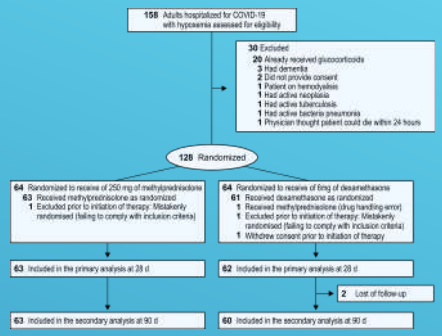
Effect of intravenous pulses of methylprednisolone 250 mg versus dexamethasone 6 mg in hospitalized adults with severe but not critical COVID-19 pneumonia: an open-label randomized trial.

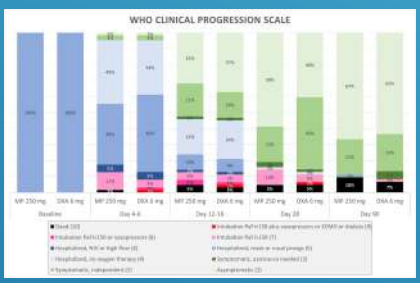
Dueñas Gutiérrez C, Abadía-Otero J, Cusacovich I, Martín-González JI, Muela-Molinero A, Corral-Gudino L, González-Fuentes R, Ruíz de Temiño A, Tapia Moral E, Cuadrado-Medina F, Martín-Asenjo M, Miramontes González P, Delgado Morales JL, Inés S, Abad-Manteca L, Usategui-Martín I, Ruíz-Albí T, Miranda-Riaño S, Rodríguez-Fortúnez P, Rodríguez-Jiménez C, López-Franco E, Marcos M, MP3 pulses COVID-19 collaborative group

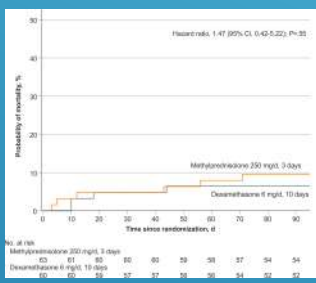
Rationale: Pulse glucocorticoid therapy is used in COVID-19 infection. We evaluated the effectiveness of methylprednisolone 250 mg/d for 3 days vs. dexamethasone 6 mg/d for 10 days in patients with severe but not critical COVID-19 pneumonia.

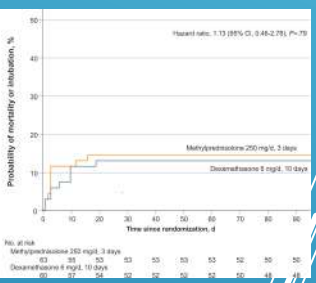
Methods: A multicentre, randomized, open-label, controlled trial was conducted between February 2021 and August 2021 at 4 hospitals in Spain and included 128 hospitalized adults with confirmed COVID-19 pneumonia needing oxygen therapy but not critically ill. Patients were randomly assigned in a 1:1 ratio to receive dexamethasone 6 once daily for 10 days or methylprednisolone 250 mg once daily for 3 days. The primary outcome was 28-day mortality.



Results: Of the 128 randomized patients, 125 were analysed (mean age 60 ± 17 years; 82 males [66%]). Mortality at 28 days was 4.8% in the 250 mg methylprednisolone group vs. 4.8 % in the 6 mg dexamethasone group (absolute risk difference, 0.1% [95% CI, -8.8 to 9.1%]; *P*=0.98). The post-hoc added composite outcome of mortality at 90 days or intubation was 15.9% in the 250 mg methylprednisolone group vs. 15% in the 6 mg dexamethasone group (absolute risk difference, -0.9% [95% CI, -13.8 to 12.3%]; *P*=0.83). Hyperglycaemia was more frequent in the methylprednisolone group, at 27.0 vs. 8.1 % (absolute risk difference, -18.9% [95% CI, -31.8 to - 5.6%]; *P*=0.007).







Subgroup	Mortality within 90 d or intubation: Methylprednisolone Events	Total	Dexamethasone Events	Total	Absolute risk difference (95% CI)	*P* value for heterogeneity
Age						
≥ 70 years	8	23	5	20	-10% [-37% to 17%]	.22
< 70 years	2	40	4	40	5% [-6% to 16%]	
Days since symptom onset						
< 7 days	5	24	5	23	1% [-23% to 24%]	.86
≥ 7 days	5	39	4	37	-2% [-17% to 12%]	
Level of inflammation						
High inflammation	9	41	7	46	-7% [-23% to 10%]	.20
Non high inflammation	1	22	2	14	10% [-11% to 30%]	
Vaccination state						
Non vaccinated	7	49	7	54	-1% [-15% to 12%]	.55
Vaccinated	3	14	2	6	12% [-32% to 55%]	
All patients	**10**	**63**	**9**	**60**	-1% [-14% to 12%]	

Conclusions: Among severe but not critical patients with COVID-19, 250 mg/d for 3 days of methylprednisolone compared with 6 mg/d for 10 days of dexamethasone did not result in a decrease in mortality or intubation.

Trial registration: EUDRA CT (2020-005026-28), Clinicaltrials.gov (NCT04780581).
Funded by the Institute of Health Science Research of Castilla y Leon (IECSCYL) and the Institute for Biomedical Research of Salamanca (IBSAL).