

# The association between obesity related adipokines and risk of breast cancer: a meta-analysis

## Supplementary Materials

### SUPPLEMENTARY REFERENCES

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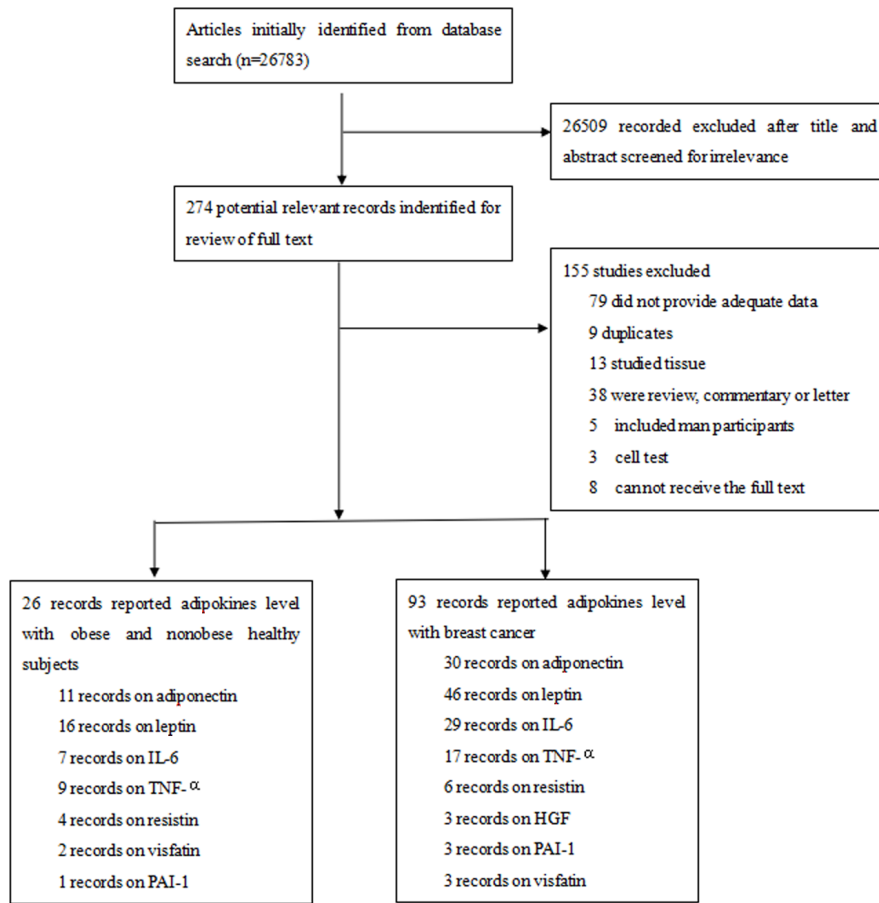


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**Supplementary Table 1: Characteristics of the studies reported adipokines level with obese and nonobese healthy subjects included in the meta-analysis.** See Supplementary\_Table\_1

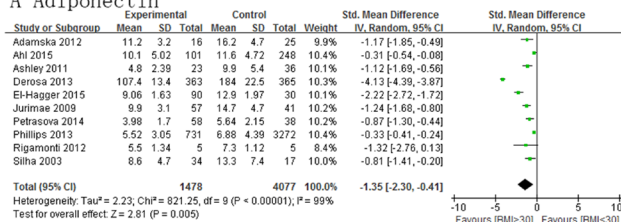
**Supplementary Table 2: Characteristics of the studies reported adipokines level with breast cancer included in the meta-analysis.** See Supplementary\_Table\_2

**Supplementary Table 3: Quality assessment score scale.** See Supplementary\_Table\_3

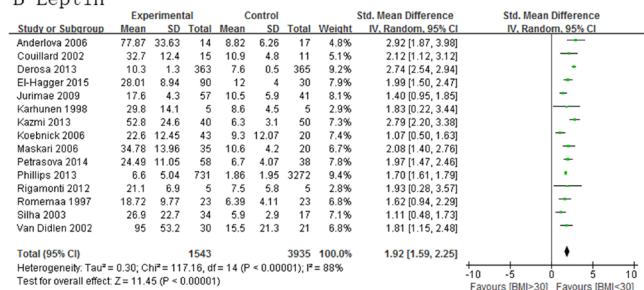


Supplementary Figure 1: Flow diagram depicting the literature search and criteria for selection of the included studies.

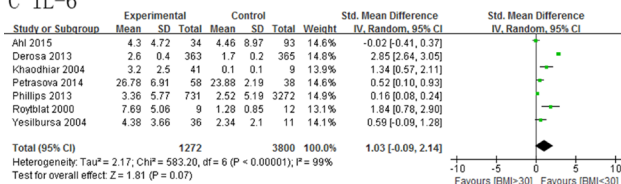
### A Adiponectin



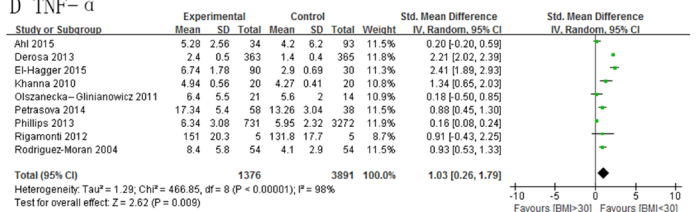
### B Leptin



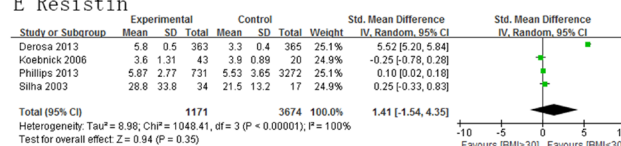
### C IL-6



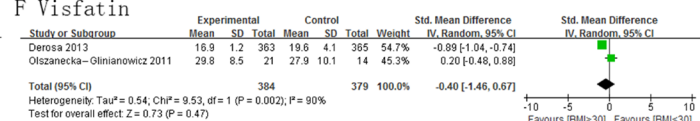
### D TNF- $\alpha$



### E Resistin

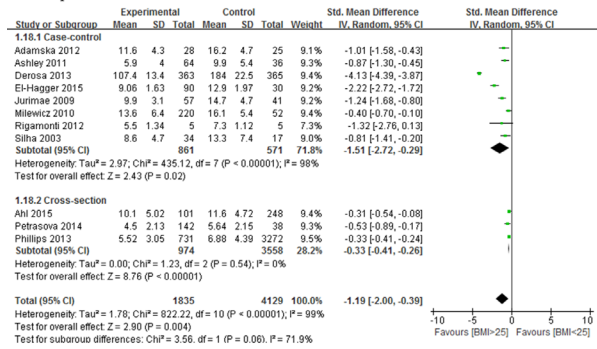


### F Visfatin

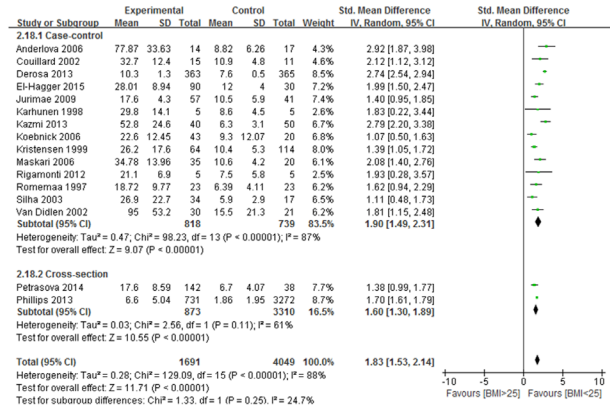


Supplementary Figure 2: Association of adiponectin, leptin, IL-6, TNF- $\alpha$ , resistin and visfatin with BMI > 30 or < 30.

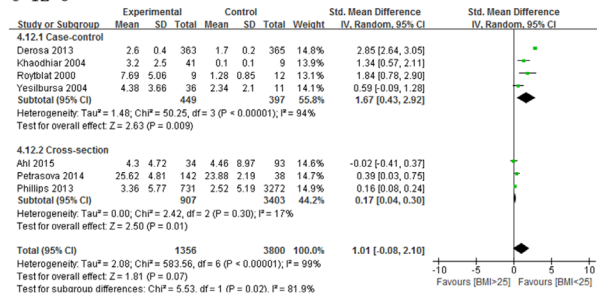
### A Adiponectin



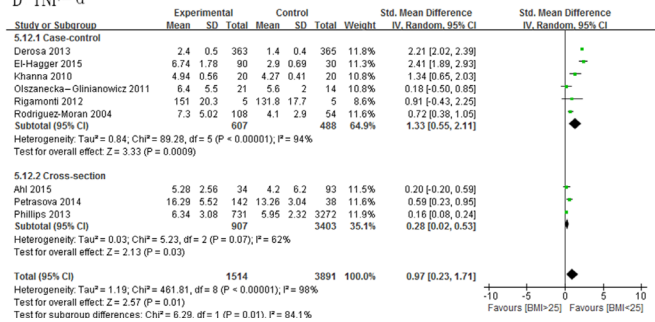
### B Leptin



### C IL-6



### D TNF-α



Supplementary Figure 3: Association of adiponectin, leptin, IL-6, and TNF-α with BMI by study method.

### A Adiponectin

Study or Subgroup	Experimental			Control			Weight	Std. Mean Difference IV, Random, 95% CI
	Mean	SD	Total	Mean	SD	Total		
<b>1.1.1 Case-Control</b>								
Ahmed 2015	6.63	1.46	175	10.17	5.29	175	3.6%	-0.91 [1.13, -0.69]
Alkhalil 2013	14.8	1	56	19.1	1.2	53	2.5%	-3.88 [4.52, -3.23]
Asari 2015	8.44	2.12	92	10.96	1.6	68	3.3%	-1.22 [1.67, -0.86]
Chen 2005-1	10.24	5.8	100	19.17	12.4	100	3.4%	-0.92 [1.21, -0.83]
Dalamaga 2013	16.9	9.8	102	19.8	10.1	102	3.5%	-0.29 [0.97, -0.01]
Outeliek 2012	6.563	2.095	93	13.905	3.293	40	3.0%	-2.09 [2.56, -1.63]
Ouo 2015	6.34	3.54	1167	6.55	3.72	1167	3.8%	-0.06 [0.14, 0.02]
Han 2007	3.264	1.665	77	7.29	2.06	36	2.9%	-2.22 [2.72, -1.73]
Hanske 2010	18.53	7.57	159	17.77	8.4	41	3.3%	0.10 [0.24, 0.45]
Hou 2007	8.6	2.92	80	10.37	2.81	50	3.3%	-0.61 [0.97, -0.25]
Kang 2007	6.93	3.2	41	7.6	3.5	43	3.1%	-0.20 [0.63, 0.23]
Kim 2009	12.602	10.363	98	14.356	6.693	96	3.4%	-0.18 [0.46, 0.10]
Korner 2007	9.1	4	74	11.3	4.7	76	3.3%	-0.50 [0.83, -0.18]
Mantoros 2004	16.7	10	174	17.4	10.5	167	3.6%	-0.07 [0.26, 0.14]
Minoyos 2015	5	3.2	63	8.1	5.7	76	3.3%	-0.65 [0.96, -0.31]
Myoshi 2003	7.57	3.13	102	8.83	3.8	100	3.5%	-0.36 [0.64, -0.08]
Olberding 2013	8.9	3.233	706	10	3.5	706	3.7%	-0.33 [0.43, -0.22]
Panis 2013	4.42	1.77	40	10.28	6.45	40	3.0%	-1.23 [1.71, -0.75]
Santillan-Benitez 2013	14.6	6	40	13.5	11.6	48	3.1%	0.12 [0.30, 0.53]
Suhair 2011	11.9	4.8	70	15.2	7.3	139	3.4%	-0.50 [0.79, -0.21]
Wang 2013	8.12	2.87	92	10.52	2.76	70	3.3%	-0.85 [1.16, -0.51]
Yang 2006	3.615	0.43	70	4.9	0.46	38	2.7%	-2.90 [3.45, -2.34]
Zhang 2012	4.54	2.6	43	6.48	4.66	43	3.1%	-0.51 [0.94, -0.08]
Zhong 2013	6.1	1.46	46	8.88	1.88	35	2.9%	-1.55 [2.05, -1.05]
Subtotal (95% CI)			3730			3568	78.0%	-0.88 [1.11, -0.62]
Heterogeneity: Tau <sup>2</sup> = 0.34, Chi <sup>2</sup> = 681.18, df = 29 (P < 0.00001), I <sup>2</sup> = 95%								
Test for overall effect: Z = 6.82 (P < 0.00001)								
<b>1.1.2 Cohort</b>								
Cust 2009	6.9	1.867	561	6.6	2.167	561	3.7%	0.15 [0.03, 0.27]
Gross 2013	7.99	3.83	272	8.704	4.042	272	3.7%	-0.18 [0.35, -0.01]
Dunler 2015	26.987	6.659	875	29.317	6.477	821	3.7%	-0.11 [0.20, -0.01]
Twoger 2006	14.4	3.125	1166	14.8	3.188	1275	3.9%	-0.13 [0.20, -0.05]
Twoger 2008a	16.7	3.021	311	15.6	2.854	621	3.7%	0.38 [0.24, 0.51]
Subtotal (95% CI)			3185			3050	18.6%	0.02 [0.16, 0.20]
Heterogeneity: Tau <sup>2</sup> = 0.04, Chi <sup>2</sup> = 54.65, df = 4 (P < 0.00001), I <sup>2</sup> = 93%								
Test for overall effect: Z = 0.22 (P = 0.83)								
<b>1.1.3 Cross-Section</b>								
Al Awadhi 2012	8	4	144	6.3	3	77	3.5%	0.46 [0.16, 0.74]
Subtotal (95% CI)			144			77	3.5%	0.46 [0.16, 0.74]
Heterogeneity: Not applicable								
Test for overall effect: Z = 3.22 (P = 0.001)								
<b>Total (95% CI)</b>								
			7059			7435	100.0%	-0.64 [0.81, -0.46]
Heterogeneity: Tau <sup>2</sup> = 0.21, Chi <sup>2</sup> = 681.78, df = 29 (P < 0.00001), I <sup>2</sup> = 96%								
Test for overall effect: Z = 7.10 (P < 0.00001)								
Test for subgroup differences: Chi <sup>2</sup> = 54.18, df = 2 (P < 0.00001), I <sup>2</sup> = 96.3%								

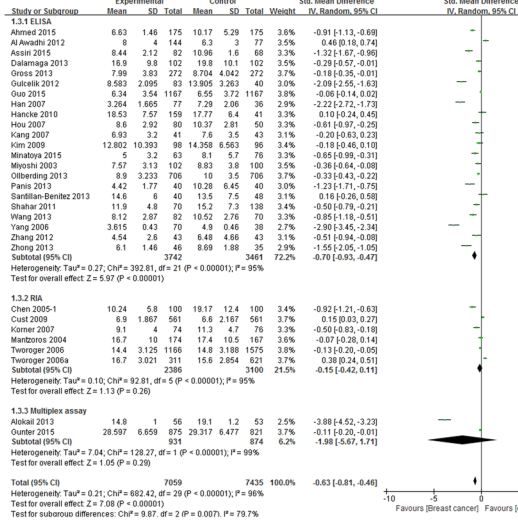
### B Leptin

Study or Subgroup	Experimental			Control			Weight	Std. Mean Difference IV, Random, 95% CI
	Mean	SD	Total	Mean	SD	Total		
<b>2.1.1 Case-Control</b>								
Alustoglu 2010	28.55	19.7	30	26.43	19.4	30	2.1%	0.11 [0.40, 0.61]
Alkhalil 2013	25.6	1.7	56	16	2.2	53	1.8%	4.67 [4.11, 5.62]
Asari 2015	24.59	5.57	92	19.82	2.03	68	2.2%	1.14 [0.76, 1.46]
Chen 2005-1	13.84	11.8	100	10.07	5.5	100	2.3%	0.39 [0.11, 0.67]
Chen 2011	31.48	20.22	50	14.21	11.56	60	2.2%	1.07 [0.66, 1.47]
Coskun 2003	38.628	18.434	85	44	16.8	15	2.0%	-0.23 [0.64, 0.26]
Dalamaga 2013	28.8	17.2	102	27.8	17.5	102	2.3%	0.06 [0.22, 0.33]
Oao 2005	31.72	29.11	74	11.65	3.07	30	2.1%	0.81 [0.37, 1.25]
Oelster 2007	27.9	6.194	44	25	1.956	114	2.2%	0.86 [0.49, 1.22]
Ou 2012	4.17	0.3	405	4.17	0.3	810	2.3%	0.00 [0.12, 0.12]
Han 2005	13.57	0.66	90	8.46	0.8	103	1.9%	6.51 [5.80, 7.23]
Hanske 2010	20.87	15.13	159	14.9	12.81	41	2.2%	0.40 [0.06, 0.75]
Hou 2007	1.35	0.42	80	1.06	0.39	50	2.2%	0.71 [0.34, 1.07]
Huang 2006	30.51	3.029	36	12.63	2.26	56	1.5%	8.66 [5.76, 11.56]
Ji 2008	19.573	7.262	64	11.2	2.1	35	2.1%	1.27 [0.82, 1.83]
Jiang 2006	33.06	27.28	68	12.42	5.57	40	2.2%	0.93 [0.52, 1.34]
Korner 2007	11	4.9	74	11.2	5.2	76	2.2%	-0.06 [0.38, 0.26]
Lj 2006	12.02	1.23	46	9.78	1.16	40	2.1%	1.64 [1.34, 2.05]
Liu 2007	10.43	7.55	47	8.13	3.16	41	2.2%	0.38 [0.04, 0.81]
Liu 2010	13.67	6.33	79	2.35	0.68	60	2.2%	2.23 [1.89, 2.76]
Liu 2012	6.85	4.82	66	2.4	0.62	35	2.1%	1.70 [1.23, 2.18]
Lv 2014	15.4	5.8	46	1.6	1.4	58	2.0%	3.43 [2.82, 4.04]
Maccio 2010	25.917	12.523	180	18.84	13.584	221	2.3%	0.54 [0.34, 0.74]
Mantoros 1999	13.69	11.97	93	18.93	14.45	68	2.2%	-0.18 [0.50, 0.14]
Mantoros 2004	24.4	16.1	174	24.1	18.4	167	2.3%	0.02 [0.19, 0.23]
Myoshi 2006	9.52	0.9	104	10.86	0.89	104	2.2%	-1.49 [1.80, -1.18]
Mohammadsadeh 2015	69.207	43.179	100	22.63	26.911	100	2.3%	1.01 [0.72, 1.31]
Olberding 2013	22.9	8.33	706	19	8.2	706	2.3%	0.47 [0.37, 0.58]
Ozer 2001	27	20.64	56	17.65	7.39	58	2.2%	0.60 [0.23, 0.97]
Pachito-Panayiotou 2007	10.9	5.16	74	11.4	5.23	76	2.3%	-0.10 [0.42, 0.22]
Santillan-Benitez 2013	22.6	15.2	40	18.5	11.6	48	2.2%	0.30 [0.12, 0.73]
Wang 2005	29.84	28.44	64	13.34	3.13	31	2.1%	0.70 [0.26, 1.14]
Wang 2015	39.3	6.1	70	12.8	5.1	60	2.1%	3.05 [2.51, 3.58]
Woo 2005	13.417	11.633	45	9.817	6.295	45	2.2%	0.38 [0.04, 0.80]
Wu 2009	10.08	6.744	266	8.4	5.2	593	2.3%	0.29 [0.14, 0.44]
Yu 2005	21.97	9.13	46	12.25	2.39	41	2.1%	1.41 [0.84, 1.98]
Zhang 2012	8.35	5.57	43	5.31	3.39	43	2.2%	0.65 [0.22, 1.09]
Zhang 2013	26.5	14.043	64	15.4	10.2	25	2.2%	0.86 [0.43, 1.29]
Zhu 2011	19.25	8.65	50	6.25	4.25	50	2.1%	1.89 [1.42, 2.37]
Subtotal (95% CI)			4952			4454	83.9%	1.10 [0.82, 1.37]
Heterogeneity: Tau <sup>2</sup> = 0.74, Chi <sup>2</sup> = 1253.45, df = 38 (P < 0.00001), I <sup>2</sup> = 97%								
Test for overall effect: Z = 7.70 (P < 0.00001)								
<b>2.1.2 Cohort</b>								
Cust 2009	14.1	4.033	561	14.5	4.5	561	2.3%	-0.09 [0.21, 0.02]
Gross 2013	32.9	36.1	272	27.4	27.4	272	2.3%	0.17 [0.00, 0.34]
Dunler 2015	13.95	5.864	875	14.406	5.908	821	2.3%	-0.08 [0.17, 0.02]
Harris 2011	15.5	5.688	330	16.2	7.5	636	2.3%	-0.10 [0.20, 0.03]
Statin 2014	16.7	7.87	149	17.1	8.667	258	2.3%	-0.05 [0.25, 0.15]
Subtotal (95% CI)			2167			2548	11.6%	-0.04 [0.13, 0.04]
Heterogeneity: Tau <sup>2</sup> = 0.00, Chi <sup>2</sup> = 8.03, df = 4 (P = 0.09), I <sup>2</sup> = 50%								
Test for overall effect: Z = 0.97 (P = 0.33)								
<b>2.1.3 Cross-Section</b>								
Al Awadhi 2012	27.5	2.1	144	20.7	11.1	77	2.3%	1.00 [0.71, 1.30]
Romero-Figueroa 2013	90.3	27.5	76	37.1	32.6	76	2.3%	1.76 [1.36, 2.13]
Subtotal (95% CI)			220			153	4.5%	1.37 [0.63, 2.11]
Heterogeneity: Tau <sup>2</sup> = 0.25, Chi <sup>2</sup> = 9.59, df = 1 (P = 0.002), I <sup>2</sup> = 90%								
Test for overall effect: Z = 3.64 (P = 0.0003)								
<b>Total (95% CI)</b>								
			6459			7155	100.0%	0.96 [0.74, 1.18]
Heterogeneity: Tau <sup>2</sup> = 0.53, Chi <sup>2</sup> = 1546.55, df = 45 (P < 0.00001), I <sup>2</sup> = 97%								
Test for overall effect: Z = 8.56 (P < 0.00001)								
Test for subgroup differences: Chi <sup>2</sup> = 70.47, df = 2 (P < 0.00001), I <sup>2</sup> = 97.3%								

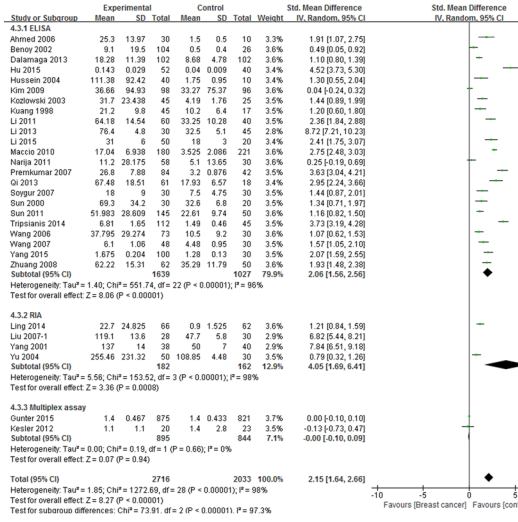
Supplementary Figure 4: Association of adiponectin and leptin with breast cancer risk by study method.



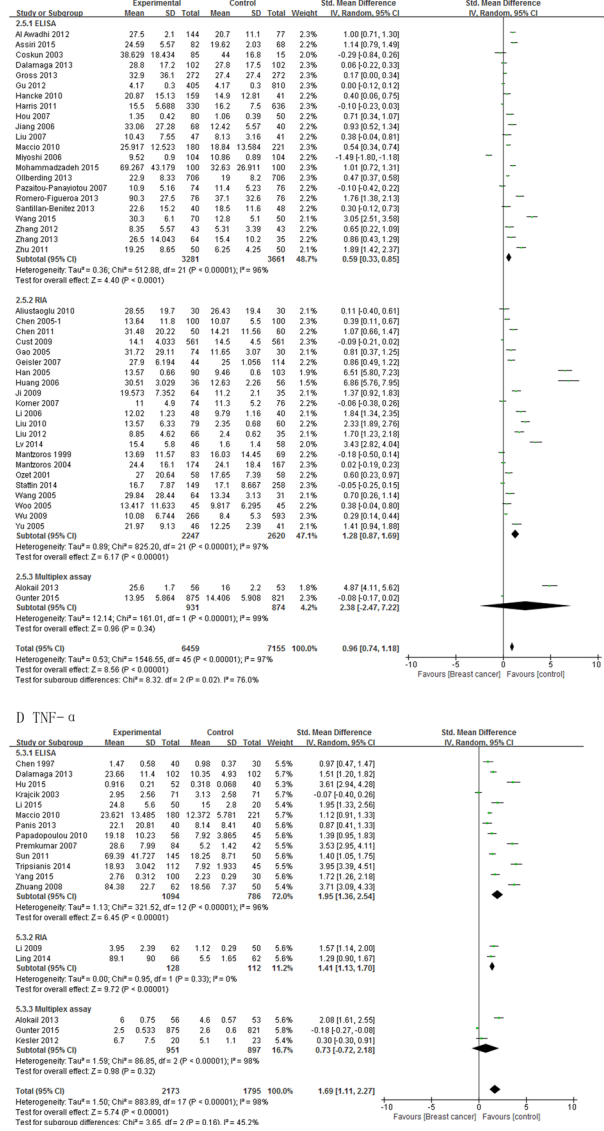
### A adiponectin



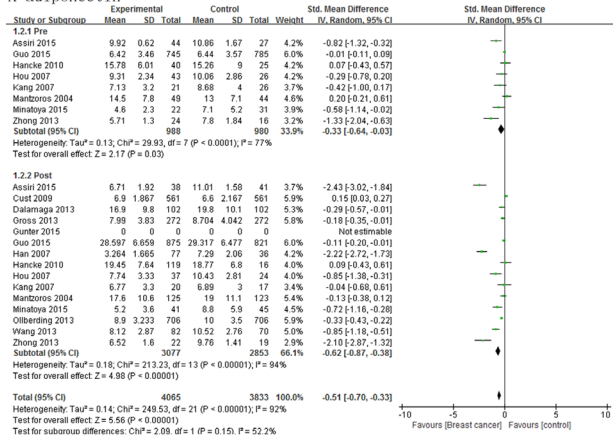
### C IL-6



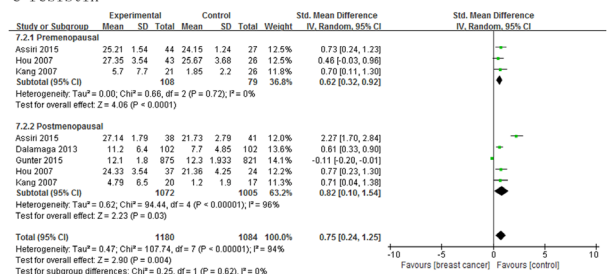
### B leptin



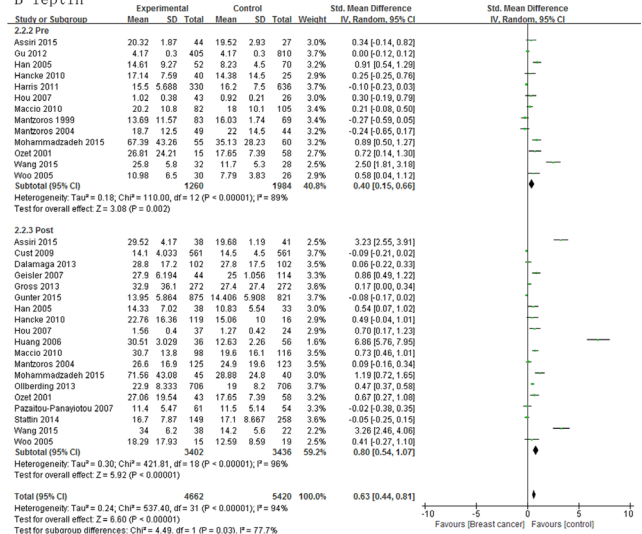
### A adiponectin



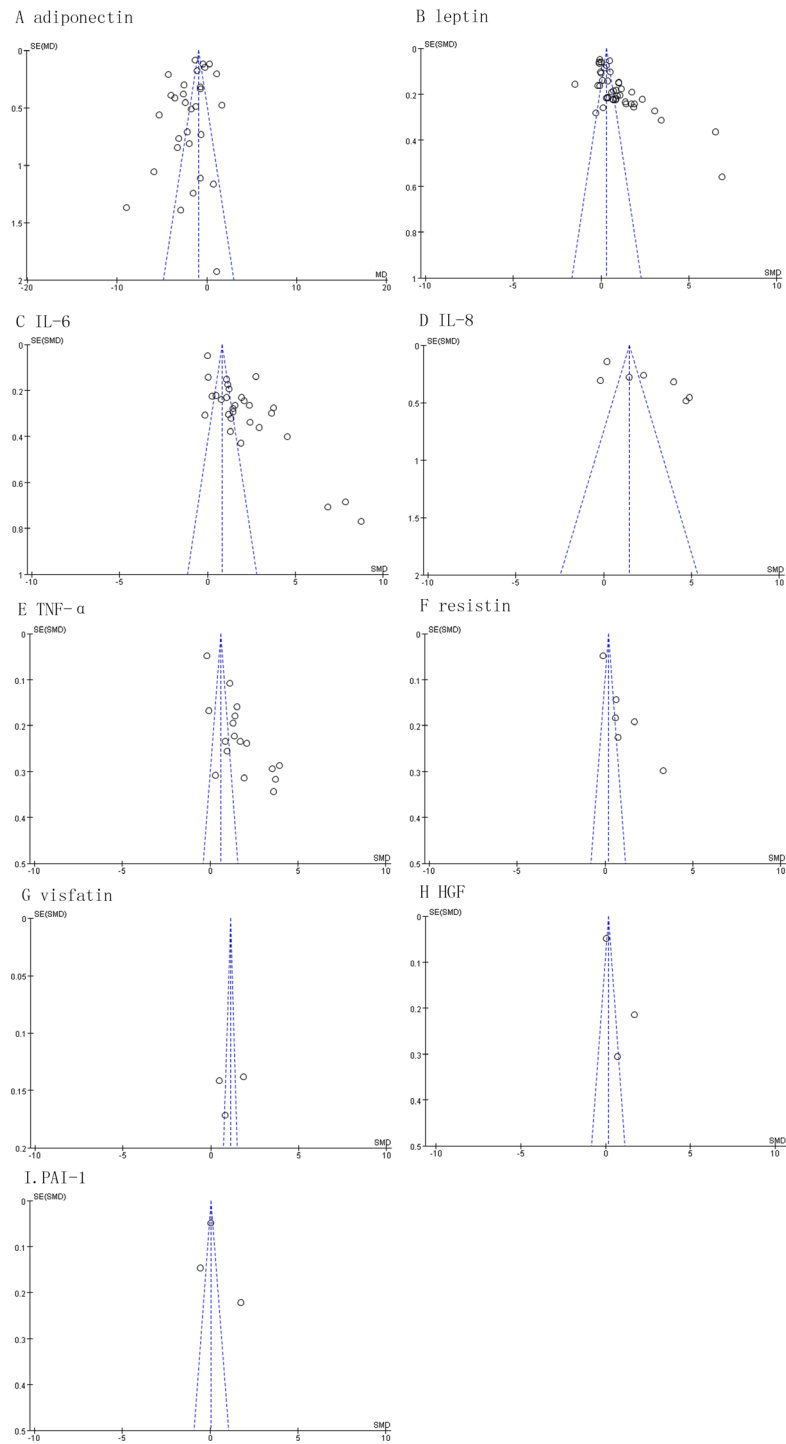
### C resistin



### B leptin



**Supplementary Figure 6: Association of adiponectin, leptin and resistin with breast cancer risk by menopausal status subtype.**



**Supplementary Figure 7: Funnel plot analysis to detect publication bias.** Each point represents a separate study for the indicated association.