Supplementary Online Content

Beveridge LA, Struthers AD, Khan F, et al; D-PRESSURE Collaboration. Effect of vitamin D supplementation on blood pressure: a systematic review and meta-analysis incorporating individual patient data. *JAMA Intern Med.* Published online March 16, 2015. doi:10.1001/jamainternmed.2015.0237

This supplementary material has been provided by the authors to give readers additional information about their work.

eAppendix: Search strategy for D-PRESSURE systematic review

[vitamin D OR vitamin D2 OR vitamin D3 OR cholecalciferol OR ergocalciferol OR alphacalcidol OR alfacalcidol OR calcitriol OR paricalcitol OR doxerocalciferol]

AND

[randomised controlled trial OR placebo]

AND

[blood pressure OR hypertension OR vascular OR cardiovascular OR mortality]

Applied to all fields within database; not restricted to MeSH headings

eTable 1. Characteristics of Included Studies

Study	*N*	*Latitude*	*Study Population*	*Outcomes*	*Mean Age*	*% Male*	*Mean baseline 25OHD* (nmol/l)	*Mean baseline SBP* (mmHg)	*Control*	*Intervention*	*Duration*
Lind et al[1], Sweden, 1987	29	60° N	Healthy volunteers with intermittent hypercalcaemia	Blood pressure	63	40	Not known	149	Placebo	Alphacalcidol 1 µg/day	6 months
Lind et al[2], Sweden, 1988a	36	61° N	Patients with primary hyperparathyroidism	Blood pressure	65	19	Not known	149	Placebo	Alphacalcidol (0.25 µg/day up-titrated to 1 µg/day after 8 weeks)	6 months
Lind et al[3], Sweden, 1988b	65	60° N	Patients with impaired glucose tolerance	Blood pressure and glucose tolerance	Not stated	100	Not known	152	Placebo	Alphacalcidol 0.75µg/day	12 weeks
Lind et al[4], Sweden, 1989	42	61° N	Patients with mild to moderate hypertension	Blood pressure and plasma renin activity	51	80	Not known	157	Placebo	Alphacalcidol 1µg/day	18 weeks
Myrup et al[5], Denmark, 1992	113	56° N	Elderly female patients	Blood pressure, cholesterol, weight	70	0	Not known	101 (MAP)	Placebo	Calcitriol 0.5µg/day	12 months
Pan et al[6], Taiwan, 1993	58	25° N	Institutionalised adults	Blood pressure	74	78	61	133	Placebo	Cholecalciferol 200IU/day + placebo	11 weeks
Scragg et al[7], England, 1995	191	52° N	Elderly patients	Blood pressure, cholesterol	70	54	35	148	Placebo	Cholecalciferol 100,000IU once-off	5 weeks
Pfeifer et al[8], Germany, 2001	148	52° N	Elderly female patients	Blood pressure, cholesterol	75	0	25	142	Calcium 1200mg/daily +Placebo	Calcium 1200mg/ daily + Cholecalciferol 800IU/day	8 weeks
Schleithoff et al[9], Germany,	123	51° N	Heart failure patients	Blood pressure, cytokine levels, survival	55	83	38 (median)	123	Calcium 500mg once/daily +	Calcium 500mg/ once daily + Cholecalciferol 2000IU/day	9 months

2006									placebo		
Alborzi et al[10], USA, 2008	24	40° N	Patients with chronic kidney disease and on ACE-I or ARB	Endothelial function, 24 hour ambulatory BP, GFR, CRP	70	83	34	125.4 (24hr BP)	Placebo	Paricalcitol 1µg daily Paricalcitol 2µg daily	1 month
Sugden et al[11], Scotland, 2008	34	56 ° N	Type 2 Diabetes patients	Endothelial function, blood pressure, insulin sensitivity	64	53	38	141	Placebo	Ergocalciferol 100,000IU single dose	8 weeks
Nagpal et al[12], India, 2009	100	28° N	Centrally obese, non-diabetic, healthy males	Insulin sensitivity, insulin secretion, lipid concentration, blood pressure	44	100	33	124	Placebo	Cholecalciferol 120,000IU /2 weekly	6 weeks
Zittermann et al[13], Germany, 2009	200	52° N	Healthy overweight subjects participating in weight reduction program	Weight loss, cardiovascular disease risk markers including blood pressure	48	33	30	128	Placebo	Cholecalciferol 3332 IU/day	12 months
Jorde et al[14], Norway, 2010	438	69° N	Overweight or obese subjects without diabetes or IHD	Cardiovascular risk factors	48	36	58	124	Placebo + 500mg calcium/day	Cholecalciferol 20,000 IU weekly + 500mg calcium/day Cholecalciferol 40,000 IU weekly + 500mg calcium/day	12 months
Witham et al[15], Scotland, 2010a	61	56° N	Type II Diabetes and baseline Vitamin D <100nmol/l	Endothelial function, blood pressure, markers of glycaemic control	65	67	45	146	Placebo	100,000 IU Cholecalciferol 200,000 IU cholecalciferol single dose	16 weeks
Witham et al[16], Scotland, 2010b	105	56° N	Older adults with heart failure	Walk test, physical activity, cardiovascular and inflammatory markers, blood pressure	80	66	22	141	Placebo	Ergocalciferol 100,000 IU 10 weekly.	20 weeks
de Zeeuw et al[17],	281	Multinational	Patients with Type II diabetes and	Albuminuria, eGFR, blood	64	65	41	142	Placebo	Paricalcitol 1µg daily Paricalcitol 2µg daily	24 weeks

Multinational, 2010			albuminuria receiving ACEi/ARBs	pressure							
Harris et al[18], USA, 2011	45	33° N	African-American Adults with no overt cardiovascular, pulmonary or metabolic disease	Endothelial function, anthropometric assessments, blood pressure	30	47	36	124	Placebo	Cholecalciferol 60,000IU/ 4 weekly	16 weeks
Shab-Bidar et al[19], Iran 2011	100	36° N	Non-insulin requiring Type II Diabetes Mellitus	Glycaemic status, lipid profile and endothelial biomarkers	53	43	38	127	Plain Yoghurt Drink with 170mg/ calcium twice a day	Cholecalciferol fortified yoghurt drink 170mg/calcium and 500IU/250ml twice daily	12 weeks
Alvarez et al[20], USA, 2012	48	34° N	Early chronic kidney disease	Vitamin D status, circulating PTH concentrations	62	95	74	129	Placebo	Cholecalciferol 50,000 IU/ week for 12 weeks then 50,000 IU every other week for 40 weeks.	12 months
Bonakdaran et al[21], Iran, 2012	51	35° N	Untreated Polycystic Ovarian syndrome Patients	Improvement in ovulation, insulin resistance, blood pressure	25	0	51	110	Placebo	Metformin 1g/day; Calcitriol 0.5µg/day	3 months
Gepner et al[22], USA, 2012	114	43° N	Healthy community dwelling postmenopausal females with serum vitamin D >10 and <60ng/ml	Endothelial function (pulse wave velocity, flow mediated dilatation, augmentation index)	64	0	78	119.4	Placebo	Cholecalciferol 2500 IU/day	4 months
Heshmat et al[23], Iran, 2012	42	36° N	Type II Diabetes Mellitus	Insulin resistance and anthropometric factors	56	36	103	119	Placebo	Cholecalciferol 300,000IU once-off	3 months
Kjaergaard et al[24], Norway, 2012	243	69° N	Adults aged 30-75 years	Depressive symptoms,	53	44	48	129	Placebo	Cholecalciferol 40,000 IU once weekly	6 months
Larsen et al[25], Denmark,2012	130	56° N	Caucasian hypertensive patients	Blood pressure, arterial stiffness	61	31	58	143	Placebo	Cholecalciferol 3000 IU/day	20 weeks

Longenecker et al[26], 2012, USA	45	42° N	Vitamin D deficient HIV infected adults	Endothelial function	45	78	21	118	Placebo	Cholecalciferol 4000 IU daily	12 weeks
Muldowney et al[27], Ireland 2012a	209	51-55° N	Older adults aged >64 years during winter	Biomarkers of cardiovascular disease risk	71	40	54	146	Placebo	Cholecalciferol 200 IU per day or 400 IU per day or 600 IU per day	22 weeks
Muldowney et al[27], Ireland 2012b	233	51-55° N	Young adults aged 20-40 years during winter	Biomarkers of cardiovascular disease risk	30	51	70	124	Placebo	Cholecalciferol 200 IU per day or 400 IU per day or 600 IU per day	22 weeks
Salehpour et a [28], Iran, 2012	85	36° N	Healthy premenopausal overweight and obese women	Blood pressure, lipid profile, anthropometric parameters	38	0	42	113.5	Placebo	Cholecalciferol 1000 IU/day	90 days
Stricker et al[29], Switzerland, 2012	62	46° N	Chronic peripheral vascular disease and vitamin D deficiency	Endothelial function and arterial stiffness, coagulation and inflammation parameters.	74	61	42	137	Placebo	Cholecalciferol (Vitamin D3) 100,000 IU single dose	1 month
Witham et al[30], Scotland, 2012	58	56° N	Older adults with previous stroke	Blood pressure, endothelial function	67	72	38	128	Placebo	100,000 IU Ergocalciferol	16 weeks
Wood et al[31], Scotland, 2012	305	57° N	Healthy Postmenopausal women aged 60-70 years	Lipid profile, insulin resistance, inflammatory biomarkers, blood pressure	64	0	34	128.5	Placebo	400 IU/day Cholecalciferol 1000 IU/day Cholecalciferol	1 year
Asemi et al[32], Iran, 2013	54	34° N	Pregnant women in Iran	C-Reactive Protein, Insulin resistance and biomarkers of oxidative stress	25	0	40	112	Placebo + 400µg/day folic acid + 60 µg/day iron	Cholecalciferol 400 IU/day + 400µg/day folic acid + 60 µg/day iron	9 weeks
Boxer et al[33], USA, 2013	64	41° N	Over 50 year olds with heart failure and vitamin D deficiency	Cardiopulmonary stress testing	66	52	46	116	Placebo once weekly + Calcium Citrate 400mg twice	Cholecalciferol 50,000 IU weekly + Calcium Citrate 400mg twice daily	6 months

									daily		
Breslavsky et al[34], Israel, 2013	47	32° N	Type II Diabetics with cardiovascular risk factors	Arterial properties, adiponectin, leptin and glucose homeostasis	66	47	30	153	Placebo	Cholecalciferol 1000 IU/day	12 months
Chai et al[35], USA, 2013	92	21° N	30 – 75 year olds with adenomatous colorectal polys	Blood pressure, serum lipids and carotenoids	61	70	Not known	126	Placebo	Calcium carbonate 2g/day OR Cholecalciferol 800 IU/day OR Calcium carbonate 2g/day + Cholecalciferol 800 IU/day	6 months
Forman et al[36], USA, 2013	283	42° N	Healthy Black Population	Systolic and diastolic blood pressure	51	35	39	122	Placebo +200mg calcium daily	Cholecalciferol 1000 IU/day or 2000 IU/day or 4000 IU/day all + 200mg calcium daily	3 months
Larsen et al[37] 2013, Denmark	30	56° N	Non-diabetic, albuminuric stage II-IV chronic kidney disease	Plasma renin concentration, albuminuria	61	73	56	136	Placebo	Paricalcitol 2 µg daily	6 weeks
Petchey et al[38], Australia, 2013	28	28° S	Chronic Kidney Disease Stage 3-4	Insulin resistance	66	71	91	135	Placebo	Cholecalciferol 2000IU daily	6 months
Roth et al[39], Bangladesh, 2013	160	24° N	Third trimester of pregnancy	Vitamin D status	22	0	45	104	Placebo	Cholecalciferol 35,000 IU weekly	Mean 10 weeks
Toxqui et al[40], Spain, 2013	129	40° N	Healthy 18-35 year old Caucasian women	Iron and bone metabolism biomarkers, blood pressure, glucose and lipid levels	25	0	63	109	15mg Iron-fortified dairy product	15mg iron fortified dairy product and 200 IU cholecalciferol daily	16 weeks
Wamberg et al[41], Denmark, 2013	55	56° N	Obese subjects aged 18-50years with low vitamin D levels	Obesity related complications such as chronic low grade inflammation, insulin resistance, hypertension and	40	29	35	133	Placebo	Cholecalciferol 7000 IU/day	26 weeks

				hyperlipidaemia							
Witham 2013 et al[42], Scotland, 2013a	159	56° N	Isolated systolic hypertension in over 70 year olds	Blood pressure, Endothelial function	77	52	45	163	Placebo	Cholecalciferol 100,000 IU three monthly	12 months
Witham et al[43], Scotland, 2013b	75	56 ° N	Recent myocardial infarction patients	Endothelial function, blood pressure, cholesterol	66	69	47	127.5	Placebo	Cholecalciferol 100,000IU/ 2 monthly	6 moths
Witham et al[44], Scotland, 2013c	50	56° N	South-east Asian women living in UK for 10 years	Macrovascular and microvascular endothelial function	41	0	27	120	Placebo	Cholecalciferol 100,000 IU once off	8 weeks
Yiu et al[45], Hong Kong 2013	100	22° N	Type II diabetes mellitus with suboptimal vitamin D status	Endothelial function, endothelial progenitor cells, CRP	65	50	54	146	Placebo	Cholecalciferol 5000 IU daily	12 weeks
Dalbeni et al[46], Italy, 2014`	36	45° N	Chronic heart failue aged >40 years	Ejection fraction and echocardiography parameters	72	74	44	133	Placebo	Cholecalciferol 600,000 IU at baseline, 100,000 IU at 10 weeks and 20 weeks	6 months
Scragg et al[47], New Zealand, 2014	322	44° S	Healthy adults	Number and severity of upper respiratory tract infections	48	25	71	123	Placebo	Cholecalciferol 200000 IU first month, 200000 IU second month then 100000 IU monthly	18 months
Sollid et al[48], Norway, 2014	511	70° N	Prediabetes	Glucose metabolism and cardiovascular risk factors	62	61	61	135	Placebo	Cholecalciferol 20000 IU weekly	12 months
Strobel et al[49], Germany 2014	86	50° N	Non-insulin requiring Type II Diabetes Mellitus	Insulin resistance and blood glucose levels	60	56	36	141	Placebo	Cholecalciferol 1904IU/day Once Weekly	6 months
Wang et al[50], Hong Kong, 2014	60	23° N	Stage 3-5 non-dialysis CKD with left ventricular hypertrophy	Change in Left Ventricular mass index	61	53	Not known	133	Placebo	Paricalcitol – if iPTH<500pg/ml Paricalcitol 1µg If iPTH >500pg/ml Paricalcitol 2µg	12 months

Witham et al[51], Scotland, 2014	68	56° N	Resistant hypertension	Blood pressure, glucose, cholesterol and Left ventricular mass index	63	65	42	154	Placebo	Cholecalciferol 100,000 IU every 2 months	6 months

eTable 2: Risk of Bias Table for All Included Studies

Study	Quality of allocation concealment	Analysis on intention to treat	Number and description of dropouts	Blinding – patients	Blinding – health care providers	Blinding – outcome assessors	Comparable treatment and placebo groups
Lind 1987[1]	+	U	+	U	U	U	-
Lind 1988a[2]	+	+	+	+	+	U	+
Lind 1988b[3]	+	U	_	+	+	+	-
Lind 1989[4]	+	+	+	+	+	U	+
Myrup 1992[5]	+	U	-	+	+	+	+
Pan 1993[6]	+	-	+	+	+	+	-
Scragg 1995[7]	+	+	+	+	+	+	+
Pfeifer 2001[8]	+	+	+	+	+	+	+
Schleithoff 2006[9]	+	-	+	+	+	+	+
Alborzi 2008[10]	+	+	+	+	+	+	-
Sugden 2008[11]	+	-	+	+	+	+	+
Nagpal 2009[12]	+	+	+	+	+	+	+
Zittermann 2009[13]	+	U	+	+	+	+	+
Jorde 2010[14]	+	-	+	+	+	+	+
Witham 2010a[15]	+	U	+	+	+	+	+
Witham 2010b[16]	+	+	+	+	+	+	+
de Zeeuw 2010[17]	+	+	+	+	+	+	+
Harris 2011[18]	+	U	+	+	+	+	+
Shab-Bidar 2011[19]	+	-	+	+	+	+	+

Alvarez 2012[20]	+	+	+	+	+	+	+
Bonakdaran 2012[21]	-	-	+	U	U	U	-
Gepner 2012[22]	+	+	+	+	+	+	+
Heshmat 2012[23]	+	U	+	+	+	+	-
Kjærgaard 2012[24]	+	-	+	+	+	+	+
Larsen 2012[25]	+	-	+	+	+	+	+
Longenecker 2012[26]	+	U	+	+	+	+	+
Muldowney 2012a[27]	+	-	+	+	+	+	+
Muldowney 2012b[27]	+	-	+	+	+	+	+
Salehpour 2012[28]	+	U	+	+	+	+	-
Stricker2012 [29]	+	+	+	+	+	+	-
Witham2012[30]	+	U	+	+	+	+	+
Wood 2012[31]	+	+	+	+	+	+	+
Asemi 2013[32]	+	-	+	+	+	-	+
Boxer 2013[33]	+	+	+	+	+	+	+
Breslavsky 2013[34]	+	-	+	U	U	U	+
Chai 2013[35]	+	U	+	+	+	+	-
Forman 2013[36]	+	+	+	+	+	+	-
Larsen 2013[37]	+	-	+	+	+	+	U
Petchey 2013[38]	+	-	+	+	+	+	-
Roth 2013[39]	+	+	+	+	+	+	+
Toxqui 2013[40]	+	-	+	+	+	+	+
Wamberg 2013[41]	+	+	+	+	+	+	+

Witham 2013a[42]	+	-	+	+	+	+	+
Witham 2013b[43]	+	+	+	+	+	+	+
Witham 2013c[44]	+	+	+	+	+	+	+
Yiu 2013[45]	+	+	+	+	+	+	+
Dalbeni 2014[46]	+	-	-	+	+	+	-
Scragg 2014[47]	+	+	+	+	+	+	+
Sollid 2014[48]	+	-	+	+	+	+	+
Strobel 2014[49]	+	-	+	+	+	+	+
Wang 2014[50]	+	+	+	+	+	+	+
Witham 2014[51]	+	+	+	+	+	+	+

+ Adequate / yes, - Inadequate / no, U: Unclear

References

1. Lind L, Wengle B, Ljunghall S. Blood pressure is lowered by vitamin D (alphacalcidol) during long-term treatment of patients with intermittent hypercalcaemia. A double-blind, placebo-controlled study. Acta Med Scand 1987;222(5):423-427.

2. Lind L, Wengle B, Wide L, Sorensen OH, Ljunghall S. Hypertension in primary hyperparathyroidism--reduction of blood pressure by long-term treatment with vitamin D (alphacalcidol). A double-blind, placebo-controlled study. Am J Hypertens 1988;1(4 Pt 1):397-402.

3. Lind L, Lithell H, Skarfors E, Wide L, Ljunghall S. Reduction of blood pressure by treatment with alphacalcidol. A double-blind, placebo-controlled study in subjects with impaired glucose tolerance. Acta Med Scand 1988;223(3):211-217.

4. Lind L, Wengle B, Wide L, Ljunghall S. Reduction of blood pressure during long-term treatment with active vitamin D (alphacalcidol) is dependent on plasma renin activity and calcium status. A double-blind, placebo-controlled study. Am J Hypertens 1989;2(1):20-25.

5. Myrup B, Jensen GF, McNair P. Cardiovascular risk factors during estrogen-norethindrone and cholecalciferol treatment. Arch Intern Med 1992;152(11):2265-2268.

6. Pan WH, Wang CY, Li LA, Kao LS, Yeh SH. No significant effect of calcium and vitamin D supplementation on blood pressure and calcium metabolism in elderly Chinese. Chin J Physiol 1993;36(2):85-94.

7. Scragg R, Khaw KT, Murphy S. Effect of winter oral vitamin D3 supplementation on cardiovascular risk factors in elderly adults. Eur J Clin Nutr 1995;49(9):640-646.

8. Pfeifer M, Begerow B, Minne HW, Nachtigall D, Hansen C. Effects of a short-term vitamin D(3) and calcium supplementation on blood pressure and parathyroid hormone levels in elderly women. J Clin Endocrinol Metab 2001 Apr;86(4):1633-1637.

9. Schleithoff SS, Zittermann A, Tenderich G, Berthold HK, Stehle P, Koerfer R. Vitamin D supplementation improves cytokine profiles in patients with congestive heart failure: a double-blind, randomized, placebo-controlled trial. Am J Clin Nutr 2006 Apr;83(4):754-759.

10. Alborzi P, Patel NA, Peterson C, et al. Paricalcitol reduces albuminuria and inflammation in chronic kidney disease: a randomized double-blind pilot trial. Hypertension 2008 Aug;52(2):249-255.

11. Sugden JA, Davies JI, Witham MD, Morris AD, Struthers AD. Vitamin D improves endothelial function in patients with type 2 diabetes mellitus and low vitamin D levels. Diabet Med 2008;25(3):320-325.

12. Nagpal J, Pande JN, Bhartia A. A double-blind, randomized, placebo-controlled trial of the short-term effect of vitamin D3 supplementation on insulin sensitivity in apparently healthy, middle-aged, centrally obese men. Diabet Med 2009;26(1):19-27.

13. Zittermann A, Frisch S, Berthold HK, et al. Vitamin D supplementation enhances the beneficial effects of weight loss on cardiovascular disease risk markers. Am J Clin Nutr 2009;89(5):1321-1327.

14. Jorde R, Sneve M, Torjesen P, Figenschau Y. No improvement in cardiovascular risk factors in overweight and obese subjects after supplementation with vitamin D3 for 1 year. J Intern Med 2010;267(5):462-472.

15. Witham MD, Dove FJ, Dryburgh M, Sugden JA, Morris AD, Struthers AD. The effect of different doses of vitamin D(3) on markers of vascular health in patients with type 2 diabetes: a randomised controlled trial. Diabetologia 2010 Oct;53(10):2112-2119.

16. Witham MD, Crighton LJ, Gillespie ND, Struthers AD, McMurdo ME. The effects of vitamin D supplementation on physical function and quality of life in older patients with heart failure: a randomized controlled trial. Circ Heart Fail 2010;3(2):195-201.

17. de Zeeuw D, Agarwal R, Amdahl M, et al. Selective vitamin D receptor activation with paricalcitol for reduction of albuminuria in patients with type 2 diabetes (VITAL study): a randomised controlled trial. Lancet 2010 Nov 6;376(9752):1543-1551.

18. Harris RA, Pedersen-White J, Guo DH, et al. Vitamin D3 supplementation for 16 weeks improves flow-mediated dilation in overweight African-American adults. Am J Hypertens 2011;24(5):557-562.

19. Shab-Bidar S, Neyestani TR, Djazayery A, et al. Regular consumption of vitamin D-fortified yogurt drink (Doogh) improved endothelial biomarkers in subjects with type 2 diabetes: a randomized double-blind clinical trial. BMC Med 2011;9:125.

20. Alvarez JA, Law J, Coakley KE, et al. High-dose cholecalciferol reduces parathyroid hormone in patients with early chronic kidney disease: a pilot, randomized, double-blind, placebo-controlled trial. Am J Clin Nutr 2012;96(3):672-679.

21. Bonakdaran S, Hami M, Hatefi A. The effects of calcitriol on albuminuria in patients with type-2 diabetes mellitus. Saudi J Kidney Dis Transpl 2012;23(6):1215-1220.

22. Gepner AD, Ramamurthy R, Krueger DC, Korcarz CE, Binkley N, Stein JH. A prospective randomized controlled trial of the effects of vitamin D supplementation on cardiovascular disease risk. PLoS One 2012;7(5):e36617.

23. Heshmat R, Tabatabaei-Malazy O, Abbaszadeh-Ahranjani S, et al. Effect of vitamin D on insulin resistance and anthropometric parameters in Type 2 diabetes; a randomized double-blind clinical trial. Daru 2012;20(1):10.

24. Kjaergaard M, Waterloo K, Wang CE, et al. Effect of vitamin D supplement on depression scores in people with low levels of serum 25-hydroxyvitamin D: nested case-control study and randomised clinical trial. Br J Psychiatry 2012 Nov;201(5):360-368.

25. Larsen T, Mose FH, Bech JN, Hansen AB, Pedersen EB. Effect of cholecalciferol supplementation during winter months in patients with hypertension: a randomized, placebo-controlled trial. Am J Hypertens 2012;25(11):1215-1222.

26. Longenecker CT, Hileman CO, Carman TL, et al. Vitamin D supplementation and endothelial function in vitamin D deficient HIV-infected patients: a randomized placebo-controlled trial. Antivir Ther 2012;17(4):613-621.

27. Muldowney S, Lucey AJ, Hill TR, et al. Incremental cholecalciferol supplementation up to 15 mug/d throughout winter at 51-55 degrees N has no effect on biomarkers of cardiovascular risk in healthy young and older adults. J Nutr 2012;142(8):1519-1525.

28. Salehpour A, Shidfar F, Hosseinpanah F, et al. Vitamin D3 and the risk of CVD in overweight and obese women: a randomised controlled trial. Br J Nutr 2012;108(10):1866-1873.

29. Stricker H, Tosi BF, Guidicelli-Nicolosi S, Limoni C, Colucci G. Effect of a single, oral, high-dose vitamin D supplementation on endothelial function in patients with peripheral arterial disease: a randomised controlled pilot study. Eur J Vasc Endovasc Surg 2012;44(3):307-312.

30. Witham MD, Dove FJ, Sugden JA, Doney AS, Struthers AD. The effect of vitamin D replacement on markers of vascular health in stroke patients - A randomised controlled trial. Nutr Metab Cardiovasc Dis 2012;22(10):864-870.

31. Wood AD, Secombes KR, Thies F, et al. Vitamin D3 Supplementation Has No Effect on Conventional Cardiovascular Risk Factors. A Parallel-Group, Double-Blind, Placebo-Controlled RCT. J Clin Endocrinol Metab 2012;97(10):3557-3568.

32. Asemi Z, Hashemi T, Karamali M, Samimi M, Esmaillzadeh A. Effects of vitamin D supplementation on glucose metabolism, lipid concentrations, inflammation, and oxidative stress in gestational diabetes: a double-blind randomized controlled clinical trial. Am J Clin Nutr 2013;98(6):1425-1432.

33. Boxer RS, Kenny AM, Schmotzer BJ, Vest M, Fiutem JJ, Pina II. A randomized controlled trial of high-dose vitamin D3 in patients with heart failure. JACC Heart Fail 2013;1(1):84-90.

34. Breslavsky A, Frand J, Matas Z, Boaz M, Barnea Z, Shargorodsky M. Effect of high doses of vitamin D on arterial properties, adiponectin, leptin and glucose homeostasis in type 2 diabetic patients. Clin Nutr 2013;32(6):970-975.

35. Chai W, Cooney RV, Franke AA, Bostick RM. Effects of calcium and vitamin D supplementation on blood pressure and serum lipids and carotenoids: a randomized, double-blind, placebo-controlled, clinical trial. Ann Epidemiol 2013;23(9):564-570.

36. Forman JP, Scott JB, Ng K, et al. Effect of vitamin D supplementation on blood pressure in blacks. Hypertension 2013;61(4):779-785.

37. Larsen T, Mose FH, Bech JN, Pedersen EB. Effect of paricalcitol on renin and albuminuria in non-diabetic stage III-IV chronic kidney disease: a randomized placebo-controlled trial. BMC Nephrol 2013 Jul 26;14(1):163.

38. Petchey WG, Hickman IJ, Prins JB, Hawley CM, Johnson DW, Isbel NM, et al. Vitamin D does not improve the metabolic health of patients with chronic kidney disease stage 3-4: a randomized controlled trial. Nephrology 2013;18(1):26-35.

39. Roth DE, Al Mahmud A, Raqib R, et al. Randomized placebo-controlled trial of high-dose prenatal third-trimester vitamin D3 supplementation in Bangladesh: the AViDD trial. Nutr J 2013;12(1):47.

40. Toxqui L, Blanco-Rojo R, Wright I, Perez-Granados AM, Vaquero MP. Changes in blood pressure and lipid levels in young women consuming a vitamin D-fortified skimmed milk: a randomised controlled trial. Nutrients 2013;5(12):4966-4977.

41. Wamberg L, Kampmann U, Stodkilde-Jorgensen H, Rejnmark L, Pedersen SB, Richelsen B. Effects of vitamin D supplementation on body fat accumulation, inflammation, and metabolic risk factors in obese adults with low vitamin D levels - results from a randomized trial. Eur J Intern Med 2013;24(7):644-649.

42. Witham MD, Price RJ, Struthers AD, et al. Cholecalciferol treatment to reduce blood pressure in older patients with isolated systolic hypertension: the VitDISH randomized controlled trial. JAMA Intern Med 2013;173(18):1672-1679.

43. Witham MD, Dove FJ, Khan F, Lang CC, Belch JJ, Struthers AD. Effects of vitamin D supplementation on markers of vascular function after myocardial infarction--a randomised controlled trial. Int J Cardiol 2013;167(3):745-749.

44. Witham MD, Adams F, Kabir G, Kennedy G, Belch JJ, Khan F. Effect of short-term vitamin D supplementation on markers of vascular health in South Asian women living in the UK--a randomised controlled trial. Atherosclerosis 2013;230(2):293-299.

45. Yiu YF, Yiu KH, Siu CW, et al. Randomized controlled trial of vitamin D supplement on endothelial function in patients with type 2 diabetes. Atherosclerosis 2013;227(1):140-146.

46. Dalbeni A, Scaturro G, Degan M, Minuz P, Delva P. Effects of six months of vitamin D supplementation in patients with heart failure: A randomized double-blind controlled trial. Nutr Metab Cardiovasc Dis 2014;24(8):861-868.

47. Scragg R, Slow S, Stewart AW, et al. Long-Term High-Dose Vitamin D3 Supplementation and Blood Pressure in Healthy Adults: A Randomized Controlled Trial. Hypertension 2014;64(4):725-730.

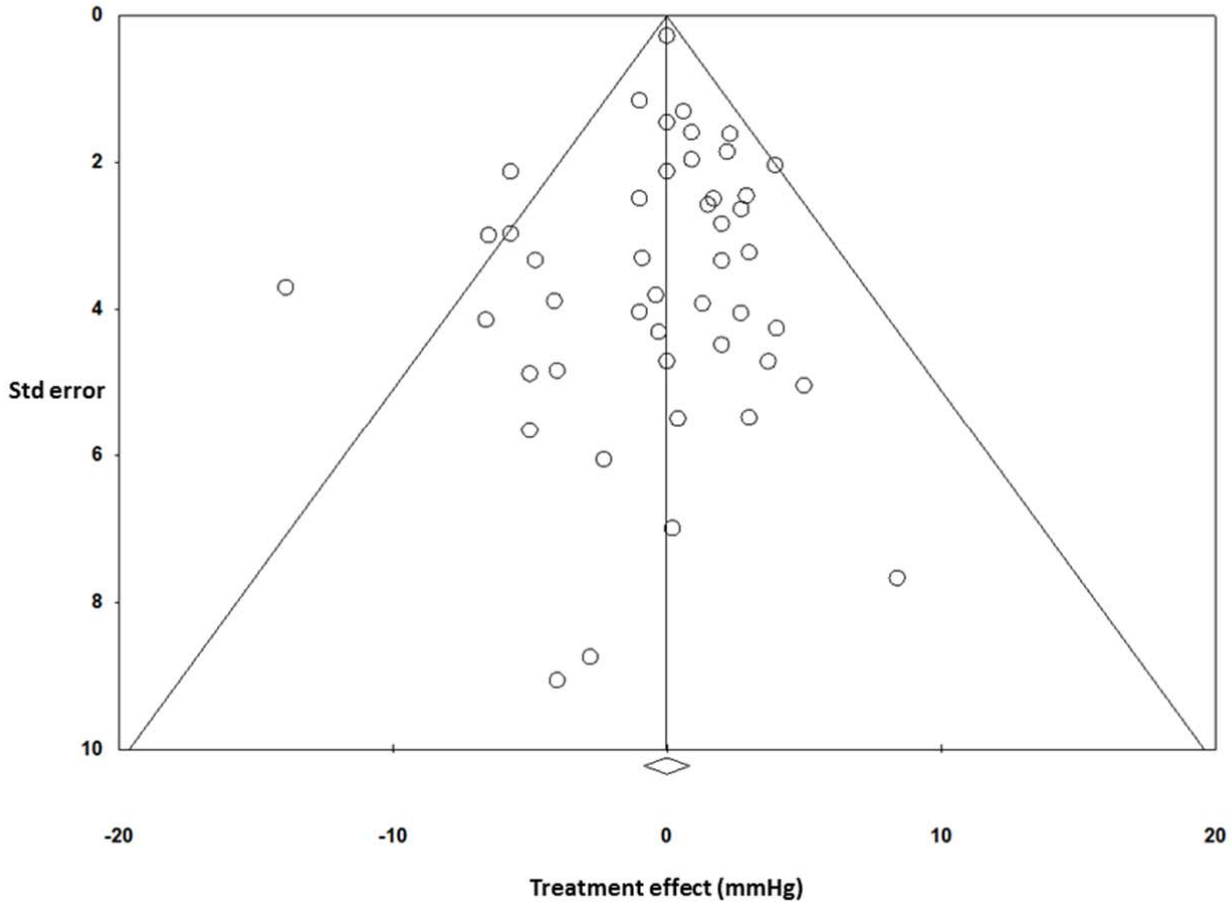
48. Sollid ST, Hutchinson MY, Fuskevag OM, et al. No Effect of High-Dose Vitamin D Supplementation on Glycemic Status or Cardiovascular Risk Factors in Subjects With Prediabetes. Diabetes Care 2014;37(8):2123-2131.

49. Strobel F, Reusch J, Penna-Martinez M, et al. Effect of a randomised controlled vitamin D trial on insulin resistance and glucose metabolism in patients with type 2 diabetes mellitus. Horm Metab Res 2014;46(1):54-58.

50. Wang AY, Fang F, Chan J, et al. Effect of paricalcitol on left ventricular mass and function in CKD--the OPERA trial. J Am Soc Nephrol 2014;25(1):175-186.

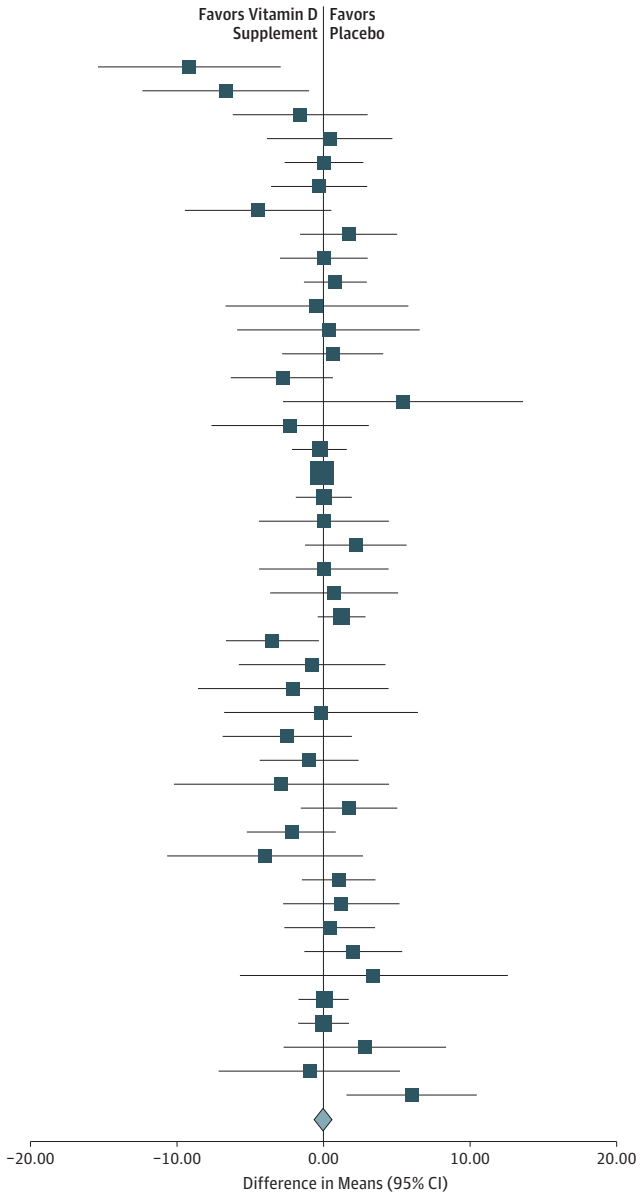
51. Witham MD, Ireland S, Houston JG, et al. Vitamin D therapy to reduce blood pressure and left ventricular hypertrophy in resistant hypertension: randomized, controlled trial. Hypertension 2014;63(4):706-712.

eFigure 1. Funnel Plot for Trial-Level Systolic Blood Pressure Treatment Effects



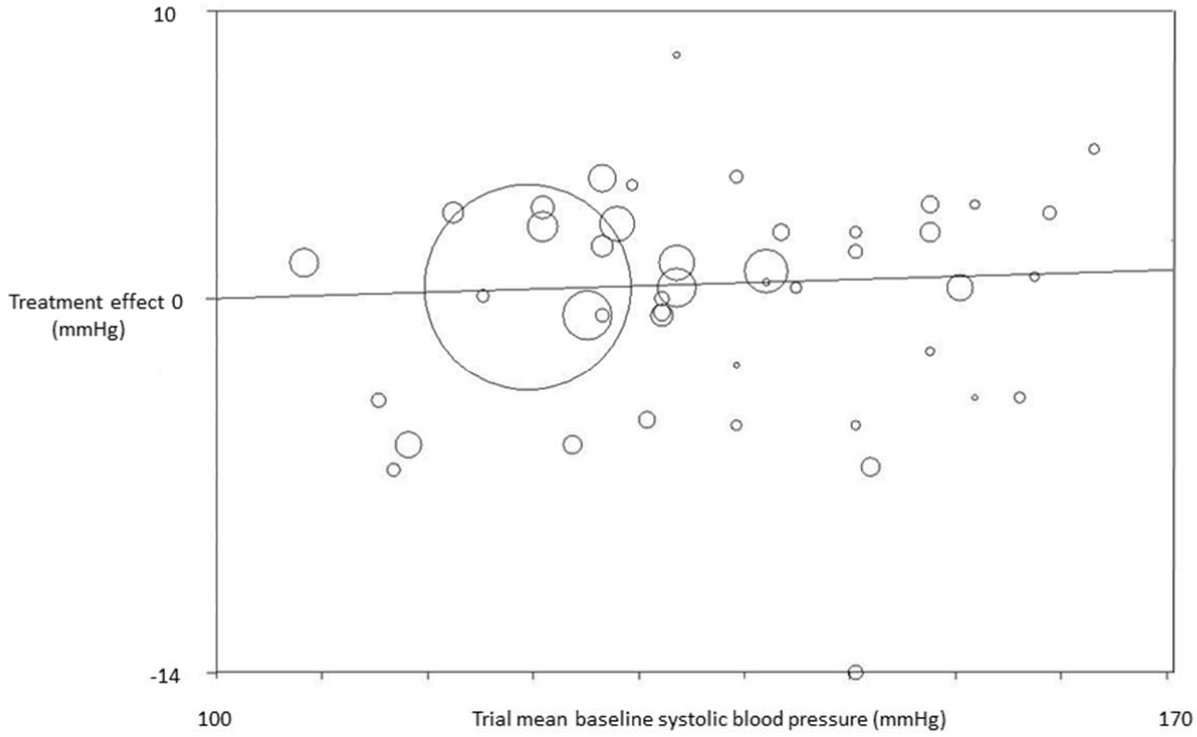
eFigure 2. Results of Trial-Level Meta-analysis for Diastolic Blood Pressure Outcomes

Source	Treatment Group, No. of Patients: Vitamin D Supplement	Treatment Group, No. of Patients: Placebo	Difference in Mean DBP Between Groups (95% CI)
Lind et al,[1] 1987	15	10	−9.2 (−15.3 to 3.1)
Lind et al,[2] 1988	15	16	−6.7 (−12.3 to −1.1)
Lind et al,[3] 1988	33	32	−1.6 (−6.1 to 2.9)
Lind et al,[4] 1989	18	21	0.4 (−3.8 to 4.6)
Scragg et al,[7] 1995	95	94	0.0 (−2.6 to 2.6)
Pfeifer et al,[8] 2001	73	72	−0.3 (−3.5 to 2.9)
Sugden et al,[11] 2008	17	17	−4.5 (−9.4 to 0.4)
Nagpal et al,[12] 2009	35	36	1.7 (−1.5 to 4.9)
Zitterman et al,[13] 2009	82	83	0.0 (−2.9 to 2.9)
Jorde et al,[14] 2010	114	112	0.8 (−1.2 to 2.8)
Witham et al,[16] 2010a	48	48	0.5 (−6.7 to 5.7)
Witham et al,[15] 2010b	19	21	0.3 (−5.8 to 6.4)
Harris et al,[18] 2011	23	22	0.6 (−2.7 to 3.9)
Shab-Bidar et al,[19] 2011	50	50	−2.9 (−6.2 to 0.5)
Alvarez et al,[20] 2012	17	20	5.4 (−2.7 to 13.5)
Bonakdaran et al,[21] 2012	15	18	−2.3 (7.6 to 3.0)
Gepner et al,[22] 2012	55	55	−0.3 (−2.1 to 1.5)
Heshmat et al,[23] 2012	21	21	−0.1 (−0.6 to 0.4)
Kjaergaard et al,[24] 2012	120	110	0.0 (−1.8 to 1.8)
Muldowney et al,[27] 2012	48	52	0.0 (−4.3 to 4.3)
Salehpour et al,[28] 2012	40	37	2.2 (−1.2 to 5.5)
Stricker et al,[29] 2012	31	31	0.0 (−4.3 to 4.3)
Witham et al,[30] 2012	29	27	0.7 (−3.6 to 5.0)
Wood et al,[31] 2012	96	100	1.2 (−0.3 to 2.7)
Asemi et al,[32] 2013	24	24	−3.5 (−6.6 to −0.4)
Boxer et al,[33] 2013	24	24	−0.8 (−5.7 to 4.1)
Breslavsky et al,[34] 2013	19	13	−2.1 (−8.5 to 4.3)
Chai et al,[35] 2013	22	21	−0.2 (−6.7 to 6.3)
Forman et al,[36] 2013	70	72	−2.5 (−6.8 to 1.8)
Larsen et al,[37] 2013	26	26	−1.0 (−4.3 to 2.3)
Petchey et al,[38] 2013	11	14	−2.9 (−10.1 to 4.3)
Roth et al,[39] 2013	67	65	1.7 (−1.4 to 4.9)
Toxqui et al,[40] 2013	55	54	−2.2 (−5.1 to 0.7)
Wamberg et al,[41] 2013	22	21	−4.0 (−10.6 to 2.6)
Witham et al,[42] 2013	73	69	1.0 (−1.4 to 3.4)
Witham et al,[43] 2013	38	36	1.2 (−2.7 to 5.1)
Witham et al,[44] 2013	24	25	0.4 (−2.6 to 3.4)
Yiu et al,[45] 2013	50	50	2.0 (−1.2 to 5.2)
Dalbeni et al,[46] 2014	13	10	3.4 (−5.6 to 12.4)
Scragg et al,[47] 2014	149	151	0.0 (−1.6 to 1.6)
Sollid et al,[48] 2014	242	242	0.0 (−1.6 to 1.6)
Strobel et al,[49] 2014	39	36	2.8 (−2.6 to 8.2)
Wang et al,[50] 2014	30	30	−1.0 (−7.1 to 5.1)
Witham et al,[51] 2014	31	30	6.0 (−1.7 to 10.3)
Overall			**0.1 (−0.6 to 0.5)**



Different sizes of data markers correspond to the relative weight assigned in the pooled analysis. Diamond marker indicates overall result.

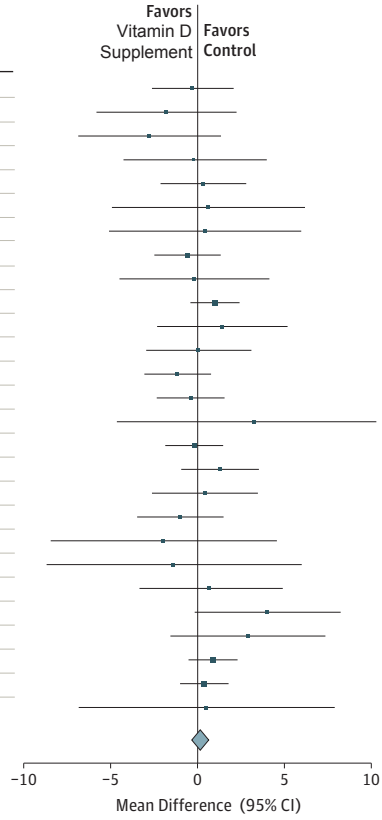
eFigure 3. Meta-regression of Treatment Effect vs Mean Trial-Level Baseline Systolic Blood Pressure



eFigure 4. Results of Individual Patient Data Analysis Using Final Diastolic Blood Pressure (BP) Adjusted for Baseline BP

Source	Vitamin D Supplement Group: Mean (SD)	Vitamin D Supplement Group: Total No. of Patients	Placebo Group: Mean (SD)	Placebo Group: Total No. of Patients	Weight,%	Mean Difference IV, Random (95% CI)
Scragg et al,[7] 1995	80.7 (7.8)	95	81 (8.7)	94	4.2	−0.3 (−2.7 to 2.1)
Schleithoff et al,[9] 2006	74.5 (9.6)	41	76.3 (9.7)	48	1.5	−1.8 (−5.8 to 2.2)
Sugden et al,[11] 2008	78.7 (6.7)	20	81.5 (6.7)	20	1.4	−2.8 (−7.0 to 1.4)
Nagpal et al,[12] 2009	76.7 (8.9)	35	76.9 (9)	36	1.4	−0.2 (−4.4 to 4.0)
Zittermann et al,[13] 2009	83.1 (8.1)	81	82.8 (8.1)	81	3.8	0.3 (−2.2 to 2.9)
Witham et al,[15] 2010	78.8 (8.9)	18	78.2 (8.7)	21	0.8	0.6 (−5.0 to 6.2)
Witham et al,[16] 2010	73 (13.6)	46	72.6 (13.6)	46	0.8	0.4 (−5.1 to 5.9)
Jorde et al,[14] 2010	75.9 (7.4)	112	76.5 (7.2)	105	6.2	−0.6 (−2.5 to 1.3)
Witham et al,[30] 2012	72.5 (7.9)	28	72.7 (8.2)	26	1.3	−0.2 (−4.5 to 4.1)
Wood et al,[31] 2012	76.5 (4.7)	90	75.5 (4.8)	93	12.2	1.0 (−0.4 to 2.4)
Witham et al,[43] 2013	73.9 (8.1)	39	72.5 (8.4)	36	1.7	1.4 (−2.3 to 5.1)
Stricker et al,[29] 2012	74.5 (6.1)	31	74.5 (6.1)	31	2.5	0.0 (−3.1 to 3.1)
Larsen et al,[25] 2012	75.8 (5.2)	55	77 (5.3)	58	6.2	−1.2 (−3.1 to 0.7)
Gepner et al,[22] 2012	71.6 (4.3)	37	72 (4.4)	39	6.2	−0.4 (−2.3 to 1.5)
Alvarez et al,[20] 2012	75.4 (12.0)	17	72.2 (12.2)	19	0.4	3.2 (−4.7 to 11.1)
Kjaergaard et al,[24] 2012	78.9 (6.6)	120	79.1 (6.3)	110	8.5	−0.2 (−1.9 to 1.5)
Witham et al,[42] 2013	77.7 (6.8)	73	76.4 (6.6)	69	4.8	1.3 (−0.9 to 3.5)
Witham et al,[44] 2013	73.6 (5.4)	24	73.2 (5.5)	25	2.5	0.4 (−2.7 to 3.5)
Toxqui et al,[40] 2013	66.4 (6.7)	56	67.4 (6.4)	51	3.8	−1.0 (−3.5 to 1.5)
Wamberg et al,[41] 2013	83 (9.7)	15	85 (9.6)	19	0.6	−2.0 (−8.5 to 4.5)
Petchey et al,[38] 2013	76.9 (9.3)	11	78.3 (9.4)	14	0.4	−1.4 (−8.8 to 6.0)
Boxer et al,[33] 2013	67.4 (7.4)	24	66.7 (7.3)	24	1.4	0.7 (−3.5 to 4.9)
Witham et al,[51] 2014	83 (8.4)	31	79 (8.1)	29	1.4	4.0 (−0.2 to 8.2)
Strobel et al,[49] 2014	86.5 (10.0)	39	83.6 (9.6)	36	1.2	2.9 (−1.5 to 7.3)
Scragg et al,[47] 2014	78.6 (6.1)	149	77.7 (6.1)	151	12.2	0.9 (−0.5 to 2.3)
Sollid et al,[48] 2014	78.9 (7.8)	242	78.5 (7.8)	242	12.2	0.4 (−1.0 to 1.8)
Dalbeni et al,[46] 2014	73.5 (9.0)	13	73 (8.9)	10	0.4	0.5 (−6.9 to 7.9)
Total		**1542**		**1533**	**100**	**0.2 (−0.3 to 0.7)**

Heterogeneity: $\tau^2 = 0.00$; $\chi^2_{20} = 16.93$ ($P = .91$); $I^2 = 0\%$
Test for overall effect: $z = 0.88$ ($P = .38$)



Different sizes of data markers correspond to the relative weight assigned in the pooled analysis. Diamond marker indicates overall result.