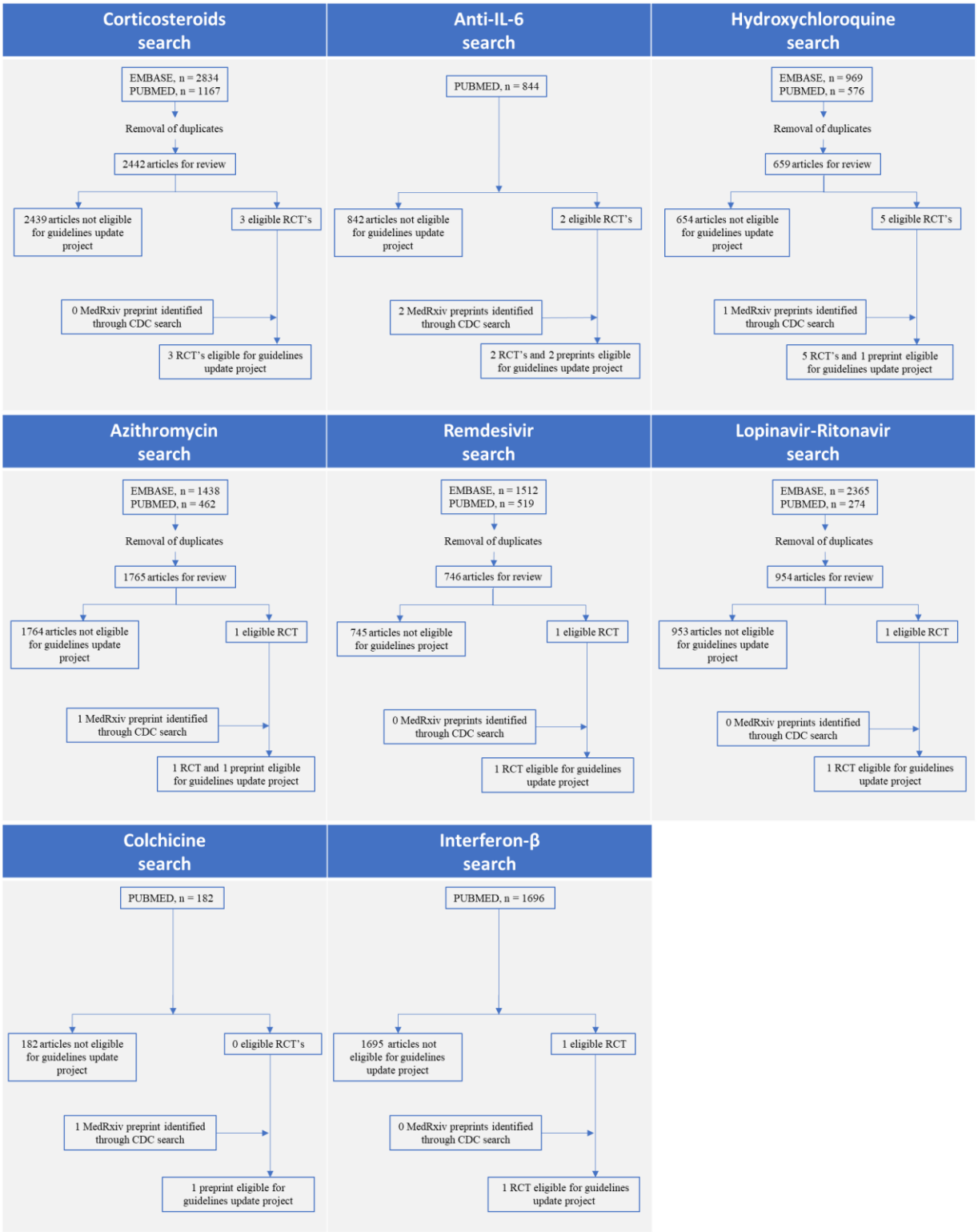

SUPPLEMENTARY INFORMATION

Figure S1. Flowcharts detailing the systematic searches for each therapy of interest.

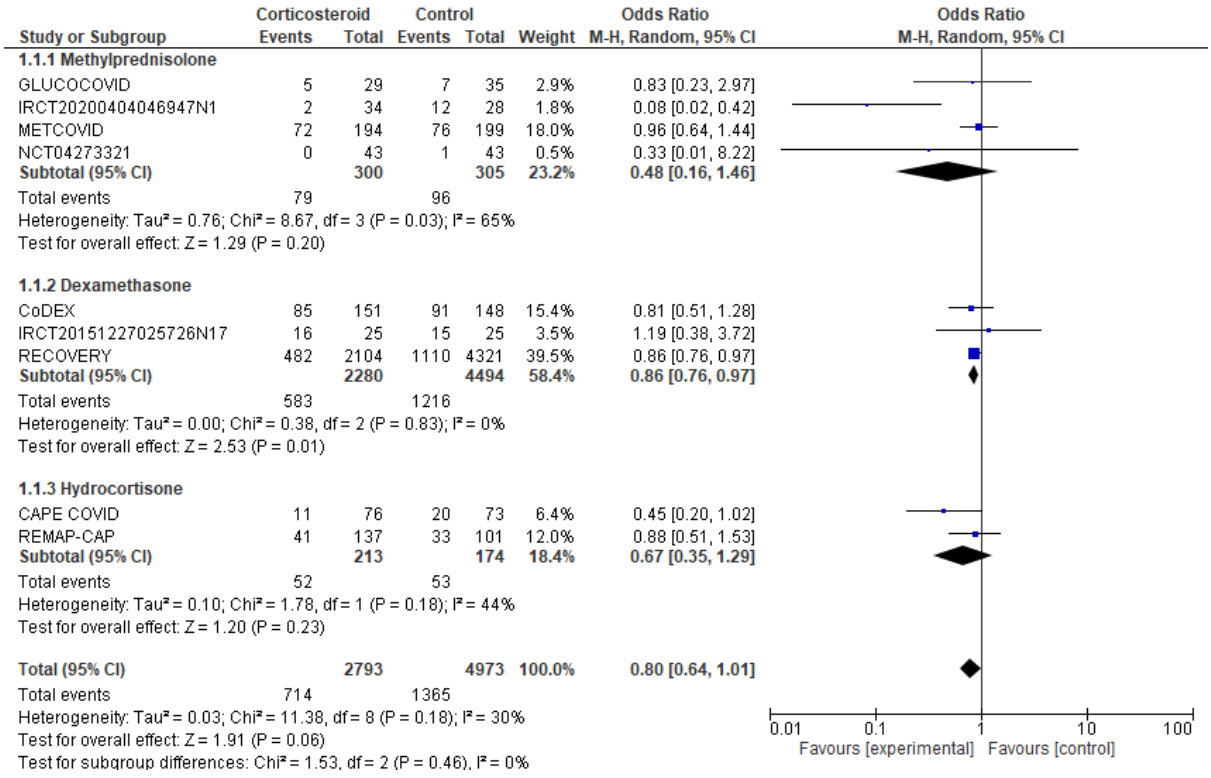

Figure S2. Forest plots showing the sub-analysis of corticosteroids grouped by class and their effects on mortality of hospitalised adult patients with COVID-19.

Study name has been used unless no name was available in which case the trial registration identifier has been used. The weight represents the percentage contribution of each study to the summary effect estimate.

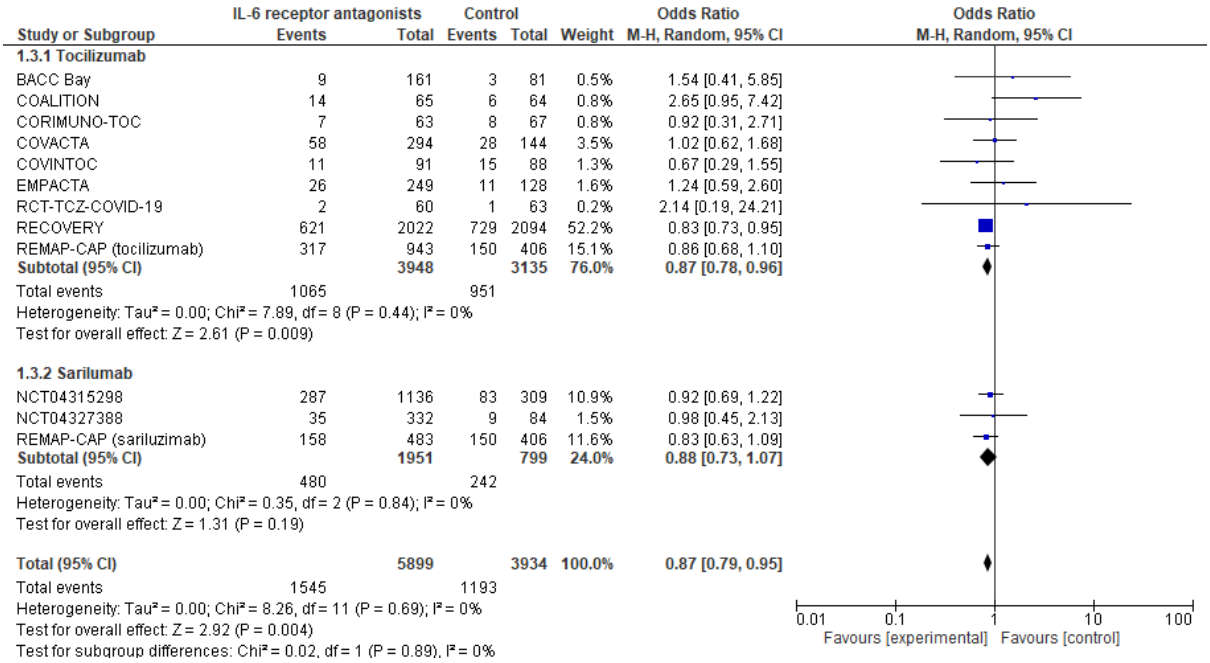

Figure S3. Forest plots showing the sub-analysis of IL-6 receptor antagonists grouped by class and their effects on mortality of hospitalised adult patients with COVID-19.

Study name has been used unless no name was available in which case the trial registration identifier has been used. The weight represents the percentage contribution of each study to the summary effect estimate.

Table S1.

Question: Corticosteroids compared to Standard care (defined as control, placebo or normal background therapy) for COVID-19

Setting:

Bibliography:
1. Angus, D. C., Derde, L., Al-Beidh, F., Annane, D., Arabi, Y., Beane, A., … Gordon, A. C. (2020). "Effect of Hydrocortisone on Mortality and Organ Support in Patients with Severe COVID-19: The REMAP-CAP COVID-19 Corticosteroid Domain Randomised Clinical Trial." JAMA - Journal of the American Medical Association, 324(13), 1317–1329. https://doi.org/10.1001/jama.2020.17022
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Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Corticosteroids	Standard care (defined as control, placebo or normal background therapy)	Relative (95% CI)	Absolute (95% CI)		
Mortality												
9	randomised trials	not serious	not serious [a]	not serious	serious [b]	none	714/2793 (25.6%)	1365/4973 (27.4%)	**OR 0.80** (0.64 to 1.01)	**42 fewer per 1,000** (from 80 fewer to 2 more)	⨁⨁⨁◯ MODERATE	CRITICAL

CI: Confidence interval; **OR:** Odds ratio

Explanations

a. one study (Jamaati) shows discordance with the other eight studies by favouring control but we have not downgraded based on this small study consisting of 50 specific participants while the other eight studies have combined 7716 participants and the confidence intervals are broadly consistent with the other trials.

b. CI's show both beneficial and detrimental effects

Table S2.

Author(s):

Question: IL-6 receptor antagonists compared to Standard care (defined as control, placebo or normal background therapy) for COVID-19

Setting:

Bibliography:
1. Abani, O., Abbas, A., Abbas, F., Abbas, M., Abbasi, S., Abbass, H., … Zuriaga-Alvaro, A. (2021). "Tocilizumab in patients admitted to hospital with COVID-19 (RECOVERY): a randomised, controlled, open-label, platform trial." The Lancet, 397(10285), 1637–1645. https://doi.org/10.1016/S0140-6736(21)00676-0

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Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	IL-6 receptor antagonists	Standard care (defined as control, placebo or normal background therapy)	Relative (95% CI)	Absolute (95% CI)		
Mortality												
11	randomised trials	serious [a]	not serious	not serious	not serious	none	1545/5899 (26.2%)	1043/3528 (29.6%)	**OR 0.87** (0.79 to 0.96)	**28 fewer per 1,000** (from 47 fewer to 8 fewer)	⨁⨁⨁◯ MODERATE	CRITICAL

CI: Confidence interval; **OR:** Odds ratio

Explanations

a. Inclusion of data from preprints

Table S3.

Author(s):

Question: Hydroxychloroquine compared to Standard care (defined as control, placebo or normal background therapy) for COVID-19

Setting:

Bibliography:
1. Abd-Elsalam, S., Esmail, E. S., Khalaf, M., Abdo, E. F., Medhat, M. A., El Ghafar, M. S. A., … Alboraie, M. (2020). “Hydroxychloroquine in the treatment of COVID-19: A multicenter randomised controlled study.” American Journal of Tropical Medicine and Hygiene, 103(4), 1635–1639. https://doi.org/10.4269/ajtmh.20-0873
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Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Hydroxychloroquine	Standard care (defined as control, placebo or normal background therapy)	Relative (95% CI)	Absolute (95% CI)		
Mortality												
13	randomised trials	not serious	not serious	not serious	serious [a]	none	628/3589 (17.5%)	984/5132 (19.2%)	**OR 1.09** (0.97 to 1.22)	**14 more per 1,000** (from 5 fewer to 33 more)	⨁⨁⨁◯ MODERATE	CRITICAL

CI: Confidence interval; **OR:** Odds ratio

Explanations

a. CI's show both beneficial and detrimental effects

Table S4.

Author(s):

Question: Azithromycin compared to Standard care (defined as control, placebo or normal background therapy) for COVID-19

Setting:

Bibliography:
1. Abaleke, E., Abbas, M., Abbasi, S., Abbott, A., Abdelaziz, A., Abdelbadiee, S., … Zuriaga-Alvaro, A. (2021). "Azithromycin in patients admitted to hospital with COVID-19 (RECOVERY): a randomised, controlled, open-label, platform trial." The Lancet, 397(10274), 605–612. https://doi.org/10.1016/S0140-6736(21)00149-5
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Certainty assessment	№ of patients	Effect	Certainty	Importance

№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Azithromycin	Standard care (defined as control, placebo or normal background therapy)	Relative (95% CI)	Absolute (95% CI)		
Mortality												
5	randomised trials	not serious	not serious	not serious	serious [a]	none	657/3169 (20.7%)	1250/5898 (21.2%)	**OR 0.97** (0.87 to 1.08)	**5 fewer per 1,000** (from 22 fewer to 13 more)	⨁⨁⨁◯ MODERATE	CRITICAL

CI: Confidence interval; **OR:** Odds ratio

Explanations

a. CI's show both beneficial and detrimental effects

Table S5.

Author(s):

Question: Hydroxychloroquine and Azithromycin compared to Standard care (defined as control, placebo or normal background therapy) for COVID-19

Setting:

Bibliography:
1. Cavalcanti, A. B., Zampieri, F. G., Rosa, R. G., Azevedo, L. C. P., Veiga, V. C., Avezum, A., … Berwanger, O. (2020). "Hydroxychloroquine with or without Azithromycin in Mild-to-Moderate Covid-19." New England Journal of Medicine, 383(21), 2041–2052. https://doi.org/10.1056/nejmoa2019014
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Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Hydroxychloroquine and Azithromycin	Standard care (defined as control, placebo or normal background therapy)	Relative (95% CI)	Absolute (95% CI)		
Mortality												
2	randomised trials	serious [a]	not serious	not serious	serious [b]	none	6/233 (2.6%)	8/229 (3.5%)	**OR 0.73** (0.25 to 2.15)	**9 fewer per 1,000** (from 26 fewer to 37 more)	⨁⨁◯◯ LOW	CRITICAL

CI: Confidence interval; **OR:** Odds ratio

Explanations

a. One trial was terminated following review by a data safety monitoring board

b. CI's show both beneficial and detrimental effects

Table S6.

Author(s):

Question: Lopinavir-ritonavir compared to Standard care (defined as control, placebo or normal background therapy for COVID-19

Setting:

Bibliography:
1. Ader, F., Peiffer-Smadja, N., Poissy, J., Bouscambert-Duchamp, M., Belhadi, D., Diallo, A., … Mentré, F. (2021). "An open-label randomised controlled trial of the effect of lopinavir/ritonavir, lopinavir/ritonavir plus IFN-β-1a and hydroxychloroquine in hospitalised patients with COVID-19." Clinical Microbiology and Infection. https://doi.org/10.1016/j.cmi.2021.05.020
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4. Solidarity, W. S. T. C., & Pan H, Peto R, Henao-Restrepo AM, Preziosi MP, Sathiyamoorthy V, Abdool Karim Q, Alejandria MM, Hernández García C, Kieny MP, Malekzadeh R, Murthy S, Reddy KS, Roses Periago M, Abi Hanna P, Ader F, Al-Bader AM, Alhasawi A, S. S. (2021). "Repurposed Antiviral Drugs for Covid-19 — Interim WHO Solidarity Trial Results." New England Journal of Medicine, 384(6), 497–511. https://doi.org/10.1056/nejmoa2023184

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	lopinavir-ritonavir	Standard care (defined as control, placebo or normal background therapy	Relative (95% CI)	Absolute (95% CI)		
Mortality												
4	randomised trials	not serious	not serious	not serious	not serious	none	555/3259 (17.0%)	950/5044 (18.8%)	**OR 1.02** (0.91 to 1.15)	**3 more per 1,000** (from 14 fewer to 22 more)	⨁⨁⨁⨁ HIGH	CRITICAL

CI: Confidence interval; **OR:** Odds ratio

Table S7.

Author(s):

Question: Remdesivir compared to Standard care (defined as control, placebo or normal background therapy) for COVID-19

Setting:

Bibliography:
1. Beigel, J. H., Tomashek, K. M., Dodd, L. E., Mehta, A. K., Zingman, B. S., Kalil, A. C., … Lane, H. C. (2020). "Remdesivir for the Treatment of Covid-19 — Final Report." New England Journal of Medicine, 383(19), 1813–1826. https://doi.org/10.1056/nejmoa2007764
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Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Remdesivir	Standard care (defined as control, placebo or normal background therapy)	Relative (95% CI)	Absolute (95% CI)		

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Remdesivir	Standard care (defined as control, placebo or normal background therapy)	Relative (95% CI)	Absolute (95% CI)		
Mortality												
5	randomised trials	not serious	not serious	not serious	serious [a]	none	392/3860 (10.2%)	397/3543 (11.2%)	**OR 0.93** (0.80 to 1.08)	**7 fewer per 1,000** (from 20 fewer to 8 more)	⨁⨁⨁◯ MODERATE	CRITICAL

CI: Confidence interval; **OR:** Odds ratio

Explanations

a. CI's show both beneficial and detrimental effects

Table S8.

Author(s):

Question: Cochicine compared to Standard care (defined as control, placebo or normal background therapy) for COVID-19

Setting:

Bibliography:
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Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Cochicine	Standard care (defined as control, placebo or normal background therapy)	Relative (95% CI)	Absolute (95% CI)		
Mortality												
3	randomised trials	serious [a]	not serious	not serious	serious [b]	none	1174/5701 (20.6%)	1196/5816 (20.6%)	**OR 0.64** (0.22 to 1.89)	**64 fewer per 1,000** (from 152 fewer to 123 more)	⨁⨁◯◯ LOW	CRITICAL

CI: Confidence interval; **OR:** Odds ratio

Explanations

a. Includes data from one preprint (Horby)

b. CI's show both beneficial and detrimental effects

Table S9

Author(s):

Question: Interferon beta compared to Standard care (defined as control, placebo or normal background therapy) for COVID-19

Setting:

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Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Interferon beta	Standard care (defined as control, placebo or normal background therapy)	Relative (95% CI)	Absolute (95% CI)		
Mortality												
4	randomised trials	not serious [a]	serious [b]	not serious	serious [c]	none	263/2165 (12.1%)	248/2142 (11.6%)	**OR 0.52** (0.22 to 1.26)	**52 fewer per 1,000** (from 88 fewer to 26 more)	⨁⨁◯◯ LOW	CRITICAL

CI: Confidence interval; **OR:** Odds ratio

Explanations

a. 3 out of 4 included studies had high risk of bias; however, we did not downgrade for RoB in the body of evidence, as the 4th included study has low risk of bias and it is including 4100 patients compared to 207 patients of all the other studies taken together.

b. Heterogeneity between studies

c. CI's show both beneficial and detrimental effects