

SUPPLEMENTARY FILE

Supplementary table A Search strategy used in the literature review for Medline and Embase (Search limited to humans and English language)

Medline	
Vitamin D terms	Vitamin d/ or 25-OHD.mp. or 25 hydroxyvitamin D.mp. or cholecalciferol/ or colecalciferol.mp. or hydroxycholecalciferols/ or hydroxycholecalciferols.mp. or calcifediol/ or dihydroxycholecalciferols/ or dihydroxycholecalciferols.mp. or calcitriol/ or 24,25-dihydroxyvitamin d 3/ or 24,25-OH2 D3.mp. or ergocalciferols/ or dihydrotachysterol/ or 25-hydroxyvitamin d 2/ or 25-OHD2.mp. or 1,25-dihydroxyvitamin d.mp. or 1,25-OH2 D.mp. or 1,25-dihydroxyvitamin d2.mp. or 1,25-dihydroxyergocalciferol.mp. or 1,25-OH2 D2.mp. or 1,25-dihydroxyvitamin d3.mp. or 1,25-OH2 D3.mp. or ergocalciferols/ or vitamin D2.mp. or vitamin D 2.mp. or vitamin D3.mp. or vitamin D 3.mp
	AND
Review terms	Review Literature as Topic/ or systematic review.mp or meta-analysis/ or meta-analysis.mp
Embase	
Vitamin D terms	Vitamin d/ or 25-OHD.mp. or 25 hydroxyvitamin D/ or colecalciferol/ or cholecalciferol.mp. or hydroxycholecalciferols/ or hydroxycholecalciferols.mp. or calcifediol/ or dihydroxycholecalciferols/ or dihydroxycholecalciferols.mp. or calcitriol/ or 24,25 dihydroxycholecalciferol/ or 24,25-OH2 D3.mp. or ergocalciferol/ or dihydrotachysterol/ or 25-hydroxyvitamin d 2.mp. or 25-OHD2.mp. or 1,25-dihydroxyvitamin d.mp. or 1,25-OH2 D.mp. or 1,25 dihydroxyergocalciferol/ or 1,25-dihydroxyvitamin d2.mp. or 1,25-OH2 D2.mp. or 1,25-dihydroxyvitamin d3.mp. or 1,25-OH2 D3.mp. or ergocalciferol/ or vitamin D2.mp. or vitamin D 2.mp. or vitamin D3.mp. or vitamin D 3.mp
	AND
Review terms	systematic review / or systematic review.mp or meta-analysis/ or meta-analysis.mp

Supplementary table B Map of 137 non-overlapping meta-analyses or systematic reviews (SR: Systematic review; MA: meta-analysis; RCTs: Randomised clinical trials)

Meta-analyses	Number of SR	Author's interpretation (in most recent SR)	Number of MA (observational studies)	Significant summary effect (in most recent MA)	Number of MA (RCTs)	Significant summary effect (in most recent MA)
Autoimmune diseases						
Ankylosing spondylitis ⁴⁹	1	Suggestive				
Crohn's disease ⁴⁹	1	Suggestive				
Multiple Sclerosis ^{49 56}	2	Suggestive				
Osteoarthritis ⁶⁴	1	Suggestive				
Rheumatoid arthritis ^{49 56}	2	Inconclusive				
Rheumatoid arthritis activity ⁶⁰	1	Definite				
Scleroderma ^{49 56}	2	Inconclusive				
Systemic Lupus Erythematosus ^{49 56 59}	3	Suggestive				
Thyroid autoimmunity ⁴⁹	1	Inconclusive				
Type 1 diabetes ^{49 56}	2	Suggestive				
Type 1 diabetes in childhood (maternal vitamin D status) ⁴⁶	1	Inconclusive				
Vitiligo ⁴⁹	1	Inconclusive				
Cancer outcomes						
Aggressive prostate cancer ⁷⁶			1	no		
Aggressive prostate cancer (1,25(OH)2D) ⁷⁶			1	no		
Breast cancer ^{47 54 68 70 75 81 94 101}	2	Inconclusive	6	yes		
Breast cancer (1,25(OH)2D) ⁶⁸			1	no		
Breast cancer prognosis ⁴⁴	1	Inconclusive				
Breast cancer pre-menopausal ¹⁰⁵			1	no		
Breast cancer post-menopausal ¹⁰⁵			1	no		
Cancer mortality ⁴⁷	1	No association				
Colon cancer ³⁵			1	no		
Colon cancer (1,25(OH)2D) ³⁵			1	no		
Colorectal adenoma ^{47 72 92 95}	1	No association	3	yes		
Colorectal adenoma recurrence ⁹⁵			1	yes		
Colorectal cancer ^{35 47 54 70 75 77 79 90 93}	2	Definite	7	yes		
Colorectal cancer (1,25(OH)2D) ^{35 47}	1	No association	1	no		
Colorectal cancer prognosis ⁴⁴	1	Inconclusive				

Kidney cancer ⁷⁴			1	no		
Lung cancer ⁵⁴	1	Inconclusive				
Melanoma prognosis ⁴⁴	1	Inconclusive				
Non-Hodgkin Lymphoma ^{54 58 86}	2	Inconclusive	1*	no		
Non-small cell lung cancer prognosis ⁴⁴	1	Inconclusive				
Oesophageal cancer ⁵⁴	1	Inconclusive				
Ovarian cancer ^{54 57 96}	2	Inconclusive	1	no		
Pancreatic cancer ^{47 54 88}	2	Inconclusive	1	yes		
Prostate cancer ^{47 54 70 75 76 97}	2	Inconclusive	4	no		
Prostate cancer (1,25(OH)2D) ^{47 76}	1	Inconclusive	1	no		
Prostate cancer prognosis ⁴⁴	1	Inconclusive				
Rectal cancer ³⁵			1	yes		
Renal cancer ⁵⁴	1	Inconclusive				
Stomach cancer ⁵⁴	1	Inconclusive				
Cardiovascular outcomes						
Cardiovascular disease ^{43 47 52 78 87 102 125 130}	4	Suggestive	3	yes	2	no
Cardiovascular disease in ethnic minorities ⁵³	1	Suggestive				
Cardiovascular disease mortality ^{43 47 78}	2	Inconclusive	1	yes		
Cardiovascular disease prevalence ⁸³			1	yes		
Hypertension: Total, diastolic, systolic ^{43 47 51 52 67 104 126 127}	4	Inconclusive	3	yes	3	no
Hypertension in children ⁶²	1	Definite				
Ischemic heart disease ⁶⁶			1	yes		
Ischemic stroke ¹⁰⁰			1**	yes		
Myocardial infarction ⁴⁷	1	No association				
Stroke ^{47 69 89}	1	No association	2	yes		
Cognitive disorders						
Alzheimer's disease ^{65 99}			2	yes		
Cognition ^{42 43 71}	2	Inconclusive	1	yes		
Depression ^{43 98}	1	Inconclusive	1	yes		
Infectious diseases						
Active tuberculosis ⁸²			1	yes		
Acute respiratory infection ⁶³	1	Suggestive				
Infectious diseases mortality ⁴⁷	1	Inconclusive				
Metabolic disorders						
Adiposity in children (maternal vitamin D status) ⁴⁶	1	No association				
Body mass index ³⁸			1	yes		

Metabolic syndrome prevalence ⁸³			1	yes		
Metabolic syndrome in ethnic minorities ⁵³	1	Inconclusive				
Metabolites: fasting glucose of diabetes patients with normal glucose tolerance ¹¹⁴					1	no
Metabolites: fasting glucose of diabetes patients with abnormal glucose tolerance ¹¹⁴					1	no
Metabolites: HDL ¹²³					1	no
Metabolites: HDL in children ⁶²	1	No association				
Metabolites: insulin/glucose metabolism in children ⁶²	1	Inconclusive				
Metabolites: insulin resistance of diabetes patients ¹¹⁴					1	no
Metabolites: LDL ¹²³					1	yes
Metabolites: LDL in children ⁶²	1	No association				
Metabolites: total cholesterol ¹²³					1	no
Metabolites: triglycerides ¹²³					1	no
Metabolites: triglycerides in children ⁶²	1	No association				
Obesity in ethnic minorities ⁵³	1	Suggestive				
Type 2 diabetes ^{52 73 80 103}	1	Inconclusive	3	yes		
Type 2 diabetes in ethnic minorities ⁵³	1	Suggestive				
Type 2 diabetes prevalence ^{11 83}			2	yes		
Neonatal/ infant/ child related outcomes						
Allergic rhinitis and atopic dermatitis/eczema (maternal vitamin D status) ^{46 47}	2	Inconclusive				
Birth length (maternal vitamin D status) ^{36 112}			1	no	1	no
Birth weight (maternal vitamin D status) ^{36 46 47 50 61 112}	4	Inconclusive	1	yes	3	yes
Cerebral function and diseases (maternal vitamin D status) ⁴⁶	1	Inconclusive				
Childhood infections (maternal vitamin D status) ^{46 61}	2	Inconclusive				
Dental caries ¹²⁸					1	yes
Head circumference (maternal vitamin D status) ^{36 112}			1	no	1	yes

Neonatal and infant growth ⁶¹	1	Suggestive				
Small for gestational age (maternal vitamin D status) ^{36 61}	1	Inconclusive	1	yes	1	no
Wheezing and asthma in childhood (maternal vitamin D status) ⁴⁶	1	Inconclusive				
Pregnancy related outcomes						
Bacterial vaginosis in pregnant women ^{36 45}	2	Definite				
Caesarean section ^{36 45}	2	No association				
Fertility ⁴⁵	1	Inconclusive				
Gestational diabetes mellitus ^{36 45 85}	1	Suggestive	2	yes		
Length of gestation/ preterm birth ^{45 61}	2	Suggestive			2	no
Maternal vitamin D levels at term ¹¹²					1	yes
Postpartum depression ⁴⁵	1	Inconclusive				
Preeclampsia in pregnant women ^{36 45 47 50 61}	4	Suggestive	1	yes		
Pregnancy-associated breast cancer ⁴⁵	1	Inconclusive				
Skeletal outcomes						
Bone health in pregnant and lactating women ⁴⁸	1	Inconclusive				
Bone mineral content in infants ⁴⁸	1	Inconclusive				
Bone mineral density ^{48 131}	1	Suggestive			1	no
Bone mineral density in children and adolescents ^{48 125}	1	Suggestive			1	no
Bone mineral density in forearm ¹³¹					1	no
Bone mineral density in forearm in children ¹²⁵					1	no
Bone mineral density in femoral neck ¹³¹					1	yes
Bone mineral density in hip ¹³¹					1	no
Bone mineral density in hip in children ¹²⁵					1	no
Bone mineral density in lumbar spine ¹³¹					1	no
Bone mineral density in lumbar spine in children ¹²⁵					1	no
Bone pain in chronic kidney disease patients requiring dialysis ¹²¹					1	no
Falls: risk of falling in older individuals ^{7 48 109 111 115 117 119}	1	Definite			11	no
Falls: rate of falls in older individuals (D2 or					2	no

D2 and D3) ¹¹¹						
Falls: rate of falls in older individuals (D3 only) ¹¹⁵					1	yes***
Fractures in older individuals ^{48 70 91 107 115 116}	1	Inconclusive	1	yes	5	no
Fractures in chronic kidney disease patients requiring dialysis ¹²¹					1	no
Fractures: hip ^{37 48 107 108 116}			1****	yes	4	no
Fractures: non-vertebral ^{5 108}					2	yes
Fractures: non-vertebral-no-hip ¹⁰⁸					1	no
Fractures: vertebral or deformity ¹⁰⁷					1	no
Performance measures in older individuals ⁴⁸	1	Inconclusive				
Balance sway ¹¹⁸					1	yes
Lower extremity strength ¹¹⁸					1	no
Muscle strength ¹¹⁸					1	yes
Rickets in children ⁴⁸	1	Definite				
Other outcomes						
Chronic kidney disease patients: Mortality ^{84 120 121}			1	yes	1*****	no
Chronic kidney disease patients not requiring dialysis: Alkaline phosphatase levels ¹²⁰					1	no
Chronic kidney disease patients not requiring dialysis: Creatinine clearance ¹²⁰					1	no
Chronic kidney disease patients not requiring dialysis: Risk of hypercalcaemia ¹²⁰					1	yes
Chronic kidney disease patients not requiring dialysis: Risk of hyperphosphataemia ¹²⁰					1	no
Chronic kidney disease patients not requiring dialysis: Parathyroid hormone levels ^{120 129}					2	yes
Chronic kidney disease patients not requiring dialysis: Risk of requiring dialysis ¹²⁰					1	no
Chronic kidney disease patients requiring dialysis: Alkaline phosphatase levels ¹²¹					1	no

Chronic kidney disease patients requiring dialysis: Parathyroid hormone levels ^{121 129}					2	yes
Chronic kidney disease patients requiring dialysis: Parathyroidectomy ¹²¹					1	no
Chronic kidney disease patients requiring dialysis: Risk of hypercalcaemia ¹²¹					1	no
Chronic kidney disease patients requiring dialysis: Risk of hyperphosphataemia ¹²¹					1	no
Chronic kidney disease patients requiring dialysis: Subperiosteal erosions ¹²¹					1	no
Chronic kidney disease patients requiring dialysis: Vascular calcification ¹²¹					1	no
Mammographic breast density ⁵⁵	1	Inconclusive				
Mortality ^{43 47 66 106 110 113 122}	2	Inconclusive	1	yes	5	no

* Non Hodgkin Lymphoma is presented in 2 meta-analyses of observational data, one for males and one for females

** Ischemic stroke outcome is presented as 2 meta-analyses one for HR and one for OR studies

*** Vitamin D3 supplementation was associated with increased rate of falls

**** Fractures: hip outcome is presented as 2 meta-analyses one with population controls and one with hospital based controls

***** Chronic kidney disease patients: Mortality is presented as 2 meta-analyses one for patients requiring dialysis and one for patients not requiring dialysis

Supplementary Table C General characteristics of the 107 systematic reviews of observational studies

Author	Year	Biomarker	Population	Outcome	N of studies	Main findings
Autoimmune diseases						
Kriegel MA	2011	25OHD	general	Ankylosing spondylitis	8	Suggestive
Kriegel MA	2011	25OHD	general	Crohn's disease	4	Suggestive
Kriegel MA	2011	25OHD	general	Multiple Sclerosis	12	Suggestive
Antico A	2012	25OHD	general	Multiple Sclerosis	11	Suggestive
Cao Y	2013	25OHD	general	Osteoarthritis	13	Suggestive
Kriegel MA	2011	25OHD	general	Rheumatoid arthritis	11	Inconclusive
Antico A	2012	25OHD	general	Rheumatoid arthritis	7	Inconclusive
Song GG	2012	25OHD	Rheumatoid arthritis patients	Rheumatoid arthritis activity	8	Definite
Kriegel MA	2011	25OHD	general	Scleroderma	8	Inconclusive
Antico A	2012	25OHD	general	Scleroderma	7	Inconclusive
Kriegel MA	2011	25OHD	general	Systemic lupus erythematosus	14	Suggestive
Antico A	2012	25OHD	general	Systemic lupus erythematosus	6	Suggestive
Sakthiswary R	2013	25OHD	general	Systemic lupus erythematosus	22	Suggestive
Kriegel MA	2011	25OHD	general	Thyroid autoimmunity	1	Inconclusive
Kriegel MA	2011	25OHD	general	Type 1 diabetes	14	Suggestive
Antico A	2012	25OHD	general	Type 1 diabetes	10	Suggestive
Christesen HT	2012	25OHD	impact of maternal vitamin D status on children health	Type 1 diabetes in childhood (maternal vitamin D status)	5	Inconclusive
Kriegel MA	2011	25OHD	general	Vitiligo	1	Inconclusive
Cancer outcomes						
van der Rhee H	2009	25OHD	general	Breast cancer	9	Inconclusive
Chung M	2009	25OHD	general	Breast cancer	3	No association
Buttigliero C	2011	25OHD	cancer patients	Breast cancer prognosis	2	Inconclusive
Chung M	2009	25OHD	general	Cancer mortality	1	No association
Chung M	2009	25OHD	general	Colorectal adenoma	1	No association
van der Rhee H	2009	25OHD	general	Colorectal cancer	8	Definite
Chung M	2009	25OHD	general	Colorectal cancer	7	Definite
Chung M	2009	1,25(OH)2D	general	Colorectal cancer	3	No association

Buttigliero C	2011	25OHD	cancer patients	Colorectal cancer prognosis	2	Inconclusive
van der Rhee H	2009	25OHD	general	Lung cancer	4	Inconclusive
Buttigliero C	2011	25OHD	cancer patients	Melanoma prognosis	1	Inconclusive
van der Rhee H	2009	25OHD	general	Non-Hodgkin Lymphoma	7	Inconclusive
Kelly LJ	2009	25OHD	general	Non-Hodgkin Lymphoma	8	Inconclusive
Buttigliero C	2011	25OHD	cancer patients	Non-small cell lung cancer prognosis	2	Inconclusive
van der Rhee H	2009	25OHD	general	Oesophageal cancer	3	Inconclusive
van der Rhee H	2009	25OHD	general	Ovarian cancer	2	Inconclusive
Cook LS	2010	25OHD	general (women)	Ovarian cancer	1	Inconclusive
van der Rhee H	2009	25OHD	general	Pancreatic cancer	3	Inconclusive
Chung M	2009	25OHD	general	Pancreatic cancer	2	Inconclusive
Chung M	2009	25OHD	general population	Prostate cancer	12	Inconclusive
van der Rhee H	2009	25OHD	general	Prostate cancer	17	Inconclusive
Chung M	2009	1,25(OH)2D	general	Prostate cancer	5	Inconclusive
Buttigliero C	2011	25OHD	cancer patients	Prostate cancer prognosis	1	Inconclusive
van der Rhee H	2009	25OHD	general	Renal cancer	1	Inconclusive
van der Rhee H	2009	25OHD	general	Stomach cancer	1	Inconclusive
Cardiovascular outcomes						
Chung M	2009	25OHD	general	Cardiovascular disease	2	Suggestive
Pittas AG	2010	25OHD	general	Cardiovascular disease	7	Suggestive
Barnard K	2010	25OHD	older adults	Cardiovascular disease	5	Inconclusive
Renzaho AM	2011	25OHD	ethnic minorities	Cardiovascular disease in ethnic minorities	5	Suggestive
Chung M	2009	25OHD	general	Cardiovascular disease mortality	1	No association
Barnard K	2010	25OHD	older adults	Cardiovascular disease mortality	6	Inconclusive
Chung M	2009	25OHD	general	Hypertension	3	Inconclusive
Pilz S	2009	25OHD	general	Hypertension	28	Inconclusive
Barnard K	2010	25OHD	older adults	Hypertension	5	Inconclusive
Pittas AG	2010	25OHD	general	Hypertension	3	Suggestive
Dolinsky DH	2013	25OHD	children	Hypertension in children	14	Definite
Chung M	2009	25OHD	general	Myocardial infarction	1	No association
Chung M	2009	25OHD	general	Stroke	1	No association
Cognitive disorders						
Annweiler C	2009	25OHD	general	Cognition	5	Inconclusive
Barnard K	2010	25OHD	older adults	Cognition	5	Inconclusive

Barnard K	2010	25OHD	older adults	Depression	4	Inconclusive
Infectious diseases						
Jolliffe DA	2013	25OHD	general	Acute respiratory infection	25	Suggestive
Chung M	2009	25OHD	general	Infectious diseases mortality	1	Inconclusive
Metabolic disorders						
Christesen HT	2012	25OHD	impact of maternal vitamin D status on children health	Adiposity in children (maternal vitamin D status)	1	No association
Renzaho AM	2011	25OHD	ethnic minorities	Metabolic syndrome in ethnic minorities	2	Inconclusive
Dolinsky DH	2013	25OHD	children	Metabolites: HDL in children	22	No association
Dolinsky DH	2013	25OHD	children	Metabolites: insulin/glucose metabolism in children	18	Inconclusive
Dolinsky DH	2013	25OHD	children	Metabolites: LDL in children	16	No association
Dolinsky DH	2013	25OHD	children	Metabolites: triglycerides in children	21	No association
Renzaho AM	2011	25OHD	ethnic minorities	Obesity in ethnic minorities	14	Suggestive
Pittas AG	2010	25OHD	general	Type 2 diabetes	3	Inconclusive
Renzaho AM	2011	25OHD	ethnic minorities	Type 2 diabetes in ethnic minorities	5	Suggestive
Neonatal/ infant/ child related outcomes						
Chung M	2009	25OHD	general	Allergic rhinitis and atopic dermatitis/eczema (maternal vitamin D status)	1	Inconclusive
Christesen HT	2012	25OHD	impact of maternal vitamin D status on children health	Allergic rhinitis and atopic dermatitis/eczema (maternal vitamin D status)	5	Inconclusive
Thorne-Lyman, A	2012	25OHD	pregnant women	Birth weight (maternal vitamin D status)	2	Inconclusive
Chung M	2009	25OHD	general	Birth weight (maternal vitamin D status)	2	No association

Christesen HT	2012	25OHD	impact of maternal vitamin D status on children health	Birth weight (maternal vitamin D status)	11	Inconclusive
Nassar N	2011	25OHD	Pregnant women	Birth weight (maternal vitamin D status)	3	Inconclusive
Christesen HT	2012	25OHD	impact of maternal vitamin D status on children health	Cerebral function and diseases (maternal vitamin D status)	2	Inconclusive
Thorne-Lyman, A	2012	25OHD	pregnant women	Childhood infections (maternal vitamin D status)	3	Inconclusive
Christesen HT	2012	25OHD	impact of maternal vitamin D status on children health	Childhood infections (maternal vitamin D status)	5	Inconclusive
Thorne-Lyman, A	2012	25OHD	pregnant women	Neonatal and infant growth	3	Suggestive
Thorne-Lyman, A	2012	25OHD	pregnant women	Small for gestational age (maternal vitamin D status)	4	Inconclusive
Christesen HT	2012	25OHD	impact of maternal vitamin D status on children health	Wheezing and asthma in childhood (maternal vitamin D status)	7	Inconclusive
Pregnancy related outcomes						
Aghajafari F	2013	25OHD	pregnant women	Bacterial vaginosis in pregnant women	3	Definite
Christesen HT	2012	25OHD	pregnant women	Bacterial vaginosis in pregnant women	4	Suggestive
Aghajafari F	2013	25OHD	pregnant women	Caesarean section	2	No association
Christesen HT	2012	25OHD	pregnant women	Caesarean section	1	Inconclusive
Christesen HT	2012	25OHD	pregnant women	Fertility	2	Inconclusive
Christesen HT	2012	25OHD	pregnant women	Gestational diabetes mellitus	7	Suggestive
Thorne-Lyman, A	2012	25OHD	pregnant women	Length of gestation/preterm birth	2	Suggestive
Christesen HT	2012	25OHD	pregnant women	Length of gestation/preterm birth	9	Suggestive
Christesen HT	2012	25OHD	pregnant women	Postpartum depression	1	Inconclusive
Thorne-Lyman, A	2012	25OHD	pregnant women	Preeclampsia in pregnant women	2	Inconclusive

Christesen HT	2012	25OHD	pregnant women	Preeclampsia in pregnant women	10	Suggestive
Chung M	2009	25OHD	pregnant women	Preeclampsia in pregnant women	1	Inconclusive
Nassar N	2011	25OHD	pregnant women	Preeclampsia in pregnant women	2	Inconclusive
Christesen HT	2012	25OHD	pregnant women	Pregnancy-associated breast cancer	1	Inconclusive
Skeletal outcomes						
Cranney A	2007	25OHD	children, women of reproductive age, postmenopausal women and elderly men	Bone health in pregnant and lactating women	4	Inconclusive
Cranney A	2007	25OHD	children, women of reproductive age, postmenopausal women and elderly men	Bone mineral content in infants	3	Inconclusive
Cranney A	2007	25OHD	children, women of reproductive age, postmenopausal women and elderly men	Bone mineral density	13	Suggestive
Cranney A	2007	25OHD	children, women of reproductive age, postmenopausal women and elderly men	Bone mineral density in children and adolescents	5	Suggestive
Cranney A	2007	25OHD	children, women of reproductive age, postmenopausal women and elderly men	Falls: risk of falling in older individuals	4	Definite
Cranney A	2007	25OHD	children, women of reproductive age, postmenopausal women and elderly men	Fractures in older individuals	15	Inconclusive

Cranney A	2007	25OHD	children, women of reproductive age, postmenopausal women and elderly men	Performance measures in older individuals	4	Inconclusive
Cranney A	2007	25OHD	children, women of reproductive age, postmenopausal women and elderly men	Rickets in children	12	Definite
Other outcomes						
Yaghjian L	2012	25OHD	general (women)	Mammographic breast density	14	Inconclusive
Chung M	2009	25OHD	general	Mortality	4	No association
Barnard K	2010	25OHD	older adults	Mortality	6	Inconclusive

Supplementary Table D General characteristics of the 74 meta-analyses of observational studies (RR: relative risk, OR: odds ratio, HR: hazard ratio, SMD: standardised mean difference, WMD: weighted mean difference, CI: confidence interval, CKD: chronic kidney disease)

Author	Date	Vitamin D measurement	Population	Outcome	Unit of comparison	Participants total	Events total	Type of metric	Meta-analysis model	N of studies	Reported RR of meta-analysis (95% CI)
Cancer outcomes											
Gilbert R	2011	25OHD	men	Aggressive prostate cancer	per 10 ng/ml	6646	1460	OR	random	6	0.98 (0.84, 1.15)
Gilbert R	2011	1,25(OH)2D	men	Aggressive prostate cancer	per 10 ng/ml	1488	696	OR	random	2	0.86 (0.72, 1.02)
Chen P	2013	25OHD	general/ Hospital based	Breast cancer	highest vs lowest quartile	26317	11771	OR	random	21	0.52 (0.40, 0.68)
Chung M	2011	25OHD	women	Breast cancer	per 10 nmol/lt	4726	2363	OR	dose-response meta-analysis	4	0.99 (0.97, 1.01)
Gandini S	2011	25OHD	adults	Breast cancer	per 10 ng/ml	29770	6175	RR	random	10	0.89 (0.81, 0.98)
Mohr SB	2011	25OHD	women	Breast cancer	highest vs lowest quintile	16337	7547	Peto OR	no info	11	0.61 (0.47, 0.80)
Yin L	2010	25OHD	general	Breast cancer	20 ng/ml	12901	6147	OR	random	9	0.73 (0.60, 0.88)
Chen P	2010	25OHD	women	Breast cancer	highest vs lowest quartile	11330	5489	OR	random	7	0.55 (0.38, 0.80)
Chen P	2010	1,25(OH)2D	women	Breast cancer	highest vs lowest quartile	3627	1802	OR	random	3	0.99 (0.68, 1.44)
Lee JE	2011	25OHD	adults	Colon cancer	highest vs lowest category	4578	1822	OR	random	10	0.77 (0.56, 1.07)

Lee JE	2011	1,25(OH)2D	adults	Colon cancer	highest vs lowest category	5284	2528	OR	no info	4	0.88 (0.57, 1.35)
Fedirko V	2010	25OHD	adults with no prior history of colorectal neoplasms	Colorectal adenoma	highest vs lowest quartile	1386	616	OR	pooled meta-analysis	3	0.59 (0.41, 0.84)
Yin L	2011	25OHD	general	Colorectal adenoma	per 20 ng/ml	7654	3539	OR	random	9	0.82 (0.69, 0.97)
Wei MY	2008	25OHD	general	Colorectal adenoma	highest vs lowest quintile	3787	2628	OR	random	7	0.7 (0.56, 0.87)
Yin L	2011	25OHD	Colorectal adenoma patients	Colorectal adenoma recurrence	per 20 ng/ml	2169	984	OR	random	3	0.84 (0.72, 0.97)
Ma Y	2011	25OHD	adults	Colorectal cancer	highest vs lowest category	6715	2767	RR	random	9	0.67 (0.54, 0.80)
Chung M	2011	25OHD	adults	Colorectal cancer	per 10nmol/lt	2249	1127	OR	dose-response meta-analysis	9	0.94 (0.91, 0.97)
Gandini S	2011	25OHD	adults	Colorectal cancer	per 10 ng/ml	no info	2630	RR	random	9	0.85 (0.79, 0.91)
Gorham ED	2007	25OHD	adults	Colorectal cancer	<6 vs ≥37 ng/ml	1448	535	OR	pooled meta-analysis	5	0.46 (0.32, 0.64)
Lee JE	2011	25OHD	adults	Colorectal cancer	highest vs lowest category	6628	2690	OR	random	9	0.66 (0.54, 0.81)
Lee JE	2011	1,25(OH)2D	adults	Colorectal cancer	highest vs lowest category	no info	no info	OR	no info	4	1.01 (0.59, 1.73)
Touvier M	2011	25OHD	general	Colorectal	per 100 IU/lt	no info	2375	RR	random	6	0.96 (0.94, 0.97)

Wang L	2012	25OHD	general	Cardiovascular disease	highest vs lowest category	64994	6123	RR	random	19	1.52 (1.30, 1.77)
Grandi NC	2010	25OHD	adults	Cardiovascular disease	lowest vs highest category	5253	756	HR	random	4	1.54 (1.22, 1.95)
Sokol SI	2011	25OHD	general	Cardiovascular disease	Hypovitaminosis D	no info	no info	RR	random	7	1.68 (1.23, 2.28)
Parker J	2010	25OHD	general	Cardiovascular disease (prevalent)	highest vs lowest category	64722	7600	OR	random	16	0.67 (0.55, 0.81)
Grandi NC	2010	25OHD	adults	Cardiovascular disease mortality	lowest vs highest category	24387	2007	HR	random	5	1.83 (1.19, 2.80)
Pittas AG	2010	25OHD	general	Hypertension	<37–51 nmol/l vs >75–81 nmol/l	2553	1149	RR	random	3	1.76 (1.27, 2.44)
Burgaz A	2011	25OHD	adults	Hypertension	highest vs lowest quartile	78028	no info	OR	random	18	0.73 (0.63, 0.84)
Kunutsor SK	2013	25OHD	general	Hypertension	highest vs lowest category	48633	4965	RR	random	7	0.70 (0.58, 0.86)
Brondum-Jacobsen P	2012	25OHD	adults	Ischemic heart disease	lowest vs highest quartile	82982	8376	HR	random	18	1.39 (1.25, 1.54)
Brondum-Jacobsen P	2013	25OHD	general	Ischemic stroke	lowest vs highest quartile	26596	1800	HR	random	5	1.52 (1.26, 1.84)
Brondum-Jacobsen P	2013	25OHD	general	Ischemic stroke	lowest vs highest quartile	31788	844	OR	random	5	1.92 (1.64, 2.26)
Sun Q	2012	25OHD	general	Stroke	highest vs lowest category	no info	1214	RR	fixed	6	1.52 (1.20, 1.85)

Chowdhury R	2012	25OHD	adults	Stroke	highest vs lowest third	47809	926	RR	random	7	0.60 (0.48, 0.72)
Cognitive disorders											
Balion C	2012	25OHD (one study measured 1,25(OH)D)	adults	Alzheimer's disease	mean 25(OH)D	888	n/a	WMD	random	6	-15.04 (-26.19, -3.89)
Annweiler C	2013	25OHD	general	Alzheimer's disease	per SD	1005	357	SMD	random	10	1.40 (0.26, 2.54)
Etgen T	2012	25OHD	adults	Cognition	lowest vs highest quartile	7688	1135	OR	random	7	2.39 (1.91, 3.00)
Anglin RE	2013	25OHD	general (cross-sectional studies)	Depression	<50 vs >50 nmol/lit	22476	2051	OR	random	9	1.13 (1.00, 1.71)
Anglin RE	2013	25OHD	general (cohort studies)	Depression	<50 vs >50 nmol/lit	8815	617	HR	random	3	2.21 (1.40, 3.49)
Infectious diseases											
Nnoaham KE	2008	25OHD	adults	Active tuberculosis	mean	534	308	SMD	random	7	0.68 (0.43, 0.93)
Metabolic disorders											
Saneei P	2013	25OHD	general	Body mass index	correlation coefficients	16525	n/a	Z score	random	37	-0.15 (-0.19, -0.11)
Parker J	2010	25OHD	general	Metabolic syndrome (prevalent)	highest vs lowest category	31416	2821	OR	random	8	0.49 (0.38, 0.64)
Forouhi NG	2012	25OHD	adults	Type 2 diabetes	highest vs lowest quartile	55713	3612	RR	random	11	0.59 (0.52, 0.67)

Mitri J	2011	25OHD	adults	Type 2 diabetes	>25 vs <14 ng/ml	5664	1153	RR	random	5	0.57 (0.43, 0.76)
Afzal S	2013	25OHD	general	Type 2 diabetes	lowest vs highest category	72204	4877	OR	random	16	1.50 (1.33, 1.68)
Pittas AG	2007	25OHD	general	Type 2 diabetes (prevalent)	25–38 vs 10–23 ng/ml			OR	random	4	0.36 (0.16, 0.80)
Parker J	2010	25OHD	general	Type 2 diabetes (prevalent)	highest vs lowest category	11892	2424	OR	random	9	0.45 (0.25, 0.82)
Neonatal/ Infant/ Child related outcomes											
Aghajafari F	2013	25OHD	pregnant women	Birth length	mean (in cm)	840	n/a	WMD	fixed	2	-0.19 (-0.65, 0.26)
Aghajafari F	2013	25OHD	pregnant women	Birth weight	mean (in grams)	5541	n/a	WMD	fixed	4	-130.92 (-186.69, -75.14)
Aghajafari F	2013	25OHD	pregnant women	Head circumference	mean (in cm)	840	n/a	WMD	fixed	2	-0.05 (-0.34, 0.24)
Aghajafari F	2013	25OHD	pregnant women	Small for gestational age	lowest vs highest category	6851	no info	OR	fixed	6	1.85 (1.52, 2.26)
Pregnancy related outcomes											
Poel YH	2012	25OHD	pregnant women	Gestational diabetes	<50 nmol/lt	2146	433	OR	random	7	1.61 (1.19, 2.17)
Aghajafari F	2013	25OHD	pregnant women	Gestational diabetes	lowest vs highest category	4112	687	OR	fixed	10	1.49 (1.18, 1.89)
Aghajafari F	2013	25OHD	pregnant women	Preeclampsia	lowest vs highest category	3230	393	OR	fixed	9	1.79 (1.25, 2.58)

Skeletal outcomes											
Weatherall M	2000	25OHD	older individuals	Fractures	per SD	2956	1572	SMD			0.66 (0.59, 0.74)
Lai JK	2010	25OHD	adults	Hip fracture (hospital-based controls)	geometric mean (in nmol/l)	2201	1116	log ratio of geometric mean	random	8	-0.26 (-0.33, -0.23)
Lai JK	2010	25OHD	adults	Hip fracture (population-based controls)	geometric mean (in nmol/l)	1655	818	log ratio of geometric mean	random	9	-0.51 (-0.64, -0.38)
Other outcomes											
Pilz S	2011	25OHD	CKD patients	Mortality	per 10 ng/mL	6853	2110	RR	mixed effects	10	0.86 (0.82, 0.91)
Brondum-Jacobsen P	2012	25OHD	adults	Mortality	lowest vs highest quartile	77155	15447	HR	random	17	1.46 (1.31, 1.64)

Supplementary Table E General characteristics of the 87 meta-analyses of RCTs of vitamin D supplementation (RR: relative risk, OR: odds ratio, RaR: rate ratio, SMD: standardised mean difference, WMD: weighted mean difference, CI: confidence interval)

Author	Date	Compound	Versus	Population	Outcome	Participants total	Events total	Type of metric	Meta-analysis model	N of studies	Reported RR (95% CI)
Cardiovascular outcomes											
Wang L	2010	vitamin D	placebo	general	Cardiovascular disease	2988	991	RR	fixed	2	0.90 (0.77, 1.05)
Myung SK	2013	vitamin D	placebo	general	Cardiovascular disease	no info	no info	RR	fixed	2	0.95 (0.86, 1.05)
Pittas AG	2010	vitamin D2 and vitamin D3	placebo	general	Diastolic blood pressure (mm Hg)	no info	n/a	WMD	no info	no info	-0.43 (-1.39, 0.53)
Witham MD	2009	Alphacalcidol or vitamin D3 or UVA + UVB (or vitamin D3 + calcium)	placebo or UVA (or calcium)	hypertensive individuals	Diastolic blood pressure (mm Hg)	545	n/a	WMD	random	8	-3.05 (-5.50, -0.60)
Wu SH	2010	vitamin D	placebo	normotensive or hypertensive individuals	Diastolic blood pressure (mm Hg)	366	n/a	WMD	no info	3	-0.03 (-1.98, 1.92)
Pittas AG	2010	vitamin D2 and vitamin D3	placebo	general	Systolic blood pressure (mm Hg)	no info	n/a	WMD	no info	no info	-2.60 (-6.60, 1.09)
Witham MD	2009	Alphacalcidol or vitamin D3 or UVA + UVB (or vitamin D3 + calcium)	placebo or UVA (or calcium)	hypertensive individuals	Systolic blood pressure (mm Hg)	545	n/a	WMD	random	8	-3.63 (-8.00, 0.74)
Wu SH	2010	vitamin D	placebo	normotensive or hypertensive individuals	Systolic blood pressure (mm Hg)	366	n/a	WMD	no info	3	-2.39 (-5.70, 0.90)

Metabolic outcomes											
George PS	2012	vitamin D or analogues	placebo	diabetes patients with normal glucose tolerance	Fasting glucose (nmol/l)	no info	n/a	WMD	no info	no info	0.01 (-0.21, 0.23)
George PS	2012	vitamin D or analogues	placebo	diabetes patients with abnormal glucose tolerance	Fasting glucose (nmol/l)	no info	n/a	WMD	no info	no info	-0.30 (-0.90, 0.30)
Wang H	2012	vitamin D (or vitamin D + calcium)	placebo (or calcium)	general	HDL (mg/dl)	1194	n/a	WMD	fixed	8	-0.14 (-0.99, 0.71)
George PS	2012	vitamin D or analogues	placebo	diabetes patients	Insulin resistance	no info	n/a	SMD	no info	5	0.16 (-0.11, 0.42)
Wang H	2012	vitamin D (or vitamin D + calcium)	placebo (or calcium)	general	Total cholesterol (mg/dl)	1314	n/a	WMD	fixed	11	1.52 (-1.42, 4.46)
Wang H	2012	vitamin D (or vitamin D + calcium)	placebo (or calcium)	general	LDL (mg/dl)	1129	n/a	WMD	fixed	7	3.23 (0.55, 5.90)
Wang H	2012	vitamin D (or vitamin D + calcium)	placebo (or calcium)	general	Triglycerides (mg/dl)	1194	n/a	WMD	fixed	8	-1.92 (-7.72, 3.88)
Neonatal/ infant/ child related outcomes											
De-Regil LM	2012	vitamin D alone or in combination with other micronutrients	placebo or no treatment	pregnant women	Birth length (cm)	326	n/a	WMD	random	2	0.97 (-0.41, 2.34)

De-Regil LM	2012	vitamin D alone or in combination with other micronutrients	placebo or no treatment	pregnant women	Birth weight (grams)	403	n/a	WMD	random	3	39.55 (-240.68, 319.78)
De-Regil LM	2012	vitamin D alone or in combination with other micronutrients	placebo or no treatment	pregnant women	Low birth weight	463	no info	RR	random	3	0.48 (0.23, 1.01)
Thorne-Lyman A	2012	vitamin D	placebo	pregnant women	Low birth weight	507	55	RR	fixed	3	0.40 (0.23, 0.71)
Hujoel PP	2013	vitamin D2 or vitamin D3 or UV therapy	no supplement or placebo	children	Dental caries	1513	no info	RR	random	38	0.53 (0.43, 0.65)
De-Regil LM	2012	vitamin D alone or in combination with other micronutrients	placebo or no treatment	pregnant women	Head circumference at birth (cm)	326	n/a	WMD	random	2	0.43 (0.06, 0.79)
Thorne-Lyman A	2012	vitamin D	placebo	pregnant women	Small-for-gestational age	305	55	RR	fixed	2	0.67 (0.40, 1.11)
Pregnancy related outcomes											
De-Regil LM	2012	vitamin D alone or in combination with other micronutrients	placebo or no treatment	pregnant women	Maternal vitamin D levels at term (nmol/l)	414	n/a	WMD	random	4	47.08 (23.76, 70.39)
Thorne-Lyman A	2012	vitamin D	placebo	pregnant women	Mean gestational age at delivery (weeks)	529	n/a	WMD	fixed	2	0.17 (-0.16, 0.51)

Thorne-Lyman A	2012	vitamin D	placebo	pregnant women	Preterm delivery	529	28	RR	fixed	2	0.77 (0.35, 1.66)
Skeletal outcomes											
Winzenberg T	2011	vitamin D3	placebo	healthy children	Bone mineral density (% change)	672	n/a	SMD	fixed	5	0.10 (-0.06, 0.26)
Reid IR	2013	vitamin D2 or D3 (no vitamin D metabolites)	placebo	community-dwelling adults	Bone mineral density (% change)	no info	n/a	WMD	random	3	-0.90 (-2.10, 0.40)
Reid IR	2013	vitamin D2 or D3 (no vitamin D metabolites)	placebo	community-dwelling adults	Bone mineral density in femoral neck (% change)	no info	n/a	WMD	random	8	1.10 (0.40, 1.90)
Reid IR	2013	vitamin D2 or D3 (no vitamin D metabolites)	placebo	community-dwelling adults	Bone mineral density in forearm (% change)	no info	n/a	WMD	random	2	-0.70 (-1.70, 0.40)
Winzenberg T	2011	vitamin D3	placebo	healthy children	Bone mineral density in forearm (% change)	563	n/a	SMD	random	3	0.04 (-0.36, 0.45)
Winzenberg T	2011	vitamin D3	placebo	healthy children	Bone mineral density in hip (% change)	639	n/a	SMD	random	4	0.06 (-0.18, 0.29)
Reid IR	2013	vitamin D2 or D3 (no vitamin D metabolites)	placebo	community-dwelling adults	Bone mineral density in hip (% change)	no info	n/a	WMD	random	6	0.70 (-0.10, 1.60)
Winzenberg T	2011	vitamin D3	placebo	healthy children	Bone mineral density in lumbar spine (% change)	660	n/a	SMD	fixed	5	0.15 (-0.01, 0.31)
Reid IR	2013	vitamin D2 or D3 (no vitamin D metabolites)	placebo	community-dwelling adults	Bone mineral density in lumbar spine (% change)	no info	n/a	WMD	random	7	0.10 (-0.60, 0.70)

Palmer SC	2009	established and newer vitamin D compounds	placebo, no treatment	chronic kidney disease requiring dialysis	Bone pain	109	no info	RR	fixed	4	0.29 (0.03, 2.63)
Bischoff-Ferrari HA	2009	vitamin D3 or vitamin D2 (or vitamin D3 or vitamin D2 + calcium)	placebo (or calcium)	older adults	Falls	1476	no info	RR	no info	6	0.77 (0.65, 0.92)
Bischoff-Ferrari HA	2009	Active form of vitamin D	placebo	older adults	Falls	624	223	RR	no info	2	0.78 (0.64, 0.94)
Bischoff-Ferrari HA	2004	vitamin D or active vitamin D analogue (or vitamin D or active vitamin D analogue + calcium)	placebo (or calcium)	older adults	Falls	1237	no info	RR		5	0.69 (0.53, 0.88)
Kalyani RR	2010	vitamin D	placebo	older adults	Falls	9508	no info	RR	random	7	1.01 (0.96, 1.07)
Murad MH	2011	vitamin D2 and vitamin D3	placebo	older adults	Falls	no info	no info	OR	random	10	0.97 (0.84, 1.11)
Murad MH	2011	vitamin D2 and vitamin D3 + calcium	calcium	older adults	Falls	no info	no info	OR	random	6	0.63 (0.50, 0.81)
Cameron ID	2012	vitamin D3 or D2 plus calcium	calcium	older individuals in care facilities or hospitals	Falls	747	no info	RR	random	2	0.85 (0.69, 1.05)
Cameron ID	2012	vitamin D2	usual care or placebo	older individuals in care facilities or hospitals	Falls	3765	no info	RR	random	2	0.80 (0.38, 1.71)
Gillespie LD	2012	vitamin D3	placebo or control	older people in the community	Falls	4516	no info	RR	random	3	1.08 (0.93, 1.26)

Gillespie LD	2012	vitamin D3 + calcium	calcium	older people in the community	Falls	379	no info	RR	random	2	0.70 (0.53, 0.92)
Gillespie LD	2012	vitamin D2	placebo or control	older people in the community	Falls	9563	no info	RR	random	2	0.98 (0.92, 1.04)
Cameron ID	2012	vitamin D3 or D2 plus calcium	calcium	older individuals in care facilities or hospitals	Falls: Rate of falls	747	no info	RaR	random	2	0.71 (0.56, 0.90)
Cameron ID	2012	vitamin D2	usual care or placebo	older individuals in care facilities or hospitals	Falls: Rate of falls	3765	no info	RaR	random	2	0.55 (0.19, 1.64)
Gillespie LD	2012	vitamin D3	placebo or control	older people in the community	Falls: Rate of falls	2478	no info	RaR	random	2	1.14 (1.03, 1.27)
Avenell A	2009	Vitamin D2, D3 or 25OHD	placebo or no intervention	Men over 65 years of age and post-menopausal women	Fractures	25016	2195	RR	fixed	10	1.01 (0.93, 1.09)
Chung M	2011	vitamin D	placebo	community dwelling or institutionalised adults	Fractures	14583	1235	RR	random	5	1.03 (0.84, 1.26)
DIPART group	2010	vitamin D2 or D3	placebo or leaflet or no treatment	general	Fractures	19316	no info	HR	fixed	4	1.01 (0.92, 1.12)
Gillespie LD	2012	vitamin D3	placebo or control	older people in the community	Fractures	4942	no info	RR	random	2	0.97 (0.63, 1.51)
Gillespie LD	2012	vitamin D3 + calcium	calcium	older people in the community	Fractures	379	no info	RR	random	2	0.54 (0.26, 1.15)
Palmer SC	2009	established and newer vitamin D compounds	placebo, no treatment	chronic kidney disease requiring dialysis	Fractures	181	no info	RR	fixed	4	1.00 (0.06, 15.41)

Avenell A	2009	Vitamin D2, D3 or 25OHD	placebo or no intervention	Men over 65 years of age and post-menopausal women	Fractures: hip	24749	695	RR	fixed	9	1.15 (0.99, 1.33)
Bergman GJ	2010	vitamin D3 (with calcium)	calcium	older women	Fractures: hip	no info	no info	OR	random	2	1.12 (0.23, 3.04)
DIPART group	2010	vitamin D2 or D3	placebo or leaflet or no treatment	general	Fractures: hip	19316	no info	HR	fixed	4	1.09 (0.92, 1.29)
Lai JK	2010	vitamin D2 or D3 (or vitamin D2 or D3 and calcium)	placebo or no treatment (or calcium)	older adults	Fractures: hip	28324	801	RR	?	8	1.13 (0.98, 1.29)
Bergman GJ	2010	vitamin D3 (with calcium)	calcium	older women	Fractures: Non-vertebral	no info	no info	OR	random	2	0.73 (0.17, 1.90)
Bischoff-Ferrari HA	2009	vitamin D3 or vitamin D2 or active vitamin D (vitamin D3 or vitamin D2 or active vitamin D + calcium)	placebo (or calcium)	people >65	Fractures: Non-vertebral	7130	610	RR		5	0.79 (0.63, 0.99)
Bergman GJ	2010	vitamin D3 (with calcium)	calcium	older women	Fractures: Non-vertebral-non-hip	no info	no info	OR	random	2	0.69 (0.21, 1.66)
Avenell A	2009	Vitamin D2, D3 or 25OHD	placebo or no intervention	Men over 65 years of age and post-menopausal women	Fractures: vertebral or deformity	9138	95	RR	random	5	0.90 (0.42, 1.92)

Muir SW	2011	vitamin D2 and vitamin D3 (or vitamin D2 and vitamin D3 + calcium)	placebo (or calcium)	older adults	Performance measures: Balance sway	207	n/a	SMD	fixed	3	-0.20 (-0.39, -0.01)
Muir SW	2011	vitamin D2 and vitamin D3 (or vitamin D2 and vitamin D3 + calcium)	placebo (or calcium)	older adults	Performance measures: Lower extremity strength	314	n/a	SMD	fixed	3	0.05 (-0.11, 0.20)
Muir SW	2011	vitamin D2 and vitamin D3 (or vitamin D2 and vitamin D3 + calcium)	placebo (or calcium)	older adults	Performance measures: Muscle strength	274	n/a	SMD	fixed	3	-0.19 (-0.35, -0.02)
Other outcomes											
Palmer SC	2009	established and newer vitamin D compounds	placebo, no treatment	chronic kidney disease not requiring dialysis	Alkaline phosphatase (U/lt)	111	n/a	WMD	fixed	2	-21.81 (-40.39, 3.22)
Palmer SC	2009	established and newer vitamin D compounds	placebo, no treatment	chronic kidney disease requiring dialysis	Alkaline phosphatase (U/lt)	135	n/a	WMD	fixed	3	-27.35 (-50.69, -4.01)
Palmer SC	2009	established and newer vitamin D compounds	placebo, no treatment	chronic kidney disease not requiring dialysis	Creatinine clearance (ml/min)	38	n/a	WMD	fixed	4	-1.68 (-6.92, 3.56)
Autier P	2007	vitamin D	placebo or no vitamin D	general	Mortality	7276	1452	RR	random	5	0.91 (0.78, 1.06)

Bjelakovic G	2011	vitamin D3	placebo or no intervention	general	Mortality	12824	1703	RR	random	9	0.91 (0.82, 1.02)
Bjelakovic G	2011	vitamin D2	placebo or no intervention	general	Mortality	17079	2850	RR	random	8	1.04 (0.97, 1.11)
Elamin MB	2011	vitamin D	placebo or no treatment	general	Mortality	13277	1865	RR	random	10	0.97 (0.90, 1.04)
Palmer SC	2009	established and newer vitamin D compounds	placebo, no treatment	chronic kidney disease not requiring dialysis	Mortality	477	no info	RR	fixed	4	1.40 (0.38, 5.15)
Palmer SC	2009	established and newer vitamin D compounds	placebo, no treatment	chronic kidney disease requiring dialysis	Mortality	233	no info	RR	fixed	5	1.34 (0.34, 5.24)
Rejnmark L	2012	vitamin D	placebo	older adults	Mortality	15515	1653	HR	participati on level analysis	4	0.96 (0.87, 1.06)
Palmer SC	2009	established and newer vitamin D compounds	placebo, no treatment	chronic kidney disease not requiring dialysis	Parathyroid hormone (nmol/lt)	153	n/a	WMD	fixed	4	-49.34 (-85.7, -12.97)
Palmer SC	2009	established and newer vitamin D compounds	placebo, no treatment	chronic kidney disease requiring dialysis	Parathyroid hormone (nmol/lt)	212	n/a	WMD	fixed	6	-196.05 (-298.43, -93.66)
Kandula P	2011	vitamin D (no active compounds)	placebo	chronic kidney disease patients	Parathyroid hormone (nmol/lt)	177	n/a	WMD	random	4	-31.53 (-57.01, -6.05)
Palmer SC	2009	established and newer vitamin D compounds	placebo, no treatment	chronic kidney disease requiring dialysis	Parathyroidectomy	133	no info	RR	fixed	2	0.82 (0.05, 12.47)

Palmer SC	2009	established and newer vitamin D compounds	placebo, no treatment	chronic kidney disease not requiring dialysis	Risk of hypercalcaemia	612	no info	RR	fixed	7	3.04 (1.17, 7.90)
Palmer SC	2009	established and newer vitamin D compounds	placebo, no treatment	chronic kidney disease requiring dialysis	Risk of hypercalcaemia	182	no info	RR	fixed	5	3.80 (0.90, 16.12)
Palmer SC	2009	established and newer vitamin D compounds	placebo, no treatment	chronic kidney disease not requiring dialysis	Risk of hyperphosphat aemia	245	no info	RR	fixed	2	1.58 (0.47, 5.30)
Palmer SC	2009	established and newer vitamin D compounds	placebo, no treatment	chronic kidney disease requiring dialysis	Risk of hyperphosphat aemia	59	no info	RR	fixed	2	1.57 (0.97, 2.54)
Palmer SC	2009	established and newer vitamin D compounds	placebo, no treatment	chronic kidney disease not requiring dialysis	Risk of requiring dialysis	301	no info	RR	fixed	4	0.76 (0.36, 1.62)
Palmer SC	2009	established and newer vitamin D compounds	placebo, no treatment	chronic kidney disease requiring dialysis	Subperiosteal erosions	120	no info	RR	fixed	3	0.41 (0.07, 2.38)
Palmer SC	2009	established and newer vitamin D compounds	placebo, no treatment	chronic kidney disease requiring dialysis	Vascular calcification	103	no info	RR	fixed	2	1.09 (0.45, 2.67)

Supplementary Table F General characteristics of 76 non overlapping systematic reviews of observational studies

Author	Year	Biomarker	Population	Outcome	N of studies	Main findings
Autoimmune diseases						
Kriegel MA	2011	25OHD	general	Ankylosing spondylitis	8	Suggestive
Kriegel MA	2011	25OHD	general	Crohn's disease	4	Suggestive
Antico A	2012	25OHD	general	Multiple Sclerosis	11	Suggestive
Cao Y	2013	25OHD	general	Osteoarthritis	13	Suggestive
Antico A	2012	25OHD	general	Rheumatoid arthritis	7	Inconclusive
Song GG	2012	25OHD	Rheumatoid arthritis patients	Rheumatoid arthritis activity	8	Definite
Antico A	2012	25OHD	general	Scleroderma	7	Inconclusive
Sakthiswary R	2013	25OHD	general	Systemic lupus erythematosus	22	Suggestive
Kriegel MA	2011	25OHD	general	Thyroid autoimmunity	1	Inconclusive
Antico A	2012	25OHD	general	Type 1 diabetes	10	Suggestive
Christesen HT	2012	25OHD	impact of maternal vitamin D status on children health	Type 1 diabetes in childhood (maternal vitamin D status)	5	Inconclusive
Kriegel MA	2011	25OHD	general	Vitiligo	1	Inconclusive
Cancer outcomes						
van der Rhee H	2009	25OHD	general	Breast cancer	9	Inconclusive
Buttigliero C	2011	25OHD	cancer patients	Breast cancer prognosis	2	Inconclusive
Chung M	2009	25OHD	general	Cancer mortality	1	No association
Chung M	2009	25OHD	general	Colorectal adenoma	1	No association
Chung M	2009	1,25(OH)2D	general	Colorectal cancer	3	No association
van der Rhee H	2009	25OHD	general	Colorectal cancer	8	Definite
Buttigliero C	2011	25OHD	cancer patients	Colorectal cancer prognosis	2	Inconclusive
van der Rhee H	2009	25OHD	general	Lung cancer	4	Inconclusive
Buttigliero C	2011	25OHD	cancer patients	Melanoma prognosis	1	Inconclusive
Kelly LJ	2009	25OHD	general	Non-Hodgkin Lymphoma	8	Inconclusive
Buttigliero C	2011	25OHD	cancer patients	Non-small cell lung cancer prognosis	2	Inconclusive
van der Rhee H	2009	25OHD	general	Oesophageal cancer	3	Inconclusive
Cook LS	2010	25OHD	General women)	Ovarian cancer	1	Inconclusive
van der Rhee H	2009	25OHD	general	Pancreatic cancer	3	Inconclusive
Chung M	2009	1,25(OH)2D	general	Prostate cancer	5	Inconclusive

van der Rhee H	2009	25OHD	general	Prostate cancer	17	Inconclusive
Buttigliero C	2011	25OHD	cancer patients	Prostate cancer prognosis	1	Inconclusive
van der Rhee H	2009	25OHD	general	Renal cancer	1	Inconclusive
van der Rhee H	2009	25OHD	general	Stomach cancer	1	Inconclusive
Pittas AG	2010	25OHD	general	Cardiovascular disease	7	Suggestive
Renzaho AM	2011	25OHD	ethnic minorities	Cardiovascular disease in ethnic minorities	5	Suggestive
Barnard K	2010	25OHD	older adults	Cardiovascular disease mortality	6	Inconclusive
Barnard K	2010	25OHD	older adults	Hypertension	5	Inconclusive
Cardiovascular outcomes						
Dolinsky DH	2013	25OHD	children	Hypertension in children	14	Definite
Chung M	2009	25OHD	general	Myocardial infarction	1	No association
Chung M	2009	25OHD	general	Stroke	1	No association
Cognitive disorders						
Barnard K	2010	25OHD	older adults	Cognition	5	Inconclusive
Barnard K	2010	25OHD	older adults	Depression	4	Inconclusive
Infectious diseases						
Jolliffe DA	2013	25OHD	general	Acute respiratory infection	25	Suggestive
Chung M	2009	25OHD	general	Infectious diseases mortality	1	Inconclusive
Metabolic disorders						
Christesen HT	2012	25OHD	impact of maternal vitamin D status on children health	Adiposity in children (maternal vitamin D status)	1	No association
Renzaho AM	2011	25OHD	ethnic minorities	Metabolic syndrome in ethnic minorities	2	Inconclusive
Dolinsky DH	2013	25OHD	children	Metabolites: HDL in children	22	No association
Dolinsky DH	2013	25OHD	children	Metabolites: insulin/glucose metabolism in children	18	Inconclusive
Dolinsky DH	2013	25OHD	children	Metabolites: LDL in children	16	No association
Dolinsky DH	2013	25OHD	children	Metabolites: triglycerides in children	21	No association
Renzaho AM	2011	25OHD	ethnic minorities	Obesity in ethnic minorities	14	Suggestive
Pittas AG	2010	25OHD	general	Type 2 diabetes	3	Inconclusive

Renzaho AM	2011	25OHD	ethnic minorities	Type 2 diabetes in ethnic minorities	5	Suggestive
Neonatal/ infant/ child related outcomes						
Christesen HT	2012	25OHD	impact of maternal vitamin D status on children health	Allergic rhinitis and atopic dermatitis/eczema (maternal vitamin D status)	5	Inconclusive
Christesen HT	2012	25OHD	impact of maternal vitamin D status on children health	Birth weight (maternal vitamin D status)	11	Inconclusive
Christesen HT	2012	25OHD	impact of maternal vitamin D status on children health	Cerebral function and diseases (maternal vitamin D status)	2	Inconclusive
Christesen HT	2012	25OHD	impact of maternal vitamin D status on children health	Childhood infections (maternal vitamin D status)	5	Inconclusive
Thorne-Lyman A	2012	25OHD	pregnant women	Neonatal and infant growth	3	Suggestive
Thorne-Lyman A	2012	25OHD	pregnant women	Small for gestational age (maternal vitamin D status)	4	Inconclusive
Christesen HT	2012	25OHD	impact of maternal vitamin D status on children health	Wheezing and asthma in childhood (maternal vitamin D status)	7	Inconclusive
Pregnancy related outcomes						
Aghajafari F	2013	25OHD	pregnant women	Bacterial vaginosis in pregnant women	3	Definite
Aghajafari F	2013	25OHD	pregnant women	Caesarean section	2	No association
Christesen HT	2012	25OHD	pregnant women	Fertility	2	Inconclusive
Christesen HT	2012	25OHD	pregnant women	Gestational diabetes mellitus	7	Suggestive
Christesen HT	2012	25OHD	pregnant women	Length of gestation/preterm birth	9	Suggestive
Christesen HT	2012	25OHD	pregnant women	Postpartum depression	1	Inconclusive
Christesen HT	2012	25OHD	pregnant women	Preeclampsia in pregnant women	10	Suggestive

Christesen HT	2012	25OHD	pregnant women	Pregnancy-associated breast cancer	1	Inconclusive
Skeletal outcomes						
Cranney A	2007	25OHD	children, women of reproductive age, postmenopausal women and elderly men	Bone health in pregnant and lactating women	4	Inconclusive
Cranney A	2007	25OHD	children, women of reproductive age, postmenopausal women and elderly men	Bone mineral content in infants	3	Inconclusive
Cranney A	2007	25OHD	children, women of reproductive age, postmenopausal women and elderly men	Bone mineral density	13	Suggestive
Cranney A	2007	25OHD	children, women of reproductive age, postmenopausal women and elderly men	Bone mineral density in children and adolescents	5	Suggestive
Cranney A	2007	25OHD	children, women of reproductive age, postmenopausal women and elderly men	Falls: risk of falling in older individuals	4	Definite
Cranney A	2007	25OHD	children, women of reproductive age, postmenopausal women and elderly men	Fractures in older individuals	15	Inconclusive
Cranney A	2007	25OHD	children, women of reproductive age, postmenopausal women and elderly men	Performance measures in older individuals	4	Inconclusive

			children, women of reproductive age, postmenopausal women and elderly men			
Cranney A	2007	25OHD		Rickets in children	12	Definite
Other outcomes						
Yaghjian L	2012	25OHD	General women)	Mammographic breast density	14	Inconclusive
Barnard K	2010	25OHD	older adults	Mortality	6	Inconclusive

Supplementary Table G General characteristics of 48 non overlapping meta-analyses of observational studies (MA: meta-analysis, RR: relative risk, OR: odds ratio, HR: hazard ratio, SMD: standardised mean difference, WMD: weighted mean difference, CI: confidence interval, CKD: chronic kidney disease)

Author	Publication date	Vitamin D measurement	Population	Outcome	Unit of comparison	Participants total	Events total	Type of metric	MA model	N of studies	Reported RR (95% CI)
Cancer outcomes											
Gilbert R	2011	25OHD	men	Aggressive prostate cancer	per 10ng/ml	4524	871	OR	random	6	0.98 (0.84, 1.15)
Gilbert R	2011	1,25(OH)2D	men	Aggressive prostate cancer	per 10ng/ml	1488	696	OR	random	2	0.86 (0.72, 1.02)
Chen P	2013	25OHD	General/ Hospital based	Breast cancer	highest vs lowest category	26317	11771	OR	random	21	0.52 (0.40, 0.68)
Chen P	2010	1,25(OH)2D	women	Breast cancer	highest vs lowest quartile	3627	1802	OR	random	3	0.99 (0.68, 1.44)
Bauer SR	2013	25OHD	post-menopausal women	Breast cancer: Post - menopausal	per 5 ng/ml	3929	8766	RR	no info	9	0.97 (0.93, 1.00)
Bauer SR	2013	25OHD	pre-menopausal women	Breast cancer: Pre-menopausal	per 5 ng/ml	1613	2890	RR	no info	6	0.99 (0.97, 1.04)
Lee JE	2011	25OHD	adults	Colon cancer	highest vs lowest category	4578	1822	OR	random	10	0.77 (0.56, 1.07)
Lee JE	2011	1,25(OH)2D	adults	Colon cancer	highest vs lowest category	no info	no info	OR	no info	4	0.88 (0.57, 1.35)
Yin L	2011	25OHD	general	Colorectal adenoma	per 20 ng/ml	7654	3539	OR	random	9	0.82 (0.69, 0.97)

Wang L	2012	25OHD	general	Cardiovascular disease	highest vs lowest category	64994	6123	RR	random	19	1.52 (1.30, 1.77)
Grandi NC	2010	25OHD	adults	Cardiovascular disease mortality	lowest vs highest category	24387	2007	HR	random	5	1.83 (1.19, 2.80)
Parker J	2010	25OHD	general	Cardiovascular disease prevalence	highest vs lowest category	64722	7600	OR	random	16	0.67 (0.55, 0.81)
Kunutsor SK	2013	25OHD	general	Hypertension	highest vs lowest category	48633	4965	RR	random	7	0.70 (0.58, 0.86)
Brondum-Jacobsen P	2012	25OHD	adults	Ischemic heart disease	lowest vs highest quartile	82982	8376	HR	random	18	1.39 (1.25, 1.54)
Brondum-Jacobsen P	2012	25OHD	general	Ischemic stroke	lowest vs highest quartile	26596	1800	HR	random	5	1.52 (1.26, 1.84)
Brondum-Jacobsen P	2012	25OHD	general	Ischemic stroke	lowest vs highest quartile	31788	844	OR	random	5	1.92 (1.64, 2.26)
Sun Q	2012	25OHD	general	Stroke	highest vs lowest category	no info	1214	RR	fixed	6	1.52 (1.20, 1.85)
Cognitive disorders											
Annweiler C	2013	25OHD	general	Alzheimer's disease	per SD	1005	357	SMD	random	10	1.40 (0.26, 2.54)
Etgen T	2012	25OHD	adults	Cognition	lowest vs highest quartile	7688	1135	OR	random	7	2.39 (1.91, 3.00)
Anglin RE	2013	25OHD	general (cross-sectional)	Depression	<50 vs >50 nmol/l	22476	2051	OR	random	9	1.31 (1.00, 1.71)

			studies)								
Anglin RE	2013	25OHD	general (cohort studies)	Depression	<50 vs >50 nmol/Lt	8815	617	HR	random	3	2.21 (1.40, 3.49)
Infectious diseases											
Nnoaham KE	2008	25OHD	adults	Active tuberculosis	mean	534	308	SMD	random	7	0.68 (0.43, 0.93)
Metabolic disorders											
Saneei P	2013	25OHD	general	Body mass index	correlation coefficients	16525	n/a	Z score	random	37	-0.15 (-0.19, -0.11)
Parker J	2010	25OHD	general	Metabolic syndrome prevalence	highest vs lowest category	31416	2821	OR	random	8	0.49 (0.38, 0.64)
Afzal S	2013	25OHD	general	Type 2 diabetes	lowest vs highest category	72204	4877	OR	random	16	1.50 (1.33, 1.68)
Parker J	2010	25OHD	general	Type 2 diabetes prevalence	highest vs lowest category	11892	2424	OR	random	9	0.45 (0.25, 0.82)
Neonatal/ infant/ child related outcomes											
Aghajafari F	2013	25OHD	pregnant women	Birth length	mean (cm)	840	n/a	WMD	fixed	2	-0.19 (-0.65, 0.26)
Aghajafari F	2013	25OHD	pregnant women	Birth weight	mean (grams)	5541	n/a	WMD	fixed	4	-130.92 (-186.69, -75.14)
Aghajafari F	2013	25OHD	pregnant women	Head circumference	mean (cm)	840	n/a	WMD	fixed	2	-0.05 (-0.34, 0.24)

Aghajafari F	2013	25OHD	pregnant women	Small for gestational age	lowest vs highest category	6851	no info	OR	fixed	6	1.85 (1.52, 2.26)
Pregnancy related outcomes											
Aghajafari F	2013	25OHD	pregnant women	Gestational diabetes	lowest vs highest category	4112	687	OR	fixed	10	1.49 (1.18, 1.89)
Aghajafari F	2013	25OHD	pregnant women	Preeclampsia	lowest vs highest category	3230	393	OR	fixed	9	1.79 (1.25, 2.58)
Skeletal diseases											
Weatherall M	2000	25OHD	older individuals	Fractures	per SD	2956	1572	SMD			-0.66 (-0.74, -0.59)
Lai JK	2010	25OHD	adults	hip fracture (hospital-based controls)	geometric mean (nmol/l)	2201	1116	log ratio of geometric mean	random	8	-0.26 (-0.33, -0.23)
Lai JK	2010	25OHD	adults	hip fracture (population-based controls)	geometric mean (nmol/l)	1655	818	log ratio of geometric mean	random	9	-0.51 (-0.64, -0.38)
Other outcomes											
Pilz S	2011	25OHD	CKD patients	Mortality	per 10 ng/ml	6853	2110	RR	mixed effects	10	0.86 (0.82, 0.91)
Brondum-Jacobsen P	2012	25OHD	adults	Mortality	lowest vs highest quartile	77155	15447	HR	random	17	1.46 (1.31, 1.64)

Supplementary Table H General characteristics of meta-analyses of observational studies for outcomes with more than one meta-analysis (RR: relative risk, OR: odds ratio, HR: hazard ratio, SMD: standardised mean difference, WMD: weighted mean difference, CI: confidence interval)

Author	Date	Vitamin D measurement	Population	Unit of comparison	Participants total	Events total	Type of metric	Meta-analysis model	N total studies	Reported RR (95% CI)	Significant summary effect	In significant bias analysis
Breast cancer												
Chen P	2013	25OHD	general/ Hospital based	highest vs lowest quintile	26317	11771	OR	random	21	0.52 (0.40, 0.68)	yes	yes
Chung M	2011	25OHD	general	per 10nmol/lt	4726	2363	OR	dose-response meta-analysis	4	0.99 (0.97, 1.01)	no	no
Gandini S	2011	25OHD	general	per 10ng/ml	no info	6175	RR	random	10	0.89 (0.81, 0.98)	yes	no
Mohr S	2011	25OHD	general	highest vs lowest quintile	no info	no info	Peto OR	no info	11	0.61 (0.47, 0.80)	yes	no
Yin L	2010	25OHD	general	per 20 ng/mL	12901	6147	OR	random	9	0.73 (0.60, 0.88)	yes	no
Chen P	2010	25OHD	general	highest vs lowest quartile	11330	5489	OR	random	7	0.55 (0.38, 0.80)	yes	no
Colorectal adenoma												
Fedirko V	2010	25OHD	adults with no colorectal cancer history	highest vs lowest quartile	1386	616	OR	pooled meta-analysis	3	0.59 (0.41, 0.84)	yes	no
Wei M	2008	25OHD	general	highest vs lowest quintile	3787	2628	OR	random	7	0.70 (0.56, 0.87)	yes	no

Forouhi NG	2012	25OHD	adults	highest vs lowest quartile	55713	3612	RR	random	11	0.59 (0.52, 0.67)	yes	no
Mitri J	2011	25OHD	adults	>25 vs <14ng/ml	5664	1153	RR	random	5 cohorts (4 studies)	0.57 (0.43, 0.76)	yes	no
Afzal S	2013	25OHD	general	lowest vs highest category	72204	4877	OR	random	16	1.50 (1.33, 1.68)	yes	yes
Type 2 diabetes (prevalent)												
Pittas AG	2007	25OHD	general	25–38 vs. 10–23 ng/ml	no info	no info	OR	random	4	0.36 (0.16, 0.80)	yes	No
Parker J	2010	25OHD	general	highest vs lowest category	no info	11892	OR	random	9	0.45 (0.25, 0.82)	yes	yes
Gestational diabetes												
Aghajafari F	2013	25OHD	pregnant women	lowest vs highest category	4112	687	OR	fixed	10	1.49 (1.18, 1.89)	yes	yes
Poel YHM	2012	25OHD	Pregnant women	<50nmol/lt	2146	433	OR	random	7	1.61 (1.19, 2.17)	yes	no

Supplementary table I Excess significance bias analysis of 40 meta-analyses (based on effect from the largest study; OR: odds ratio, HR: hazards ratio)

Variable	Outcome group	Number of Studies	Number of meta-analyses	Expected Significant	Observed significant	Observed/expected	p-value
All meta-analyses		369	40	218	158	0.72	
Outcome							
<i>Cancer</i>							
Aggressive prostate cancer	2	6	1	0.7	1	1.52	0.66
Aggressive prostate cancer (1,25(OH)2D)	2	2	1	0.8	0	0.00	
Breast cancer	2	21	1	20.9	13	0.62	
Breast cancer (1,25(OH)2D)	2	3	1	1.4	0	0.00	
Breast cancer: Post-menopausal	2	9	1	9	0	0.00	
Breast cancer: Pre-menopausal	2	6	1	6	1	0.17	
Colon cancer	2	10	1	9.0	2	0.22	
Colorectal cancer	2	10	1	3.8	0	0.00	
Kidney cancer	2	6	1	3.2	0	0.00	
Non-Hodgkin Lymphoma	2	6	1	0.5	1	2.17	0.41
Non-Hodgkin Lymphoma	2	4	1	0.2	0	0.00	
Ovarian cancer	2	10	1	4.9	0	0.00	
Pancreatic cancer	2	6	1	0.6	1	1.75	0.55
Prostate cancer	2	14	1	2.6	0	0.00	
Prostate cancer (1,25(OH)2D)	2	7	1	0.4	1	2.50	0.26
Rectal cancer	2	9	1	0.7	2	2.86	0.10
Sporadic colorectal adenoma	2	9	1	3.6	4	1.11	0.76
Sporadic colorectal adenoma recurrence	2	3	1	0.2	1	5.26	0.05
<i>Cardiovascular diseases</i>							
Cardiovascular disease	3	19	1	17.2	8	0.47	
Cardiovascular disease mortality	3	5	1	2.5	3	1.20	0.62
Cardiovascular disease prevalent	3	16	1	15.3	11	0.72	
Hypertension	3	7	1	6.4	3	0.47	
Ischemic heart disease	3	19	1	8.1	12	1.48	0.07
Ischemic stroke (HR)	3	5	1	2.7	3	1.11	0.76
Ischemic stroke (OR)	3	5	1	3.8	4	1.05	0.81
Stroke	3	7	1	4.3	3	0.70	
<i>Cognition disorders</i>							
Alzheimer's diseases	4	7	1	0.9	5	5.56	3.8x10 ⁻⁶
Cognition	4	7	1	6.5	7	1.08	0.47

Depression (case-control studies)	4	9	1	2.0	3	1.50	0.40
Depression (cohort studies)	4	3	1	3.0	2	0.67	
<i>Infectious diseases</i>							
Tuberculosis	5	7	1	4.6	5	1.09	0.72
<i>Metabolic diseases</i>							
Metabolic syndrome prevalent	6	8	1	8	4.0	0.50	
Type 2 diabetes	6	16	1	9.5	6	0.63	
Type 2 diabetes prevalent	6	9	1	9.0	5	0.56	
<i>Neonatal/ infant/ child related outcomes</i>							
Small for gestational age	7	6	1	4.9	4	0.82	
<i>Pregnancy related outcomes</i>							
Gestational diabetes	8	10	1	8.4	2	0.24	
Preeclampsia	8	7	1	5.3	1	0.19	
<i>Skeletal outcomes</i>							
Fractures	9	28	1	9.0	19	2.11	6.2x10 ⁻⁵
<i>Other</i>							
All-cause mortality in CKD patients	7	10	1	6.2	6	0.97	
All-cause mortality	7	18	1	12.0	15	1.25	0.13
Outcome group							
Cancer	2	141	18	68.3	27	0.40	
Cardiovascular diseases	3	83	8	60.2	47	0.78	
Cognition disorders	4	26	4	12.4	17	1.37	0.07
Infectious diseases	5	7	1	4.6	5	1.09	0.72
Metabolic diseases	6	33	3	26.5	15	0.57	
Neonatal/ infant/ child related outcomes	7	6	1	4.9	4	0.82	
Pregnancy related outcomes	8	17	2	13.7	3	0.22	
Skeletal outcomes	9	28	1	9.1	19	2.09	6.2x10 ⁻⁵
Other	10	28	2	18.2	21	1.15	0.27
Heterogeneity							
I ² ≤50%		185	25	107	47	0.44	
I ² >50%		184	15	111	111	1.00	0.94
Statistically significant summary effect							
Yes		277	26	178	150	0.84	
No		92	14	39.3	8	0.20	
Type of biomarker							
1,25(OH)2D		12	3	2.6	1	0.38	
25OHD		357	37	215	157	0.73	

Supplementary Table J: General characteristics of meta-analyses of RCTs for outcomes with more than one meta-analysis (RR: relative risk, OR: odds ratio, HR: hazard ratio, SMD: standardised mean difference, WMD: weighted mean difference, CI: confidence interval)

Author	Date	Compound	Versus	Population	Outcome	Participants total	Events total	Type of metric	Meta-analysis model	N of studies	Reported RR (95% CI)
Cardiovascular disease											
Wang L	2010	vitamin D	placebo	general population	Cardiovascular disease	2988	991	RR	fixed	2	0.90 (0.77, 1.05)
Myung SK	2013	vitamin D	placebo	general population	Cardiovascular disease	no info	no info	RR	fixed	2	0.95 (0.86, 1.05)
Hypertension											
Pittas AG	2010	vitamin D2 and vitamin D3	placebo	general population	Diastolic blood pressure (mm Hg)	no info	NA	WMD	no info	no info	-0.43 (-1.39, 0.53)
Witham MD	2009	Alphacalcidol or vitamin D3 or UVA + UVB (or vitamin D3 + calcium)	placebo or UVA (or calcium)	hypertensive individuals	Diastolic blood pressure (mm Hg)	545	NA	WMD	random	8	-3.05 (-5.50, -0.60)
Wu SH	2010	vitamin D	placebo	normotensive or hypertensive individuals	Diastolic blood pressure (mm Hg)	366	NA	WMD	no info	3	-0.03 (-1.98, 1.92)

Pittas AG	2010	vitamin D2 and vitamin D3	placebo	general population	Systolic blood pressure (mm Hg)	no info	NA	WMD	no info	no info	-2.60 (-6.60, 1.09)
Witham MD	2009	Alphacalcidol or vitamin D3 or UVA + UVB (or vitamin D3 + calcium)	placebo or UVA (or calcium)	hypertensive individuals	Systolic blood pressure (mm Hg)	545	NA	WMD	random	8	-3.63 (-8.00, 0.74)
Wu SH	2010	vitamin D	placebo	normotensive or hypertensive individuals	Systolic blood pressure (mm Hg)	366	NA	WMD	no info	3	-2.39 (-5.70, 0.90)
Birth weight											
De-Regil LM	2012	vitamin D alone or in combination with other micronutrients	placebo or no treatment	pregnant women	Birth weight (grams)	403	NA	WMD	random	3	39.55 (-240.68, 319.78)
De-Regil LM	2012	vitamin D alone or in combination with other micronutrients	placebo or no treatment	pregnant women	Birth weight	463	no info	RR	random	3	0.48 (0.23, 1.01)
Thorne-Lyman A	2012	vitamin D	placebo	pregnant women	Birth weight	507	55	RR	fixed	3	0.4 (0.23, 0.71)
Preterm											

delivery											
Thorne-Lyman A	2012	vitamin D	placebo	pregnant women	Mean gestational age at delivery (weeks)	529	NA	WMD	fixed	2	0.17 (-0.16, 0.51)
Thorne-Lyman A	2012	vitamin D	placebo	pregnant women	Preterm delivery	529	28	RR	fixed	2	0.77 (0.35, 1.66)
Falls											
Bischoff-Ferrari HA	2009	vitamin D3 or vitamin D2 (or vitamin D3 or vitamin D2 + calcium)	placebo (or calcium)	older adults	Falls	1476	no info	RR	no info	6	0.77 (0.65, 0.92)
Bischoff-Ferrari HA	2009	Active form of vitamin D	placebo	older adults	Falls	624	223	RR	no info	2	0.78 (0.64, 0.94)
Bischoff-Ferrari HA	2004	vitamin D or active vitamin D analogue (or vitamin D or active vitamin D analogue + calcium)	placebo (or calcium)	older adults	Falls	1237	no info	RR	no info	5	0.69 (0.53, 0.88)
Kalyani RR	2010	vitamin D	placebo	older adults	Falls	9508	no info	RR	random	7	1.01 (0.96, 1.07)
Murad MH	2011	vitamin D2 and vitamin	placebo	older adults	Falls	no info	no info	OR	random	10	0.97 (0.84, 1.11)

Cameron ID	2012	vitamin D3 or D2 plus calcium	calcium	older individuals in care facilities or hospitals	Falls: Rate of falls	747	no info	RaR	random	2	0.71 (0.56, 0.90)
Cameron ID	2012	vitamin D2	usual care or placebo	older individuals in care facilities or hospitals	Falls: Rate of falls	3765	no info	RaR	random	2	0.55 (0.19, 1.64)
Gillespie LD	2012	vitamin D3	placebo or control	older people in the community	Falls: Rate of falls	2478	no info	RaR	random	2	1.14 (1.03, 1.27)
Fractures											
Avenell A	2009	Vitamin D2, D3 or 25OHD	placebo or no intervention	Men over 65 years of age and post-menopausal women	Fractures	25016	2195	RR	fixed	10	1.01 (0.93, 1.09)
Chung M	2011	vitamin D	placebo	community dwelling or institutionalised adults	Fractures	14583	1235	RR	random	5	1.03 (0.84, 1.26)
DIPART group	2010	vitamin D2 or D3	placebo or leaflet or no treatment	general population	Fractures	19316	no info	HR	fixed	4	1.01 (0.92, 1.12)

Gillespie LD	2012	vitamin D3	placebo or control	older people in the community	Fractures	4942	no info	RR	random	2	0.97 (0.63, 1.51)
Gillespie LD	2012	vitamin D3 + calcium	calcium	older people in the community	Fractures	379	no info	RR	random	2	0.54 (0.26, 1.15)
Palmer SC	2009	established and newer vitamin D compounds	placebo, no treatment	chronic kidney disease requiring dialysis	Fractures	181	no info	RR	fixed	4	1.00 (0.06, 15.41)
Fractures: hip											
Avenell A	2009	Vitamin D2, D3 or 25OHD	placebo or no intervention	Men over 65 years of age and post-menopausal women	Fractures: hip	24749	695	RR	fixed	9	1.15 (0.99, 1.33)
Bergman GJ	2010	vitamin D3 (with calcium)	calcium	older women	Fractures: hip	no info	no info	OR	random	2	1.12 (0.23, 3.04)
DIPART group	2010	vitamin D2 or D3	placebo or leaflet or no treatment	general population	Fractures: hip	19316	no info	HR	fixed	4	1.09 (0.92, 1.29)
Lai JK	2010	vitamin D2 or D3 (or vitamin D2 or D3 and calcium)	placebo or no treatment (or calcium)	older adults	Fractures: hip	28324	801	RR	no info	8	1.13 (0.98, 1.29)

Fractures: Non-vertebral											
Bergman GJ	2010	vitamin D3 (with calcium)	calcium	older women	Fractures: Non-vertebral	no info	no info	OR	random	2	0.73 (0.17, 1.90)
Bischoff- Ferrari HA	2009	vitamin D3 or vitamin D2 or active vitamin D (vitamin D3 or vitamin D2 or active vitamin D + calcium)	placebo (or calcium)	people >65	Fractures: Non-vertebral	7130	610	RR	no info	5	0.79 (0.63, 0.99)
Mortality											
Autier P	2007	vitamin D	placebo or no vitamin D	general population	Mortality	7276	1452	RR	random	5	0.91 (0.78, 1.06)
Bjelakovic G	2011	vitamin D3	placebo or no intervention	general population	Mortality	12824	1703	RR	random	9	0.91 (0.82, 1.02)
Bjelakovic G	2011	vitamin D2	placebo or no intervention	general population	Mortality	17079	2850	RR	random	8	1.04 (0.97, 1.11)
Elamin MB	2011	vitamin D	placebo or no treatment	general population	Mortality	13277	1865	RR	random	10	0.97 (0.90, 1.04)

Rejnmark L	2012	vitamin D	placebo	older adults	Mortality	15515	1653	HR	participation level analysis	4	0.96 (0.87, 1.06)
Chronic kidney disease patients: Parathyroid hormone levels											
Palmer SC	2009	established and newer vitamin D compounds	placebo, no treatment	chronic kidney disease not requiring dialysis	Parathyroid hormone (pmol/l)	153	NA	WMD	fixed	4	-49.34 (-85.7, -12.97)
Palmer SC	2009	established and newer vitamin D compounds	placebo, no treatment	chronic kidney disease requiring dialysis	Parathyroid hormone (pmol/l)	212	NA	WMD	fixed	6	-196.05 (-298.43, -93.66)
Kandula P	2011	vitamin D (no active compounds)	placebo	chronic kidney disease patients	Parathyroid hormone (pmol/l)	177	NA	WMD	random	4	-31.53 (-57.01, -6.05)

Supplementary Figure A Correlation between the summary relative risk in each meta-analysis (random effects) and the relative risk in the largest study. Axes are in logarithmic scale.

