Supplemental material 2: Supplemental Figures.

A. IL-1β

	Expe	erimenta	l.	(Control			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% Cl
Constantinidis J. 2008	0.28	0.11	13	0.66	0.21	12	10.5%	-0.38 [-0.51, -0.25]	•
Huang Y.S. 2016	0.36	0.16	47	0.42	0.27	32	10.5%	-0.06 [-0.16, 0.04]	•
Dalesio N.M. 2020	0.17	0.07	7	0.22	0.4	12	10.5%	-0.05 [-0.28, 0.18]	•
Sahiman J. 2010	0.19	1.51	84	0.23	1.31	40	10.3%	-0.04 [-0.56, 0.48]	t
Medeiros C.A.M. 2012	1.22	4.6	35	0	0	15		Not estimable	
Tomiyama H. 2008	0.43	0.33	28	0.33	0.16	15	10.5%	0.10 [-0.05, 0.25]	t the second sec
Huang Y.S. 2020	1.51	2.25	55	0.42	1.38	32	10.1%	1.09 [0.33, 1.85]	•
Tang T. 2019	23	2.87	120	20.86	2.56	127	10.2%	2.14 [1.46, 2.82]	•
Chen V.G. 2020	102.03	112.98	17	97.26	139.67	17	0.0%	4.77 [-80.63, 90.17]	· · · · · · · · · · · · · · · · · · ·
Kong Y. 2018	27.15	5.91	50	21.17	1.7	40	8.4%	5.98 [4.26, 7.70]	+
Chen B. 2021	13.17	5.5	23	2.67	1.89	30	7.2%	10.50 [8.15, 12.85]	+
Gamsiz-Isik H. 2017	38.82	26.42	83	19.25	17.65	80	2.1%	19.57 [12.70, 26.44]	
Celikhisar H. 2020	23.74	2.98	30	1.7	0.21	82	9.6%	22.04 [20.97, 23.11]	•
Total (95% CI)			592			534	100.0%	4.07 [2.96, 5.18]	•
Heterogeneity: Tau ² = 3.0	15; Chi² =	1872.19,	df = 11	(P < 0.	00001); F	²= 99%	6		
Test for overall effect: Z =	7.18 (P <	0.00001)						Favours [experimental] Favours [control]

B. IL-2

	Expe	erimen	tal	C	ontrol			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% Cl	IV, Random, 95% Cl
Said E.A. 2017	0.3	0.2	22	1.1	3.3	21	29.1%	-0.80 [-2.21, 0.61]	•
Zhang Z. 2017	3.41	0.21	50	3.38	0.19	52	30.0%	0.03 [-0.05, 0.11]	•
Sarinc Ulasli S. 2015	101.4	9.4	28	97.2	10.2	20	20.1%	4.20 [-1.47, 9.87]	+=-
Shi C. 2019	59.98	8.57	15	36.58	6.2	15	20.8%	23.40 [18.05, 28.75]	
Total (95% CI)			115			108	100.0%	5.49 [1.07, 9.92]	◆
Heterogeneity: Tau ² = 1 Test for overall effect: 2	16.97; Ch I = 2.44 (ni² = 76 P = 0.0	6.62, df 01)	-50 -25 0 25 50					

Favours [experimental] Favours [control]

C. IL-4

	Expe	erimenta	al	С	ontrol			Mean Difference	Mean Difference	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	
Said E.A. 2017	1.2	0.6	22	5.6	20.4	21	2.7%	-4.40 [-13.13, 4.33]		
Akinnusi M. 2013	0.39	0.21	25	0.36	0.2	18	33.2%	0.03 [-0.09, 0.15]	•	
Chen V.G. 2020	6.67	2.37	17	6.49	3.29	17	21.4%	0.18 [-1.75, 2.11]		
Zhang Z. 2017	2.45	0.21	50	1.21	0.22	52	33.2%	1.24 [1.16, 1.32]		
Ye J. 2015	36.72	16.58	25	33.24	15.69	19	2.3%	3.48 [-6.11, 13.07]		
Su M. 2017	234.24	12.16	42	186.42	11.43	48	7.2%	47.82 [42.92, 52.72]		•
Total (95% CI)			181			175	100.0%	3.89 [2.40, 5.38]	•	
Heterogeneity: Tau ² =	1.74; Ch	i ² = 607.	83, df =	= 5 (P < 0	.00001)); I ² = 99	3%			
Test for overall effect: 2	Z = 5.11 ((P < 0.0)	0001)						-10 -5 0 5 10	
		`							Favours (experimental) Favours (control)	

D. IL-6

	Experimental		Control				Mean Difference Mean Difference		
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
Roytblat L. 2000	5.58	0.37	11	7.69	5.06	9	1.1%	-2.11 [-5.42, 1.20]	+
Chen V.G. 2020	6.66	3.91	17	7.22	4.96	17	1.2%	-0.56 [-3.56, 2.44]	+
Kurt O.K. 2013	1.35	0.32	48	1.31	0.3	37	3.3%	0.04 [-0.09, 0.17]	
Deboer M.D. 2012	1.69	1.1	9	1.61	1.27	15	2.8%	0.08 [-0.88, 1.04]	-
Zychowski K.E. 2016	2.23	0.04	8	2.15	0.05	7	3.3%	0.08 [0.03, 0.13]	
Dalesio N.M. 2020	0.74	0.29	7	0.59	0.2	18	3.2%	0.15 [-0.08, 0.38]	
Sahlman J. 2010	2.36	1.9	84	2.14	2.01	40	3.0%	0.22 [-0.52, 0.96]	
Antonopoulou S. 2008	0.53	0.3	45	0.21	0.2	25	3.3%	0.32 [0.20, 0.44]	
Akinnusi M. 2013	1.71	0.99	25	1.36	0.92	18	3.1%	0.35 [-0.23, 0.93]	
Steiropoulos P. 2010	2.73	1.14	38	2.36	1.41	23	3.0%	0.37 [-0.31, 1.05]	
Constantinidis J. 2008	0.84	0.08	13	0.42	0.08	12	3.3%	0.42 [0.36, 0.48]	
Huang Y.S. 2020	1.59	1.58	55	1.1	0.92	32	3.1%	0.49 [-0.04, 1.02]	
Nobili Y. 2015	11.5	5.9	52	11	5.6	28	1.5%	0.50 [-2.12, 3.12]	+
Kim J. 2010	3.57	2.74	28	3.02	2.44	22	2.4%	0.55 [-0.89, 1.99]	ł
Huang Y.S. 2016	1.66	0.23	47	1.1	0.18	32	3.3%	0.56 [0.47, 0.65]	
Takahashi K.I. 2008	1.56	2.49	41	0.99	0.94	12	2.8%	0.57 [-0.36, 1.50]	+
Arias M.A. 2008	4.2	3.4	30	3.6	1.8	15	2.3%	0.60 [-0.92, 2.12]	Ļ
Liu Z. 2011	1.62	0.43	20	0.92	0.34	20	3.2%	0.70 [0.46, 0.94]	
Gileles-Hillel A. 2014	8	4.8	75	7.3	3.2	129	2.6%	0.70 [-0.52, 1.92]	-
Oian X. 2012	89.56	36.19	30	88.85	41.48	40	0.1%	0.71 [-17.54, 18.96]	
Yang D. 2013	1.89	1.29	25	1	0.12	25	3.1%	0.89 [0.38, 1.40]	
Tomiyama H. 2008	2.4	1.6	28	1.5	0.6	15	3.0%	0.90 [0.23, 1.57]	
Nakra N. 2008	3.9	4.3	24	3	2.4	9	1.6%	0.90 [-1.43, 3.23]	Ļ
Mônico-Neto M. 2018	10.1	0.8	123	9.1	0.9	211	3.3%	1.00 [0.81, 1.19]	
Dogan D. 2016	2.02	1.19	39	1.01	0.19	12	3.2%	1.01 [0.62, 1.40]	
Kotsiou O. S. 2022	3.4	1	15	2.3	0.3	15	3.1%	1.10 [0.57, 1.63]	
Tauman R. 2007	2.26	2.7	38	1.12	0.7	33	2.9%	1.14 [0.25, 2.03]	
Zhang 7, 2017	3.75	0.19	50	2.54	0.17	52	3.3%	1.21 [1.14, 1.28]	
Damiani M.F. 2015	3.14	1.27	30	1.46	0.69	30	3.1%	1.68 [1.16, 2.20]	
Shalitin S. 2018	4.56	2.92	9	2.83	1.54	29	1.9%	1.73 [-0.26, 3.72]	-
Ciccone M.M. 2014	3.33	1.35	54	1.5	0.67	40	3.2%	1.83 [1.41, 2.25]	
Bozic I. 2018	3.58	1.55	25	1.26	0.69	25	3.0%	2.32 [1.65, 2.99]	-
Ifergane G. 2016	6.64	5.27	21	3.14	2.05	22	1.6%	3 50 [1 09 5 91]	-
Tang T. 2019	63.6	8.29	120	59.16	12.27	127	1.5%	4.44 [1.84, 7.04]	-
Smith D F 2017	29.2	62	42	24.6	51.9	90	0.0%	4 60 [-17 00 26 20]	
Bhatt S.P. 2021	20.1	5.6	190	15.4	3.5	57	2.6%	4.70 [3.49, 5.91]	
Ciftci T.U. 2004	11.71	9.8	43	6.12	4.44	22	1.0%	5.59 [2.12, 9.06]	-
Kong Y. 2018	61.59	9.76	50	54.46	9.43	40	0.8%	7.13 [3.15, 11, 11]	-
Medeiros C.A.M. 2012	9.4	13.2	35	0.77	2.53	15	0.7%	8.63 [4.07, 13.19]	-
Ye I. 2012	55.09	17.02	44	42.56	21.15	20	0.2%	12.53 [1.98, 23.08]	
Nizam N 2016	99.2	41 1	22	82.4	27.2	13	0.0%	16 80 [-5 86 39 46]	
Rilal N 2021	57.98	5.96	10	40.57	3 47	30	0.9%	17 41 [13 51 21 31]	-
Li Y 2008	65.3	15.4	28	37.5	10.9	22	0.3%	27 80 [20 50 35 10]	
Chen I. 2007	143.12	33.52	100	107.43	27.66	40	0.1%	35.69 [24.89, 46 49]	
Liu H. 2000	50.67	4.7	22	12.69	2.75	16	1.6%	37.98 [35.60, 40.36]	-
Li Y 2009	83.4	6.4	24	37.5	10.9	22	0.5%	45.90 [40.67, 51 13]	· -
Lu D. 2018	58.49	8.03	35	9.11	10.13	22	0.6%	49 38 [44 38 54 38]	— —
Ye L. 2010	144.5	10.9	45	53.6	3.5	52	1.1%	90.90 [87.58, 94.22]	-
Total (95% CI)			1974			1657	100.0%	3 49 [3 07 2 02]	
Hotorogonoitu Ta2 - 1	42. Ch ¹²	- 5625	23/4	- 47 (2	~ 0.000	01): 12	- 0.0%	3.49 [3.07, 3.92]	
Test for overall effect: 7	+3; Cni*	= 5035. (P < 0 0	.01, 01	= 47 (P -	< 0.000	01); 1, 1	= 99%		-100 -50 0 50 100
rescior overall effect. Z	- 10.15	(r < 0.0	(0001)						Favours [experimental] Favours [control]

E. IL-8

	Exp	Experimental Control						Mean Difference	Mean Difference		
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI		
Said E.A. 2017	75.2	32.9	22	91.5	43.5	21	5.4%	-16.30 [-39.43, 6.83]			
Archontogeorgis K. 2016	31.79	20.09	64	34.09	14.37	20	8.8%	-2.30 [-10.29, 5.69]	-		
Cheng J. 2021	43.5	7.22	29	45.65	6.87	22	9.4%	-2.15 [-6.04, 1.74]	-		
Akinnusi M. 2013	4.98	1.67	25	4.57	1.453	18	9.6%	0.41 [-0.53, 1.35]			
Kim J. 2010	13.35	5.63	28	12.89	4.3	22	9.5%	0.46 [-2.29, 3.21]	+		
Smith D.F. 2017	11.6	16.7	42	9.8	18.8	90	9.1%	1.80 [-4.57, 8.17]	+		
Bhatt S.P. 2021	8.29	5.2	190	4.98	3.67	57	9.6%	3.31 [2.10, 4.52]	-		
Bao H.R. 2005	35.95	10.63	35	22.27	7.62	25	9.3%	13.68 [9.06, 18.30]	-		
Ming H. 2019	34.6	7.1	684	19.4	8.5	192	9.6%	15.20 [13.89, 16.51]			
Bilal N. 2021	126.31	11.73	10	100.12	5.13	30	8.9%	26.19 [18.69, 33.69]			
Jin F. 2017	40.72	1.6	100	13.28	3.15	50	9.6%	27.44 [26.51, 28.37]			
Zhang D. 2019	229.71	175.61	21	69.4	26.7	10	1.0%	160.31 [83.40, 237.22]	$ \longrightarrow$		
Chen V.G. 2020	1,088.77	1,012.05	17	664.44	565.13	17	0.0%	424.33 [-126.68, 975.34]	· · · · · · · · · · · · · · · · · · ·		
Total (95% CI)			1267			574	100.0%	8.68 [0.56, 16.80]	◆		
Heterogeneity: $Tau^2 = 178$.16: Chi ² =	2046.15. c	if = 12	(P < 0.0	0001); I ²	= 99%					
Test for overall effect: Z =	2.10 (P = 0	.04)							–100 –50 0 50 100 Favours [experimental] Favours [control]		

F. IL-10

	Expe	riment	al	С	ontrol			Mean Difference	Mean Difference			
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI			
Su M. 2017	261.71	18.55	42	338.24	25.2	48	0.3%	-76.53 [-85.60, -67.46]	•			
Li Y 2009	24.6	5.1	24	50.1	6.9	22	1.7%	-25.50 [-29.03, -21.97]				
Leon-Cabrera S. 2015	74.4	17	29	97.2	10.9	13	0.3%	-22.80 [-31.37, -14.23]				
Li Y 2008	37.5	12.4	28	50.1	6.9	22	0.8%	-12.60 [-18.02, -7.18]				
Bao H.R. 2005	36.39	4.96	35	42.06	4.09	25	3.5%	-5.67 [-7.97, -3.37]				
Ye J. 2012	47.84	10.72	44	52.17	23.18	20	0.2%	-4.33 [-14.97, 6.31]				
Said E.A. 2017	0.5	0.3	22	1.8	5.9	21	3.0%	-1.30 [-3.83, 1.23]	-+			
Rogers V.E. 2018	1.7	1.06	20	2.03	1.76	7	6.5%	-0.33 [-1.71, 1.05]	+			
Akinnusi M. 2013	0.96	0.48	25	0.89	0.43	18	12.4%	0.07 [-0.20, 0.34]	•			
Dalesio N.M. 2020	0.59	0.17	7	0.46	0.16	18	12.7%	0.13 [-0.02, 0.28]	•			
Zhang Z. 2017	3.45	0.19	50	3.01	0.17	52	12.8%	0.44 [0.37, 0.51]				
Bhatt S.P. 2021	2.62	0.39	190	2.1	0.28	57	12.8%	0.52 [0.43, 0.61]	•			
Huang Y.S. 2016	2.62	0.39	47	2.1	0.28	32	12.7%	0.52 [0.37, 0.67]	•			
Sahiman J. 2010	1.28	2.34	84	0.7	1.51	40	10.4%	0.58 [-0.11, 1.27]	+			
Huang Y.S. 2020	2.74	2.94	55	2.1	1.41	32	9.0%	0.64 [-0.28, 1.56]	+			
Sarinc Ulasli S. 2015	34.7	12.4	28	32.5	14	20	0.4%	2.20 [-5.46, 9.86]				
Chen V.G. 2020	13.08	11.77	17	10.69	12.95	17	0.4%	2.39 [-5.93, 10.71]				
Total (95% CI)			747			464	100.0%	-0.77 [-1.27, -0.27]	•			
Heterogeneity: Tau ² = 0.1	51: Chi ² =											
Test for overall effect: Z =	= 3.00 (P =	= 0.003)							-20 -10 0 10 20			
									Favours [experimental] Favours [control]			

G. IL-12

	Expe	erimen	tal	C	ontrol			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% Cl
Rogers V.E. 2018	4.88	2.97	20	5.37	4.15	7	2.9%	-0.49 [-3.83, 2.85]	
Huang Y.S. 2020	1.77	1.15	55	0.97	0.75	6	70.2%	0.80 [0.13, 1.47]	
Said E.A. 2017	1	2.6	22	0	0.1	21	26.9%	1.00 [-0.09, 2.09]	
Leon-Cabrera S. 2015	405.3	57.4	29	394	64.7	13	0.0%	11.30 [-29.61, 52.21]	· · · · · · · · · · · · · · · · · · ·
Total (95% CI)			126			47	100.0%	0.82 [0.26, 1.38]	•
Heterogeneity: Chi ² = 0.9	95, df = 3	(P = 0	.81); I²	= 0%					-10 -5 0 5 10
Test for overall effect: Z =	: 2.85 (P	= 0.00	14)						Favours (experimental) Favours (control)

H. IL-17

	Exp	eriment	al	0	Control			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
Bhatt S.P. 2021	15.12	1.38	190	10.2	1.25	57	24.8%	4.92 [4.54, 5.30]	•
Huang Y.S. 2016	15.12	1.38	47	10.2	1.25	32	24.5%	4.92 [4.33, 5.51]	•
Huang Y.S. 2020	13.78	7.18	55	10.2	6.36	32	18.2%	3.58 [0.67, 6.49]	-
Toujani S. 2017	20.3	3.9	92	10.05	3	30	23.1%	10.25 [8.91, 11.59]	•
Ye J. 2012	70.3	13.65	44	55.12	18.23	20	5.6%	15.18 [6.23, 24.13]	— —
Ye J. 2015	88.36	14.96	25	38.18	21.63	19	3.8%	50.18 [38.82, 61.54]	
Total (95% CI)			453			190	100.0%	8.19 [5.79, 10.59]	•
Heterogeneity: Tau ² =	6.01; C	hi² = 123	3.96, d1	f= 5 (P ·	< 0.000	01); I 2 =	96%		-50 -25 0 25 50
Test for overall effect:	Z = 6.70) (P < 0.1	00001)						Favours [experimental] Favours [control]

I. IL-18

	Exp	erimenta	al 👘	C	ontrol			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
Tang T. 2019	94.13	7.98	120	89.72	12.71	127	41.4%	4.41 [1.78, 7.04]	•
Zhang S.W. 2015	19.26	9.87	34	10.58	2.02	25	41.3%	8.68 [5.27, 12.09]	•
Li C 2009	797.64	109.83	18	250.27	76.48	18	17.3%	547.37 [485.54, 609.20]	
Total (95% CI)			172			170	100.0%	100.14 [66.45, 133.84]	•
Heterogeneity: Tau² = Test for overall effect:	712.26; (Z = 5.83 (Chi² = 29 (P < 0.00	7.96, di 001)	f=2(P <	0.0000	1); I² = 9	99%		-500 -250 0 250 500 Favours [experimental] Favours [control]

J. IL-23

	Expe	rimen	tal	С	ontrol			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% Cl	IV, Random, 95% Cl
Huang Y.S. 2016	14.58	0.75	47	12.29	0.73	32	25.3%	2.29 [1.96, 2.62]	
Bhatt S.P. 2021	14.58	0.75	190	12.29	0.73	57	25.3%	2.29 [2.07, 2.51]	•
Huang Y.S. 2020	20.14	7.08	55	12.29	3.66	32	24.4%	7.85 [5.59, 10.11]	•
Can M. 2016	30.9	1.4	12	6.9	1.3	27	25.1%	24.00 [23.07, 24.93]	•
Total (95% CI)			304			148	100.0%	9.10 [3.21, 14.98]	
Heterogeneity: Tau² = Test for overall effect:	35.66; (Z = 3.03	Chi² = 0 (P = 0	2026.5 .002)	8, df = 3	(P < 0	.00001); I² = 100	1%	-100 -50 0 50 100 Favours [experimental] Favours [control]

Supplemental Figure 1. Forest plots of interleukins (ILs) concentration differences between OSA patients and controls. (A) IL-1 β ; (B) IL-2; (C) IL-4; (D) IL-6; (E) IL-8; (F) IL-10; (G) IL-12; (H) IL-17; (I) IL-18; (J) IL-23.

The study of Medeiros C.A.M made no contribution to the pooled analysis in IL-1β.





Supplemental Figure 2. Funnel plots of Interleukins (ILs) concentration differences between OSA patients and controls. (A) IL-1β; (B) IL-2; (C) IL-4; (D) IL-6; (E) IL-8; (F) IL-10; (G) IL-12; (H) IL-17; (I) IL-18; (J) IL-23.

Α. IL-1β

	Exp	eriment	tal	0	Control			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
2.3.1 mild OSA VS no (DSA								
Kong Y. 2018	20.1	1.47	10	21.17	1.7	40	6.0%	-1.07 [-2.12, -0.02]	1
Tang T. 2019	20.1	1.48	9	20.86	2.56	127	6.0%	-0.76 [-1.82, 0.30]	-
Sahlman J. 2010	0.19	1.51	84	0.23	1.31	40	6.3%	-0.04 [-0.56, 0.48]	
Medeiros C.A.M. 2012	0	0	15	0	0	15		Not estimable	
Tomiyama H. 2008	0.35	0.12	10	0.33	0.16	15	6.4%	0.02 [-0.09, 0.13]	
Chen B. 2021	7.29	3.43	20	2.67	1.89	30	5.5%	4.62 [2.97, 6.27]	-
Celikhisar H. 2020	11.8	7.04	28	1.7	0.21	82	4.6%	10.10 [7.49, 12.71]	-
Gamsiz-Isik H. 2017	34.35	24.2	16	19.25	17.65	80	0.6%	15.10 [2.63, 27.57]	
Subtotal (95% CI)			192			429	35.6%	1.59 [0.33, 2.86]	•
Heterogeneity: Tau ² = 2	11; Chi ²	= 99.07	, df = 6	6 (P < 0	.00001);	l ² = 94	%		
Test for overall effect: Z	= 2.47 (P = 0.01)						
2.3.2 moderate OSA VS	S no OS	A							
Tomiyama H 2008	0.4	0.28	12	0.33	0.16	15	64%	0.07 [-0.11 0.25]	+
Tang T 2019	22.89	1 92	33	20.86	2 56	127	6.2%	2 03 [1 24 2 82]	-
Kong Y 2018	24.35	3.83	15	21 17	17	40	5.2%	3 18 [1 17 5 19]	-
Chen B 2021	10.69	3.83	24	2.67	1 89	30	5.5%	8 02 [6 35 9 69]	-
Celikhisar H 2020	17.2	5.96	26	17	0.21	82	4 9%	15 50 [13 21 17 79]	-
Gamsiz-Isik H 2017	39.82	26.92	67	19 25	17 65	80	1.4%	20 57 [13 05 28 09]	
Subtotal (95% CI)	00.02	20.02	177	10.20	11.00	374	29.7%	7.14 [3.61, 10.68]	•
Heterogeneity: Tau ² = 1	7.45: Ch	i ² = 310.	68. df	= 5 (P <	0.0000	1); ² =	98%		
Test for overall effect: Z	= 3.96 (P < 0.00	01)	,					
2.3.3 severe OSA VS n	o OSA								
Dalesio N.M. 2020	0.17	0.07	7	0.22	0.4	12	6.4%	-0.05 [-0.28, 0.18]	
Medeiros C.A.M. 2012	1.22	4.6	35	0	0	15		Not estimable	
Tomiyama H. 2008	0.43	0.33	28	0.33	0.16	15	6.4%	0.10 [-0.05, 0.25]	
Tang T. 2019	24.92	2.86	78	20.86	2.56	127	6.2%	4.06 [3.28, 4.84]	
Kong Y. 2018	29.15	5.91	25	21.17	1.7	40	4.8%	7,98 [5,60, 10,36]	-
Chen B. 2021	13.17	5.5	23	2.67	1.89	30	4.8%	10.50 [8.15, 12.85]	-
Celikhisar H. 2020	23.74	2.98	30	1.7	0.21	82	6.0%	22.04 [20.97, 23.11]	
Subtotal (95% CI)			226			321	34.8%	7.34 [4.18, 10.51]	•
Heterogeneity: Tau ² = 1	5.09; Ch	i² = 180	3.46, d	f = 5 (P	< 0.000	01); l ² :	= 100%		
Test for overall effect: Z	= 4.55 (P < 0.00	001)						
Total (95% CI)			595			1124	100.0%	4.96 [3.94, 5.99]	•
Heterogeneity: Tau ² = 4.	25; Chi ²	= 2245	35, df	= 18 (P	< 0.000	01); l ² :	= 99%		
_ /									

Test for overall effect: Z = 9.47 (P < 0.00001) Test for suboroup differences: Chi² = 17.19. df = 2 (P = 0.0002). I² = 88.4%

B. IL-6

	Exp	eriment	al	C	Control			Mean Difference	Mean Difference
Study or Subgroup 2.5.1 mild OSA VS no 0	Mean DSA	SD	Total	Mean	SD	Total	Weight	IV. Random, 95% CI	IV. Random, 95% Cl
Kong Y. 2018	46.2	6.09	10	54.46	9.43	40	1.4%	-8.26 [-13.03, -3.49]	
Tang T. 2019	52.86	5.47	9	59.16	12.27	127	1.6%	-6.30 [-10.46, -2.14]	
Tomiyama H. 2008	1.6	0.8	10	1.5	0.6	15	3.0%	0.10 [-0.48, 0.68]	+
Dogan D. 2016	1.21	0.41	12	1.01	0.19	12	3.0%	0.20 [-0.06, 0.46]	•
Sahlman J. 2010	2.36	1.9	84	2.14	2.01	40	2.9%	0.22 [-0.52, 0.96]	ł
Ciccone M.M. 2014	1.89	0.88	26	1.5	0.67	40	3.0%	0.39 [-0.01, 0.79]	•
Tauman R 2007	1.63	1.67	40	1 12	0.7	33	3.0%	0.51 [-0.06, 1.08]	-
Nobili V 2015	11.00	6.4	20	1.12	5.6	28	2.0%	0.80 [-2.32, 3.92]	<u>+</u> -
Mônico-Neto M 2018	10.5	0.4	201	9.1	0.0	211	3.0%	1 40 [1 23 1 57]	
Modeiros C A M 2012	4.4	4.5	15	0.77	2 53	15	2 20%	3 63 [1.02 6 24]	
Bilal N. 2021	44.46	5.01	10	40.57	2.00	20	1 70/	3 89 10 02 7 761	
Vol. 2010	64.2	4.2	10	52.6	3.47	50	2 70/	10 60 10 02 12 19	
Yo L 2012	56.2	22 /1	40	42.56	21 15	20	2.7 /0	12 64 [0 61 26 67]	
Nizom N 2016	00.2	40 5	17	42.00	21.10	12	0.3%	16 70 [9 34 41 74]	
Nizam N. 2016	99.1	42.5	17	02.4	21.2	13	0.1%	10.70 [-0.34, 41.74]	
LI Y 2009	55.2	9.6	22	37.5	10.9	22	1.0%	17.70 [11.63, 23.77]	
Smith D.F. 2017	76.9	114.9	23	24.6	51.9	90	0.0%	52.30 [4.13, 100.47]	4
Subtotal (95% CI)			5/4			/00	31.0%	1.63 [0.74, 2.52]	•
Heterogeneity: Tau ² = 1. Test for overall effect: Z	.76; Chi ² = 3.57 (F	= 295.7 P = 0.00	7, df = 04)	15 (P <	0.0000	1); l² =	95%		
2.5.3 moderate OSA VS	S no OS	A							
Kim J. 2010	2.87	2.53	9	3.02	2.44	22	2.5%	-0.15 [-2.09, 1.79]	+
Akinnusi M. 2013	1.71	0.99	25	1.36	0.92	18	3.0%	0.35 [-0.23, 0.93]	r
Tomiyama H. 2008	1.9	1.4	12	1.5	0.6	15	2.9%	0.40 [-0.45, 1.25]	+
Liu Z. 2011	1.62	0.43	20	0.92	0.34	20	3.0%	0.70 [0.46, 0.94]	•
Tang T. 2019	60.16	7.08	33	59.16	12.27	127	2.0%	1.00 [-2.22, 4.22]	
Tauman R. 2007	2.26	2.7	38	1.12	0.7	33	2.9%	1.14 [0.25, 2.03]	-
Bozic J. 2018	2.62	0.71	25	1.26	0.69	25	3.0%	1.36 [0.97, 1.75]	•
Damiani M F. 2015	3.14	1.27	30	1.46	0.69	30	3.0%	1 68 [1 16, 2 20]	
Ciccone M.M. 2014	3.33	1.35	54	1.5	0.67	40	3.0%	1 83 [1 41 2 25]	
Mônico-Neto M 2018	11	0.9	123	91	0.9	211	3.0%	1 90 [1 70 2 10]	
Bilal N 2021	42 74	2 49	10	40.57	3 47	30	2.5%	2 17 [0 19 4 15]	
Kong V 2018	58 34	7.00	15	54.46	9.43	40	1 4%	3 88 [_0 75 8 51]	
Smith D E 2017	20.24	62	12	24.6	51.9	90	0.1%	4 60 [-17 00 26 20]	
Li V 2009	73.5	8.0	22	37.5	10.0	22	1 10/	36 00 [30 12 41 88]	
LIT 2009	121.0	0.9	20	57.5	2.5	52	2.0%	67 60 [64 25 70 95]	
Subtotal (95% CI)	121.2	9.9	407	53.0	3.5	775	2.0%	6 94 [5 13 9 55]	▲
Subtotal (95 % Cl)	50. Chi2	- 1000	431	- 11 (D	- 0.000	011.12.	- 000/	0.04 [0.15, 0.55]	
Test for overall effect: Z	= 7.85 (F	= 1809. > < 0.00	95, di 001)	= 14 (P	< 0.000	01); 1-	= 99%		
2.5.5 severe OSA VS n	o OSA								
Nobili Y. 2015	10.5	4.3	23	11	5.6	28	2.2%	-0.50 [-3.22, 2.22]	+
Zychowski K.E. 2016	2.23	0.04	8	2.15	0.05	7	3.0%	0.08 [0.03, 0.13]	
Dalesio N.M. 2020	0.74	0.29	7	0.59	0.2	18	3.0%	0.15 [-0.08, 0.38]	•
Kim J. 2010	3.57	2.74	28	3.02	2.44	22	2.7%	0.55 [-0.89, 1.99]	+
Qian X. 2012	89.56	36.19	30	88.85	41.48	40	0.2%	0.71 [-17.54, 18.96]	
Tomiyama H. 2008	2.4	1.6	28	1.5	0.6	15	3.0%	0.90 [0.23, 1.57]	-
Mônico-Neto M. 2018	10.1	0.8	123	9.1	0.9	211	3.0%	1.00 [0.81, 1.19]	•
Dogan D. 2016	2.38	1.25	27	1.01	0.19	12	3.0%	1.37 [0.89. 1.85]	•
Bozic J. 2018	3.58	1.55	25	1.26	0.69	25	3.0%	2.32 [1.65, 2.99]	-
Tang T. 2019	66.29	7.62	78	59.16	12.27	127	2.2%	7.13 [4.41, 9.85]	-
Medeiros C.A.M. 2012	9.4	13.2	35	0.77	2.53	15	1.5%	8.63 [4.07, 13.19]	
Kong Y. 2018	64.76	9,05	25	54.46	9.43	40	1.4%	10.30 [5.70, 14.90]	
Ye J. 2012	53.75	19,52	21	42.56	21.15	20	0.3%	11.19 [-1.28, 23.66]	+
Nizam N. 2016	99.2	41.1	22	82.4	27.2	13	0.1%	16.80 [-5.86, 39.46]	
Bilal N. 2021	57.98	5.96	10	40.57	3.47	30	1.7%	17.41 [13.51, 21.31]	
LI Y 2009	83.4	64	24	37.5	10.9	22	1 2%	45.90 [40.67 51 13]	
Yel 2010	144 5	10.9	45	53.6	3.5	52	1 9%	90 90 [87 58 94 22]	
Subtotal (95% CI)	144.0	10.9	559	00.0	0.0	697	33.5%	10.87 [9.23, 12,52]	◆
Heterogencity: Tou? - 9	10. Chi2	= 3452	37 Af	= 16 (P	< 0.000	01). 12 .	= 100%	icion [oiro, irior]	
Test for overall effect: Z	= 12.95	– 3453. (P < 0.0	0001)	- 10 (P	~ 0.000	01), 123	- 100%		
Total (95% CI)			1630			2260	100.0%	5.97 [5.21, 6.73]	•
Heterogeneity: Tau ² = 4	.98; Chi ²	= 6020.	14. df	= 47 (P	< 0.000	01); l ² :	= 99%		
Test for overall effect: 7	= 15.37	(P < 0.0	0001)		2.000	.,, .			-20 -10 0 10 20
Test for subaroup differe	ences: Cl	$hi^2 = 104$.03. d	f = 2 (P	< 0.000	01). I² :	= 98.1%		Favours [experimental] Favours [control]

Supplemental Figure 3. Forest plots of IL-1 β for IL-6 concentration differences between mild, moderate, severe OSA patients and controls. (A) IL-1 β ; (B) IL-6.

The study of Medeiros C.A.M made no contribution to the pooled analysis in IL-1 β .

A. IL-8



B. IL-10

	Expe	eriment	al	0	Control			Mean Difference	Mean Difference	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	
2.7.1 mild OSA VS no	OSA									
Ye J. 2012	46.79	11.69	23	52.17	23.18	20	5.2%	-5.38 [-16.61, 5.85]		
Li Y 2009	46.7	4.6	22	50.1	6.9	22	15.8%	-3.40 [-6.87, 0.07]	+	
Sahiman J. 2010	1.28	2.34	84	0.7	1.51	40	20.0%	0.58 [-0.11, 1.27]	.†	
Subtotal (95% CI)			129			82	41.0%	-1.38 [-4.91, 2.16]	•	
Heterogeneity: Tau ² =	5.79; Cl	hi² = 5.9	0, df=	2 (P = 0	.05); l² =	66%				
Test for overall effect: Z = 0.76 (P = 0.45)										
2.7.3 severe OSA VS no OSA										
Li Y 2009	24.6	5.1	24	50.1	6.9	22	15.7%	-25.50 [-29.03, -21.97]	+	
Ye J. 2012	49.06	8.51	21	52.17	23.18	20	5.5%	-3.11 [-13.90, 7.68]		
Said E.A. 2017	0.5	0.3	22	1.8	5.9	21	17.6%	-1.30 [-3.83, 1.23]	-	
Dalesio N.M. 2020	0.59	0.17	7	0.46	0.16	18	20.2%	0.13 [-0.02, 0.28]		
Subtotal (95% CI)			74			81	59.0%	-7.58 [-18.06, 2.89]	◆	
Heterogeneity: Tau ² =	106.71;	Chi ² = 3	203.40	, df = 3 ((P < 0.0)	0001); F	²= 99%			
Test for overall effect: Z = 1.42 (P = 0.16)										
Total (95% CI)			203			163	100.0%	-5.08 [-8.03, -2.12]	•	
Heterogeneity: Tau ² =	11 27.0	hi² = 2°	10.18	df = 6 (F	<pre>< 0 000</pre>	101): P	= 97%			
Test for overall effect:	7 = 3.36	(P = 0)	0008)	ur – 0 (r	- 0.001	5017,11	- 51 70		-50 -25 0 25 50	
Test for subgroup diff	erences	: Chi ² =	1.21. d	f=1 (P	= 0.27).	$ ^{2} = 17$	4%		Favours [experimental] Favours [control]	
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C. IL-18



Supplemental Figure 4. Forest plots of interleukins (ILs) concentration differences between 2 subgroups of OSA patients and controls. (A) IL-8 in moderate, severe subgroups; (B) and (C) IL-10, IL-18 in mild, severe subgroups.



Supplemental Figure 5. Funnel plots of Interleukins (ILs) concentration differences between mild, moderate, severe OSA patients and controls. (A) IL-1 β ; (B) IL-6; (C) IL-8; (D) IL-10; (E) IL-18.

A. IL-1β

	post pre							Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
Tirado R. 2017	0.46	0.47	66	0.67	0.61	66	40.3%	-0.21 [-0.40, -0.02]	-
Chuang H.H. 2020	0.3	0.2	60	0.8	0.8	60	39.2%	-0.50 [-0.71, -0.29]	+
Huang Y.S. 2020	0.35	0.29	55	1.51	2.25	55	20.5%	-1.16 [-1.76, -0.56]	
Total (95% CI)			181			181	100.0%	-0.52 [-0.89, -0.15]	•
Heterogeneity: Tau ² =	0.08; C	hi²=1	0.99, dt						
Test for overall effect:	Z = 2.78	6 (P = 0).006)		Favours [experimental] Favours [control]				

B. IL-6

	post			pre			Mean Difference		Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
Arnardottir E.S. 2015	2.8	2	177	2.4	1.7	177	5.5%	0.40 [0.01, 0.79]	
Recoquillon S. 2019	1.3	1.2	55	1.1	0.5	55	5.5%	0.20 [-0.14, 0.54]	
Dorkova Z. 2008	1.28	1.05	16	1.25	1.1	16	5.5%	0.03 [-0.72, 0.78]	t the second sec
Li A. M. 2008	0.2	0.3	16	0.3	0.4	16	5.5%	-0.10 [-0.34, 0.14]	
Campos-Rodriguez F. 2019	3.5	2.6	120	3.6	2.8	120	5.5%	-0.10 [-0.78, 0.58]	
Akinnusi M. 2013	1.48	0.97	25	1.71	0.99	25	5.5%	-0.23 [-0.77, 0.31]	
Steiropoulos P. 2009	2.46	1.08	32	2.71	1.27	32	5.5%	-0.25 [-0.83, 0.33]	
Tirado R. 2017	0.39	0.58	66	0.64	0.69	66	5.6%	-0.25 [-0.47, -0.03]	
Huang Y.S. 2020	1.22	1.21	55	1.59	1.58	55	5.5%	-0.37 [-0.90, 0.16]	
Salman M.A. 2020	1.8	0.45	79	2.27	0.4	79	5.6%	-0.47 [-0.60, -0.34]	
Ryan S. 2006	4.46	16.39	49	5.13	22.65	49	2.0%	-0.67 [-8.50, 7.16]	+
Kezirian E.J. 2010	2	1.3	21	2.96	2.74	21	5.3%	-0.96 [-2.26, 0.34]	4
Borges Y.G. 2020	7	4.2	18	8	3.1	18	4.7%	-1.00 [-3.41, 1.41]	+
Takahashi K.I. 2008	0.634	0.619	27	1.68	2.87	27	5.4%	-1.05 [-2.15, 0.06]	•
Kheirandish-Gozal L. 2015	7.1	4.7	100	9.2	5.4	100	5.3%	-2.10 [-3.50, -0.70]	-
Bilal N. 2021	55.17	3.74	10	57.98	5.96	10	3.5%	-2.81 [-7.17, 1.55]	-
Martínez-Cerón E. 2016	8	4.6	26	11.1	4.7	26	4.7%	-3.10 [-5.63, -0.57]	-
Eun Y.G. 2010	2.4	3.4	51	7.6	10.4	51	4.4%	-5.20 [-8.20, -2.20]	-
Li Y 2008	62.2	14.2	2	76.3	1.2	2	0.4%	-14.10 [-33.85, 5.65]	
Li Y 2008	59.9	13.2	33	75.7	12.3	33	2.6%	-15.80 [-21.96, -9.64]	
Li Y 2008	51.6	23.8	5	71.4	15.4	5	0.3%	-19.80 [-44.65, 5.05]	
Wang X 2020	18.68	1.33	54	43.31	2.93	54	5.4%	-24.63 [-25.49, -23.77]	•
Ye L. 2010	66.04	10.05	10	131.66	20.39	10	0.8%	-65.62 [-79.71, -51.53]	
Total (95% CI)			1047			1047	100.0%	-3.21 [-4.58, -1.85]	•
Heterogeneity: $Tau^2 = 8.75$; C	$Chi^2 = 32$	223.89.	df = 2	2 (P < 0.0	00001):	$l^2 = 99$	9%		
Test for overall effect: $Z = 4.6$	51 (P < 0)	0.00001)		,,				-100 -50 0 50 100
· · · · · · · · · · · · · · · · · · ·									Favours [experimental] Favours [control]

C. IL-8

	F F	ost			pre			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% Cl
Akinnusi M. 2013	4.73	1.56	25	4.98	1.67	25	15.6%	-0.25 [-1.15, 0.65]	+
Li A. M. 2008	1.1	0.6	16	1.9	1	16	16.0%	-0.80 [-1.37, -0.23]	•
Ryan S. 2006	4.68	1.56	49	5.48	1.53	49	16.0%	-0.80 [-1.41, -0.19]	•
Martínez-Cerón E. 2016	9.7	4	26	10.7	3.3	26	13.6%	-1.00 [-2.99, 0.99]	
Chuang H.H. 2020	4.1	2.2	60	6.4	3.6	60	15.4%	-2.30 [-3.37, -1.23]	+
Jin F. 2017	35.79	1.63	100	40.72	1.6	100	16.1%	-4.93 [-5.38, -4.48]	•
Bao H.R. 2005	33.73	8.07	10	38.97	9.72	10	4.1%	-5.24 [-13.07, 2.59]	
Bilal N. 2021	112.87	8.99	10	126.31	11.73	10	3.2%	-13.44 [-22.60, -4.28]	
Total (95% CI)			296			296	100.0%	-2.22 [-4.06, -0.39]	◆
Heterogeneity: Tau ² = 5.3	7; Chi ² = 2	209.15	, df = 7	(P < 0.00	1001); I ^z	= 97%		-	
Test for overall effect: Z =	2.38 (P =	0.02)							Favours [experimental] Favours [control]

D. IL-10

	post pre							Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
Huang Y.S. 2020	1.68	1.05	55	2.74	2.94	55	17.9%	-1.06 [-1.89, -0.23]	-
Chuang H.H. 2020	0.4	0.2	60	1.2	2.1	60	20.4%	-0.80 [-1.33, -0.27]	•
Ryan S. 2006	1.08	0.6	49	1.31	0.49	49	22.3%	-0.23 [-0.45, -0.01]	•
Borges Y.G. 2020	4	3.5	18	4	1.6	18	10.1%	0.00 [-1.78, 1.78]	+
Akinnusi M. 2013	1.03	0.62	25	0.96	0.48	25	21.9%	0.07 [-0.24, 0.38]	•
Bao H.R. 2005	39.39	3.78	10	33.91	4.29	10	3.8%	5.48 [1.94, 9.02]	
Li Y 2008	44.3	5	2	36.1	13.2	2	0.1%	8.20 [-11.36, 27.76]	
Li Y 2008	44.9	7.3	33	33.8	8.7	33	3.3%	11.10 [7.23, 14.97]	
Li Y 2008	50.9	12.2	5	33.2	8.2	5	0.3%	17.70 [4.82, 30.58]	
Total (95% CI)			257			257	100.0%	0.25 [-0.50, 1.01]	•
Heterogeneity: Tau ² =	0.65; CI	hi² = 6:	2.77, df	= 8 (P	< 0.000	001); I ^z	= 87%		
Test for overall effect:	Z = 0.66	(P = 0).51)	Favours [experimental] Favours [control]					

Supplemental Figure 6. Forest plots of interleukins (ILs) treatment concentration differences between post and pre OSA patients. (A) IL-1 β ; (B) IL-6; (C) IL-8; (D) IL-10



Supplemental Figure 7. Funnel plots of Interleukins (ILs) treatment concentration differences between post and pre OSA patients. (A) IL-1 β ; (B) IL-6; (C) IL-8; (D) IL-10.



Supplemental Figure 8. Verification of the negative results about the causal relationships between OSA and Interleukins (ILs) of IL-6, IL-8 and Il-18 using another large-sample GWAS

(A). Causality was analyzed with OSA as exposure, IL-6, IL-8, IL-18 individually as outcomes by MR.

(B). Causality was analyzed with IL-6, IL-8, IL-18 respectively as exposure and OSA as outcome by MR. The presented results were performed by method of inverse variance weighted (IVW). The statistically threshold was p < 0.05.