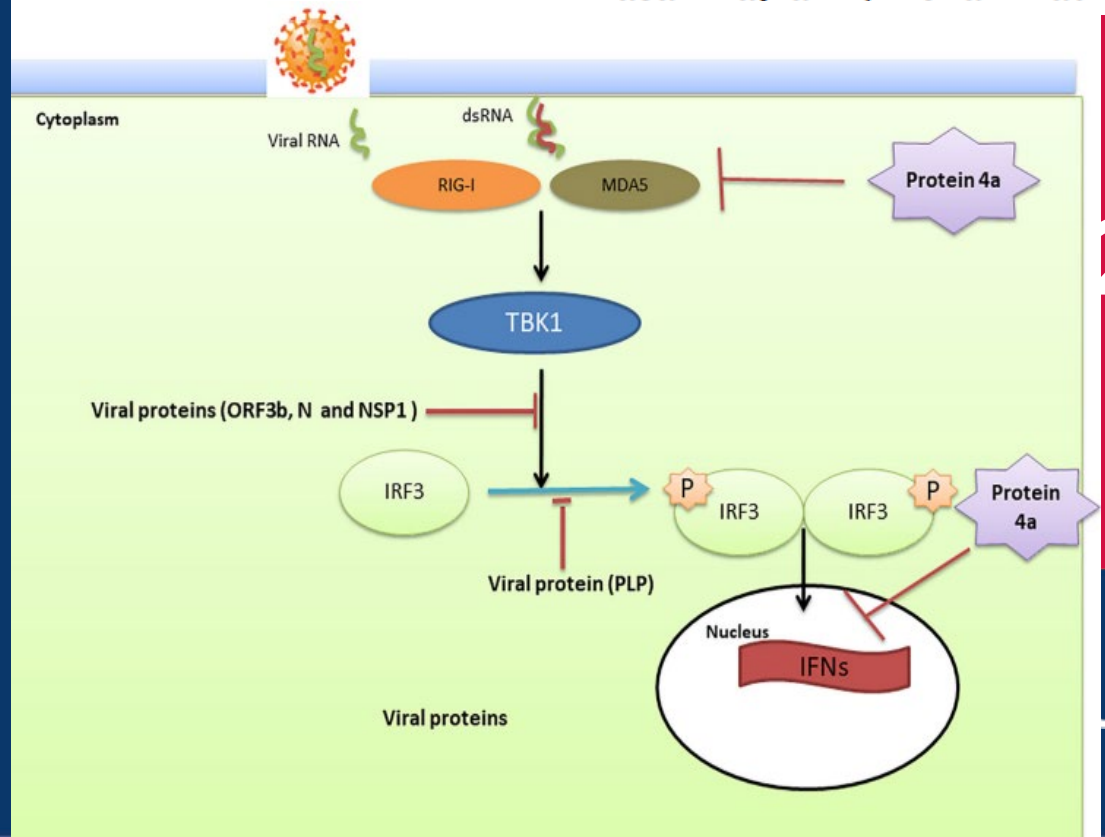
- Reducing the extravasation of plasma through intercellular junctions of the capillary
- Inhibiting the adhesion and migration of leukocytes across the capillary wall
- Corticosteroids diffuse across leukocyte cell membranes and bind to glucocorticoid receptors in the cytoplasm.
- The activated corticosteroid–receptor complexes translocate into the nucleus, which may encode anti-inflammatory proteins
- Activated nuclear corticosteroid receptors also inhibit, or switch off, inflammation genes, thereby blocking the transcription of inflammatory proteins by nuclear factor-κB (NF-κB) and activator protein 1

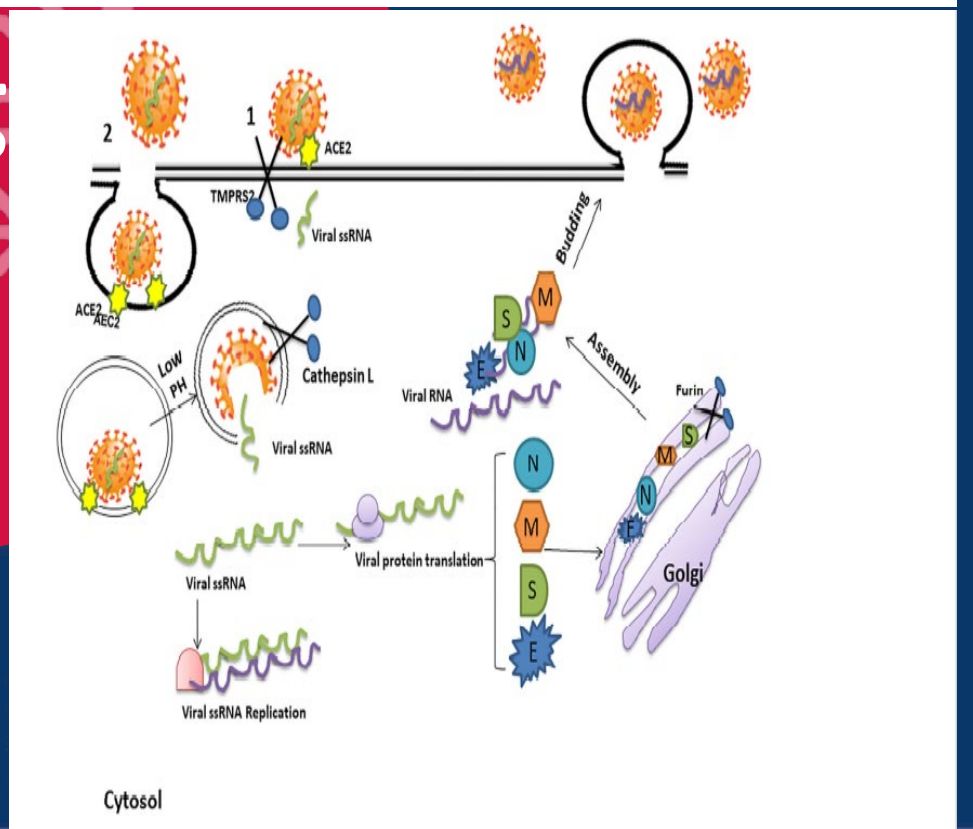
frontiers in Cellular and Infection Microbiology

REVIEW
published: 11 February 2021
doi: 10.3389/fcimb.2021.563085

COVID-19: Molecular and Cellular Response

Shamila D. Alipoor[1], Esmaeil Mortaz[2,3], Hamidreza Jamaati[4], Payam Tabarsi[2], Hasan Bayram[5], Mohammad Varahram[6] and Ian M. Adcock[7,8]*



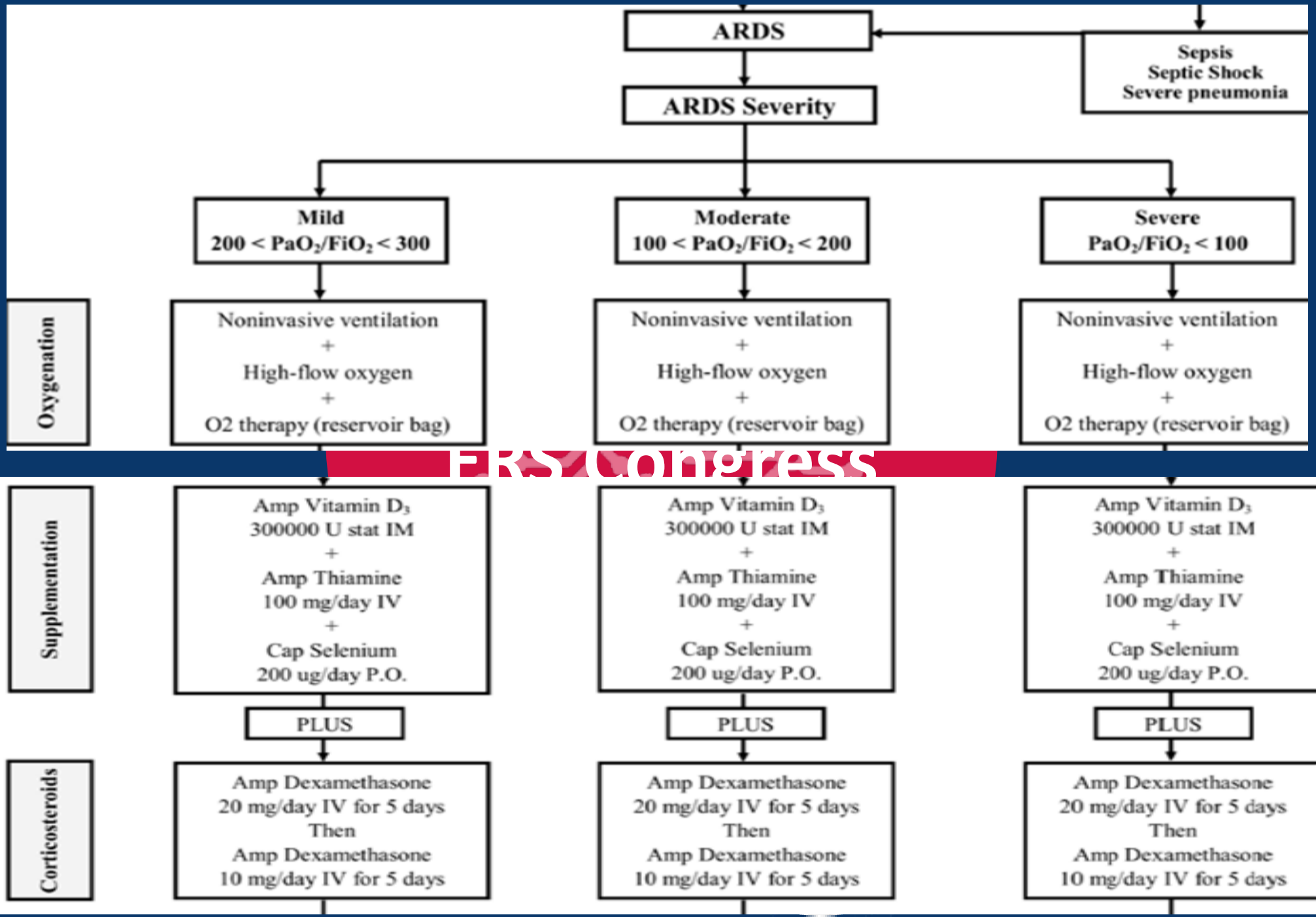


Iranian Journal of Pharmaceutical Research (2020), 19 (1): 31-36
DOI: 10.22037/ijpr.2020.113337.14239
Received: March 2020
Accepted: March 2020

Original Article

A Fourteen-day Experience with Coronavirus Disease 2019 (COVID-19) Induced Acute Respiratory Distress Syndrome (ARDS): An Iranian Treatment Protocol

Hamidreza Jamaati[a], Farzaneh Dastan[a, b*], Payam Tabarsi[c], Majid Marjani[c], Ali Saffaei[d] and Seyed MohammadReza Hashemian[a*]



COVID-19-Related Severe Heterogeneous Acute Respiratory Distress Syndrome: A Therapeutic Challenge

Hamidreza Jamaati[1], Lida Fadaizadeh[2], Batoul Khoundabi[3], Seyed Mohammad Reza Hashemian[1], Fatemeh Monjazabi[4], Alireza Jahangirifard[1], Mohammad Taghi Beigmohammadi[5], Behrooz Farzanegan[6], Seyedpouzhia Shojaei[7], Payam Tabarsi[8], Farzaneh Dastan[1,9], Seyed Ali Reza Nadji[10], Mihan Pourabdollah Toutkaboni[11], Majid Malekmohammad[6], Abdolreza Mohamadnia[1], Esmail Mortaz[12], Maryam Mirenayat[13], Fatemeh Yassari[14], Jalal Heshmatnia[14], Alireza Eslaminejad[1], Ali Akbar Velayati[15]

Table 2: Transpulmonary thermodilution technique results and mortality in patients requiring further assessment

Items	L Type (n=18)	H Type (n=18)		P
	Assessment required (n=6)	Assessment required (n=10)		
	EVLWI <10 and PVPI <3	Ha (n=5) EVLWI <10 and PVPI <3	Hb (n=5) EVLWI >10 and PVPI >3	
Mean EVLWI (ml/kg) (range)	8.8±1.3 (6.9-9.7)	8.7±0.8 (7.5-9.8)	17.5±1.9 (15.7-20.6)	<0.050*
Mean PVPI (range)	2.4±0.1 (2.2-2.6)	2.6±0.3 (2.1-2.8)	3.9±0.4 (3.5-4.5)	<0.050*
Mortality before assessment and intervention (3±1 days)	3 (16.7)	8 (44.4)		0.048$
Total mortality	6 (33.3)	15 (83.3)		0.002$

*Significant at level 0.05 for the comparison of three groups, $Significant at level 0.05 for two group high and low compliance. L Type: Compliance >40 and decrease in the elastance. H Type: Compliance <40 and increase in the elastance. EVLWI: Extravascular lung water index, PVPI: Pulmonary vascular permeability index

Intensive Care Med (2020) 46:2200–2211
https://doi.org/10.1007/s00134-020-06192-2

ORIGINAL

Clinical features, ventilatory management, and outcome of ARDS caused by COVID-19 are similar to other causes of ARDS

Carlos Ferrando[1,2*], Fernando Suarez-Sipmann[2,3,4], Ricard Mellado-Artigas[1], María Hernández[5], Alfredo Gea[6], Egoitz Arruti[7], César Aldecoa[8], Graciela Martínez-Pallí[1], Miguel A. Martínez-González[9,10], Arthur S. Slutsky[11,12] and Jesús Villar[2,11,13] on behalf of the COVID-19 Spanish ICU Network

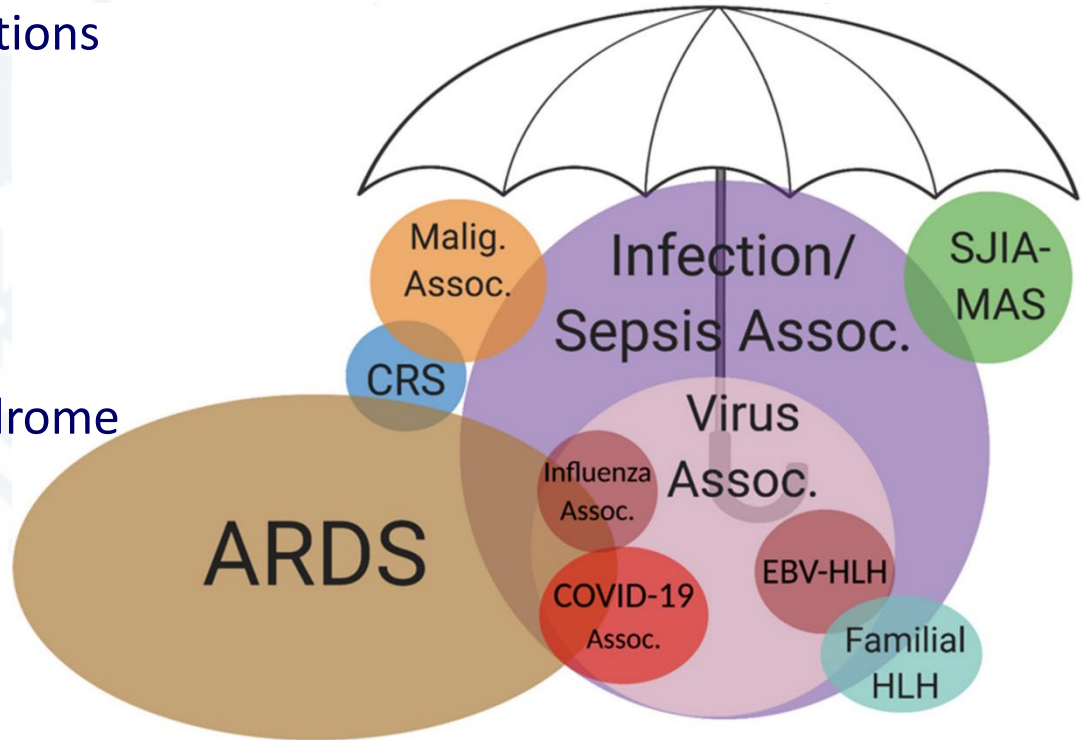
Corticosteroids in the Acute Respiratory Distress Syndrome

- Actions of corticosteroids
- Cytokine Storm Syndromes
- Determinants of clinical efficacy of corticosteroids in ARDS
- DEXA-ARDS trial
- Recovery trial
- WHO REACT meta-analysis
- Corticosteroids in ARDS. More questions than answers
- Takeaways

Cytokine Storm Syndromes: *An Umbrella Term*

Types of Cytokine Storm Syndromes

- Malig. Assoc.: malignancy associations
- CRS: cytokine release syndromes
- ARDS: acute respiratory distress syndrome
- SJIA: systemic juvenile idiopathic arthritis
- MAS: macrophage activation syndrome
- EBV: Epstein-Barr virus
- HLH: hemophagocytic lymphohistiocytosis



Henderson et al, Arthritis & Rheumatology 2020, 72:1059; Tothova Z et al, J Intensive Care Med 2015, 30:401

Determinants of clinical efficacy of corticosteroids in ARDS

Timing of initiation: early better than late.

Dosage: sufficient to achieve close to maximal saturation of glucocorticoid receptor (MP 80-100 mg, DEXA 20 mg).

Mode of administration: iv bolus and/or continuous infusion.

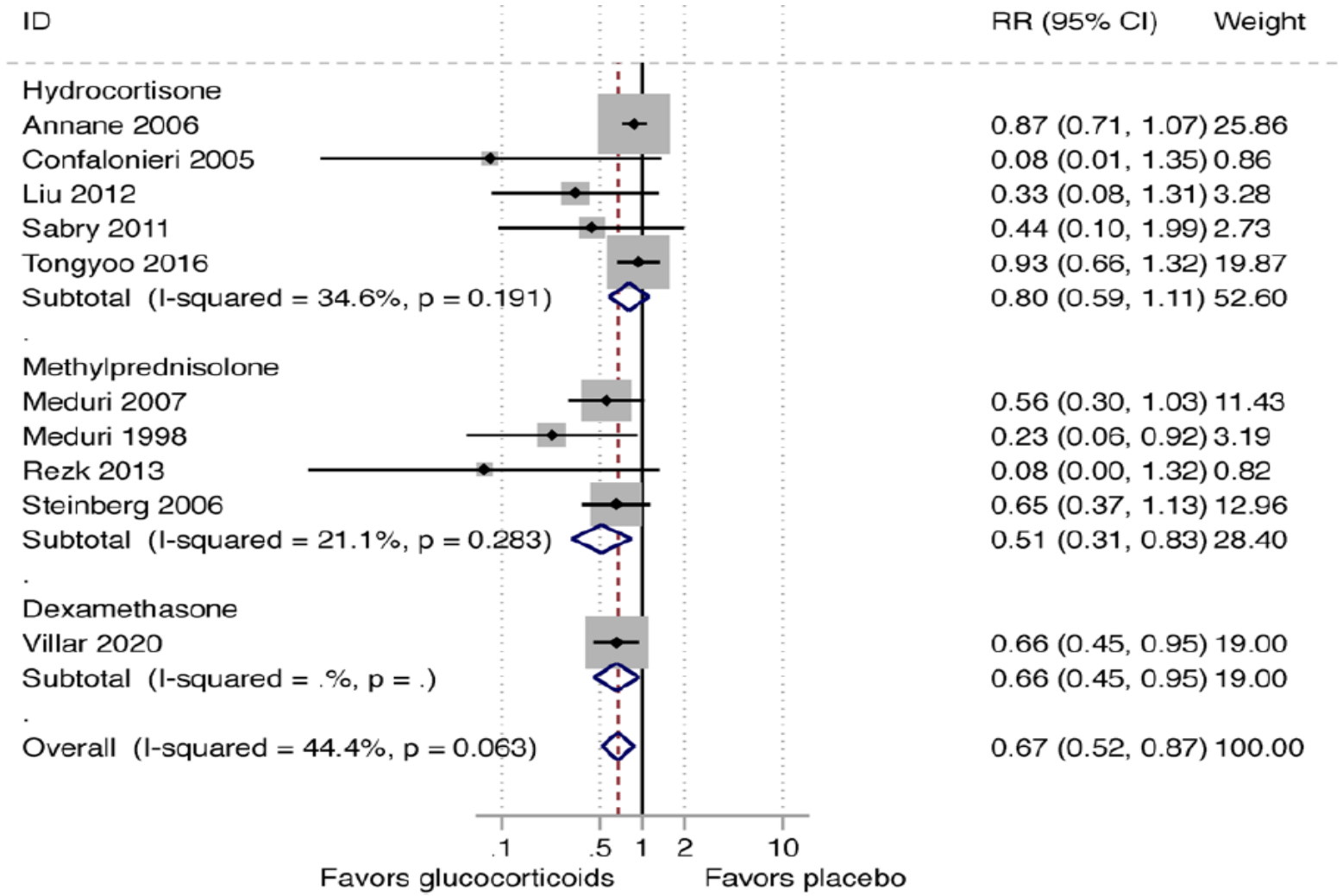
Duration of exposure: no concerns about higher doses or prolonged (up to 28 days) treatment.

Dose tapering: gradual de-escalation to avoid inflammation rebound (when prolonged therapy).

Meduri et al, Intensive Care Med 2020, 46:2284-96; Meduri et al, Intensive Care Med 2021

Hospital mortality in ARDS patients without COVID-19 randomized before day 14

10 RCTs, 1093 patients, 8 countries *Villar et al, Crit Care Expl 2020, 2:e0111*



The aggregate data from 10 RCTs (n = 1,093)

- CST is associated with a sizable reduction in duration of MV and hospital mortality

- Prolonged CST on reduction of ventilator dependence and hospital mortality

RCTs of corticosteroids in ARDS

(Arulkumaran et al, ICM 2020, 26:2108)

Author (Year)	Enrolment criteria & No. Patients	Initiation timing	Corticosteroids	Risk ratio for death
Meduri et al (1998)	AEC definition & LIS 24 patients	After 7 days of MV	MP: 2 mg/kg x 14 days then tapering	0.05 (0-0.78)
Steinberg et al (2006)	P/F <200 180 patients	Between days 7 and 28	MP: 0.5 mg/kg 6 hourly x 14 d then tapering	1.02 (0.65-1.62)
Meduri et al (2007)	AEC definition 91 patients	Within 72 h	MP: 1 mg/kg/day x 14 d then tapering	1.25 (0.9-1.74)
Liu et al (2012)	P/F ≤ 200 26 patients	Within 72 h	HC: 300 mg/day for 7 days	0.33 (0.08-1.31)
Rezk et al (2013)	P/F ≤ 200 27 patients	Within 48 h	MP: 1 mg/kg/day x 14 days then tapering	0.08 (0.0-1.32)
Tongyoo et al (2016)	AEC definition 197 patients	Within 12 h	HC: 50 mg 6 hourly x 7 days	0.86 (0.6-1.23)
Villar et al (2020)	P/F ≤ 200 277 patients	Within 24 h	DEXA: 20 mg/day x 5 days then 10 mg/day x 5 days	0.58 (0.39-0.85)
Recovery trial (2020)	COVID-19 requiring MV 1007	Not stated	DEXA: 6 mg/day x up to 10 days (median 6 days)	0.64 (0.51-0.81)

Dexamethasone treatment for the acute respiratory distress syndrome: a multicenter, randomized controlled trial

JesúsVillarMD[acd]CarlosFerrandoMD[abe]DomingoMartínezMD[f]AlfonsoAmbrósMD[g]TomásMuñozMD[h]Juan ASolerMD[f]GerardoAguilarMD[e]FranciscoAlbaMD[i]ElenaGonzález-HigueraMD[j]Luís AConesaMD[f]CarmenMartín-RodríguezMD[g]Francisco JDíaz-DomínguezMD[k]PabloSerna-GrandeMD[h]RosanaRivasMD[l]JoséFerreresMD[m]JavierBeldaMD[e]LucíaCapillaMD[no]AlecTalletMD[p]…JesúsVillar

Summary

Background

There is no proven specific pharmacological treatment for patients with the acute respiratory distress syndrome (ARDS). The efficacy of corticosteroids in ARDS remains controversial.

Methods

We did a multicenter, randomized controlled trial in a network of 17 intensive care units (ICUs) in teaching hospitals across Spain in patients with established moderate-to-severe ARDS

Patients with brain death, terminal-stage disease, or receiving corticosteroids or immunosuppressive drugs were excluded.

Patients in the dexamethasone group received an intravenous dose of 20 mg once daily from day 1 to day 5, which was reduced to 10 mg once daily from day 6 to day 10

Dexamethasone treatment for the acute respiratory distress syndrome: a multicenter, randomized controlled trial

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Findings

Between March 28, 2013, and Dec 31, 2018, we enrolled 277 patients and randomly assigned 139 patients to the dexamethasone group and 138 to the control group.

At 60 days, 29 (21%) patients in the dexamethasone group and 50 (36%) patients in the control group had died (between-group difference −15·3% [–25·9 to −4·9]; p=0·0047).

The proportion of adverse events did not differ significantly between the dexamethasone group and control group.

The most common adverse events were hyperglycaemia in the ICU (105 [76%] patients in the dexamethasone group *vs* 97 [70%] patients in the control group), new infections in the ICU (eg, pneumonia or sepsis; 33 [24%] *vs* 35 [25%]), and barotrauma (14 [10%] *vs* 10 [7%]).

Interpretation

Early administration of dexamethasone could reduce duration of mechanical ventilation and overall mortality in patients with established moderate-to-severe ARDS

THE LANCET
Respiratory Medicine

QUESTION Does treatment with systemic dexamethasone provide clinical benefit in adults with **established** moderate-to-severe acute respiratory distress syndrome (ARDS)?

CONCLUSION This randomized trial found that in patients with ARDS, intravenous dexamethasone administered for 10 days, compared with no-dexamethasone, resulted in significant reduction in ventilator-free days over 28 days and number of deaths over 60 days.

POPULATION

191 men
86 women

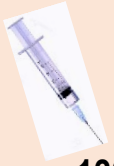
Adults with established moderate to severe ARDS ($PaO_2/FiO_2 \leq 200$ on a PEEP-FiO_2 trial at 24 h of meeting Berlin criteria.

Mean age: **57** years

LOCATIONS

17 ICUs
in 15 cities
of Spain

INTERVENTION



277 patients randomized

139 Dexamethasone

10 intravenous doses:
20 mg/day (day 1-5),
10 mg/day (day 6-10)

138 Control

No dexamethasone

Lung-protective ventilation in both groups

PRIMARY OUTCOME

Number of ventilator-free days at 28 days.

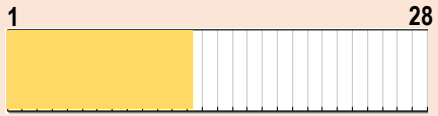
SECONDARY OUTCOME

All-cause mortality 60 days after randomization.

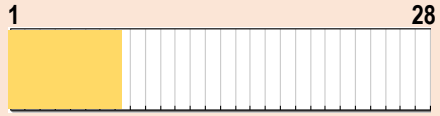
FINDINGS

Ventilator-free days (VFDs)

Dexamethasone
Mean VFDs
12.3 days



Control
Mean VFDs
7.5 days



Absolute difference: **4.8 days** (95% CI: 2.6 - 7.0)

All-cause mortality at day 60

Dexamethasone	**21%**	(29/139)
Control	**36%**	(50/138)

Absolute difference: **-15%** (95% CI: -26 to -5)

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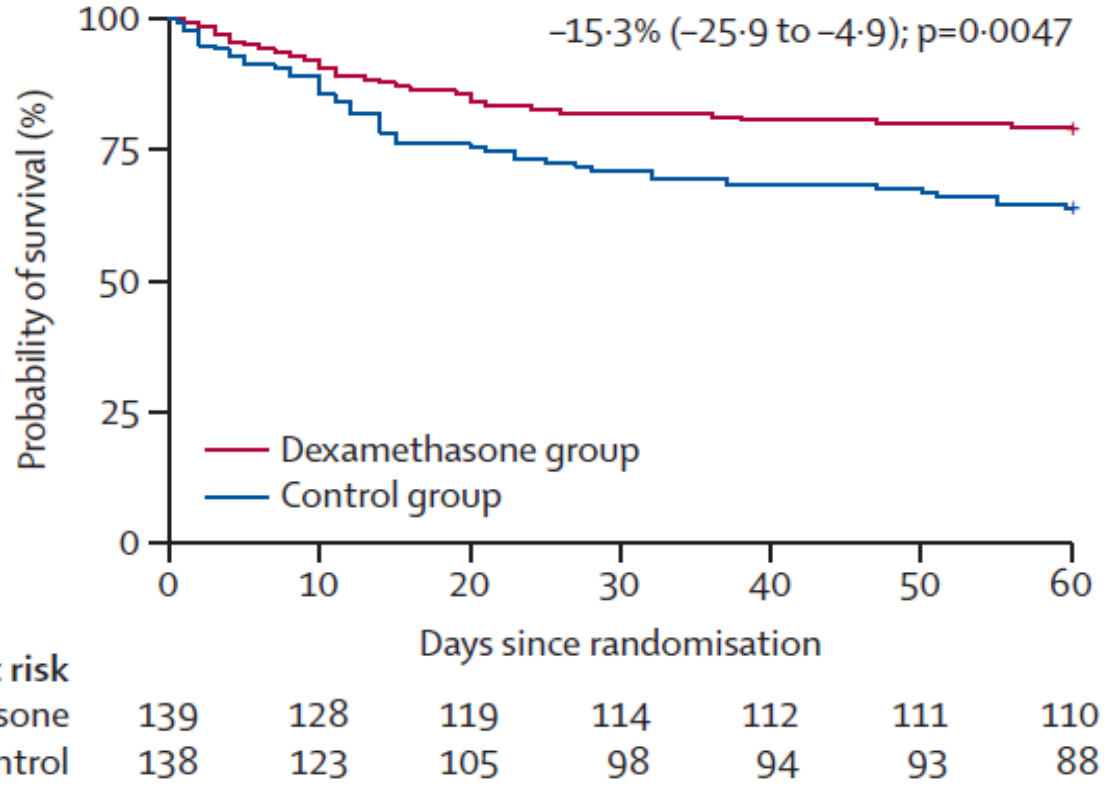
Villar J, Ferrando C, Martínez D, et al; DEXA in ARDS Network. Dexamethasone treatment for the acute respiratory distress syndrome: a multicentre, randomised controlled trial. Lancet Respir Med 2020, 8:267-76.

Dexamethasone treatment for the acute respiratory distress syndrome: a multicentre, randomised controlled trial

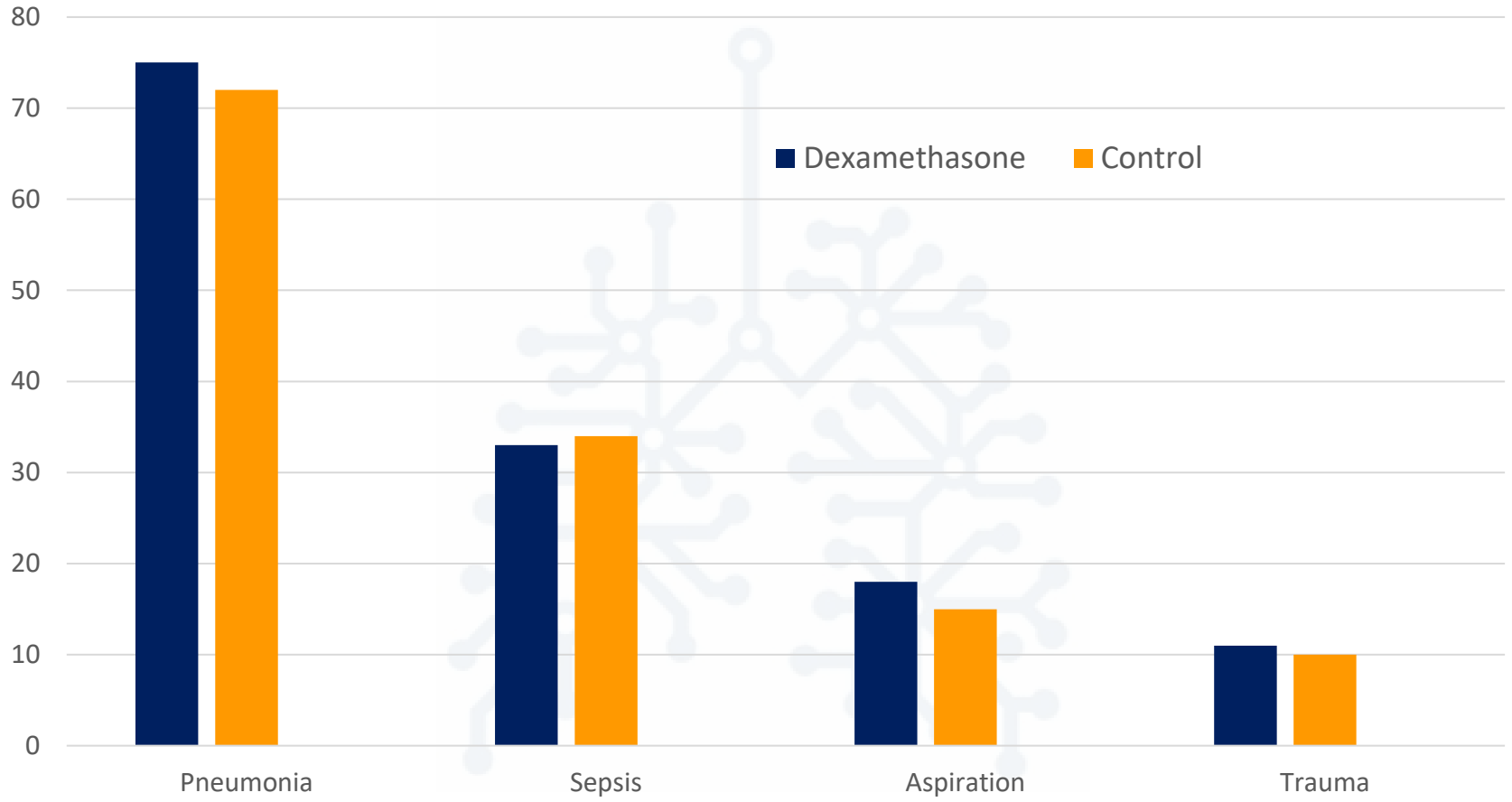
*Jesús Villar, Carlos Ferrando, Domingo Martínez, Alfonso Ambrós, Tomás Muñoz, Juan A Soler, Gerardo Aguilar, Francisco Alba, Elena González-Higueras, Luís A Conesa, Carmen Martín-Rodríguez, Francisco J Díaz-Domínguez, Pablo Serna-Grande, Rosana Rivas, José Ferreres, Javier Belda, Lucía Capilla, Alec Tallet, José M Añón, Rosa L Fernández, Jesús M González-Martín for the dexamethasone in ARDS network**



Number at risk							
Dexamethasone	139	128	119	114	112	111	110
Control	138	123	105	98	94	93	88

Lancet Respir Med 2020; 8: 267–76

Main causes of ARDS



Debate: Subgroup analyses in clinical trials – fun to look at, but don't believe them!

Peter Sleight

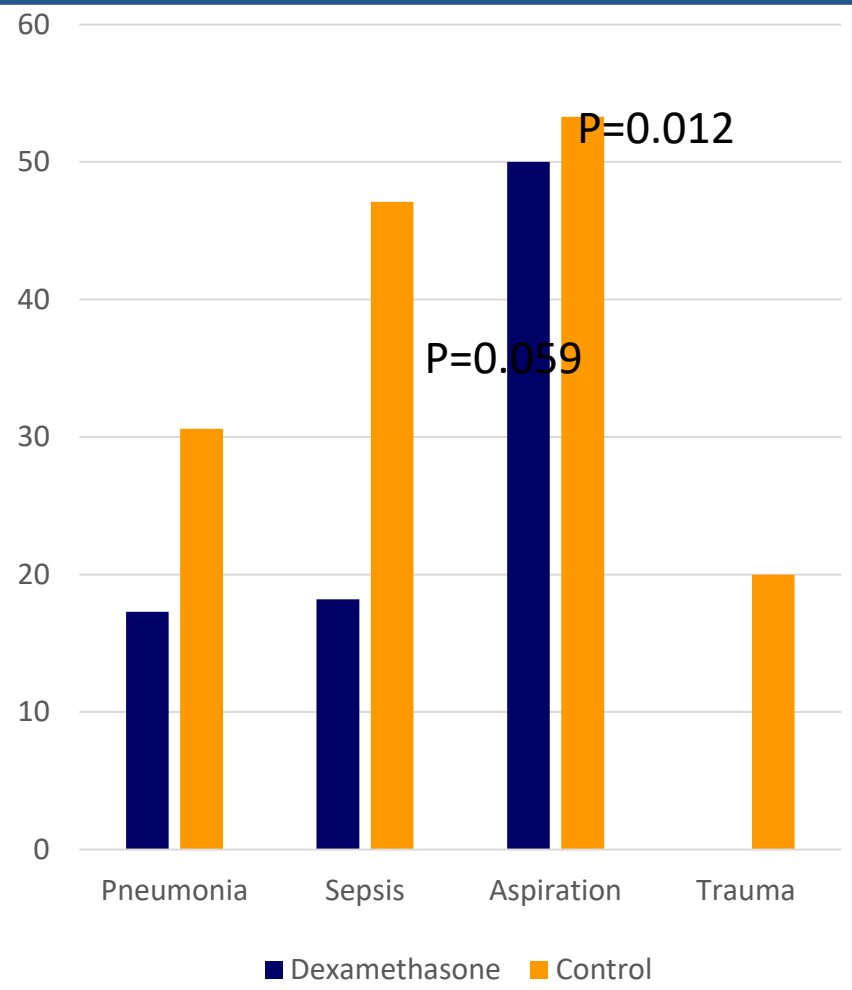
John Radcliffe Hospital, Oxford, UK

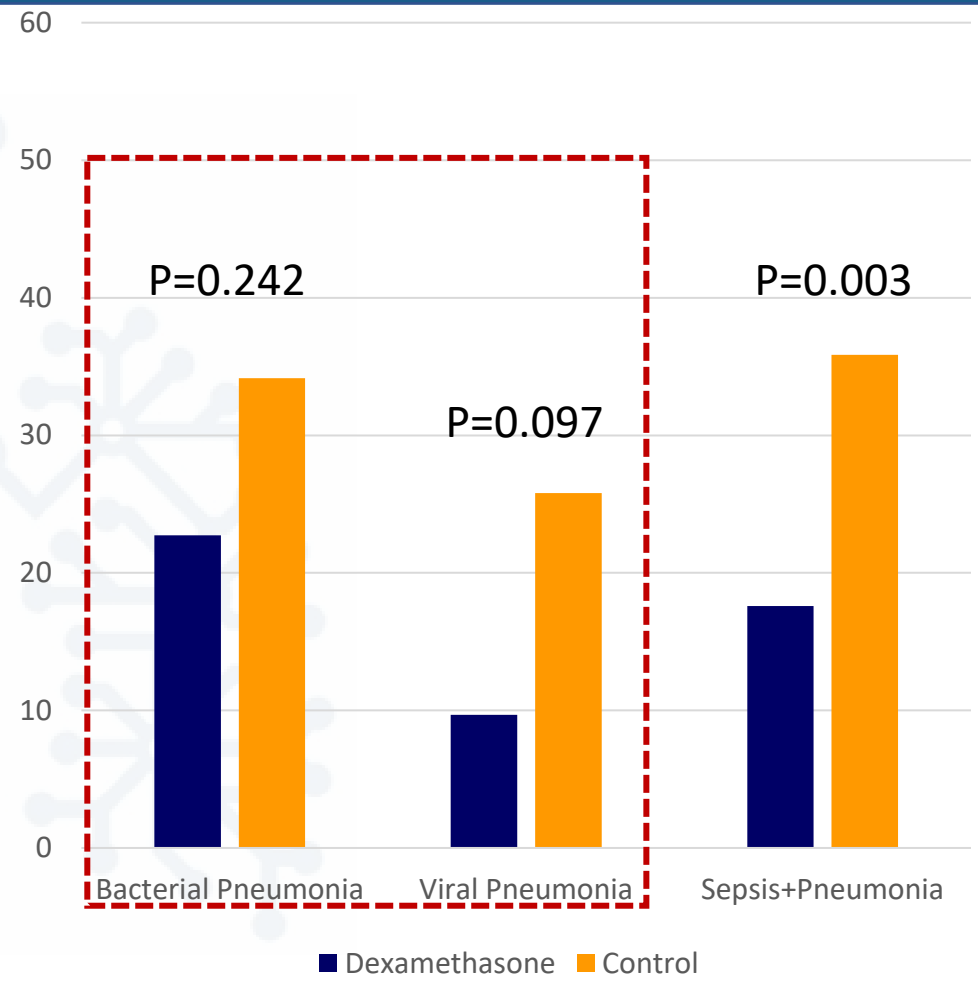
Curr Control Trials Cardiovasc Med 2000, 1:25-7

- Analysis of subgroups results in a clinical trial is unreliable, even in a large trial.
- This is the result of a combination of:
  - Reduced statistical power
  - Increased variance
  - Play of chance
- The lack of a statistically significant effect is not evidence of lack of a real effect.

> **"Subgroup-specific trial mortality results can provide wrong answers for individualising patient care"**
>
> R. Peto *(British J Cancer 2011, 104:1057-8)*

DEXA-ARDS trial: 60-day all-cause mortality (%) by etiology





Villar J, Ferrando C, Martínez D, et al; DEXA in ARDS Network. Dexamethasone treatment for the acute respiratory distress syndrome: a multicentre, randomised controlled trial. Lancet Respir Med 2020, 8:267-76.

Dexamethasone in Hospitalized Patients with Covid-19 — Preliminary Report

The RECOVERY Collaborative Group*

Multicenter (176), randomized controlled, open-label (March–June 2020). Dexamethasone: 6 mg/day x 10 days

Respiratory Support at Randomization	Dexamethasone	Usual Care	Rate Ratio (95% CI)
	no. of events/total no. (%)		
Invasive mechanical ventilation	95/324 (29.3)	283/683 (41.4)	0.64 (0.51–0.81)
Oxygen only	298/1279 (23.3)	682/2604 (26.2)	0.82 (0.72–0.94)
No oxygen received	89/501 (17.8)	145/1034 (14.0)	1.19 (0.91–1.55)
All Patients	**482/2104 (22.9)**	**1110/4321 (25.7)**	**0.83 (0.75–0.93)**
			P<0.001

Chi-square trend across three categories: 11.5

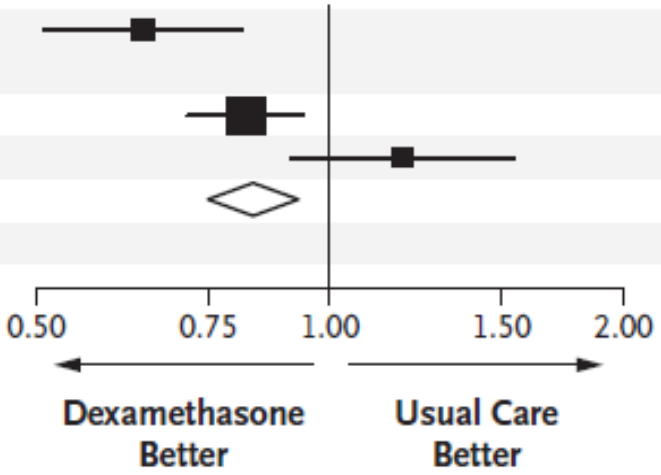


Figure 3. Effect of Dexamethasone on 28-Day Mortality, According to Respiratory Support at Randomization.

Table 2. Primary and Secondary Outcomes.

Outcome	Dexamethasone (N=2104)	Usual Care (N=4321)	Rate or Risk Ratio (95% CI)*
	no./total no. of patients (%)		
Primary outcome			
Mortality at 28 days	482/2104 (22.9)	1110/4321 (25.7)	0.83 (0.75–0.93)
Secondary outcomes			
Discharged from hospital within 28 days	1413/2104 (67.2)	2745/4321 (63.5)	1.10 (1.03–1.17)
Invasive mechanical ventilation or death†	456/1780 (25.6)	994/3638 (27.3)	0.92 (0.84–1.01)
Invasive mechanical ventilation	102/1780 (5.7)	285/3638 (7.8)	0.77 (0.62–0.95)
Death	387/1780 (21.7)	827/3638 (22.7)	0.93 (0.84–1.03)

Meta-Analysis: Steroids in COVID-19

7 RCTs, 1703 patients, 12 countries

Table 1. Characteristics of Included Trials

	DEXA-COVID 19	CoDEX	RECOVERY	CAPE COVID	COVID STEROID	REMAP-CAP	Steroids-SARI[a]
ClinicalTrials.gov identifier	NCT04325061	NCT04327401	NCT04381936	NCT02517489	NCT04348305	NCT02735707	NCT04244591
Planned sample size	200	350	NA	290	1000	NA[b]	80
Eligibility criteria	• Intubation • Mechanical ventilation • Moderate to severe ARDS per Berlin criteria[9] • Confirmed COVID-19	• Intubation • Mechanical ventilation • Moderate to severe ARDS per Berlin criteria[9] • Onset of ARDS <48 h before randomization • Probable or confirmed COVID-19	Criteria[c] used for this meta-analysis: Intubation Suspected or confirmed COVID-19	• Minimal severity • Admitted to ICU or intermediate care unit • Oxygen (≥6 L/min) • Probable or confirmed COVID-19	• Oxygen (≥10 L/min) • Confirmed COVID-19	• Admitted to ICU receiving high-flow nasal oxygen with Fio_2 ≥0.4 at ≥30 L/min, noninvasive or invasive ventilatory support, or receiving vasopressors • Probable or confirmed COVID-19	• Admitted to ICU with Pao_2:Fio_2 <200 mm Hg on positive pressure ventilation (invasive or noninvasive) or high-flow nasal canulae >45 L/min • Confirmed COVID-19
Corticosteroid							
Drug name	Dexamethasone	Dexamethasone	Dexamethasone	Hydrocortisone	Hydrocortisone	Hydrocortisone	Methylprednisolone
Dosage and administration	20 mg/d intravenously × 5 d and then 10 mg/d intravenously × 5 d	20 mg/d intravenously × 5 d and then 10 mg/d intravenously × 5 d	6 mg/d orally or intravenously	Continuous intravenous infusion × 8 d or 14 d (200 mg/d × 4 d or 7 d; 100 mg/d × 2 d or 4 d; 50 mg/d × 2 d or 3 d)	200 mg/d intravenously × 7 d (continuous or bolus dosing every 6 h)	50 mg intravenously every 6 h × 7 d[d]	40 mg intravenously every 12 h × 5 d
Dose classification	High	High	Low	Low	Low	Low	High
Control intervention	Usual care	Usual care	Usual care	Placebo	Placebo	Usual care	Usual care
Primary outcome	60-d mortality	Ventilator-free days	28-d mortality	21-d treatment failure (death or persistent requirement for mechanical ventilation or high-flow oxygen therapy)	Days alive without life support at 28 d	Composite of hospital mortality and ICU organ support-free days to 21 d	Lower lung injury score at 7 d and 14 d
Mortality outcome, d	28	28	28	21	28	28	30
Serious adverse event definitions	• Secondary infections of pneumonia, sepsis, or other similar • Pulmonary embolism	• Mortality • Infections • Insulin use	• Cause-specific mortality • Ventilation • Dialysis • Cardiac arrhythmia (in a subset) • Other that were believed to be related to study treatment	• Any • Excluded some listed in protocol • Excluded expected adverse events related to the patient's disease or comorbidity	• New episodes of septic shock (Sepsis-3 criteria) • Invasive fungal infection • Clinically important gastrointestinal bleeding • Anaphylaxis	• Per ICH good clinical practice guidelines (events not already captured as a trial end point; eg, mortality) • When the event may reasonably have occurred because of study participation	• Secondary bacterial infections • Barotrauma • Severe hyperglycemia • Gastrointestinal bleeding requiring transfusion • Acquired weakness
Location	Spain	Brazil	UK	France	Denmark	Australia, Canada, European Union, New Zealand, UK, US	China

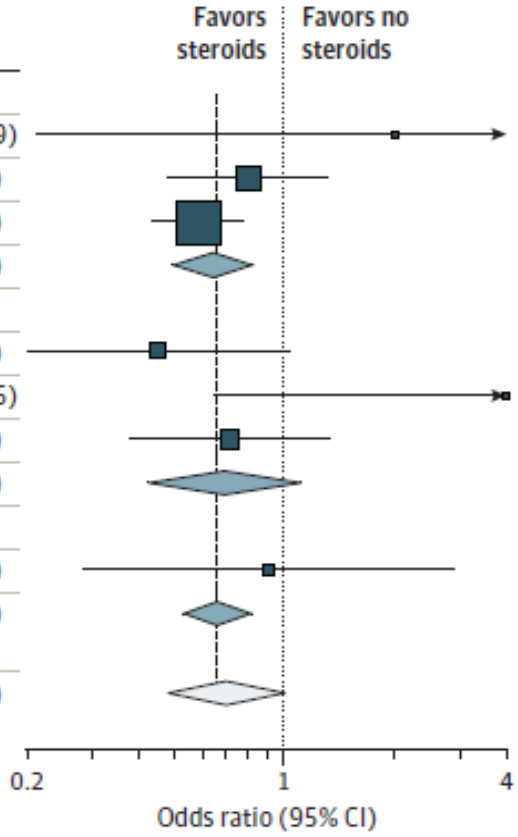
WHO Rapid Evidence Appraisal for COVID-19 Therapies (REACT) Working Group, et al. JAMA 2020, 324:1330-41

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

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

Drug and trial	ClinicalTrials.gov identifier	Initial dose and administration	No. of deaths/total No. of patients: Steroids	No. of deaths/total No. of patients: No steroids	Odds ratio (95% CI)
Dexamethasone					
DEXA-COVID 19	NCT04325061	High: 20 mg/d intravenously	2/7	2/12	2.00 (0.21-18.69)
CoDEX	NCT04327401	High: 20 mg/d intravenously	69/128	76/128	0.80 (0.49-1.31)
RECOVERY	NCT04381936	Low: 6 mg/d orally or intravenously	95/324	283/683	0.59 (0.44-0.78)
Subgroup fixed effect			166/459	361/823	0.64 (0.50-0.82)
Hydrocortisone					
CAPE COVID	NCT02517489	Low: 200 mg/d intravenously	11/75	20/73	0.46 (0.20-1.04)
COVID STEROID	NCT04348305	Low: 200 mg/d intravenously	6/15	2/14	4.00 (0.65-24.66)
REMAP-CAP	NCT02735707	Low: 50 mg every 6 h intravenously	26/105	29/92	0.71 (0.38-1.33)
Subgroup fixed effect			43/195	51/179	0.69 (0.43-1.12)
Methylprednisolone					
Steroids-SARI	NCT04244591	High: 40 mg every 12 h intravenously	13/24	13/23	0.91 (0.29-2.87)
Overall (fixed effect) $P = .31$ for heterogeneity; $I^2 = 15.6\%$			222/678	425/1025	0.66 (0.53-0.82)
Overall (random effects[a])			222/678	425/1025	0.70 (0.48-1.01)



Sterne et al, JAMA 2020, 324:1330-41

Intensive Care Med (2021) 47:521–537 https://doi.org/10.1007/s00134-021-06394-2

Corticosteroids in COVID-19 and non-COVID-19 ARDS: a systematic review and meta-analysis

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Purpose

Corticosteroids are now recommended for patients with severe COVID-19 including those with COVID related ARDS. This has generated renewed interest regarding whether corticosteroids should be used in non-COVID ARDS as well.

The main outcome for this review was 28-day-mortality

Results

We included 18 RCTs enrolling 2826 patients. The use of corticosteroids probably reduced mortality in patients with ARDS of any etiology (2740 patients in 16 trials, RR 0.82, 95% CI 0.72–0.95, ARR 8.0%, 95% CI 2.2–12.5%, moderate certainty). Patients who received a longer course of corticosteroids (over 7 days) had higher rates of survival compared to a shorter course

Conclusion

The use of corticosteroids probably reduces mortality in patients with ARDS. This effect was consistent between patients with COVID-19 and non-COVID-19 ARDS, corticosteroid types, and dosage

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No clinical benefit of high dose corticosteroid administration in patients with COVID-19: A preliminary report of a randomized clinical trial

Hamidreza Jamaati [a], Seyed MohammadReza Hashemian [a], Behrooz Farzanegan [b], Majid Malekmohammad [b], Payam Tabarsi [c], Majid Marjani [c], Afshin Moniri [d], Zahra Abtahian [a], Sara Haseli [a], Esmaeil Mortaz [c,e], Alireza Dastan [f], Abdolreza Mohamadnia [a], Abdolbaset Vahedi [a], Fatemeh Monjazebi [g], Fatemeh Yassari [a], Lida Fadaeizadeh [h], Ali Saffaei [i], Farzaneh Dastan [a,j,*]

The aim of this study was to evaluate the clinical effects of dexamethasone administration in patients with mild to moderate acute respiratory distress syndrome (ARDS) due to coronavirus disease 2019 (COVID-19).

RESULT

No significant differences were observed in the other outcomes. This study showed that corticosteroid administration had no clinical benefit in patients with COVID-19-induced mild to moderate ARDS.

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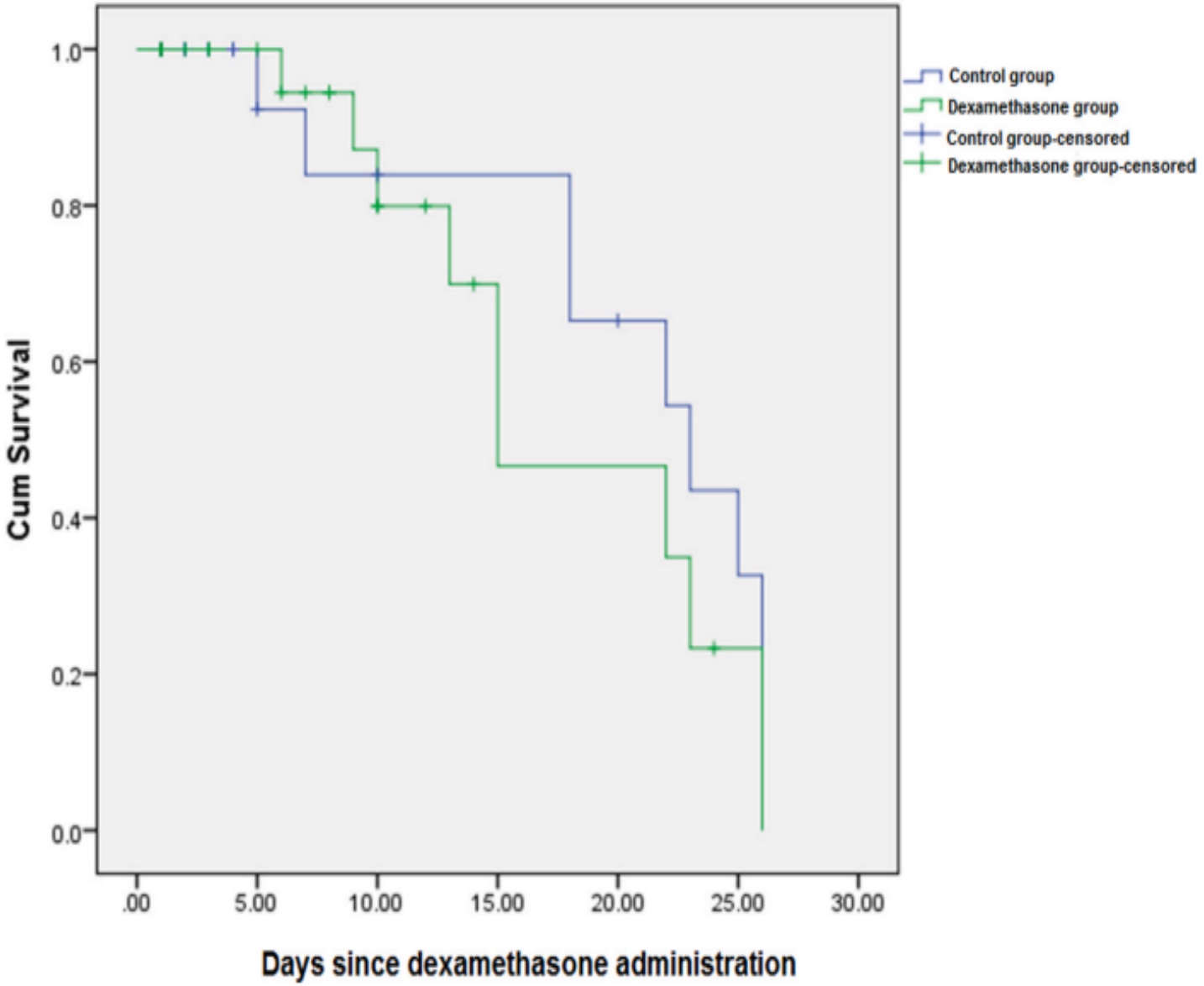

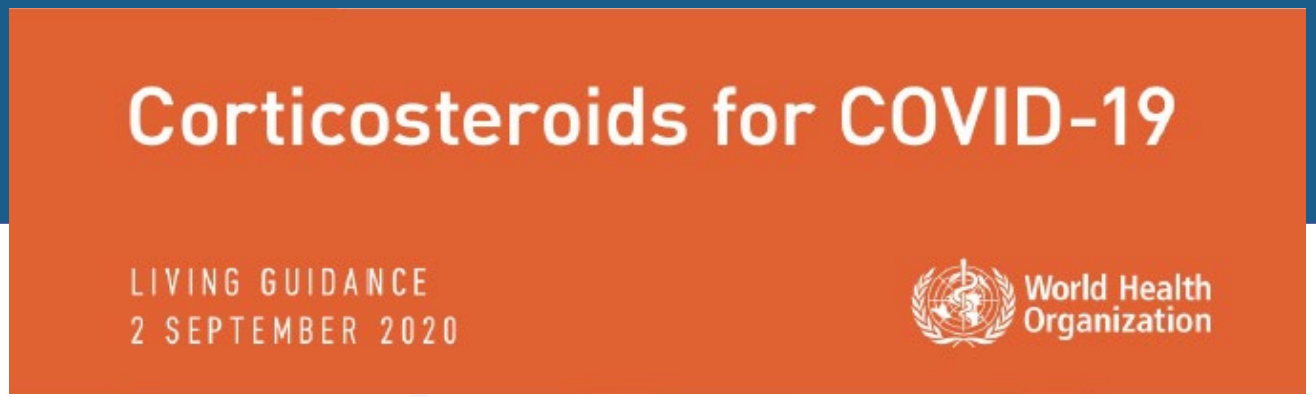

Understanding the recommendations

Recommendation 1:
We recommend systemic corticosteroids rather than no corticosteroids for the treatment of patients with severe and critical COVID-19 (strong recommendation, based on moderate certainty evidence).

Recommendation 2:
We suggest not to use corticosteroids in the treatment of patients with non-severe COVID-19 (conditional recommendation, based on low certainty evidence).

WHO website. Corticosteroids for COVID-19. 2020.

Ten reasons why corticosteroid therapy reduces mortality in severe COVID-19

José M. Añón[1,2*] and Jesús Villar[2,3]

*Intensive Care Med 2021**

Why a dose of 6 mg was selected in the RECOVERY trial?

Reporting overall all-cause mortality

DEXA-ARDS: ICU, hospital, and 60-day
RECOVERY: 28-day
WHO REACT meta-analysis: 5 at 28-day, 1 at 21-day, 1 at 30-day

Management: MV vs. Non-invasive MV vs. Oxygen

No definitive conclusions: type of corticosteroids, timing of initiation, optimum dose, duration of treatment, etc.

IT IS TIME to know the LONG-TERM outcome data of RECOVERY trial.

**Commentary to a paper by Arabi et al (Intensive Care Med 2020, 46:2067)*

Corticosteroids in ARDS: More questions than answers

Which one?	When?	Dose?	How long?
Methylprednisolone Hydrocortisone Dexamethasone	At ARDS onset Within 24 hours	Low dose Medium dose Higher dose	10 vs 14 vs 28 days With/without tapering
DEXAMETHASONE merits priority	At ARDS onset *(if intubated)* merits further attention	Near corticosteroid receptor saturation merits attention	10 days merits priority

New RCTs addressing dosage, duration, type of corticosteroids, and dose tapering

NCT04509973: COVID STEROID 2 (Higher vs. Lower Doses of Dexamethasone in Patients with COVID-19 and Severe Hypoxia)

NCT04545242: DEXA-REFINE (Efficacy of Higher vs. Lower Doses of Dexamethasone in Patients with Acute Hypoxemic Respiratory Failure Caused by Infections).

NCT04636671: MEDEAS (Methylprednisolone vs. Dexamethasone in COVID-19 Pneumonia).

Concluding Remarks

Key

- We have STRONG evidence that corticosteroids can reduce the risk of death in patients with ARDS.
- We have STRONG evidence that corticosteroids can reduce the risk of death in patients with non-ARDS AHRF.

Takeaways

We DO NOT have strong evidence for when to initiate and for how long to use corticosteroids in ARDS.

Whether DEXAMETHASONE is the corticosteroid of choice in ARDS merits further studies.

Thank You

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