Supplemental Materials

Effects of Oral Vitamin D Supplementation on Vitamin D Levels and Glycemic Parameters in Patients with Type 2 Diabetes Mellitus: A Systematic Review and Network Meta-analysis

Contents

Supplementary Method S1. Details of the literature search strategy

Data base: PubMed

Number of studies: 163

1. (Diabetes Mellitus, Type 2 [Mesh])OR (Diabetes Mellitus, Adult-Onset[Title/Abstract]) OR (Adult-Onset Diabetes Mellitus[Title/Abstract]) OR (Diabetes Mellitus, Adult Onset[Title/Abstract]) OR (Diabetes Mellitus, Ketosis-Resistant[Title/Abstract]) OR (Diabetes Mellitus, Ketosis Resistant[Title/Abstract]) OR (Ketosis-Resistant Diabetes Mellitus[Title/Abstract]) OR (Diabetes Mellitus, Non Insulin Dependent[Title/Abstract]) OR (Diabetes Mellitus, Non-Insulin-Dependent[Title/Abstract]) OR (Non-Insulin-Dependent Diabetes Mellitus[Title/Abstract]) OR (Diabetes Mellitus, Stable[Title/Abstract]) OR (Stable Diabetes Mellitus[Title/Abstract]) OR (Diabetes Mellitus, Type II [Title/Abstract]) OR (NIDDM[Title/Abstract])OR (Diabetes Mellitus, Noninsulin Dependent [Title/Abstract]) OR (Diabetes Mellitus, Maturity-Onset[Title/Abstract]) OR (Diabetes Mellitus, Maturity Onset[Title/Abstract]) OR (Maturity-Onset Diabetes Mellitus[Title/Abstract]) OR (Maturity Onset Diabetes Mellitus[Title/Abstract]) OR (MODY[Title/Abstract]) OR (Diabetes Mellitus, Slow-Onset[Title/Abstract]) OR (Diabetes Mellitus, Slow Onset[Title/Abstract]) OR (Slow-Onset Diabetes Mellitus[Title/Abstract]) OR (Type 2 Diabetes Mellitus[Title/Abstract]) OR (Noninsulin-Dependent Diabetes Mellitus[Title/Abstract]) OR (Noninsulin Dependent Diabetes Mellitus[Title/Abstract]) OR (Maturity-Onset Diabetes[Title/Abstract]) OR (Diabetes, Maturity-Onset[Title/Abstract])OR (Maturity Onset Diabetes[Title/Abstract])OR (Type 2 Diabetes[Title/Abstract])OR (Diabetes, Type 2[Title/Abstract]) OR (Diabetes Mellitus, Noninsulin-Dependent)

2. Search: (Vitamin D[Mesh]) OR (Cholecalciferol[Mesh]) OR (Vitamin D 3[Title/Abstract]) OR (Vitamin D3[Title/Abstract]) OR ((3 beta,5Z,7E)-9,10-Secocholesta-5,7,10(19)-trien-3-ol[Title/Abstract]) OR (Calciol[Title/Abstract]) OR (Cholecalciferols[Title/Abstract])OR (Ergocalciferols[Mesh]) OR (Calciferols[Title/Abstract])OR (Vitamin D 2[Title/Abstract])OR (Ergocalciferol[Title/Abstract])OR (Vitamin D2[Title/Abstract])OR (D2, Vitamin[Title/Abstract])

3. (Randomized Controlled Trials as Topic[MeSH Terms]) OR (Randomized Controlled Trial[Publication Type]) OR (Random Allocation[MeSH Terms])

4. #1 AND #2 AND #3

Database: Embase

Number of studies: 1357

1. 'diabetes mellitus, type 2'/exp OR 'diabetes mellitus, type 2' OR 'diabetes mellitus, adult-onszet' OR 'adult-onset diabetes mellitus'/exp OR 'adult-onset diabetes mellitus' OR 'diabetes mellitus, adult onset' OR 'diabetes mellitus, ketosis-resistant' OR 'diabetes mellitus, ketosis resistant' OR 'ketosis-resistant diabetes mellitus'/exp OR 'ketosis-resistant diabetes mellitus' OR 'diabetes mellitus, non insulin dependent'/exp OR 'diabetes mellitus, non insulin dependent' OR 'diabetes mellitus, non-insulin-dependent'/exp OR 'diabetes mellitus, non-insulin-dependent' OR 'non-insulin-dependent diabetes mellitus'/exp OR 'non-insulin-dependent diabetes mellitus' OR 'diabetes mellitus, stable' OR '(stable diabetes mellitus' OR 'diabetes mellitus, type ii'/exp OR 'diabetes mellitus, type ii' OR 'niddm'/exp OR 'niddm' OR 'diabetes mellitus, noninsulin dependent' OR 'diabetes mellitus, maturity-onset'/exp OR 'diabetes mellitus, maturity-onset' OR 'diabetes mellitus, maturity onse' OR '(maturity-onset diabetes mellitus'/exp OR '(maturity-onset diabetes mellitus' OR 'maturity onset

diabetes mellitus'/exp OR 'maturity onset diabetes mellitus' OR 'mody' OR 'diabetes mellitus, slow-onset' OR 'diabetes mellitus, slow onset' OR 'slow-onset diabetes mellitus' OR 'type 2 diabetes mellitus'/exp OR 'type 2 diabetes mellitus' OR 'noninsulin-dependent diabetes mellitus'/exp OR 'noninsulin-dependent diabetes mellitus' OR 'noninsulin dependent diabetes mellitus'/exp OR 'noninsulin dependent diabetes mellitus' OR 'maturity-onset diabetes'/exp OR 'maturity-onset diabetes' OR 'diabetes, maturity-onset' OR 'maturity onset diabetes'/exp OR 'maturity onset diabetes' OR 'type 2 diabetes'/exp OR 'type 2 diabetes' OR 'diabetes, type 2'/exp OR 'diabetes, type 2' OR 'diabetes mellitus, noninsulin-dependent'

2. 'vitamin d' OR 'cholecalciferol' OR 'vitamin d 3' OR 'vitamin d3' OR '(3 beta,5z,7e)-9,10-secocholesta-5,7,10(19)-trien-3-ol' OR 'calciol' OR 'cholecalciferols' OR 'ergocalciferols' OR 'calciferols' OR 'vitamin d 2' OR 'ergocalciferol' OR 'vitamin d2' OR 'd2, vitamin'

3. 'randomized controlled trial*' OR 'clinical trial*' OR 'rct' OR 'clinical research*':ab,ti

4. #1 AND #2 AND #3

Database: Cochrane Library
Number of studies: 613

1. ("Diabetes Mellitus, Type 2" OR "Diabetes Mellitus, Adult-Onset" OR "Adult-Onset Diabetes Mellitus" OR "Diabetes Mellitus, Adult Onset" OR "Diabetes Mellitus, Ketosis-Resistant" OR "Diabetes Mellitus, Ketosis Resistant" OR "Ketosis-Resistant Diabetes Mellitus" OR "Diabetes Mellitus, Non Insulin Dependent" OR "Diabetes Mellitus, Non-Insulin-Dependent" OR "Non-Insulin-Dependent Diabetes Mellitus" OR "Diabetes Mellitus, Stable" OR "Stable Diabetes Mellitus" OR "Diabetes Mellitus, Type II" OR "NIDDM" OR "Diabetes Mellitus, Noninsulin Dependent" OR "Diabetes Mellitus, Maturity-Onset" OR "Diabetes Mellitus, Maturity Onset" OR "Maturity-Onset Diabetes Mellitus" OR "Maturity Onset Diabetes Mellitus" OR "MODY" OR "Diabetes Mellitus, Slow-Onset" OR "Diabetes Mellitus, Slow Onset" OR "Slow-Onset Diabetes Mellitus" OR "Type 2 Diabetes Mellitus" OR "Noninsulin-Dependent Diabetes Mellitus" OR "Noninsulin Dependent Diabetes Mellitus" OR "Maturity-Onset Diabetes" OR "Diabetes, Maturity-Onset" OR "Maturity Onset Diabetes" OR "Type 2 Diabetes" OR "Diabetes, Type 2" OR "Diabetes Mellitus, Noninsulin-Dependent"):ti,ab,kw

2. ("Vitamin D" OR "Cholecalciferol" OR "Vitamin D 3" OR "Vitamin D3" OR "(3 beta,5Z,7E)-9,10-Secocholesta-5,7,10(19)-trien-3-ol" OR "Calciol" OR "Cholecalciferols" OR "Ergocalciferols" OR "Calciferols" OR "Vitamin D 2" OR "Ergocalciferol" OR "Vitamin D2" OR "D2, Vitamin"):ti,ab,kw

3. (Randomized Controlled Trial) OR (randomized) OR (Random Allocation)

4. #1 and #2 and #3 in Trials

Database: Web of science
Number of studies: 807

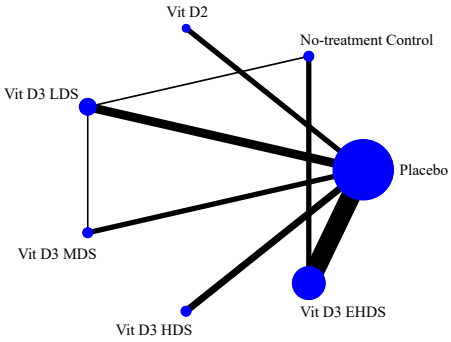
1. TS=("Diabetes Mellitus, Type 2" OR "Diabetes Mellitus, Adult-Onset" OR "Adult-Onset Diabetes Mellitus" OR "Diabetes Mellitus, Adult Onset" OR "Diabetes Mellitus, Ketosis-Resistant" OR "Diabetes Mellitus, Ketosis Resistant" OR "Ketosis-Resistant Diabetes Mellitus" OR "Diabetes Mellitus, Non Insulin Dependent" OR "Diabetes Mellitus, Non-Insulin-Dependent" OR "Non-Insulin-Dependent Diabetes Mellitus" OR "Diabetes Mellitus, Stable" OR "Stable Diabetes Mellitus" OR "Diabetes Mellitus, Type II" OR "NIDDM" OR "Diabetes Mellitus, Noninsulin

Dependent" OR "Diabetes Mellitus, Maturity-Onset" OR "Diabetes Mellitus, Maturity Onset" OR "Maturity-Onset Diabetes Mellitus" OR "Maturity Onset Diabetes Mellitus" OR "MODY" OR "Diabetes Mellitus, Slow-Onset" OR "Diabetes Mellitus, Slow Onset" OR "Slow-Onset Diabetes Mellitus" OR "Type 2 Diabetes Mellitus" OR "Noninsulin-Dependent Diabetes Mellitus" OR "Noninsulin Dependent Diabetes Mellitus" OR "Maturity-Onset Diabetes" OR "Diabetes, Maturity-Onset" OR "Maturity Onset Diabetes" OR "Type 2 Diabetes" OR "Diabetes, Type 2" OR "Diabetes Mellitus, Noninsulin-Dependent") and Preprint Citation Index (Exclude – Database)

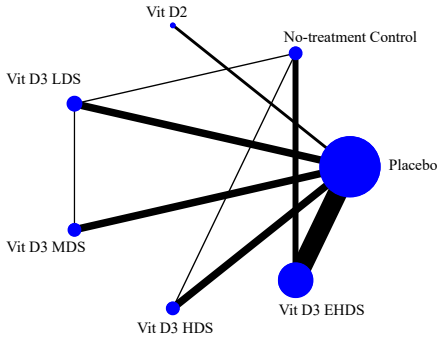
2. TS=("Vitamin D" OR "Cholecalciferol" OR "Vitamin D 3" OR "Vitamin D3" OR "(3 beta,5Z,7E)-9,10-Secocholesta-5,7,10(19)-trien-3-ol" OR "Calciol" OR "Cholecalciferols" OR "Ergocalciferols" OR "Calciferols" OR "Vitamin D 2" OR "Ergocalciferol" OR "Vitamin D2" OR "D2, Vitamin") and Preprint Citation Index (Exclude – Database)

3. TS= (“randomized control* trial*” OR “clinical trial*” OR “RCT” OR“clinical research*”) and Preprint Citation Index (Exclude – Database)

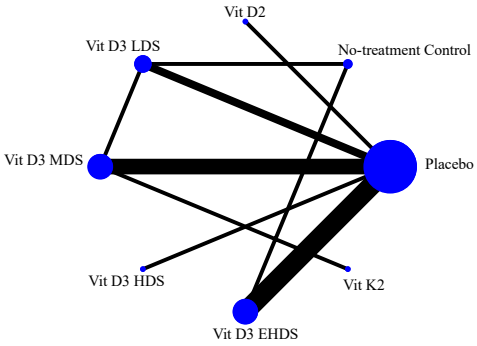
4. #1 AND #2 AND #3 and Preprint Citation Index (Exclude – Database)



25-(OH)-D



HbA1c



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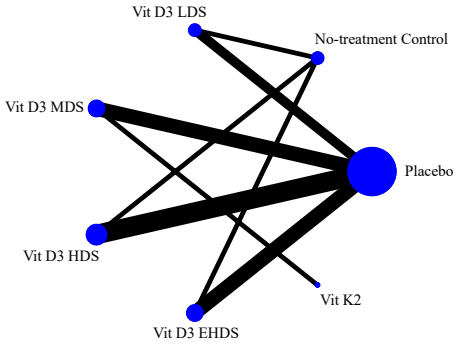
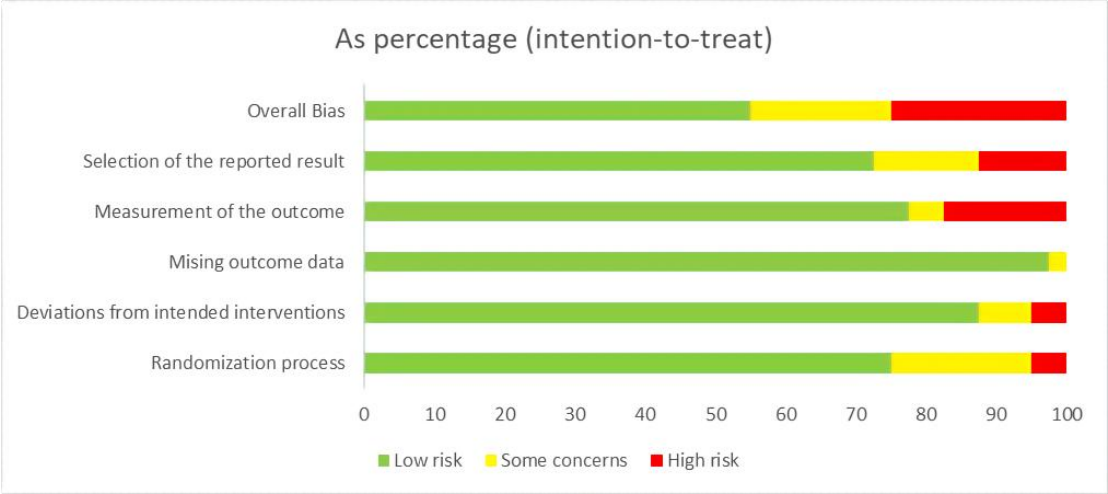
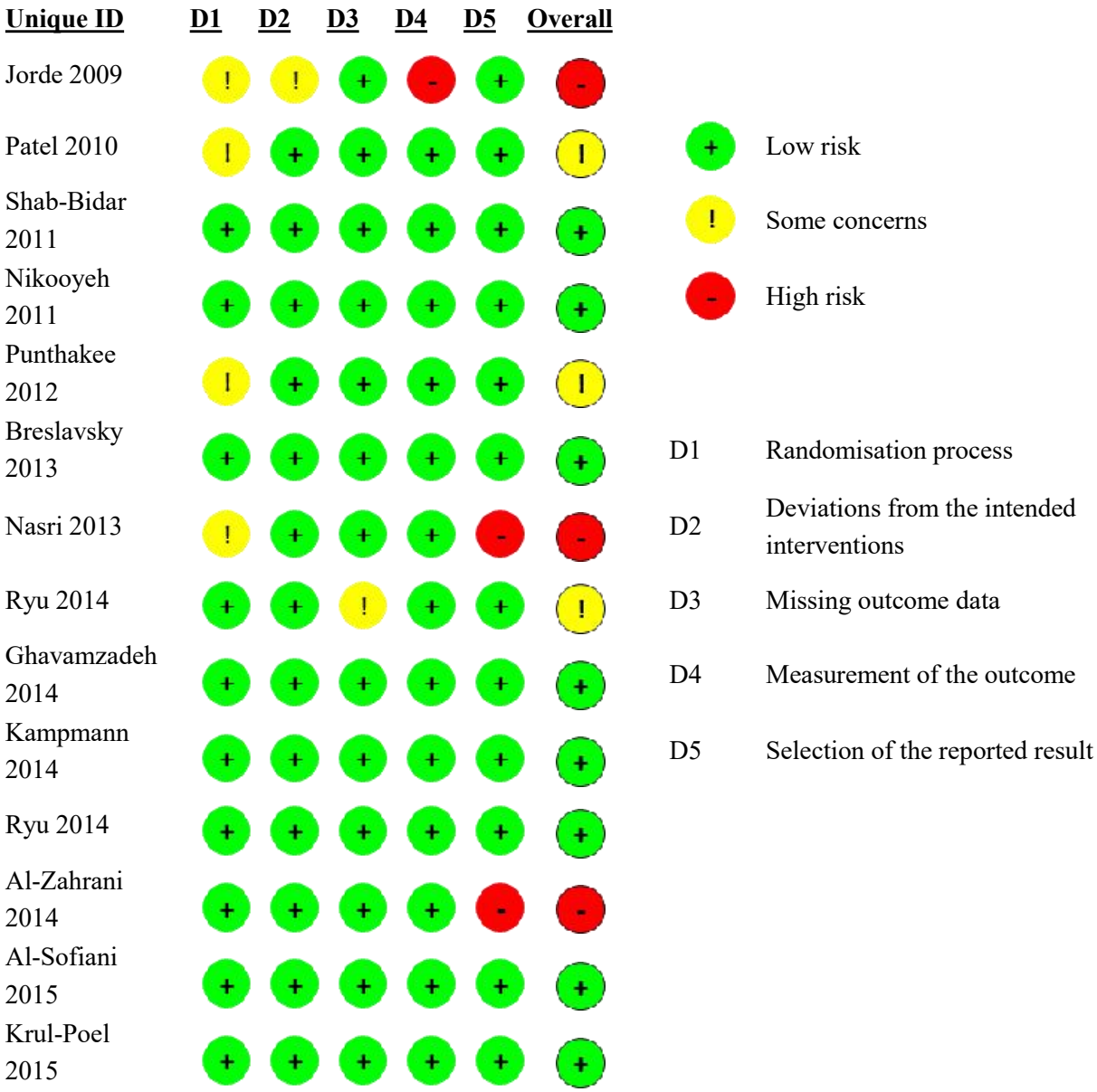
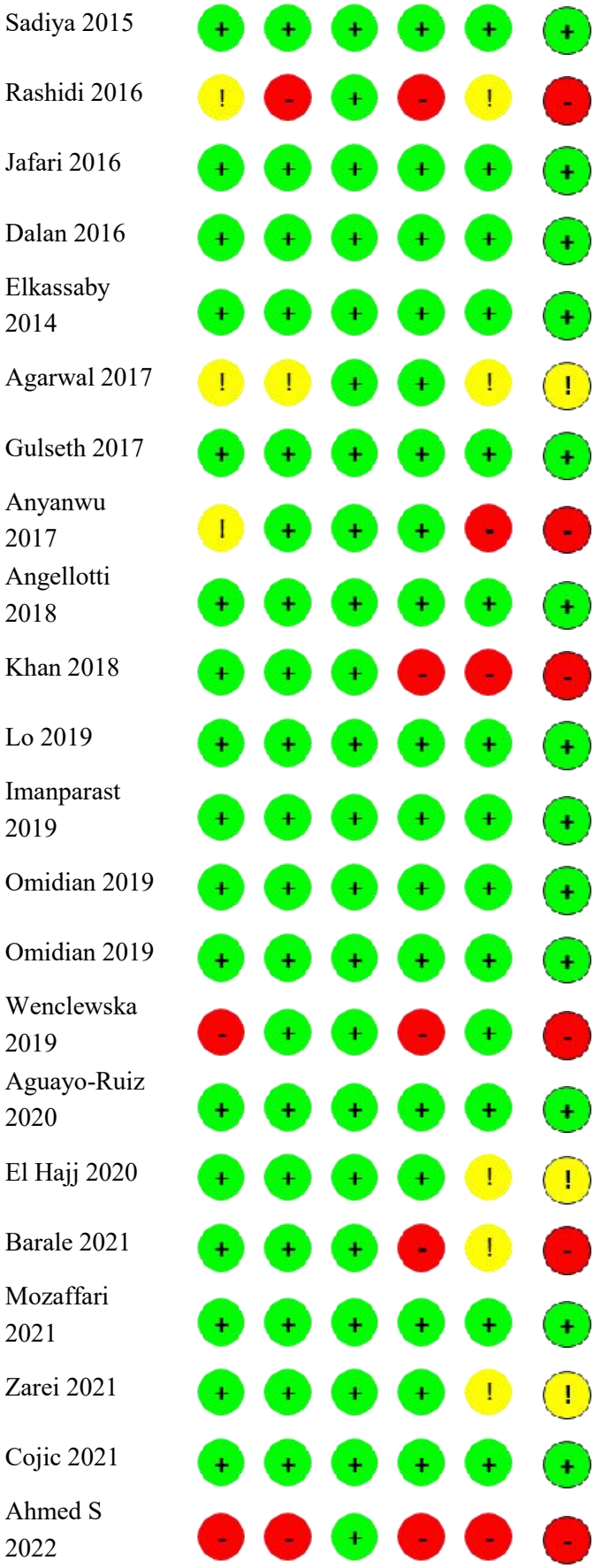


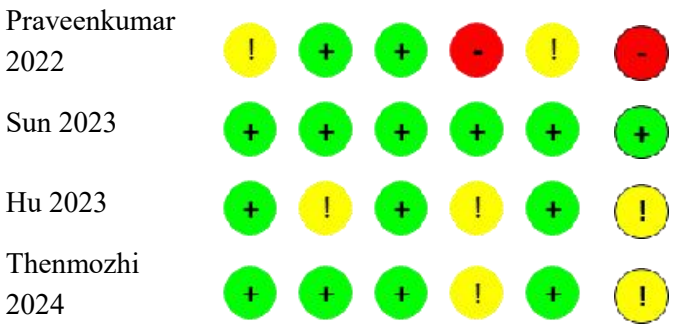
HOMA-IR

Supplementary Figure S1. Evidence plots 25-(OH)-D, HbA1c, FIN, and HOMA-IR. LDS, low dose strategy; MDS, medium dose strategy; HDS, high dose strategy; EHDS, extremely high dose strategy; 25-(OH)-D, 25-hydroxyvitamin D; HbA1c, hemoglobin A1c; FIN, fasting insulin; HOMA-IR, homeostasis model assessment-insulin

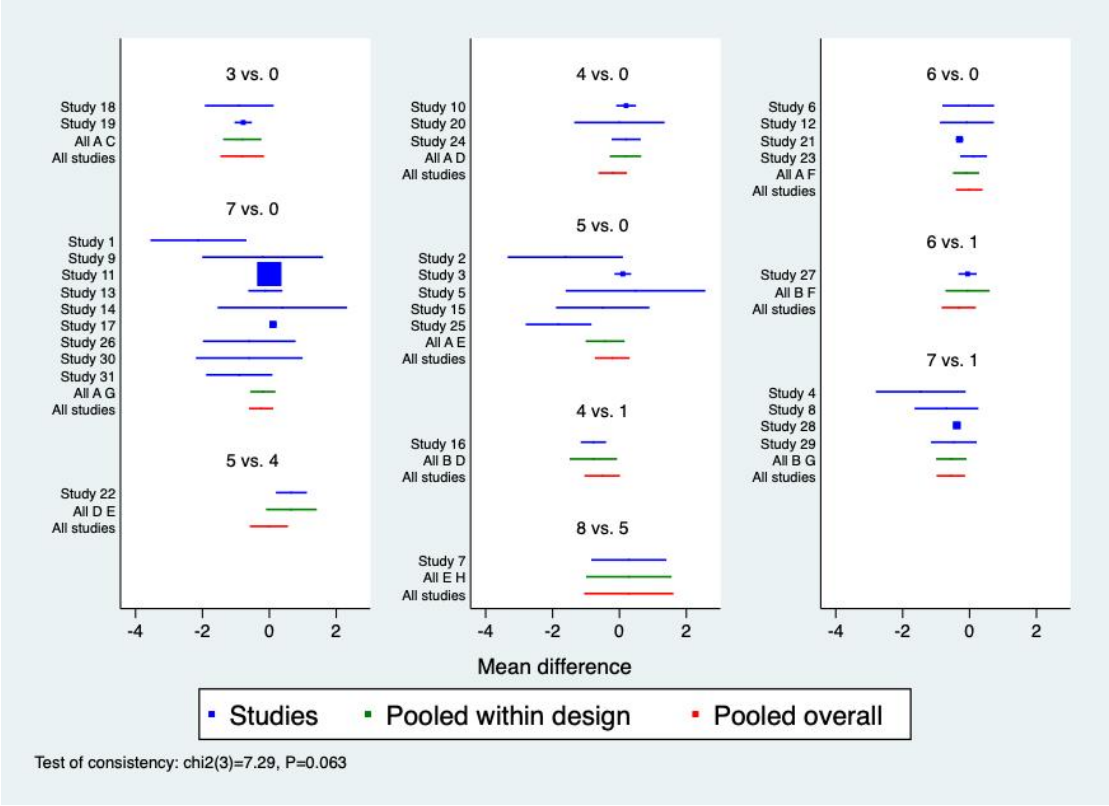

As percentage (intention-to-treat)
Overall Bias
Selection of the reported result
Measurement of the outcome
Mising outcome data
Deviations from intended interventions
Randomization process
0
10
20
30
40
50
60
70
80
90
100
Low risk
Some concerns
High risk


Unique ID
D1
D2
D3
D4
D5
Overall
Jorde 2009
Patel 2010
Shab-Bidar 2011
Nikooyeh 2011
Punthakee 2012
Breslavsky 2013
Nasri 2013
Ryu 2014
Ghavamzadeh 2014
Kampmann 2014
Ryu 2014
Al-Zahrani 2014
Al-Sofiani 2015
Krul-Poel 2015
Low risk
Some concerns
High risk
D1 Randomisation process
D2 Deviations from the intended interventions
D3 Missing outcome data
D4 Measurement of the outcome
D5 Selection of the reported result

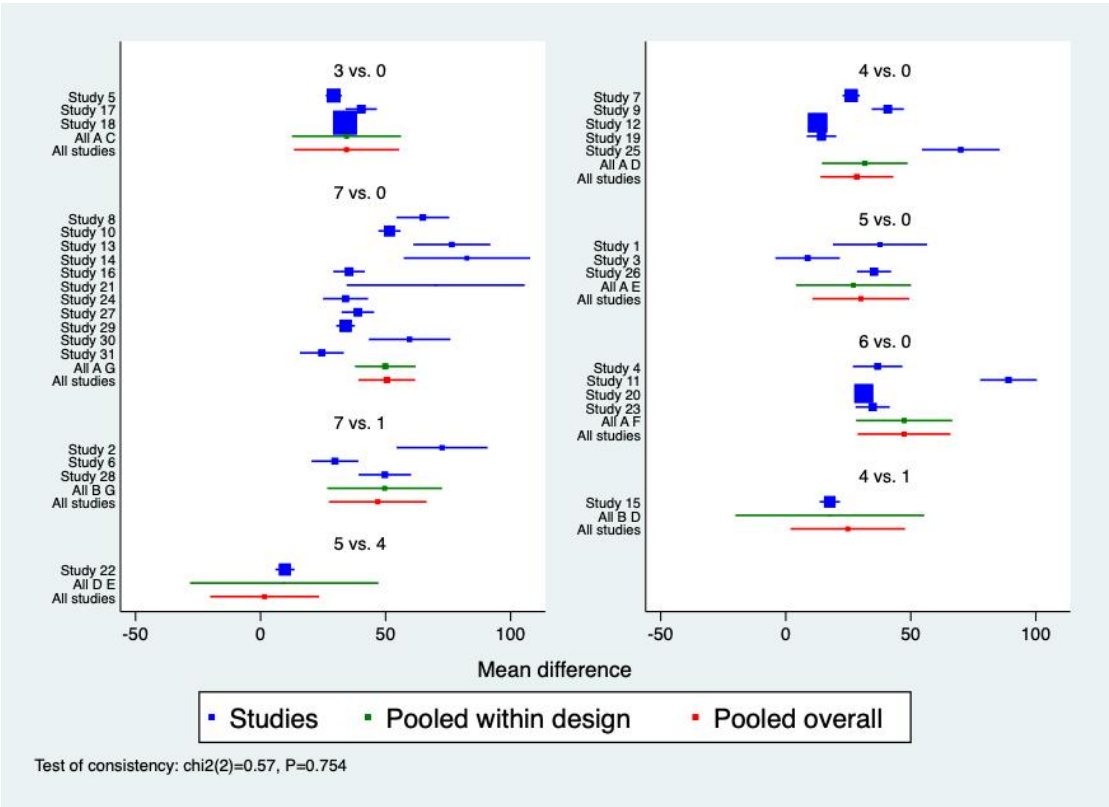

Sadiya 2015
Rashidi 2016
Jafari 2016
Dalan 2016
Elkassaby 2014
Agarwal 2017
Gulseth 2017
Anyanwu 2017
Angellotti 2018
Khan 2018
Lo 2019
Imanparast 2019
Omidian 2019
Omidian 2019
Wenclewska 2019
Aguayo-Ruiz 2020
El Hajj 2020
Barale 2021
Mozaffari 2021
Zarei 2021
Cojic 2021
Ahmed S 2022



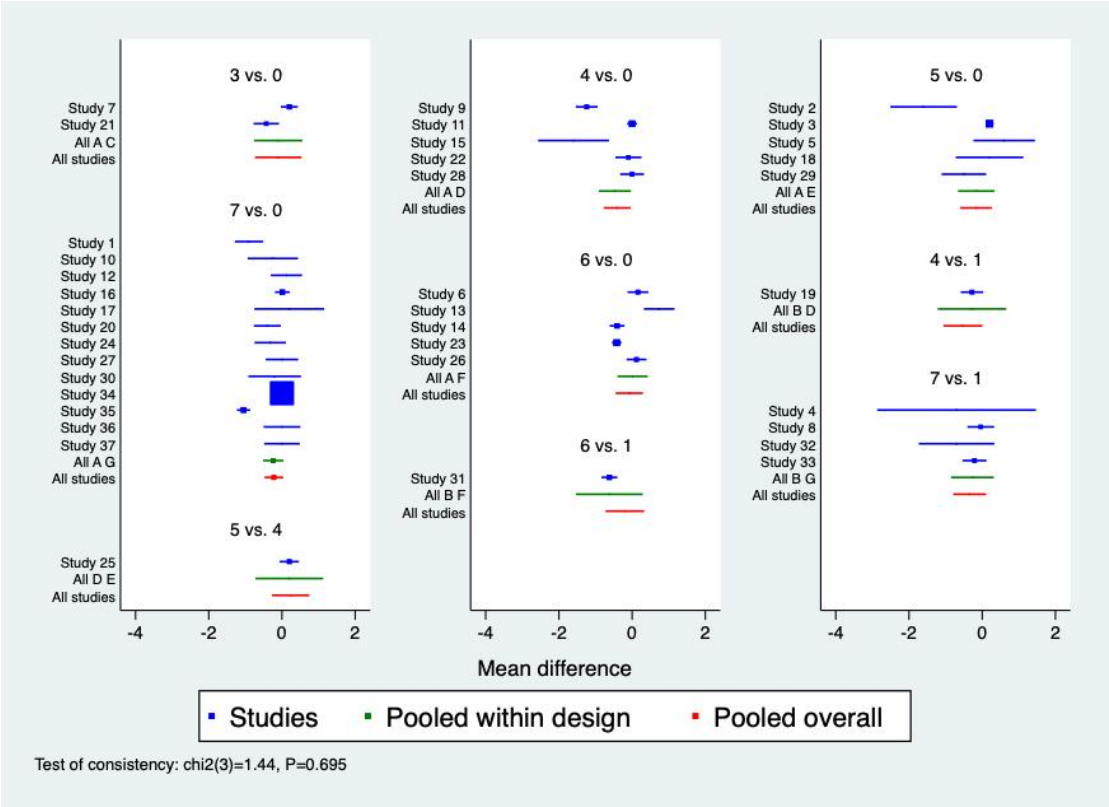
Supplementary Figure S2. Results of bias assessment of included studies.


3 vs. 0
Study 18
Study 19
All A C
All studies
7 vs. 0
Study 1
Study 9
Study 11
Study 13
Study 14
Study 17
Study 26
Study 30
Study 31
All A G
All studies
5 vs. 4
Study 22
All D E
All studies
4 vs. 0
Study 10
Study 20
Study 24
All A D
All studies
5 vs. 0
Study 2
Study 3
Study 5
Study 15
Study 25
All A E
All studies
4 vs. 1
Study 16
All B D
All studies
8 vs. 5
Study 7
All E H
All studies
6 vs. 0
Study 6
Study 12
Study 21
Study 23
All A F
All studies
6 vs. 1
Study 27
All B F
All studies
7 vs. 1
Study 4
Study 8
Study 28
Study 29
All B G
All studies
-4
-2
0
2
Mean difference
Studies
Pooled within design
Pooled overall
Test of consistency: chi2(3)=7.29, P=0.063

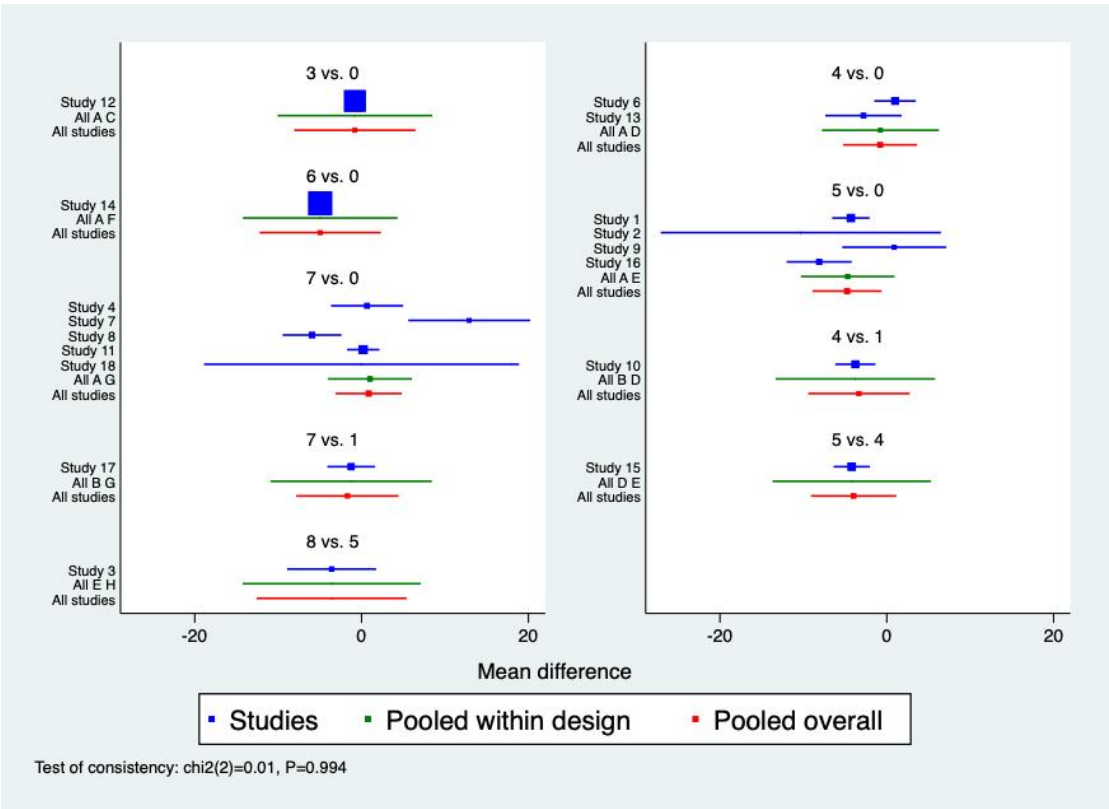
FBG


3 vs. 0
Study 5
Study 17
Study 18
All A C
All studies
7 vs. 0
Study 8
Study 10
Study 13
Study 14
Study 16
Study 21
Study 24
Study 27
Study 29
Study 30
Study 31
All A G
All studies
7 vs. 1
Study 2
Study 6
Study 28
All B G
All studies
5 vs. 4
Study 22
All D E
All studies
4 vs. 0
Study 7
Study 9
Study 12
Study 19
Study 25
All A D
All studies
5 vs. 0
Study 1
Study 3
Study 26
All A E
All studies
6 vs. 0
Study 4
Study 11
Study 20
Study 23
All A F
All studies
4 vs. 1
Study 15
All B D
All studies
-50
0
50
100
Mean difference
Studies
Pooled within design
Pooled overall
Test of consistency: chi2(2)=0.57, P=0.754

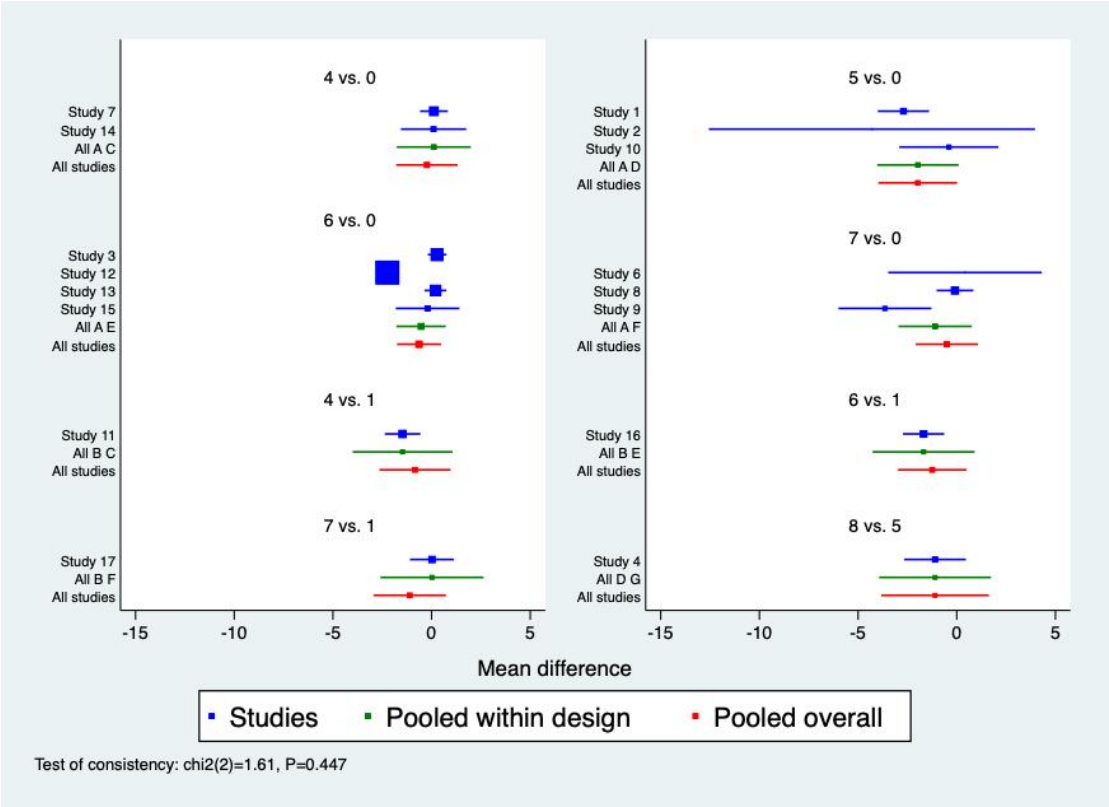
25-(OH)-D


3 vs. 0
Study 7
Study 21
All A C
All studies
7 vs. 0
Study 1
Study 10
Study 12
Study 16
Study 17
Study 20
Study 24
Study 27
Study 30
Study 34
Study 35
Study 36
Study 37
All A G
All studies
5 vs. 4
Study 25
All D E
All studies
4 vs. 0
Study 9
Study 11
Study 15
Study 22
Study 28
All A D
All studies
6 vs. 0
Study 6
Study 13
Study 14
Study 23
Study 26
All A F
All studies
6 vs. 1
Study 31
All B F
All studies
5 vs. 0
Study 2
Study 3
Study 5
Study 18
Study 29
All A E
All studies
4 vs. 1
Study 19
All B D
All studies
7 vs. 1
Study 4
Study 8
Study 32
Study 33
All B G
All studies
-4
-2
0
2
Mean difference
Studies
Pooled within design
Pooled overall
Test of consistency: chi2(3)=1.44, P=0.695

HbA1c

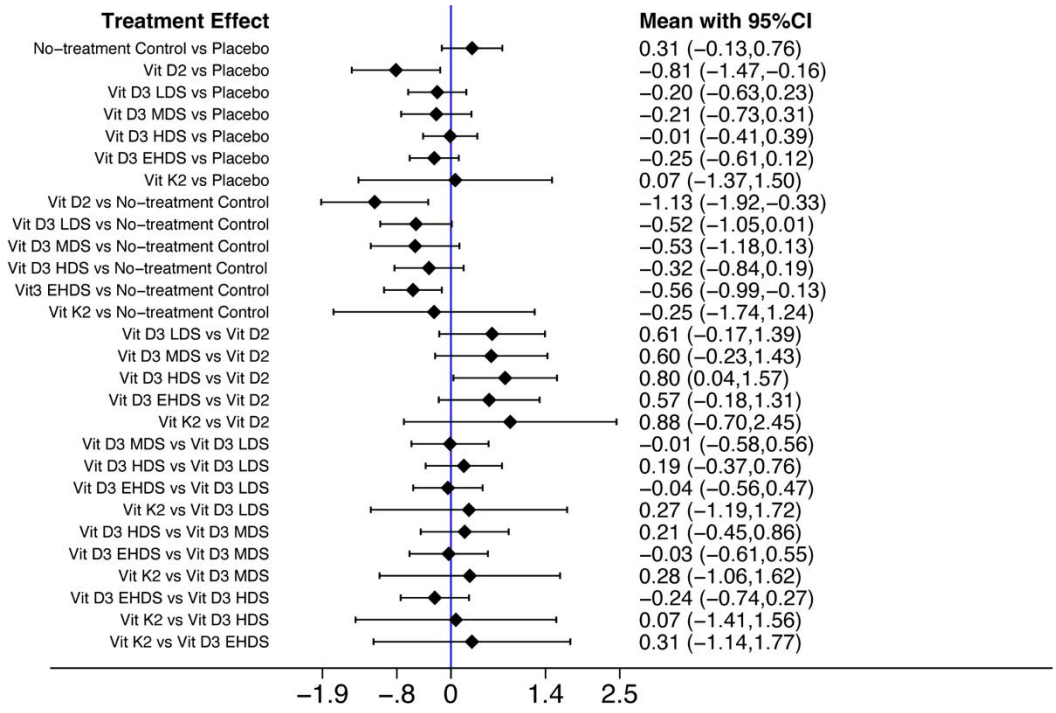

3 vs. 0
Study 12
All A C
All studies
6 vs. 0
Study 14
All A F
All studies
7 vs. 0
Study 4
Study 7
Study 8
Study 11
Study 18
All A G
All studies
7 vs. 1
Study 17
All B G
All studies
8 vs. 5
Study 3
All E H
All studies
4 vs. 0
Study 6
Study 13
All A D
All studies
5 vs. 0
Study 1
Study 2
Study 9
Study 16
All A E
All studies
4 vs. 1
Study 10
All B D
All studies
5 vs. 4
Study 15
All D E
All studies
-20
0
20
Mean difference
Studies
Pooled within design
Pooled overall
Test of consistency: chi2(2)=0.01, P=0.994

FIN

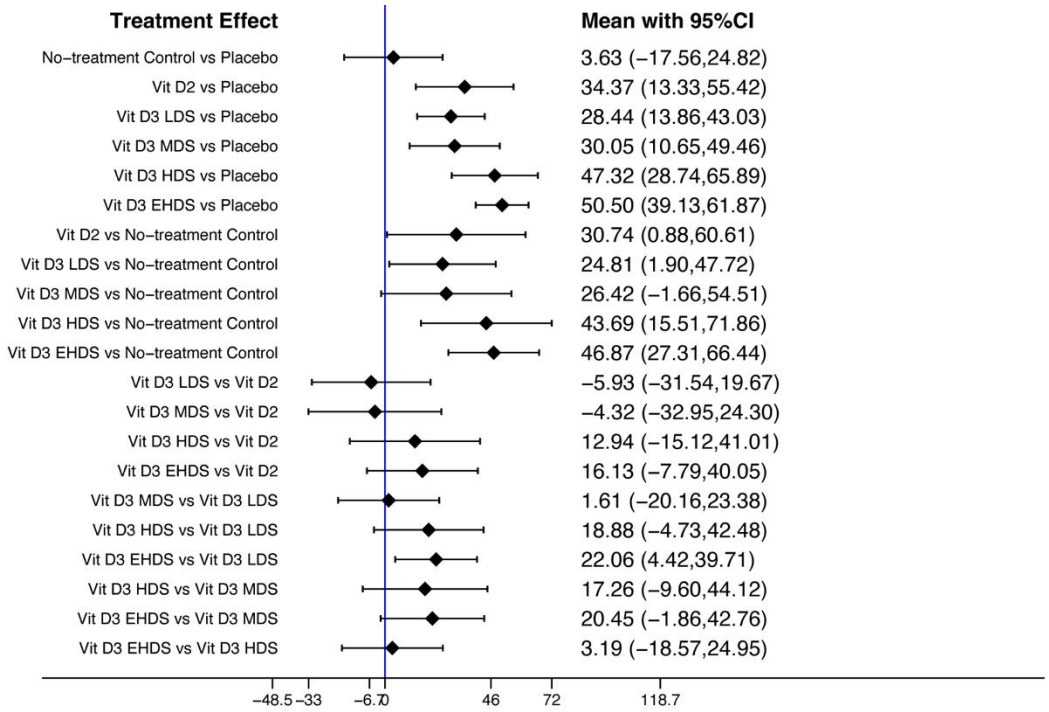


HOMA-IR

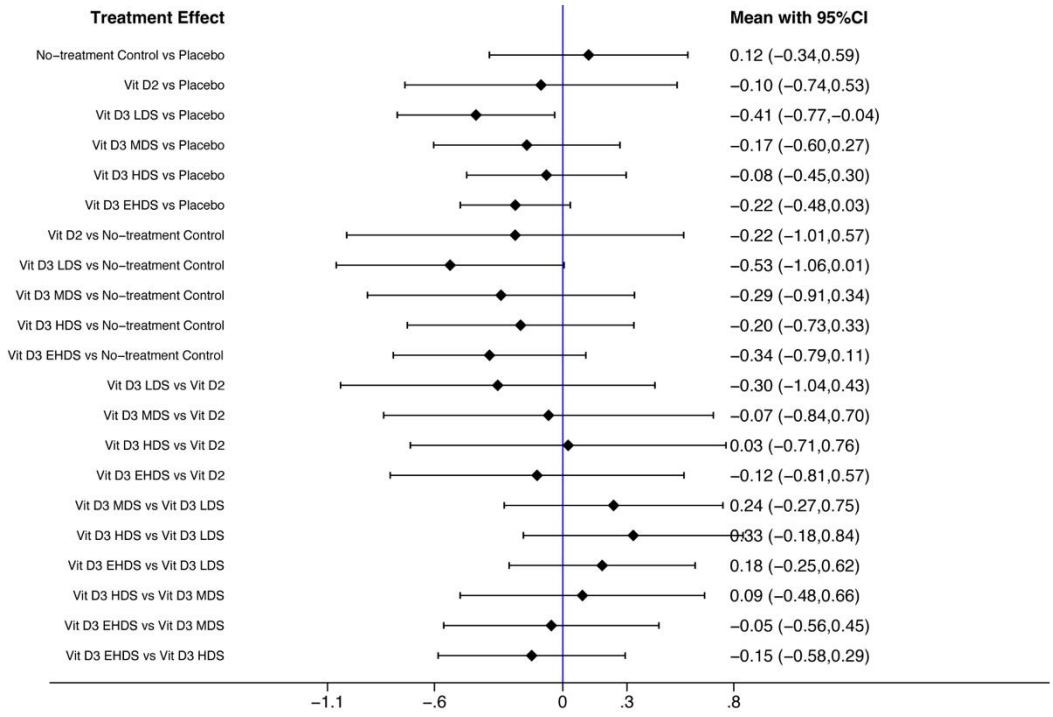
Supplementary Figure S3. Global consistency model test for FBG, 25-(OH)-D, HbA1c, FIN, and HOMA-IR. LDS, low dose strategy; MDS, medium dose strategy; HDS, high dose strategy; EHDS, extremely high dose strategy; FBG, fasting blood glucose; 25-(OH)-D, 25-hydroxyvitamin D; HbA1c, hemoglobin A1c; FIN, fasting insulin; HOMA-IR, homeostasis model assessment-insulin


Treatment Effect
Mean with 95%CI
No−treatment Control vs Placebo
0.31 (−0.13,0.76)
Vit D2 vs Placebo
−0.81 (−1.47,−0.16)
Vit D3 LDS vs Placebo
−0.20 (−0.63,0.23)
Vit D3 MDS vs Placebo
−0.21 (−0.73,0.31)
Vit D3 HDS vs Placebo
−0.01 (−0.41,0.39)
Vit D3 EHDS vs Placebo
−0.25 (−0.61,0.12)
Vit K2 vs Placebo
0.07 (−1.37,1.50)
Vit D2 vs No−treatment Control
−1.13 (−1.92,−0.33)
Vit D3 LDS vs No−treatment Control
−0.52 (−1.05,0.01)
Vit D3 MDS vs No−treatment Control
−0.53 (−1.18,0.13)
Vit D3 HDS vs No−treatment Control
−0.32 (−0.84,0.19)
Vit3 EHDS vs No−treatment Control
−0.56 (−0.99,−0.13)
Vit K2 vs No−treatment Control
−0.25 (−1.74,1.24)
Vit D3 LDS vs Vit D2
0.61 (−0.17,1.39)
Vit D3 MDS vs Vit D2
0.60 (−0.23,1.43)
Vit D3 HDS vs Vit D2
0.80 (0.04,1.57)
Vit D3 EHDS vs Vit D2
0.57 (−0.18,1.31)
Vit K2 vs Vit D2
0.88 (−0.70,2.45)
Vit D3 MDS vs Vit D3 LDS
−0.01 (−0.58,0.56)
Vit D3 HDS vs Vit D3 LDS
0.19 (−0.37,0.76)
Vit D3 EHDS vs Vit D3 LDS
−0.04 (−0.56,0.47)
Vit K2 vs Vit D3 LDS
0.27 (−1.19,1.72)
Vit D3 HDS vs Vit D3 MDS
0.21 (−0.45,0.86)
Vit D3 EHDS vs Vit D3 MDS
−0.03 (−0.61,0.55)
Vit K2 vs Vit D3 MDS
0.28 (−1.06,1.62)
Vit D3 EHDS vs Vit D3 HDS
−0.24 (−0.74,0.27)
Vit K2 vs Vit D3 HDS
0.07 (−1.41,1.56)
Vit K2 vs Vit D3 EHDS
0.31 (−1.14,1.77)
−1.9
−.8
0
1.4
2.5

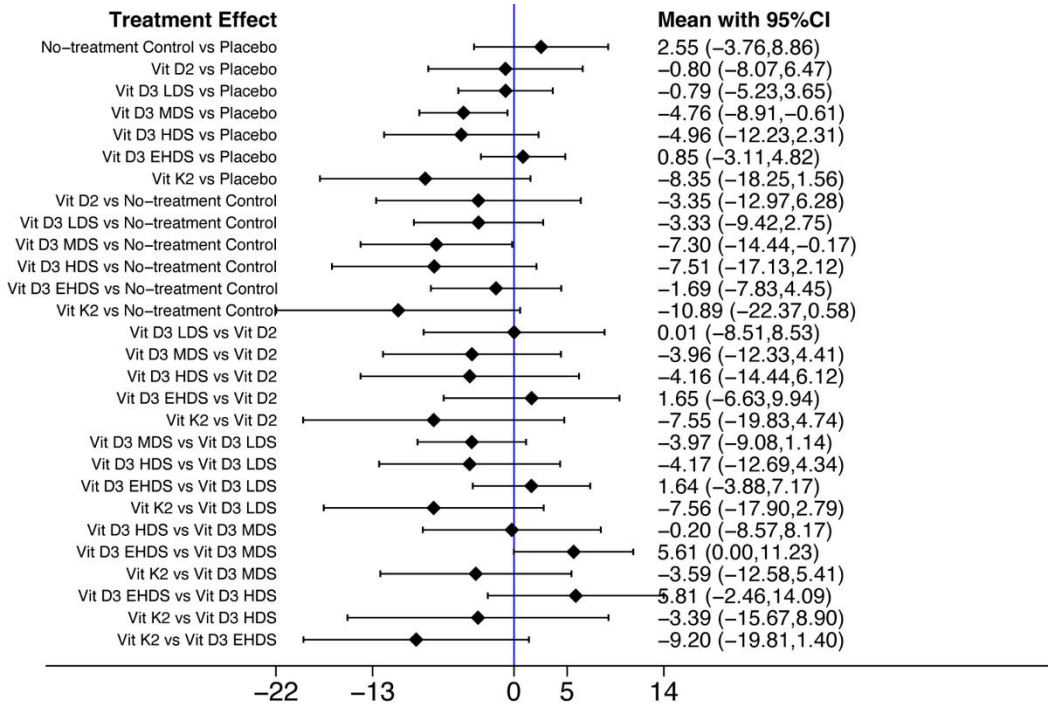
FBG


Treatment Effect
Mean with 95%CI
No−treatment Control vs Placebo
3.63 (−17.56,24.82)
Vit D2 vs Placebo
34.37 (13.33,55.42)
Vit D3 LDS vs Placebo
28.44 (13.86,43.03)
Vit D3 MDS vs Placebo
30.05 (10.65,49.46)
Vit D3 HDS vs Placebo
47.32 (28.74,65.89)
Vit D3 EHDS vs Placebo
50.50 (39.13,61.87)
Vit D2 vs No−treatment Control
30.74 (0.88,60.61)
Vit D3 LDS vs No−treatment Control
24.81 (1.90,47.72)
Vit D3 MDS vs No−treatment Control
26.42 (−1.66,54.51)
Vit D3 HDS vs No−treatment Control
43.69 (15.51,71.86)
Vit D3 EHDS vs No−treatment Control
46.87 (27.31,66.44)
Vit D3 LDS vs Vit D2
−5.93 (−31.54,19.67)
Vit D3 MDS vs Vit D2
−4.32 (−32.95,24.30)
Vit D3 HDS vs Vit D2
12.94 (−15.12,41.01)
Vit D3 EHDS vs Vit D2
16.13 (−7.79,40.05)
Vit D3 MDS vs Vit D3 LDS
1.61 (−20.16,23.38)
Vit D3 HDS vs Vit D3 LDS
18.88 (−4.73,42.48)
Vit D3 EHDS vs Vit D3 LDS
22.06 (4.42,39.71)
Vit D3 HDS vs Vit D3 MDS
17.26 (−9.60,44.12)
Vit D3 EHDS vs Vit D3 MDS
20.45 (−1.86,42.76)
Vit D3 EHDS vs Vit D3 HDS
3.19 (−18.57,24.95)
−48.5
−33
−6.7
0
46
72
118.7

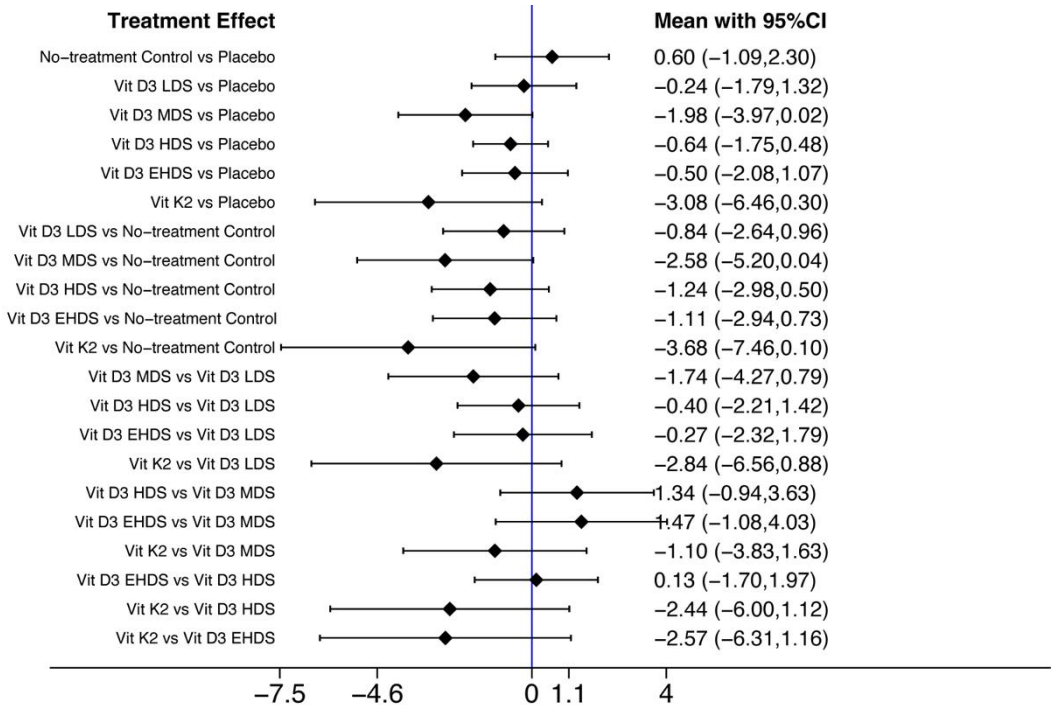
25-(OH)-D


Treatment Effect
Mean with 95%CI
No−treatment Control vs Placebo
0.12 (−0.34,0.59)
Vit D2 vs Placebo
−0.10 (−0.74,0.53)
Vit D3 LDS vs Placebo
−0.41 (−0.77,−0.04)
Vit D3 MDS vs Placebo
−0.17 (−0.60,0.27)
Vit D3 HDS vs Placebo
−0.08 (−0.45,0.30)
Vit D3 EHDS vs Placebo
−0.22 (−0.48,0.03)
Vit D2 vs No−treatment Control
−0.22 (−1.01,0.57)
Vit D3 LDS vs No−treatment Control
−0.53 (−1.06,0.01)
Vit D3 MDS vs No−treatment Control
−0.29 (−0.91,0.34)
Vit D3 HDS vs No−treatment Control
−0.20 (−0.73,0.33)
Vit D3 EHDS vs No−treatment Control
−0.34 (−0.79,0.11)
Vit D3 LDS vs Vit D2
−0.30 (−1.04,0.43)
Vit D3 MDS vs Vit D2
−0.07 (−0.84,0.70)
Vit D3 HDS vs Vit D2
0.03 (−0.71,0.76)
Vit D3 EHDS vs Vit D2
−0.12 (−0.81,0.57)
Vit D3 MDS vs Vit D3 LDS
0.24 (−0.27,0.75)
Vit D3 HDS vs Vit D3 LDS
0.33 (−0.18,0.84)
Vit D3 EHDS vs Vit D3 LDS
0.18 (−0.25,0.62)
Vit D3 HDS vs Vit D3 MDS
0.09 (−0.48,0.66)
Vit D3 EHDS vs Vit D3 MDS
−0.05 (−0.56,0.45)
Vit D3 EHDS vs Vit D3 HDS
−0.15 (−0.58,0.29)
−1.1
−.6
0
.3
.8

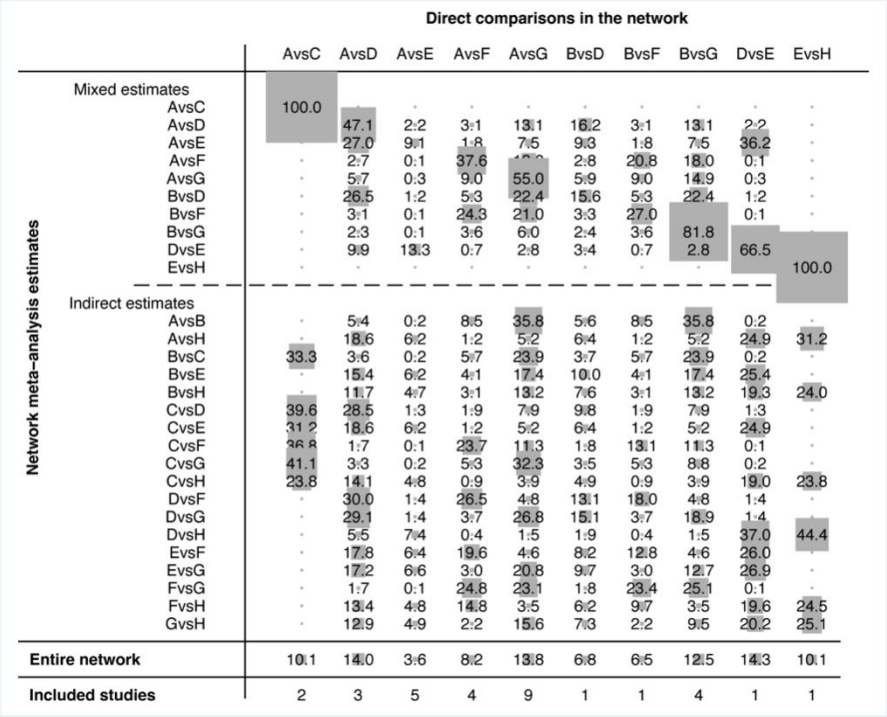
HbA1c


Treatment Effect
Mean with 95%CI
No−treatment Control vs Placebo
2.55 (−3.76,8.86)
Vit D2 vs Placebo
−0.80 (−8.07,6.47)
Vit D3 LDS vs Placebo
−0.79 (−5.23,3.65)
Vit D3 MDS vs Placebo
−4.76 (−8.91,−0.61)
Vit D3 HDS vs Placebo
−4.96 (−12.23,2.31)
Vit D3 EHDS vs Placebo
0.85 (−3.11,4.82)
Vit K2 vs Placebo
−8.35 (−18.25,1.56)
Vit D2 vs No−treatment Control
−3.35 (−12.97,6.28)
Vit D3 LDS vs No−treatment Control
−3.33 (−9.42,2.75)
Vit D3 MDS vs No−treatment Control
−7.30 (−14.44,−0.17)
Vit D3 HDS vs No−treatment Control
−7.51 (−17.13,2.12)
Vit D3 EHDS vs No−treatment Control
−1.69 (−7.83,4.45)
Vit K2 vs No−treatment Control
−10.89 (−22.37,0.58)
Vit D3 LDS vs Vit D2
0.01 (−8.51,8.53)
Vit D3 MDS vs Vit D2
−3.96 (−12.33,4.41)
Vit D3 HDS vs Vit D2
−4.16 (−14.44,6.12)
Vit D3 EHDS vs Vit D2
1.65 (−6.63,9.94)
Vit K2 vs Vit D2
−7.55 (−19.83,4.74)
Vit D3 MDS vs Vit D3 LDS
−3.97 (−9.08,1.14)
Vit D3 HDS vs Vit D3 LDS
−4.17 (−12.69,4.34)
Vit D3 EHDS vs Vit D3 LDS
1.64 (−3.88,7.17)
Vit K2 vs Vit D3 LDS
−7.56 (−17.90,2.79)
Vit D3 HDS vs Vit D3 MDS
−0.20 (−8.57,8.17)
Vit D3 EHDS vs Vit D3 MDS
5.61 (0.00,11.23)
Vit K2 vs Vit D3 MDS
−3.59 (−12.58,5.41)
Vit D3 EHDS vs Vit D3 HDS
5.81 (−2.46,14.09)
Vit K2 vs Vit D3 HDS
−3.39 (−15.67,8.90)
Vit K2 vs Vit D3 EHDS
−9.20 (−19.81,1.40)
−22
−13
0
5
14

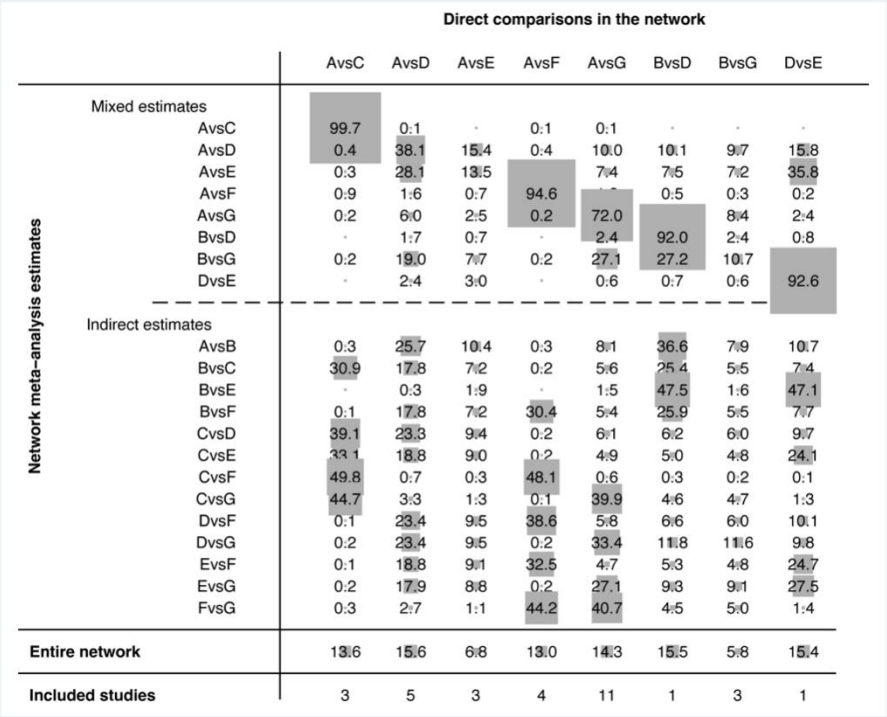
FIN



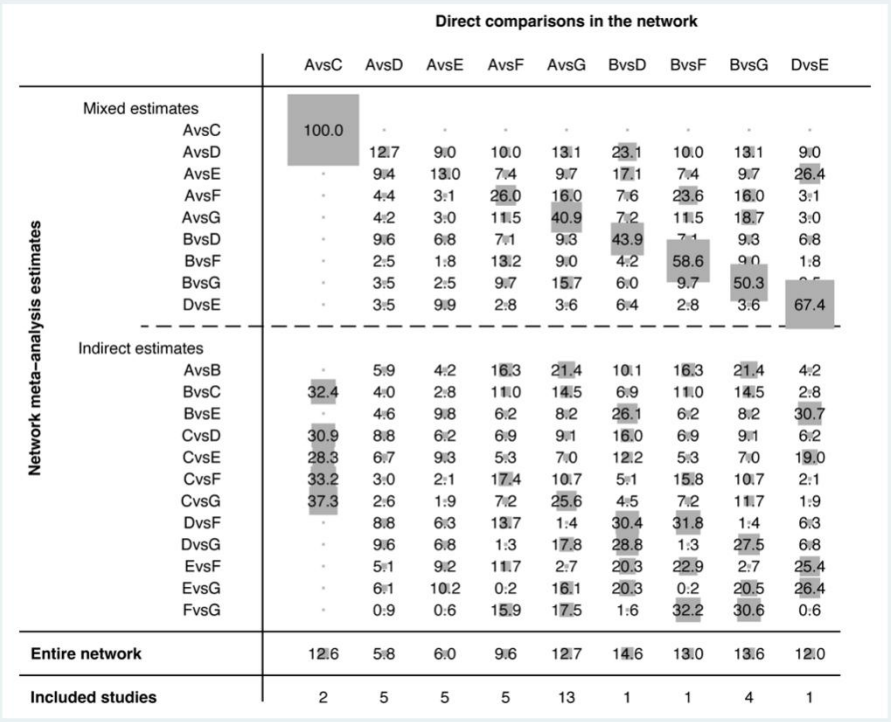
Supplementary Figure S4. Forest plot for FBG, 25-(OH)-D, HbA1c, FIN, and HOMA-IR. LDS, low dose strategy; MDS, medium dose strategy; HDS, high dose strategy; EHDS, extremely high dose strategy; FBG, fasting blood glucose; 25-(OH)-D, 25-hydroxyvitamin D; HbA1c, hemoglobin A1c; FIN, fasting insulin; HOMA-IR, homeostasis model assessment-insulin


Direct comparisons in the network
AvsC AvsD AvsE AvsF AvsG BvsD BvsF BvsG DvsE EvsH
Network meta−analysis estimates
Mixed estimates
AvsC 100.0
AvsD 47.1 2.2 3.1 13.1 16.2 3.1 13.1 2.2
AvsE 27.0 9.1 1.8 7.5 9.3 1.8 7.5 36.2
AvsF 2.7 0.1 37.6 2.8 20.8 18.0 0.1
AvsG 5.7 0.3 9.0 55.0 5.9 9.0 14.9 0.3
BvsD 26.5 1.2 5.3 22.4 15.6 5.3 22.4 1.2
BvsF 3.1 0.1 24.3 21.0 3.3 27.0 0.1
BvsG 2.3 0.1 3.6 6.0 2.4 3.6 81.8
DvsE 9.9 13.3 0.7 2.8 3.4 0.7 2.8 66.5
EvsH 100.0
Indirect estimates
AvsB 5.4 0.2 8.5 35.8 5.6 8.5 35.8 0.2
AvsH 18.6 6.2 1.2 5.2 6.4 1.2 5.2 24.9 31.2
BvsC 33.3 3.6 0.2 5.7 23.9 3.7 5.7 23.9 0.2
BvsE 15.4 6.2 4.1 17.4 10.0 4.1 17.4 25.4
BvsH 11.7 4.7 3.1 13.2 7.6 3.1 13.2 19.3 24.0
CvsD 39.6 28.5 1.3 1.9 7.9 9.8 1.9 7.9 1.3
CvsE 31.2 18.6 6.2 1.2 5.2 6.4 1.2 5.2 24.9
CvsF 26.8 1.7 0.1 23.7 11.3 1.8 13.1 11.3 0.1
CvsG 41.1 3.3 0.2 5.3 32.3 3.5 5.3 8.8 0.2
CvsH 23.8 14.1 4.8 0.9 3.9 4.9 0.9 3.9 19.0 23.8
DvsF 30.0 1.4 26.5 4.8 13.1 18.0 4.8 1.4
DvsG 29.1 1.4 3.7 26.8 15.1 3.7 18.9 1.4
DvsH 5.5 7.4 0.4 1.5 1.9 0.4 1.5 37.0 44.4
EvsF 17.8 6.4 19.6 4.6 8.2 12.8 4.6 26.0
EvsG 17.2 6.6 3.0 20.8 9.7 3.0 12.7 26.9
FvsG 1.7 0.1 24.8 23.1 1.8 23.4 25.1 0.1
FvsH 13.4 4.8 14.8 3.5 6.2 9.7 3.5 19.6 24.5
GvsH 12.9 4.9 2.2 15.6 7.3 2.2 9.5 20.2 25.1
Entire network 10.1 14.0 3.6 8.2 13.8 6.8 6.5 12.5 14.3 10.1
Included studies 2 3 5 4 9 1 1 4 1 1

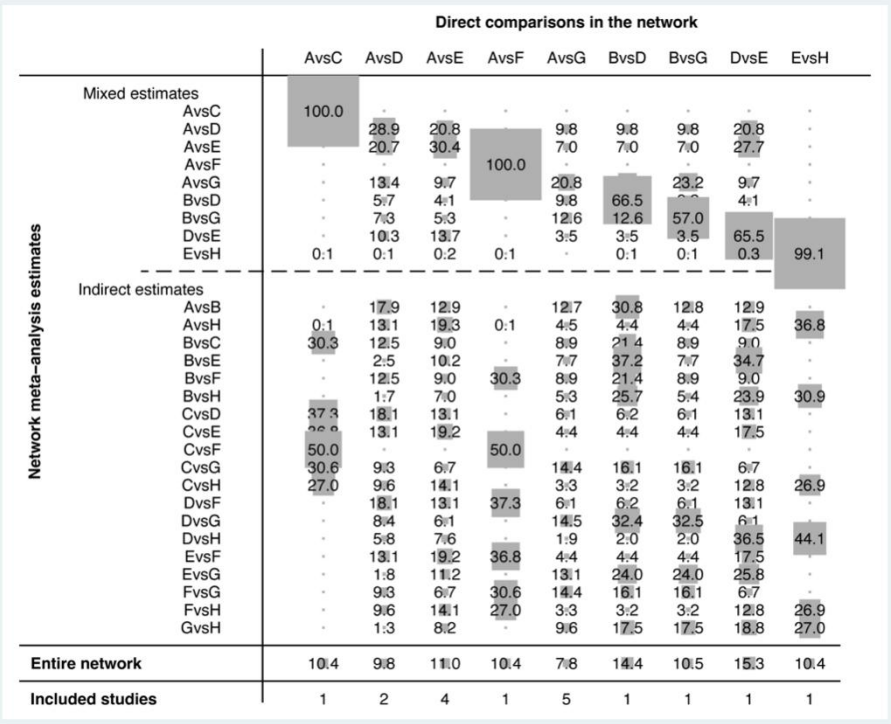
FBG


Direct comparisons in the network
AvsC AvsD AvsE AvsF AvsG BvsD BvsG DvsE
Network meta−analysis estimates
Mixed estimates
AvsC 99.7 0.1 0.1 0.1
AvsD 0.4 38.1 15.4 0.4 10.0 10.1 9.7 15.8
AvsE 0.3 28.1 13.5 7.4 7.5 7.2 35.8
AvsF 0.9 1.6 0.7 94.6 0.5 0.3 0.2
AvsG 0.2 6.0 2.5 0.2 72.0 8.4 2.4
BvsD 1.7 0.7 2.4 92.0 2.4 0.8
BvsG 0.2 19.0 7.7 0.2 27.1 27.2 10.7
DvsE 2.4 3.0 0.6 0.7 0.6 92.6
Indirect estimates
AvsB 0.3 25.7 10.4 0.3 8.1 36.6 7.9 10.7
BvsC 30.9 17.8 7.2 0.2 5.6 25.4 5.5 7.4
BvsE 0.3 1.9 1.5 47.5 1.6 47.1
BvsF 0.1 17.8 7.2 30.4 5.4 25.9 5.5 7.7
CvsD 39.1 23.3 9.4 0.2 6.1 6.2 6.0 9.7
CvsE 33.1 18.8 9.0 0.2 4.9 5.0 4.8 24.1
CvsF 49.8 0.7 0.3 48.1 0.6 0.3 0.2 0.1
CvsG 44.7 3.3 1.3 0.1 39.9 4.6 4.7 1.3
DvsF 0.1 23.4 9.5 38.6 5.8 6.6 6.0 10.1
DvsG 0.2 23.4 9.5 0.2 33.4 11.8 11.6 9.8
EvsF 0.1 18.8 9.1 32.5 4.7 5.3 4.8 24.7
EvsG 0.2 17.9 8.8 0.2 27.1 9.3 9.1 27.5
FvsG 0.3 2.7 1.1 44.2 40.7 4.5 5.0 1.4
Entire network 13.6 15.6 6.8 13.0 14.3 15.5 5.8 15.4
Included studies 3 5 3 4 11 1 3 1

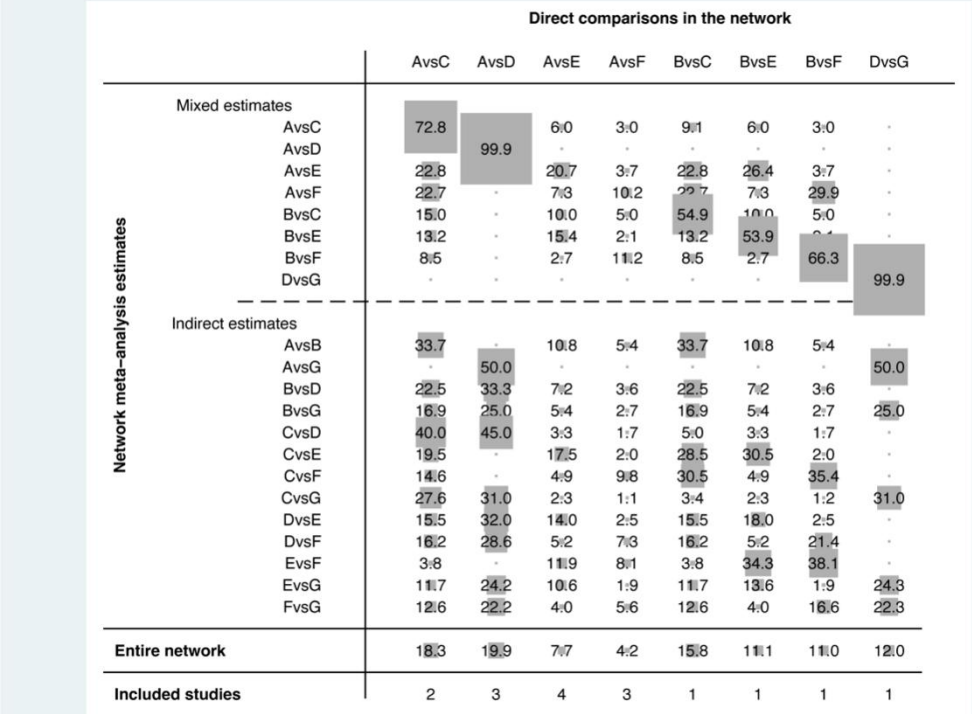
25-(OH)-D


Direct comparisons in the network
AvsC AvsD AvsE AvsF AvsG BvsD BvsF BvsG DvsE
Network meta−analysis estimates
Mixed estimates
AvsC 100.0
AvsD 12.7 9.0 10.0 13.1 23.1 10.0 13.1 9.0
AvsE 9.4 13.0 7.4 9.7 17.1 7.4 9.7 26.4
AvsF 4.4 3.1 26.0 16.0 7.6 23.6 16.0 3.1
AvsG 4.2 3.0 11.5 40.9 7.2 11.5 18.7 3.0
BvsD 9.6 6.8 7.1 9.3 43.9 7.1 9.3 6.8
BvsF 2.5 1.8 13.2 9.0 4.2 58.6 9.0 1.8
BvsG 3.5 2.5 9.7 15.7 6.0 9.7 50.3
DvsE 3.5 9.9 2.8 3.6 6.4 2.8 3.6 67.4
Indirect estimates
AvsB 5.9 4.2 16.3 21.4 10.1 16.3 21.4 4.2
BvsC 32.4 4.0 2.8 11.0 14.5 6.9 11.0 14.5 2.8
BvsE 4.6 9.8 6.2 8.2 26.1 6.2 8.2 30.7
CvsD 30.9 8.8 6.2 6.9 9.1 16.0 6.9 9.1 6.2
CvsE 28.3 6.7 9.3 5.3 7.0 12.2 5.3 7.0 19.0
CvsF 33.2 3.0 2.1 17.4 10.7 5.1 15.8 10.7 2.1
CvsG 37.3 2.6 1.9 7.2 25.6 4.5 7.2 11.7 1.9
DvsF 8.8 6.3 13.7 1.4 30.4 31.8 1.4 6.3
DvsG 9.6 6.8 1.3 17.8 28.8 1.3 27.5 6.8
EvsF 5.1 9.2 11.7 2.7 20.3 22.9 2.7 25.4
EvsG 6.1 10.2 0.2 16.1 20.3 0.2 20.5 26.4
FvsG 0.9 0.6 15.9 17.5 1.6 32.2 30.6 0.6
Entire network 12.6 5.8 6.0 9.6 12.7 14.6 13.0 13.6 12.0
Included studies 2 5 5 5 13 1 1 4 1

HbA1c

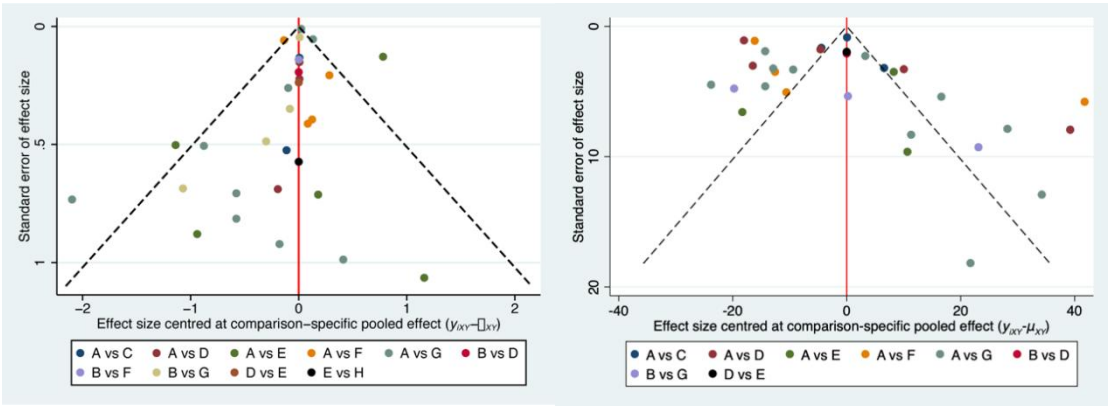

Direct comparisons in the network
AvsC AvsD AvsE AvsF AvsG BvsD BvsG DvsE EvsH
Network meta−analysis estimates
Mixed estimates
AvsC 100.0
AvsD 28.9 20.8 9.8 9.8 9.8 20.8
AvsE 20.7 30.4 7.0 7.0 7.0 27.7
AvsF 100.0
AvsG 13.4 9.7 20.8 23.2 9.7
BvsD 5.7 4.1 9.8 66.5 4.1
BvsG 7.3 5.3 12.6 12.6 57.0 65.5
DvsE 10.3 13.7 3.5 3.5 3.5
EvsH 0.1 0.1 0.2 0.1 0.1 0.1 0.3 99.1
Indirect estimates
AvsB 17.9 12.9 12.7 30.8 12.8 12.9
AvsH 0.1 13.1 19.3 0.1 4.5 4.4 4.4 17.5 36.8
BvsC 30.3 12.5 9.0 8.9 21.4 8.9 9.0
BvsE 2.5 10.2 7.7 37.2 7.7 34.7
BvsF 12.5 9.0 30.3 8.9 21.4 8.9 9.0
BvsH 1.7 7.0 5.3 25.7 5.4 23.9 30.9
CvsD 37.3 18.1 13.1 6.1 6.2 6.1 13.1
CvsE 13.1 19.2 4.4 4.4 4.4 17.5
CvsF 50.0 50.0
CvsG 30.6 9.3 6.7 14.4 16.1 16.1 6.7
CvsH 27.0 9.6 14.1 3.3 3.2 3.2 12.8 26.9
DvsF 18.1 13.1 37.3 6.1 6.2 6.1 13.1
DvsG 8.4 6.1 14.5 32.4 32.5 6.1
DvsH 5.8 7.6 1.9 2.0 2.0 36.5 44.1
EvsF 13.1 19.2 36.8 4.4 4.4 4.4 17.5
EvsG 1.8 11.2 13.1 24.0 24.0 25.8
FvsG 9.3 6.7 30.6 14.4 16.1 16.1 6.7
FvsH 9.6 14.1 27.0 3.3 3.2 3.2 12.8 26.9
GvsH 1.3 8.2 9.6 17.5 17.5 18.8 27.0
Entire network 10.4 9.8 11.0 10.4 7.8 14.4 10.5 15.3 10.4
Included studies 1 2 4 1 5 1 1 1 1

FIN

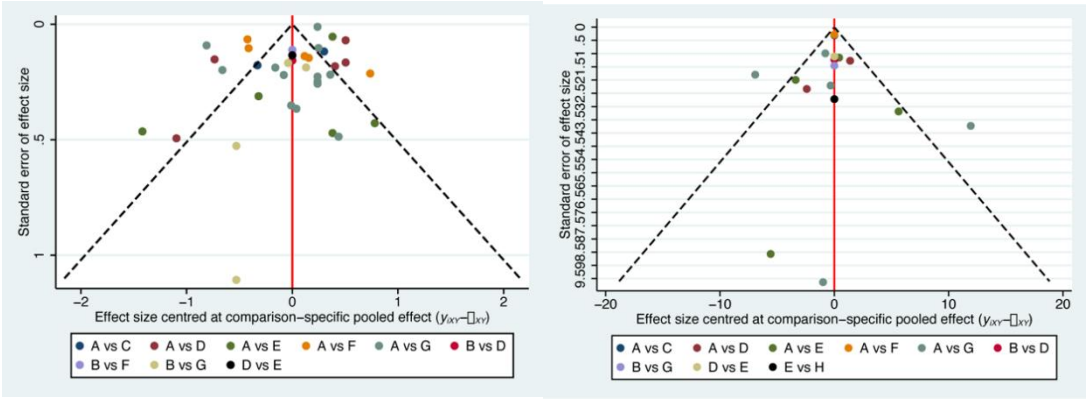


HOMA-IR

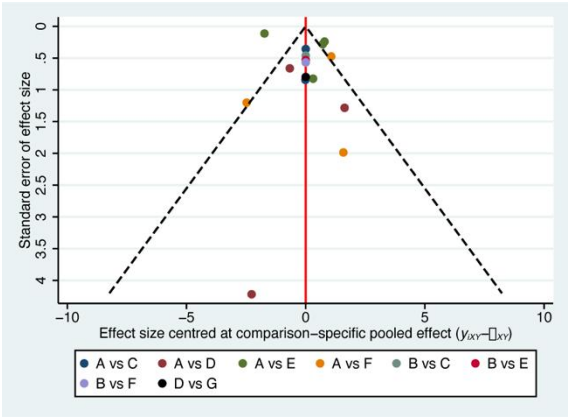
Supplementary Figure S5. Contribution Plot for FBG, 25-(OH)-D, HbA1c, FIN, and HOMA-IR. LDS, low dose strategy; MDS, medium dose strategy; HDS, high dose strategy; EHDS, extremely high dose strategy; FBG, fasting blood glucose; 25-(OH)-D, 25-hydroxyvitamin D; HbA1c, hemoglobin A1c; FIN, fasting insulin; HOMA-IR, homeostasis model assessment-insulin



FBG 25-(OH)-D



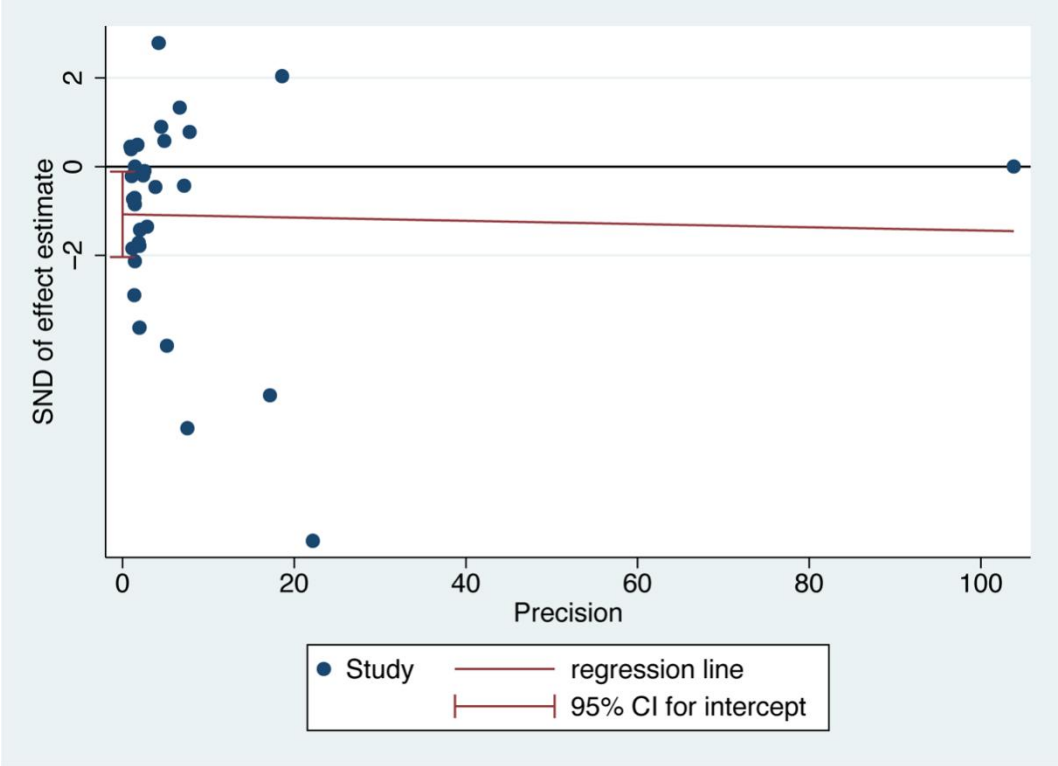
HbA1c FIN



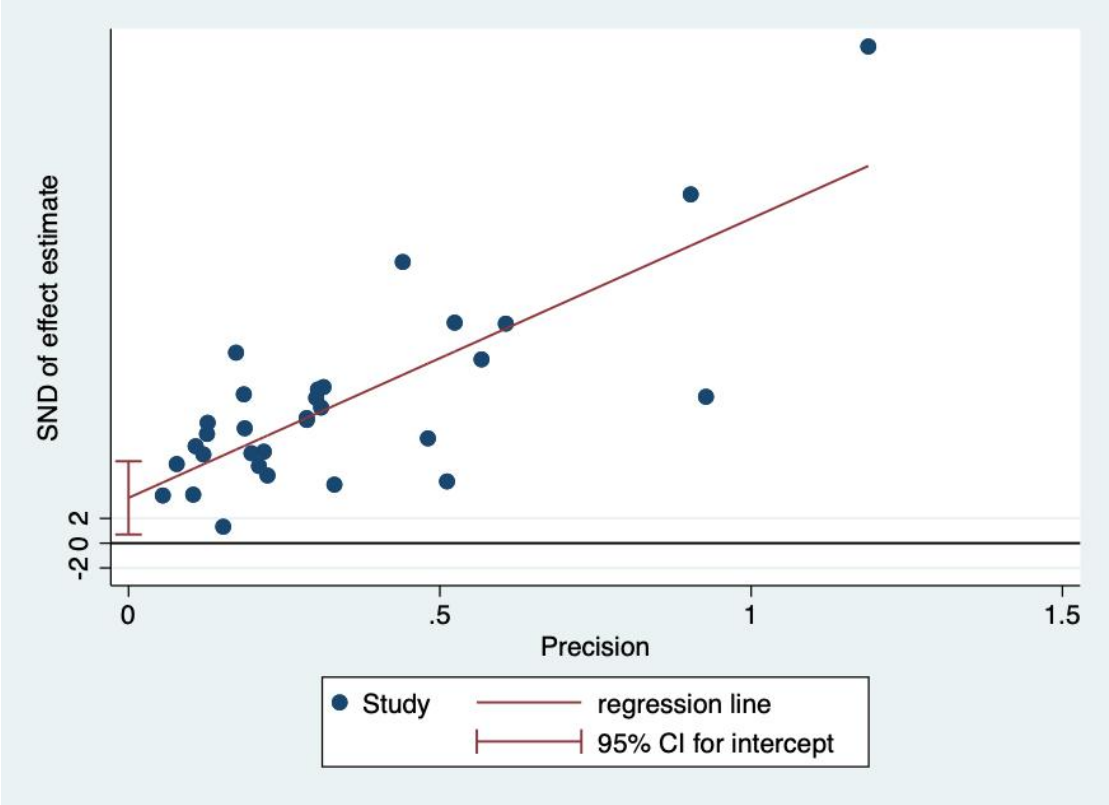
A. Placebo.
B. No-treatment Control.
C. Vit D2
D. Vit D3 LDS
E. Vit D3 MDS
F. Vit D3 HDS
G. Vit D3 EHDS
H. Vit K2.

HOMA-IR

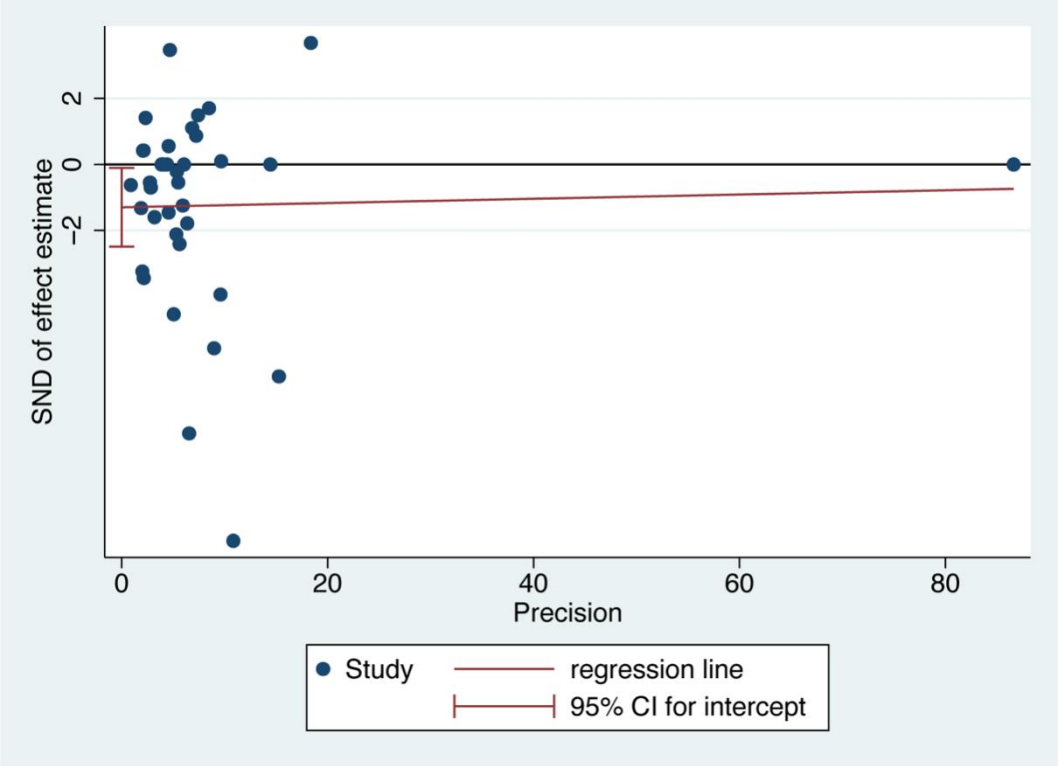
Supplementary Figure S6. Funnel plots for FBG, 25-(OH)-D, HbA1c, FIN, and HOMA-IR. LDS, low dose strategy; MDS, medium dose strategy; HDS, high dose strategy; EHDS, extremely high dose strategy; FBG, fasting blood glucose; 25-(OH)-D, 25-hydroxyvitamin D; HbA1c, hemoglobin A1c; FIN, fasting insulin; HOMA-IR, homeostasis model assessment-insulin


SND of effect estimate
2
0
−2
0
20
40
60
80
100
Precision
Study
regression line
95% CI for intercept

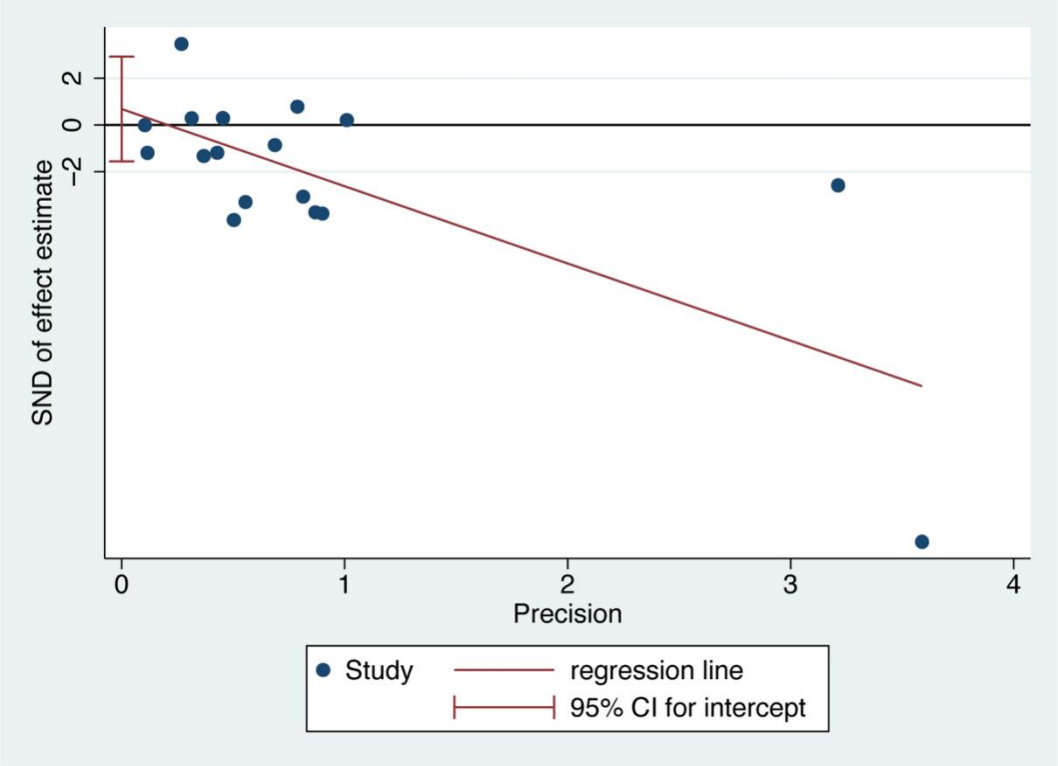
FBG


SND of effect estimate
-2 0 2
0
.5
1
1.5
Precision
Study
regression line
95% CI for intercept

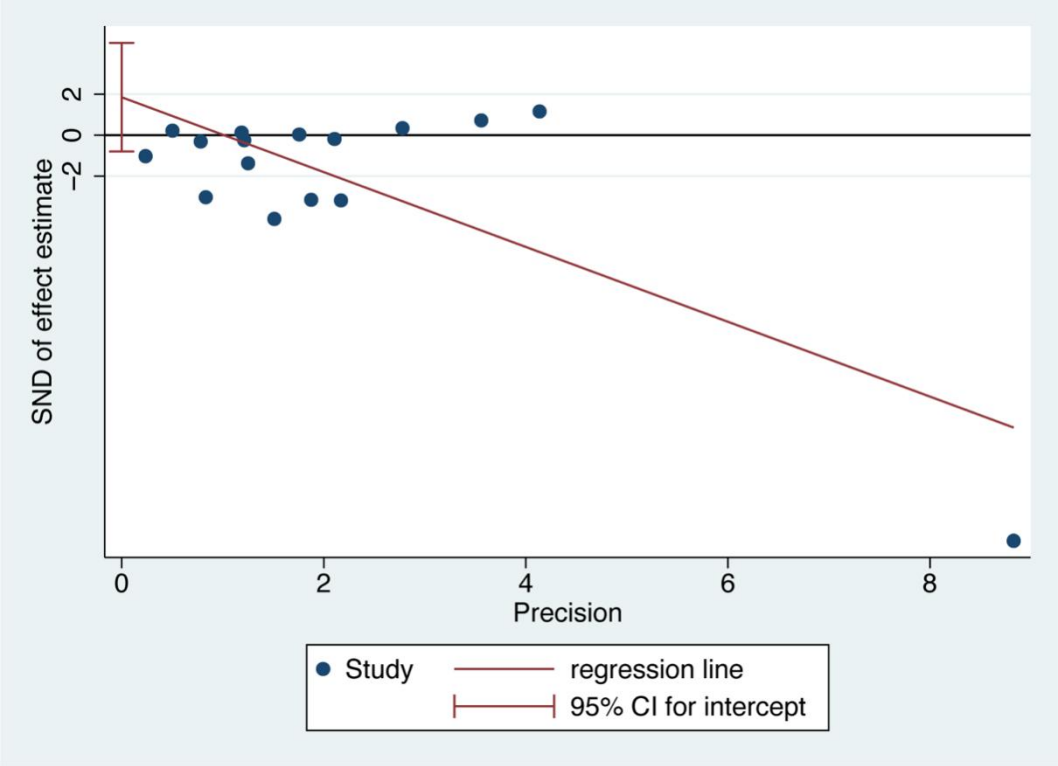
25-(OH)-D


SND of effect estimate
2
0
−2
0
20
40
60
80
Precision
Study
regression line
95% CI for intercept

HbA1c

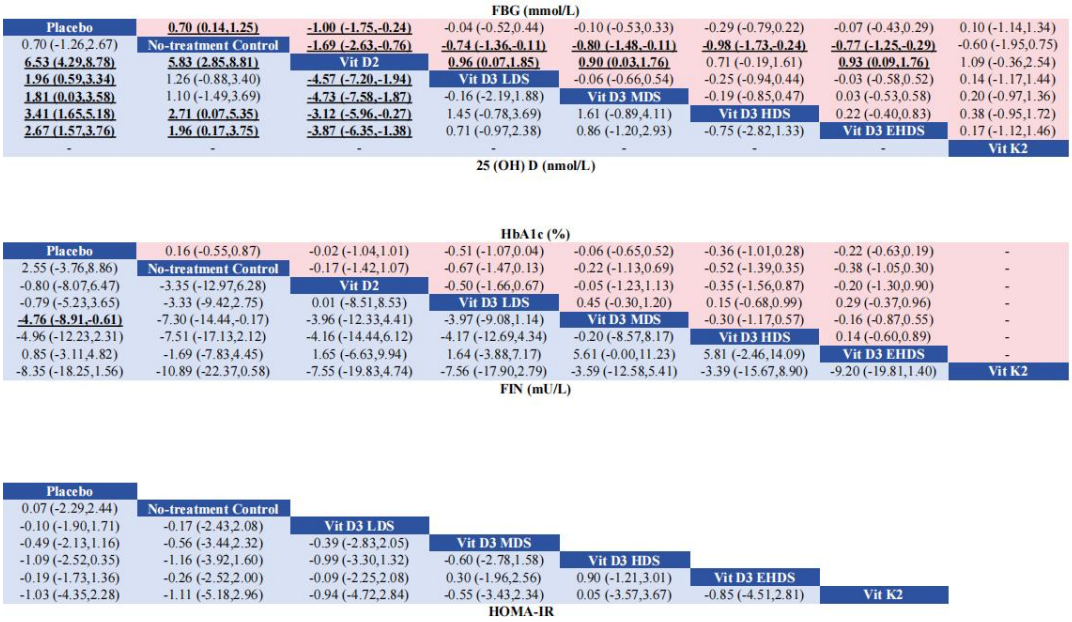

SND of effect estimate
2
0
−2
0
1
2
3
4
Precision
Study
regression line
95% CI for intercept

FIN

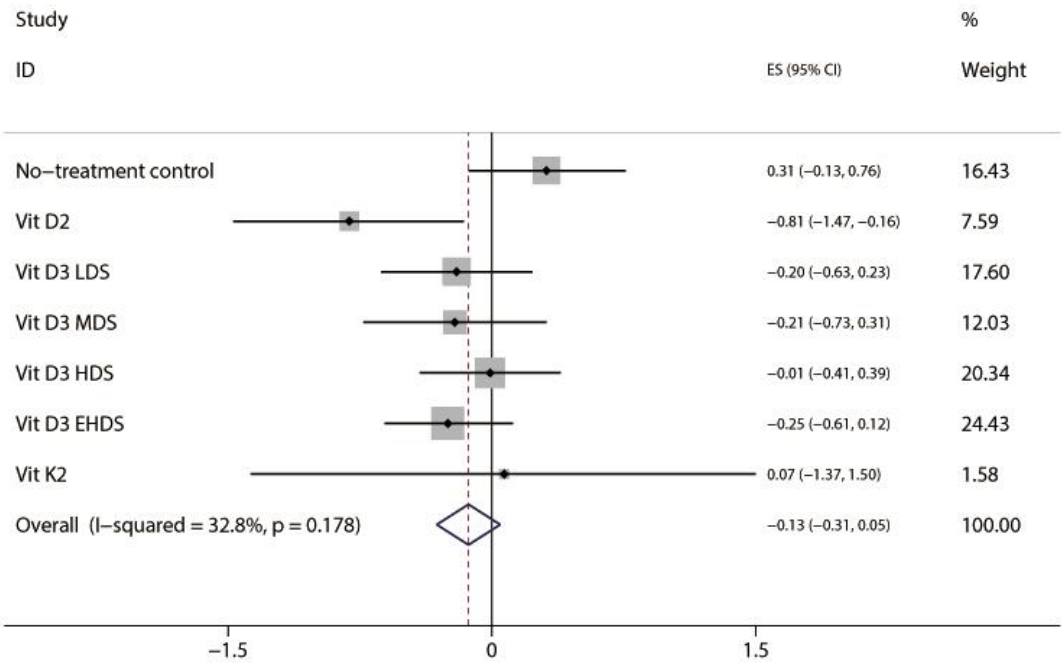


HOMA-IR

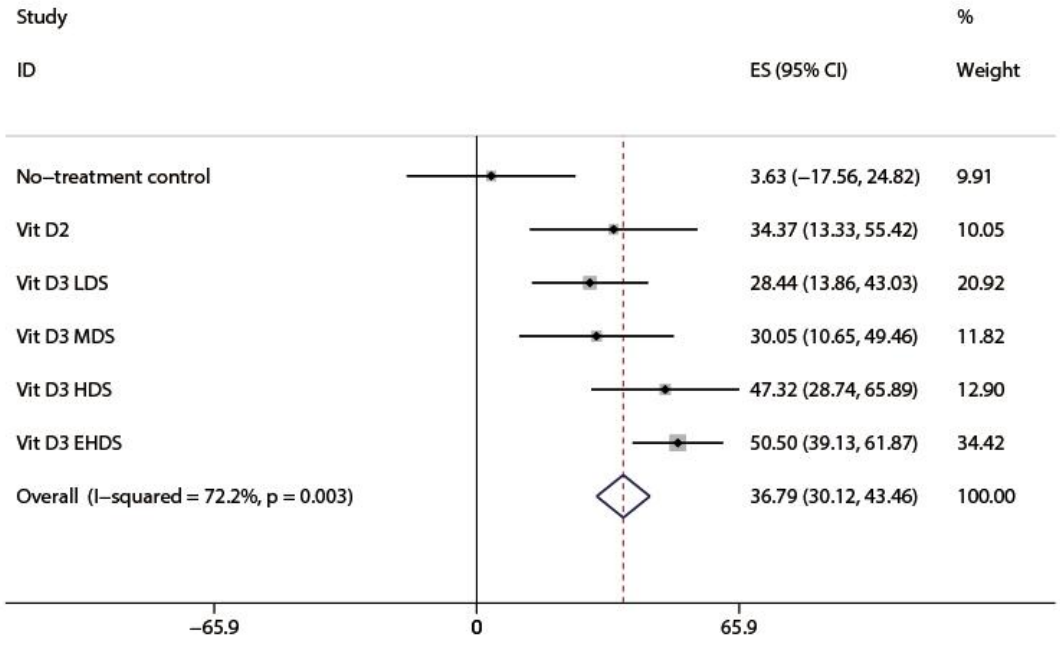
Supplementary Figure S7. Egger's test for FBG, 25-(OH)-D, HbA1c, FIN, and HOMA-IR. LDS, low dose strategy; MDS, medium dose strategy; HDS, high dose strategy; EHDS, extremely high dose strategy; FBG, fasting blood glucose; 25-(OH)-D, 25-hydroxyvitamin D; HbA1c, hemoglobin A1c; FIN, fasting insulin; HOMA-IR, homeostasis model assessment-insulin



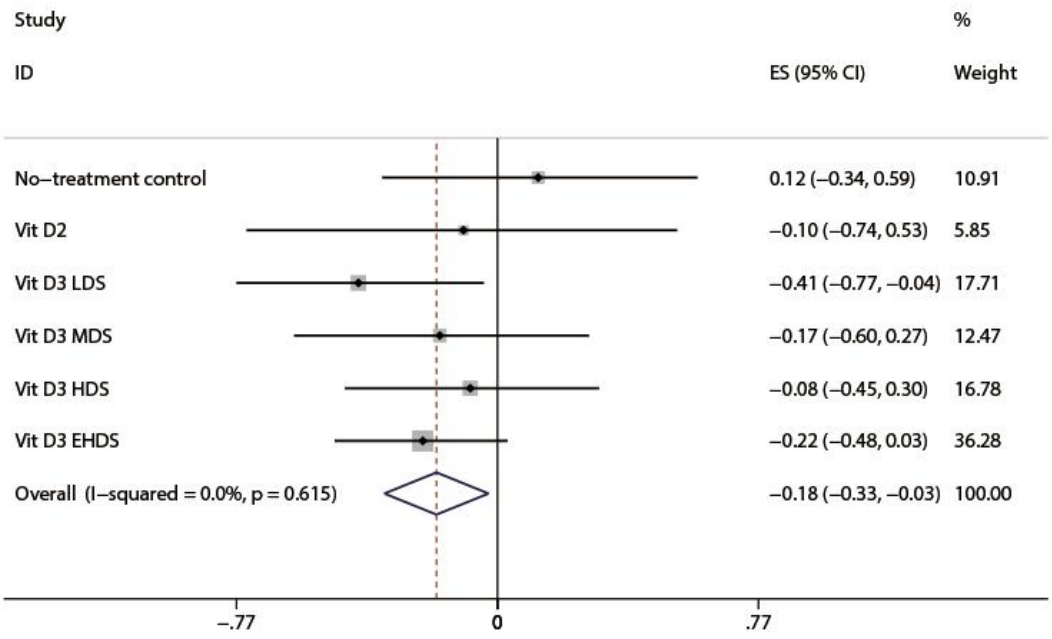
Supplementary Figure S8. Sensitivity analysis for FBG, 25-(OH)-D, HbA1c, FIN, and HOMA-IR. LDS, low dose strategy; MDS, medium dose strategy; HDS, high dose strategy; EHDS, extremely high dose strategy; FBG, fasting blood glucose; 25-(OH)-D, 25-hydroxyvitamin D; HbA1c, hemoglobin A1c; FIN, fasting insulin; HOMA-IR, homeostasis model assessment-insulin


Study
ID
ES (95% CI)
%
Weight
No–treatment control
0.31 (–0.13, 0.76)
16.43
Vit D2
–0.81 (–1.47, –0.16)
7.59
Vit D3 LDS
–0.20 (–0.63, 0.23)
17.60
Vit D3 MDS
–0.21 (–0.73, 0.31)
12.03
Vit D3 HDS
–0.01 (–0.41, 0.39)
20.34
Vit D3 EHDS
–0.25 (–0.61, 0.12)
24.43
Vit K2
0.07 (–1.37, 1.50)
1.58
Overall (I–squared = 32.8%, p = 0.178)
–0.13 (–0.31, 0.05)
100.00
–1.5
0
1.5

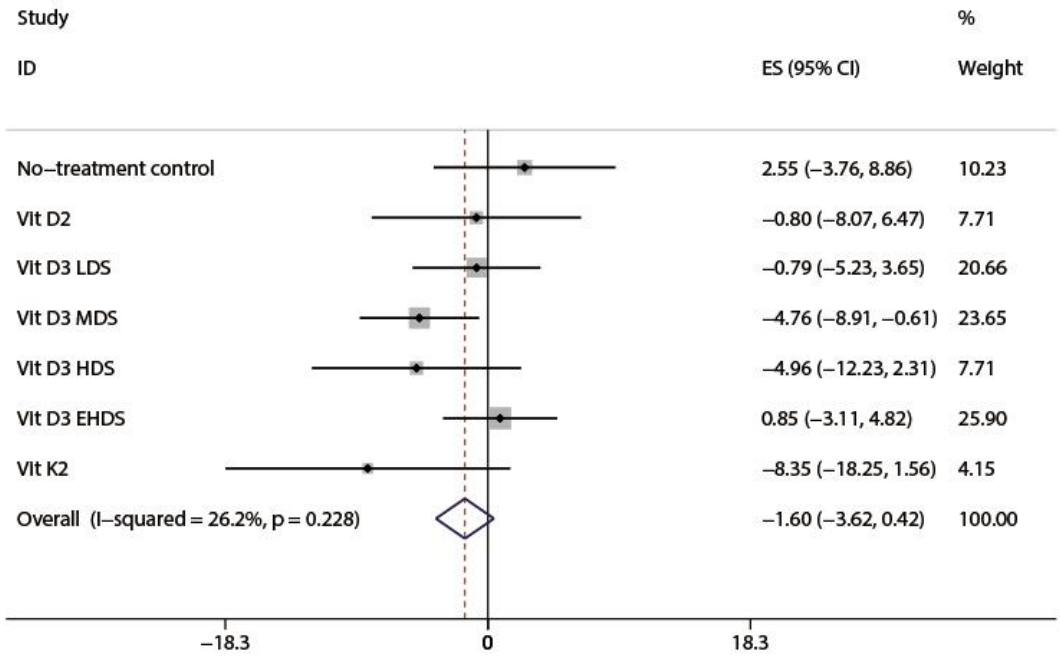
FBG


Study
ID
ES (95% CI)
%
Weight
No–treatment control
3.63 (–17.56, 24.82)
9.91
Vit D2
34.37 (13.33, 55.42)
10.05
Vit D3 LDS
28.44 (13.86, 43.03)
20.92
Vit D3 MDS
30.05 (10.65, 49.46)
11.82
Vit D3 HDS
47.32 (28.74, 65.89)
12.90
Vit D3 EHDS
50.50 (39.13, 61.87)
34.42
Overall (I–squared = 72.2%, p = 0.003)
36.79 (30.12, 43.46)
100.00
–65.9
0
65.9

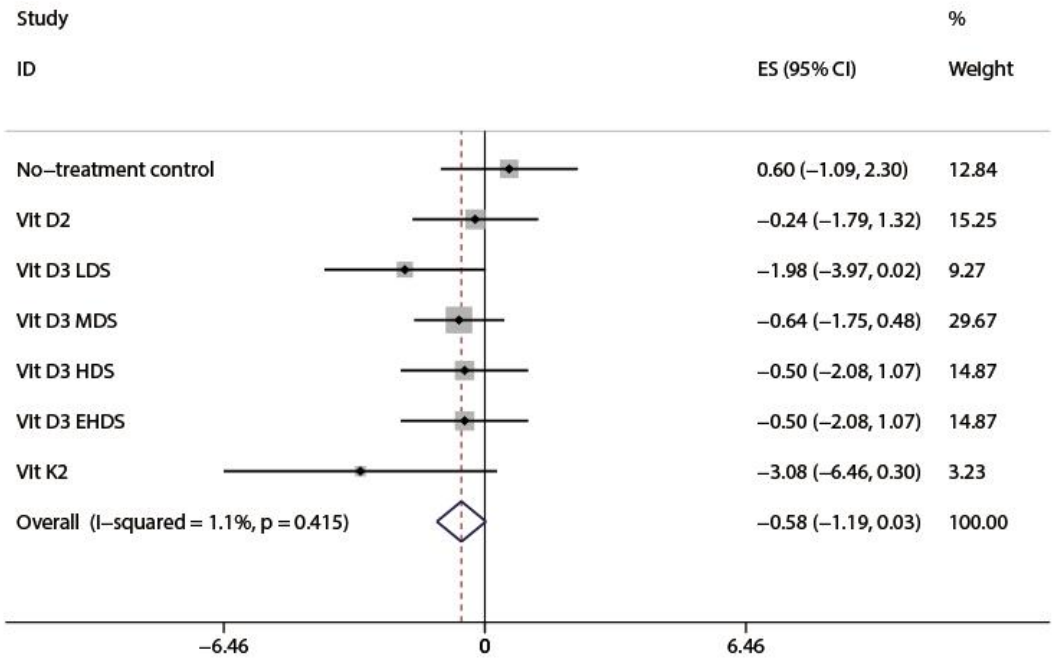
25-(OH)-D


Study
ID
ES (95% CI)
%
Weight
No–treatment control
0.12 (–0.34, 0.59)
10.91
Vit D2
–0.10 (–0.74, 0.53)
5.85
Vit D3 LDS
–0.41 (–0.77, –0.04)
17.71
Vit D3 MDS
–0.17 (–0.60, 0.27)
12.47
Vit D3 HDS
–0.08 (–0.45, 0.30)
16.78
Vit D3 EHDS
–0.22 (–0.48, 0.03)
36.28
Overall (I–squared = 0.0%, p = 0.615)
–0.18 (–0.33, –0.03)
100.00
–.77
0
.77

HbA1c

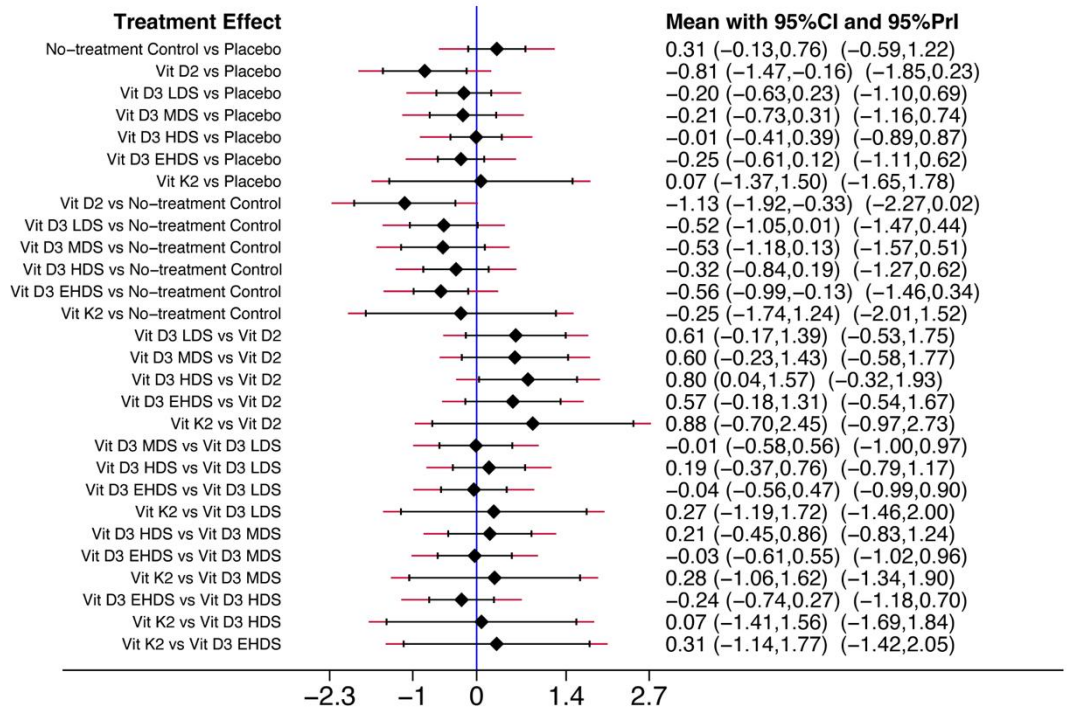

Study
ID
ES (95% CI)
%
Weight
No–treatment control
2.55 (–3.76, 8.86)
10.23
Vit D2
–0.80 (–8.07, 6.47)
7.71
Vit D3 LDS
–0.79 (–5.23, 3.65)
20.66
Vit D3 MDS
–4.76 (–8.91, –0.61)
23.65
Vit D3 HDS
–4.96 (–12.23, 2.31)
7.71
Vit D3 EHDS
0.85 (–3.11, 4.82)
25.90
Vit K2
–8.35 (–18.25, 1.56)
4.15
Overall (I–squared = 26.2%, p = 0.228)
–1.60 (–3.62, 0.42)
100.00
–18.3
0
18.3

FIN

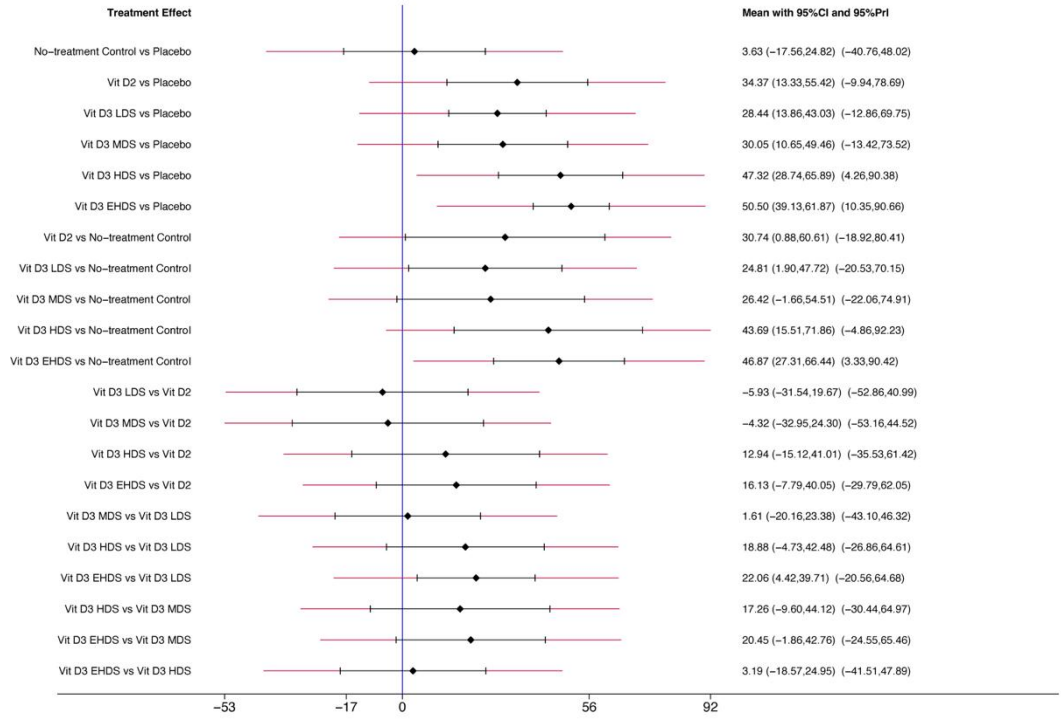


HOMA-IR

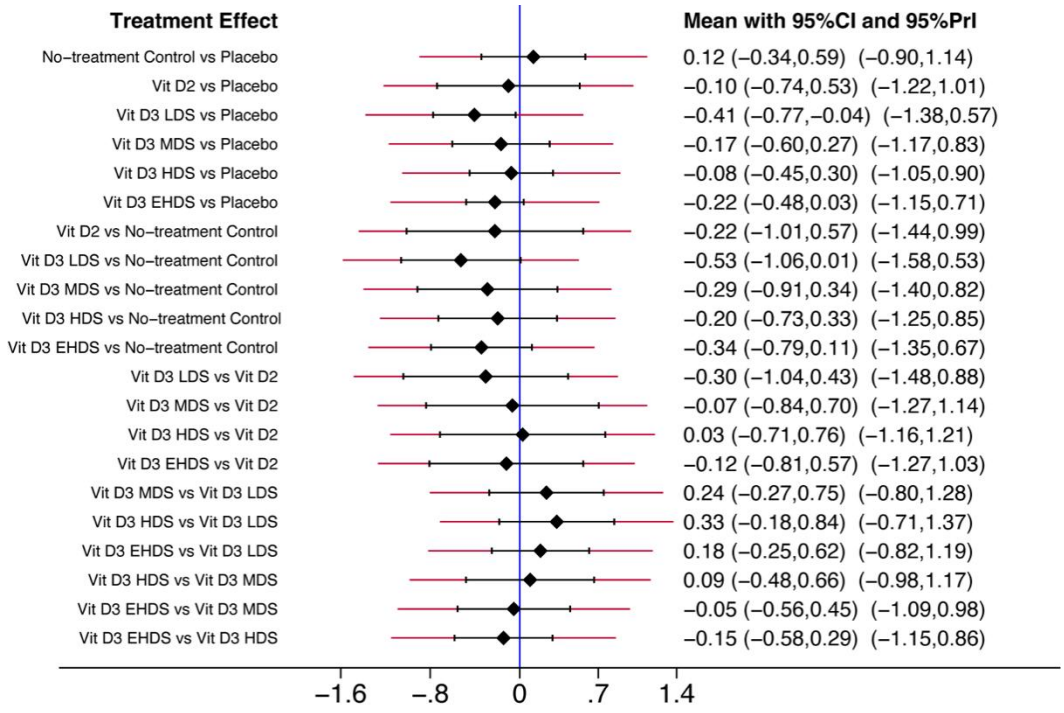
Supplementary Figure S9. Comparative Effectiveness of Paired Meta-Analysis for FBG, 25-(OH)-D, HbA1c, FIN, and HOMA-IR. LDS, low dose strategy; MDS, medium dose strategy; HDS, high dose strategy; EHDS, extremely high dose strategy; FBG, fasting blood glucose; 25-(OH)-D, 25-hydroxyvitamin D; HbA1c, hemoglobin A1c; FIN, fasting insulin; HOMA-IR, homeostasis model assessment-insulin


Treatment Effect
Mean with 95%CI and 95%PrI
No−treatment Control vs Placebo
0.31 (−0.13,0.76) (−0.59,1.22)
Vit D2 vs Placebo
−0.81 (−1.47,−0.16) (−1.85,0.23)
Vit D3 LDS vs Placebo
−0.20 (−0.63,0.23) (−1.10,0.69)
Vit D3 MDS vs Placebo
−0.21 (−0.73,0.31) (−1.16,0.74)
Vit D3 HDS vs Placebo
−0.01 (−0.41,0.39) (−0.89,0.87)
Vit D3 EHDS vs Placebo
−0.25 (−0.61,0.12) (−1.11,0.62)
Vit K2 vs Placebo
0.07 (−1.37,1.50) (−1.65,1.78)
Vit D2 vs No−treatment Control
−1.13 (−1.92,−0.33) (−2.27,0.02)
Vit D3 LDS vs No−treatment Control
−0.52 (−1.05,0.01) (−1.47,0.44)
Vit D3 MDS vs No−treatment Control
−0.53 (−1.18,0.13) (−1.57,0.51)
Vit D3 HDS vs No−treatment Control
−0.32 (−0.84,0.19) (−1.27,0.62)
Vit D3 EHDS vs No−treatment Control
−0.56 (−0.99,−0.13) (−1.46,0.34)
Vit K2 vs No−treatment Control
−0.25 (−1.74,1.24) (−2.01,1.52)
Vit D3 LDS vs Vit D2
0.61 (−0.17,1.39) (−0.53,1.75)
Vit D3 MDS vs Vit D2
0.60 (−0.23,1.43) (−0.58,1.77)
Vit D3 HDS vs Vit D2
0.80 (0.04,1.57) (−0.32,1.93)
Vit D3 EHDS vs Vit D2
0.57 (−0.18,1.31) (−0.54,1.67)
Vit K2 vs Vit D2
0.88 (−0.70,2.45) (−0.97,2.73)
Vit D3 MDS vs Vit D3 LDS
−0.01 (−0.58,0.56) (−1.00,0.97)
Vit D3 HDS vs Vit D3 LDS
0.19 (−0.37,0.76) (−0.79,1.17)
Vit D3 EHDS vs Vit D3 LDS
−0.04 (−0.56,0.47) (−0.99,0.90)
Vit K2 vs Vit D3 LDS
0.27 (−1.19,1.72) (−1.46,2.00)
Vit D3 HDS vs Vit D3 MDS
0.21 (−0.45,0.86) (−0.83,1.24)
Vit D3 EHDS vs Vit D3 MDS
−0.03 (−0.61,0.55) (−1.02,0.96)
Vit K2 vs Vit D3 MDS
0.28 (−1.06,1.62) (−1.34,1.90)
Vit D3 EHDS vs Vit D3 HDS
−0.24 (−0.74,0.27) (−1.18,0.70)
Vit K2 vs Vit D3 HDS
0.07 (−1.41,1.56) (−1.69,1.84)
Vit K2 vs Vit D3 EHDS
0.31 (−1.14,1.77) (−1.42,2.05)
−2.3
−1
0
1.4
2.7

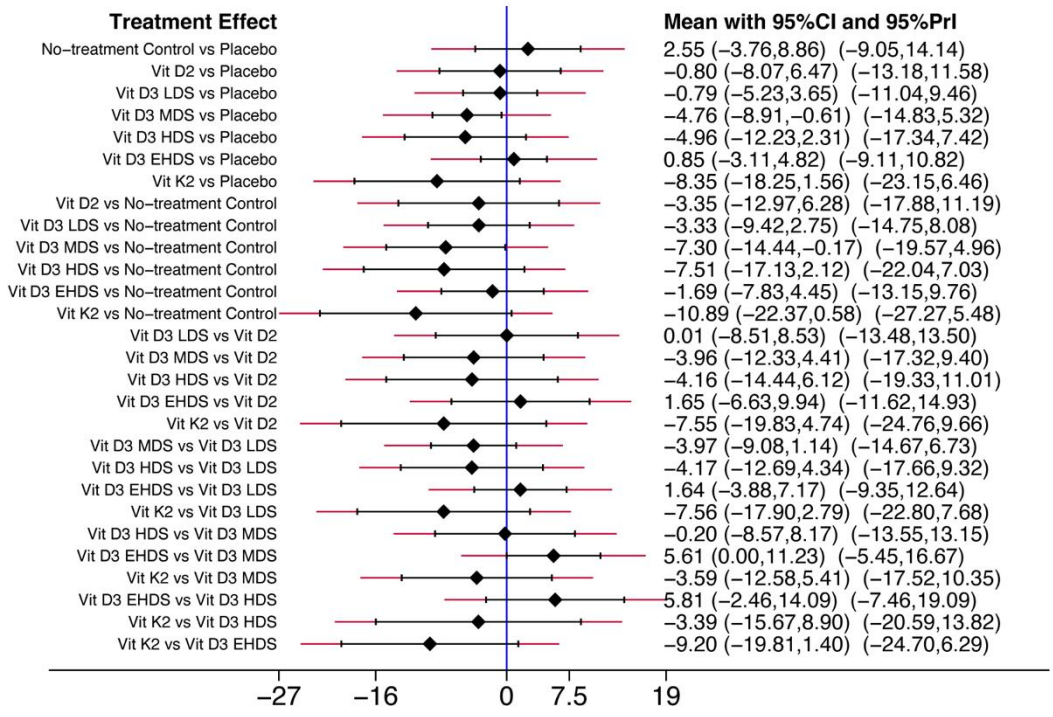
FBG


Treatment Effect
Mean with 95%CI and 95%PrI
No−treatment Control vs Placebo
3.63 (−17.56,24.82) (−40.76,48.02)
Vit D2 vs Placebo
34.37 (13.33,55.42) (−9.94,78.69)
Vit D3 LDS vs Placebo
28.44 (13.86,43.03) (−12.86,69.75)
Vit D3 MDS vs Placebo
30.05 (10.65,49.46) (−13.42,73.52)
Vit D3 HDS vs Placebo
47.32 (28.74,65.89) (4.26,90.38)
Vit D3 EHDS vs Placebo
50.50 (39.13,61.87) (10.35,90.66)
Vit D2 vs No−treatment Control
30.74 (0.88,60.61) (−18.92,80.41)
Vit D3 LDS vs No−treatment Control
24.81 (1.90,47.72) (−20.53,70.15)
Vit D3 MDS vs No−treatment Control
26.42 (−1.66,54.51) (−22.06,74.91)
Vit D3 HDS vs No−treatment Control
43.69 (15.51,71.86) (−4.86,92.23)
Vit D3 EHDS vs No−treatment Control
46.87 (27.31,66.44) (3.33,90.42)
Vit D3 LDS vs Vit D2
−5.93 (−31.54,19.67) (−52.86,40.99)
Vit D3 MDS vs Vit D2
−4.32 (−32.95,24.30) (−53.16,44.52)
Vit D3 HDS vs Vit D2
12.94 (−15.12,41.01) (−35.53,61.42)
Vit D3 EHDS vs Vit D2
16.13 (−7.79,40.05) (−29.79,62.05)
Vit D3 MDS vs Vit D3 LDS
1.61 (−20.16,23.38) (−43.10,46.32)
Vit D3 HDS vs Vit D3 LDS
18.88 (−4.73,42.48) (−26.86,64.61)
Vit D3 EHDS vs Vit D3 LDS
22.06 (4.42,39.71) (−20.56,64.68)
Vit D3 HDS vs Vit D3 MDS
17.26 (−9.60,44.12) (−30.44,64.97)
Vit D3 EHDS vs Vit D3 MDS
20.45 (−1.86,42.76) (−24.55,65.46)
Vit D3 EHDS vs Vit D3 HDS
3.19 (−18.57,24.95) (−41.51,47.89)
−53
−17
0
56
92

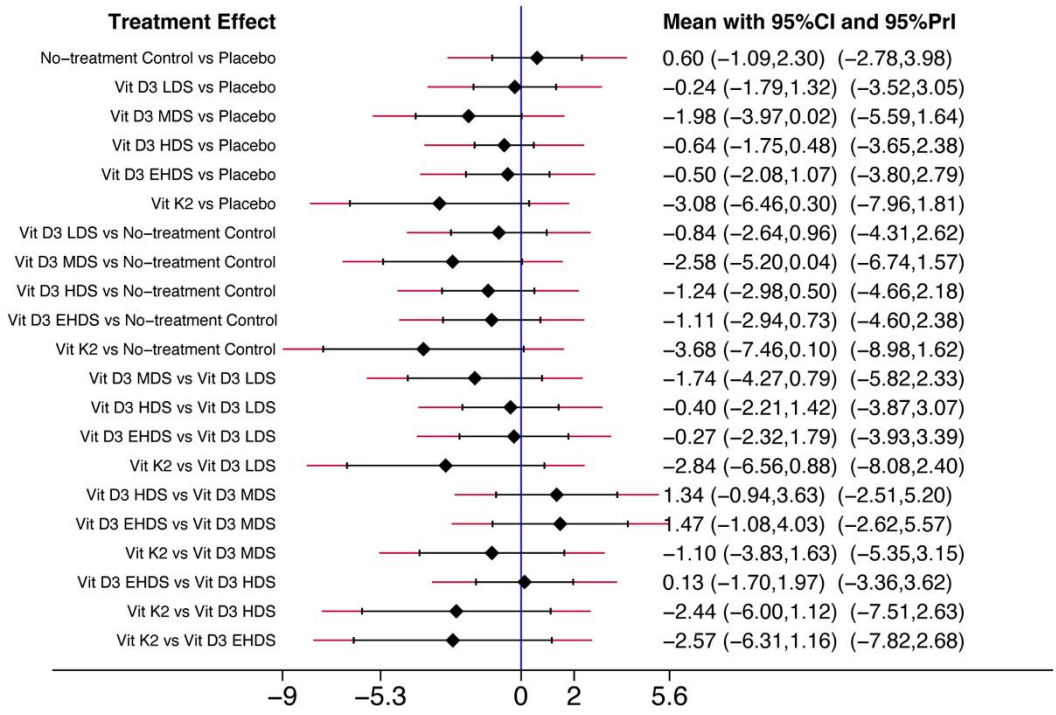
25-(OH)-D


Treatment Effect
Mean with 95%CI and 95%PrI
No−treatment Control vs Placebo
0.12 (−0.34,0.59) (−0.90,1.14)
Vit D2 vs Placebo
−0.10 (−0.74,0.53) (−1.22,1.01)
Vit D3 LDS vs Placebo
−0.41 (−0.77,−0.04) (−1.38,0.57)
Vit D3 MDS vs Placebo
−0.17 (−0.60,0.27) (−1.17,0.83)
Vit D3 HDS vs Placebo
−0.08 (−0.45,0.30) (−1.05,0.90)
Vit D3 EHDS vs Placebo
−0.22 (−0.48,0.03) (−1.15,0.71)
Vit D2 vs No−treatment Control
−0.22 (−1.01,0.57) (−1.44,0.99)
Vit D3 LDS vs No−treatment Control
−0.53 (−1.06,0.01) (−1.58,0.53)
Vit D3 MDS vs No−treatment Control
−0.29 (−0.91,0.34) (−1.40,0.82)
Vit D3 HDS vs No−treatment Control
−0.20 (−0.73,0.33) (−1.25,0.85)
Vit D3 EHDS vs No−treatment Control
−0.34 (−0.79,0.11) (−1.35,0.67)
Vit D3 LDS vs Vit D2
−0.30 (−1.04,0.43) (−1.48,0.88)
Vit D3 MDS vs Vit D2
−0.07 (−0.84,0.70) (−1.27,1.14)
Vit D3 HDS vs Vit D2
0.03 (−0.71,0.76) (−1.16,1.21)
Vit D3 EHDS vs Vit D2
−0.12 (−0.81,0.57) (−1.27,1.03)
Vit D3 MDS vs Vit D3 LDS
0.24 (−0.27,0.75) (−0.80,1.28)
Vit D3 HDS vs Vit D3 LDS
0.33 (−0.18,0.84) (−0.71,1.37)
Vit D3 EHDS vs Vit D3 LDS
0.18 (−0.25,0.62) (−0.82,1.19)
Vit D3 HDS vs Vit D3 MDS
0.09 (−0.48,0.66) (−0.98,1.17)
Vit D3 EHDS vs Vit D3 MDS
−0.05 (−0.56,0.45) (−1.09,0.98)
Vit D3 EHDS vs Vit D3 HDS
−0.15 (−0.58,0.29) (−1.15,0.86)
−1.6
−.8
0
.7
1.4

HbA1c

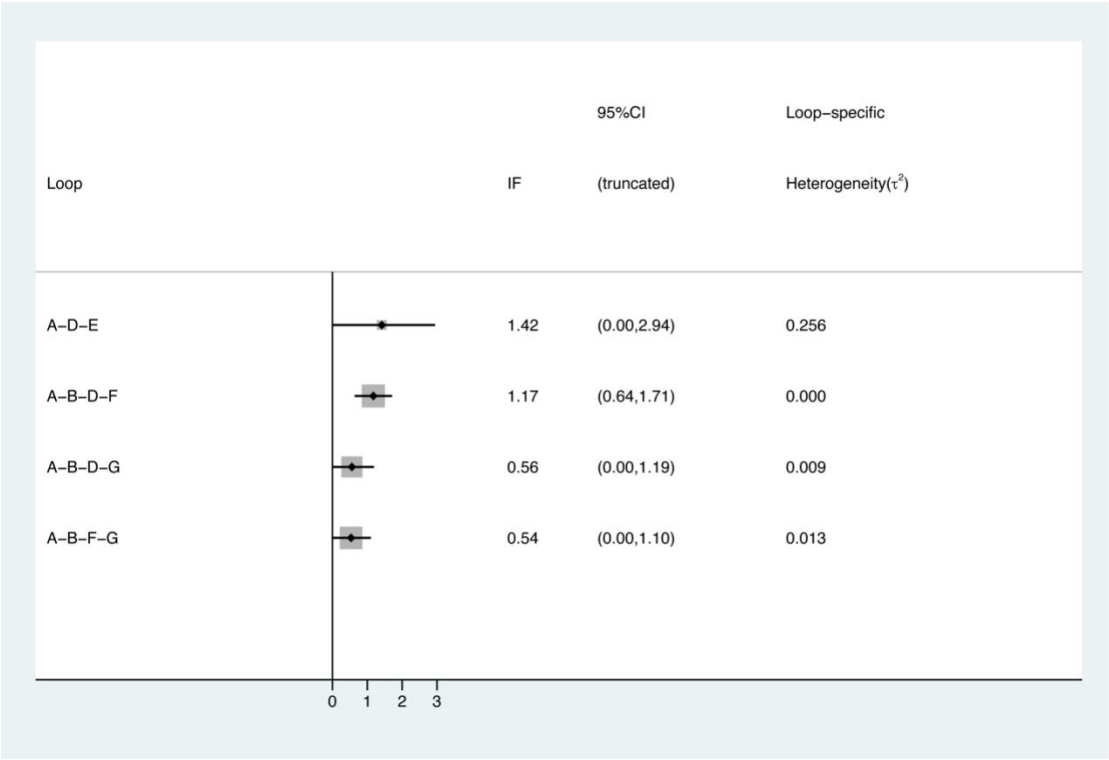

Treatment Effect
Mean with 95%CI and 95%PrI
No−treatment Control vs Placebo
2.55 (−3.76,8.86) (−9.05,14.14)
Vit D2 vs Placebo
−0.80 (−8.07,6.47) (−13.18,11.58)
Vit D3 LDS vs Placebo
−0.79 (−5.23,3.65) (−11.04,9.46)
Vit D3 MDS vs Placebo
−4.76 (−8.91,−0.61) (−14.83,5.32)
Vit D3 HDS vs Placebo
−4.96 (−12.23,2.31) (−17.34,7.42)
Vit D3 EHDS vs Placebo
0.85 (−3.11,4.82) (−9.11,10.82)
Vit K2 vs Placebo
−8.35 (−18.25,1.56) (−23.15,6.46)
Vit D2 vs No−treatment Control
−3.35 (−12.97,6.28) (−17.88,11.19)
Vit D3 LDS vs No−treatment Control
−3.33 (−9.42,2.75) (−14.75,8.08)
Vit D3 MDS vs No−treatment Control
−7.30 (−14.44,−0.17) (−19.57,4.96)
Vit D3 HDS vs No−treatment Control
−7.51 (−17.13,2.12) (−22.04,7.03)
Vit D3 EHDS vs No−treatment Control
−1.69 (−7.83,4.45) (−13.15,9.76)
Vit K2 vs No−treatment Control
−10.89 (−22.37,0.58) (−27.27,5.48)
Vit D3 LDS vs Vit D2
0.01 (−8.51,8.53) (−13.48,13.50)
Vit D3 MDS vs Vit D2
−3.96 (−12.33,4.41) (−17.32,9.40)
Vit D3 HDS vs Vit D2
−4.16 (−14.44,6.12) (−19.33,11.01)
Vit D3 EHDS vs Vit D2
1.65 (−6.63,9.94) (−11.62,14.93)
Vit K2 vs Vit D2
−7.55 (−19.83,4.74) (−24.76,9.66)
Vit D3 MDS vs Vit D3 LDS
−3.97 (−9.08,1.14) (−14.67,6.73)
Vit D3 HDS vs Vit D3 LDS
−4.17 (−12.69,4.34) (−17.66,9.32)
Vit D3 EHDS vs Vit D3 LDS
1.64 (−3.88,7.17) (−9.35,12.64)
Vit K2 vs Vit D3 LDS
−7.56 (−17.90,2.79) (−22.80,7.68)
Vit D3 HDS vs Vit D3 MDS
−0.20 (−8.57,8.17) (−13.55,13.15)
Vit D3 EHDS vs Vit D3 MDS
5.61 (0.00,11.23) (−5.45,16.67)
Vit K2 vs Vit D3 MDS
−3.59 (−12.58,5.41) (−17.52,10.35)
Vit D3 EHDS vs Vit D3 HDS
5.81 (−2.46,14.09) (−7.46,19.09)
Vit K2 vs Vit D3 HDS
−3.39 (−15.67,8.90) (−20.59,13.82)
Vit K2 vs Vit D3 EHDS
−9.20 (−19.81,1.40) (−24.70,6.29)
−27
−16
0
7.5
19

FIN

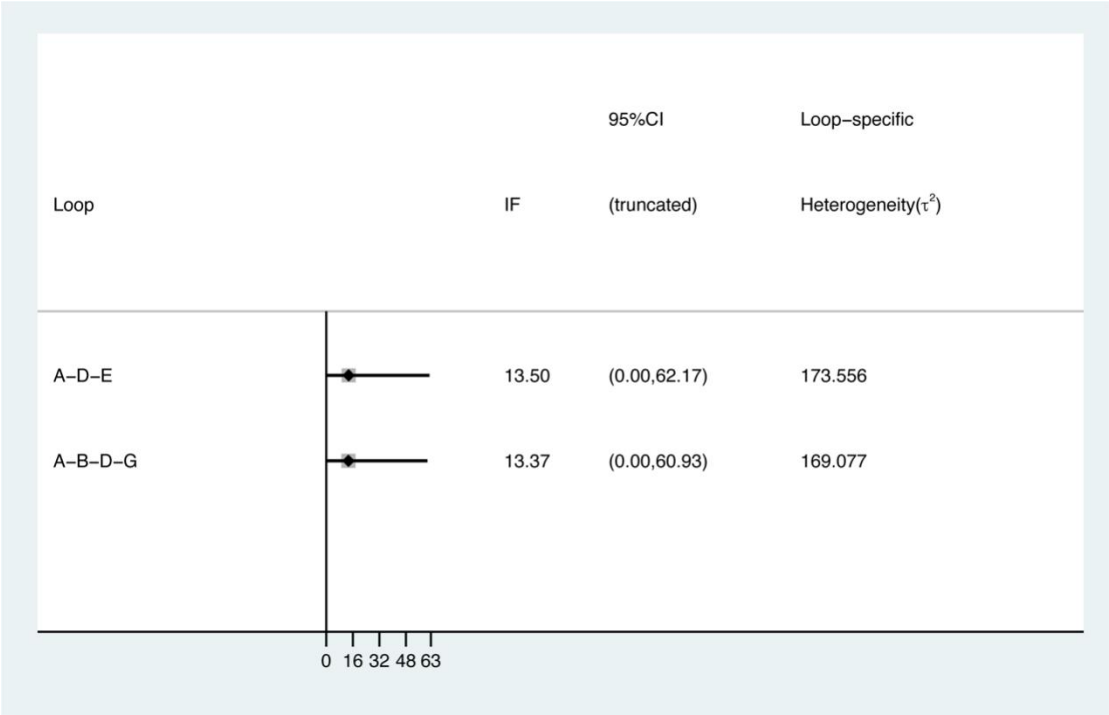


HOMA-IR

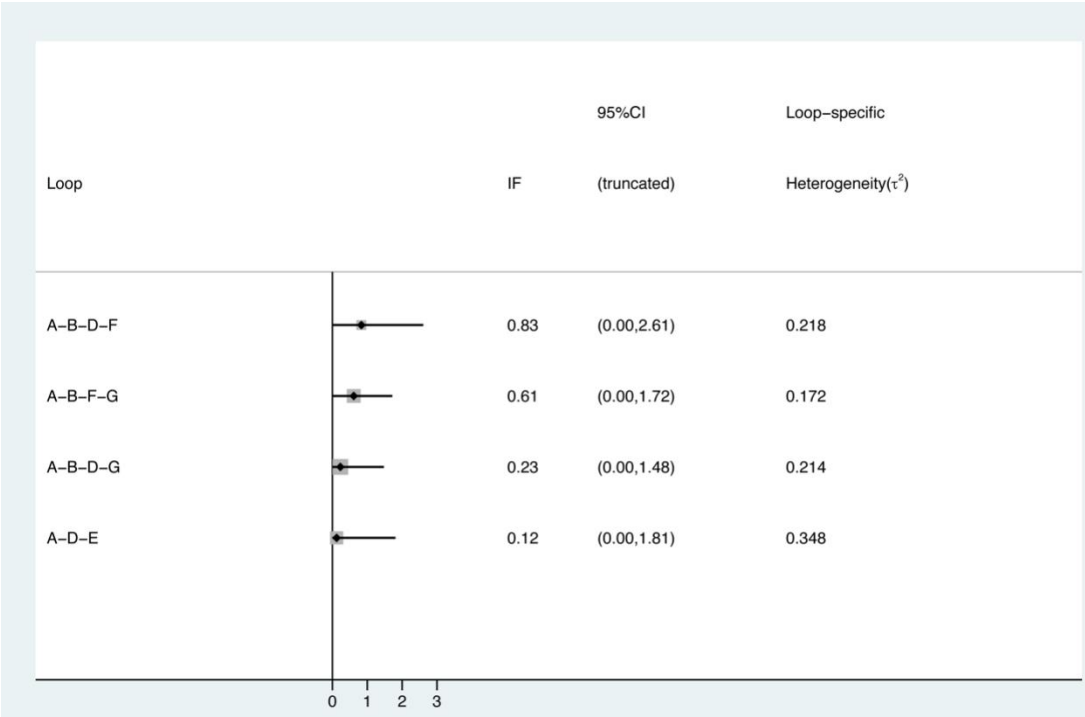
Supplementary Figure S10. Prediction interval for FBG, 25-(OH)-D, HbA1c, FIN ,and HOMA-IR. LDS, low dose strategy; MDS, medium dose strategy; HDS, high dose strategy; EHDS, extremely high dose strategy; FBG, fasting blood glucose; 25-(OH)-D, 25-hydroxyvitamin D; HbA1c, hemoglobin A1c; FIN, fasting insulin; HOMA-IR, homeostasis model assessment-insulin


Loop
IF
95%CI
(truncated)
Loop−specific
Heterogeneity(τ^2)
A−D−E
1.42
(0.00,2.94)
0.256
A−B−D−F
1.17
(0.64,1.71)
0.000
A−B−D−G
0.56
(0.00,1.19)
0.009
A−B−F−G
0.54
(0.00,1.10)
0.013
0
1
2
3

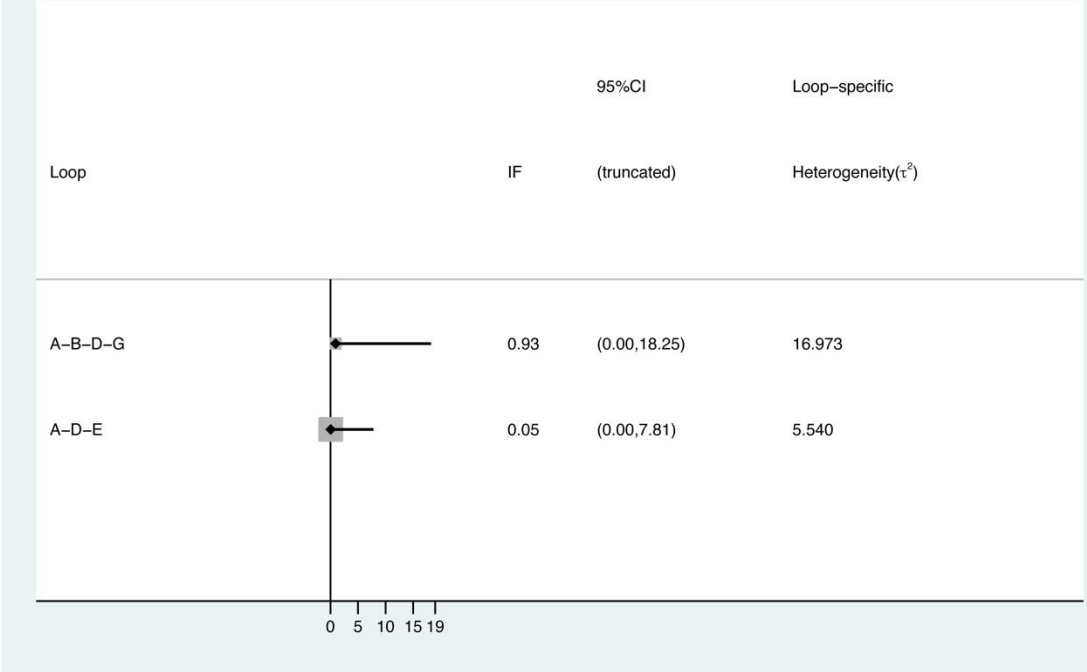
FBG


Loop
IF
95%CI
(truncated)
Loop−specific
Heterogeneity(τ^2)
A−D−E
13.50
(0.00,62.17)
173.556
A−B−D−G
13.37
(0.00,60.93)
169.077
0
16
32
48
63

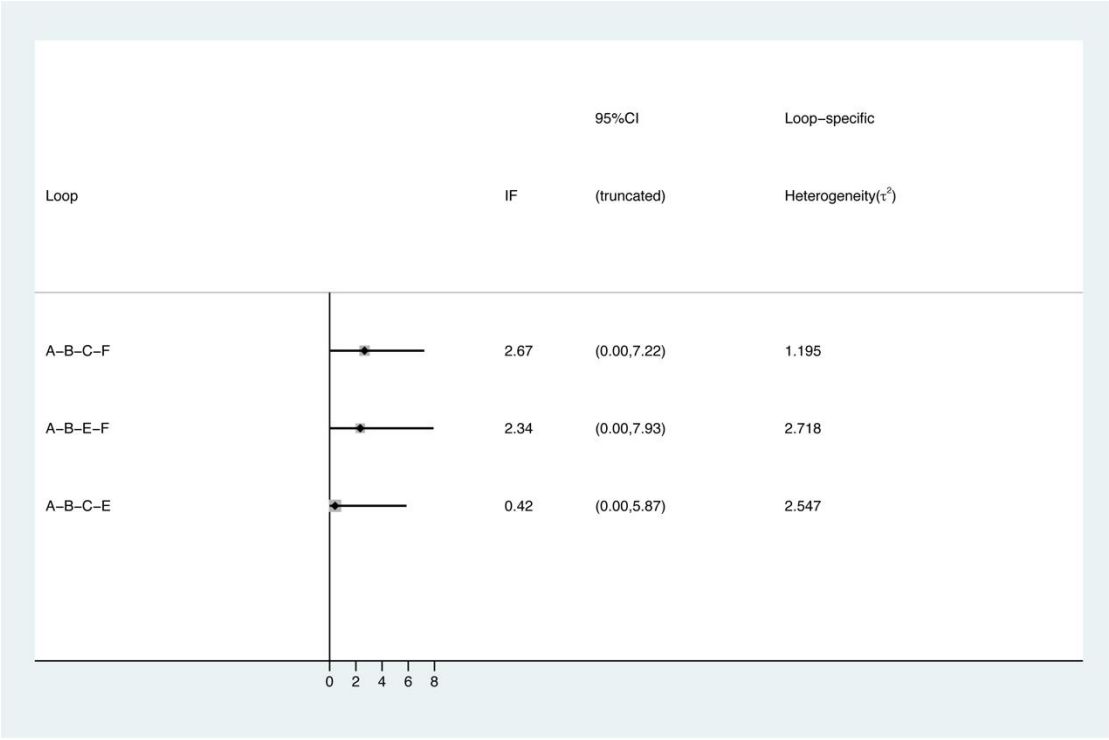
25-(OH)-D


Loop
IF
95%CI (truncated)
Loop−specific Heterogeneity(τ^2)
A−B−D−F
0.83
(0.00,2.61)
0.218
A−B−F−G
0.61
(0.00,1.72)
0.172
A−B−D−G
0.23
(0.00,1.48)
0.214
A−D−E
0.12
(0.00,1.81)
0.348
0 1 2 3

HbA1c


Loop
IF
95%CI (truncated)
Loop−specific Heterogeneity(τ^2)
A−B−D−G
0.93
(0.00,18.25)
16.973
A−D−E
0.05
(0.00,7.81)
5.540
0 5 10 15 19

FIN



HOMA-IR

Supplementary Figure S11. Loop inconsistency assessment for FBG, 25-(OH)-D, HbA1c, FIN, and HOMA-IR. LDS, low dose strategy; MDS, medium dose strategy; HDS, high dose strategy; EHDS, extremely high dose strategy; FBG, fasting blood glucose; 25-(OH)-D, 25-hydroxyvitamin D; HbA1c, hemoglobin A1c; FIN, fasting insulin; HOMA-IR, homeostasis model assessment-insulin

Supplementary Table S1. Characteristics of studies included in the meta-analysis

Study	Registration	Country	Females, %	Follow-up, years	Treatment	Sample size	Mean age, years	BMI, kg/m^2
Jorde 2009	NCT00400491	Norway	43.8	6	vitamin D3 (40000IU/week)	16	55.7±9.7	32.8±6.8
					placebo	16	54.8±5.9	31.3±6.3
Patel 2010	NR	Israel	70.8	4	vitamin D3 (400IU/d)	13	61±4	32.9±2.0
					vitamin D3 (1200IU/d)	11	54±3	31.8±2.1
Nikooyeh 2011	NCT01229891	Iran	61.1	3	fortified yogurt (1000IU vitamin D3 and 300 mg Ca/d)	30	51.4±5.4	29.2±4.4
					plain yogurt (300 mg Ca/d)	30	50.8±6.6	29.9±4.7
Shab-Bidar 2011	NCT01236846	Iran	57	3	fortified yogurt (1000IU vitamin D3 and 340 mg Ca/d)	50	52.6±6.3	28.6±4.0
					plain yogurt (340 mg Ca/d)	50	52.4±8.4	30.0±4.2
Punthakee 2012	NCT00879970	33 country	40.9	4	vitamin D3 (1000IU/d)	607	66.7±6.7	30.6±5.3
					placebo	614	66.6±6.3	30.7±5.3
Breslavsky 2013	NR	Israel	53.2	12	vitamin D3 (1000IU/d)	24	66.8±9.2	27.9±5.2
					placebo	23	65.8±9.7	30.6±5.1
Nasri 2013	IRCT201011185191N6	Iran	71.7	3	vitamin D3 (50000IU/week)	30	55±10.7	NR
					placebo	30		NR
Ryu 2014	NCT01854463	Korea	NR	24	vitamin D3 (2000IU/d)	32	54.5±7.9	24.4±5.0
					placebo	30	56.7±7.9	25.3±3.4
Ghavamzadeh, Mobasseri 2014	NR	Iran	58.8	3.5	vitamin D3 (400IU/d)	26	52.26±10.66	28.9±0.86
					placebo	25	49.28±10	27.9±0.93
Kampmann 2014	NCT00812578	Denmark	46.7	3	vitamin D3 (11200 IU/d)	7	61.6±4.4	35.3±2.9
					placebo	8	57±4.5	32.4±2.0

Study	Registration	Country	Females, %	Follow-up, years	Treatment	Sample size	Mean age, years	BMI, kg/m^2
Ryu 2014	NCT01854463	Korea	50	6	vitamin D3 (2000IU/d)+Ca(200mg/d)	64	54.8±7.6	25.0±3.3
					Ca (200mg/d)	65	55.9±8.1	25.6±3.6
Elkassaby 2014	ACTRN 12611001023943	Australia	42	6	vitamin D3 (10000 IU × 2 weeks + 6000 IU × 22 weeks)	26	53	30.6(26.6–36.4)
					placebo	24	51	31.1(26.7–38.0)
Al-Zahrani 2014	NR	Saudi	51.4	3	vitamin D3 (45000 IU / week)	91	56.9±9.4	31.3±4.5
					placebo	92	52.5±8.1	32±5.7
Al-Sofiani 2015	ACTRN12612000714886	Saudi Arabia	25	12	vitamin D3 (5000IU/d)	10	54.8±9.16	28.8±3.1
					placebo	10	55±11.99	33.35±6.09
Krul-Poel 2015	NTR3154	Netherlands	34.9	6	vitamin D3 (5000IU/week)	129	67±8	28.7±4.6
					placebo	132	67±9	28.5±4.5
Sadiya 2015	NR	United Arab Emirates	82	6	vitamin D3 (4500IU/d)	43	49±8	37.9±6.1
					placebo	39	48±8	37.6±7.7
Rashidi 2016	NR	Iran	41.7	3	vitamin D3 (50000IU/2 weeks)	48	47.09±7.38	28.08±3.46
					placebo	46		28.65±2.9
Jafari 2016	IRCT2013110515294N1	Iran	100	3	fortified yogurt (vitamin D3 2000IU/d + Ca 150mg)	30	57.8±5.5	28±0.82

Study	Registration	Country	Females, %	Follow-up, years	Treatment	Sample size	Mean age, years	BMI, kg/m^2
					plain yogurt (150 mg Ca/d)	29	56.8±5.7	29.3±0.72
Dalan 2016	NCT01741181	Singapore	48.4	4	vitamin D3 (4000IU/d or 2000IU/d)	33	52.2±8.2	27.3±5.8
					placebo	31	54.8±10.8	28.9±6.0
Agarwal 2017	NR	India	50	3	vitamin D3 (4000IU/d)	30	57.1±11.7	NR
					No-treatment Control	30	53.6±10	NR
Gulseth 2017	NCT00992797	Norway	40.3	6	vitamin D3 (400000IU/once)	33	55.5±9.2	32.5±5.1
					placebo	29	55.9±9.2	31.1±4.7
Anyanwu 2017		Nigeria	57.6	3	vitamin D3 (3000IU/d)	17	52±2	28.4±4
					placebo	16	51±2	26.5±0.9
Angellotti 2018	NCT01736865	United States	29.9	12	vitamin D3 (4000IU/d)	68	60.1±8.4	30.7±3.9
					placebo	61	60.3±8.5	31.2±3.8
Khan 2018	NR	Pakistan	NR	3	Metformin+VitaminD3 (50000IU/week)	70	54.8±8.55	NR
					Metformin	70	58.4±7.98	NR
Lo 2019	NCT01855321	United States	76.7	6	vitamin D2 (50000 IU/week)	14	60.1±2.2	37.4±2.4
					placebo	16	56.1±1.5	39.8±2.5
Imanparast 2019	IRCT 2017052034038N1	Iran	47.8	4	vitamin D3 (50000IU/week)	23	53.63±12.29	28.29±2.64
					placebo	23	51.72±9.11	28.38±2.14
Omidian 2019	NCT03008057	Iran	37.9	3	vitamin D2 (4000IU/d)	32	49.7±6.5	27.3±2.3
					placebo	34	51.3±5.9	27.5±1.6

Study	Registration	Country	Females, %	Follow-up, years	Treatment	Sample size	Mean age, years	BMI, kg/m^2
Omidian 2019	NCT03008057	Iran	50	3	vitamin D2 (4000IU/d)	23	51.3±4.7	26.8±1.4
					placebo	23	52.4±5.7	27.5±1.6
Wenclewska 2019	NR	Poland	NR	3	vitamin D3 (2000IU/d)	18	69.78±2.19	29.95±0.88
					No-treatment Control	14	72.57±3.02	29.41±0.78
Aguayo-Ruiz 2020	NCT04041492	Mexico	60	3	vitamin D3 (1000IU/d)	16	55.31±8.85	30.23±6.25
					vitamin K2 (100µg/d)	12	55.42±12.62	28.49±7.44
El Hajj 2020	NCT03782805	Lebanon	48.9	6	vitamin D3 (30000IU/week)	45	66.9±4.1	22.6±1.72
					placebo	43	65.7±4.5	23.2±5.71
Barale 2021	NR	Italy	30	12	vitamin D3 (5000IU/d)	16	71.6±3.5	29.7±3.8
					No-treatment Control	14	71.4±3.5	30.0±3.6
Mozaffari 2021	IRCT 20190505043480N1	Iran	61.2	3	vitamin D3 (50000IU/week)	40	55.1±9.4	29.66±4.58
					placebo	40	55.8±12.28	29.39±4.58
Zarei 2021	IRCT20170813035665N2	Iran	50	3	vitamin D3 (4000IU/d)	37	50.57±5.6	NR
					placebo	37	51.04±6.31	NR
Cojic 2021	ISRCTN25609316	Serbia	50	6	Metformin+VitaminD3 (32000IU/week)	49	60.41±8.5	30.13±4.6
					Metformin	65	63.65±8.2	29.79±5.0
Ahmed S 2022	NR	Iraq	100	4	vitamin D3 (5000IU/d)	65	NR	NR
					placebo	65	NR	NR
Praveenkumar 2022	NR	India	48.5	4	vitamin D3 (6000IU/week)	34	61±6.46	25±3.22
					placebo	34	60±7.97	24±3.29
Sun 2023	ChiCTR1800015383	China	NR	3	vitamin D3 (1000IU/d)	16	NR	25.3±3.3

Study	Registration	Country	Females, %	Follow-up, years	Treatment	Sample size	Mean age, years	BMI, kg/m^2
					placebo	15	NR	27.2±3.3
Hu 2023	NR	China	73.6	30	vitamin D3 (800IU/d)	115	66.05±9.35	24.86±3.88
					No-treatment Control	105	66.12±7.75	24.55±3.23
Thenmozhi 2024	NR	India	7	3	vitamin D3 (120000IU/week)	30	46±5.62	37.21±3.12
					No-treatment Control	30	47±7.42	38.34±2.19

Note: BMI, body mass index; IU, International Unit; NR, no response.

Supplementary Table S2. Node-splitting method for fasting blood glucose (FBG), 25-(OH)-D, hemoglobin A1c (HbA1c), fasting insulin (FIN), homeostasis model assessment-insulin resistance (HOMA-IR).

FBG

Side	Direct		Indirect		Difference			tau
	Coef.	Std. Err.	Coef.	Std. Err.	Coef.	Std. Err.	*P*>|z|	
A C								
A D	0.1816553	0.2251788	-0.7844327	0.3056006	0.966088	0.3779774	0.011	0.2775019
A E	-0.4624032	0.2908977	0.6595226	0.4690167	-1.121926	0.5510669	0.042	0.2775019
A F	-0.4624032	0.2908977	0.6595226	0.4690167	-1.121926	0.5510669	0.042	0.3372658
A G	-0.2570677	0.2103003	-0.2873574	0.4416796	0.0302897	0.4819313	0.95	0.3952905
B D	-0.7800006	0.418893	-0.3242826	0.3586649	-0.455718	0.5514632	0.409	0.3716459
B F	-0.060008	0.3897234	-0.5307466	0.349016	0.4707386	0.5231592	0.368	0.3638001
B G	-0.5817958	0.270493	-0.5515185	0.4075371	-0.0302773	0.4828702	0.95	0.3953985
D E	0.6600019	0.4120857	-0.4621219	0.3660006	1.122124	0.5511545	0.042	0.3372647
E H *	0.28	0.6814264	0.4695289	83.85602	-0.1895289	83.85627	0.998	0.3681517

25-(OH)-D

Side	Direct		Indirect		Difference			tau
	Coef.	Std. Err.	Coef.	Std. Err.	Coef.	Std. Err.	*P*>|z|	
A C								
A D	31.68891	8.549884	17.41001	15.80033	14.2789	17.96421	0.427	18.67838
A E	27.09104	11.56174	39.36546	20.50512	-12.27442	23.53983	0.602	18.82344
A F								
A G	49.82787	6.093655	61.61739	23.55438	-11.78951	24.31884	0.628	18.83154
B D	17.60003	18.94744	29.53384	15.29858	-11.9338	24.35266	0.624	18.83299
B G	49.57475	11.53038	37.71557	21.44398	11.85918	24.34411	0.626	18.83256
D E	9.750725	18.92755	-2.948213	14.09691	12.69894	23.60028	0.591	18.82634

HbA1c

Side	Direct		Indirect		Difference			tau
	Coef.	Std. Err.	Coef.	Std. Err.	Coef.	Std. Err.	*P*>|z|	
A C								
A D	-0.4712112	0.2210493	-0.2211934	0.3780122	-0.2500177	0.4377502	0.568	0.4429383
A E	-0.1594787	0.2520941	-0.2152154	0.5076953	0.0557367	0.5663865	0.922	0.4446868
A F	0.0103967	0.2018973	-0.6528647	0.5176961	0.6632615	0.5554855	0.232	0.4291119
A G	-0.2392442	0.1384403	-0.0278633	0.4616074	-0.2113809	0.4822156	0.661	0.4403126
B D	-0.28	0.4698221	-0.6597305	0.341187	0.3797305	0.5806388	0.513	0.442766
B F	-0.6200005	0.4433391	0.0438798	0.3351054	-0.6638803	0.5557387	0.232	0.4291182
B G	-0.2649756	0.2928941	-0.4764187	0.3825075	0.2114431	0.4823141	0.661	0.4403165
D E	0.199994	0.4645567	0.2562248	0.3243429	-0.0562308	0.5665782	0.921	0.4446949

FIN

Side	Direct		Indirect		Difference			tau
	Coef.	Std. Err.	Coef.	Std. Err.	Coef.	Std. Err.	*P*>|z	
A C								
A D	-0.7215316	3.229365	-0.8956764	4.017083	0.1741449	5.157305	0.973	4.180138
A E	-4.673203	2.609695	-5.086289	5.207429	0.4130861	5.824783	0.943	4.18438
A F								
A G	0.8728809	2.34001	1.86131	6.757748	-0.9884288	7.156629	0.89	4.16565
B D	-3.760002	4.34303	-2.769441	5.690143	-0.9905603	7.158184	0.89	4.16584
B G	-1.250001	4.413164	-2.239513	5.635949	0.9895118	7.158207	0.89	4.165841
D E	-4.199932	4.330014	-3.776122	3.904798	-0.4238102	5.830645	0.942	4.185247
E H *	-3.59	4.589796	9.004492	450.7486	-12.59449	450.7697	0.978	3.696538

HOMA-IR

Side	Direct		Indirect		Difference			tau
	Coef.	Std. Err.	Coef.	Std. Err.	Coef.	Std. Err.	*P*>|z	
A C	0.1115824	0.9476821	-1.326445	1.674366	1.438027	1.923929	0.455	1.192233
A D *	-1.978848	1.018052	4714284	59.09903	-2.450276	59.1078	0.967	1.140028
A E	-0.5284093	0.6484695	-1.42825	1.775049	0.8998411	1.890719	0.634	1.228802
A F	-1.067712	0.8957149	1.362185	1.596591	-2.429897	1.831417	0.185	1.103134
B C	-1.47	1.278188	-0.0318504	1.438123	-1.43815	1.924048	0.455	1.192246
B E	-1.680006	1.339522	-0.779551	1.335229	-0.9004555	1.891344	0.634	1.228872
B F	0.0199999	1.241393	-2.410154	1.346644	2.430154	1.831532	0.185	1.103145
D G *	-1.1	1.391565	3.800553	118.2091	-4.900553	118.214	0.967	1.140028
A C	0.1115824	0.9476821	-1.326445	1.674366	1.438027	1.923929	0.455	1.192233