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1. Search strategy

1.1. Table S1.

Search strategy for each database, number of results, and execution date.

Database	Query/Search Strategy	Items founds/Results	Search time limits
PubMed	("diabetes mellitus, type 1"[MeSH Terms] OR "type 1 diabetes"[All Fields] OR "T1DM"[All Fields]) AND ("interleukin-1beta"[MeSH Terms] OR "il-1b"[All Fields] OR "il-1beta"[All Fields] OR "interleukin-1b"[All Fields] OR "interleukin-1beta"[All Fields])	626	October 25 - 2020
Embase	('type 1 diabetes' OR 'T1DM') AND ('interleukin 1beta'/exp OR 'il-1beta' OR 'il-1b' OR 'interleukin-1b')	817	October 25 - 2020
Web of Science	TS=("diabetes") AND TS=("type 1") AND TS=(interleukin 1 beta)	826	October 25 - 2020
Scopus	("diabetes mellitus,type 1" OR "type 1 diabetes" OR "T1DM") AND ("interleukin-1beta" OR "il-1b" OR "il-1beta" OR "interleukin-1b")	874	October 25 - 2020
Total			3,143

2. List of full-text articles excluded with reasons
-Non control group

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4. Characteristics of analyzed studies.

4.1. Table S2. Variables of study.

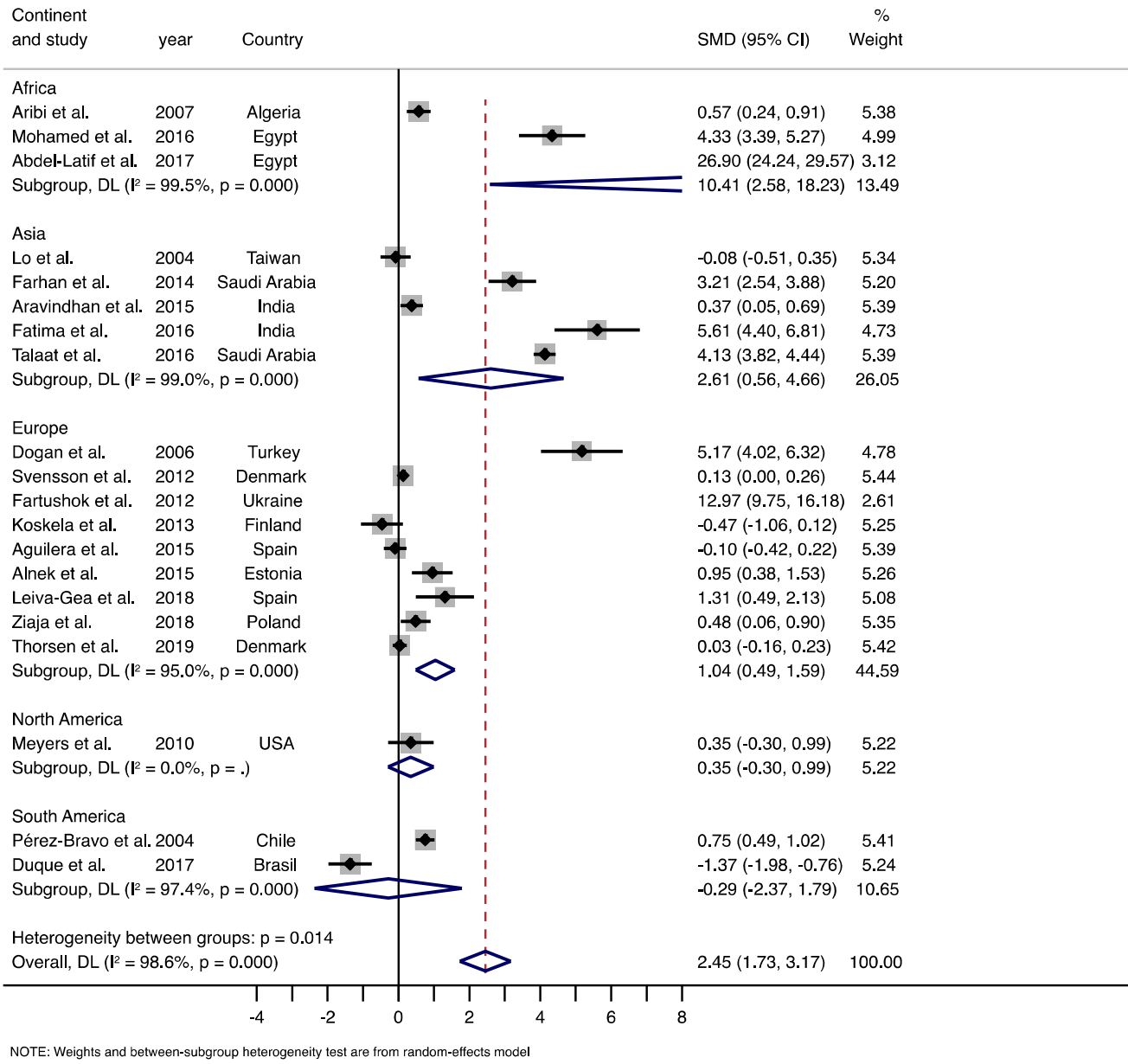
Study	Year	Country	Population (n) (Male, Female)		Age (Years)		Sample	IL1-β (pg/ml or mRNA/GADPH)		Technique	Evolution (years)	HbA1c%	Study design
					T1DM	Control		T1DM	Control				
			T1DM	Control	Mean (SD)	Mean (SD)		Mean (SD)	Mean (SD)		Mean (SD)	Mean (SD)	
Pérez-Bravo *et al.*	2004	Chile	120 (66, 54)	118 (62, 56)	8.5 (3.5)	9.1 (5.5)	Serum	9.4 (7.3)	4.96 (4)	ELISA	NA	NA	CC
Lo *et al.*	2004	Taiwan	58 (22, 36)	33 (16, 17)	10.98 (4.61)	10.06 (4.9)	Serum	46.43 (79.71)	52.98 (82.13)	ELISA	NA	8.7 (1.59)	CC
Holm *et al.*	2006	Sweden	13 (NA, NA)	82 (NA, NA)	0.72 (1)	0.77 (1.6)	CBP	178.60 (236.73)	52.77 (106.68)	FC	NA	NA	CC
Dogan *et al.*	2006	Turkey	27 (15, 12)	25 (14, 11)	10.05 (1.85)	10.5 (1)	Serum	12.86 (2.27)	3.8 (0.9)	ELISA	NA	8.95 (1.4)	CC
Arabi *et al.*	2007	Algeria	69 (29, 40)	74 (36, 38)	15.3 (0.32)	15.71 (0.37)	Plasma	3 (3.32)	0.5 (5.16)	ELISA	13.41 (0.25)	9.5 (0.83)	CC
Duarte *et al.*	2007	Brazil	20 (7, 13)	20 (8, 12)	50.19 (11.41)	49.5 (8.11)	GB	1.16 (0.7)	2.61 (0.83)	RT-PCR	12.06 (7.52)	NA	CC
Salvi *et al.*	2010	Switzerland	9 (NA, NA)	9 (NA, NA)	25.6 (5.8)	24.8 (5.7)	GCF	3130.09 (653.53)	1444.66 (275.17)	ELISA	9.0 (5.3)	8.1 (0.7)	C
Meyers *et al.*	2010	USA	20 (NA, NA)	18 (NA, NA)	16.2 (6.6)	12.9 (3.4)	Serum	48.49 (30.86)	32.89 (56.99)	IP	0.19	8.8 (2.7)	CC
Gabbay *et al.*	2012	Brazil	35 (20, 15)	25 (16, 9)	13 (5)	13.6 (5.4)	Serum	1 (3)	0.01 (0.01)	FC	NA	8.4 (2.2)	CC
Svensson *et al.*	2012	Denmark	482 (255, 227)	479 (266, 213)	9.83	10.2	Serum	5115.69 (1418.09)	4940.51 (1257.73)	IP	NA	NA	CC
Ururahya *et al.*	2012	Brazil	76 (23, 53)	100 (43, 57)	12.2 (3.8)	11.9 (3.6)	PB	1.86 (0.9)	1.44 (0.72)	RT-PCR	5.3 (3.7)	10.26 (3.1)	CC
Fartushok *et al.*	2012	Ukraine	25 (10, 15)	10 (NA, NA)	35	35	Plasma	11.71 (0.69)	3 (0.62)	ELISA	NA	NA	CC
Koskela *et al.*	2013	Finland	38 (17, 21)	16 (5, 11)	59.4 (14.3)	66.6 (9.3)	Plasma	29.9 (63.5)	66.7 (108)	ELISA	24.7 (12.3)	8.5 (1.5)	CSS
							Vitreo	0.3 (0.9)	1.2 (2.4)				
Allam *et al.*	2014	Saudi Arabia	150 (75, 75)	150 (75, 75)	9.82	10.19	Serum	9.54 (3.43)	2.45 (1.13)	FC	NA	9.45 (2.9)	CSS
Farhan *et al.*	2014	Saudi Arabia	37 (18, 19)	42 (27, 15)	33.1 (16.2)	43 (17)	Serum	1.57 (0.504)	0.34 (0.23)	ELISA	NA	NA	
Aguilera *et al.*	2015	Spain	150 (87, 63)	50 (28, 22)	38.6 (8.1)	38.1 (7.2)	Serum	1 (1.1)	1.1 (0.8)	IP	20.4 (8.1)	8.1 (2.3)	CC
Aravindhan *et al.*	2015	India	97 (49, 48)	64 (32, 32)	29.02 (16.94)	30.4 (15.76)	Serum	15.21 (14.36)	9.88 (14.34)	ELISA	8.23 (7.14)	10.7 (3.8)	CC
Alnek *et al.*	2015	Estonia	36 (17, 19)	20 (8, 12)	9.53 (5.94)	13.87 (10.85)	Plasma	6.36 (3.32)	3.24 (3.19)	IP	<1	NA	CC
Mohamed *et al.*	2016	Egypt	30 (NA, NA)	30 (NA, NA)	8.8 (2.85)	9.83 (2.81)	Serum	7.763 (1.119)	3.403 (0.88)	ELISA	NA	7.067 (0.872)	CC
Fatima *et al.*	2016	India	29 (17, 12)	25 (NA, NA)	14.25 (4)	14.25 (4)	Serum	18.46 (3.5)	4.04 (0.2)	ELISA	NA	9.17 (1.33)	CC
Talaat *et al.*	2016	Saudi Arabia	250 (NA, NA)	250 (NA, NA)	8.5 (0.5)	8.5 (0.5)	Serum	12.09 (2.94)	3.39 (0.5)	ELISA	3.5 (4.69)	11.35 (3.1)	CSS
Duque *et al.*	2017	Brazil	24 (12, 12)	27 (13, 14)	9.45 (1.69)	9.62 (1.86)	Serum	1.57 (0.31)	1.98 (0.29)	ELISA	NA	6.94 (1.58)	CC
Abdel-Latif *et al.*	2017	Egypt	100 (50, 50)	100 (50, 50)	9.8 (2.9)	9.1 (2.7)	Serum	12.46 (0.37)	2.56 (0.366)	ELISA	NA	8.87 (1.07)	CC
Leiva-Gea *et al.*	2018	Spain	15 (7, 8)	13 (7, 6)	12.56 (3.59)	12.25 (2.92)	Serum	119.41 (27.12)	83.21 (28.25)	ELISA	5.68 (1.84)	6.26 (0.38)	CC
Ziaja *et al.*	2018	Poland	39 (17, 22)	52 (23, 29)	48.8 (9.1)	44.8 (12)	Plasma	2.67 (3.92)	1.3 (1.6)	ELISA	35.8 (8.6)	7.7 (1.1)	CSS
Thorsen *et al.*	2019	Denmark	199 (96, 103)	199 (104, 95)	Neonatal	Neonatal	Serum	176.17 (112.39)	172.34 (120.22)	ELISA	NA	NA	C

Abbreviation: T1DM, Type 1 Diabetes Mellitus; SD, Standard Deviation; IL1β, Interleukin-1 beta; mRNA, messenger ribonucleic acid; GADPH, glyceraldehyde-3-phosphate dehydrogenase; HbA1c, Glycated hemoglobin A1c; ELISA, Enzyme-Linked ImmunoSorbent Assay; NA, Non Available; CC, case control; CBP, Cord Blood Plasma; FC, Flow cytometry; GB, Gingival biopsies; RT-PCR, Reverse transcription polymerase chain reaction; GCF, Gingival crevicular fluid; IP, Innmunoassay panel; C, cohort; PB, Peripheral blood; CSS, cross-sectional study.

5. Subgroup meta-analyses

5.1. Figure S1. Geographical area.

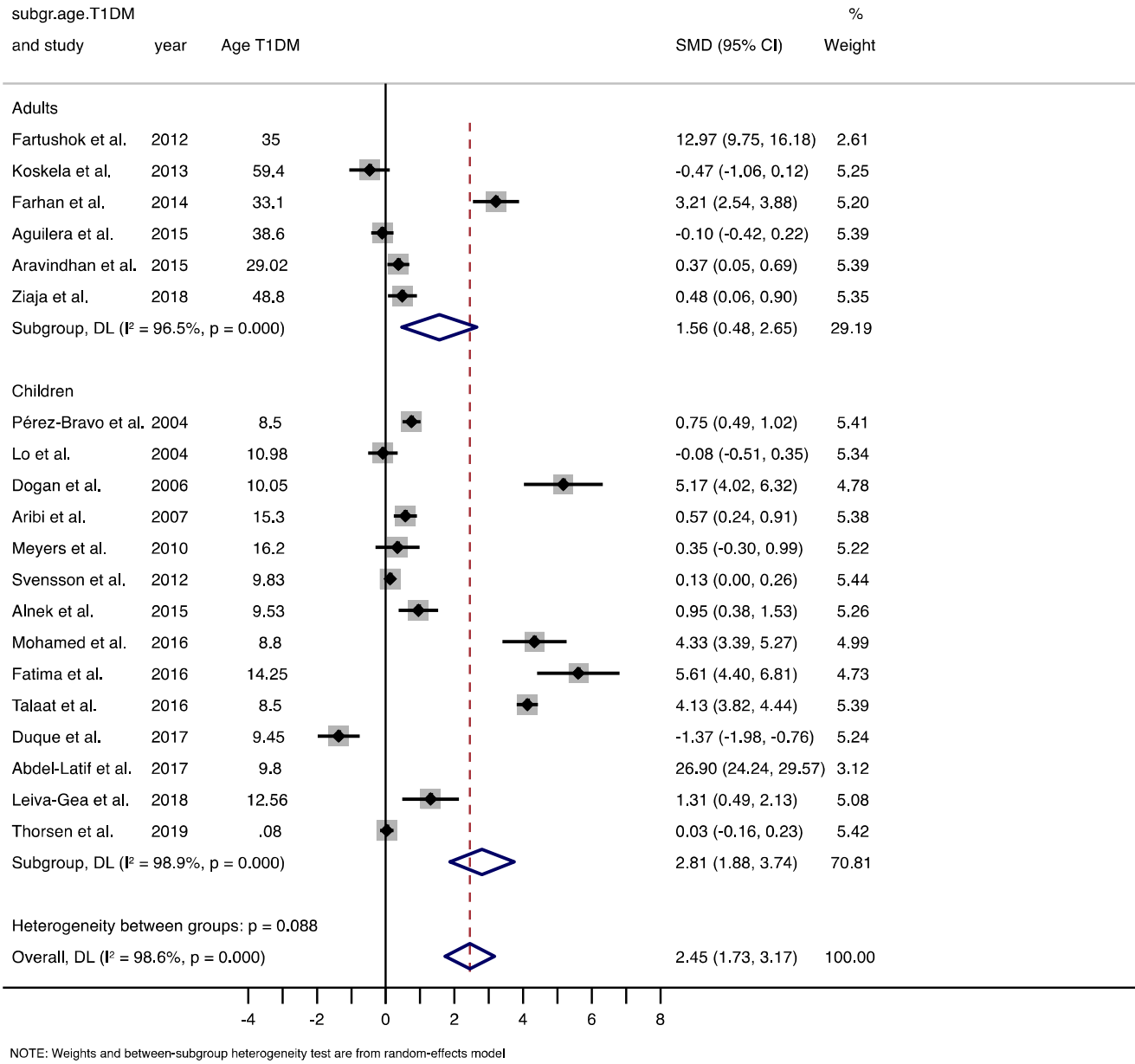
Forest plot graphically representing the meta-analyses evaluating the changes in circulating IL-1β levels (immunoassays determination) between T1DM patients and controls by geographical area.



Random-effects model, inverse-variance weighting based on the DerSimonian and Laird method. Standardized mean difference (SMD) was chosen as effect size measure. An SMD>0 suggests that IL-1β levels are higher in T1DM. Diamonds indicate the overall pooled SMDs with their corresponding 95% confidence intervals (CI).

5.2. Figure S2. Age

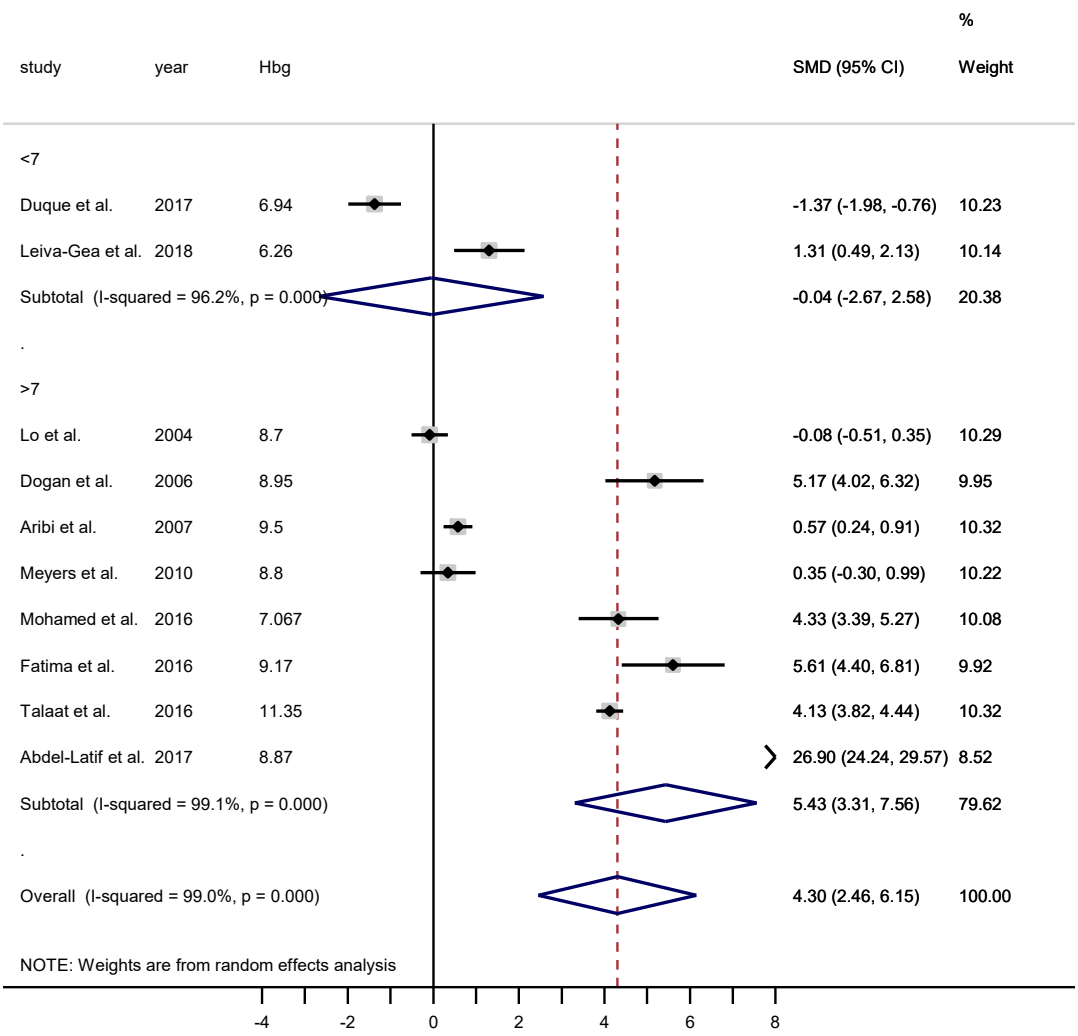
Forest plot graphically representing the meta-analyses evaluating the changes in circulating IL-1β levels (immunoassays determination) between T1DM patients and controls by age (<18, children vs >18 years old, adults).



Random-effects model, inverse-variance weighting based on the DerSimonian and Laird method. Standardized mean difference (SMD) was chosen as effect size measure. An SMD>0 suggests that IL-1β levels are higher in T1DM. Diamonds indicate the overall pooled SMDs with their corresponding 95% confidence intervals (CI).

5.3. Figure S3. HbAc1 levels in patients <18 years

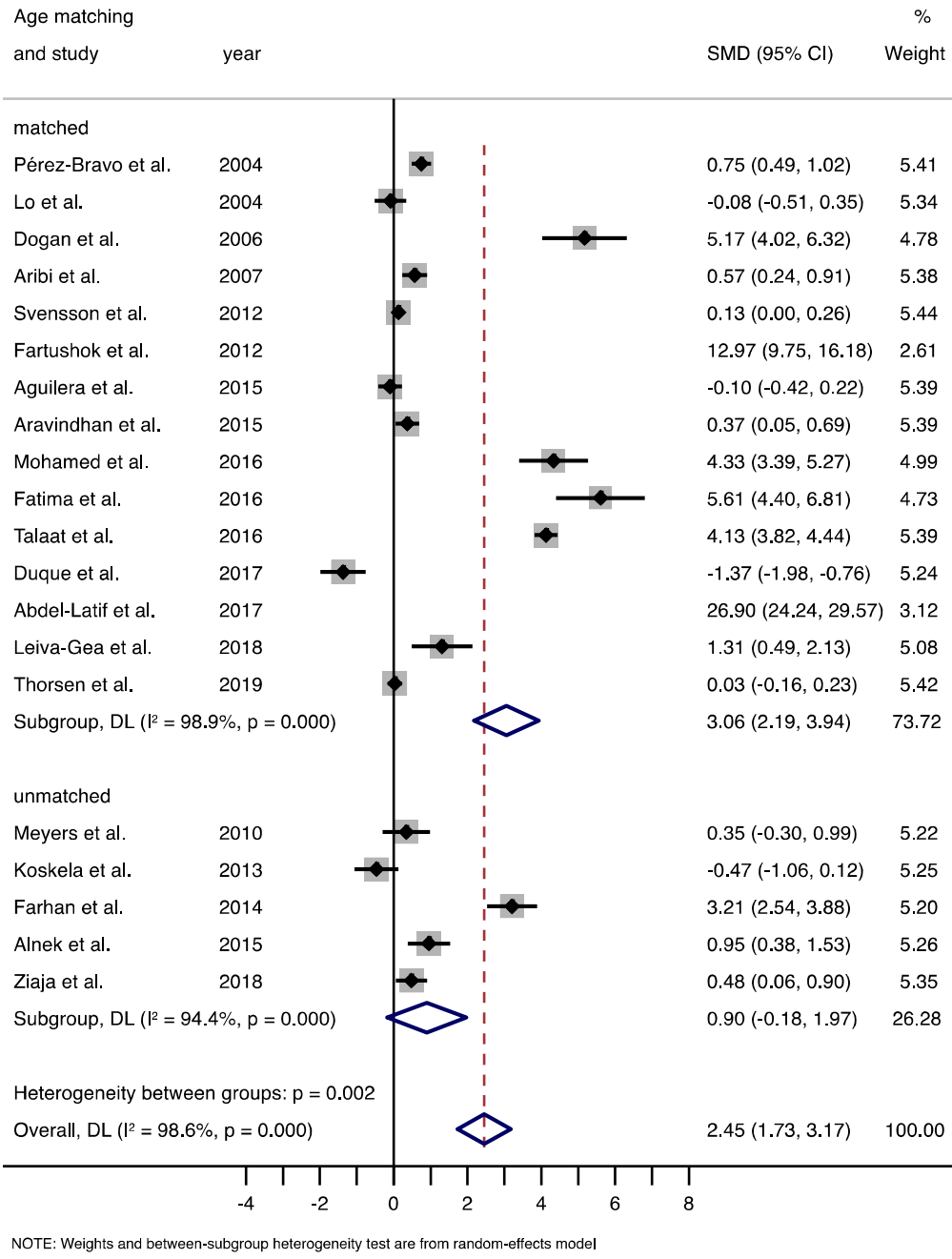
Forest plot graphically representing the meta-analyses evaluating the changes in circulating IL-1β levels (immunoassays determination) between T1DM patients and controls by HbAc1levels in patients <18 years (<7 vs >7).



Random-effects model, inverse-variance weighting based on the DerSimonian and Laird method. Standardized mean difference (SMD) was chosen as effect size measure. An SMD>0 suggests that IL-1β levels are higher in T1DM. Diamonds indicate the overall pooled SMDs with their corresponding 95% confidence intervals (CI).

5.4. Figure S4. Age matching

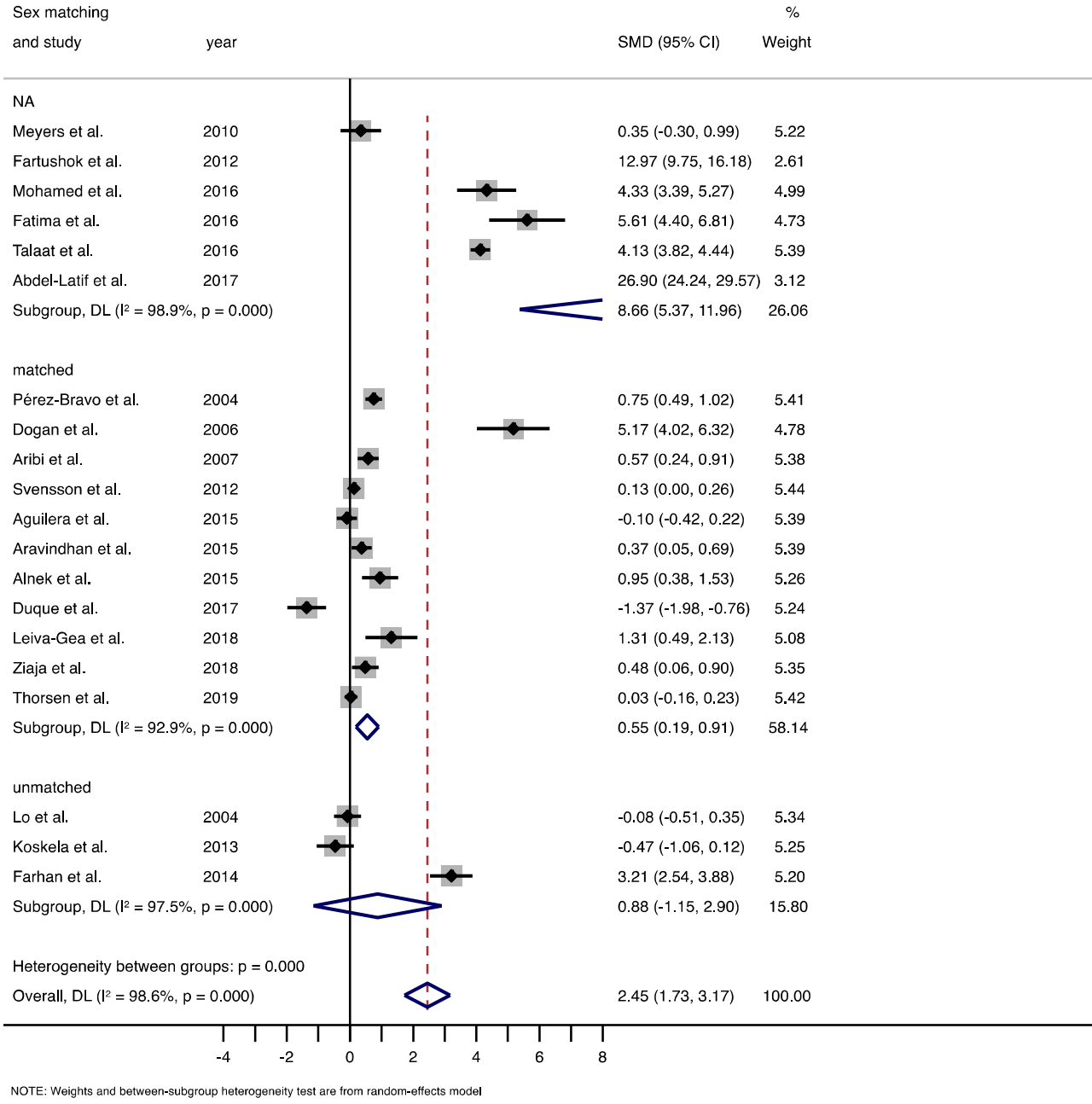
Forest plot graphically representing the meta-analyses evaluating the changes in circulating IL-1β levels (immunoassays determination) between T1DM patients and controls by age matching (matched vs unmatched).



Random-effects model, inverse-variance weighting based on the DerSimonian and Laird method. Standardized mean difference (SMD) was chosen as effect size measure. An SMD>0 suggests that IL-1β levels are higher in T1DM. Diamonds indicate the overall pooled SMDs with their corresponding 95% confidence intervals (CI).

5.5. Figure S5. Sex matching

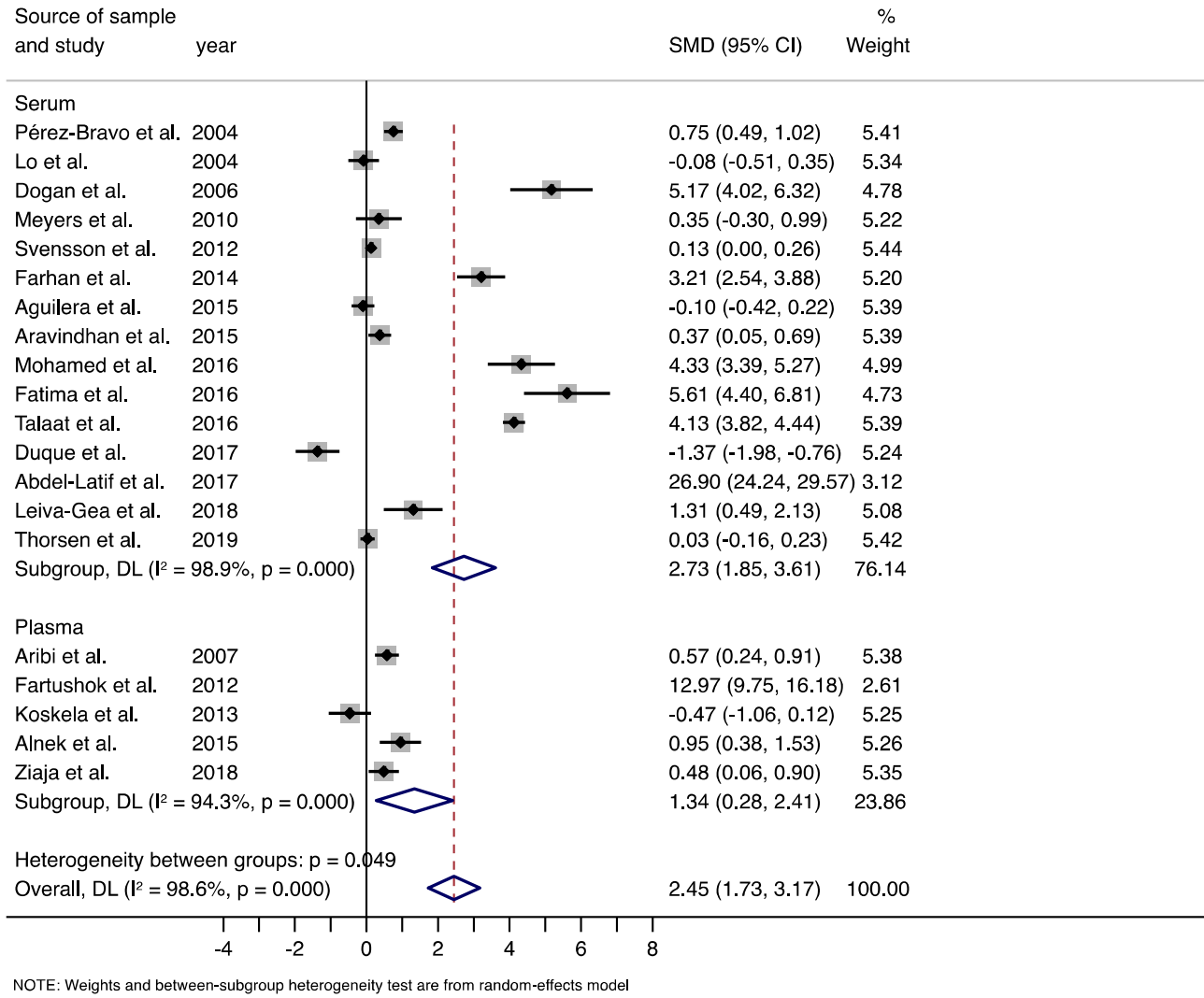
Forest plot graphically representing the meta-analyses evaluating the changes in circulating IL-1β levels (immunoassays determination) between T1DM patients and controls by sex matching (matched vs unmatched).



Random-effects model, inverse-variance weighting based on the DerSimonian and Laird method. Standardized mean difference (SMD) was chosen as effect size measure. An SMD>0 suggests that IL-1β levels are higher in T1DM. Diamonds indicate the overall pooled SMDs with their corresponding 95% confidence intervals (CI).

5.6. Figure S6. Source of sample

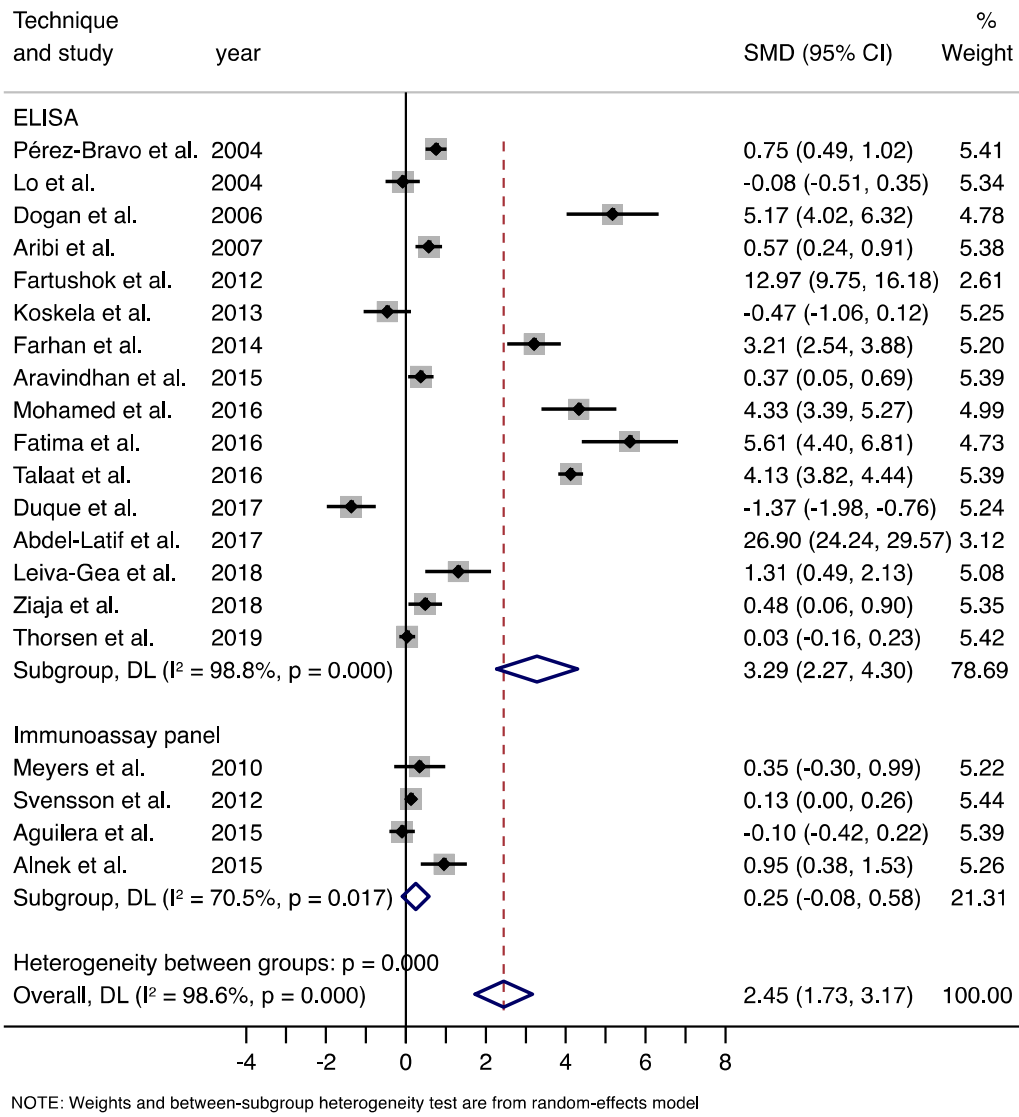
Forest plot graphically representing the meta-analyses evaluating the changes in circulating IL-1β levels (immunoassays determination) between T1DM patients and controls by source of sample (Serum, Plasma, Gingival crevicular fluid or Vitreous humour).



Random-effects model, inverse-variance weighting based on the DerSimonian and Laird method. Standardized mean difference (SMD) was chosen as effect size measure. An SMD>0 suggests that IL-1β levels are higher in T1DM. Diamonds indicate the overall pooled SMDs with their corresponding 95% confidence intervals (CI).

5.7. Figure S7. Type of analysis

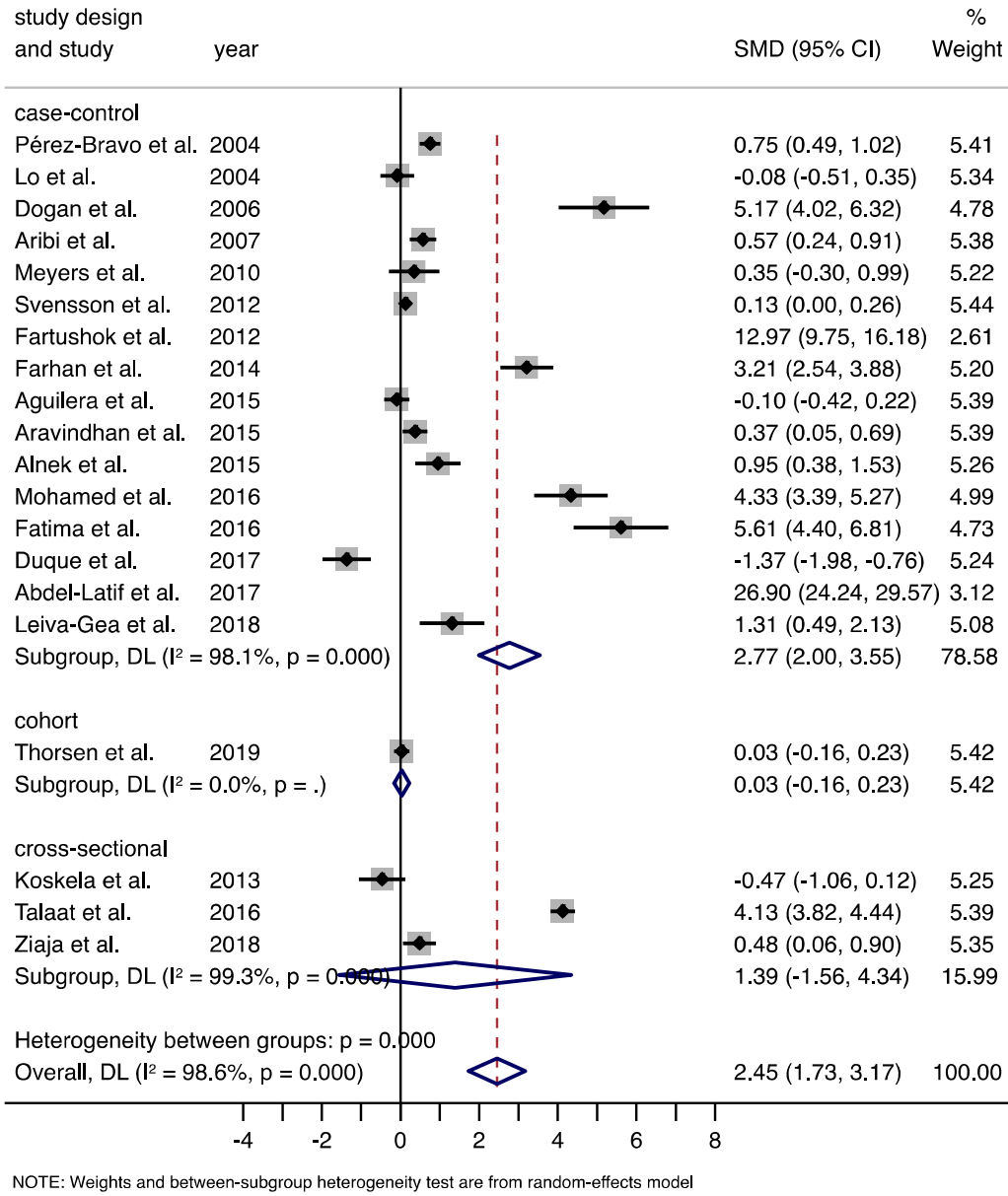
Forest plot graphically representing the meta-analyses evaluating the changes in circulating IL-1β levels (immunoassays determination) between T1DM patients and controls by type of analysis (ELISA vs immunoassay panel).



Random-effects model, inverse-variance weighting based on the DerSimonian and Laird method. Standardized mean difference (SMD) was chosen as effect size measure. An SMD>0 suggests that IL-1β levels are higher in T1DM. Diamonds indicate the overall pooled SMDs with their corresponding 95% confidence intervals (CI).

5.8. Figure S8. Study design

Forest plot graphically representing the meta-analyses evaluating the changes in circulating IL-1β levels (immunoassays determination) between T1DM patients and controls by study design (Case-control, or Cohort, or Cross-sectional).

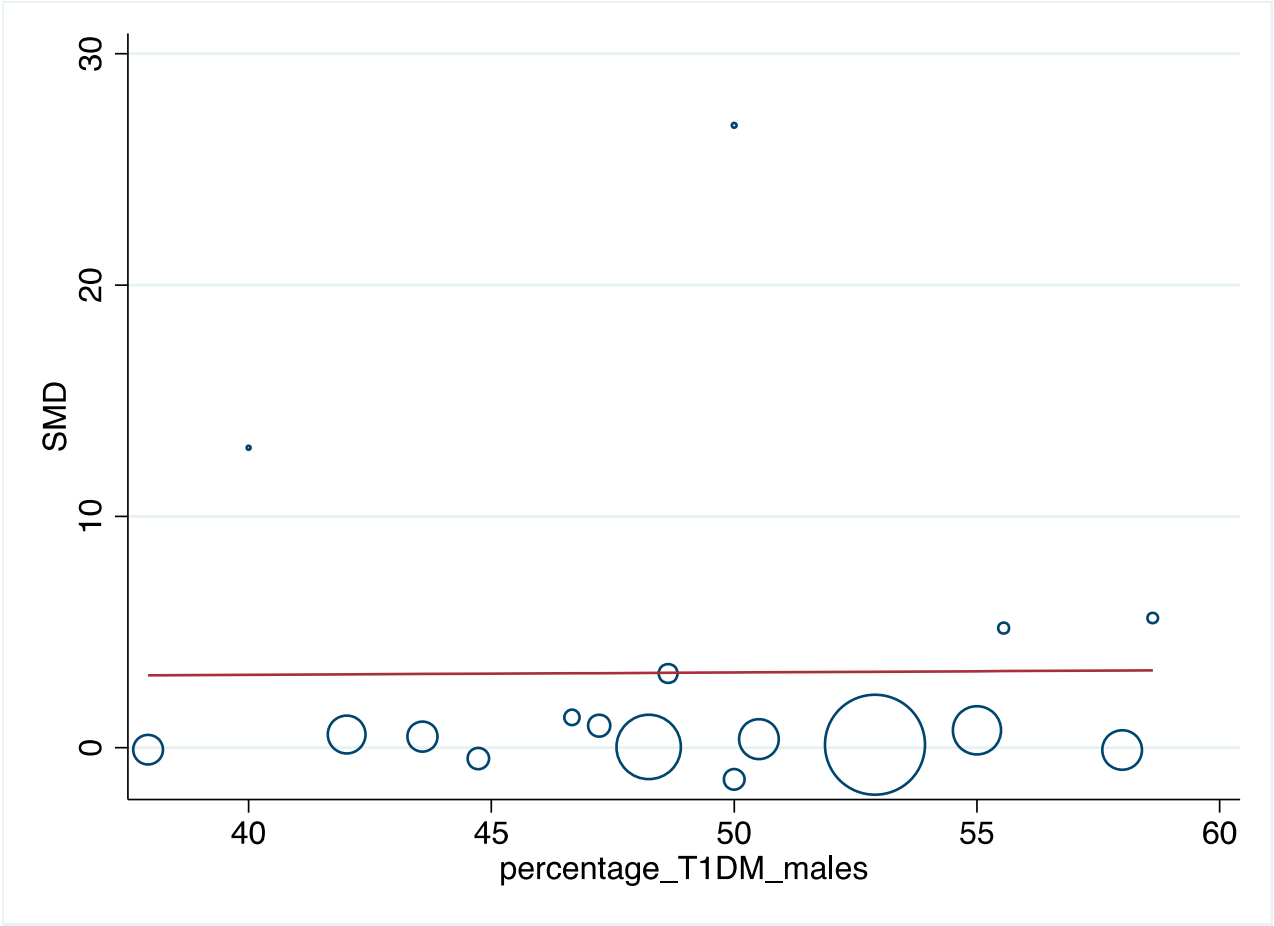


Random-effects model, inverse-variance weighting based on the DerSimonian and Laird method. Standardized mean difference (SMD) was chosen as effect size measure. An SMD>0 suggests that IL-1β levels are higher in T1DM. Diamonds indicate the overall pooled SMDs with their corresponding 95% confidence intervals (CI).

6. Meta-regression analyses

6.1. Figure S9. Effect of the covariate Sex

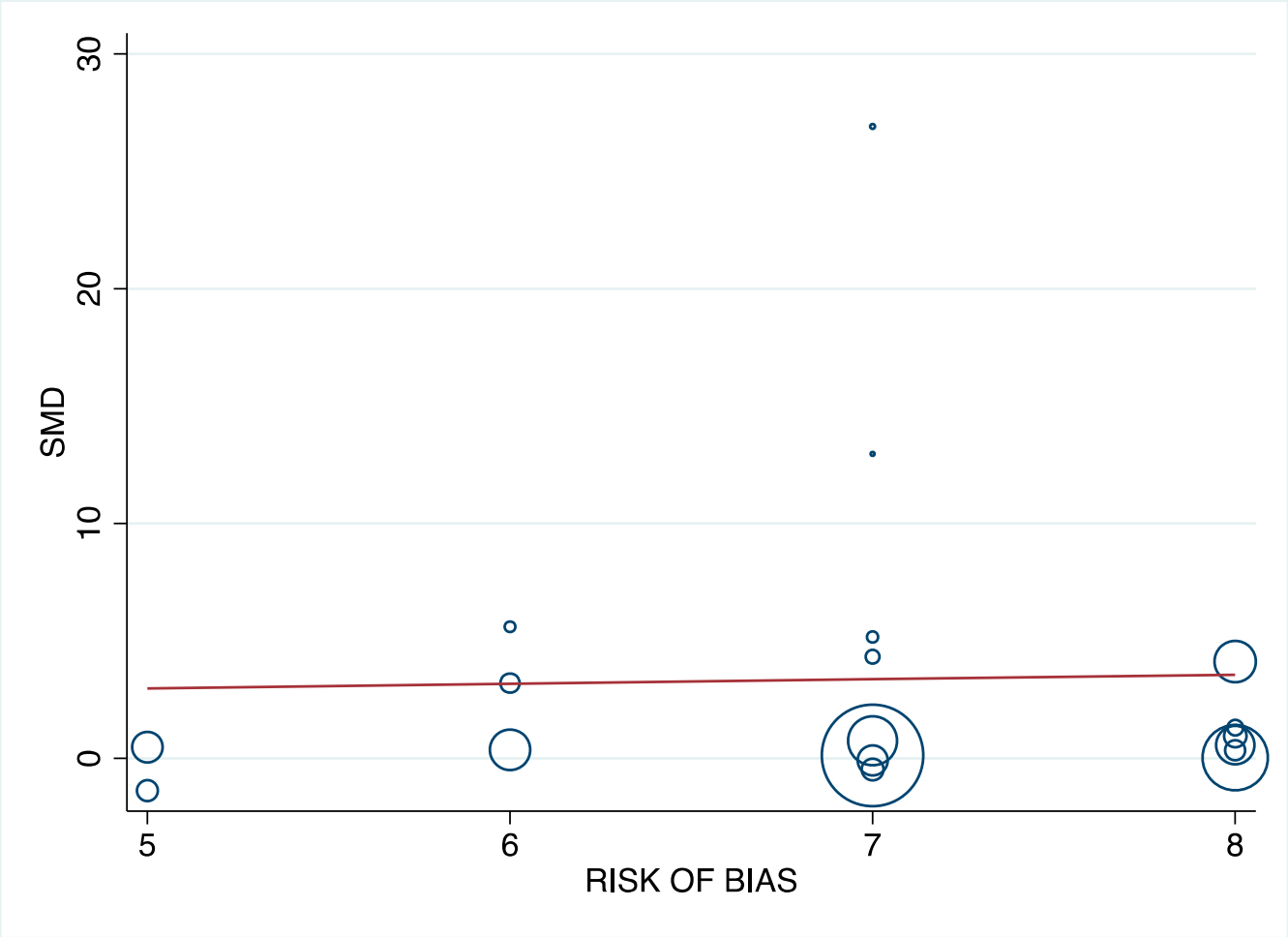
Bubble plot graphically representing the univariable meta-regression analysis of the potential effect of sex (% of males) on circulating IL-1β levels among patients with T1DM compared with controls.



Random-effects univariable meta-regression. The red line exhibits the fitted regression line together with blue circles representing the estimates from each individual study, sized according to the precision of each estimate (the inverse of its within-study variance).

6.2. Figure S10. Effect of the covariate Risk of Bias

Bubble plot graphically representing the univariable meta-regression analysis of the potential effect of risk of bias (scored using Newcastle-Ottawa Scale) on circulating IL-1β levels among patients with T1DM compared with controls.



Random-effects univariable meta-regression. The red line exhibits the fitted regression line together with blue circles representing the estimates from each individual study, sized according to the precision of each estimate (the inverse of its within-study variance).

7. Table S3. Sensitivity analysis.

Sensitivity analyses evaluating the influence of individual studies on the combined results of the meta-analyses.

Sensitivity analysis ("leave-one-out" method) of the meta-analysis results, sequentially omitting one study at a time.

Study omitted	Estimate	95% confidence intervals	
Meta-analysis on IL-1β determination by immunoassays			
Pérez-Bravo et al. (2004)	2.608	1.825	3.392
Lo et al. (2004)	2.614	1.860	3.368
Dogan et al. (2006)	2.294	1.570	3.018
Aribi et al. (2007)	2.596	1.829	3.363
Meyers et al. (2010)	2.577	1.831	3.324
Svensson et al. (2012)	2.739	1.878	3.601
Fartushok et al. (2012)	2.153	1.438	2.868
Koskela et al. (2013)	2.621	1.875	3.366
Farhan et al. (2014)	2.396	1.666	3.126
Aguilera et al. (2015)	2.631	1.866	3.395
Aravindhan et al. (2015)	2.611	1.841	3.380
Alnek et al. (2015)	2.547	1.798	3.295
Mohamed et al. (2016)	2.333	1.608	3.059
Fatima et al. (2016)	2.272	1.550	2.994
Talaat et al. (2016)	2.128	1.521	2.736
Duque et al. (2017)	2.659	1.921	3.396
Abdel-Latif et al. (2017)	1.596	0.970	2.221
Leiva-Gea et al. (2018)	2.518	1.775	3.260
Ziaja et al. (2018)	2.586	1.829	3.343
Thorsen et al. (2019)	2.681	1.873	3.490
Combined	2.451	1.731	3.171
Meta-analysis on IL-1β determination by qRT-PCR			
Duarte et al. (2007)	.523	.220	.827
Ururahya et al. (2012)	-1.889	-2.641	-1.138
Combined	-.658	-3.022	1.706
Meta-analysis on IL-1β determination by Flow cytometry			
Holm et al. (2006)	1.613	-.685	3.912
Gabbay et al. (2012)	1.887	.1087	3.666
Allam et al. (2014)	.673	.1559	1.191
Combined	1.401	-.1949	2.998