Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: The RECOVERY Collaborative Group. Dexamethasone in hospitalized patients with Covid-19 — preliminary report. N Engl J Med. DOI: 10.1056/NEJMoa2021436

Effect of Dexamethasone in Hospitalized Patients with COVID-19 – Preliminary Report

SUPPLEMENTARY APPENDIX

RECOVERY Collaborative Group

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Supplementary Methods

Study organization

The RECOVERY trial is an investigator-initiated, individually randomized, open-label, controlled trial to evaluate the efficacy and safety of a range of putative treatments in patients hospitalized with COVID-19. The protocol is available at NEJM.org. The trial was conducted at 176 National Health Service (NHS) hospital organizations in the United Kingdom. The trial was coordinated by a team drawn from the Clinical Trial Service Unit and the National Perinatal Epidemiology Clinical Trials Unit within the Nuffield Department of Population Health at University of Oxford, the trial sponsor. Support for local site activities was provided by the National Institute for Health Research Clinical Research Network.

Treatment supply to local sites was supported by National Health Service (NHS) England and Public Health England. Access to relevant routine health care and registry data was supported by NHS DigiTrials, the Intensive Care National Audit and Research Centre, Public Health Scotland, National Records Service of Scotland, and the Secure Anonymised Information Linkage (SAIL) at University of Swansea.

Protocol changes

RECOVERY is a randomized trial among patients hospitalized for COVID-19. All eligible patients receive usual standard of care in the participating hospital and are randomly allocated between no additional treatment and one of several active treatment arms. Over time, additional treatment arms have been added (see Table). In version 4.0 of the protocol, a second randomization was introduced for those trial participants with hypoxia (oxygen saturation <92% on air or receiving oxygen) and inflammation (C-reactive protein ≥75 mg/dL), comparing the addition of tocilizumab vs. control on top of the treatment assigned in the first randomization. In version 6.0, a factorial design was introduced to the first randomization such that participants were also randomized to convalescent plasma vs. no additional treatment. As outlined in the protocol, if one or more of the active treatments was not available at the hospital or is believed, by the attending clinician, to be contraindicated (or definitely indicated) for the specific patient, then random allocation was between the remaining treatment arms.

The original and final protocol are included in the supplementary material to this publication, together with summaries of the changes made.

Table. Protocol changes to treatment comparisons

Protocol version	Date	Randomization	Treatment arms
1.0	13-Mar-2020	Main (part A)	No additional treatment Lopinavir-ritonavir Low-dose corticosteroid Nebulised Interferon-ß-1a (never activated)
2.0	23-Mar-2020	Main (part A)	No additional treatment Lopinavir-ritonavir Low-dose corticosteroid Hydroxychloroquine
3.0	07-Apr-2020	Main (part A)	No additional treatment Lopinavir-ritonavir Low-dose corticosteroid Hydroxychloroquine Azithromycin

Protocol version	Date	Randomization	Treatment arms
4.0	14-Apr-2020	Main (part A)	No additional treatment Lopinavir-ritonavir Low-dose corticosteroid Hydroxychloroquine Azithromycin
		Second[a]	No additional treatment Tocilizumab
5.0	24-Apr-2020	-	(no change – extension to children <18 years old)
6.0	14-May-2020	Main (part A)	No additional treatment Lopinavir-ritonavir Low-dose corticosteroid[b] Hydroxychloroquine[c] Azithromycin
		Main (part B factorial)	No additional treatment Convalescent plasma
		Second[a]	No additional treatment Tocilizumab

[a] for patients with (a) oxygen saturation <92% on air or requiring oxygen or children with significant systemic disease with persistent pyrexia; and (b) C-reactive protein ≥75 md/dL)
[b] enrolment ceased 8 June 2020 as more than 2,000 patients had been recruited to the active arm
[c] enrolment ceased 5 June 2020 when the Data Monitoring Committee advised that the Chief Investigators review the unblinded data.

Ascertainment and classification of study outcomes
Information on baseline characteristics and study outcomes was collected through a combination of electronic case report forms (see below) completed by members of the local research team at each participating hospital and linkage to National Health Service, clinical audit, and other relevant health records. Full details are provided in the RECOVERY Definition and Derivation of Baseline Characteristics and Outcomes Document which was published online (www.recoverytrial.net) on 9 June 2020.

Randomisation form

The Randomisation form (shown below) was completed by trained study staff. It collected baseline information about the participant (including demographics, COVID-19 history, comorbidities and suitability for the study treatments) and availability of the study treatments. Once completed and electronically signed, the treatment allocation was displayed.

The following modifications were made to the Randomisation form during the trial:

Randomisation form version	Date of release	Major modifications from previous version
1.0	19-Mar-20	Initial version (protocol V1.0)
2.0	25-Mar-20	For protocol V2.0 • Hydroxycholoroquine added as treatment • Known long QT syndrome added to comorbidities • Severe depression removed from comorbidities
3.0	09-Apr-20	For protocol V3.0

		• Azithromycin added as treatment • Suspected SARS-CoV-2 infection included in eligibility criteria
[Second randomisation form introduced]	23-Apr-20	For protocol 4.0 • Eligibility criteria for second randomisation • Tocilizumab vs control as treatment allocations
4.0	09-May-20	For protocol V5.0 • Age ≥18 years removed from eligibility criteria • Additional questions on child's age and weight added
5.0	21-May-20	For protocol V6.0 • Convalescent plasma added as treatment
6.0	28-May-20	Baseline use of remdesivir
7.0	05-Jun-20	Removal of hydroxychloroquine as treatment

RECOVERY
Randomised Evaluation of COVID-19 Therapy

Test version only (v6.03 - 27/05/20)

Randomisation Program

Call Freefone **0800 138 5451** to contact the RECOVERY team for **URGENT** problems using the Randomisation Program or for medical advice. All **NON-URGENT queries** should be emailed to **recoverytrial@ndph.ox.ac.uk**

Logged in as: **Barts Health NHS Trust**

Section A: Baseline and Eligibility

Date and time of randomisation: 27 May 2020 11:17

Treating clinician

A1. Name of treating clinician

Patient details

A2. Patient surname

Patient forename

A3. NHS number ☐ Tick if not available

A4. What is the patient's date of birth? / /

A5. What is the patient's sex?

Inclusion criteria

A6. Has consent been taken in line with the protocol?
If answer is No patient cannot be enrolled in the study

A7. Does the patient have proven or suspected SARS-CoV-2 infection?
If answer is No patient cannot be enrolled in the study

A8. Does the patient have any medical history that might, in the opinion of the attending clinician, put the patient at significant risk if they were to participate in the trial?

A8B. Is the patient willing to receive convalescent plasma?

A9. COVID-19 symptom onset date: / /

A10. Date of hospitalisation: / /

A11. Does the patient require oxygen?

A12. Does the patient **CURRENTLY** require ventilation or ECMO?
Invasive mechanical ventilation or extra-corporeal membrane oxygenation

Does the patient have any CURRENT comorbidities or other medical problems?

A13.1 Diabetes

A13.2 Heart disease

A13.3 Chronic lung disease

A13.4 Tuberculosis

A13.5 HIV

A13.6 Severe liver disease

A13.7 Severe kidney impairment (eGFR<30 or on dialysis)

A13.8 Known long QT syndrome

A13.9 Current treatment with macrolide antibiotics which are to continue
Macrolide antibiotics include clarithromycin, azithromycin and erythromycin

A13.10 Previous adverse reaction to blood or blood product transfusion

Are the following treatments UNSUITABLE for the patient?
If you answer Yes it means you think this participant should NOT receive this drug.

A14.1 Lopinavir-Ritonavir

A14.2 Corticosteroids

A14.3 Hydroxychloroquine

A14.4 Azithromycin

A14B.1 Convalescent plasma

Are the following treatments available?

A15.1 Lopinavir-Ritonavir

A15.2 Corticosteroids

A15.3 Hydroxychloroquine

A15.4 Azithromycin

A15B.1 Convalescent plasma

Current medication

A16 Is the patient currently prescribed remdesivir?

Please sign off this form once complete

Surname:

Forename:

Professional email:

Continue

Cancel

Follow-up form

The Follow-up form (shown on the next page) collected information on study treatment adherence (including both the randomised allocation and use of other study treatments), vital status (including date and provisional cause of death if available), hospitalisation status (including date of discharge), respiratory support received during the hospitalisation, occurrence of any major cardiac arrhythmias and renal replacement therapy received.

The following modifications were made to the Follow-up form during the trial:

Follow-up form version	**Date of release**	**Modifications from previous version**
1.0	31-Mar-20	Initial version
2.0	09-Apr-20	Information on other treatments used during admission: • Azithromycin, IL-6 receptor antagonist Fact and result of SARS-CoV-2 PCR test
3.0	23-Apr-20	Duration of treatments added
4.0	12-May-20	Capture of major cardiac arrhythmias added
5.0	28-May-20	Information on other treatments used during admission: • Remdesivir, convalescent plasma

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Follow-up

Date of randomisation

Patient's date of birth

yyyy-mm-dd

1. Which of following treatment(s) did the patient definitely receive as part of their hospital admission after randomisation? *

(NB Include RECOVERY study-allocated drug, only if given, PLUS any of the other treatments if given as standard hospital care)

- [ ] No additional treatment
- [ ] Lopinavir-ritonavir
- [ ] Corticosteroid (dexamethasone, prednisolone or hydrocortisone)
- [ ] Hydroxychloroquine
- [ ] Azithromycin or other macrolide (eg, clarithromycin, erythromycin)
- [ ] Tocilizumab or sarilumab
- [ ] Remdesivir

The following questions only appear if the treatments have been allocated at randomisation

Please select number of days the patient received lopinavir-ritonavir

1 2 3 4 5 6 7 8 9 10

Please select number of days the patient received corticosteroid (dexamethasone, prednisolone or hydrocortisone)

1 2 3 4 5 6 7 8 9 10

Please select number of days the patient received hydroxychloroquine

1 2 3 4 5 6 7 8 9 10

Please select number of days the patient received azithromycin

This question and the following question cannot both be zero

0 1 2 3 4 5 6 7 8 9 10

Please select number of days the patient received other macrolides (eg, clarithromycin, erythromycin)

0 1 2 3 4 5 6 7 8 9 10

Please select number of doses of tocilizumab or sarilumab the patient received

1 >1

Please select number of days the patient received remdesivir

1 2 3 4 5 6 7 8 9 10

» Convalescent Plasma

How many convalescent plasma infusions did the patient receive?

This is plasma given as part of trial, not any standard fresh frozen plasma or other blood products that the patient may have been given

0 1 2

Were any infusions stopped early for any reason ie, the patient did not receive the full amount?

Yes No

How many were stopped early?

1 2

» Health Status

2. Was a COVID-19 test done for this patient?

(If multiple tests were done, and the results were positive and negative, please tick Yes – positive result and Yes – negative result)

- [ ] Yes – positive result
- [ ] Yes – negative result
- [ ] Not done

3. What is the patient's vital status? *

- Alive
- Dead

3.1 What is the patient's current hospitalisation status?

Q3.1 is only completed if the patients is alive at Q3

- Inpatient
- Discharged

The patient has been enrolled in the trial for **NaN** days

3.1.1 Date follow-up form completed **Q3.1.1 is only completed if patient is still an inpatient at Q3**

yyyy-mm-dd

3.1.1 What was the date of discharge? **Q3.1.1 is only completed if patient has been discharged at Q3**

yyyy-mm-dd

3.1 What was the date of death? **Q3.1.1 is only completed if patient has died at Q3** *

yyyy-mm-dd

3.2 What was the underlying cause of death? *

This can be obtained from the last entry in part 1 of the death certificate

- ◯ COVID-19
- ◯ Other infection
- ◯ Cardiovascular
- ◯ Other

Please give details

4. Did the patient require any form of assisted ventilation (ie, more than just supplementary oxygen)? *

- ◯ Yes
- ◯ No

Please answer the following questions:

4.1 For how many days did the patient require assisted ventilation? *

4.2 What type of ventilation did the patient receive?

	Yes	No	Unknown
CPAP alone	◯	◯	◯
Non-invasive ventilation (eg, BiPAP)	◯	◯	◯
High-flow nasal oxygen (eg, AIRVO)	◯	◯	◯
Mechanical ventilation (intubation/tracheostomy)	◯	◯	◯

ECMO	◯	◯	◯

Total number of days the patient received invasive mechanical ventilation (intubation/tracheostomy) (from randomisation until discharge/death/28 days after randomisation)

Complete if invasive mechanical ventilation (intubation/tracheostomy) is Yes

5. Has the participant been documented to have a NEW cardiac arrhythmia at any point since the main randomisation?

- ◯ Yes
- ◯ No
- ◯ Unknown

5.1 Please select all of the following which apply

If Q5 is answered Yes, you must select at least one option here

- ☐ Atrial flutter or atrial fibrillation
- ☐ Supraventricular tachycardia
- ☐ Ventricular tachycardia (including torsades de pointes)
- ☐ Ventricular fibrillation
- ☐ Atrioventricular block requiring intervention (eg, cardiac pacing)

6. Did the patient require use of renal dialysis or haemofiltration?

- ◯ Yes
- ◯ No

7. Please enter UKOSS case ID if known *

Enter the full UKOSS case ID ie, COR_123

Complete only if patient was pregnant at randomisation

(select if you do not know the UKOSS case ID)

- ☐ Not known

Interim analyses: role of the Data Monitoring Committee

The independent Data Monitoring Committee reviews unblinded analyses of the study data and any other information considered relevant at intervals of around 2 weeks. The committee is charged with determining if, in their view, the randomized comparisons in the study provide evidence on mortality that is strong enough (with a range of uncertainty around the results that was narrow enough) to affect national and global treatment strategies. In such a circumstance, the Committee would inform the Steering Committee who would make the results available to the public and amend the trial arms accordingly. Unless that happened, the Steering Committee, investigators, and all others involved in the trial would remain blind to the interim results until 28 days after the last patient had been randomized to a particular intervention arm. Further details about the role and membership of the independent Data Monitoring Committee are provided in the protocol.

The Data Monitoring Committee determined that to consider recommending stopping a treatment early for benefit would require at least a 3 to 3.5 standard error reduction in mortality. The Committee concluded that examinations of the data at every 10% (or even 5%) of the total data would lead to only a marginal increase in the overall type I error rate.

The Data Monitoring Committee met to review interim outcome data on dexamethasone on five occasions prior to being informed by the Steering Committee that recruitment to dexamethasone was to be stopped. With the requirement of a 3.5 standard error overall mortality benefit before a recommendation to stop would be made, this means that the alpha ‘spent’ at these interim analyses was only of the order of about 0.06% (hence the alpha preserved to claim significance at the final analysis was 4.94%).

Supplementary Tables

Table S1: Treatments given, by randomized allocation

	Treatment allocation	
	Dexamethasone (n=2104)	**Usual care (n=4321)**
Follow-up forms received	2079	4278
Treatments given		
Dexamethasone	1975 (95%)	336 (8%)
Lopinavir/ritonavir	2 (<0.5%)	4 (<0.5%)
Hydroxychloroquine	17 (1%)	22 (1%)
Azithromycin	499 (24%)	1082 (25%)
Tocilizumab or sarilumab	43 (2%)	128 (3%)
Not recorded	7 (<0.5%)	12 (<0.5%)

Percentages are of those with a completed follow-up form. Among patients allocated dexamethasone, it was taken for a median of 7 days [IQR 3-10 days].

Table S2: Impact of adjusting for the 1.1-year age imbalance between randomised arms on the estimated effect of allocation to dexamethasone on 28-day mortality, both in all randomized patients and in subgroups defined by respiratory support received at randomization

	Treatment allocation		Age-adjusted Cox regression*		One-step estimate†	
Subgroup	**Dexamethasone (n=2104)**	**Usual care (n=4321)**	**RR (95% CI)**	**p**	**RR (95% CI)**	**p**
No oxygen received	89/501 (17.8%)	145/1034 (14.0%)	1.19 (0.91-1.55)	0.20	1.30 (0.99-1.71)	0.06
Oxygen only	298/1279 (23.3%)	682/2604 (26.2%)	0.82 (0.72-0.94)	0.0042	0.86 (0.75-0.99)	0.0305
Invasive mechanical ventilation	95/324 (29.3%)	283/683 (41.4%)	0.64 (0.51-0.81)	0.0002	0.67 (0.54-0.84)	0.0003
All participants	**482/2104 (22.9%)**	**1110/4321 (25.7%)**	**0.83 (0.75-0.93)**	**0.0009**	**0.87 (0.78-0.97)**	**0.0089**

RR=rate ratio, CI=confidence interval. P-values shown to 2 dp if >0.05 and 4 dp if between 0.0001 and 0.05.

* Main analysis shown in Figures 2 and 3, in which the 28-day age-adjusted (ie, conditional) mortality rate ratio is estimated by the hazard ratio from a Cox regression analysis adjusted for age in three categories (<70 years, 70-79 years, and 80 years or older). With this analysis, a test for linear trend in the log RRs across the three respiratory support subgroups gives a chi-squared trend statistic of 11.5 (corresponding to a p-value for trend of 0.0007, or a 1 in ~1400 chance of observing effect modification this extreme by chance alone).

† Original pre-specified analysis without adjustment for the 1.1-year age-imbalance between the randomized groups. With this method the 'one-step' method is used to estimate the average unadjusted (ie, marginal) mortality rate ratio from the log-rank 'observed minus expected' statistic (O –E) and its variance (V), through the formula $\exp([O - E] \div V)$. Its 95% CI is then given by $\exp([O - E] \div V \pm 1.96 \div \sqrt{V})$. With this analysis, a test for linear trend in the log RRs across the three respiratory support subgroups gives a chi-squared trend statistic of 13.1 (corresponding to a p-value for trend of 0.0003, or a 1 in ~3300 chance of observing effect modification this extreme by chance alone).

Table S3: Baseline characteristics by randomized allocation, separately among those not receiving oxygen at randomization, those receiving oxygen only, and those on invasive mechanical ventilation

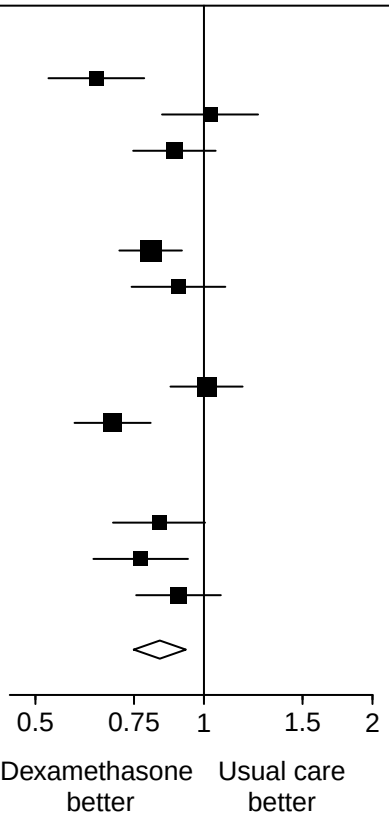
	No oxygen received		Oxygen only		Invasive mechanical ventilation	
	Dexamethasone (n=501)	**Usual care (n=1034)**	**Dexamethasone (n=1279)**	**Usual care (n=2604)**	**Dexamethasone (n=324)**	**Usual care (n=683)**
Age, years	71.1 (16.3)	68.5 (18.0)	67.2 (15.2)	66.4 (15.3)	58.8 (11.3)	59.2 (11.5)
<70	197 (39%)	462 (45%)	675 (53%)	1473 (57%)	269 (83%)	569 (83%)
≥70 to <80	114 (23%)	224 (22%)	306 (24%)	531 (20%)	49 (15%)	104 (15%)
≥80	190 (38%)	348 (34%)	298 (23%)	600 (23%)	6 (2%)	10 (1%)
Sex						
Male	286 (57%)	605 (59%)	819 (64%)	1643 (63%)	233 (72%)	501 (73%)
Female*	215 (43%)	429 (41%)	460 (36%)	961 (37%)	91 (28%)	182 (27%)
Number of days since symptom onset	6 (3-10)	7 (3-10)	8 (5-13)	9 (5-12)	13 (9-18)	13 (8-18)
Number of days since hospitalization	2 (1-6)	2 (1-5)	2 (1-4)	2 (1-4)	5 (3-10)	5 (3-9)
Previous diseases						
Diabetes	119 (24%)	223 (22%)	320 (25%)	630 (24%)	82 (25%)	172 (25%)
Heart disease	180 (36%)	339 (33%)	357 (28%)	717 (28%)	49 (15%)	115 (17%)
Chronic lung disease	121 (24%)	230 (22%)	259 (20%)	624 (24%)	35 (11%)	77 (11%)
Tuberculosis	2 (<0.5%)	6 (1%)	1 (<0.5%)	10 (<0.5%)	3 (1%)	3 (<0.5%)
HIV	2 (<0.5%)	3 (<0.5%)	9 (1%)	12 (<0.5%)	1 (<0.5%)	5 (1%)
Severe liver disease	13 (3%)	19 (2%)	20 (2%)	52 (2%)	4 (1%)	11 (2%)
Severe kidney impairment	28 (6%)	91 (9%)	85 (7%)	168 (6%)	53 (16%)	99 (14%)
Any of the above	313 (62%)	598 (58%)	702 (55%)	1473 (57%)	159 (49%)	346 (51%)
SARS-Cov-2 test result						
Positive	425 (85%)	908 (88%)	1123 (88%)	2293 (88%)	302 (93%)	647 (95%)
Negative	74 (15%)	119 (12%)	152 (12%)	300 (12%)	21 (6%)	34 (5%)
Test result not yet known	2 (<0.5%)	7 (1%)	4 (<0.5%)	11 (<0.5%)	1 (<0.5%)	2 (<0.5%)

Results are count (%), mean ± standard deviation, or median (inter-quartile range). * Includes 6 pregnant women. The 'oxygen only' group includes non-invasive ventilation. Severe liver disease defined as requiring ongoing specialist care. Severe kidney impairment defined as estimated glomerular filtration rate <30 mL/min/1.73m². 4 (0.2%) patients allocated dexamethasone and 13 (0.3%) patients allocated usual care had missing data for days since symptom onset; these patients are excluded from estimates of the median (IQR) days since onset above.

Supplementary Figures

Figure S1: Effect of allocation to dexamethasone on 28−day mortality by other pre−specified baseline characteristics

Characteristic	Dexamethasone	Usual care	RR (95% CI)
Age, years (χ^2_1=4.9; p=0.03)			
<70	129/1141 (11.3%)	428/2504 (17.1%)	0.64 (0.53−0.78)
≥70 <80	155/469 (33.0%)	271/859 (31.5%)	1.03 (0.84−1.25)
≥80	198/494 (40.1%)	411/958 (42.9%)	0.89 (0.75−1.05)
Sex (χ^2_1=0.9; p=0.33)			
Men	331/1338 (24.7%)	782/2749 (28.4%)	0.80 (0.71−0.91)
Women	151/766 (19.7%)	328/1572 (20.9%)	0.90 (0.74−1.09)
Days since symptom onset (χ^2_1=12.3; p<0.001)			
≤7	269/916 (29.4%)	500/1801 (27.8%)	1.01 (0.87−1.17)
>7	212/1184 (17.9%)	604/2507 (24.1%)	0.69 (0.59−0.80)
Baseline risk (χ^2_1=0.4; p=0.51)			
<30%	150/1268 (11.8%)	377/2682 (14.1%)	0.83 (0.69−1.00)
≥30% <45%	146/464 (31.5%)	334/878 (38.0%)	0.77 (0.63−0.94)
≥45%	186/372 (50.0%)	399/761 (52.4%)	0.90 (0.76−1.07)
All participants	**482/2104 (22.9%)**	**1110/4321 (25.7%)**	**0.83 (0.75−0.93) p<0.001**



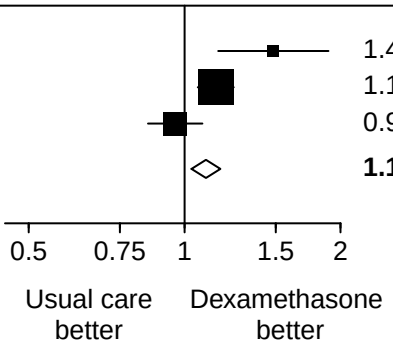
RR=age−adjusted (or age−specific) rate ratio (with the exception of RR estimates by baseline−predicted risk, which are not adjusted for age). CI=confidence interval. Subgroup−specific RR estimates are represented by squares (with areas of the squares proportional to the amount of statistical information) and the lines through them correspond to the 95% confidence intervals. For each of the four subgroups shown, the RRs and CIs are estimated from a regression model that includes a relevant interaction term enabling the effect of allocation to dexamethasone on mortality to be estimated separately at each level of the subgroup. Baseline−predicted risk is calculated as exp(a)/(1 + exp(a)), where a = −1.23 − 2.85 (if age <50) − 2.03 (if age 50−59) − 1.21 (if age 60−69) − 0.51 (if age 70−79) + 0.42 (if male) − 0.34 (if >7 days since symptom onset) + 0.86 (if on oxygen only) + 2.18 (if on invasive mechanical ventilation) − 0.01 (if history of diabetes) + 0.22 (if history of heart disease) + 0.21 (if history of chronic lung disease) + 0.50 (if history of kidney disease).

Figure S2: Effect of allocation to dexamethasone on: a) discharge from hospital alive within 28 days; and b) invasive mechanical ventilation or death, by level of respiratory support received at randomization

a) Discharge from hospital alive within 28 days

Respiratory support at randomization	Dexamethasone	Usual care	RR (95% CI)
Invasive mechanical ventilation	107/324 (33.0%)	159/683 (23.3%)	1.48 (1.16−1.90)
Oxygen only	921/1279 (72.0%)	1755/2604 (67.4%)	1.15 (1.06−1.24)
No oxygen received	385/501 (76.8%)	831/1034 (80.4%)	0.96 (0.85−1.08)
All participants	**1413/2104 (67.2%)**	**2745/4321 (63.5%)**	**1.10 (1.03−1.17)**

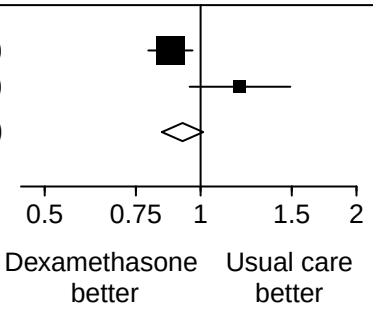
Trend across three categories: χ^2_1=11.5; p<0.001



b) Invasive mechanical ventilation or death (among those not on invasive mechanical ventilation at randomization)

Respiratory support at randomization	Dexamethasone	Usual care	RR (95% CI)
Oxygen only	359/1279 (28.1%)	834/2604 (32.0%)	0.87 (0.79−0.96)
No oxygen received	97/501 (19.4%)	160/1034 (15.5%)	1.19 (0.95−1.49)
Subtotal	**456/1780 (25.6%)**	**994/3638 (27.3%)**	**0.92 (0.84−1.01)**

Trend across two categories: χ^2_1=6.2; p=0.01



RR=age−adjusted rate ratio for panel a and age−adjusted risk ratio for panel b. CI=confidence interval. Subgroup−specific RR estimates are represented by squares (with areas of the squares proportional to the amount of statistical information) and the lines through them correspond to the 95% confidence intervals. For each analysis, the RRs and CIs are estimated from a regression model that includes a relevant interaction term enabling the effect of allocation to dexamethasone to be estimated separately for each level of the subgroup. The 'oxygen only' group includes non−invasive ventilation.