

SUPPLEMENTAL MATERIAL

Table S1. Number of participants (n) at baseline and 6 months for individual biomarkers.

Biomarker	Baseline	Month 6
hsCRP	281	281
Glucose	282	282
Insulin	281	281
HOMA-IR	281	279
NT-proBNP	281	281
Renin	251	274
Aldosterone	264	252
Lipid profile*	282	282
25-OH-D	288	277

*Lipid profile includes total cholesterol, triglycerides, high-density lipoprotein, low-density lipoprotein; hsCRP, high-sensitivity C-Reactive Protein; Glucose, Fasting Plasma Glucose; HOMA-IR, Homeostatic Model Assessment of Insulin Resistance; NT-proBNP, N-terminal pro-B-type natriuretic peptide; 25-OH-D, 25-hydroxyvitamin D.

Table S2. Circulating glycemic, inflammatory, neurohormonal, and lipid biomarkers at baseline and 6-month follow-up, stratified by baseline vitamin D level.

Biomarker	Low-dose Vitamin D Group			High-dose Vitamin D Group			*P-value
	Baseline	Month 6	Change	Baseline	Month 6	Change	
<i>Baseline 25-OH-D ≤ 10 ng/ml</i>							
hsCRP (mg/L)	2.6 (1.0, 12.5)	2.9 (1.1, 5.6)	-0.2 (-1.7, 0.5)	2.0 (0.7, 4.1)	1.7 (0.7, 3.5)	0.03 (-1.0, 1.0)	0.4
Glucose (mg/dL)	77.0 (71.0, 88.0)	77.0 (68.0, 94.0)	0.0 (-10.0, 4.0)	79.0 (70.0, 92.0)	81.0 (73.0, 92.0)	4.0 (-8.5, 13.0)	0.3
Insulin (μU/mL)	13.0 (9.2, 23.6)	9.1 (6.0, 23.0)	-0.2 (-7.6, 4.0)	8.0 (4.4, 16.3)	11.6 (5.9, 18.2)	0.5 (-4.4, 5.7)	0.5
HOMA-IR	2.7 (1.5, 6.5)	1.8 (0.9, 5.3)	-0.2 (-1.3, 0.3)	1.5 (0.8, 3.5)	2.4 (1.1, 4.0)	0.06 (-1.1, 1.0)	0.4
NT-proBNP (pg/mL)	27.8 (7.7, 42.4)	21.7 (9.8, 67.1)	1.5 (-6.3, 18.3)	23.6 (11.8, 42.2)	21.4 (7.1, 39.4)	-5.6 (-17.6, 9.0)	0.09
Renin (pg/mL)	6.3 (3.9, 16.1)	7.6 (3.3, 14.5)	-1.2 (-3.5, 3.1)	7.3 (3.5, 10.6)	7.0 (5.1, 16.3)	0.2 (-1.2, 4.2)	0.3
Aldosterone (ng/dL)	10.9 (8.3, 13.1)	9.6 (7.2, 11.9)	-0.5 (-2.9, 1.6)	9.4 (6.3, 12.6)	10.9 (6.3, 13.9)	-0.03 (-1.7, 3.8)	0.3
Total Cholesterol (mg/dL)	172.0 (150.0, 198.0)	160.0 (143.0, 200.0)	-8.0 (-15.0, 8.0)	162.0 (152.0, 193.0)	169.0 (146.0, 205.0)	8.0 (-13.0, 21.0)	0.08
Triglyceride (mg/dL)	102.0 (72.0, 150.0)	94.0 (68.0, 134.0)	-18.0 (-28.0, .0)	85.0 (70.0, 110.0)	97.0 (73.0, 146.0)	7.0 (-19.0, 37.0)	0.04
HDL (mg/dL)	49.0 (44.0, 60.0)	54.0 (44.0, 64.0)	1.5 (-2.0, 7.8)	60.0 (53.0, 74.0)	61.0 (52.0, 72.0)	1.0 (-7.5, 8.0)	0.3
LDL (mg/dL)	94.0 (67.0, 115.0)	94.0 (68.0, 105.0)	-5.0 (-15.3, 5.3)	86.0 (68.0, 100.0)	86.0 (70.0, 110.0)	4.0 (-6.5, 16.5)	0.1
<i>Baseline 25-OH-D > 10 and < 20 ng/ml</i>							
hsCRP (mg/L)	1.9 (1.1, 4.7)	1.9 (0.9, 3.9)	-0.3 (-1.4, 0.5)	1.2 (0.5, 2.5)	1.3 (0.7, 2.5)	-0.2 (-0.7, 0.8)	0.5
Glucose (mg/dL)	79.0 (70.0, 90.0)	80.0 (72.0, 91.0)	-1.0 (-10.0, 13.0)	79.0 (68.0, 89.0)	80.0 (70.0, 88.0)	-0.5 (-10.3, 13.0)	0.9
Insulin (μU/mL)	11.2 (6.1, 22.2)	9.5 (6.2, 14.9)	-0.2 (-7.1, 3.6)	9.3 (6.1, 14.9)	11.0 (6.2, 18.3)	1.1 (-3.1, 5.0)	0.09
HOMA-IR	2.2 (1.1, 4.4)	1.9 (1.2, 3.3)	-0.04 (-1.6, 1.2)	1.6 (1.1, 3.1)	2.1 (1.2, 3.3)	0.1 (-0.6, 1.2)	0.2
NT-proBNP (pg/mL)	20.8 (9.1, 48.8)	14.0 (8.1, 39.6)	-0.07 (20.0, 8.7)	19.0 (10.5, 38.4)	15.4 (5.0, 33.2)	-3.8 (-9.8, 0.6)	0.5
Renin (pg/mL)	9.8 (3.7, 18.5)	8.4 (4.5, 14.5)	-0.4 (-7.0, 4.1)	9.6 (3.4, 15.1)	8.8 (3.7, 14.5)	0.0 (-3.4, 4.0)	0.7
Aldosterone (ng/dL)	10.9 (7.8, 13.6)	9.9 (7.5, 14.4)	-0.7 (-2.9, 2.6)	8.8 (6.5, 13.9)	11.2 (8.1, 15.0)	0.7 (-1.0, 4.5)	0.06
Total Cholesterol (mg/dL)	178.0 (153.0, 196.0)	175.0 (152.0, 199.0)	2.0 (-15.0, 16.0)	173.0 (152.0, 187.0)	179.0 (156.0, 195.0)	7.5 (-5.0, 19.0)	0.07
Triglyceride (mg/dL)	98.0 (74.0, 148.0)	98.0 (70.0, 135.0)	-5.0 (-29.0, 20.0)	89.0 (68.0, 125.0)	100.0 (68.0, 131.0)	7.0 (-6.0, 28.0)	0.045
HDL (mg/dL)	50.0 (45.0, 59.0)	52.0 (45.0, 64.0)	2.0 (-2.0, 7.0)	50.0 (44.0, 59.0)	52.0 (46.0, 64.0)	3.0 (-1.0, 9.0)	0.2
LDL (mg/dL)	97.0 (76.0, 122.0)	96.0 (73.0, 115.0)	2.0 (-16.0, 13.0)	96.0 (74.0, 114.0)	100.0 (76.0, 113.0)	2.0 (-8.8, 11.0)	0.7
<i>Baseline 25-OH-D ≥ 20 ng/ml</i>							
hsCRP (mg/L)	1.4 (0.5, 2.3)	1.1 (0.4, 3.3)	0.1 (-0.6, 1.3)	1.1 (0.5, 2.0)	1.2 (0.6, 3.6)	0.1 (-0.4, 0.8)	0.9
Glucose (mg/dL)	78.0 (72.0, 100.0)	78.0 (70.0, 96.0)	2.0 (-9.5, 8.5)	75.0 (71.0, 84.0)	79.0 (69.0, 94.0)	1.0 (-8.5, 12.8)	0.6
Insulin (μU/mL)	9.1 (5.5, 17.1)	9.3 (6.6, 20.4)	-0.3 (-2.7, 4.4)	8.3 (5.4, 15.2)	9.5 (5.4, 19.6)	1.0 (-2.4, 6.6)	0.7
HOMA-IR	1.5 (1.0, 4.5)	1.8 (1.3, 4.1)	0.07 (-0.5, 1.0)	1.7 (0.9, 3.0)	1.9 (1.0, 4.1)	0.009 (-0.5, 1.3)	0.9
NT-proBNP (pg/mL)	21.0 (14.0, 41.0)	14.8 (9.1, 47.0)	-4.0 (16.4, 2.9)	22.0 (14.0, 38.0)	22.8 (12.2, 43.2)	-1.2 (-11.4, 9.9)	0.2
Renin (pg/mL)	8.6 (5.0, 14.9)	9.2 (6.0, 14.7)	-0.3 (-5.3, 7.5)	10.6 (6.8, 20.1)	9.7 (4.3, 14.2)	-1.4 (-8.6, 2.3)	0.2
Aldosterone (ng/dL)	11.2 (7.3, 16.6)	12.3 (8.9, 17.9)	0.3 (-3.2, 4.4)	11.7 (7.8, 18.2)	10.2 (7.5, 15.4)	-0.7 (-4.5, 2.8)	0.6
Total Cholesterol (mg/dL)	162.0 (140.0, 192.0)	164.0 (151.0, 186.0)	-2.0 (-9.5, 19.5)	172.0 (154.0, 190.0)	175.0 (152.0, 190.0)	1.5 (-13.0, 7.3)	0.5
Triglyceride (mg/dL)	99.0 (65.0, 143.0)	99.0 (62.0, 126.0)	-5.0 (-30.0, 6.5)	88.0 (62.0, 120.0)	94.0 (74.0, 135.0)	3.5 (-10.8, 24.8)	0.03
HDL (mg/dL)	49.0 (45.0, 56.0)	53.0 (49.0, 62.0)	5.0 (0.5, 9.5)	53.0 (47.0, 63.0)	54.0 (47.0, 63.0)	-1.0 (-5.8, 6.0)	0.003
LDL (mg/dL)	82.0 (72.0, 100.0)	86.0 (72.0, 113.0)	2.0 (-9.0, 11.5)	96.0 (82.0, 111.0)	96.0 (74.0, 108.0)	-4.5 (-12.8, 1.5)	0.1

Data presented as median (lower quartile, upper quartile); 25-OH-D, 25-hydroxyvitamin D; hsCRP, high-sensitivity C-Reactive Protein; HOMA-IR, Homeostatic Model Assessment of Insulin Resistance; NT-proBNP, N-terminal pro-B-type natriuretic peptide; HDL, High-density Lipoprotein; LDL, Low-density Lipoprotein. *P-value refers to the difference between the change for low-dose group vs. change for high-dose group.

Table S3. Circulating glycemc, inflammatory, neurohormonal, and lipid biomarkers at baseline and 6-month follow-up, stratified by vitamin D status at the end of the study.

Biomarker	Low-dose Vitamin D Group			High-dose Vitamin D Group		
	Baseline	Month 6	Change	Baseline	Month 6	Change
<i>Final 25-OH-D > 20 ng/ml</i>						
hsCRP (mg/L)	1.9 (0.9, 3.3)	1.5 (0.7, 2.4)	-0.3 (-1.2, 0.5)	1.2 (0.6, 3.2)	1.3 (0.7, 3.2)	0.02 (-0.6, 0.8)
Glucose (mg/dL)	81.0 (74.0, 96.0)	79.0 (69.0, 92.0)	-1.0 (-12.0, 8.0)	78.0 (69.0, 87.0)	79.0 (70.0, 88.0)	0.5 (-9.0, 12.8)
Insulin (μU/mL)	9.8 (5.3, 18.3)	7.5 (5.7, 14.5)	-0.4 (-5.2, 4.2)	8.3 (5.1, 14.0)	7.9 (5.2, 14.5)	-0.1 (-3.4, 4.3)
HOMA-IR	1.7 (1.1, 3.9)	1.5 (1.0, 3.4)	-0.06 (-1.2, 1.1)	1.4 (0.9, 2.9)	1.5 (1.0, 2.9)	-0.05 (-0.7, 0.9)
NT-proBNP (pg/mL)	20.8 (8.6, 40.2)	14.8 (9.5, 41.0)	-0.07 (-16.1, 9.8)	20.5 (10.6, 39.3)	18.3 (6.9, 37.1)	-2.7 (-11.4, 5.5)
Renin (pg/mL)	10.2, (4.5, 17.5)	10.3 (6.7, 15.5)	0.0 (-6.3, 5.1)	8.9 (4.5, 14.5)	9.0 (5.2, 15.6)	0.05 (-3.4, 4.7)
Aldosterone (ng/dL)	12.3 (8.5, 15.7)	11.7 (9.2, 16.3)	-0.05 (-4.5, 3.0)	9.4 (6.5, 14.1)	11.7 (8.1, 14.9)	0.3 (-1.8, 3.9)
Total Cholesterol (mg/dL)	168.0 (144.0, 191.0)	166.0 (147.0, 188.0)	-2.0 (-11.0, 9.0)	170.0 (152.0, 188.0)	175.0 (147.0, 196.0)	5.0 (-12.5, 17.0)
Triglyceride (mg/dL)	99.0 (70.0, 147.0)	92.0 (65.0, 124.0)	-6.0 (-33.0, 11.0)	88.0 (68.0, 122.0)	98.0 (70.0, 140.0)	7.0 (-15.0, 31.0)
HDL (mg/dL)	53.0 (45.0, 59.0)	53.0 (48.0, 64.0)	2.0 (-2.0, 7.0)	54.0 (46.0, 63.0)	54.0 (46.0, 63.0)	1.0 (-4.0, 6.0)
LDL (mg/dL)	83.0 (74.0, 110.0)	88.0 (72.0, 113.0)	0.0 (-10.0, 9.0)	92.0 (75.0, 112.0)	95.0 (73.0, 112.0)	-1.5 (-11.8, 13.8)
<i>Final 25-OH-D ≤ 20 ng/ml</i>						
hsCRP (mg/L)	1.8 (0.7, 5.6)	2.4 (0.9, 5.4)	-0.05 (-1.0, 1.2)	1.2 (0.6, 2.2)	2.0 (0.7, 3.2)	-0.2 (-0.5, 1.1)
Glucose (mg/dL)	77.0 (70.0, 89.0)	77.0 (69.0, 91.0)	0.0 (-8.0, 9.0)	82.0 (73.0, 92.0)	81.0 (75.0, 94.0)	1.0 (-11.0, 13.0)
Insulin (μU/mL)	12.3 (5.9, 28.0)	9.8 (7.1, 16.6)	0.03 (-7.0, 3.7)	11.8 (5.6, 17.2)	14.2 (11.3, 23.2)	3.7 (-2.6, 9.8)
HOMA-IR	2.3 (1.1, 5.3)	1.9 (1.2, 3.5)	-0.04 (-1.5, 0.6)	2.3 (1.3, 4.0)	2.8 (2.1, 5.5)	0.6 (-0.9, 1.8)
NT-proBNP (pg/mL)	25.0 (10.0, 49.0)	14.9 (7.2, 41.7)	-3.5 (-19.5, 6.4)	24.0 (13.0, 41.0)	19.9 (6.7, 33.4)	-6.8 (-17.8, 0.6)
Renin (pg/mL)	9.4 (3.9, 16.1)	7.1 (3.7, 13.0)	-0.6 (-5.8, 3.5)	9.2 (3.7, 17.3)	6.1 (3.0, 14.0)	-0.3 (-4.9, 2.5)
Aldosterone (ng/dL)	10.6 (7.3, 12.4)	9.0 (7.1, 12.9)	-0.6 (-2.6, 2.4)	9.4 (6.9, 14.3)	10.0 (6.8, 12.8)	0.2 (-1.7, 2.7)
Total Cholesterol (mg/dL)	170.0 (152.0, 196.0)	175.0 (156.0, 198.0)	7.0 (-14.5, 20.5)	167.0 (159.0, 189.0)	176.0 (162.0, 205.0)	11.0 (-3.0, 22.0)
Triglyceride (mg/dL)	103.0 (74.0, 148.0)	101.0 (71.0, 144.0)	-10.0 (-25.0, 19.0)	88.0 (68.0, 113.0)	94.0 (66.0, 121.0)	7.0 (-16.0, 29.0)
HDL (mg/dL)	49.0 (45.0, 58.0)	53.0 (45.0, 65.0)	4.0 (-1.0, 9.5)	53.0 (47.0, 64.0)	59.0 (50.0, 70.0)	6.0 (-3.0, 10.0)
LDL (mg/dL)	95.0 (71.0, 122.0)	95.0 (73.0, 113.0)	2.0 (-13.5, 14.0)	94.0 (80.0, 112.0)	95.0 (72.0, 107.0)	3.0 (-4.0, 11.0)

Data presented as median (lower quartile, upper quartile); 25-OH-D, 25-hydroxyvitamin D; hsCRP, high-sensitivity C-Reactive Protein; HOMA-IR, Homeostatic Model Assessment of Insulin Resistance; NT-proBNP, N-terminal pro-B-type natriuretic peptide; HDL, High-density Lipoprotein; LDL, Low-density Lipoprotein. **P*-value refers to the difference between the change for low-dose group vs. change for high-dose group.

Table S4. General characteristics of studies investigating effects of vitamin D supplementation on LDL.

Author	Year	Country	Subject Characteristics	Mean Age, Control	Mean Age, Intervention	Sex (n) male	Intervention (n)	Control (n)	Baseline 25 OH-D (ng/mL)		Vit D Dose (IU/day)	Duration (Weeks)	Delta, Intervention	Delta, Control	p-value
									Intervention	Control					
Angelloti ²⁶	2019	USA	T2D	60.3	60.1	89	66	61	25.8 (10.3)	27.5 (12.0)	4000	48	-0.07 (3.3)	-2.0 (3.4)	0.7
Dastorani ¹⁹	2018	Iran	PCOS	30.1	29.9	0	20	20	10.5 (2.5)	11.0 (2.4)	7142	8	-4.5 (10.3)	2.5 (10.6)	0.04
Foroozanfard ¹¹	2017	Iran	PCOS	NR	NR	0	60	30	13.5 (3.1) (high dose) 14.0 (4.6) (low dose)	14.0 (3.5)	4000	12	-10.8 (8.3) (high dose) -5.7 (21.9) (low dose)	6.8 (28.2)	0.005
Ghaderi ¹³	2017	Iran	MMT	42.5	40.1	NR	34	34	13.9 (4.5)	13.5 (4.5)	3571	12	-11.1 (17.9)	5.9 (27.5)	0.004
Dalan ²¹	2016	Singapore	T2D	54.8	52.2	33	33	31	18.0 (7.0)	17.0 (11.0)	4000	16	0.1 (0.5)	-0.1 (0.6)	0.2
Maktabi ¹⁴	2017	Iran	PCOS	23.1	22.0	0	35	35	12.8 (4.5)	14.5 (5.1)	3571	12	-6.3 (24.1)	3.2 (26.8)	0.1
Tabassi ¹⁵	2017	Iran	Endometrial hyperplasia	43.2	41.5	0	30	30	NR	NR	3571	12	0.9 (4.0)	3.3 (4.0)	0.7
Sepehrmanesh ¹⁷	2015	Iran	MDD	36.1	36.5	6	20	20	13.6 (7.9) µg/L	9.2 (6.0) µg/L	7142	8	4.0 (17.0)	-3.0 (16.0)	0.3
Asemi ¹⁸	2015	Iran	PCOS, obesity	24.3	25.0	0	26	26	13.9 (2.0) (Calcium) 11.6 (4.7) (Vit D) 15.1 (3.6) (Calcium+ Vit D)	14.0 (4.1)	7142	8	-4.5 (20.8)	-2.2 (31.7)	0.4
Yousefi Rad ¹²	2014	Iran	T2D	49.9	50.0	12	28	30	15.6 (1.9)	14.6 (2.2)	4000	8	0.9 (7.2)	1.3 (8.7)	1.0
Ryu ¹⁶	2014	South Korea	T2D	56.7	54.5	NR	32	30	12.3 (3.0)	10.7 (2.6)	2000	24	10.2 (17.5)	0.3 (26.0)	0.09
Sollid ²³	2014	Norway	Prediabetes	61.9	62.3	314	256	255	23.9 (8.8)	24.4 (8.5)	2857	52	-0.1 (0.7)	0.09 (0.66)	<0.05
Raja-Khan ²²	2014	USA	PCOS	28.7	28.2	0	13	15	19.9 (9.5)	22.2 (6.9)	12000	12	-0.1 (20.6)	-0.4 (20.9)	0.9
Ponda ²⁰	2012	USA	Vit D deficient	47.4	48.4	75	76	75	13.4 (5.3)	14.1 (5.7)	7142	8	-0.3 (18.6)	-4.1 (20.8)	0.1
Rajpathak ¹⁰	2010	USA	Postmenopausal	62.1	61.6	0	592	599	NR	NR	400	260	-6.5 (1.6)	-6.3 (1.7)	NS
Jorde ²⁴	2009	Norway	T2D	54.8	57.7	18	16	16	24.0 (5.6)	23.4 (8.4)	5714	26	-0.1 (0.4)	0.0 (0.3)	0.6
Zittermann ²⁵	2009	Germany	Overweight	48.8	47.4	53	82	83	30.0 (17.5)	30.3 (20.1)	3332	52	0.2 (1.0)	-0.09 (0.9)	0.2

Data are presented as mean (SD). LDL, Low-density Lipoprotein; 25-OH-D, 25-hydroxyvitamin D; IU, International Units; PCOS, Polycystic

Ovarian Syndrome; MMT, Methadone Maintenance Treatment; MDD, Major Depressive Disorder; T2D, Type 2 Diabetes; NR, Not Reported; NS,

Not Significant.

Table S5. General characteristics of included studies investigating effects of vitamin D supplementation on HOMA-IR.

Author	Year	Country	Subject Characteristics	Mean Age, Control	Mean Age, Intervention	Sex (n) male	Intervention (n)	Control (n)	Baseline 25 OH-D (ng/mL)		Vit D Dose (IU/day)	Duration (Weeks)	Delta, Intervention	Delta, Control	p-value
									Intervention	Control					
Seyyed ²⁹	2018	Iran	PCOS	22.8	26.2	0	22	22	8.65 (4.3)	9.8 (5.1)	7142	8	0.04 (1.2)	0.3 (1.4)	0.3
Maktabi ¹⁴	2017	Iran	PCOS	23.1	22.0	0	35	35	12.8 (4.5)	14.5 (5.1)	3571	12	-0.3 (0.8)	0.6 (1.6)	0.003
Ghaderi ¹³	2017	Iran	MMT	42.5	40.1	NR	34	34	13.9 (4.5)	13.5 (4.5)	3571	12	-1.0 (1.3)	-0.2 (0.7)	0.003
Jamilian ²⁷	2017	Iran	PCOS	25.0	26.0 (low dose) 28.0 (high dose)	0	60	30	12.6 (3.4) (low dose) 12.6 (2.7) (high dose)	12.9 (2.4) (high dose)	4000 (high dose) 1000 (low dose)	12	-0.5 (0.4) (high dose) -0.3 (0.7) (low dose)	0.1 (2.6)	0.004
Tabassi ¹⁵	2017	Iran	Endometrial hyperplasia	43.2	41.5	0	30	30	NR	NR	3571	12	-0.2 (0.1)	0.3 (0.1)	0.006
Foroozanfard ¹¹	2017	Iran	PCOS	NR	NR	0	60	30	13.5 (3.1) (high dose) 14.0 (4.6) (low dose)	14.0 (3.5)	4000	12	-0.4 (1.0) (low dose) -0.6 (0.6) (high dose)	-0.1 (0.9)	0.02
Sepehrmanesh ¹⁷	2016	Iran	MDD	36.1	36.5	6	20	20	13.6 (7.9) µg/L	9.2 (6.0) µg/L	7142	8	-1.0 (1.5)	0.6 (2.2)	0.01
Osati ²⁸	2016	Iran	Vit D deficient	38.0	38.0	49	105	105	13.8 (3.6) mg/dL	13.9 (3.7) mg/dL	7142	8	-0.8 (0.4)	-0.3 (0.3)	<0.001
Asemi ¹⁸	2015	Iran	PCOS, obesity	24.3	25.0	0	26	26	13.9 (2.0) (Calcium) 11.6 (4.7) (Vit D) 15.1 (3.6) (Calcium+ Vit D)	14.0 (4.1)	7142	8	-0.7 (2.4) (Calcium +Vit D)	0.8 (1.9)	0.04
Yousefi Rad ¹²	2014	Iran	T2D	49.9	50.0	12	28	30	15.6 (1.9)	14.6 (2.2)	4000	8	-0.1 (0.1)	0.2 (0.1)	0.06
Raja-Khan ²²	2014	USA	PCOS	28.7	28.2	0	13	15	19.9 (9.5)	22.2 (6.9)	12000	12	2.57 (4.9)	-0.5 (4.9)	0.2
Jorde ²⁴	2009	Norway	T2D	54.8	57.7	18	16	16	24.0 (5.6)	23.4 (8.4)	5714	26	0.3 (23.5)	-0.2 (13.7)	0.6

Data are presented as mean (SD). HOMA-IR, Homeostatic Model Assessment of Insulin Resistance; 25-OH-D, 25-hydroxyvitamin D; IU,

International Units; PCOS, Polycystic Ovarian Syndrome; MMT, Methadone Maintenance Treatment; MDD, Major Depressive Disorder; T2D, Type

2 Diabetes; NR, Not Reported.

Table S6. General characteristics of included studies investigating effects of vitamin D supplementation on hsCRP.

Author	Year	Country	Subject Characteristics	Mean Age, Control	Mean Age, Intervention	Sex (n) male	Intervention (n)	Control (n)	Baseline 25 OH-D (ng/mL)		Vit D Dose (IU/day)	Duration (Weeks)	Delta, Intervention	Delta, Control	p-value
									Intervention	Control					
Angelloti ²⁶	2019	USA	T2D	60.3	60.1	89	66	61	25.8 (10.3)	27.5 (12.0)	4000	48	-0.8 (0.3)	-0.6 (0.3)	0.6
Maktabi ³⁰	2018	Iran	PCOS	24.8	23.8	0	30	30	10.1 (4.9)	10.8 (4.6)	400	12	-0.7 (0.8)	0.2 (0.8)	<0.001
Zheng ³²	2018	Australia	Knee OA, Vit D deficient	62.8	63.3	93	106	94	17.0 (4.7)	17.4 (5.0)	1667	104	0.3 (2.1)	0.0 (2.4)	0.4
Ghaderi ¹³	2017	Iran	MMT	42.5	40.1	NR	34	34	13.9 (4.5)	13.5 (4.5)	3571	12	-2.2 (4.2)	2.0 (3.7)	<0.001
Mousa ³¹	2017	Australia	Obese/ Overweight	29.5	30.5	35	28	26	12.6 (5.0)	13.7 (4.0)	4893	16	-0.1 (1.4)	-0.4 (2.3)	0.9
Jamilian ²⁷	2017	Iran	PCOS	25	26 (low dose) 28 (high dose)	0	30 (low dose) 30 (high dose)	30	12.6 (2.7) (high dose) 12.6 (3.4) (low dose)	12.9 (2.4)	4000 (high dose) 1000 (low dose)	12	-0.7 (1.4) (high dose) -0.5 (0.9) (low dose)	0.5 (2.4)	0.01
Maktabi ¹⁴	2017	Iran	PCOS	23.1	22	0	35	35	12.8 (4.5)	14.5 (5.1)	3571	12	-0.7 (1.4)	0.5 (2.1)	0.009
Tabassi ¹⁵	2017	Iran	Endometrial hyperplasia	43.2	41.5	0	30	30	NR	NR	3571	12	-1.7 (0.4)	-0.2 (0.4)	0.007
Sepehrmanesh ¹⁷	2016	Iran	MDD	36.1	36.5	6	20	20	13.6 (7.9)	9.2 (6.0)	7142	8	0.01 (1.0)	0.02 (1.7)	1.0
Sollid ²³	2014	Norway	Prediabetes	61.9	62.3	314	256	255	24.0 (8.8)	24.4 (8.5)	2857	52	2.7 (3.2)	3.1 (4.1)	NS
Raja-Khan ²²	2014	USA	PCOS	28.7	28.2	0	13	15	19.9 (9.5)	22.2 (6.9)	12000	12	0.9 (4.8)	2.0 (4.8)	0.6
Zittermann ²⁵	2009	Germany	Overweight	48.8	47.4	53	82	83	30.0 (17.5)	30.3 (20.1)	3332	52	-0.03 (0.5)	-0.05 (0.7)	0.5

Data are presented as mean (SD). hsCRP, high-sensitivity C-reactive protein; 25-OH-D, 25-hydroxyvitamin D; IU, International Units; PCOS, Polycystic Ovarian Syndrome; OA, Osteoarthritis; MMT, Methadone Maintenance Treatment; MDD, Major Depressive Disorder; T2D, Type 2 Diabetes; NR, Not Reported; NS, Not Significant.

Figure S1. Flow diagram detailing study selection for randomized-controlled trials included in the meta-analysis.

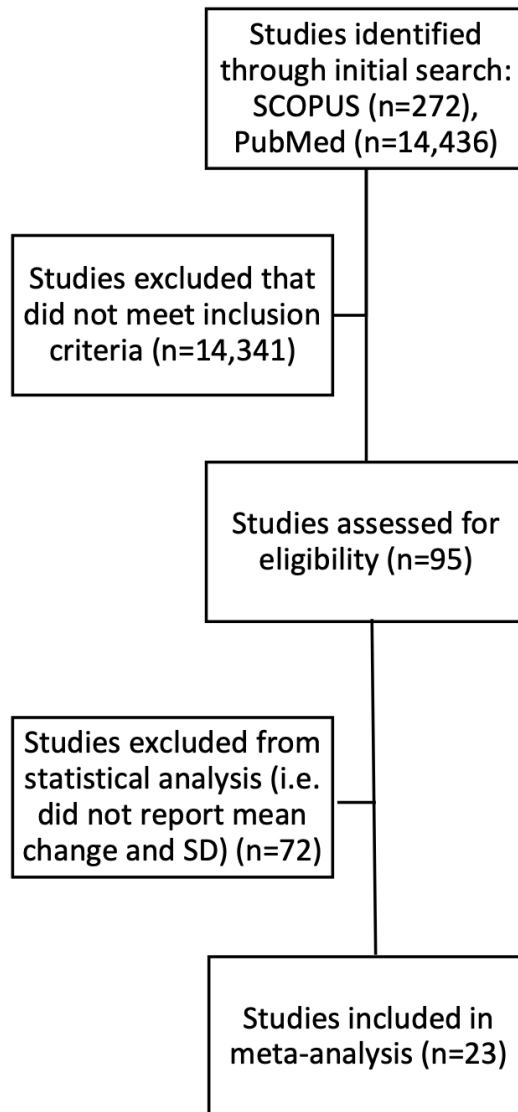
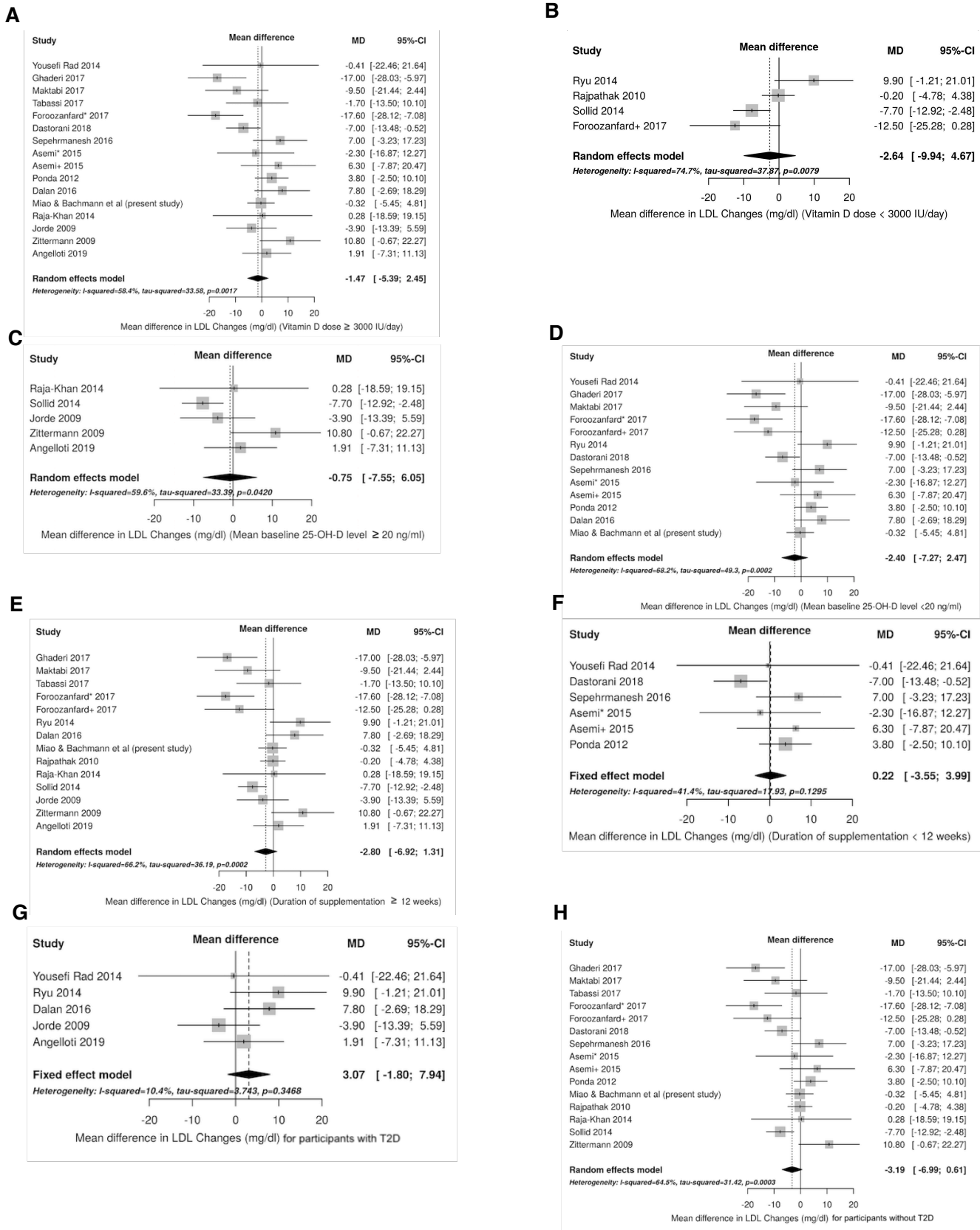
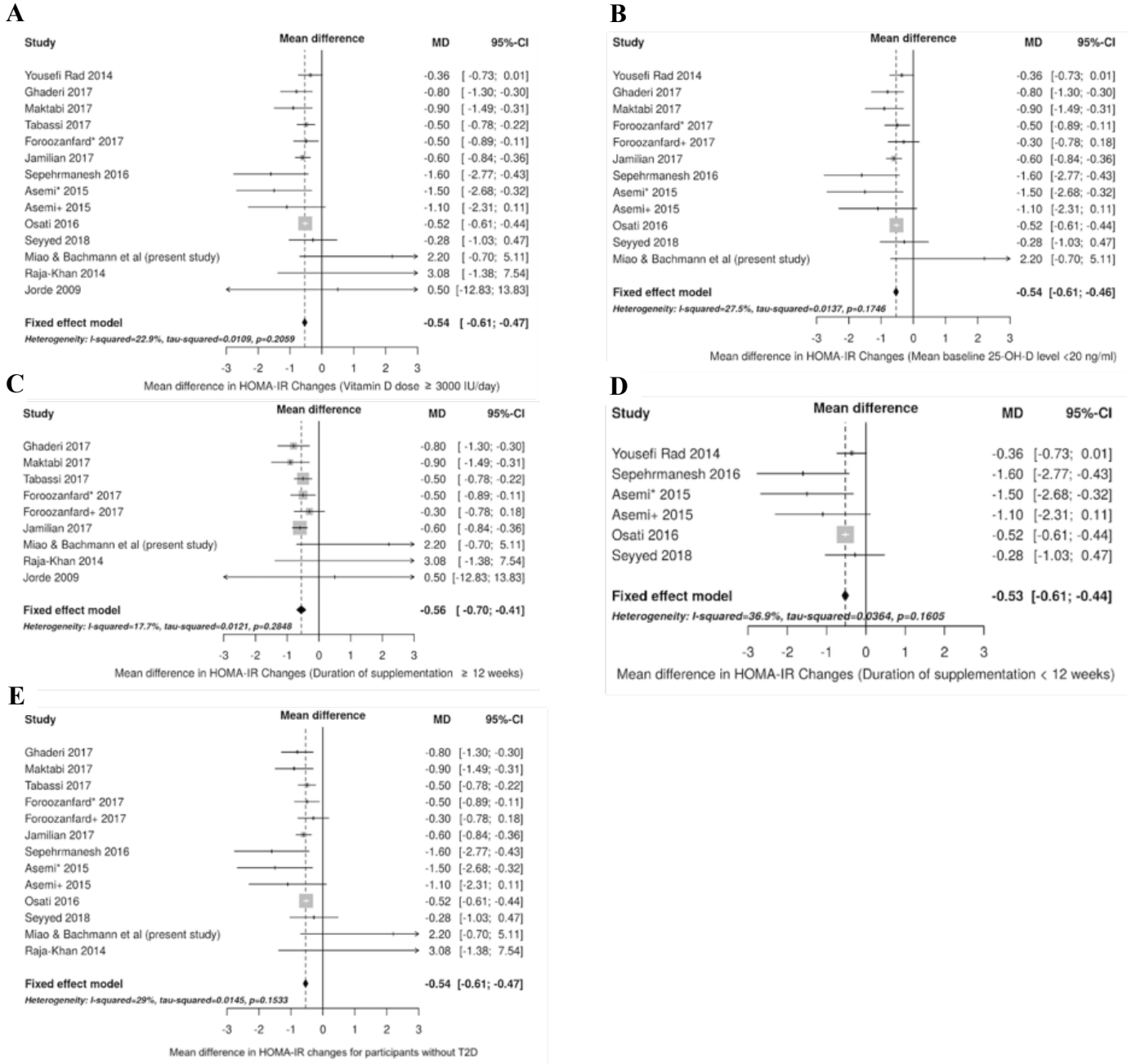


Figure S2. Forest plots comparing effects of vitamin D supplementation on changes in LDL stratified by dose of vitamin D supplementation, mean baseline 25-hydroxyvitamin D concentration, duration of vitamin D supplementation, and diabetes status.



Subgroup analyses are presented for daily vitamin D supplementation dose \geq or $<$ 3000 IU/day (panels A and B, respectively), mean baseline 25-hydroxyvitamin-D level \geq or $<$ 20 ng/ml (panels C and D, respectively), supplementation duration \geq or $<$ 12 weeks (panels E and F, respectively), and participants with or without T2D (panels G and H, respectively). Meta-analysis was not performed for subgroups consisting of 2 or fewer studies. The gray boxes correspond with study precision, lines denote 95% CI. MD, mean difference; IU, International Units; 25-OH-D, 25-hydroxyvitamin D; T2D, Type 2 Diabetes; LDL, Low-density Lipoprotein.

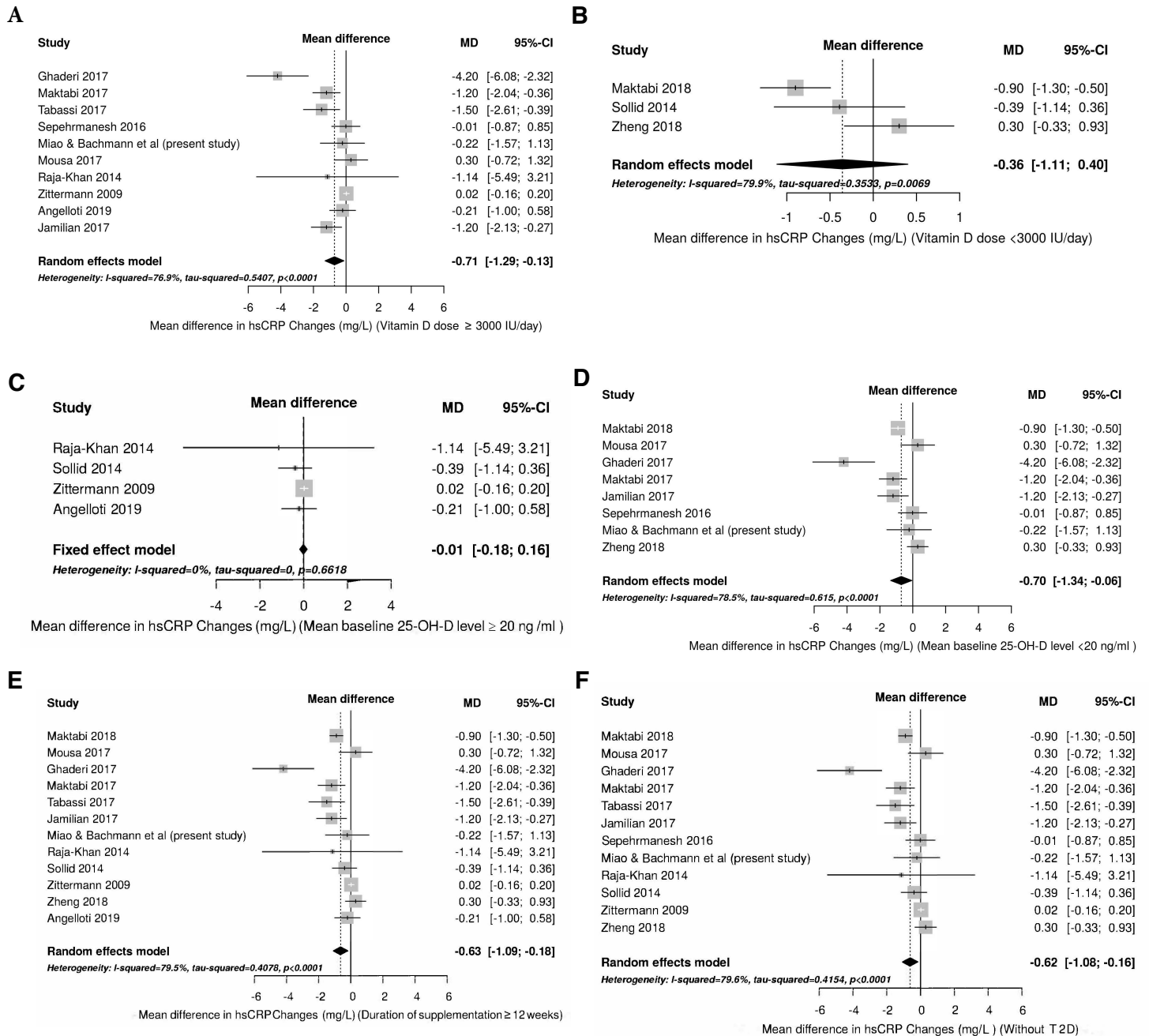
Figure S3. Forest plots comparing effects of vitamin D supplementation on changes in HOMA-IR stratified by dose of vitamin D supplementation, mean baseline 25-hydroxyvitamin D concentration, duration of vitamin D supplementation, and diabetes status.



Subgroup analyses are presented for daily vitamin D supplementation dose ≥ 3000 IU/day (panel A), mean baseline 25-hydroxyvitamin-D level < 20 ng/ml (panel B), supplementation duration \geq or < 12 weeks (panels C and D, respectively), and participants without T2D (panel E). Meta-analysis was not performed for subgroups consisting of 2 or fewer studies. The gray boxes correspond with study precision, lines denote 95% CI. MD,

mean difference; IU, International Units; 25-OH-D, 25-hydroxyvitamin D; T2D, Type 2 Diabetes; HOMA-IR, Homeostatic Model Assessment of Insulin Resistance. Foroozanfard*, Vitamin D 4000 IU daily; Foroozanfard+, Vitamin D 1000 IU daily; Asemi*, Vitamin D 50,000 IU weekly + calcium 1000 mg daily; Asemi+, Vitamin D 50,000 IU weekly.

Figure S4. Forest plots comparing effects of vitamin D supplementation on changes in hsCRP between studies included in the meta-analysis stratified by dose of vitamin D supplementation, mean baseline 25-hydroxyvitamin D concentration, duration of vitamin D supplementation, and diabetes status.



Subgroup analyses are presented for daily vitamin D supplementation dose \geq or < 3000 IU/day (panels A and B, respectively), mean baseline 25-OH-D level \geq or < 20 ng/ml (panels C and D, respectively), supplementation duration \geq 12 weeks (panel E), and participants without T2D (panel F). Meta-analysis was not performed for subgroups consisting of 2 or fewer studies. The gray boxes correspond with study precision, lines denote 95%

CI, MD, mean difference; IU, International Units; 25-OH-D, 25-hydroxyvitamin D; T2D, Type 2 Diabetes; hsCRP, high-sensitivity C-reactive protein.