Supplementary Material

Blood eosinophil count-guided corticosteroid therapy and as a prognostic biomarker of exacerbations of chronic obstructive pulmonary disease: A systematic review and meta-analysis

Table S1. Risk of bias in observational studies assessed using NOS scales

Figure S1. Risk of bias summary in RCTs assessed using the Cochrane Handbook for Systematic Reviews of Interventions

Figure S2. Risk of bias graph in RCTs assessed using the Cochrane Handbook for Systematic Reviews of Interventions

Figure S3. The mean difference of FEV_1 change from baseline ICS vs non-ICS treatment among patients with baseline BEC < 2%

Figure S4. The mean difference of FEV_1 change from baseline ICS vs non-ICS treatment among patients with baseline BEC ≥ 2%

Figure S5. The mean difference of FEV_1 change from baseline ICS vs placebo treatment among patients with baseline BEC < 2%

Figure S6. The mean difference of FEV_1 change from baseline ICS vs placebo treatment among patients with baseline BEC ≥ 2%

Figure S7. The mean difference of FEV_1 change from baseline ICS+LAMA/LABA vs LAMA/LABA treatment among patients with baseline BEC < 2%

Figure S8. The mean difference of FEV_1 change from baseline ICS+LAMA/LABA vs LAMA/LABA treatment among patients with baseline BEC ≥ 2%

Figure S9. The mean difference of FEV_1 change from baseline ICS vs non-ICS treatment among patients with baseline BEC < 150cells/μL

Figure S10. The mean difference of FEV_1 change from baseline ICS vs non-ICS treatment among patients with baseline BEC ≥ 150cells/μL

Figure S11. The mean difference of FEV_1 change from baseline ICS vs non-ICS treatment among patients with baseline BEC < 300cells/μL

Figure S12. The mean difference of FEV_1 change from baseline ICS vs non-ICS treatment among patients with baseline BEC ≥ 300cells/μL

Figure S13. The mean difference of SGRQ score change from baseline ICS vs non-ICS treatment among patients with baseline BEC < 2%

Figure S14. The mean difference of SGRQ score change from baseline ICS vs non-ICS treatment among patients with baseline BEC ≥ 2%

Figure S15. The mean difference of SGRQ score change from baseline ICS vs placebo treatment among patients with baseline BEC < 2%

Figure S16. The mean difference of SGRQ score change from baseline ICS vs placebo treatment among patients with baseline BEC ≥ 2%

Figure S17. The mean difference of SGRQ score change from baseline ICS+LAMA/LABA vs LAMA/LABA treatment among patients with baseline BEC < 2%

Figure S18. The mean difference of SGRQ score change from baseline ICS+LAMA/LABA vs LAMA/LABA treatment among patients with baseline BEC ≥ 2%

Figure S19. The risk ratio of exacerbations COPD ICS vs non-ICS treatment among patients with baseline BEC ≥ 2%

Figure S20. The risk ratio of exacerbations COPD ICS vs non-ICS treatment among patients with baseline BEC < 2%

Figure S21. The risk ratio of exacerbations COPD ICS vs non-ICS treatment among patients with baseline BEC ≥3%

Figure S22. The risk ratio of exacerbations COPD ICS vs non-ICS treatment among patients with baseline BEC < 3%

Figure S23. The risk ratio of exacerbations COPD ICS vs non-ICS treatment among patients with baseline BEC ≥ 150 cells/μL

Figure S24. The risk ratio of exacerbations COPD ICS vs non-ICS treatment among patients with baseline BEC < 150 cells/μL

Figure S25. The risk ratio of exacerbations COPD ICS vs non-ICS treatment among patients with baseline BEC ≥ 200 cells/μL

Figure S26. The risk ratio of exacerbations COPD ICS vs non-ICS treatment among patients with baseline BEC < 200 cells/μL

Figure S27. The risk ratio of exacerbations COPD ICS vs non-ICS treatment among patients with baseline BEC ≥ 300 cells/μL

Figure S28. The risk ratio of exacerbations COPD ICS vs non-ICS treatment among patients with baseline BEC < 300 cells/μL

Figure S29. The odds ratio of exacerbations COPD baseline BEC ≥ 2% vs baseline BEC < 2%

Figure S30. The odds ratio of exacerbations COPD baseline BEC ≥ 3% vs baseline BEC < 3%

Figure S31. The odds ratio of exacerbations COPD baseline BEC ≥ 4% vs baseline BEC < 4%

Figure S32. The odds ratio of exacerbations COPD baseline BEC ≥ 5% vs baseline BEC < 5%

Figure S33. The odds ratio of exacerbations COPD baseline BEC ≥ 150 cells/μL vs baseline BEC < 150 cells/μL

Figure S34. The odds ratio of exacerbations COPD baseline BEC ≥ 200 cells/μL vs baseline BEC < 200 cells/μL

Figure S35. The odds ratio of exacerbations COPD baseline BEC ≥ 300 cells/μL vs baseline BEC < 300 cells/μL

Figure S36. The odds ratio of exacerbations COPD baseline BEC ≥ 400 cells/μL vs baseline BEC < 400 cells/μL

Figure S37. The odds ratio of exacerbations COPD baseline BEC ≥ 500 cells/μL vs baseline BEC < 500 cells/μL

Figure S38. The hazard ratio of mortality baseline BEC ≥ 2% vs baseline BEC < 2%

Figure S39. The hazard ratio of mortality baseline BEC ≥ 200 cells/μL vs baseline BEC < 200 cells/μL

Figure S40. The hazard ratio of mortality baseline BEC ≥ 300 cells/μL vs baseline BEC < 300 cells/μL

Figure S41. The odds ratio of GOLD III+IV in patients with baseline high BEC vs low BEC

Figure S42. The mean difference of baseline FEV1/FVC in patients with baseline high BEC vs low BEC

Table S1. Risk of bias in observational studies assessed using NOS scales

Reference	Selection	Comparability	outcome
Aksoy2018 [1]	☆☆☆☆	☆☆	☆☆☆
Bafadhel2016 [2]	☆☆☆	☆☆	☆☆
Bélanger2018 [3]	☆☆☆	☆☆	☆☆☆
Chan2020 [4]	☆☆☆	☆☆	☆☆
Cheng2016 [5]	☆☆☆	☆☆	☆☆
Couillard2017 [6]	☆☆	☆☆	☆☆
Disantostefano2016 [7]	☆☆☆☆	☆☆	☆☆☆
Duman2015 [8]	☆☆☆	☆☆	☆☆
Gonzalez-Barcala2019 [9]	☆☆☆	☆☆	☆☆
Hasegawa2016 [10]	☆☆☆☆	☆☆	☆☆
Hastie2017 [11]	☆☆☆☆	☆☆	☆☆☆
Hegewald2020 [12]	☆☆☆☆	☆☆	☆☆☆
Kerkhof2017 [13]	☆☆☆☆	☆☆	☆☆☆
Landis2018 [14]	☆☆☆☆	☆☆	☆☆
Lv2021 [15]	☆☆☆	☆☆	☆☆
Mendy2018 [16]	☆☆☆	☆☆	☆☆☆
Nishimura2021 [17]	☆☆☆	☆☆	☆☆
Oh2018 [18]	☆☆☆	☆☆	☆☆☆
Oshagbemi 2018 [19]	☆☆☆☆	☆☆	☆☆☆
Peng2021 [20]	☆☆☆	☆☆	☆☆
Poder2018 [21]	☆☆☆	☆☆	☆☆☆
Prins2017 [22]	☆☆☆	☆☆	☆☆
Roche2017 [23]	☆☆☆☆	☆☆	☆☆☆
Serafino-Agrusa2016 [24]	☆☆	☆☆	☆☆
Song 2017 [25]	☆☆☆☆	☆☆	☆☆☆
Vedel-Krogh2018 [26]	☆☆☆☆	☆☆	☆☆☆
Yun2018 [27]	☆☆☆	☆☆	☆☆☆
Zeiger2018 [28]	☆☆☆☆	☆☆	☆☆☆
Zhang2020 [29]	☆☆☆	☆☆	☆☆☆
Zysman2017 [30]	☆☆☆	☆☆	☆☆

NOS: Newcastle-Ottawa scale

Figure S1. Risk of bias summary in RCTs assessed using the Cochrane Handbook for Systematic Reviews of Interventions

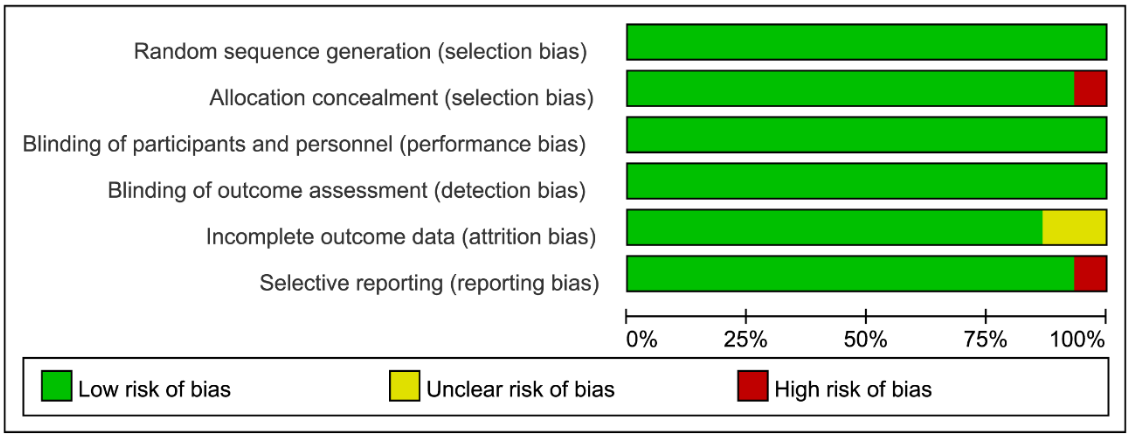


Figure S2. Risk of bias graph in RCTs assessed using the Cochrane Handbook for Systematic Reviews of Interventions

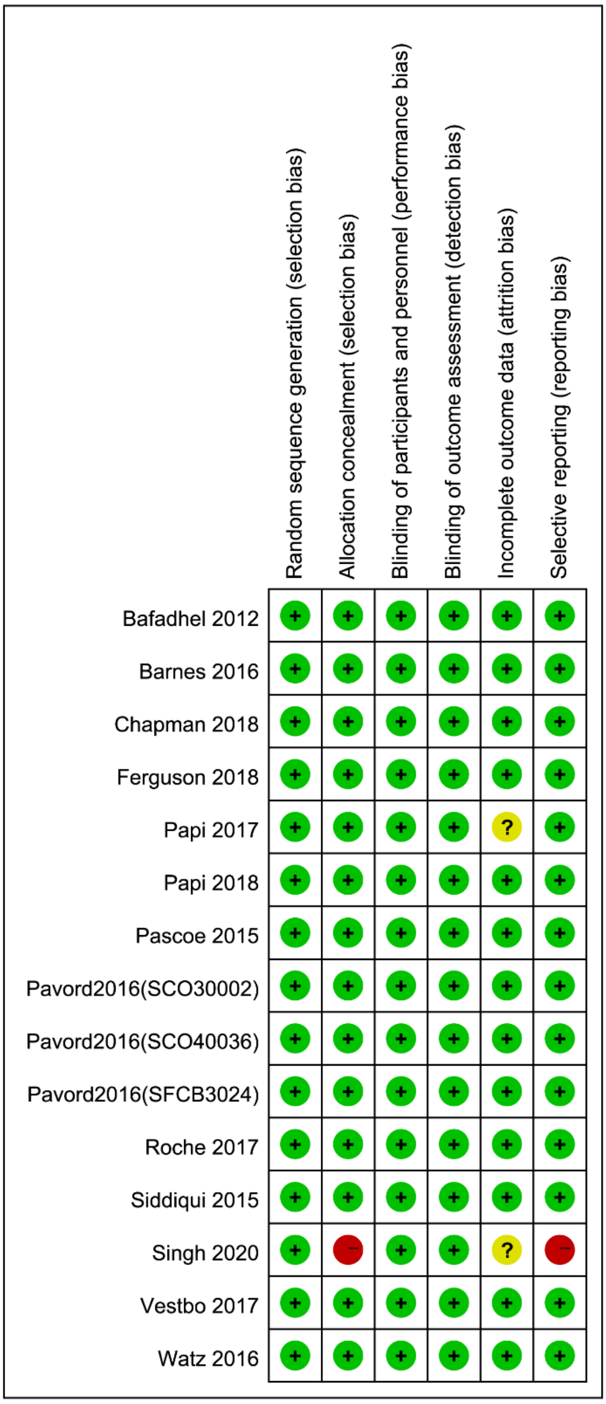


Figure S3. The mean difference of FEV_1 change from baseline ICS vs non-ICS treatment among patients with baseline BEC < 2%

Study or Subgroup	Mean Difference	SE	Weight	Mean Difference IV, Random, 95% CI
Barnes 2016	33.9	11.403	14.2%	33.90 [11.55, 56.25]
Chapman 2018	45	15.8166	13.3%	45.00 [14.00, 76.00]
Pascoe 2015	49	12.245	14.0%	49.00 [25.00, 73.00]
Pavord(SCO30002)	66.795	44.963	6.8%	66.80 [-21.33, 154.92]
Pavord(SCO40036)	-18.27	14.604	13.6%	-18.27 [-46.89, 10.35]
Pavord(SFCB3024)	80.846	18.978	12.5%	80.85 [43.65, 118.04]
Roche 2017	-56	16.993	13.0%	-56.00 [-89.31, -22.69]
Siddiqui 2015	64.61	18.936	12.6%	64.61 [27.50, 101.72]
Total (95% CI)			**100.0%**	**30.71 [-0.11, 61.52]**

Heterogeneity: Tau² = 1610.06; Chi² = 51.07, df = 7 (P < 0.00001); I² = 86%
Test for overall effect: Z = 1.95 (P = 0.05)

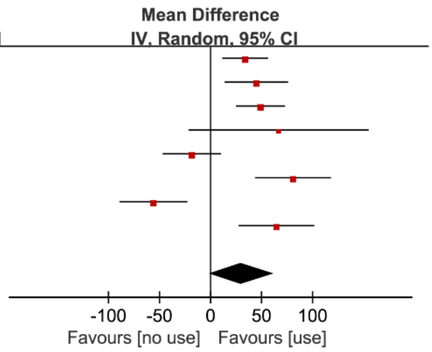


Figure S4. The mean difference of FEV_1 change from baseline ICS vs non-ICS treatment among patients with baseline BEC ≥ 2%

Study or Subgroup	Mean Difference	SE	Weight	Mean Difference IV, Random, 95% CI
Bafadhel 2012	-30	136.224	1.1%	-30.00 [-296.99, 236.99]
Barnes 2016	-2.9	7.219	20.2%	-2.90 [-17.05, 11.25]
Chapman 2018	-41	28.572	11.7%	-41.00 [-97.00, 15.00]
Pascoe 2015	27	16.071	16.9%	27.00 [-4.50, 58.50]
Pavord(SCO30002)	98.246	59.269	4.7%	98.25 [-17.92, 214.41]
Pavord(SCO40036)	-14	17.653	16.2%	-14.00 [-48.60, 20.60]
Pavord(SFCB3024)	73.958	32.408	10.4%	73.96 [10.44, 137.48]
Roche 2017	-72	21.829	14.4%	-72.00 [-114.78, -29.22]
Siddiqui 2015	85.89	61.242	4.5%	85.89 [-34.14, 205.92]
Total (95% CI)			**100.0%**	**2.36 [-26.23, 30.95]**

Heterogeneity: Tau² = 1001.86; Chi² = 26.33, df = 8 (P = 0.0009); I² = 70%
Test for overall effect: Z = 0.16 (P = 0.87)

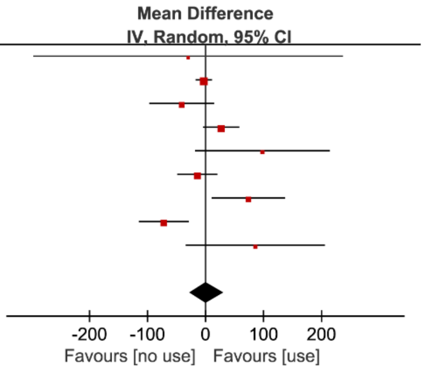


Figure S5. The mean difference of FEV_1 change from baseline ICS vs placebo treatment among patients with baseline BEC < 2%

Study or Subgroup	Mean Difference	SE	Weight	Mean Difference IV, Random, 95% CI
Bafadhel 2012	-30	136.224	3.1%	-30.00 [-296.99, 236.99]
Barnes 2016	-2.9	7.219	54.7%	-2.90 [-17.05, 11.25]
Pavord(SCO30002)	38.287	56.057	14.4%	38.29 [-71.58, 148.16]
Pavord(SFCB3024)	74.085	33.576	27.7%	74.08 [8.28, 139.89]
Total (95% CI)			**100.0%**	**23.56 [-24.64, 71.77]**

Heterogeneity: Tau² = 1052.95; Chi² = 5.52, df = 3 (P = 0.14); I² = 46%
Test for overall effect: Z = 0.96 (P = 0.34)

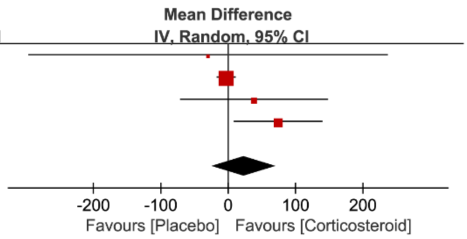


Figure S6. The mean difference of FEV_1 change from baseline ICS vs placebo treatment among patients with baseline BEC ≥ 2%

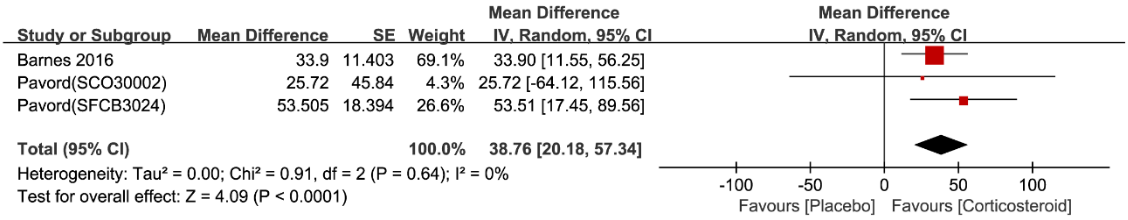


Figure S7. The mean difference of FEV_1 change from baseline ICS+LAMA/LABA vs LAMA/LABA treatment among patients with baseline BEC < 2%

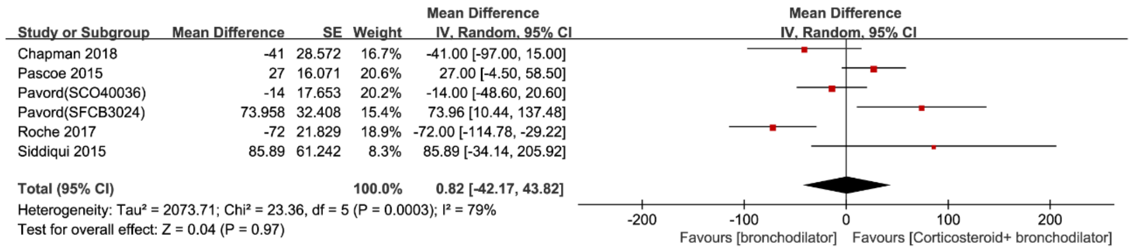


Figure S8. The mean difference of FEV_1 change from baseline ICS+LAMA/LABA vs LAMA/LABA treatment among patients with baseline BEC ≥ 2%

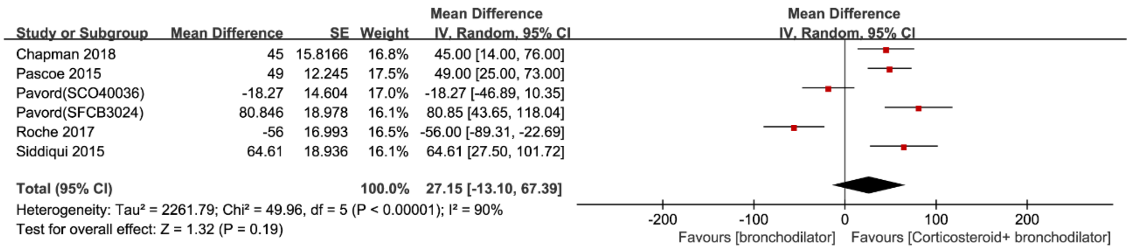


Figure S9. The mean difference of FEV_1 change from baseline ICS vs non-ICS treatment among patients with baseline BEC < 150cells/Μl

Study or Subgroup	Mean Difference	SE	Weight	Mean Difference IV, Random, 95% CI
Chapman 2018	13	21.429	30.8%	13.00 [-29.00, 55.00]
Ferguson 2018	-13	13.7758	37.7%	-13.00 [-40.00, 14.00]
Roche 2017	-68	20.62	31.5%	-68.00 [-108.41, -27.59]
Total (95% CI)			**100.0%**	**-22.33 [-64.20, 19.54]**

Heterogeneity: Tau² = 1021.94; Chi² = 8.05, df = 2 (P = 0.02); I² = 75%
Test for overall effect: Z = 1.05 (P = 0.30)

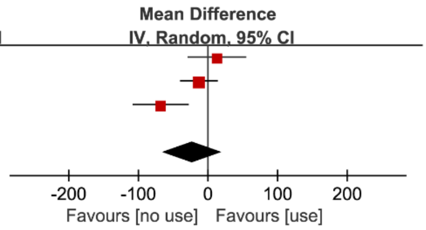


Figure S10. The mean difference of FEV_1 change from baseline ICS vs non-ICS treatment among patients with baseline BEC ≥ 150cells/μL

Study or Subgroup	Mean Difference	SE	Weight	Mean Difference IV, Random, 95% CI
Chapman 2018	51.98	18.0207	32.8%	51.98 [16.66, 87.30]
Ferguson 2018	35	17.3473	32.9%	35.00 [1.00, 69.00]
Roche 2017	-59	11.23	34.3%	-59.00 [-81.01, -36.99]
Total (95% CI)			**100.0%**	**8.33 [-66.82, 83.49]**

Heterogeneity: Tau² = 4162.72; Chi² = 37.44, df = 2 (P < 0.00001); I² = 95%
Test for overall effect: Z = 0.22 (P = 0.83)

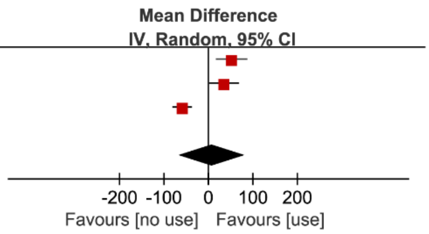


Figure S11. The mean difference of FEV_1 change from baseline ICS vs non-ICS treatment among patients with baseline BEC < 300cells/μL

Study or Subgroup	Mean Difference	SE	Weight	Mean Difference IV, Random, 95% CI
Chapman 2018	13	15.8166	34.1%	13.00 [-18.00, 44.00]
Roche 2017	-67	20.34	32.4%	-67.00 [-106.87, -27.13]
Siddiqui 2015	53.2	17.5718	33.5%	53.20 [18.76, 87.64]
Total (95% CI)			**100.0%**	**0.52 [-63.72, 64.77]**

Heterogeneity: Tau² = 2900.39; Chi² = 20.29, df = 2 (P < 0.0001); I² = 90%
Test for overall effect: Z = 0.02 (P = 0.99)

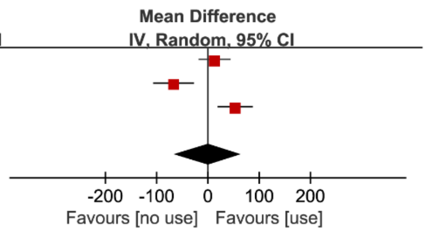


Figure S12. The mean difference of FEV_1 change from baseline ICS vs non-ICS treatment among patients with baseline BEC ≥ 300cells/μL

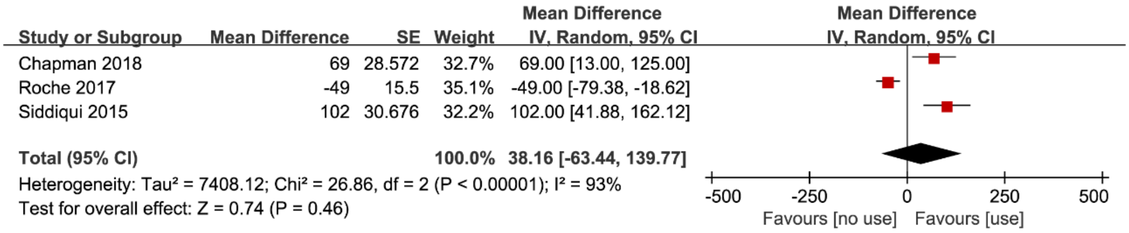


Figure S13. The mean difference of SGRQ score change from baseline ICS vs non-ICS treatment among patients with baseline BEC < 2%

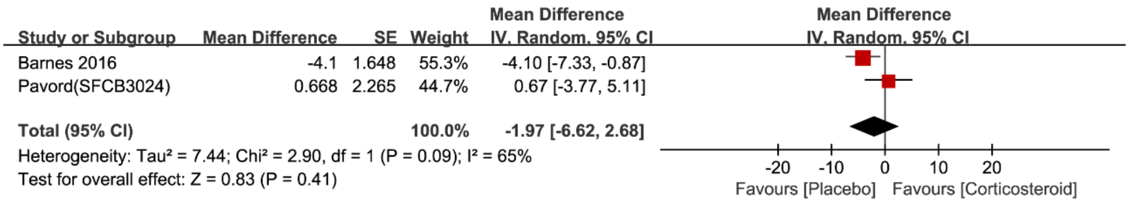


Figure S14. The mean difference of SGRQ score change from baseline ICS vs non-ICS treatment among patients with baseline BEC ≥ 2%

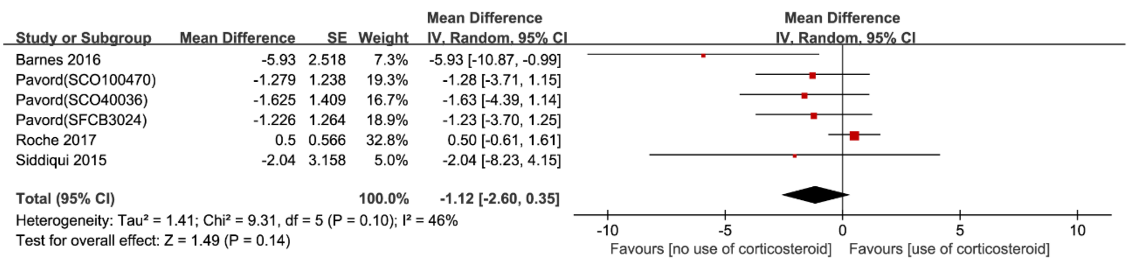


Figure S15. The mean difference of SGRQ score change from baseline ICS vs placebo treatment among patients with baseline BEC < 2%

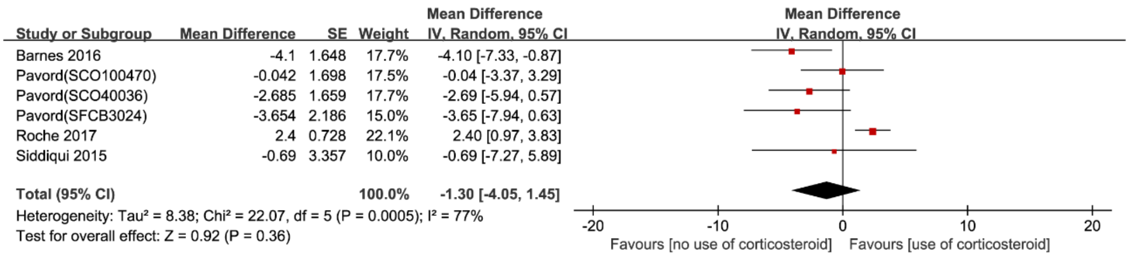


Figure S16. The mean difference of SGRQ score change from baseline ICS vs placebo treatment among patients with baseline BEC ≥ 2%

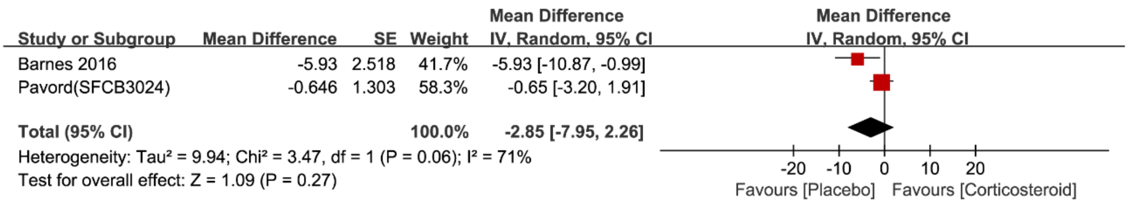


Figure S17. The mean difference of SGRQ score change from baseline ICS+LAMA/LABA vs LAMA/LABA treatment among patients with baseline BEC < 2%

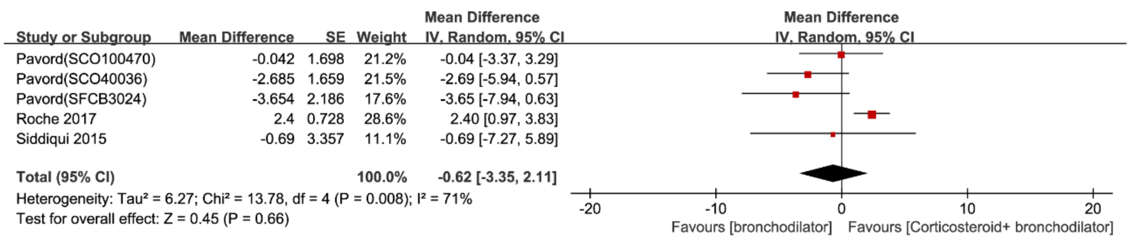


Figure S18. The mean difference of SGRQ score change from baseline ICS+LAMA/LABA vs LAMA/LABA treatment among patients with baseline BEC ≥ 2%

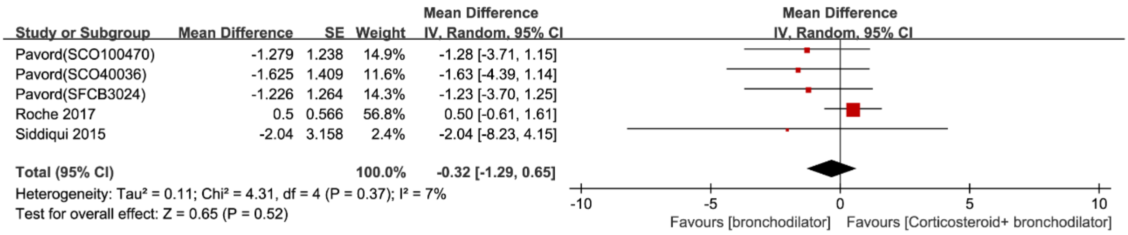


Figure S19. The risk ratio of exacerbations COPD ICS vs non-ICS treatment among patients with baseline BEC ≥ 2%

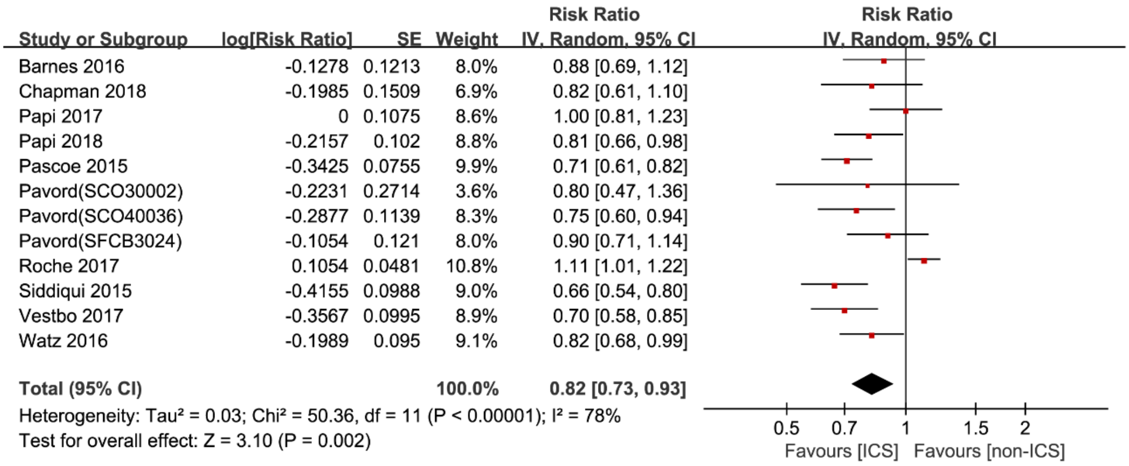


Figure S20. The risk ratio of exacerbations COPD ICS vs non-ICS treatment among patients with baseline BEC < 2%

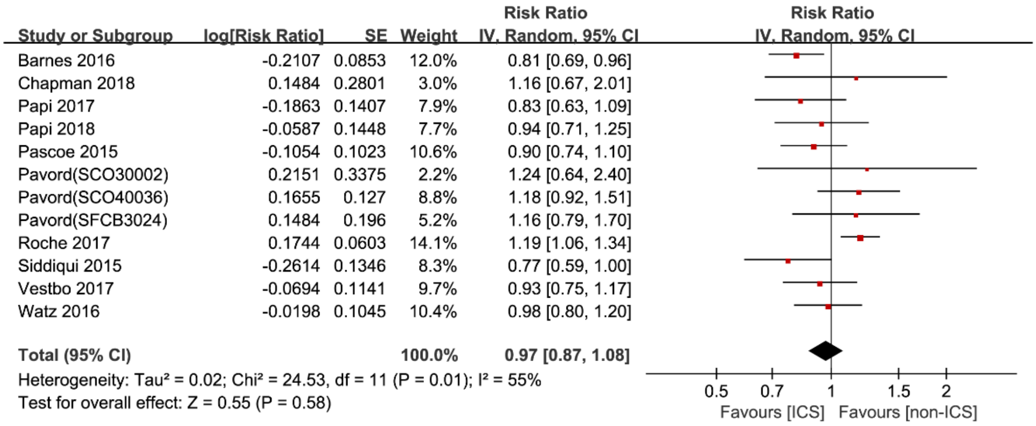
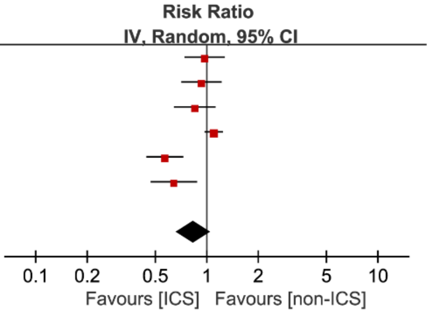


Figure S21. The risk ratio of exacerbations COPD ICS vs non-ICS treatment among patients with baseline BEC ≥3%

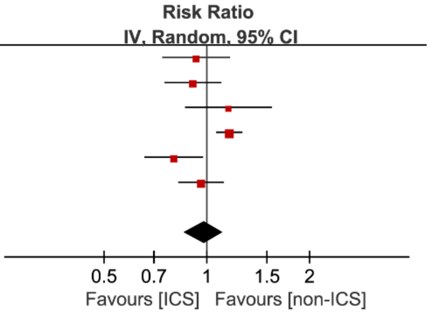


Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Random, 95% CI
Papi 2017	-0.0305	0.1381	16.2%	0.97 [0.74, 1.27]
Pavord(SCO40036)	-0.0726	0.1381	16.2%	0.93 [0.71, 1.22]
Pavord(SFCB3024)	-0.1625	0.1428	16.0%	0.85 [0.64, 1.12]
Roche 2017	0.0944	0.0632	19.8%	1.10 [0.97, 1.24]
Siddiqui 2015	-0.5656	0.1264	16.8%	0.57 [0.44, 0.73]
Watz 2016	-0.4447	0.1595	15.1%	0.64 [0.47, 0.88]
Total (95% CI)			**100.0%**	**0.83 [0.66, 1.04]**

Heterogeneity: $Tau^2 = 0.06$; $Chi^2 = 28.06$, df = 5 (P < 0.0001); $I^2 = 82\%$

Test for overall effect: Z = 1.60 (P = 0.11)

Figure S22. The risk ratio of exacerbations COPD ICS vs non-ICS treatment among patients with baseline BEC < 3%

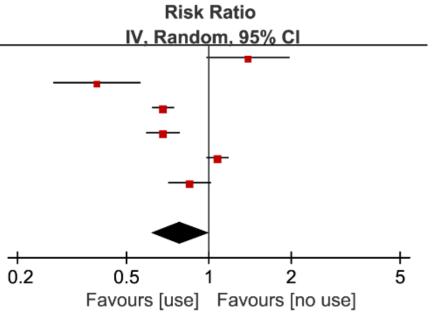


Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Random, 95% CI
Papi 2017	-0.0726	0.1166	14.4%	0.93 [0.74, 1.17]
Pavord(SCO40036)	-0.0943	0.0977	16.5%	0.91 [0.75, 1.10]
Pavord(SFCB3024)	0.1454	0.1491	11.3%	1.16 [0.86, 1.55]
Roche 2017	0.151	0.0454	22.7%	1.16 [1.06, 1.27]
Siddiqui 2015	-0.2231	0.1008	16.2%	0.80 [0.66, 0.97]
Watz 2016	-0.0392	0.0784	18.9%	0.96 [0.82, 1.12]
Total (95% CI)			**100.0%**	**0.98 [0.86, 1.12]**

Heterogeneity: $Tau^2 = 0.02$; $Chi^2 = 17.13$, df = 5 (P = 0.004); $I^2 = 71\%$

Test for overall effect: Z = 0.28 (P = 0.78)

Figure S23. The risk ratio of exacerbations COPD ICS vs non-ICS treatment among patients with baseline BEC ≥ 150 cells/μL



Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Random, 95% CI
Chapman 2018	0.3293	0.1783	13.8%	1.39 [0.98, 1.97]
Ferguson 2018	-0.9416	0.1876	13.4%	0.39 [0.27, 0.56]
Lipson 2018	-0.3857	0.0471	18.7%	0.68 [0.62, 0.75]
Pascoe 2015	-0.3857	0.0724	18.0%	0.68 [0.59, 0.78]
Roche 2017	0.0723	0.0472	18.7%	1.07 [0.98, 1.18]
Watz 2016	-0.1625	0.0918	17.4%	0.85 [0.71, 1.02]
Total (95% CI)			**100.0%**	**0.79 [0.62, 1.01]**

Heterogeneity: $Tau^2 = 0.08$; $Chi^2 = 80.00$, df = 5 (P < 0.00001); $I^2 = 94\%$

Test for overall effect: Z = 1.89 (P = 0.06)

Figure S24. The risk ratio of exacerbations COPD ICS vs non-ICS treatment among patients with baseline BEC < 150 cells/μL

Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Random, 95% CI
Chapman 2018	-0.1863	0.21	10.5%	0.83 [0.55, 1.25]
Ferguson 2018	-0.4943	0.2027	10.9%	0.61 [0.41, 0.91]
Lipson 2018	-0.1278	0.0615	21.1%	0.88 [0.78, 0.99]
Pascoe 2015	-0.0513	0.1006	18.2%	0.95 [0.78, 1.16]
Roche 2017	0.2231	0.0606	21.2%	1.25 [1.11, 1.41]
Watz 2016	-0.0726	0.103	18.0%	0.93 [0.76, 1.14]
Total (95% CI)			**100.0%**	**0.93 [0.77, 1.11]**

Heterogeneity: Tau² = 0.04; Chi² = 25.36, df = 5 (P = 0.0001); I² = 80%
Test for overall effect: Z = 0.82 (P = 0.41)

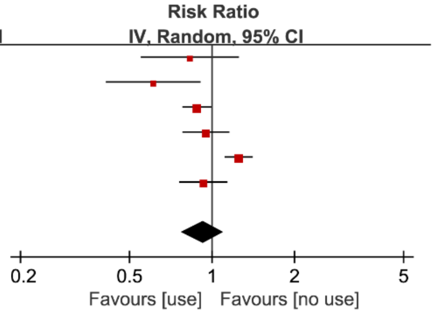


Figure S25. The risk ratio of exacerbations COPD ICS vs non-ICS treatment among patients with baseline BEC ≥ 200 cells/μL

Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Random, 95% CI
Papi 2018	-0.2157	0.1098	27.2%	0.81 [0.65, 1.00]
Pavord(SCO30002)	-0.1625	0.372	2.8%	0.85 [0.41, 1.76]
Pavord(SCO40036)	-0.1393	0.1037	29.9%	0.87 [0.71, 1.07]
Pavord(SFCB3024)	-0.1393	0.1487	16.0%	0.87 [0.65, 1.16]
Vestbo 2017	-0.4447	0.1176	24.2%	0.64 [0.51, 0.81]
Total (95% CI)			**100.0%**	**0.79 [0.70, 0.89]**

Heterogeneity: Tau² = 0.00; Chi² = 4.51, df = 4 (P = 0.34); I² = 11%
Test for overall effect: Z = 3.76 (P = 0.0002)

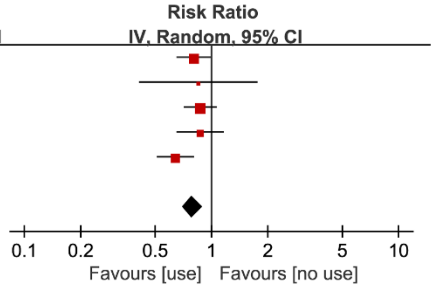


Figure S26. The risk ratio of exacerbations COPD ICS vs non-ICS treatment among patients with baseline BEC < 200 cells/μL

Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Random, 95% CI
Papi 2018	-0.137	0.1194	21.5%	0.87 [0.69, 1.10]
Pavord(SCO30002)	0.3716	0.2606	4.9%	1.45 [0.87, 2.42]
Pavord(SCO40036)	-0.0305	0.0983	30.1%	0.97 [0.80, 1.18]
Pavord(SFCB3024)	0.1398	0.1788	10.2%	1.15 [0.81, 1.63]
Vestbo 2017	-0.0866	0.0925	33.3%	0.92 [0.76, 1.10]
Total (95% CI)			**100.0%**	**0.97 [0.86, 1.08]**

Heterogeneity: Tau² = 0.00; Chi² = 4.43, df = 4 (P = 0.35); I² = 10%
Test for overall effect: Z = 0.60 (P = 0.55)

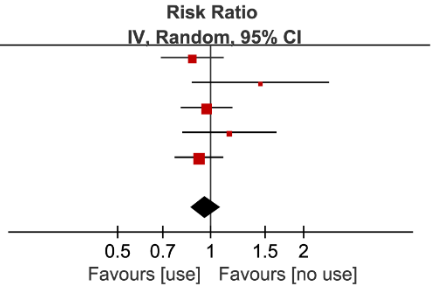


Figure S27. The risk ratio of exacerbations COPD ICS vs non-ICS treatment among patients with baseline BEC ≥ 300 cells/μL

Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Random, 95% CI
Chapman 2018	-0.6162	0.2999	25.1%	0.54 [0.30, 0.97]
Roche 2017	0.0943	0.0826	39.7%	1.10 [0.93, 1.29]
Watz 2016	-0.4463	0.1575	35.2%	0.64 [0.47, 0.87]
Total (95% CI)			**100.0%**	**0.76 [0.48, 1.21]**

Heterogeneity: Tau² = 0.14; Chi² = 12.94, df = 2 (P = 0.002); I² = 85%
Test for overall effect: Z = 1.15 (P = 0.25)

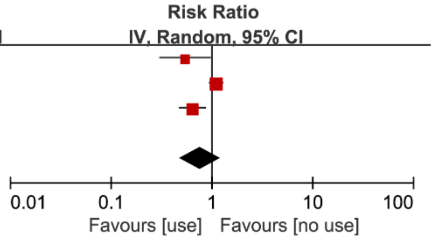


Figure S28. The risk ratio of exacerbations COPD ICS vs non-ICS treatment among patients with baseline BEC < 300 cells/μL

Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Random, 95% CI
Chapman 2018	0.0296	0.1551	16.2%	1.03 [0.76, 1.40]
Roche 2017	0.151	0.0401	48.0%	1.16 [1.08, 1.26]
Watz 2016	-0.0408	0.0742	35.8%	0.96 [0.83, 1.11]
Total (95% CI)			**100.0%**	**1.06 [0.92, 1.23]**

Heterogeneity: Tau² = 0.01; Chi² = 5.41, df = 2 (P = 0.07); I² = 63%
Test for overall effect: Z = 0.84 (P = 0.40)

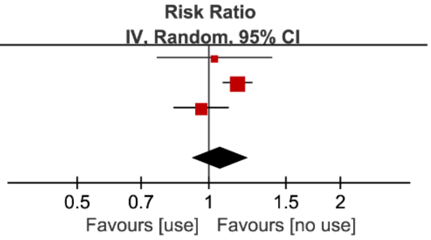


Figure S29. The odds ratio of exacerbations COPD baseline BEC ≥ 2% vs baseline BEC < 2%

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI
Aksoy 2018	-1.1335	0.0526	10.3%	0.32 [0.29, 0.36]
Bélanger 2018	0.604	0.233	9.0%	1.83 [1.16, 2.89]
Chan 2020	1.0919	0.3782	7.3%	2.98 [1.42, 6.25]
Couillard 2017	1.2726	0.4095	7.0%	3.57 [1.60, 7.97]
Duman 2015	-0.3392	0.1378	9.9%	0.71 [0.54, 0.93]
Hastie 2017	0.018	0.0926	10.2%	1.02 [0.85, 1.22]
Kerkhof 2017	0.122	0.056	10.3%	1.13 [1.01, 1.26]
Oshagbemi 2018	0.0198	0.0363	10.4%	1.02 [0.95, 1.10]
Prins 2017	1.075	0.3696	7.4%	2.93 [1.42, 6.05]
Song 2017	-0.198	0.32	8.0%	0.82 [0.44, 1.54]
Watz 2016	0.1689	0.0929	10.2%	1.18 [0.99, 1.42]
Total (95% CI)			**100.0%**	**1.19 [0.82, 1.72]**

Heterogeneity: Tau² = 0.34; Chi² = 454.74, df = 10 (P < 0.00001); I² = 98%
Test for overall effect: Z = 0.90 (P = 0.37)

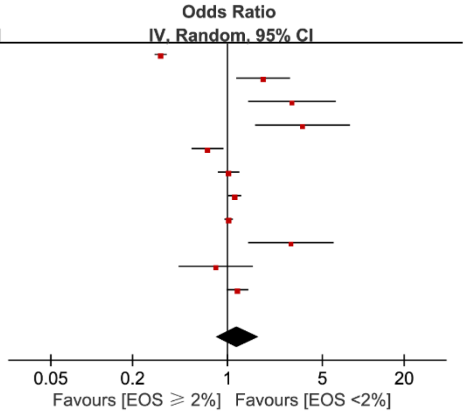


Figure S30. The odds ratio of exacerbations COPD baseline BEC ≥ 3% vs baseline BEC < 3%

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI
Bélanger 2018	0.688	0.26	8.3%	1.99 [1.20, 3.31]
Cheng 2016	-0.6808	0.3733	4.9%	0.51 [0.24, 1.05]
Couillard 2017	1.166	0.446	3.7%	3.21 [1.34, 7.69]
Song 2017	0.166	0.357	5.3%	1.18 [0.59, 2.38]
Vedel-Krogh 2018	0.784	0.591	2.3%	2.19 [0.69, 6.98]
Watz 2016	0.2539	0.1229	16.6%	1.29 [1.01, 1.64]
Yun(COPDGene)	0.565	0.099	18.5%	1.76 [1.45, 2.14]
Yun(ECLIPSE)	0.199	0.084	19.6%	1.22 [1.03, 1.44]
Zeiger 2018	0.223	0.067	20.8%	1.25 [1.10, 1.43]
Total (95% CI)			**100.0%**	**1.38 [1.15, 1.66]**

Heterogeneity: Tau² = 0.04; Chi² = 23.75, df = 8 (P = 0.003); I² = 66%
Test for overall effect: Z = 3.48 (P = 0.0005)

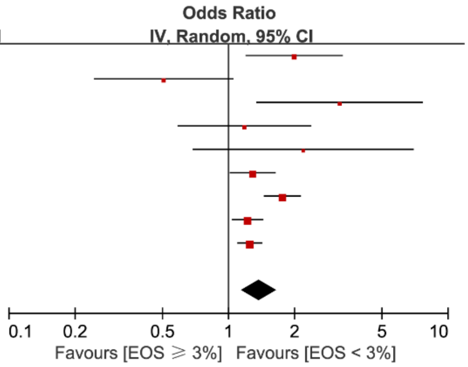


Figure S31. The odds ratio of exacerbations COPD baseline BEC ≥ 4% vs baseline BEC < 4%

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI
Bélanger 2018	0.742	0.286	6.3%	2.10 [1.20, 3.68]
Song 2017	0.293	0.474	2.3%	1.34 [0.53, 3.39]
Watz 2016	0.4161	0.1641	19.0%	1.52 [1.10, 2.09]
Zeiger 2018	0.392	0.084	72.5%	1.48 [1.26, 1.74]
Total (95% CI)			**100.0%**	**1.52 [1.32, 1.74]**

Heterogeneity: Tau² = 0.00; Chi² = 1.45, df = 3 (P = 0.69); I² = 0%
Test for overall effect: Z = 5.82 (P < 0.00001)

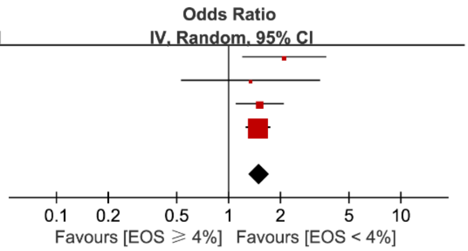


Figure S32. The odds ratio of exacerbations COPD baseline BEC ≥ 5% vs baseline BEC < 5%

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI
Song 2017	0.784	0.591	2.3%	2.19 [0.69, 6.98]
Watz 2016	0.511	0.2191	16.6%	1.67 [1.08, 2.56]
Zeiger 2018	0.565	0.099	81.2%	1.76 [1.45, 2.14]
Total (95% CI)			**100.0%**	**1.75 [1.47, 2.09]**

Heterogeneity: Tau² = 0.00; Chi² = 0.20, df = 2 (P = 0.91); I² = 0%
Test for overall effect: Z = 6.29 (P < 0.00001)

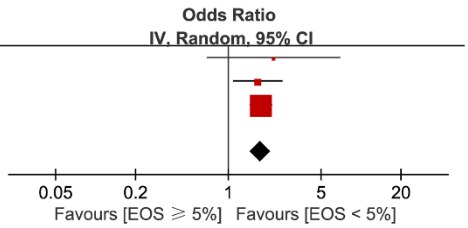


Figure S33. The odds ratio of exacerbations COPD baseline BEC ≥ 150 cells/μL vs baseline BEC < 150 cells/μL

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI
Singh 2020	0.0677	0.0194	72.7%	1.07 [1.03, 1.11]
Watz 2016	0.1345	0.0932	9.9%	1.14 [0.95, 1.37]
Zeiger 2018	-0.0305	0.0674	17.4%	0.97 [0.85, 1.11]
Total (95% CI)			**100.0%**	**1.06 [1.00, 1.12]**

Heterogeneity: Tau² = 0.00; Chi² = 2.57, df = 2 (P = 0.28); I² = 22%
Test for overall effect: Z = 1.85 (P = 0.06)

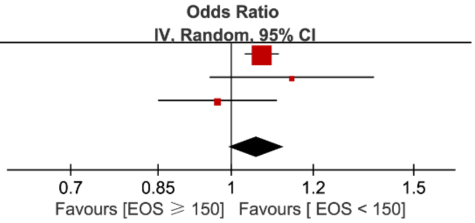


Figure S34. The odds ratio of exacerbations COPD baseline BEC ≥ 200 cells/μL vs baseline BEC < 200 cells/μL

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI
Bélanger 2018	0.6471	0.2002	18.0%	1.91 [1.29, 2.83]
Hasegawa 2016	1.1378	0.4016	8.1%	3.12 [1.42, 6.85]
Peng 2021	1.1436	0.4399	7.1%	3.14 [1.32, 7.43]
Song 2017	-0.1985	0.3176	11.2%	0.82 [0.44, 1.53]
Yun(COPDGene)	0.2151	0.0897	26.7%	1.24 [1.04, 1.48]
Yun(ECLIPSE)	0.0953	0.0538	28.9%	1.10 [0.99, 1.22]
Total (95% CI)			**100.0%**	**1.42 [1.10, 1.85]**

Heterogeneity: Tau² = 0.06; Chi² = 19.91, df = 5 (P = 0.001); I² = 75%
Test for overall effect: Z = 2.64 (P = 0.008)

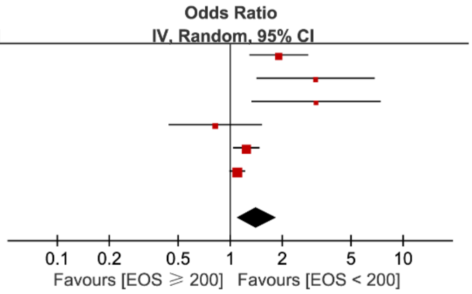


Figure S35. The odds ratio of exacerbations COPD baseline BEC ≥ 300 cells/μL vs baseline BEC < 300 cells/μL

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI
Bélanger 2018	0.7701	0.2591	2.5%	2.16 [1.30, 3.59]
Couillard 2017	1.1663	0.4457	0.9%	3.21 [1.34, 7.69]
Hasegawa 2016	0.1133	0.0139	23.6%	1.12 [1.09, 1.15]
Nishimura 2021	0.4075	0.3393	1.5%	1.50 [0.77, 2.92]
Peng 2021	0.9828	0.4427	0.9%	2.67 [1.12, 6.36]
Siddiqui 2015	-0.3467	0.1707		Not estimable
Singh 2020	0.0862	0.0289	21.8%	1.09 [1.03, 1.15]
Song 2017	0.1655	0.3537	1.4%	1.18 [0.59, 2.36]
Vedel-Krogh 2018	1.1442	0.4049	1.1%	3.14 [1.42, 6.94]
Watz 2016	0.4266	0.1589	5.6%	1.53 [1.12, 2.09]
Yun(COPDGene)	0.2776	0.1024	10.2%	1.32 [1.08, 1.61]
Yun(ECLIPSE)	0.1823	0.0681	15.0%	1.20 [1.05, 1.37]
Zeiger 2018	0.2231	0.0652	15.5%	1.25 [1.10, 1.42]
Total (95% CI)			**100.0%**	**1.24 [1.14, 1.35]**

Heterogeneity: Tau² = 0.01; Chi² = 33.72, df = 11 (P = 0.0004); I² = 67%
Test for overall effect: Z = 5.09 (P < 0.00001)

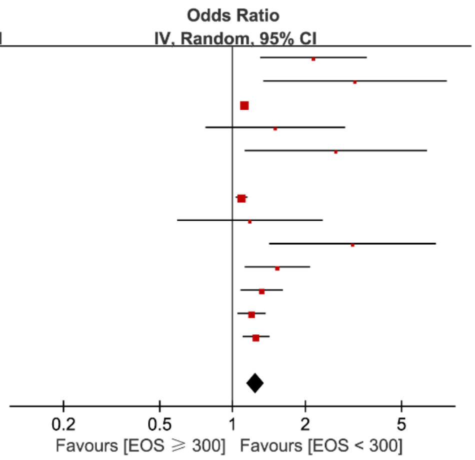


Figure S36. The odds ratio of exacerbations COPD baseline BEC ≥ 400 cells/μL vs baseline BEC < 400 cells/μL

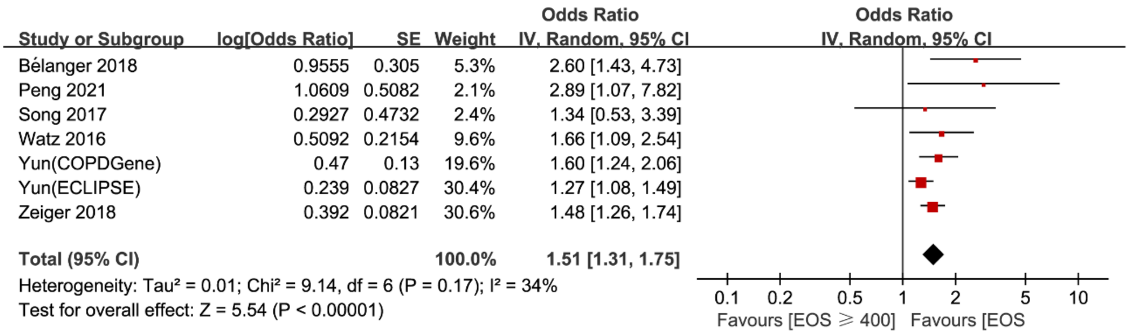


Figure S37. The odds ratio of exacerbations COPD baseline BEC ≥ 500 cells/μL vs baseline BEC < 500 cells/μL

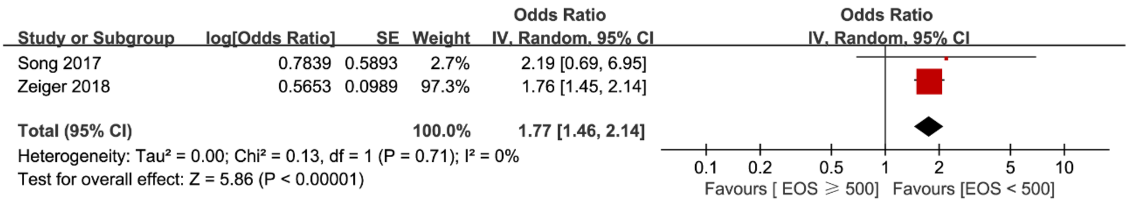


Figure S38. The hazard ratio of mortality baseline BEC ≥ 2% vs baseline BEC < 2%

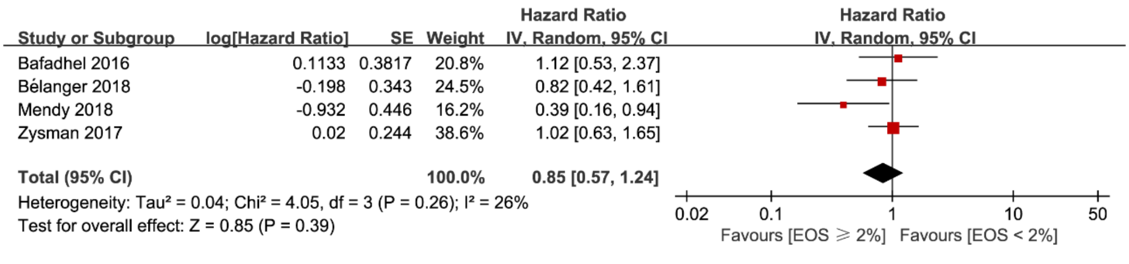


Figure S39. The hazard ratio of mortality baseline BEC ≥ 200 cells/μL vs baseline BEC < 200 cells/μL

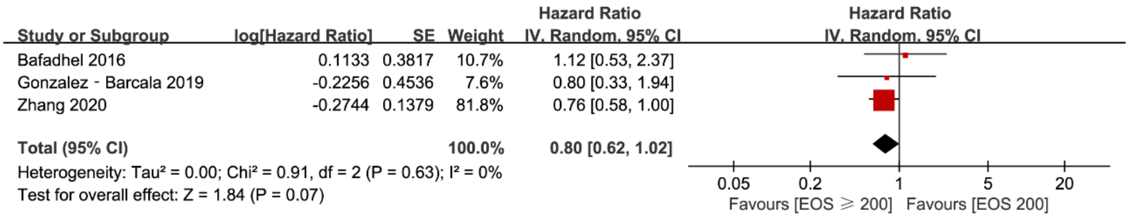


Figure S40. The hazard ratio of mortality baseline BEC ≥ 300 cells/μL vs baseline BEC < 300 cells/μL

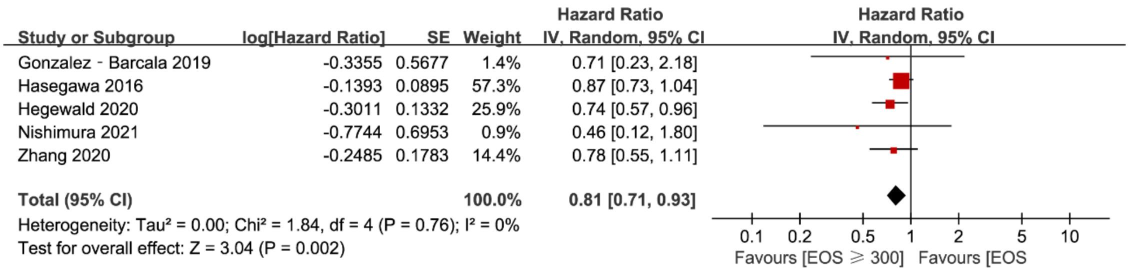


Figure S41. The odds ratio of GOLD III+IV in patients with baseline high BEC vs low BEC

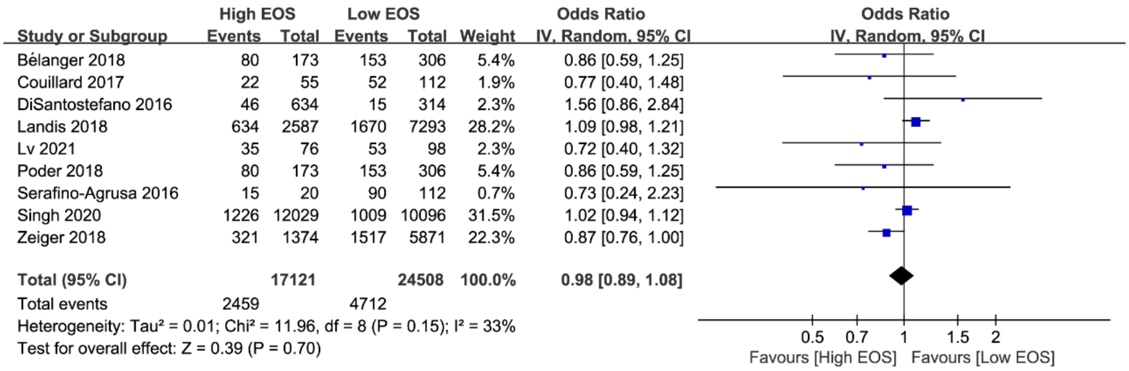
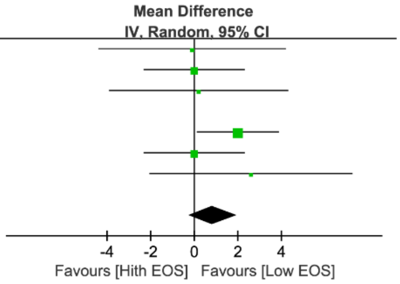


Figure S42. The mean difference of baseline FEV1/FVC in patients with baseline high BEC vs low BEC

	High EOS			Low EOS				Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
Bafadhel 2016	46.6	14.9606	62	46.7	14.799	181	6.6%	-0.10 [-4.40, 4.20]
Bélanger 2018	47	12.9	173	47	11.6	306	22.9%	0.00 [-2.32, 2.32]
Couillard 2017	47.7	13.1	55	47.5	12	112	7.3%	0.20 [-3.91, 4.31]
Lv 2021	58.74	10.14	0	57.22	11.32	0		Not estimable
Oh 2018	51.7	11.5	424	49.7	11.2	205	34.7%	2.00 [0.12, 3.88]
Poder 2018	47	12.9	173	47	11.6	306	22.9%	0.00 [-2.32, 2.32]
Prins 2017	42.5	13.6	39	39.9	12.4	168	5.7%	2.60 [-2.06, 7.26]
Total (95% CI)			**926**			**1278**	**100.0%**	**0.85 [-0.26, 1.96]**

Heterogeneity: Tau² = 0.00; Chi² = 3.29, df = 5 (P = 0.66); I² = 0%

Test for overall effect: Z = 1.50 (P = 0.13)



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