

Supplementary – intended for publication

Abbreviations

<i>Abbreviation</i>	<i>Meaning</i>
<i>BMI</i>	Body Mass Index
<i>Hcy</i>	Homocysteine
<i>HDL-c</i>	HDL-Cholesterol
<i>HHcy</i>	Hyperhomocysteine
<i>LD</i>	Linkage disequilibrium
<i>PICOC</i>	Population, Intervention, Comparison, Outcome, Context, Study method
<i>PN</i>	Personalized nutrition
<i>RBC</i>	Red blood cell
<i>SNP</i>	Single nucleotide polymorphism
<i>VDD</i>	Vitamin D deficiency

Search Strategy

Table S1: Inclusion and exclusion criteria

<i>Inclusion Criteria</i>	<i>Exclusion Criteria</i>
• Peer-reviewed primary studies • Languages: English or German • Subjects: healthy adults of any physical fitness, ethnicity, or socioeconomic status • Focused on the aspect of personalized nutrition and genetic variations (e.g. SNPs) • any type of nutrition-based observation and intervention • any outcome measure or follow-up duration	• Animal studies • Children <18 years • Diseased, pregnant, or infertile subjects • Overweight & obese subjects (BMI >25 kg/m²) • Papers published prior to 2007 • Non-validated studies • Studies with nonsignificant correlations • Studies using genetic risk scores • Studies on alcohol intake, food intake and food preferences. • Reviews, meta-analyses, conference abstracts

Table S2: PICOC methodology

<i>PICOC</i>	<i>Description</i>
<i>Population</i>	adult participants of any age and physical fitness
<i>Intervention</i>	any types of nutrition-based observation and interventions
<i>Comparison</i>	controlled quantitative studies (any type of controls)
<i>Outcome</i>	any kind of outcome measures and lengths of follow-up
<i>Context</i>	clinical and nutrition context

Table S3: Search strategies for the systematic literature search

Database	Date	Concepts	Results
Cochrane	First search: 30.05.2022	(('single nucleotide' OR gen* OR allele* OR homozygo* OR heterozygo*) NEAR/3 (polymorphism* OR varia* OR pattern* OR diversit* OR mutation* OR differentiat* OR divergenc*)):ti,ab,kw OR ((nutritional* NEAR/3 (genomic* OR genetic*)):ti,ab,kw) OR nutrigenomic*:ti,ab,kw OR AND ((personal* OR precis* OR individuali* OR tailored OR custom*) NEAR/3 (nutri* OR macronutri* OR micronutri* OR alimentary OR metabolism* OR diet* OR feed* OR food* OR intake* OR uptake*)):ti,ab,kw OR ((nutri* OR macronutri* OR micronutri* OR alimentary OR diet* OR feed* OR food*) NEAR/20 (intake* OR uptake* OR advice* OR intervention* OR choice* OR recommend*)):ti,kw OR (daily NEAR/20 (intake* OR uptake*)):ti,kw OR ((deficien* OR defective* OR insufficien*) NEAR/20 (nutri* OR macronutri* AND ((gen* OR allele* OR homozygo* OR heterozygo*) NEAR/4 (interact* OR affect* OR modulat* OR influenc* OR associat* OR correlate* OR determinant* OR based OR linkage* OR diathes* OR predisposition* OR prognos* OR propensit* OR proneness* OR anticipation* OR Filter: Cochrane Library publication date Between Jan 2007 and Dec 2022	252
	Last search: 05.09.2023		276
EMBASE	First search: 30.05.2022	'single nucleotide polymorphism'/exp OR 'genetic variability'/exp OR 'genetic variation'/de OR 'nutrigenomics'/exp OR 'nutrigenetics'/exp OR (('single nucleotide' OR gen* OR allele* OR homozygo* OR heterozygo*) NEAR/3 (polymorphism* OR varia* OR pattern* OR diversit* OR mutation* OR differentiat* OR divergenc*)):ti,ab,kw) OR ((nutritional* NEAR/3 (genomic* OR genetic*)):ti,ab,kw) OR nutrigenomic*:ti,ab,kw OR nutrigenetic*:ti,ab,kw AND 'personalized nutrition'/exp OR 'dietary intake'/exp/mj OR 'food intake'/exp/mj OR 'nutritional deficiency'/exp/mj OR 'nutrient uptake'/exp OR (((personal* OR precis* OR individuali* OR tailored OR custom*) NEAR/3 (nutri* OR macronutri* OR micronutri* OR alimentary OR metabolism* OR diet* OR feed* OR food* OR intake* OR uptake*)):ti,ab,kw) OR (((nutri* OR macronutri* OR micronutri* OR alimentary OR diet* OR feed* OR food*)	2401

		NEAR/20 (intake* OR uptake* OR advice* OR intervention* OR choice* OR recommend*)):ti,kw) OR ((daily NEAR/20 (intake* OR uptake*)):ti,kw) OR (((deficien* OR defective* OR insufficien*) NEAR/20 (nutri* OR macronutri* OR micronutri* OR alimentary OR diet* OR feed* OR food*)):ti,kw) AND 'gene interaction'/exp OR 'genetic association'/exp OR 'genetic association study'/exp OR 'genetic predisposition'/de OR 'genetic susceptibility'/exp OR (((gen* OR allele* OR homozygo* OR heterozygo*) NEAR/4 (interact* OR affect* OR modulat* OR influenc* OR associat* OR correlate* OR determinant* OR based OR linkage* OR diathes* OR predisposition* OR prognos* OR propensit* OR proneness* OR anticipation* OR susceptibilit*)):ti,ab,kw) AND ([english]/lim OR [german]/lim) AND [2007-2022]/py NOT [conference abstract]/lim NOT ([animals]/lim NOT [humans]/lim) NOT ('juvenile'/exp NOT 'adult'/exp)	
	Last search: 05.09.2023		2564
MEDLINE (OVID)	First search: 30.05.2022	exp Polymorphism, Single Nucleotide/ or Genetic Variation/ or exp Genomic Structural Variation/ or exp Nutrigenomics/ or (('single nucleotide' or gen* or allele* or homozygo* or heterozygo*) adj3 (polymorphism* or varia* or pattern* or diversit* or mutation* or differentiat* or divergenc*)):ti,ab,kw. or (nutritional* adj3 (genomic* or genetic*)):ti,ab,kw. or nutrigenomic*.ti,ab,kw. or nutrigenetic*.ti,ab,kw. AND exp *Diet/ or exp *Dietary Supplements/ or exp *Eating/ or exp *Deficiency Diseases/ or ((personal* or precis* or individual* or tailored or custom*) adj3 (nutri* or macronutri* or micronutri* or alimentary or metabolism* or diet* or feed* or food* or intake* or uptake*)):ti,ab,kw. or ((nutri* or macronutri* or micronutri* or alimentary or diet* or feed* or food*) adj20 (intake* or uptake* or advice* or intervention* or choice* or recommend*)):ti,kw. or (daily adj20 (intake* or uptake*)):ti,kw. or ((deficien* or defective* or insufficien*) adj20 (nutri* or macronutri* or micronutri* or alimentary or diet* or feed* or food*)):ti,kw. AND exp Genetic Association Studies/ or Genetic Predisposition to Disease/ or ((gen* or allele* or homozygo* or heterozygo*) adj4 (interact* or affect* or modulat* or influenc* or associat* or correlate* or determinant* or based or linkage* or diathes* or predisposition* or prognos* or propensit* or proneness* or anticipation* or susceptibilit*)):ti,ab,kw.	1804

	Last search: 13.09.2023	limit to ((english or german) and yr="2007 - 2022") AND NOT (animals not humans).sh. NOT ((exp infant/ OR exp child/ OR adolescent/) NOT exp adult/)	1975
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JB1 Quality Assessment

Red numbers indicate rating scores < 60%

Table S4: Cross-Sectional Studies

Source / Question		1. Were the criteria for inclusion in the sample clearly defined?	2. Were the study subjects and the setting described in detail?	3. Was the exposure measured in a valid and reliable way?	4. Were objective, standard criteria used for measurement of the condition?	5. Were confounding factors identified?	6. Were strategies to deal with confounding factors stated?	7. Were the outcomes measured in a valid and reliable way?	8. Was appropriate statistical analysis used?	Rating
Vitamin D	Zhang et al., 2013	Y	Y	Y	N/A	Y	Y	Y	Y	7/8
	Sinotte et al., 2009	Y	Y	Y	N/A	Y	Y	Y	Y	7/8
	Santos et al., 2019	Y	Y	Y	N/A	Y	Y	Y	Y	7/8
	Robien et al., 2013	Y	Y	Y	N/A	Y	Y	Y	Y	7/8
	Rivera-Parodex et al., 2020	Y	Y	Y	Y	Y	Y	Y	Y	8/8
	Perna et al., 2013	Y	Y	Y	N/A	Y	Y	Y	Y	7/8
	Nissen et al., 2014	Y	Y	Y	N/A	Y	Y	Y	Y	7/8
	Pooyen et al., 2020	Y	Y	Y	Y	Y	Y	Y	Y	8/8
	Mehdizadeh et al., 2021	n	Y	Y	Y	n	n	Y	Y	5/8
	Li et al., 2014	Y	Y	Y	Y	Y	Y	Y	Y	8/8
	Lali et al., 2015	n	Y	Y	Y	n	n	Y	Y	5/8
	Fohner et al., 2016	n	Y	Y	N/A	Y	Y	Y	Y	6/8
	Engelman et al., 2008	n	Y	Y	N/A	Y	Y	Y	Y	6/8
	Gozdzik et al., 2011	Y	Y	Y	N/A	Y	Y	Y	Y	7/8
	Engelman et al., 2012	Y	Y	Y	N/A	Y	Y	Y	Y	7/8
	Lu et al., 2011	Y	Y	Y	Y	Y	Y	Y	Y	8/8
	Xu et al., 2015	Y	Y	Y	Y	Y	Y	Y	Y	8/8
	Bu et al., 2010	Y	Y	Y	N/A	Y	Y	Y	Y	7/8
	Xu et al., 2014	Y	Y	Y	Y	Y	Y	Y	Y	8/8
	Selli et al., 2018	Y	Y	Y	N/A	Y	Y	Y	Y	7/8
	Batai et al., 2014	n	Y	Y	Y	Y	Y	Y	Y	7/8
	Elkum et al., 2014	u	Y	Y	N/A	Y	Y	Y	Y	6/8
	Rivera-Parodex et al., 2018	Y	Y	Y	Y	Y	Y	Y	Y	8/8
	Engelman et al., 2010	Y	Y	Y	N/A	Y	Y	Y	Y	7/8
	Wang et al., 2010	Y	Y	Y	Y	Y	Y	Y	Y	8/8
	Ahn et al., 2010	u	Y	Y	N/A	Y	Y	Y	Y	6/8
	Lee et al., 2021	Y	Y	Y	N/A	Y	Y	Y	Y	7/8
	Kwak et al., 2018	Y	Y	Y	N/A	Y	Y	Y	Y	7/8
	Kandemir et al., 2021	Y	Y	Y	Y	n	u	Y	Y	6/8
	Didriksen et al., 2013	Y	Y	Y	N/A	Y	Y	Y	Y	7/8
	Truemmer et al., 2012	Y	Y	Y	N/A	Y	Y	Y	Y	7/8
	Slater et al., 2015	Y	Y	Y	Y	Y	Y	u	Y	7/8
	Simon et al., 2011	Y	n	Y	N/A	Y	Y	u	Y	5/8
	Thongthai et al., 2015	Y	Y	Y	Y	Y	Y	Y	Y	8/8
	Hansen et al., 2015	Y	Y	Y	N/A	Y	Y	Y	Y	7/8
	Tuncel et al., 2019	Y	Y	Y	N/A	n	n	Y	Y	5/8
	Larcombe et al., 2012	Y	Y	Y	N/A	Y	Y	Y	Y	7/8
	Sallinen et al., 2021	Y	Y	u	N/A	Y	Y	Y	Y	6/8
	Man et al., 2022	Y	Y	n	Y	Y	Y	Y	Y	7/8
	Grant et al., 2022	Y	Y	Y	N/A	Y	Y	Y	Y	7/8
	Parfeto et al., 2023	Y	Y	Y	N/A	Y	Y	Y	Y	7/8
	Retamoso et al., 2023	Y	Y	Y	Y	u	Y	Y	Y	7/8
	Cheung et al., 2013	Y	Y	Y	N/A	Y	Y	Y	Y	7/8
Homocysteine metabolism	A. Walkiewicz, 2011	Y	Y	Y	N/A	Y	Y	Y	Y	7/8
	E. Zittan, 2007	Y	Y	Y	Y	Y	Y	Y	Y	8/8
	B. H. Thuesen, 2010	Y	Y	Y	N/A	Y	Y	Y	Y	7/8
	Q. H. Yang, 2008	Y	Y	Y	N/A	Y	Y	Y	Y	7/8
	J. Ni, 2017	Y	Y	Y	N/A	n	n	Y	n	4/8
	M. Lucock, 2012	Y	Y	Y	N/A	Y	Y	Y	n	6/8
	N. Fukuda, 2014	Y	Y	Y	N/A	Y	Y	Y	Y	7/8
	A. Fredriksem, 2007	Y	Y	Y	N/A	Y	Y	u	Y	6/8
	J. P. du Plessis, 2019	Y	Y	Y	N/A	Y	Y	Y	Y	7/8
	J. Srebnik, 2018	Y	Y	Y	N/A	Y	Y	Y	Y	7/8
	A. Stanislawski-Sachadyn, 2010	Y	Y	Y	N/A	Y	Y	Y	Y	7/8
	Wang et al., 2023	n	Y	Y	N/A	Y	Y	Y	Y	6/8
	M. G. Garrod, 2010	Y	Y	Y	N/A	Y	Y	Y	Y	7/8
	K. K. Sukla and R. Raman, 2012	n	Y	Y	N/A	Y	n	Y	Y	5/8
	F. Wang, 2019	u	Y	Y	Y	Y	n	u	Y	5/8
	S. M. Naushad, 2017	Y	Y	Y	N/A	Y	Y	Y	Y	7/8
	C. Nienaber-Rouseau, 2013	Y	Y	Y	N/A	Y	Y	Y	Y	7/8
	K. Sun, 2017	Y	Y	Y	N/A	u	u	Y	Y	5/8
	J. Kumar, 2009	Y	Y	Y	N/A	Y	Y	Y	Y	7/8
	M. A. Caudill, 2009	Y	Y	Y	N/A	Y	Y	Y	Y	7/8
	H. Ara, A. 2007	n	n	Y	N/A	n	n	Y	Y	3/8
	de Battlle et al., 2016	Y	Y	Y	u	Y	Y	Y	Y	7/8
	Stanislawski-Sachadyn et al., 2008	Y	Y	Y	N/A	u	Y	Y	Y	6/8
	Galmiche et al., 2008	Y	Y	Y	N/A	Y	Y	Y	Y	7/8
	Hu et al., 2018	Y	Y	Y	N/A	Y	Y	Y	Y	7/8
Antioxidants	Combet et al., 2011	Y	Y	Y	N/A	Y	Y	Y	Y	7/8
	Yabuta et al., 2016	Y	Y	Y	N/A	Y	Y	Y	Y	7/8
	Ferrucci et al., 2009	Y	Y	Y	N/A	Y	Y	Y	Y	7/8

Table S5: Randomized Controlled Trials

Source / Question		1. Was true randomization used for assignment of participants to treatment groups?	2. Was allocation to treatment groups concealed?	3. Were treatment groups similar at the baseline?	4. Were participants blind to treatment assignment?	5. Were those delivering treatment blind to treatment assignment?	6. Were outcomes assessors blind to treatment assignment?	7. Were treatment groups treated identically other than the intervention of interest?	8. Was follow up complete and if not, were differences between groups in terms of their follow up adequately described and analyzed?	9. Were participants analyzed in the groups to which they were randomized?	10. Were outcomes measured in the same way for treatment groups?	11. Were outcomes measured in a reliable way?	12. Was appropriate statistical analysis used?	13. Was the trial design appropriate, and any deviations from the standard RCT design (individual randomization, parallel groups) accounted for in the conduct and analysis of the trial?	Rating
Vitamin D	Nissen, Vogel et al., 2014	u	y	y	y	y	y	y	y	u	y	y	y	y	11/13
	Gaffney-Stomberg et al., 2017	y	y	n	y	y	y	y	y	y	y	y	y	y	12/13
	Barry et al., 2014	y	y	y	y	y	y	y	y	y	y	y	y	y	13/13
	Waterhouse et al., 2014	y	y	y	y	y	y	y	y	y	y	y	y	y	13/13
	Slow et al., 2020	y	y	y	y	y	y	y	y	y	y	y	y	y	13/13
Hcy	Crider et al., 2011	u	y	y	y	y	y	n	u	y	y	y	y	u	9/13
Anti-oxidants	Batai et al., 2021	y	y	y	y	y	y	y	y	y	y	y	y	y	13/13
	Kopp et al., 2018	y	n	y	n	n	n	y	y	y	y	y	y	y	9/13

Table S6: Case-Control Studies

Source / Question		1. Were the groups comparable other than the presence of disease in cases or the absence of disease in controls?	2. Were cases and controls matched appropriately?	3. Were the same criteria used for identification of cases and controls?	4. Was exposure measured in a standard, valid and reliable way?	5. Was exposure measured in the same way for cases and controls?	6. Were confounding factors identified?	7. Were strategies to deal with confounding factors stated?	8. Were outcomes assessed in a standard, valid and reliable way for cases and controls?	9. Was the exposure period of interest long enough to be meaningful?	10. Was appropriate statistical analysis used?	Rating
Vitamin D	Janssens et al., 2010	u	y	y	y	y	y	y	y	N/A	y	8/10
	Mohamed et al., 2022	y	n	n	y	y	n	n	y	N/A	y	5/10
	Liu et al., 2021	n	y	y	y	y	y	y	y	N/A	y	8/10
Hcy	Al-Batayneh et al., 2018 *	y	y	u	y	y	n	n	y	N/A	y	6/10
	Al-Batayneh et al., 2020 *	y	y	y	y	y	y	n	y	N/A	y	8/10
	Rupalika et al., 2018	u	u	y	y	y	n	n	y	N/A	y	5/10

* same cohort

Table S7: Quasi-Experimental Studies

Source / Question		1. Is it clear in the study what is the 'cause' and what is the 'effect' (i.e. there is no confusion about which variable comes first)?	2. Were the participants included in any comparisons similar?	3. Were the participants included in any comparisons receiving similar treatment/care, other than the exposure or intervention of interest?	4. Was there a control group?	5. Were there multiple measurements of the outcome both pre and post the intervention/exposure?	6. Was follow up complete and if not, were differences between groups in terms of their follow up adequately described and analyzed?	7. Were the outcomes of participants included in any comparisons measured in the same way?	8. Were outcomes measured in a reliable way?	9. Was appropriate statistical analysis used?	Rating
Vitamin D	Tomei et al., 2020	y	u	y	n	n	u	u	u	y	3/9
	Ammar et al., 2023	y	y	y	n	n	y	y	y	y	7/9
Hcy	Solis et al., 2008	y	y	y	n	y	y	y	y	y	8/9

Table S8: Cohort Studies

Source / Question		1. Were the two groups similar and recruited from the same population?	2. Were the exposures measured similarly to assign people to both exposed and unexposed groups?	3. Was the exposure measured in a valid and reliable way?	4. Were confounding factors identified?	5. Were confounding factors identified?	6. Were the groups/participants free of the outcome at the start of the study (or at the moment of exposure)?	7. Were the outcomes measured in a valid and reliable way?	8. Was the follow up time reported and sufficient to be long enough for outcomes to occur?	9. Was follow up complete, and if not, were the reasons to loss to follow up described and explored?	10. Were strategies to address incomplete follow up utilized?	11. Was appropriate statistical analysis used?	Rating
Hcy	Du et al., 2018	y	y	y	y	y	y	y	y	y	y	y	11/11
Antioxidants	Méplán et al., 2007	y	y	y	y	y	y	y	y	y	N/A	y	10/11

Table S9: Case Series

Source / Question		1. Were there clear criteria for inclusion in the case series?	2. Was the condition measured in a standard, reliable way for all participants included in the case series?	3. Were valid methods used for identification of the condition for all participants included in the case series?	4. Did the case series have consecutive inclusion of participants?	5. Did the case series have complete inclusion of participants?	6. Was there clear reporting of the demographics of the participants in the study?	7. Was there clear reporting of clinical information of the participants?	8. Were the outcomes or follow up results of cases clearly reported?	9. Was there clear reporting of the presenting site(s)/clinic(s) demographic information?	10. Was statistical analysis appropriate?	Rating
Hcy	Petr et al., 2013	y	y	y	y	n	y	y	y	y	N/A	8/10

Table S10: Vitamins parameter study

Table S10: Vitamins parameter study																				
	Gene and SNP	Source	Vitamin										Ancestry	Outcome				Risk of bias	Notes	
			Vitamin D					Vit. B12	Vit. B9 (Folate)		Vit. B6 (PLP)	Hcy		Absolute Values	Effect size	Other	P-value			JBI assessment
			Calf-folate (25(OH)D)	Calf-folate (25(OH)D)239	Ergocalciferol (D2)	VDBP	Vit. D Deficiency	Red blood cell folate	Folate / Folic acid	Serum / Plasma Folate										
Homocysteine metabolism	MTHFR rs1801133 (C677T)	Solis et al., 2008							x				Hispanic	Mean ± SEM [nmol/L] CC (Wt): 1704 ± 143 TT : 1622 ± 113 Mean ± SEM [nmol/L] CC (Wt): 30.4 ± 5.2 TT: 23.8 ± 5.2 Mean ± SEM [μmol/L] CC (Wt): 9.8 ± 0.7 TT: 11.5 ± 1.4	CC: 1 TT: 0.952 CC: 1 TT: 0.783 CC: 1 TT: 1.173		P = 0.015 P = 0.002 P < 0.0001	8/9		
		Yang et al., 2008 [†]										x	non-Hispanic white non-hispanic black Mexican American	Adjusted geometric Mean (95%CI) [ng/mL] non-Hispanic White CC (Wt): 6.7 (6.2, 7.2) CT: 6.4 (5.9, 6.8) TT: 5.4 (4.9, 5.8) non-Hispanic Black CC (Wt): 4.8 (4.6, 5.1) CT: 4.4 (4.1, 4.7) TT: 3.2 (2.6, 4.0) Mexican-American (Hispanic) CC (Wt): 5.5 (5.1, 6.0) CT: 5.0 (4.7, 5.2) TT: 4.4 (4.0, 4.7) Adjusted geometric Mean (95%CI) [μmol/L] non-Hispanic White CC (Wt): 8.5 (8.2, 8.7) CT: 9.0 (8.8, 9.2) TT: 10.7 (9.9, 11.4) non-Hispanic Black CC: 8.6 (8.4, 8.8) CT: 9.3 (9.0, 9.6) TT: 12.0 (9.1, 15.9) Mexican-American (Hispanic) CC: 7.7 (7.4, 8.1) CT: 7.9 (7.7, 8.1) TT: 9.4 (8.9, 10.0)	non-Hispanic White CC: 1 CT: 0.955 TT: 0.806 non-Hispanic Black CC: 1 CT: 0.917 TT: 0.667 Mexican-American (Hispanic) CC: 1 CT: 0.909 TT: 0.8 non-Hispanic White CC: 1 CT: 1.059 TT: 1.259 non-Hispanic Black - NS Mexican-American (Hispanic) CC: 1 CT: 1.026 TT: 1.221	Adjusted geometric mean serum folate concentration was non-Hispanic White 19.6% (95% CI: 12.5%, 26.2%) non-Hispanic Black 33.6% (17.9%, 46.3%) Mexican-American 21.3% (15.2%, 27.0%) ...lower for the TT genotype than the CC wild type Adjusted geometric mean serum folate concentration was non-Hispanic White 26.1% (17.6%, 35.2%) non-Hispanic Black 39.7% (5.3%, 85.2%) Mexican-American 21.4% (14.6%, 28.6%) ...higher for the TT genotype than the CC wild type	non-Hispanic White P = 0.0002 non-Hispanic Black P = 0.0052 Mexican-American P < 0.0001 non-Hispanic White P < 0.0001 non-Hispanic Black P = 0.0890 (NS) Mexican-American P < 0.0001	7/8	SNP effect on tHcy significantly higher when B12 low.	
		Lucock et al., 2013						x					Caucasian	Slope estimate (SE) All: -217.5(54.4) Subjects for which RBC folate ≥ Median: -216.8 (63.2)			P = 0.0004 P = 0.0111	6/8	median RBC folate: 848 nmol/L.	
	Fukuda et al., 2014 [†]											x	Asian (Japanese)	MLR tHcy against folate intake by genotype, β (95%CI) CC (Wt): - 0.141(-0.251, -0.030) CT: -0.072 (-0.156, 0.012) TT: 0.070 (-0.115, 0.254) Simple Linear Regression tHcy against folate intake by genotype, Coef. (95%CI) CC (Wt): -0.204 (-0.327, -0.080) CT: -0.093 (-0.192, 0.006) TT: 0.109 (-0.090, -0.307) Simple Linear Regression Plasma folate against folate intake by genotype, Coef (95%CI) CC (Wt): 0.273 (0.107, 0.438) CT: 0.318 (0.188, 0.447) TT: 0.247 (-0.067, -0.561)			MLR P = 0.013 P = 0.93 P = 0.454 Folate intake * genotype: P = 0.056 Simple regression P = 0.001 P = 0.066 P = 0.281	7/8		
	MTHFR rs1801133 (C677T)	de Batlle et al., 2018 [†]								x			N/R (likely Caucasian)	CC: Ref. CT: -6.48% TT: -15.89%			P = 0.038 P < 0.001	7/8		
		Grider et al., 2011									x		Asian (Chinese)	Mean (95%CI) [nmol/L] CC (Wt): 10.3 (9.7, 11.1) CT: 9.8 (9.5, 10.2) TT: 9.1 (8.7, 9.5) Mean (95%CI) [μmol/L] CC (Wt): 6.1 (5.7, 6.4) CT: 6.7 (6.5, 7.0) TT: 10.2 (9.8, 10.6) Mean (95%CI) [nmol/L] CC (Wt): 669.0 (630.6, 709.8) CT: 616.3 (594.7, 638.8) TT: 552.2 (529.7, 575.6)	CC: 1 CT: NS TT: 0.883 CC: 1 CT: 1.098 TT: 1.672 CC: 1 CT: 0.921 TT: 0.825		Odds fo tHcy, OR (95%CI) TT: 23.0 (9.2, 57.6)	CC < TT P = 0.025 CC < CT P = 0.67 CT < TT P = 0.005 CC < CT P = 0.013 CC < TT P < 0.001 CT < TT P < 0.001 CC < CT P = 0.06 CC < TT P < 0.001 CT < TT P < 0.001	7/10	
		Caudill et al., 2009										x	Hispanic	Mean ± SEM [nmol/L] CC (Wt): 11.4 ± 0.9 TT: 8.0 ± 0.6 Mean ± SEM [μmol/L] CC (Wt): 11.6 ± 0.3 TT: 30.9 ± 3.1	CC: 1 TT: 0.702 CC: 1 TT: 2.664		P = 0.004 P < 0.001	7/8	Effect on tHcy: CC interacts with Creatinine TT interacts with folate, riboflavin,	
		Ni et al., 2017											x	Asian (Chinese)	Mean ± SD [μM] ^b CC (Wt): 11.69 ± 3.87 CT: 13.32 ± 5.50 TT: 21.28 ± 15.22 Mean ± SD [nM] CC (Wt): 648.14 ± 385.20 CT: 811.54 ± 446.41 TT: 731.22 ± 388.00	CC: 1 CT: 1.139 TT: 1.820 CC: 1 CT: 1.252 TT: 1.128		P < 0.01 for both TT: P < 0.05	4/8	HWE equilibrium not met for this SNP ^b Interaction depends on folate levels. For results stratified by B12 & folate refer to Ni et al. (2017)
		Stanislawska et al., 2008 [†]									x			N/R (likely Caucasian)	Coef. (SE) [nmol/L] Men CC: Ref. CT: -0.06 (0.02) TT: -0.15 (0.04) Women CC: Ref. CT: -0.05 (0.03) TT: -0.10 (0.04)		R2: 0.08 R2: 0.03	P < 0.01 P < 0.05	6/8	
												x		Coef. (SE) [nmol/L] Men* CC: Ref. CT: -0.07 (0.03) TT: -0.10 (0.05)		R2: 0.03	P = 0.05		* results in women not significant	

Gene and SNP	Source	Vitamin										Ancestry	Outcome				Risk of bias JBI assessment	Notes		
		Vitamin D					Vit. B12	Vit. B9 (Folate)	Vit. B6 (PLP)	Hcy	Absolute Values		Effect size	Other	P-value					
		Calfedol (25(OH)D)	Calfedol (1,25(OH)2D)	Ergocalciferol (D3)	VDPP	Vit. D deficiency	Mean ± SD	Red blood cell folate	Folate / folic acid	Serum / Plasma Folate						Hcy				
Homocysteine metabolism	MTHFR rs1801133 (C677T)	Zittan et al., 2007										x	Israeli	Mean ± SD [μmol/l] CC (Wt): 20.6 ± 18 CT + TT: 9.4 ± 3.2	CC: 1 CT + TT: 0.456	Prevalence of Hhcy CC: 46% TT + CT: 3.75% Allele freq. P < 0.0001	8/8	Hhcy: Hcy >15μmol/L		
							x								Prevalence of B12 deficiency CC: 29.8% TT + CT: 9.2% Odds for B12 deficiency, OR(95%CI) CC: 4.2 (2.1, 8.3)	P < 0.001		B12 deficiency: B12 ≤ 150pmol/L		
		Thuesen et al., 2010						x					Caucasian	Geometric mean (95%CI) [pmol/L] CC (Wt): 293 (288, 297) CT: 287 (282, 292) TT: 274 (264, 285)	CC: 1 CT: 0.980 TT: 0.935	Prevalence of B12 < 148pmol/L CC: 4.9% CT: 4.5% TT: 8.4% Odds for B12 deficiency, OR(95%CI) TT: 1.78 (1.25, 2.54)	Absolute values P = 0.004 Prevalence P = 0.001 OR P = 0.003	7/8		
										x				Geometric Mean (95% CI) [nmol/L] CC (Wt): 9.3 (9.2, 9.5) CT: 8.6 (8.4, 8.8) TT: 7.5 (7.2, 7.9)	CC: 1 CT: 0.925 TT: 0.806	Prevalence of folate < 6.8nmol/L CC: 27.5% CT: 33.9% TT: 45.9% Odds for low folate, OR(95%CI) TT: OR (95%CI): 2.24 (1.85, 2.70)	Absolute values P < 0.001 Prevalence P < 0.001 OR P < 0.001			
	Wang et al., 2023											x	Asian (Chinese)	Mean ± SD [μg/L] CC (Wt): 5.00 ± 2.95 CT: 6.19 ± 4.74 TT: 4.09 ± 2.52	CC: 1 CT: 1.238 TT: 0.818		P = 0.014	6/8	Values apply to men only	
	MTHFR rs1801133 (C677T)	Al-Batayneh et al., 2018						x					Arab (Jordanian)			Genotype frequencies by B12 status Deficient CC (Wt): 36% CT: 43% TT: 21% C: 115%; T: 85% Sufficient CC (Wt): 46% CT: 47% TT: 7% C: 139%; T: 61% χ²= 8.397 Odds to be B12 deficient, OR(95%CI) T allele carrier: 1.684 (1.116, 2.542) Mean age * Vit. B12 deficiency [yrs ± SD] CC: 31.4 ± 11.9 CT: 36.4 ± 14.5 TT: 43.7 ± 10.9	Genotype Freq. P = 0.015 OR P = 0.017 age * B12 def. P = 0.007	3/5	B12 deficiency: B12 < 200 mg/mL	
		Fredriksen et al., 2007 [†]					x					N/R (likely Caucasian)		Mean (95%CI) [pmol/L] CC (Wt): 335.75 (325.67, 345.83) CT: 329.90 (321.64, 338.17) TT: 324.43 (310.49, 338.38)	CC: 1 CT: 0.983 TT: 0.966	P = 0.020	6/8		P for trend test	
									x						Mean (95%CI) [nmol/L] CC (Wt): 18.72 (18.14, 19.29) CT: 17.30 (16.83, 17.77) TT: 13.34 (12.54, 14.13)	CC: 1 CT: 0.924 TT: 0.713				P < 0.001
										x					Mean (95%CI) [pmol/L] CC (Wt): 63.19 (60.68, 65.69) CT: 62.44 (60.38, 64.49) TT: 57.96 (54.50, 61.43)	CC: 1 CT: 0.988 TT: 0.917				P < 0.001
	MTHFR rs1801133 (C677T)	Wasikiewicz et al., 2011 [†]											x	Caucasian	Mean [μmol/L] Men CC/CT: 10.18 TT: 13.14 Women CC/CT: 8.77 TT: 9.77	CC/CT: 1 TT: 1.291 CC/CT: 1 TT: 1.114	Frequency of Hhcy by genotype * Men CC/CT: 25.8% TT: 52.5% Women CC/CT: 14.9% TT: 22.4%	Absolute values Men P < 0.0001 Women P < 0.0001 Frequencies Men P < 0.0001 Women P = 0.0129	7/8	Hhcy: Hcy > 12μmol/L * E.g. 25.8% of male carriers of the CC or CT genotype had Hhcy
		Wang et al., 2019											x	Asian (Chinese)	Mean ± SD [μmol/L] CC (Wt): 12.8 ± 7.5 CT: 14.74 ± 6.98 TT: 20.92 ± 10.75	CC: 1 CT: 1.152 TT: 1.634	Hcy status by genotype * Hhcy TT: 47.58% T: 69.17% Hcy normal TT: 21.92% T: 50.58%	Absolute values P = 0.00 Frequencies P = 0.00	5/8	Hhcy: Hcy ≥ 15 μmol/L * E.g. 47.58% of Hhcy subjects had the TT genotype, while 21.92% of subjects with normal Hcy levels were TT homomzygotes.
		Sun et al., 2017 [†]											x	Asian (Chinese)	Mean ± SD [μmol/L] CC (Wt): 2.53 ± 0.50 CT: 2.56 ± 0.40 TT: 2.77 ± 0.46	CC: 1 CT: 1.012 TT: 1.095		P = 0.012	5/8	
		Sukla et al., 2012											x	Asian (Indian)	Mean [μmol/L] CC (Wt): 11.2 CT: 14.6 TT: 20.8	CC: 1 CT: 1.304 TT: 1.857	Relative risk for Hhcy TT: 35.50	P < 0.0001	5/8	Hhcy: Hcy > 15 μmol/L
		Petr et al., 2013											x	Caucasian	Mean ± SD [μmol/L] Baseline CC (Wt): 5.9±1.3 CT: 6.6±1.3 TT: 33.2 Post-intervention * CC: 9.9±2.9 CT: 11.6±3.3 TT: 17.1	CC: 1 CT: 1.119 TT: 5.627 CC: 1 CT: 1.172 TT: 1.727		NS	8/10	* Intervention: 5g/d creatinine for 30 days
		Nienaber-Rousseau et al., 2013 [†]											x	Black-African	Mean (95%CI) [μmol/L] CC (Wt): 9.74 (9.56, 9.91) CT: 10.5 (10, 10.9) TT: 16.6 (12.9, 21.5)	CC: 1 CT: 1.078 TT: 1.704		P < 0.05 for all	7/8	

	Gene and SNP	Source	Vitamin										Hcy	Ancestry	Outcome				Risk of bias JBI assessment	Notes	
			Vitamin D					Vit. B12	Vit. B9 (Folate)	Vit. B6 (PLP)	Absolute Values	Effect size			Other	P-value					
			Calcifediol (25(OH)D)	Calcitriol (1,25(OH)2D)	Ergocalciferol (D2)	VDBP	Vit.D deficiency	Red blood cell folate	Folate / folic acid	Serum / Plasma Folate											
Homocysteine metabolism	MTHFR rs1801133 (C677T)	Naushad et al., 2017											✕	Asian (Indian)	Estimated Mean [μmol/L] Men CC: 18 CT: 19.5 TT: 21 Women CC: 13.2 CT: 14.7 TT: 16.2	Men CC: 1 CT: 1.083 TT: 1.167 Women CC: 1 CT: 1.114 TT: 1.227	Genotype effect was associated with vegetarian diet only. A non-vegetarian diet compensated the genetic effect, protecting against high Hcy.		7/8	Absolute values are estimated based on Fig. 2 in Naushad et al. (2017)	
		Kumar et al., 2009											✕	Asian (Indian)	Median [μmol/L] Phase I Codominant model CC: 13.4; CT: 13.1; TT: 23.3 P(q-value): 0.000458 (0.027) Recessive model CC + CT: 13.3; TT: 23.3 P(q-value): 0.0010 (0.024) Phase II Dominant model CC: 17.8; CT+ TT: 19.9; P= 0.007 Allelic association C: 18.0; T: 20.0; P value= 0.0001 Pooled sample Codominant model CC: 15.0; CT: 15.4; TT: 22.0 P(q-value): 0.00276 (0.027) Recessive model CC + CT: 15.0; TT: 22.0 P(q-value): 0.00165 (0.024) Dominant Model CC: 15.0; CT + TT: 15.9 P(q-value): 0.036 (0.15)	Phase I Codominant model CC: 1 CT: 0.978 TT: 1.739 Recessive model CC + CT: 1 TT: 1.752 Phase II Dominant model CC: 1 CT+ TT: 1.118 Allelic association C: 1 CT: 1.111 TT: 1.111 Pooled sample Codominant model CC: 15.0 CT: 1.027 TT: 1.467 Recessive model	Phase I Codominant model P(q-value): 0.000458 (0.027) Recessive model P(q-value): 0.0010 (0.024) Phase II Dominant model P= 0.007 Allelic association P = 0.0001 Pooled sample Codominant model P(q-value): 0.00276 (0.027) Recessive model P(q-value): 0.00165 (0.024) Dominant Model P(q-value): 0.036 (0.15)		7/8	Phase I 546 individuals genotyped and checked for associations between of 14 rsSNPs with Hcy levels. Phase II SNPs that were significantly associated with Hcy levels under multiple genetic models were further genotyped in an additional 330 individuals	
		du Plessis et al., 2020 ¹											✕	Black-African	Mean (95%CI) [μmol/L] CC (WT): 10.1 (9.9, 10.3) CT: 11.1 (10.6, 11.6) TT: 18.5 (16.2, 20.7)	CC: 1 CT: 1.099 TT: 1.832 Cohen's d= 0.22		P = 0.00001	7/8	P value for GLM, remained significant after adjusting for multiple testing	
		Arai et al., 2007												✕	Asian (Japanese)	Mean ± SEM [μmol/L] CC (WT): 10.9 ± 0.3 CT: 11.6 ± 0.24 TT: 15.7 ± 1.23	CC: 1 CT: 1.064 TT: 1.440		P < 0.001	3/8	Values were also significant when men & women were analyzed individually (see source for details)
	MTHFR rs1801133 (C677T)	Du et al., 2018											✕	Asian (Chinese)	Allele freq. by Hcy therapy status Success grp TT: 47.29% TT + CT: 89.14% T: 55.85% Failure grp TT: 33.85% TT + CT: 77.85% T: 68.21% Odds for treatment failure OR (95%CI) TT: 2.68 (1.59, 4.54) CT + TT: 2.12 (1.3, 3.44) T: 1.69 (1.35, 2.13)		Allele freq. by Hcy therapy status Success grp TT: 47.29% TT + CT: 89.14% T: 55.85% Failure grp TT: 33.85% TT + CT: 77.85% T: 68.21% Odds for treatment failure OR (95%CI) TT: 2.68 (1.59, 4.54) CT + TT: 2.12 (1.3, 3.44) T: 1.69 (1.35, 2.13)	P < 0.05 for all P < 0.000 P = 0.003 P = 0.000	10/10	Therapy: 5 mg/d oral folate for 90d Success group: patients whose Hcy levels decreased to ≤ 15 μmol/L Failure group: patients whose Hcy levels were ≥15 μmol/L	
		Rupalika et al., 2018											✕	Asian (Indian)	TT genotype was present in low frequency (0.72%) only among the HHcy case group: OR (95%CI): 0.81 (0.22, 2.91) No TT genotype was observed in Control grp			P = 0.61 (NS)	5/10	The association was not significant due to low sample size (only 21 controls).	
Footnotes Effect directions refer to minor allele T; reference genotype: CC (WT) ¹ Nienaber-Rousseau et al. (2013) and du Plessis et al (2020) both conducted their studies on the South African arm of the PURE study. Overlaps in subject samples can not be excluded. ² Statistical analyses in this study were performed on log-transformed values. Abbreviations: NS, Not significant; N/R, not reported; SE, standard error; MLR, multilinear regression; OR, odds ratio; R2, coefficient of determination; Coef, Coefficient; HHcy, hyperhomocysteinemia; grp, group																					
Homocysteine metabolism	rs1801133 x rs1801394	Yang et al., 2008 ¹											✕	non-Hispanic white	Adjusted geometric Mean (95%CI) [μmol/L] TT + GG: 9.3 (8.2, 10.5) TT + AA: 12.5 (10.8, 14.5)	TT + AA: 1 TT + GG: 0.744	Adjusted geometric mean serum folate concentration was 25.6% (95% CI: 16.0, 34.4) ..lower for the 677TT + 66GG haplotype than the TT/AA genotypes	P = 0.0138	7/8	P for trend test	
Footnotes ¹ Statistical analyses in this study were performed on log-transformed values.																					
Homocysteine metabolism	rs1801133 x rs1801131	Wang et al., 2019											✕	Asian (Chinese)	Mean (95%CI) [μmol/L] TT x TT: 24.5 (20.5, 28.8) TT x TC: 15 (12, 18.2) TT x CC: 12.2 (1, 21.2)	TT: 1 TC: 0.612 CC: 0.498	Odds for HHcy, OR (95%CI) C/A: 0.634 (0.469, 0.859) C/C: 0.440 (0.298, 0.648) T/A: 1.842 (1.418, 2.394)	P = 0.003 P < 0.00 P < 0.00		5/8	HHcy: Hcy ≥ 15 μmol/L
		Du et al., 2018											✕	Asian (Chinese)	Haplotype freq. by Hcy therapy status Success grp C/A: 28.8% C/C: 15.4% T/A: 55.2% Failure grp C/A: 21.9% C/C: 9.9% T/A: 68.2% Odds for treatment failure OR (95%CI) C/A: 0.69 (0.53, 0.89) C/C: 0.60 (0.43, 0.84) T/A: 1.72 (1.36, 2.16)	C/A: P = 0.004 C/C: P = 0.003 T/A: P = 0.000 C/A: P = 0.004 C/C: P = 0.003 T/A: P = 0.000			10/10	Therapy: 5 mg/d oral folate for 90d Success group: patients whose Hcy levels decreased to ≤ 15 μmol/L Failure group: patients whose Hcy levels were ≥15 μmol/L	
Homocysteine metabolism	rs1801133 x T833C/844ins68	Nienaber-Rousseau et al., 2013											✕	Black-African	Mean (95%CI) [μmol/L] TT x TT: 24.5 (20.5, 28.8) TT x TC: 15 (12, 18.2) TT x CC: 12.2 (1, 21.2)	TT: 1 TC: 0.612 CC: 0.498		P < 0.01	7/8	Absolute values are estimated based on Fig. 1 in Nienaber-Rousseau et al. (2013)	
Homocysteine metabolism	rs1801133 TT x rs7946	Caudill et al., 2009											✕	Hispanic	Mean ± SEM [μmol/L] TT x GG: 42.5 ± 4 TT x GA: 25 ± 2.5 TT x AA: 22.5 ± 2.5	TT x GG: 1 TT x GA: 0.588 TT x AA: 0.529	R2: 0.12	P < 0.001 for both	7/8	Absolute values are estimated based on Fig. 4 in Caudill et al. (2009) Co-variable Creatinine excluded from this	
Homocysteine metabolism	rs1801133 x rs9001	Kumar et al., 2009											✕	Asian (Indian)	Median [μmol/L] CC x CC: 11.2 TT x AA: 22.0	CC x CC: 1 TT x AA: 1.964	1.7% of variation explained	P = 0.0002	7/8		

Homocysteine metabolism	Gene and SNP	Source	Vitamin										Ancestry	Outcome				Risk of bias	Notes
			Vitamin D			Vit. B12	Vit. B9 (Folate)	Vit. B6 (PLP)	Hcy	Absolute Values	Effect size	Other		P-value	JBI assessment				
			Calc./folate (25(OH)D)	Cerebral (1,25(OH)2D)	Serum/urinary (25(OH)D)	Vit. D	Vit. B12	Red blood cell folate	Folate / Folic acid							Serum / Plasma folate	Hcy		
	MTNFR rs1801131 (A1298C)	Wang et al., 2019										x	Asian (Chinese)	Mean $\pm$ SD [μ mol/L] AA (Wt): 16.99 $\pm$ 9.57 AC: 16.48 $\pm$ 8.48 CC: 11.66 $\pm$ 5.04	AA: 1 AC: 0.970 CC: 0.686	Hcy status by genotype * <u>Hcy</u> A: 80.1% C: 19.90% CC: 1.94% <u>Hcy normal</u> A: 73.46% AC: 0.003 C: 26.54% CC: 8.85% Odds for Hcy, OR (95%CI) A allele: 0.69 (0.50, 0.94) CC: 0.20 (0.07, 0.60)	<u>Absolute values</u> P = 0.01 <u>Frequencies</u> CC: P = 0.003 C: P = 0.02 A: P = 0.02	5/8	* E.g. 1.94% of Hcy subjects had the CC genotype, while 8.85% of subjects with normal Hcy levels were CC homomzygotes.
		Sukla et al., 2012										x	Asian (Indian)	Mean [μ mol/L] AA (Wt): 11.6 AC: 12.3 CC: 13.1	AA: 1 AC: 1.06 CC: 1.129			5/8	
		Frederiksen et al., 2007										x	N/R (likely Caucasian)	Mean (95%CI) [μ mol/L] AA (Wt): 10.15 (10.02, 10.28) AC: 10.35 (10.24, 10.45) CC: 10.65 (10.51, 10.80) Mean (95%CI) [μ mol/L] AA (Wt): 37.55 (36.95, 38.15) AC: 37.59 (37.12, 38.06) CC: 36.36 (35.71, 37.02) Mean (95%CI) [μ mol/L] AA (Wt): 18.73 (18.16, 19.30) AC: 17.76 (17.32, 18.21) CC: 16.98 (16.35, 17.60)	AA: 1 AC: 1.02 CC: 1.049 AA: 1 AC: 1.001 CC: 0.968 AA: 1 AC: 0.948 CC: 0.907	P < 0.001 P = 0.008 P < 0.001		6/8	P for trend test
		Wang et al., 2023										x	Asian (Chinese)	Mean $\pm$ SD [μ g/L] AA (Wt): 4.86 $\pm$ 3.56 AC + CC: 6.55 $\pm$ 4.87	AA: 1 AC + CC: 1.348		P = 0.028	6/8	Values apply to men only
		Du et al., 2018										x	Asian (Chinese)	<u>Failure grp</u> AA (Ref.): 81.47% AC: 17.25% C: 1.28 CC + AC: 18.53% C: 9.90% <u>Success grp</u> AA (Ref.): 71.39% AC: 25.23% CC: 3.58 CC+AC: 28.62% C: 16% Odds for treatment failure compared to AA (Ref.), OR (95%CI) AC: 0.52 (0.33, 0.81) CC: 0.26 (0.07, 0.93) AC + CC: 0.48 (0.32, 0.74) C: 0.58 (0.41, 0.81)	AA: 1 AC: 1.001 CC: 0.968 AC: 1 AC + CC: 1.348	Allele freq. by Hcy therapy status <u>Failure grp</u> AA (Ref.): 81.47% AC: 17.25% C: 1.28 CC + AC: 18.53% C: 9.90% <u>Success grp</u> AA (Ref.): 71.39% AC: 25.23% CC: 3.58 CC+AC: 28.62% C: 16% Odds for treatment failure compared to AA (Ref.), OR (95%CI) AC: 0.52 (0.33, 0.81) CC: 0.26 (0.07, 0.93) AC + CC: 0.48 (0.32, 0.74) C: 0.58 (0.41, 0.81)	AC: P = 0.009 CC: NS CC+ AC: P = 0.003 C: P = 0.001 P = 0.004 P = 0.035 P = 0.001 P = 0.001	10/10	Therapy: 5 mg/d oral folate for 90d Success group: patients whose Hcy levels decreased to $\leq$ 15 μ mol/L Failure group: patients whose Hcy levels were $\geq$ 15 μ mol/L

Homocysteine metabolism														
MTHFR rs2274976 (G1793A)	Lucock et al., 2013								x	Caucasian	Slope estimate (SE) All: -597.8 (173.1) Subjects for which RBC folate $\geq$ Median: -202.5 (87.1)	P = 0.0173 P = 0.0352 Subjects for which RBC folate < Median: P = 0.0087	6/8	median RBC folate: 848 nmol/L
	Wang et al., 2023								x	Asian (Chinese)	Mean $\pm$ SD [μ g/L] GG (Wt): 4.96 $\pm$ 3.60 GA: 7.93 $\pm$ 5.96 AA: not observed	GG (Wt): 1 GA: 1.599	P = 0.006	6/8

Study	Genotype	Allele	Frequency	OR (95%CI)	P-value	Haplotype	Linkage Disequilibrium (r ²)	Population	Sex	Estimated Mean [μmol/L]		P-value	Dose	Outcome	
										Men	Women				
Homocysteine metabolism	MTRR rs1801394 (66AG)	Naushad et al., 2017						Asian (Indian)	x		Men AA (Wt): 18 AG: 20.1 GG: 22.5 Women AA (Wt): 13.2 AG: 15.6 GG: 17.7	Men AA: 1 AG: 1.117 G: 1.25 Women AA: 1 AG: 1.182 GG: 1.341	N/R	7/8	Absolute values are estimated based on Fig. 2 in Naushad et al. (2017)
		Du et al., 2018						Asian (Chinese)	x			<i>Allele freq. by Hcy therapy status</i> <u>Success grp</u> G: 24.31% <u>Failure grp</u> G: 36.74% <i>Odds for treatment failure compared to A allele</i> G: OR (95%CI): 1.81 (1.42, 2.30)	P = 0.000 P = 0.000	10/10	Therapy: 5 mg/d oral folate for 90d <u>Success group</u> : patients whose Hcy levels decreased to ≤ 15 μmol/L <u>Failure group</u> : patients whose Hcy levels were ≥ 15 μmol/L

	Gene and SNP	Source	Vitamin										Ancestry	Outcome				Risk of bias	Notes
			Vitamin D					Vit. B12	Vit. B9 (Folate)	Vit. B6 (PLP)	Hcy	Absolute Values		Effect size	Other	P-value	JBI assessment		
			Calc(folac) (25(OH)D)	Calc(folac) 1,25(OH)2D	Ergocalciferol (D2)	WDRP	Vit D deficiency	Red blood cell folate	Folate / Folic acid	Serum / Plasma Folate									
Homocysteine metabolism	rs1801394 x rs162036	Du et al., 2018										x	Asian (Chinese)			Allele freq. by Hcy therapy status <u>Success grp</u> A/G: 16.6% G/A: 22.8% <u>Failure grp</u> A/G: 11.7% G/A: 33% Odds for treatment failure OR(95%CI) A/G: 0.66 (0.48, 0.91) G/A: 1.68 (1.31, 2.15)	A/G: P = 0.011 G/A: P = 0.000 A/G: P= 0.011 G/A: P = 0.000	10/10	Therapy: 5 mg/d oral folate for 90d <u>Success group:</u> patients whose Hcy levels decreased to ≤ 15 μmol/L <u>Failure group:</u> patients whose Hcy levels were ≥15 μmol/L
	MTR rs1805087 (A2756G)	Nienaber-Rousseau et al., 2013 ¹										x	Black-African	Mean (95%CI) [μmol/L] AA (Wt): 10.1 (9.86, 10.3) AG: 9.5 (9.22, 9.79) GG: 9.5 (8.79, 10.2)	AA: 1 AG: 0.941 GG: 0.941	P < 0.05	7/8		
		Fredriksen et al., 2007 ¹										x	N/R (likely Caucasian)	Mean (95%CI) [μmol/L] AA (Wt): 10.90 (10.81, 10.98) AG: 10.65 (10.52, 10.78) GG: 10.36 (10.00, 10.72)	AA: 1 AG: 0.977 GG: 0.950	P < 0.001	6/8		
		du Plessis et al., 2020 ¹										x	Black-African	Means (95%CI) [μmol/L] AA (Wt): 10.6 (10.3; 10.8) AG + GG: 9.9 (9.5; 10.2)	AA: 1 AG + GG: 0.934 Cohen's d = 0.16	AA: 1 AG + GG: 0.934 Cohen's d = 0.16	P = 0.004	7/8	P value for GLIM, remained significant after adjusting for multiple testing
		Naushad et al., 2017										x	Asian (Indian)	Estimated Mean [μmol/L] <u>Men</u> AA (Wt): 18 AG: 20.7 GG: 23.4 <u>Women</u> AA (Wt): 13.2 AG: 15.9 GG: 18.6	<u>Men</u> AA: 1 AG: 1.15 GG: 1.3 <u>Women</u> AA: 1 AG: 1.205 GG: 1.409	Genotype effect associated with vegetarian diet, and a non-vegetarian diet compensated genetic effect		7/8	Absolute values are estimated based on Fig. 2 in Naushad et al. (2017)

Footnotes
Effect directions refer to minor allele G; reference genotype: AA (Wt)
¹Statistical analyses in this study were performed on log-transformed values.
²Nienaber-Rousseau et al. (2013) and du Plessis et al (2020) both conducted their studies on the South African arm of the PURE study. Overlaps in subject samples are possible.

Homocysteine metabolism	RFC1 rs1051266 (G80A)	Sukla et al., 2012								x	Asian (Indian)	Mean [μmol/L] GG (Wt): 12.2 GA: 12.6 AA: 9.9	GG: 1 GA: 1.033 AA: 0.811	P < 0.0001	5/8			
		Naushad et al., 2017									x	Asian (Indian)	Estimated Mean [μmol/L] Men GG: 18 GA: 16.6 AA: 14.8 Women GG: 13.2 GA: 11 AA: 9.8	Men GG: 1 GA: 0.922 AA: 0.822 Women GG: 1 GA: 0.833 AA: 0.742	Genotype effect associated with vegetarian diet, and a non-vegetarian diet compensated the genetic effect	7/8	Absolute values are estimated based on Fig. 2 in Naushad et al. (2017)	
Homocysteine metabolism	DHFR 19-bp deletion	Steluti et al., 2018								x		N/R (likely Hispanic)		19bp del. * Folate conc. β (95%CI): 1.02 (1.01, 1.03)	P =0.002	7/8		
		Stanislawska et al., 2008 ¹									x		N/R (likely Caucasian)	Coef. [SE] [nmol/L] ins/rs: Ref. ins/del: -0.006 (0.04) del/del: 0.12 (0.05)	R2: 0.05	P = 0.02	6/8	The results were only significant in women
		Lucock et al., 2013									x		Caucasian	θ [SE] SNP * Vit. C Wt: NS het.: 0.576 (0.298) homozyg.: 1.380 (0.588) SNP * PreGlu Wt: 0.735 (0.378) Het.: 0.745 (0.204) homozyg.: NS	"SNP associated with RBCF in subjects with values >848 nmol/L"	SNP * Vit. C Het.: P = 0.056 Homozyg. P = 0.0245 SNP * PreGlu Wt: P = 0.0555 Het.: P = 0.0004 SNP * RBCF >848 nmol/L P = 0.0343	6/8	
		Kalmbach et al., 2008 ¹									x		N/R (likely Caucasian)	Mean (95%CI) [nmol/L] when folic acid intake <250μg/d Wt: 844.4 (787.8, 905.1) ins/del: 793.0 (750.3, 837.4) del/del: 732.3 (669.1, 801.4)	Wt: 1 het.: 0.939 hom.: 0.867	del/del: P < 0.05	7/8	High folic acid: >1.35nmol/L
											x			Prevalence of high folic acid when intake >500μg/d Wt: 24.4%, 95% CI: 13.9, 35.0 ins/del: 21.4%, 95% CI: 13.6, 29.3 del/del: 47.0%, 95% CI: 31.6, 62.5	ins/del: P < 0.05 del/del: P < 0.05			

Footnotes
Effect directions refer to the double deletion (del/del); reference genotype: double insertion (ins/ins; Wt)
¹Statistical analyses in this study were performed on log-transformed values.
Abbreviations: Coef, Coefficient; SE, standard error; Ref., Reference; PteGlu, Pteroylmonoglutamic acid (= folic acid)

	Gene and SNP	Source	Vitamin										Ancestry	Outcome				Risk of bias	Notes	
			Vitamin D					Vit. B12	Vit. B9 (Folate)		Vit. B6 (PLP)	Hcy		Absolute Values	Effect size	Other	P-value			JBI assessment
			Cabo/total (25(OH)D)	Caloric (1.25(OH)2D)	Epigallocatechin (D2)	VDBP	Vit.D deficiency	Red blood cell folate	Folate / Folic acid	Serum / Plasma Folate										
Homocysteine metabolism	TCN2 rs1801198 (C776G)	Stanislawska et al., 2010						x					Caucasian	Median (IQR), [pmol/L] CC (Wt): 243.5 (182.8–333.0) CG: 269.7 (212.8–343.7) GG: 279.7 (213.9–351.5)	Wt: 1 CG: 1.11 GG: 1.15		P overall = 0.01 CG: P = 0.03 GG: P = 0.045	7/8	Bonferroni corrected P-values P overall = P value by Kruskal-Wallis	
												x		Median (IQR), [pmol/L] ...when B12 ≤ 261.96 pmol/L CC (Wt): 7.5 (6.1–9.4) CG: 7.4 (6.2–8.9) GG: 8.5 (6.5–10.9)	CC: 1 CG: 0.987 GG: 1.133		P overall = 0.04 CG: P = 0.01 * CC + CG: P = 0.06		Bonferroni corrected P-values P overall = P value by Kruskal-Wallis * unadjusted	
		Garrod et al., 2010 [†]						x					Hispanic	Mean ± SD, [%] HoloTC/B12 Ratio CC (Wt): 26.5 ± 0.1 GG: 22.8 ± 0.1	CC: 1 GG: 0.860		P = 0.04			
												x		Mean (95%CI), [μmol/L] ...when holoTC < 35pmol/L CC (Wt): 17 (11, 23) CG + GG: 14 (11.5, 16)	Wt: 1 CG + GG: 0.824	Odds for Hcy, OR (95%CI) P = 0.02 Model 1 (incl. B12) Total B12 * genotype 5.41 (1.08, 27.0) CG+GG (compared to CC) 18.8 (1.04, 339) Model 2 (incl. holoTC) holoTC * genotype 5.99 (1.14, 31.6) CG+GG (compared to CG) 27.9 (1.33, 584)	Absolute values P = 0.02 OR Model 1 P = 0.04 P = 0.05 OR Model 2 P = 0.03 P = 0.03	7/8	Absolute values are estimated based on Fig. 2 in Garrod et al. (2010) Hcy: Hcy >13 μmol/L	
		Al-Batayneh et al., 2020						x				Arab			Genotype frequencies by B12 status Deficient GG: 15% G: 28% Sufficient GG: 0% G: 6.5% Odds for B12 deficiency, OR (95%CI) 5.6 (2.95, 10.63)		GG: P = 0.0001 G: P = 0.0001 P = 0.0001	8/10	B12 deficiency: B12 < 200 mg/mL	
Footnotes Effect directions refer to minor allele G; reference genotype: CC (Wt) * Statistical analyses in this study were performed on log-transformed values. Abbreviations: IQR, interquartile range; holoTC, Holotranscobalamin (bioavailable B12); OR, odds ratio; Hcy, hyperhomocysteinemia, freq., frequency;																				
Homocysteine metabolism	CBS 844ins68 (LD with rs5742905 (T833C))	du Plessis et al., 2020										x	Black-African	844ins68 * biotin intake, Slope ± SE [μg/day] TT (Wt): -0.02 ± 0.01 CT: -0.01 ± 0.01 CC: 0.03 ± 0.02		SNP * biotin intake Interaction P = 0.04 Slope P = 0.05 for all genotypes		7/8		
		Fredriksen et al., 2007 [†]										x	N/R (likely Caucasian)	Mean (95%CI) [μmol/L] Wt: 10.90 (10.78, 11.02) het.: 10.61 (10.38, 10.83) hom.: 10.35 (9.74, 10.96)	Wt: 1 het.: 0.973 hom.: 0.949		P < 0.001	6/8	HWE not met for this SNP in this cohort	
Footnotes Effect directions refer to minor allele C; reference genotype: TT (Wt) * Statistical analyses in this study were performed on log-transformed values.																				
Homocysteine metabolism	TCN1 rs34530014	Hu et al., 2018						x						Association with B12, 0 ± SE JHS cohort: - 0.817 ± 0.104 BioVU cohort: - 0.158 ± 0.038 BioME cohort: - 0.272 ± 0.037		P= 6.48E-15 P= 3.28E-5 P= 2.76E-13		7/8		
Footnotes Rs34530014 was not directly genotyped or imputed in BioVU or BioMe, therefore LD proxy rs1822978 (r2=0.98 in JHS) was used to confirm its association with lower Vit. B12 levels in BioVU and BioMe (n= 9,924) Effect directions refer to minor allele A; reference genotype: AC (Wt) for rs34530014 and minor allele T; reference genotype: CC (Wt) for rs1822978																				
Vitamin D	GC rs4588	Zhang et al., 2013	x										Asian (Chinese)	Mean [ng/mL] GG (Wt): 20.3 GT: 19.55 TT: 17.88	Wt: 1 GT: 0.963 TT: 0.881	β = -0.1635 Odds for VDD, OR (95%CI) 1.403 (1.245–1.583)	P = 0.002016 * OR: P = 2.7E-8	7/8	* Bonferroni corrected	
							x							Mean [mg/mL] GG (Wt): 317 GT: 307 TT: 300	GG: 1 GT: 0.968 TT: 0.946				Values estimated based on Fig. 4 in Zhang et al. (2013)	
	GC rs4588	Sinotte et al., 2009	x										Caucasian	Mean ± SE [nmol/L] CC (Wt): 67.2 ± 0.9; Ref. CA: 63.2 ± 0.9; P = 0.0018 AA: 58.4 ± 2.0; P < 0.0001 Seasonal Association May-Oct: CC: 74.1 ± 1.1 CA: 69.3 ± 1.3 AA: 61.5 ± 2.7 Nov-Apr CC: 58.2 ± 1.3 CA: 54.8 ± 1.5 AA: 52.7 ± 3.2	CC (Wt): 1 CA: 0.940 AA: 0.869 May-Oct CC: 1 CA: 0.935 AA: 0.830 Nov-Apr CC: 1 CA: 0.942 AA: 0.905	Total β ± SE = 24.22 ± 0.93 May-Oct: β = -5.73 Nov-Apr β = -3.03	Total P for trend < 0.0001 Summer P for trend < 0.0001 Winter P for trend = 0.037	7/8		
		Santos et al., 2019				x							Caucasian (20% African + Caucasian mixed)	Mean ± SD [μg/mL] CC (Wt): 202.98±28.28 CA: 196.49±29.88 AA: 183.95±36.85	CC (Wt): 1 CA: 0.968 AA: 0.906	β = -8.4	P < 0.001	7/8		

Vitamin D	Gene and SNP	Source	Vitamin											Ancestry	Outcome				Risk of bias		Notes
			Vitamin D					Vit. B12	Vit. B9 (Folate)			Vit. B6 (PLP)	Hcy		Absolute Values	Effect size	Other	P-value	JBI assessment		
			Calcifediol (25(OH)D)	Calcitriol (1,25(OH)2D)	Ergocalciferol (D2)	VDBP	VitD deficiency	Red blood cell folate	Folate /Folic acid	Serum / Plasma Folate											
GC	rs4588	Sallinen et al., 2021 [†]	x											Caucasian	Mean ± SD [nmol/L] CC (Wt): 69.3 ± 13.2 CA: 65.7 ± 12.6 AA: 60.5 ± 10.8	CC (Wt): 1 CA: 0.948 AA: 0.873	β = -3.7	P = 1.2E-22	6/8		
		Robien et al., 2013 [†]	x											Asian (Chinese)	Geometric Mean (95%CI) [nmol/L] CC (Wt): 68.7 (66.7, 70.8) CA: 64.3 (61.9, 66.8) AA: 57.2 (52.8, 61.9)	CC (Wt): 1 CA: 0.936 AA: 0.833	Variance explained: 3.7%	P for trend < 0.001	7/8		
		Rivera-Paredes et al., 2020					x							Hispanic			"rs4588 was positively associated with higher odds of VDD" AA & AC had higher prevalence of VDD compared to CC	AA: P = 0.003 AC: P = 0.021	8/8	VDD: 25(OH)D <20 ng/mL	
	rs4588	Perna et al., 2013	x											Caucasian	Median (IQR), [nmol/L] Women CC (Wt): 41.1 (31.3, 53.7) CA: 39.1 (30.3, 50.1) AA: 34.9 (29.7, 47.5) Men CC (Wt): 55.1 (39.2, 73.4) CA: 51.5 (35.8, 69.8) AA: 44.3 (33.9, 62.7)	Women CC (Wt): 1 CA: 0.951 AA: 0.849 Men CC (Wt): 1 CA: 0.935 AA: 0.804	Adjusted Estimates (SE) [nmol/L] CC (Ref.): 0.0 CA: -2.3 (0.7) AA: -5.5 (1.4)		7/8		
		Pooyan et al., 2020					x							Iranian			Allele Freq. CC (Wt) VDD: 70.4% <> Normal: 29.6% AC/AA VDD: 75.3% <> Normal: 24.7%		8/8	VDD: Vit D < 30ng/mL SNP was not associated with Vit.D in binary regression model	
		Nissen, Vogel et al., 2014 ^{1,†}	x											Caucasian	Geometric Mean (95%CI) [nmol/L] CC (Wt): 75.1 (73.1, 77.2) CA: 69.9 (67.7, 72.1) AA: 61.2 (56.9, 62.9)	CC (Wt): 1 CA: 0.927 AA: 0.812		P < 0.0001	6/8		
	rs4588	Nissen et al., 2014 ^{1,†}	x											Caucasian	Geometric Mean (95%CI) [nmol/L] CC (Wt): 74.1 (71.0, 77.3) CA: 69.7 (66.3, 73.2) AA: 63.6 (57.1, 70.8)	CC (Wt): 1 CA: 0.941 AA: 0.858		P = 0.0008	7/8		
		Li et al., 2014	x											Asian (Chinese)			β (SE): -3.084 (0.899)	P = 0.0006 P = 0.005 *	8/8	* Bonferroni corrected	
		Lafi et al., 2015	x											Mostly Caucasian (Mixed)	Mean ± SD [ng/mL] CC (Wt): 32.7 ± 20.9 CA: 24.6 ± 20.0 AA: 12.4 ± 6.9 CC + AC: 28.7 ± 20.5 AA + AC: 18.5 ± 15.6	CC (Wt): 1 CA: 0.752 AA: 0.379 CC + AC: 1 AA + AC: 0.645	Odds for low Vit. D, OR (95%CI) CC (Wt): Ref. CA: 2.60 (1.36, 4.96) AA: 11.58 (1.39, 96.78) CC + AC: 7.95 (4.48, 14.12) AA + AC: 3.01 (1.61, 5.61)	CA: P= 0.004 AA: P = 0.0024 CC + AC: P < 0.0001 AA + AC: P = 0.0005	5/8		
	GC	rs4588	Janssens et al., 2010 ²	x											Caucasian	Mean ± SD [ng/mL] CC (Wt): 21.0 ± 7.9 CA: 19.2 ± 7.0 AA: 15.6 ± 7.2	CC (Wt): 1 CA: 0.914 AA: 0.743	Multivariate analysis: association of rs4588 with 25-OHD when correcting for age, gender, current smoking status, BMI and seasonal variation	Univariate analysis CA: P = 0.15 (NS) AA: P = 0.01 Multivariate analysis controls: P = 0.03 patients: P = 0.05	8/10	
			Gaffney-Stomberg et al., 2017	x											Caucasian			Discovery cohort β (SE) = -2.53 (0.797) Replication β (SE) = -3.952 (0.955)	Discovery cohort P = 0.0016 Replication P = 4.97E-5 * P = 0.0013 **	7/8	* FDR corrected ** Bonferroni corrected
Engelman et al., 2008			x											Hispanic & African American	Effect of SNP, Coef ± SE <u>San Antonio Hispanics</u> 0.199 ± 0.068 <u>San Luis Hispanics</u> 0.285 ± 0.075 <u>Los Angeles African Americans</u> 0.234 ± 0.087		P = 0.004 P < 0.001 P = 0.007		6/8		
GC	rs4588			x											Effect of SNP, Coef ± SE <u>San Antonio Hispanics</u> 0.255 ± 0.093 <u>San Luis Hispanics</u> 0.182 ± 0.085		P= 0.007 P=0.032				
		Barry et al., 2014 [†]	x											Caucasian			Estimated diff. in serum level per variant allele: -8.87% 95%CI: -10.90, -6.78	P < 0.0001 (Wald test)	7/8		
		Gordzik et al., 2011 [†]	x											Diverse (East & South Asian, European, other)	Mean ± SD [nmol/L] East Asians Fall: CC: 54.4 ± 15.7 AC: 42.5 ± 12.0 AA: 34.2 ± 6.50 Winter: CC: 31.3 ± 17.1 CA: 29.5 ± 12.5 AA: 24.4 ± 7.39 Europeans Fall: CC: 81.4 ± 26.1 CA: 73.4 ± 22.6 AA: 59.6 ± 20.6	East Asians Fall: CC (Wt): 1 AC: 0.781 AA: 0.629 Winter: CC (Wt): 1 AC: 0.942 AA: 0.780 Caucasians Fall: CC (Wt): 1 AC: 0.902 AA: 0.732	A allele partial correlations East Asians Fall: -0.463, Winter: -0.384 Europeans Fall: -0.256	P < 0.001 P < 0.001 P = 0.009	7/8		

	Gene and SNP	Source	Vitamin										Ancestry	Outcome				Risk of bias	Notes
			Vitamin D					Vit. B12	Vit. B9 (Folate)	Vit. B6 (PLP)	Hcy	Absolute Values		Effect size	Other	P-value	JBI assessment		
			Calcitriol (25(OH)D)	Calcitriol (1,25(OH)2D)	Ergocalciferol (D2)	VDBP	Vit.D deficiency		Red blood cell	Folate / Folic acid	Serum / Plasma Folate								
Vitamin D	GC rs4588	Engelman et al., 2012	x										Caucasian	Mean stratified by season [†] [nmol/L] <u>High exposure</u> CC (Wt): 65.6 CA: 62.0 AA: 53.5		<u>Additive genetic model</u> β = -0.25 <u>SNP * High exposure</u> β = -0.33	P < 0.001 <u>High exposure</u> P = 0.0002	7/8	
		Ammar et al., 2023	x										Arab		<u>Odds of non-response *, OR (95%CI)</u> GG (Wt): 1 GT: 7.58 (1.97, 27.2) TT: 11.51 (3.36, 39.4)	P = 0.002 P < 0.001	7/9	* non-response: serum 25(OH)D <30ng/ml after Vit. D supplementation	
		Grant et al., 2022	x										Mixed	<u>Adjusted Mean Difference (95%CI), [nmol/L]</u> TT: Ref. (0.00) TG: 6.12 (3.71, 8.77) GG (Wt): 10.94 (8.52, 13.69)		both P < 0.001	7/8		
		Parlato et al., 2023	x										Black-African	<u>UK Biobank Sample</u> β (SE) = -0.11 (0.01) <u>SCCS Sample *</u> β (SE) = -0.12 (0.06) <u>SCCS Sample *</u> β (SE) = 0.13 (0.05)	Variance explained: 0.01% P = 1.48E-13 P = 2.28E-02 P = 0.01	P = 1.48E-13 P = 2.28E-02 P = 0.01	7/8	* Southern Community Cohort Study	
	GC rs4588	Szili et al., 2018				x							Caucasian	<u>Mean [mg/L]</u> GG (Wt): 320.2 GT: 305.5 TT: 277.3	GG: 1 GT: 0.954 TT: 0.866	TT: P = 0.004 *	7/8	* remained signif. After FDR correction	
		Lu et al., 2011 [†]	x										Asian (Chinese)	<u>GLR</u> Beijing: β (SE) = -0.087 (0.01) Shanghai: β (SE) = -0.064 (0.01) Meta-analysis: β (SE) = -0.076 (0.01) <u>Conditional analyses</u> Beijing: β (SE) = -0.086 (0.02) Shanghai: β (SE) = -0.057 (0.02) Meta-analysis: β (SE) = -0.072 (0.01)	P = 4.5E-9 P = 2.6E-6 P = 1.3E-26 P = 1.7E-4 P = 0.0045 P = 4.3E-7	P = 4.5E-9 P = 2.6E-6 P = 1.3E-26 P = 1.7E-4 P = 0.0045 P = 4.3E-7	8/8	<u>GLR</u> Analyses performed under additive model with adjusting for covariates. <u>Conditional analyses:</u> including all variants, which were in the same locus, in one multiple regression model.	

Footnotes
Effect directions refer to minor allele T (A on reverse DNA strand); reference genotype: GG (Wt) (CC on reverse DNA strand)
β = variation in serum 25(OH)D per risk-allele.
[†]Statistical analyses in these studies were performed on log-transformed 25(OH)D values.
*Both studies by Nissen et al. were conducted in the same cohort.
[†]Mean values & corresponding P-values derive from univariate analysis in COPD patients.
[†]association not significant for low sun exposure (winter)
Abbreviations: Wt, wild type; VDB, Vitamin D deficiency; Coef., coefficient; GLR, general linear regression; FDR, False discovery rate

Vitamin D	rs12512631 x rs2282679 x rs3755967 x rs4588	Barry et al., 2014 [†]	x										Caucasian		Ref.: CTCC Estimated diff. in baseline 25(OH)D level for TTCC: -9.34% 95%CI: -11.63, -6.99	P < 0.0001 (Wald test)	7/8	
	rs7041 x rs4588 x rs1155563 x rs2282679	Lu et al., 2011 [†]	x										Asian (Chinese)		Ref.: GCTA TACC Beijing: β (SE)= -0.098 (0.02) Shanghai: β (SE)= -0.071 (0.02) Meta-analysis: β (SE)= -0.085 (0.01)	Beijing P = 4.8E-6 Shanghai P = 2.4E-4 Meta-analysis P = 2.3E-9	8/8	Analyses performed under additive model with adjusting for covariates. Meta-analysis: fixed-effect model

Footnotes
β = variation in serum 25(OH)D per haplotype, compared to reference haplotype.
[†]Statistical analyses in these studies were performed on log-transformed 25(OH)D values.
Abbreviations: Ref., Reference haplotype

Vitamin D	GC rs222020	Xu et al., 2014	x										Asian (Chinese)	Pearson correlation r = 0.080	P = 0.001	8/8	
		Barry et al., 2014 [†]	x										Caucasian	Estimated diff. in 25(OH)D level per variant allele: 3.21% 95% CI: 0.24, 6.26	P = 0.03 (Wald test)	7/8	
		Bu et al., 2010	x										Caucasian	Discovery cohort β = 8.42 Replication cohort β = 4.42 Pooled β = 5.79	Discovery cohort P (Wald test) = 0.010 P = 0.009 * P = NS ** Replication cohort P (Wald test) = 0.037 P = 0.038 * P = NS ** Pooled P (Wald test) = 0.001 P = 0.002 * P = 0.006 **	7/8	* empirical P-value ** adjusted for multiple testing

Footnotes
Pearson correlation coefficient r indicates direction & strength of linear correlation. Value 0-1 indicates a positive correlation. In this case, 25(OH)D is positively (but weakly) associated with the GC SNP.
β = variation in serum 25(OH)D per risk-allele.
[†]Statistical analyses in this study were performed on log-transformed 25(OH)D values.

Vitamin D	rs222020 x rs2298849	Xu et al., 2014	x						Asian (Chinese)		GLR β (SE) = 0.104 (0.030)	Pearson correlation TA: r = -0.082 CG: r = 0.094	GLR: P = 0.001 TA: P = 0.001 CG: P < 0.001	8/8	
	rs222020 x rs16847015 [†] x rs1155563	Barry et al., 2014 [†]	x						Caucasian		Ref.: TGT Estimated diff. in baseline 25(OH)D level for TGC: -8.44% 95%CI: -10.55, - 6.28	P < 0.0001		7/8	

Footnotes
Pearson correlation coefficient r indicates direction & strength of linear correlation. Value 0-1 indicates a positive correlation. In this case, 25(OH)D is negatively (but weakly) associated with the GC SNPs.
[†]Statistical analyses in this study were performed on log-transformed 25(OH)D values.
[†]Associations of rs16847015 were not replicated in this review.
Abbreviations: Ref., reference haplotype; GLR, general linear regression

Vitamin D	GC rs2298849	Xu et al., 2014	x										Asian (Chinese)	GLR β (SE) = 0.105 (0.029)	Pearson correlation r = 0.095	GLR: P < 0.001 P < 0.001	8/8	
		Robien et al., 2013 [†]	x										Asian (Chinese)	Geometric Mean (95%CI), [nmol/L] TT (Wt): 63.9 (61.6, 66.3) TC: 66.1 (64.0, 68.3) CC: 72.2 (68.2, 76.4)	TT (Wt): 1 TC: 1.034 CC: 1.130	Variance explained: 2.1% P for trend = 0.001	7/8	
		Bu et al., 2010	x										Caucasian		Discovery cohort β = 6.38 Discovery + Replication cohort β = 3.59	Discovery cohort P (Wald test) = 0.026 P* = NS Pooled P (Wald test) = 0.021 P* = 0.020 P** = NS	7/8	* empirical P-value ** adjusted for multiple testing

Footnotes
Pearson correlation coefficient r indicates direction & strength of linear correlation. Value 0-1 indicates a positive correlation. In this case, 25(OH)D is positively (but weakly) associated with the GC SNPs.
[†]Statistical analyses in this study were performed on log-transformed 25(OH)D values.
Abbreviations: Wt, wild type; GLR, general linear regression

Vitamin D	Gene and SNP	Source	Vitamin										Ancestry	Outcome				Risk of bias JBI assessment	Notes
			Vitamin D					Vit. B12	Vit. B9 (Folate)	Vit. B6 (PLP)	Hcy								
			Calcitriol (25(OH)D)	Calcitriol (1,25(OH)2D)	Ergocalciferol (D2)	MDBP	Vit.D deficiency	Red blood cell folate	Folate / Folic acid	Serum / Plasma folate									
			Absolute Values	Effect size	Other	P-value													
GC rs17467825		Rivera-Paredes et al., 2018					x					Amerindian (Hispanic-Caucasian range)			Odds to be VDD, OR (95%CI) <u>Codominant model</u> AA (Wt): Ref. AG: 1.64 (1.04, 2.60) GG: 3.48 (1.19, 10.20) <u>Additive model</u> : 1.73 (1.19, 2.52)	P = 0.033 P = 0.023 P = 0.004	8/8	VDD: 25(OH)D < 20 ng/mL	
		Nissen et al., 2014 [†]	x									Caucasian	Geometric Mean (95%CI), [nmol/L] AA (Wt): 73.8 (70.7, 77.0) GA: 70.0 (66.6, 73.6) GG: 63.6 (57.1, 70.8)	AA (Wt): 1 GA: 0.949 GG: 0.862	P = 0.0015	7/8			
		Elkum et al., 2014	x									Mixed (59% Arab, 41% Asian)	Mean [ng/mL] <u>Arabs</u> AA (Wt): 14.4 AG: 13.4 GG: 10.3 <u>South Asians</u> AA (Wt): 15.8 AG: 12.9 GG: 13.0	<u>Arabs</u> AA (Wt): 1 AG: 0.931 GG: 0.715 <u>South Asians</u> AA (Wt): 1 AG: 0.816 GG: 0.823	P = 0.0165 <u>South Asians</u> P = 0.0013	6/8			
		Batal et al., 2014 [†]	x									Caucasian			β = -0.04	P = 0.003	7/8		

Footnotes
Effect directions refer to minor allele G; reference group: AA (WT)
Pearson correlation coefficient *r* indicates direction & strength of linear correlation. Value 0-1 indicates a positive correlation. In this case, 25(OH)D is positively (but weakly) associated with the GC SNPs.
β = variation in serum 25(OH)D per risk allele.
[†] Statistical analyses in these studies were performed on log-transformed 25(OH)D values.
Abbreviations: Wt, wild type; VDD, Vitamin D deficiency

Vitamin D	GC rs3755967	Rivera-Paredes et al., 2018							x						Amerindian (Hispanic-Caucasian range)				Odds to be VDD, OR (95%CI) <u>Codominant model</u> CC Ref. CT: 1.61 (1.02, 2.54) TT: 3.48 (1.19, 10.18) <u>Additive model</u> : 1.71 (1.18, 2.49)	P= 0.040 P= 0.023 P = 0.005	8/8	VDD: 25(OH)D < 20 ng/mL
		Elkum et al., 2014	x											Mixed (59% Arab, 41% Asian)	Mean (ng/mL) <u>Arabs</u> CC (WT): 14.4 CT: 13.3 TT: 10.5 <u>South Asians</u> CC (WT): 15.8 CT: 12.8 TT: 13.0	<u>Arabs</u> AA (WT): 1 AG: 0.924 GG: 0.729 <u>South Asians</u> AA (WT): 1 AG: 0.810 GG: 0.823	<u>Arabs</u> P = 0.0368 <u>South Asians</u> P = 0.0007	6/8				
		Batal et al., 2014 [†]	x											Caucasian			β = -0.04	P= 0.002	7/8			

Footnotes
Effect directions refer to minor allele T; reference group: CC (WT)
rs12512631 has also been observed to affect Vitamin D in association with other GC SNPs (view Haplotype: rs12512631 x rs2282679 x rs3755967 x rs4588)
[†] Statistical analyses in these studies were performed on log-transformed 25(OH)D values.
Abbreviations: Wt, wild type; VDD, Vitamin D deficiency; Ref., reference

Vitamin D	GC rs12512631	Nissen et al., 2014 [†]	x								Caucasian	Geometric Mean (95% CI), [nmol/L] TT (WT): 66.8 (71.3, 78.0) TC: 74.6 (71.3, 78.0) CC: 75.3 (69.0, 82.1)	TT (WT): 1 TC: 1.117 CC: 1.127		P = 0.0004	7/8	
		Barry et al., 2014 [†]	x								Caucasian			Estimated diff. in serum level per variant allele: -4.69% 95%CI: 2.50, 6.92	P < 0.0001 (Wald test)	7/8	
		Rivera-Paredes et al., 2018	x								Amerindian (Hispanic-Caucasian range)			"SNP rs12512631 had an inverse association with VD deficiency, only with the unadjusted model."	P = 0.03	8/8	

Footnotes
Effect directions refer to minor allele C; reference group: TT (WT)
rs12512631 has also been observed to affect Vitamin D in association with other GC SNPs (view Haplotype: rs12512631 x rs2282679 x rs3755967 x rs4588)
[†] Statistical analyses in these studies were performed on log-transformed 25(OH)D values.
Abbreviations: Wt, wild ; VDD, Vitamin D deficient

Vitamin D	GC rs2298850	Elkum et al., 2014	x						Mixed (59% Arab, 41% Asian)	Mean (ng/mL) <u>Arabs</u> GG (WT): 14.4 GC: 13.3 CC: 10.3 <u>South Asians</u> GG (WT): 15.5 GC: 13.2 CC: 13.0	<u>Arabs</u> GG (WT): 1 GC: 0.924 CC: 0.715 <u>South Asians</u> GG (WT): 1 GC: 0.852 CC: 0.839		<u>Arabs</u> P = 0.0374 <u>South Asians</u> P = 0.0103	6/8		
		Rivera-Paredes et al., 2018					x			Amerindian (Hispanic-Caucasian range)			Odds to be VDD, OR (95%CI) <u>Codominant model</u> GG (WT): Ref. GC: 1.64 (1.04, 2.60) CC: 2.88 (0.98, 8.51) <u>Additive model</u> : 1.67 (1.14, 2.43)	P= 0.034 P= 0.055 P = 0.008	8/8	VDD: 25(OH)D <20 ng/mL
		Batal et al., 2014 [†]	x							Caucasian			β = -0.03	P = 0.04	7/8	

Footnotes
Effect directions refer to minor allele C; reference group: GG (WT), except for Batal et al. (2014), who refer to the G allele as the minor allele (possibly genotyped the reverse DNA strand).
Pearson correlation coefficient *r* indicates direction & strength of linear correlation. Value 0-1 indicates a positive correlation. In this case, 25(OH)D is positively (but weakly) associated with the GC SNPs.
β = variation in serum 25(OH)D per risk allele.
[†] Statistical analyses in this study were performed on log-transformed 25(OH)D values.

Vitamin D	Gene and SNP	Source	Vitamin											Ancestry	Outcome				Risk of bias JBI assessment	Notes
			Vitamin D					Vit. B12	Vit. B9 (Folate)	Vit. B6 (PLP)	Hcy	Absolute Values	Effect size		Other	P-value				
			Calcifediol (25(OH)D)	Calcitriol (1,25(OH)2D)	Ergocalciferol (D2)	VDBP	Vit. D deficiency	Red blood cell folate	Folate / Folic acid	Serum / Plasma Folate										
GC rs2282679	GC rs2282679	Zhang et al., 2013	x										Asian (Chinese)	Mean [ng/mL] Wt: 19.32 Het.: 18.33 Hom.: 16.87	Wt: 1 Het.: 0.949 Hom.: 0.873	β = - 0.1529	P = 0.006206	7/8	* Bonferroni corrected P-value	
						x							Mean [mg/mL] ¹ TT (Wt): 317 TG: 308.5 GG: 296	TT (Wt): 1 TG: 0.973 GG: 0.934	"rs2282679 was associated with concentrations of DBP, with the minor allele G related to reduced protein concentrations."			¹ Values estimated based on Fig. 4 in Zhang et al. (2013)		
		Santos et al., 2019	x					x					Caucasian (20% African + Caucasian mixed)	Mean ± SD [ng/mL] AA (Wt): 23.39 ± 8.79 AC: 22.83 ± 7.80 CC: 19.70 ± 7.17	AA (Wt): 1 AC: 0.976 CC: 0.842	β = -1.3	P = 0.034	7/8	PR for AC not significant VDD: 25(OH)D < 20 ng/mL	
								x					Mean ± SD [µg/mL] AA (Wt): 203.13 ± 27.90 AC: 196.41 ± 30.04 CC: 180.88 ± 38.20	AA (Wt): 1 AC: 0.967 CC: 0.890	β = -9.3	P < 0.001				
		Perna et al., 2013	x										Caucasian	Median (IQR) [nmol/L] Women AA (Wt): 41.1 (31.3; 53.7) AC: 39.3 (30.3; 50.5) CC: 34.7 (29.7; 46.1) Men AA (Wt): 55.1 (39.2; 73.4) AC: 51.5 (35.8; 69.8) CC: 44.4 (33.9; 62.7)	Women AA (Wt): 1 AC: 0.956 CC: 0.844 Men AA (Wt): 1 AC: 0.935 CC: 0.806	Adjusted Estimates (SE) [nmol/L] AA: Ref. 0.0 AC: -2.2 (0.7) CC: -5.8 (1.4)	"Linear regression analysis showed strong associations between Vit. D and the genetic variant in the total population and by sex"	7/8	Estimates adjusted for covariates	
		Nissen et al., 2014 [†]	x										Caucasian	Geometric mean (95%CI), [nmol/L] AA (Wt): 73.8 (70.7, 77.0) CA: 70.1 (66.6, 73.7) CC: 63.6 (57.1, 70.8)	AA (Wt): 1 AC: 0.950 CC: 0.862		P = 0.0020	7/8		
		Li et al., 2014	x										Asian (Chinese)			β (SE): -3.077 (0.903)	P = 0.0007 P = 0.006 *	8/8	* Bonferroni corrected	
		Barry et al., 2014 [†]	x										Caucasian			"baseline associations were statistically significant."				Results not shown, authors did not respond to request for absolute values.
		Lu et al., 2011 [†]	x										Asian (Chinese)			GLR Beijing: β (SE) = -0.080 (0.01) Shanghai: β (SE) = -0.063 (0.01) Meta-analysis: β (SE) = -0.072 (0.01) Conditional analyses Beijing: β (SE) = -0.069 (0.02) Shanghai: β (SE) = -0.052 (0.02) Meta-analysis: β (SE) = -0.061 (0.01)	P = 7.4E-8 P = 4.1E-6 P = 4.9E-24 P = 0.0022 P = 0.0080 P = 1.9E-5	8/8	GLR Analyses performed under additive model with adjusting for covariates. Conditional analyses: incl. all variants, which were in the same locus, in one multiple regression model.	
		GC rs2282679	GC rs2282679	Wang et al., 2010 [†]	x									Caucasian	Mean ± SE [nmol/L] Wt: 82.6 ± 0.73 het.: 74.8 ± 0.81 hom.: 64.6 ± 1.79	Wt: 1 het.: 0.906 hom.: 0.782		Candidate gene analysis Discovery Cohort P = 4.57E-63 Replication Cohort P = 2.88E-48 Overall P = 2.9E-108	8/8	All Analyses reached genome-wide significance
							x								Odds for low Vit. D, OR (95%CI) < 75nmol/L: 1.63 (1.53, 1.73) < 50nmol/L: 1.49 (1.40, 1.59)	P = 3.5E-50 P = 7.5E-33		OR per copy of the risk allele		
								x							"minor allele related to lower DBP concentration"	P = 4.0E-42		"rs2282679 was strongly associated with DBP, with the minor allele related to lower DBP conc."		
Batal et al., 2014 [†]	x											Caucasian			β = -0.05	P = 0.001	7/8			
Elkum et al., 2014	x											Mixed (59% Arab, 41% Asian)	Mean [ng/mL] Arabs TT (Wt): 14.4 GT: 13.3 GG: 10.4 South Asians TT (Wt): 15.8 GT: 12.8 GG: 13.0	Arabs AA (Wt): 1 AG: 0.924 GG: 0.722 South Asians AA (Wt): 1 AG: 0.810 GG: 0.823		Arabs P = 0.0377 South Asians P = 0.0007	6/8			
Rivera-Paredes et al., 2018						x					Amerindian (Hispanic-Caucasian range)			Odds to be VDD, OR (95%CI) Subsample (n=400) 1.73 (1.19, 2.52) Whole sample (n= 689) 1.53 (1.15, 2.04)	P = 0.004 P = 0.003	8/8	VDD: 25(OH)D < 20 ng/mL			
Ahn et al., 2010 ¹	x										Caucasian	Mean [nmol/L] ATBC AA (Wt): 42.1 AC: 37.2 CC: 35.2 CLUE II AA (Wt): 67.5 AC: 58.4 CC: 44.3 PLCO AA (Wt): 61.5 AC: 55.3 CC: 53.4 NHS-CGEMS AA (Wt): 86.8 AC: 77.3 CC: 72.5 NHS-T2D AA (Wt): 58.8 AC: 55.8 CC: 48.8	ATBC AA (Wt): 1 AC: 0.884 CC: 0.836 CLUE II AA (Wt): 1 AC: 0.865 CC: 0.656 PLCO AA (Wt): 1 AC: 0.899 CC: 0.868 NHS-CGEMS AA (Wt): 1 AC: 0.891 CC: 0.835 NHS-T2D AA (Wt): 1 AC: 0.949 CC: 0.830	ATBC β(SE): -0.36 (0.05) CLUE II β(SE): -0.69 (0.22) PLCO β(SE): -0.37 (0.05) NHS-CGEMS β(SE): -0.46 (0.09) NHS-T2D β(SE): -0.24 (0.07)	ATBC P = 1.5E-8 CLUE II P = 2.2E-3 PLCO P = 5.8E-13 NHS-CGEMS P = 1.2E-7 NHS-T2D P = 9.5E-4	6/8				

Gene and SNP	Source	Vitamin										Ancestry	Outcome				Risk of bias JBI assessment	Notes	
		Vitamin D					Vit. B12	Vit. B9 (Folate)		Vit. B6 (PLP)	Hcy		Absolute Values	Effect size	Other	P-value			
		Calcitriol (25(OH)D)	Calcitriol (1,25(OH)2D)	Ergocalciferol (D2)	VDBP	Vit.D deficiency		Red blood cell folate / Folate / Folic acid / Serum / Plasma Folate											
Vitamin D	Slow et al., 2020	x										Caucasian			Baseline 25(OH)D [nmol/L] β (95% CI): -6.34 (-10.29, -2.39) ^{2,3}	P = 0.00181	12/13	² association remained significant after 2 mo of Vit. D3 supplementation and after Bonferroni correction at that time point ³ association remained significant after 18 mo of Vit. D3 supplementation	
					x									Baseline VDBP [nmol/L] β (95% CI): -298.81 (-440.35, -157.26)	P = 0.00005 *	*remained signif. after Bonferroni correction			
	Kwak et al., 2018	x										Asian (Korean)			*found negative associations btw serum 25(OH)D level and the effect allele G*	P = 0.004	7/8		
	Man et al., 2022	x										Asian (Chinese)			Odds to be VDD, OR (95%CI): <u>Genotypic model</u> AC: 2.30 (1.37, 3.87) <u>Univariate model</u> 1.52 (1.03, 2.24) <u>Multivariate model</u> 1.57 (1.04, 2.39)	P < 0.01 * P = 0.04 P = 0.03	7/8	VDD: 25(OH)D < 30 ng/ mL *remained signif. after Bonferroni correction	
	Waterhouse et al., 2014	x										Caucasian	Mean change (95%CI) [nmol/L] AA (WT): 43.3 (41.9, 44.8) AC: 41.0 (39.3, 42.7) CC: 36.0 (32.3, 39.7)	AA (WT): 1 AC: 0.947 CC: 0.831		P < 0.005 (P trend < 0.005)	12/13	significant after Bonferroni correction (P trend = 2E-4)	
	Cheung et al., 2013 ¹	x										Asian (Chinese)			β (95%CI): -0.066 (-0.100, 0.033) <u>SNP * season</u> <u>Summer/Autumn</u> β (95%CI): -0.063 (-0.105, -0.021) <u>Winter/Spring</u> β (95%CI): -0.072 (-0.126, -0.019)	 <u>SNP * season</u> <u>Summer/Autumn</u> P = 0.003 <u>Winter/Spring</u> P = 0.008	7/8	¹ model adjusted for rs12785879 Association for Winter/Spring was not significant VDD: 25(OH)D < 20 ng/mL	
						x									Odds to be VDD, OR (95%CI): 1.51 (1.19, 1.93) <u>Independent association*</u> OR (95%CI): 1.52 (1.19, 1.94) <u>SNP * season</u> <u>Summer/Autumn</u> OR (95%CI): 1.64 (1.19, 2.27)	 P = 8.6E-4 P = 8.1E-4 <u>SNP * season</u> <u>Summer/Autumn</u> P = 0.003			
	Didriksen et al., 2013	x										Caucasian	Mean ± SD [nmol/L] TT (WT): 61.9 ± 24.5 TG: 53.4 ± 20.3 GG: 46.5 ± 16.4	TT (WT): 1 TG: 0.863 GG: 0.751		GG baseline: 46.0 ± 15.5 GG 6mo: 139.2 ± 23.9 MD: 93.2 ± 21.6	GG: P < 0.01 Delta: P < 0.05	7/8	TG not significant
	Trummer et al., 2012	x										Caucasian	Mean ± SD [ng/mL] <u>Cross-sectional study cohort</u> TT (WT): 35.9 ± 13.3 TG: 31.8 ± 12.9 GG: 26.1 ± 8.7 <u>Prospective cohort study</u> TT (WT): 9.4 ± 7.6 TG: 8.7 ± 5.5 GG: 7.5 ± 4.6	 <u>Cross-sectional</u> TT (WT): 1 TG: 0.886 GG: 0.727 <u>Prospective cohort</u> TT (WT): 1 TG: 0.926 GG: 0.798			P = 0.001 P = 0.048	7/8	94% of subjects in the prospective cohort were Vit. D deficient (thus the low mean values)
	Slater et al., 2017					x						Caucasian			Odds to be VDD for T allele, OR (95%CI) <u>Initial model</u> 0.42 (0.18, 0.93) <u>Final model</u> 0.346 (0.143, 0.838)	P = 0.037 P = 0.019	7/8	Initial model: all potential confounders Final model: significant confounders only VDD: 25(OH)D < 30ng/mL	
	Simon et al., 2011	x										Caucasian			*Each additional 'C' allele was associated with a 7.8 nmol/L decrease in 25(OH)D*		5/8		
	Thongthai et al., 2015	x										Asian (Thai)	Mean ± SD [ng/mL] AA (WT): 30.1 ± 9.0 AC: 27.5 ± 8.7 CC: 25.2 ± 8.3	AA (WT): 1 AC: 0.914 CC: 0.837	Multivariate analysis Association C allele: β = -0.17	P < 0.001 Multivariate P<0.001	8/8	VDD: 25(OH)D < 20ng/mL	
						x									*A allele: 34% lower risk of VDD* Odds to be VDD for each C allele OR (95%CI): 1.80 (1.57, 2.01) VDD prevalence by genotype AA (WT): 10.6% AC: 16.7% CC: 26.4%	P < 0.001			

Footnotes
 Unless specified, effect directions refer to minor allele C (G on reverse strand); reference group: AA (WT) (T on reverse strand)
 β = variation in serum 25(OH)D per risk allele.
¹ Statistical analyses in these studies were performed on log-transformed 25(OH)D values.
² Ahn et al (2020) analyzed 5 GWAS for associations between SNPs and 25(OH)D, the cohorts listed here found significant results. Subjects include cases (VDD) and contrors.
 Abbreviations: WT, wild type; VDD, Vitamin D deficiency; PR, prevalence ratio; Ref., reference; GLR, general linear regression; MD, mean difference; VDBP, Vitamin D binding protein

Vitamin D	Gene and SNP	Source	Vitamin										Ancestry	Outcome				Risk of bias JBI assessment	Notes
			Vitamin D					Vit. B12	Vit. B9 (Folate)	Vit. B6 (PLP)	Hcy	Absolute Values		Effect size	Other	P-value			
			Calcifediol (25(OH)D)	Calcitriol (1,25(OH)2D)	Ergocalciferol (D2)	VDBP	Vit D deficiency												
																	Red blood cell folate		
	rs705117 x rs2282679 x rs1491710	Zhang et al., 2013	x									Asian (Chinese)			TGA β = - 0.1529 freq.: 0.3083 CTA β = 0.1 freq.: 0.1758	P = 6.6E-5 P = 0.03234	7/8		
Vitamin D	GC rs1155563	Perna et al., 2013	x									Caucasian	Median (IQR) [nmol/L] Women TT (Wt): 41.0 (31.3; 53.7) TC: 39.1 (30.5; 50.0) CC: 34.5 (29.5; 46.1) Men TT (Wt): 54.6 (38.4; 73.2) TC: 51.5 (36.8; 69.8) CC: 45.6 (33.9; 63.9)	Women TT (Wt): 1 TC: 0.954 CC: 0.841 Men TT (Wt): 1 TC: 0.943 CC: 0.835	Adjusted Estimates (SE) [nmol/L] TT: Ref. 0.0 TC: -2.1 (0.7) CC: -5.8 (1.4)	N/R *	7/8	* "Linear regression analysis showed strong associations between Vit. D and the genetic variant in the total population and by sex"	
		Barry et al., 2014 [†]	x									Caucasian			Estimated diff. in serum level per variant allele: -8.44% 95%CI: -10.48, -6.35	P < 0.0001 (Wald test)	7/8		
		Batal et al., 2014 [†]	x									Black African			African American: β= -0.04	P = 0.048	7/8		
		Elkum et al., 2014	x									Arab	TT (Wt): 14.4 TC: 13.3 CC: 10.4	TT (Wt): 1 TC: 0.924 CC: 0.722		P = 0.0289	6/8		
		Rivera-Paredes et al., 2018					x					Amerindian (Hispanic-Caucasian range)			Odds to be VDD, OR (95%CI) Codominant model TT: Ref. TC: 1.76 (1.13, 2.76) CC: 2.96 (0.71, 12.34) Additive model: 1.76 (1.18, 2.61)	P= 0.013 P= 0.135 P = 0.006	8/8	VDD 25(OH)D <20 ng/mL	
		Slow et al., 2020	x									Caucasian			Baseline 25(OH)D [nmol/L] β (95% CI): -5.48 (-9.37, -1.59) [‡]	P = 0.00609	12/13	[‡] association remained significant after 2 mo of Vit. D3 supplementation and after Bonferroni correction at that time point * Remained significant after Bonferroni correction	
						x									Baseline VDBP [nmol/L] β (95% CI): -257.38 (-397.16, -117.59)	P= 0.00036 *			
			Lu et al., 2011 [†]	x									Asian (Chinese)			GLB Beijing: β (SE)= -0.048 (0.01) Shanghai: β (SE)= -0.042 (0.01) Meta-analysis: β (SE)= -0.045 (0.01)	P= 9.8E-4 P= 0.0015 P= 2.0E-10	8/8	Analyses performed under additive model, adjusted for covariates. Meta-analysis: fixed-effect model
Footnotes																			
Effect directions refer to minor allele C (G on reverse strand) ; reference group: AA (Wt) (T on reverse strand)																			
β = variation in serum 25(OH)D per haplotype, compared to reference haplotype. Lu et al (2011) refer to changes in log-25(OH)D																			
[†] Statistical analyses in these studies were performed on log-transformed 25(OH)D values.																			
[‡] Ahn et al (2020) analyzed 5 GWAS for associations between SNPs and 25(OH)D, the cohorts listed here found significant results. Subjects include cases and controls.																			
Vitamin D	GC rs7041	Sinotte et al., 2009	x									Caucasian	Mean ± SE [nmol/L] GG: 67.5 ± 1.1 GT: 64.5 ± 0.8 TT: 60.8 ± 1.5 Seasonal Association May-Oct GG: 73.4 ± 1.4 GT: 71.4 ± 1.1 TT: 64.8 ± 2.1	GG: 1 GT: 0.956 TT: 0.901 May-Oct GG: 1 GT: 0.973 TT: 0.883		GG: Ref. GT: P = 0.034 TT: P = 0.0003 Total β ± SE = 23.29 ± 0.89 May-Oct β = -3.78	Total P for trend = 0.0003 Summer P for trend = 0.0018	7/8	Association not significant for Winter
		Santos et al., 2019	x									Caucasian (20% African + Caucasian mixed)	Mean ± SD [ng/mL] TT (Wt) : 21.48 ± 7.54 TG: 23.20 ± 8.24 GG: 23.78 ± 9.14	GG: 1 TG: 0.976 TT: 0.903	β = 1.2	P= 0.030	7/8		
		Robien et al., 2013 [†]	x									Asian (Chinese)	Geometric Mean (95%CI) [nmol/L] TT (Wt): 64.0 (61.9, 66.1) TG: 67.7 (65.4, 70.0) GG: 70.6 (65.9, 75.6)	GG: 1 TG: 0.959 TT: 0.907	Variance explained: 1.6%	P for trend = 0.003	7/8		
		Rivera-Paredes et al., 2020					x					Hispanic			"Carriers of the GG & GT had lower prevalence of VDD compared to TT genotype"	GG: P = 0.019 GT: P = 0.022	8/8	VDD: 25(OH)D <20 ng/mL	
		Pooyan et al., 2020		x								Iranian			"T allele carriers had lower Vitamin D compared to others" β ± SE = -0.46 ± 0.14 GT: 0.63	P < 0.0001 (P-trend: 0.002)	8/8		
		Meshkibaf et al., 2021						x				Iranian (Persian)			Allele freq(n) VDD GG: 35.4% (17) GT: 31.3% (15) TT: 33% (n= 16) * Insufficient GG 34.2% (40) GT: 52.1% (61) ** TT: 13.7% (n=16) Normal GG: 41.9% (13) GT: 35.5% (11) TT: 22.6% (7)	* P = 0.03 ** P= 0.02	5/8	VDD: 25(OH)D < 20 ng/ml Insufficient: 25(OH)D 21–29 ng/ml Normal: 25(OH)D > 30 ng/ml P-values after Bonferroni correction	
		Lafi et al., 2015	x									Mostly Caucasian (Mixed)	Mean ± SD [ng/mL] GG (Wt): 36.1 ± 20.4 GT: 28.5 ± 21.8 TT: 24.6 ±17.7 TT + GT: 27.2 ± 20.5 GG + GT: 31.3 ± 21.5	GG (Wt): 1 GT: 0.789 TT: 0.681 TT + GT: 1 GG + GT: 1.151		GT: P = 0.001 TT: P= 0.004 TT + GT: P = 0.0006 GG + GT: P= 0.026	5/8		
															Odds for low Vit. D, OR (95%CI) GG (Wt):Ref. GT: 3.25 (1.59, 6.63) TT: 3.31 (1.46, 7.50) TT + GT: 3.27 (1.66, 6.42) GG+ GT: 2.15 (1.10, 4.20)				
	Janssens et al., 2010	x									Caucasian	Mean ± SD [ng/mL] GG (Wt): 26.3 ± 8.7 GT: 24.6 ± 9.1 TT: 20.9 ± 5.0	GG (Wt): 1 GT: 0.935 TT: 0.795	Multivariate analysis β (95%CI): -4.5 (-6.5, -2.4)	P < 0.0001 GT: P = 0.5 (NS) TT: P = 0.03				

Gene and SNP	Source	Vitamin										Ancestry	Outcome				Risk of bias	Notes	
		Vitamin D					Vit. B12	Vit. B9 (Folate)	Vit. B6 (PLP)	Hcy	Absolute Values		Effect size	Other	P-value	JBI assessment			
		Calcifediol (25(OH)D)	Calcitriol (1,25(OH)2D)	Ergocalciferol (D2)	VDBP	Vit.D deficiency	Red blood cell folate	Folate/Folic acid	Serum / Plasma Folate										
GC rs7041	Gaffney-Stomberg et al., 2017	x										Caucasians, African Americans, other		Entire cohort Discovery cohort β (SE) = 3.201 (0.614) Replication β (SE) = 4.458 (0.667) Caucasians only Discovery cohort β (SE) = -2.179 (0.696) Replication β (SE) = -3.268 (0.863)	Entire cohort P = 2.88E-7 P* = 1.97E-10 P** = 5.32E-09 Caucasians P = 0.0019 P* = 0.0002 P** = 0.0053	7/8	*FDR corrected ** Bonferroni corrected		
		x											Entire cohort Discovery cohort β (SE) = 4.127 (1.665) Replication β (SE) = 9.633 (2.504) African Americans only Discovery cohort β (SE) = -9.705 (4.067) Replication: NS	Entire cohort P = 0.0136 P* = 0.04701 P** = 0.0039 African Americans P = 0.0198					
	Engelman et al., 2008	x									Hispanic & African American		Effect of SNP (T allele), Coef ± SE San Antonio Hispanics -0.181 ± 0.061 San Luis Hispanics -0.220 ± 0.063 Los Angeles African Americans -0.2159 ± 0.071	P = 0.003 P < 0.001 P = 0.025	6/8	Association between rs7041 and 1,25(OH)2D was not significant			
	Barry et al., 2014 [†]	x									Caucasian		Estimated diff. in serum level per variant allele: -6.69% 95%CI: -8.57, -4.76	P < 0.0001 (Wald test)	7/8				
	Engelman et al., 2012	x									Caucasian	Association stratified by season [‡] [nmol/L] High exposure GG (WT): 67.8 GT: 63.1 TT: 57.4	GG (WT): 1 GT: 0.931 TT: 0.847	Additive genetic model β = -0.1 SNP * High exposure β = -0.33	P = 0.002 SNP * season P = 0.01 SNP * exposure P < 0.0001	7/8			
	Szili et al., 2018	x									Caucasian	Mean [ng/mL] AA (WT): 13.6 AC: 14.6 CC: 16.2	CC: 1 CA: 0.901 AA: 0.840	Explained variance: 2.6% MLR dependent: β (SE): -2.959 (0.905) univariate: β (SE): -1.228 (0.718)	CC: P = 0.006 * MLR P = 0.005	7/8	* remained signif. After FDR correction Association was not significant after Benjamini-Hochberg correction A allele noted as ref. Allele in this study		
	Wang et al., 2010 [†]	x									Caucasian			after adjusting for rs7041, no other SNP in GC remained significant in this cohort.	Candidate gene analysis Discovery Cohort P = 3.74E-42 Replication Cohort P = 1.78E-18 Overall P = 6.31E-59	8/8	All analyses reached genome-wide significance		
	Batal et al., 2014 [†]	x									Caucasian			β = -0.04	P = 0.0007	7/8	after adjusting for rs7041, no other SNP in GC remained significant in this cohort.		
	Elkum et al., 2014	x									Mixed (59% Arab, 41% Asian)	Mean [ng/mL] Arabs CC (WT): 14.5 AC: 14.3 AA: 11.7 South Asians CC (WT): 15.8 AC: 14.4 AA: 12.3	Arabs CC (WT): 1 AC: 0.986 AA: 0.807 South Asians CC (WT): 1 AC: 0.911 AA: 0.778		Arabs P = 0.0110 South Asians P = 0.0072	6/8			
	GC rs7041	Slow et al., 2020	x									Caucasian		Baseline 25(OH)D [nmol/L] β (95% CI): -7.40 (-10.90, -3.89) [‡] Baseline free 25(OH)D [pmol/L] β (95% CI): -2.45 (-4.36, -0.54) [‡]	P = 0.00005* P = 0.01249	12/13	[‡] association remained significant after 2 mo of Vit. D3 supplementation *remained signif. after Bonferroni correction		
					x								Baseline VDBP [nmol/L] β (95% CI): -162.79 (-292.66, -32.92)	P = 0.01461					
Lee et al., 2021		x									Asian (Korean)	Mean ± SE [ng/mL] CC (WT): 21.0 ± 0.50 AC: 19.8 ± 0.22 AA: 18.5 ± 0.18	CC: 1 CA: 0.0.943 AA: 0.881	Associations in multivariate model β = 1.2090 P = 3.20E-9 **	P = 2.44E-8 *	7/8	* obtained through GLM ** obtained thorough additive linear model		
Parlato et al., 2023					x						Black-African			SCCS Sample* β (SE) = 0.48 µg/mL Variance explained: 0.01% *C allele was associated with a 1.83µg/L increase of VDBP. CC: 28.12% higher VDBP than AA."	P = 4.1E-21	7/8	Southern Community Cohort Study These results refer to the major allele C		
Didriksen et al., 2013		x									Caucasian	Mean ± SD [nmol/L] Wt: 63.7 ± 24.8 Het.: 57.2 ± 22.4 Hom.: 50.0 ± 19.2	Wt: 1 Het: 0.898 Hom: 0.785		Hom.: P < 0.01	7/8	Difference for heterozygotes was not significant		
Simon et al., 2011	x									Caucasian			"Each additional 'T' allele was associated with a 5.5 nmol/L decrease in 25(OH)D"		5/8				
Hansen et al., 2015	x									African-American	Mean in supplement users [mg/L] GG/GT: 29 TT: 25.3	GG/GT: 1 TT: 0.872	β ± SE = -0.93 ± 0.53	β: P = 0.08 Mean values P = 0.002	7/8	The association was not significant in non-supplement users (Vit.D & multivitamin)			
Larcombe et al., 2012				x						Canadian First Nation (Dene)	Mean ± SD [µg/mL] GG (WT): 469.4 ± 72.85 GT: 277.26 ± 6.40 TT: 208.1 ± 153.8	GG (WT): 1 GT: 0.591 TT: 0.443		P < 0.005		Associations shown apply to winter-time, those for summer were not significant			

[†]Footnotes
Effect directions refer to risk allele T (A on reverse DNA strand); reference genotype: GG (CC on reverse DNA strand) - Exception: Parlato et al., 2023 refer effect size to major allele C
 β = variation in serum 25(OH)D per risk allele.
[‡] Statistical analyses in these studies were performed on log-transformed 25(OH)D values.
[§] association not significant for low sun exposure (winter)
Abbreviations: Wt, wild type; VDD, Vitamin D deficiency; VDBP, Vitamin D binding protein; GLR, general linear regression; FDR, False discovery rate; Coef., coefficient

Vitamin D	Gene and SNP	Source	Vitamin										Ancestry	Outcome				Risk of bias	Notes	
			Vitamin D					Vit. B12	Vit. B9 (Folate)	Vit. B6 (PLP)	Hcy	Absolute Values		Effect size	Other	P-value	JBI assessment			
			Cxk/fcd/ol (25(OH)D)	Cxk/fcd/ol 1,25(OH)2D	Eggsal/fcd/ol (D3)	VDBP	Vit.D deficiency	Red blood cell folate	Folate / Folic acid	Serum / Plasma Folate										
GC rs4588 x rs7041 Haplotypes	Fohner et al., 2016	x										Alaskan Native (Yup'ik)			Variance explained by GC1s haplotype: 2.8%	GC2: P = 1.4E-4 GC1f: NS GCx (TC): NS	6/8	The p-values signify the associations with 25(OH)D3 in comparison with the reference haplotype GC		
	Li et al., 2014	x										Asian (Chinese)	Mean ± SE [nmol/L] GC2-2(Ref.): 51.9 ± 1.9 GC1s-1s: 62.0 ± 1.9 GC1s-1f: 59.9 ± 1.2 GC2-1s: 58.6 ± 1.5	GC2-2(Ref.): 1 GC1s-1s: 1.195 GC1s-1f: 1.154 GC2-1s: 1.129		All P < 0.05	8/8			
	Gordzik et al., 2011 [†]	x										Diverse (East & South Asian, European, other)	Mean ± SD [nmol/L] Fall GC1f-1f (Ref.): 55.5 ± 18.2 GC2-1f: 43.4 ± 12.7 GC2-1s: 41.2 ± 11.2 GC2-2: 34.2 ± 6.53 Winter GC1f-1f (Ref.): 40.8 ± 18.9 GC2-1f: 26.6 ± 12.0 GC2-2: 24.4 ± 7.39	Fall GC1f-1f (Ref.): 1 GC2-1f: 0.782 GC2-1s: 0.742 GC2-2: 0.616 Winter GC1f-1f (Ref.): 1 GC2-1f: 0.652 GC2-2: 0.598	Partial correlations Fall GC2-1f: -0.256 GC2-1s: -0.240 GC2-2: -0.303 Winter GC2-1f: -0.311 GC2-2: 0.291 Variance explained by GC2-2: 7%	Fall P=0.014 P=0.021 P=0.003 Winter P= 0.005 P= 0.009	7/8			
	Robien et al., 2013 [†]	x										Asian (Chinese)	Geometric Mean (95%CI) [nmol/L] GC2-2 (Ref.): 56.6 (52.1, 61.4) GC1s-1s: 70.9 (66.1, 76.2) GC1s-1f: 67.6 (64.7, 70.6) GC2-1s: 67.3 (63.3, 71.5) GC1f-1f: 68.9 (65.1, 72.8) GC2-1f: 62.3 (59.3, 65.5)	GC2-2 (Ref.): 1 GC1s-1s: 1.253 GC1s-1f: 1.194 GC2-1s: 1.189 GC1f-1f: 1.217 GC2-1f: 1.101		All haplotypes were significantly different from GC2-2 at P < 0.01 P for trend = 0.0001	7/8			
	Santos et al., 2019	x										Caucasian (20% African + Caucasian mixed)	Mean ± SD [ng/mL] GC1s-1s (Ref.): 23.83 ± 9.19 GC1f-1f: 20.63 ± 8.29 GC2-2: 20.25 ± 7.39	GC1s-1s (Ref.): 1 GC1f-1f: 0.866 GC2-2: 0.850	β = -1.9	P = 0.015	7/8	PR's adjusted for age, BMI, & vitamin D supplementation. Associations were also significant in the unadjusted model (view source)		
													Mean ± SD [µg/mL] GC1s-1s (Ref.): 199.41 ± 29.89 GC1f-1f: 204.83 ± 31.58 GC2-2: 180.75 ± 37.58	GC1s-1s (Ref.): 1 GC1f-1f: 1.027 GC2-2: 0.906	β = -7.7	P = 0.012		VDD: 25(OH)D < 20ng/mL PR's adjusted for age, BMI, & vitamin D supplementation. Associations were also significant in the unadjusted model (view source)		
															GC2 frequency by Vit.D status VDD: 28.4% Sufficient: 15.0% Prevalence Ratio for VDD, PR (95%CI) GC1s-1s: Ref. GC1f-1f: 1.593 (1.120, 2.265) GC2-2: 0.881 (0.790, 0.982)	P = 0.016 P = 0.010 P = 0.022				
	Rivera-Paredes et al., 2020					x						Hispanic			Odds for VDD, OR (95%CI) GC1fs-1f: Ref. GC2-2: 2.83 (1.14, 7.02) GC2-1f: 2.30 (1.40, 3.78)	N/R	8/8	VDD: 25(OH)D < 20ng/mL		
	Pooyan et al., 2020						x						Iranian			Frequencies of VDD by haplotype Gct1 (GC) VDD: 76.5% < Normal: 23.5% Gcx (TC) VDD: 66.7% < Normal: 33.3% Gc2 (TA) VDD: 79.3% < Normal: 20.7% Gctf (GA) VDD: 78.7% < Normal: 21.3%	N/R	8/8	VDD: 25(OH)D < 30 ng/ mL	
	Meshkibaf et al., 2021							x					Iranian (Persian)			Frequencies of haplotype by VDD Gctf (GA) VDD: 42.7% (41/96) * Insufficient: 20.5% (48/234) Normal: 33.9% (21/62) Gc2 (TA) VDD: 6.4% (6/97) Insufficient: 19.3% (45/234) ** Normal: 6.5% (4/62)	P < 0.001* P = 0.001 **	5/8	VDD: 25(OH)D < 20 ng/ml Insufficiency: 25(OH)D 21–29 ng/ml Normal: 25(OH)D > 30 ng/ml P-values remained significant after Bonferroni correction	
Lafi et al., 2015								x				Mostly Caucasian (Mixed)			GC1s-1f (n= 56) VDD: 46.5% (26) Insuff.: 8.9% (5) Suff.: 44.6% (25) OR (95%CI): 2.5 (1.1,5.5) Gc2-1f (n = 15) VDD: 53.3% (8) Insuff.: 6.7% (1) Suff.: 40.0% (6) OR (95%CI): 3.3 (1, 10.6) Gc2-1s (n= 38) VDD: 65.8% (25) Insuff.: 7.9% (3) Suff.: 26.3% (10) OR (95%CI): 5.5 (2.3–13.4) Gc2-2 (n= 8) VDD: 87.5% (7) Insuff.: 12.5% (1) Suff.: 0% (0) OR (95%CI): 20.1 (2.3, 177) Gc2 (n= 69) VDD: 68.1% (47)	P = 0.024 P = 0.047 P = 0.0002 P = 0.007 P < 0.0001	5/8	VDD: 25(OH)D < 20 ng/mL		

Footnotes
 All Alleles are noted as on the forward DNA strand. Notations in papers using the reverse DNA allele were adapted for easier comparison in this table.
[†] Statistical analyses in these studies were performed on log-transformed 25(OH)D values.
 Haplotype codes explained (rs4588 x rs7041): GC1s/1s: GG x CA; GC1f/1f: GG x AA; GC2/1s: GT x CA; GC2/1f: GT x AA. GCx: TT x CC; GC2x: TT x AA; GC1f: GxA; GC1s: GxC; GC2: TxA
 Abbreviations: VDD, Vitamin D deficiency; Ref., reference haplotype

Vitamin D	Gene and SNP	Source	Vitamin										Ancestry	Outcome				Risk of bias	Notes
			Vitamin D					Vit. B12	Vit. B9 (Folate)	Vit. B6 (PLP)	Hcy	Absolute Values		Effect size	Other	P-value	JBI assessment		
			Calcifediol (25(OH)D)	Ergocalciferol (25(OH)D2)	Ergocalciferol (25(OH)D2)	VDBP	VLD deficiency												
CYP2R1 rs10766197	Zhang et al., 2013	x											Asian (Chinese)	Mean [ng/mL] GG (WT): 19.48 GA: 18.17 AA: 17.87	GG (WT): 1 GA: 0.933 AA: 0.917	β = -0.1484 Odds for VDD, OR (95%CI) 1.215 (1.037, 1.424)	P = 0.004411 * P = 0.016	7/8	* Bonferroni corrected
	Ammar et al., 2023	x											Arab			Odds of non-response *, OR (95%CI) GG (WT): 1 GA: 5.31 (1.21, 35.7) AA: 6.92 (1.70, 28.31)	P = 0.011 P = 0.008	7/9	* non-response: serum 25(OH)D <30ng/mL after Vit. D supplementation
	Xu et al., 2015						x						Asian (Chinese) Uygur ethnic group			Odds for VDD, OR (95%CI) 6.533 (1.361, 31.357) Allele Freq. VDD GG: 0.39 GA: 0.48 AA: 0.13 Control GG: 0.69 GA: 0.12 AA: 0.19	P = 0.019	8/8	VDD: 25(OH)D <20ng/mL
	Nissen, Vogel et al., 2014 ^{1,†}	x											Caucasian	Geometric Mean (95% CI) [nmol/L] GG (WT): 74.3 (71.6, 77.1) GA: 72.9 (70.8, 75.1) AA: 66.9 (64.2, 69.8)	GG (WT): 1 GA: 0.981 AA: 0.900		P < 0.0001	6/8	
	Nissen et al., 2014 ^{1,†}	x											Caucasian	Geometric Mean (95% CI) [nmol/L] GG (WT): 73.0 (69.0, 77.3) GA: 73.2 (69.9, 76.6) AA: 66.2 (62.1, 70.5)	GG (WT): 1 GA: 1.003 AA: 0.907		P = 0.0081	7/8	
	Barry et al., 2014 [†]	x											Caucasian			Baseline Estimated diff. in serum level per variant allele: -3.83% 95%CI: -5.79, -1.83 After 1 yr D3 supplementation [‡] Estimated diff. in serum level per variant allele: -4.12% 95%CI: -7.40, -0.76 Only optimally adherent subjects: -4.21% 95%CI: -7.66, -0.63	P = 0.0002 (Wald test) Genotype * D3: P = 0.02 (Wald test) Optimally adherent: P = 0.02	7/8	
	Bu et al., 2010	x											Caucasian			Discovery cohort β = -6.45 Replication cohort β = -3.55 Pooled β = -4.53	Discovery P (Wald test) = 0.005 P* = 0.005 P** = NS Replication P (Wald test) = 0.022 P* = 0.024 P** = NS Pooled P (Wald test) = 4.04E-4 P* = 3E-4 P** = 0.002	7/8	* empirical P-value ** adjusted for multiple testing
	Slow et al., 2020	x											Caucasian			Baseline 25(OH)D [nmol/L] β (95% CI): -4.00 [-7.45, -0.54]	P = 0.03413	12/13	Each copy of the minor allele A for rs10766197 was associated with a 4.00 nmol/L lower 25(OH) D conc.
		Waterhouse et al., 2014 [†]	x											Caucasian			Coef. (95%CI) Model 2: -3.7 (-6.2, -1.1) Model 3: -3.5 (-6.0, -1.0)	P < 0.005 * P = 0.01	12/13

Vitamin D	Gene and SNP	Source	Vitamin										Ancestry	Outcome				Risk of bias	Notes	
			Vitamin D					Vit. B12	Vit. B9 (Folate)		Vit. B6 (PLP)	Hcy								
			Calc./refol 25(OH)D	Calc./refol 25(OH)D	L-25(OH)D2	Ergocalciferol (12)	VDBP		VLD deficiency	Red blood cell folate										Folate / Folic acid
													Absolute Values	Effect size	Other	P-value	JBI assessment			
	CYP2R1 rs1562902	Nissen et al., 2014 [†]	x										Caucasian	Geometric Mean (95% CI) [nmol/L] TT (WT): 67.5 (63.9, 71.4) TC: 73.3 (70.0, 76.6) CC: 73.4 (68.6, 78.5)	TT (WT): 1 TC: 1.086 CC: 1.087		P = 0.0353	7/8		
		Barry et al., 2014 [†]	x										Caucasian			Estimated diff. in serum level per variant allele: 3.30% 95%CI: 1.21, 5.42	P = 0.002	7/8		
		Bu et al., 2010	x										Caucasian			Discovery cohort β= 6.08 Discovery + Replication cohort β= 2.69	Discovery P (Wald test) = 0.011 P*= 0.011 P**= NS Pooled P (Wald test) = 0.030 P*= 0.031 P**= NS	7/8	* empirical P-value ** adjusted for multiple testing	

Footnotes
Effect directions refer to minor allele C (G on reverse DNA strand); reference group: TT (WT) (AA on reverse DNA strand)
β = variation in serum 25(OH)D per risk-allele.
[†] Statistical analyses in these studies were performed on log-transformed 25(OH)D values.
rs1562902 was also associated with 25(OH)D when occurring with rs10766197 (view Haplotype rs1562902 x rs10766197)

Vitamin D	rs1562902 x rs10766197	Barry et al., 2014 [†]	x										Caucasian			Estimated % diff. in serum level per genotype (95%CI) AA: Ref. AG: 3.89 (1.67, 6.15) GG: 4.29 (0.56, 8.15)	AG: P= 0.001 GG: P= 0.02	7/8	
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Footnotes
[†] Statistical analyses in this study were performed on log-transformed 25(OH)D values.

Vitamin D	CYP2R1 rs11023374	Fohner et al., 2016	x										Alaskan Native (Yup'ik)	Mixed-effects model linear regression 1 [ns 744] Mean ± SE (ng/mL) TT (WT) + CT: 31.3 ± 0.5 CC: 25.0 ± 2.2	TT + CT : 1 CC: 0.799	Mixed-effects model linear regression 2 [ns 526] TT (WT) + CT: Ref. CC: β (SE) = -3.8 (1.7) Heritability: 0.46 MLR [ns 526] TT (WT) + CT: Ref. CC: β (SE) = -4.5 (2.0)	Mixed-model 1: P = 0.0067 Mixed model 2: P = 2.3E-2 MLR: P= 1.5E-2	6/8	Specified outcome measure: 25(OH)D3
		Engelman et al., 2012	x										Caucasian	Association stratified by season [‡] [nmol/L] High exposure AA (WT): 66.4 AG: 60.2 GG: 59.4	AA (WT): 1 AG: 0.907 GG: 0.895	Additive genetic model β = -0.19 SNP * high exposure β = -0.29	P=0.005 P = 0.001	7/8	

Footnotes
Effect directions refer to minor allele C (G on reverse DNA strand); reference group: TT (WT) (AA on reverse DNA strand)
β = variation in serum 25(OH)D per risk-allele.
[†] Statistical analyses in these studies were performed on log-transformed 25(OH)D values.
[‡] association not significant for low sun exposure (winter)
Abbreviations: WT, wild type; MLR, Multiple linear regression

Vitamin D	CYP2R1 rs1993116	Robien et al., 2013 [†]	x										Asian (Chinese)	Geometric Mean (95% CI), [nmol/L] CC (WT): 64.6 (62.6, 66.7) CT: 67.8 (65.5, 70.2) TT: 68.5 (63.5, 73.9)	CC (WT): 1 CT: 1.050 TT: 1.060	Variance explained: 0.8%	P for trend = 0.04	7/8	
		Batal et al., 2014 [†]	x										African-American & Caucasian			African American: β = 0.03 European American: β = 0.04 Odds for VDD in European Americans OR (95%CI): 0.51 (0.35, 0.76)	P = 0.02 P = 0.0006 P = 0.0008	7/8	VDD: 25(OH)D <20 ng/mL (<50nmol/L)
		Li et al., 2014	x										Asian (Chinese)			β (SE): -1.789 (0.865)	P = 0.04 P = 0.30 *	8/8	* corrected for Bonferroni
		Ahn et al., 2010 [‡]	x										Caucasian	Mean [nmol/L] NHS-Polyps GG (WT): 62.5 GA: 68.8 AA: 75.0 NHS-CRC GG (WT): 65.5 GA: 68.8 AA: 73.8 HPFS GG (WT): 56.0 GA: 62.3 GG: 67.0	NHS-Polyps GA: 1.101 AA: 1.200 NHS-CRC GA: 1.050 AA: 1.127 HPFS GA: 1.113 GG: 1.196	NHS-Polyps β (SE): -0.39 (0.07) NHS-CRC β (SE): 0.29 (0.08) HPFS β (SE): 0.33 (0.06)	NHS-Polyps P= 6.2E-9 NHS-CRC P= 5.2E-4 HPFS P= 1.6E-8	6/8	rs1993116 was r ² =1 with rs2060793 in the HapMap CEU panel
		Slow et al., 2020	x										Caucasian			Increase per minor allele Baseline 25(OH)D [nmol/L] β (95% CI): 3.95 (0.49, 7.41) Baseline free 25(OH)D [pmol/L] β (95% CI): 2.00 (0.16, 3.84)	P= 0.02584 P = 0.03409	P= 0.02584 P = 0.03409	Associations did not remain significant after Bonferroni correction

Footnotes
Effect directions refer to minor allele T ; reference group: CC (wt)
β = variation in serum 25(OH)D per risk-allele
[†] Statistical analyses in these studies were performed on log-transformed 25(OH)D values.
[‡] Ahn et al (2020) analyzed 3 case-control studies for associations between SNPs and 25(OH)D, the cohorts listed here found significant results. Subjects include cases and controls.
A trend toward association with log-25(OH)D levels was observed in a Chinese cohorts too, however associations were not significant (P = 0.08) (Lu et al., 2011)
Abbreviations: NHS-Polyps, NHS colon polyp study; NHS-CRC, NHS colorectal cancer study; HPFS, study of prostatecancer in the Health Professionals Follow-up Study

Vitamin D	Gene and SNP	Source	Vitamin										Ancestry	Outcome				Risk of bias	Notes
			Vitamin D					Vit. B12	Vit. B9 (Folate)	Vit. B6 (PLP)	Hcy	Absolute Values		Effect size	Other	P-value			
			Calcitriol (25(OH)D)	Calcitriol (1,25(OH)2D)	Ergocalciferol (D2)	VDBP	Vit.D deficiency		Red blood cell / folic acid	Folate / Folic acid	Serum / Plasma Folate								
																JBI assessment			
	CYP2R1 rs7116978	Tomei et al., 2020	x										Arab			Genotype frequency by Vit.D status Deficient: 0% CC, 80% CT, 20% TT Insuff.: 13% CC, 80% CT, 7% TT Sufficient: 30% CC, 45% CT, 25% TT *CC genotype showed higher response to Vit. D supplementation than CT or TT (no data)*	P = 0.0163	3/9	VDD: 25(OH)D < 20ng/mL (50nmol/L) Insufficiency: 21 < 29 ng/mL Sufficiency: ≥ 30ng/mL
		Nissen et al., 2014 [†]	x										Caucasian	Geometric Mean (95% CI) [nmol/L] CC (Wt): 67.5 (64.2, 71.0) CT: 72.8 (69.5, 76.3) TT: 77.5 (71.8, 83.8)	TT (Wt): 1 TC: 1.079 CC: 1.148		P = 0.0093	7/8	

Footnotes
Effect directions refer to minor allele T; reference group: CC (wt)
[†] Statistical analyses in this study were performed on log-transformed 25(OH)D values.

Vitamin D	CYP2R1 rs10500804	Lee et al., 2021	x							Asian (Korean)	Mean ± SE [ng/mL] <u>Total</u> TT (Wt): 20.0 ± 0.22 GT: 18.9 ± 0.20 GG: 18.0 ± 0.33 <u>Summer/Fall</u> TT (Wt): 25.3 ± 0.31 GT: 23.7 ± 0.24 GG: 22.0 ± 0.38	<u>Total</u> TT (Wt): 1 TG: 0.945 GG: 0.900 <u>Summer/Fall</u> TT (Wt): 1 TG: 0.937 GG: 0.870	Associations in multivariate model β = - 1.0149 P = 3.02E-8 <u>SNP * Season</u> β = - 1.4964 P = 8.01E-5	<u>Total</u> P = 1.79E-7 <u>Summer/Fall</u> P = 6.56E-9	7/8	
		Elkum et al., 2014	x							Arab	Mean [ng/mL] TT (Wt): 14.4, TG: 14.3 GG: 12.0	TT (Wt): 1 TG: 0.993 GG: 0.933		P= 0.0379	6/8	
		Engelman et al., 2012	x								Caucasian	Association stratified by season ² [nmol/L] <u>High exposure</u> AA (Wt): 66.0 AC: 63.9 CC: 57.1	AA (Wt): 1 AC: 0.968 CC: 0.865	Additive genetic model β = - 0.19 SNP * high exposure β = - 0.25	P = 0.001 P = 0.002	7/8

Footnotes
Effect directions refer to minor allele G (C on reverse stand) ; reference group: TT (Wt) (AA on reverse strand)
[‡] association not significant for low sun exposure (winter)

Vitamin D	CYP2R1 rs731236	Tomei et al., 2020	x									Arab			Genotype frequency by Vit.D status Deficient: 0% GG, 20% AG, 80% AA Insuff.: 0% GG, 5% AG, 95% AA Sufficient: 4% GG, 44% AG, 54% AA *GG genotype showed higher response to Vit. D supplementation than GA or AA (no data)*	P = 0.0336	3/9	VDD: 25(OH)D < 20ng/mL (50nmol/L) Insufficiency: 21 < 29 ng/mL Sufficiency: ≥ 30ng/mL
		Nissen et al., 2014 [†]	x									Caucasian	Geometric Mean (95% CI) [nmol/L] TT (Wt): 69.3 (67.0, 71.7) TC: 73.2 (71.1, 75.4) CC: 73.7 (70.1, 77.5)	TT (Wt): 1 TC: 1.056 CC: 1.063		P = 0.0346	7/8	

Footnotes
Effect directions refer to minor allele G (C on reverse strand) ; reference group: AA (Wt) (TT on reverse strand)
[†] Statistical analyses in this study were performed on log-transformed 25(OH)D values.
Data by Nissen et al (2014) refer to the entire cohort, which includes adults and children (not adults only).

Gene and SNP	Source	Vitamin										Ancestry	Outcome				Risk of bias	Notes	
		Vitamin D					Vit. B12	Vit. B9 (Folate)	Vit. B6 (PLP)	Hcy	Absolute Values		Effect size	Other	P-value	JBI assessment			
		Calc/fetol (25(OH)D)	Calc/fetol (1,25(OH)2D)	Ergocalciferol (D2)	VDBP	Vit D deficiency	Red blood cell folate	Folate / folic acid	Serum / Plasma Folate										
CYP2R1 rs10741657	Sallinen et al., 2021, [†]	x										Caucasian	Mean ± SD [nmol/L] GG (Wt): 65.9 ± 12.5 GA: 68.4 ± 13.1 AA: 69.9 ± 13.9	GG (Wt): 1 GA: 1.038 AA: 1.061	β = 2.2	P = 4.9E-12	6/8		
	Robien et al., 2013 [†]	x										Asian (Chinese)	Geometric Mean (95%CI) [nmol/L] GG (Wt): 64.9 (62.9, 67.0) GA: 67.6 (65.3, 70.0) AA: 70.0 (65.3, 75.3)	GG (Wt): 1 GA: 1.042 AA: 1.079	Variance explained: 1%	P for trend = 0.02	7/8		
	Nissen, Vogel et al., 2014 ^{1,†}	x										Caucasian	Geometric Mean (95%CI) [nmol/L] GG (Wt): 67.2 (65.0, 69.5) GA: 73.9 (71.8, 76.1) AA: 76.6 (73.0, 80.5)	GG (Wt): 1 GA: 1.1 AA: 1.140		P < 0.0001	6/8		
	Nissen et al., 2014 ^{1,†}	x										Caucasian	Geometric Mean (95%CI) [nmol/L] GG (Wt): 66.6 (63.3, 70.1) GA: 74.0 (70.7, 77.4) AA: 75.2 (69.9, 80.9)	GG (Wt): 1 GA: 1.111 AA: 1.129		P= 0.0067	7/8		
	Li et al., 2014	x										Asian (Chinese)			R(SE): -1.866 (0.863)	P = 0.04 P* = 0.30	8/8	* corrected for Bonferroni	
	Grant et al., 2022	x										Mixed		Adjusted Mean Difference (95%CI), [nmol/L] GG: Ref. (0.00) GA: 2.94 (1.38, 4.50) AA: 4.44 (2.38, 6.51)		both P < 0.001	7/8		
	Lafi et al., 2015	x										Mostly Caucasian (Mixed)	Mean ± SD [ng/mL] GG (Wt): 25.3 ± 18.1 GA: 31.8 ± 21.4 AA: 38.7 ± 24.9 GG + AG: 28.5 ± 20.0	GG (Wt): 1 GA: 1.257 AA: 1.530		GA: P= 0.013 AA: P= 0.026 AA+AG: P= 0.004	5/8	Associations for GG + AG NS	
						x									Odds for low Vit. D, OR (95%CI) GG (Wt):Ref. GA: 0.47 (0.26, 0.85) AA: 0.33 (0.12, 0.87) AA+AG: 0.44 (0.25–0.77)			VDD: 25(OH) < 20 ng/mL	
	Barry et al., 2014 [†]	x										Caucasian			Estimated diff. in serum level per variant allele: 4.91% 95%CI: 2.76, 7.10	P < 0.0001 (Wald test)	7/8		
	Bu et al., 2010	x										Caucasian			Discovery cohort β= 7.56 Replication cohort NS Pooled β= 4.12	Discovery cohort P (Wald test) = 0.001 P* = 0.002 P** = 0.051 Replication cohort NS Pooled P (Wald test) = 0.002 P* = 0.002 P** = 0.010	7/8	* empirical P-value ** adjusted for multiple testing	
CYP2R1 rs10741657	Wang et al., 2010 [†]	x										Caucasian	Mean ± SE [nmol/L] <u>Framingham heart study</u> Wt: 75.4 ± 0.87 Het.: 78.6 ± 0.76 Hom.: 81.6 ± 1.26 <u>1958 British Birth Cohort</u> Wt: 56.8 ± 0.34 Het.: 60.2 ± 0.32 Hom.: 61.1 ± 0.29	<u>Framingham Heart</u> Wt: 1 Het.: 1.042 Hom.: 1.082 <u>1958 British Birth</u> Wt: 1 Het.: 1.060 Hom.: 1.076		Candidate gene analysis <u>Discovery Cohort</u> P = 3.91E-8 <u>Replication Cohort</u> P = 2.09E-14 Overall P = 3.27E-20		8/8	All associations reached genome-wide significance (P < 5E-8)
						x									Odds for Vit. D insufficiency per risk allele OR (95%CI) <75nmol/L: 1.21 (1.45-1.29) <50nmol/L: 1.06 (1.00-1.13)	P = 9.4E-11 P = 0.06			
	Batal et al., 2014 [†]	x										African-American & Caucasian			African American: β= 0.04 European American: β= 0.04	P= 0.01 P= 0.003	7/8		
Elkum et al., 2014	x										Arabs	Mean [ng/mL] GG (Wt): 13.4 GA: 14.6 AA: 16.2	GG (Wt): 1 GA: 1.090 AA: 1.209		P= 0.0437	6/8			
Didriksen et al., 2013	x										Caucasian	Mean ± SD [nmol/L] Wt.: 55.6 ± 21.9 Het.: 56.2 ± 22.5 Hom.: 61.4 ± 24.4	Wt.: 1 Het.: 1.011 Hom.: 1.104	Increase (delta) in serum 25(OH)D after Vit.D supplementation Hom. baseline: 64.0 ± 26.6 Hom. 6mo: 176.8 ± 37.4 MD: 112.8± 33.0	Hom.: P < 0.05 Delta: P < 0.01	7/8	Difference for heterozygotes NS		
Slater et al., 2017						x					Caucasian			Odds to be VDD, OR (95%CI) Initial model: 3.67 (1.35, 9.99) Final model: 4.040 (1.429, 11.420)	P= 0.011 P= 0.008		7/8	Initial model: all potential confounders final model: significant confounders only	
Simon et al., 2011	x										Caucasian			"Each additional 'A' allele was associated with a 5.3 nmol/L increase in 25(OH)D level"		5/8			

Footnotes
Effect directions refer to minor allele A (T on reverse DNA strand); reference genotype: GG (wt) (CC on reverse DNA strand)
β = variation in serum 25(OH)D per risk-allele, Sallinen et al (2021) refer to changes in log-25(OH)D
[†]Statistical analyses in these studies were performed on log-transformed 25(OH)D values.
[‡]Both studies by Nissen et al. were conducted in the same cohort.
Abbreviations: NS, not significant; hom., homozygote; het., heterozygote; VDD, Vitamin D deficiency

	Gene and SNP	Source	Vitamin											Ancestry	Outcome				Risk of bias	Notes				
			Vitamin D					Vit. B12	Vit. B9 (Folate)		Vit. B6 (PLP)	Hcy												
			Calcifediol (25(OH)D)	Calcitriol (1,25(OH)2D)	Ergocalciferol level (D2)	VDBP	Vit D deficiency		Red blood cell folate	Folate / Folic acid								Serum / Plasma Folate						
																			Absolute Values	Effect size	Other	P-value	JBI assessment	
Vitamin D	CYP2R1 rs12794714	Robien et al., 2013 [†]	x											Asian (Chinese)	Geometric Mean (95%CI) [nmol/L] GG (Wt): 69.2 (66.8, 71.7) GA: 66.0 (64.0, 68.2) AA: 58.6 (54.9, 62.5)	GG (Wt): 1 GA: 0.954 AA: 0.847	Variance explained: 3.1%	P for trend < 0.001	7/8					
		Barry et al., 2014 [†]	x											Caucasian			Baseline Estimated diff. in serum level per variant allele: -4.74 95%CI: -6.68, -2.75 After 1 yr D3 supplementation [‡] Analysis restricted to optimally adherent subjects Estimated diff. in serum level per variant allele: -3.69% 95%CI: -7.18, -0.07	P < 0.0001 (Wald test) P = 0.05	7/8					
		Bu et al., 2010	x											Caucasian	Mean ± SE [nmol/L] (ANOVA) Discovery cohort GG: 77.82 ± 21.96 GA: 70.65 ± 21.70 AA: 62.03 ± 17.82 Replication cohort GG: 75.09 ± 23.67 GA: 74.94 ± 19.90 AA: 66.13 ± 16.18 Pooled GG: 76.62 ± 23.32 GA: 74.44 ± 20.83 AA: 65.20 ± 16.96	Discovery cohort GG: 1 GA: 0.908 AA: 0.797 Replication cohort GG: 1 GA: 0.998 AA: 0.881 Pooled GG: 1 GA: 0.972 AA: 0.851	Discovery cohort β = -7.63 Replication cohort β = -3.61 Pooled β = -5.03	Discovery cohort P ANOVA = 0.001 P (Wald test) = 0.001 P* = 0.001 P** = 0.022 Replication cohort P ANOVA = 0.017 P (Wald test) = 0.018 P* = 0.016 P** = NS Pooled P ANOVA = 0.0002 P (Wald test) = 5.74E-5 P* = 1E-4 P** = 1E-4	7/8	* empirical P-value ** adjusted for multiple testing				
	CYP2R1 rs12794714	Batal et al., 2014 [†]	x											African-American & Caucasian			African American: β = -0.04 European American: β = -0.04	P = 0.01 P = 0.005	7/8	VDD: 25(OH)D <20 ng/mL (<50nmol/L)				
							x										Odds for VDD in AA OR (95%CI): 1.72 (1.20, 2.47)	P = 0.003						
		Elkum et al., 2014	x											Arab	Mean [ng/mL] GG (Wt): 14.4 GA: 14.3 AA: 12.0	GG (Wt): 1 GA: 0.993 AA: 0.833		P = 0.0402	6/8					
		Ammar et al., 2023	x											Arab			Odds of non-response *, OR (95%CI) GG (Wt): 1 GA: 3.45 (1.49, 7.99) AA: 5.09 (1.70, 24.08)	P = 0.014 P = 0.004	7/9	* non-response: serum 25(OH)D <30ng/mL after Vit. D supplementation				
		Slow et al., 2020	x											Caucasian			Baseline 25(OH)D [nmol/L] β (95% CI): -4.62 (-8.15, -1.08) Baseline free 25(OH)D [pmol/L] β (95% CI): -2.71 (-4.61, -0.81)	P = 0.01095 P = 0.00545	12/13					
	Kwak et al., 2018	x												Asian (Korean)			*found negative associations btw serum 25(OH)D level and the effect allele A [‡]	P = 0.020	7/8					
	Hansen et al., 2015	x												African- American			Estimated change in serum 25(OH)D per A allele β ± SE = 1.30 ± 0.56	P = 0.02	7/8	This SNP was imputed in this cohort				

Footnotes
Effect directions refer to minor allele A; reference group: GG (wt)
β = variation in serum 25(OH)D per risk allele
[†] Statistical analyses in these studies were performed on log-transformed 25(OH)D values.
[‡] shows that the SNP negatively impacts the efficacy of Vit. D3 treatment to increase year 1 [25(OH)D]

Vitamin D	CYP2R1 rs7936142 x rs12794714 x rs2060793 x rs16930609	Hansen et al., 2015	x										African- American	AAGA β = 0.0899 Frequency = 0.1332	P = 0.1123	7/8		
Vitamin D	CYP24A1 rs6013897	Wang et al., 2010 [†]	x										Caucasian		Candidate gene analysis Discovery Cohort P = 7.2 E-4 (NS) Replication Cohort P = 8.4E-8 Overall P = 6.0E-10 *	8/8	* Genome-wide significant	
		Ammar et al., 2023	x										Arab	Mean [median min, max] [ng/mL] TT (WT): 20.6 (6.3, 24.9) TG: 12.4 (0, 24.4) GG: 13.5 (3.9, 23.3)	TT: 1 TG: 0.602 GG: 0.655	P < 0.001	7/9	
		Barry et al., 2014 [†]	x										Caucasian	After 1 yr D3 supplementation [‡] Estimated diff. in serum level per variant allele: -4.24 % 95%CI: -8.22, -0.09 Only optimally adherent subjects: -4.86 % 95%CI: -9.10, -0.42	Genotype * D3 P = 0.04 (Wald test) Optimally adherent P = 0.03	7/8		

Footnotes
Effect directions refer to minor allele C ; reference group: GG (Wt)
β = variation in serum 25(OH)D per risk-allele
[†] Statistical analyses in these studies were performed on log-transformed 25(OH)D values.
[‡] shows that the SNP negatively impacts the efficacy of Vit. D3 treatment to increase year 1 [25(OH)D]

Vitamin D	CYP24A1 rs2762939	Szili et al., 2018	x										Caucasian	Mean total-25(OH)D [ng/mL] GG(Wt): 15.5 GC: 14.0 CC: 11.3	GG (Wt): 1 GC: 0.903 CC: 0.729		GG (Wt) vs. CC P = 0.018 *	7/8	* remained signif. after FDR correction, became non-significant after adjusting for BMI, age, and sex.
		Barry et al., 2014 [†]	x										Caucasian			Estimated diff. in serum level per variant allele: 2.75% 95%CI: 0.32, 5.23	P = 0.03 (Wald test)	7/8	

Footnotes
Effect directions refer to minor allele C ; reference group: GG (Wt)
[†] Statistical analyses in these studies were performed on log-transformed 25(OH)D values.
rs2762939 was also associated with 25(OH)D when occurring with rs4809958 and rs2244719 (view Haplotype rs2762939 x rs4809958 x rs2244719)

Vitamin D	rs2762939 x rs4809958 [‡] x rs2244719	Barry et al., 2014 [†]	x										Caucasian			Ref.: GTC Estimated % diff. in baseline 25(OH)D level for GGT: -3.11% 95%CI: 0.50, 5.79	P = 0.02	7/8	
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Footnotes
[‡] Associations of rs4809958 were not replicated in this review
[†] Statistical analyses in these studies were performed on log-transformed 25(OH)D values.
Abbreviations: Ref., reference haplotype

Vitamin D	Gene and SNP	Source	Vitamin										Ancestry	Outcome				Risk of bias	Notes	
			Vitamin D					Vit. B12	Vit. B9 (Folate)	Vit. B6 (PLP)	Hcy	Absolute Values		Effect size	Other	P-value				
			Calc (refed) (25(OH)D)	Calc (unrefed) (1,25(OH)2D)	Ergocalciferol (D2)	VitD	Vit.D deficiency	Red blood cell folate	Folate / Folic acid	Serum / Plasma Folate	PLP						Hcy			
	CYP24A1 rs2209314	Szili et al., 2018	x											Caucasian	Mean total-25(OH)D [ng/mL] TT (Wt): 15.6 TC: 13.6 CC: 13.1 Mean free-25(OH)D [pmol/L] TT (Wt): 9.9 TC: 8.9 CC: 5.8 Mean Bioavailable-25(OH)D [nmol/mL] TT (Wt): 4.1 TC: 3.6 CC: 3.1 Mean, [mg/L] TT (Wt): 306.2 TC: 309.8 CC: 360.9	Total TT (Wt): 1 TC: 0.872 CC: 0.840 Free TT (Wt): 1 TC: 0.899 CC: 0.586 Bioavailable TT (Wt): 1 TC: 0.878 CC: 0.756	Total β (SE): -5.787 (2.844) P = 0.005 Explained variance: 2.7%	Total: P = 0.017 * Free: P = 0.012 Bioavailable: P = 0.008	7/8	* remained signif. after FDR correction but non-significant after adjusting for BMI, age, and sex. P-values by Szili et al. (2018) refer to the differences between Wt and CC genotype
		Barry et al., 2014 [†]	x				x							Caucasian	TT (Wt): 306.2 TC: 309.8 CC: 360.9	TT (Wt): 1 TC: 1.012 CC: 1.179	Estimated diff. In serum level per variant allele: 2.67% 95%CI: 0.19, 5.21	P = 0.03 (Wald test)	7/8	

	Gene and SNP	Source	Vitamin											Ancestry	Outcome				Risk of bias	Notes
			Vitamin D						Vit. B12	Vit. B9 (Folate)	Vit. B6 (PLP)	Hcy	Absolute Values		Effect size	Other	P-value			
			Calcifediol (25(OH)D)	Calcitriol 1,25(OH)2D	Ergocalciferol (D2)	VDPP	Vitamin D deficiency	Red blood cell folate	Folate / Folic acid	Serum / plasma folate	Hcy									
Vitamin D	DAB1 rs6680429 ¹	Engelman et al., 2010		x										Hispanic	Mean ± SD [pmol/L] GG (Wt): 44.9 ± 15.3 GA: 45.8 ± 14.4 AA: 50.0 ± 18.3	GG (Wt):1 GA: 1.020 AA: 1.114	Subsample P = 6.6E-9 Total sample P = 1.4E-3	7/8		
	N/A rs2806508	Engelman et al., 2010	x											Hispanic	Mean ± SD [nmol/L] CC (Wt): 15.0 ± 6.5 CT: 16.4 ± 7.3 TT: 18.6 ± 8.0	CC (Wt): 1 CT: 1.093 TT: 1.240	Subsample P = 1.6E-6 Total sample P = 4.1E-5	7/8		
	N/A rs10141935	Engelman et al., 2010	x											Hispanic	Mean ± SD [nmol/L] AA (Wt): 16.1 ± 7.6 AG: 16.5 ± 7.0 GG: 18.2 ± 7.7	AA (Wt): 1 AG: 1.025 GG: 1.130	Subsample P = 3.1E-5 Total sample P = 3.9E-4	7/8		
	N/A rs4778359	Engelman et al., 2010	x											Hispanic	Mean ± SD [nmol/L] TT (Wt): 15.6 ± 6.9 TG: 18.0 ± 7.8 GG: 19.1 ± 7.7	TT (Wt): 1 TG: 1.154 GG: 1.224	Subsample P = 4.0E-6 Total sample P = 5.5E-5	7/8		
	A2BP1 rs1507023	Engelman et al., 2010	x											Hispanic	Mean ± SD [nmol/L] TT (Wt): 17.0 ± 7.1 TC: 16.3 ± 7.6 CC: 15.8 ± 7.1	TT (Wt): 1 TC: 0.959 CC: 0.929	Subsample P = 7.5E-6 Total sample P = 5.1E-4	7/8		
	GPR114 rs937918	Engelman et al., 2010	x											Hispanic	Mean ± SD [nmol/L] CC (Wt): 17.0 ± 7.2 CT: 16.8 ± 7.2 TT: 15.4 ± 7.5	CC (Wt): 1 CT: 0.988 TT: 0.906	Subsample P = 3.3E-5 Total sample P = 8.2E-3	7/8		
	N/A rs1348864	Engelman et al., 2010		x										Hispanic	Mean ± SD [pmol/L] GG(Wt): 45.0 ± 14.7 GT: 45.8 ± 15.3 TT: 48.5 ± 17.9	GG (Wt):1 GT: 1.018 TT: 1.078	Subsample P = 1.8E-5 Total sample P = 1.5E-5	7/8		
	N/A rs4559029	Engelman et al., 2010		x										Hispanic	Mean ± SD [pmol/L] AA (Wt): 48.8 ± 16.0 AG: 45.2 ± 15.0 GG: 42.2 ± 15.3	AA (Wt): 1 AG: 0.926 GG: 0.865	Subsample P = 1.5E-5 Total sample P = 1.2E-4	7/8		
	N/A rs12667374	Engelman et al., 2010		x										Hispanic	Mean ± SD, [pmol/L] GG (Wt): 45.5 ± 15.2 GA: 55.4 ± 19.8 AA: 55.3 ± 30.6	GG(Wt):1 GA: 1.218 AA: 1.215	Subsample P = 2.4E-5 Total sample P = 1.8E-3	7/8		
	MLL3 rs7781309	Engelman et al., 2010		x										Hispanic	Mean ± SD [pmol/L] TT (Wt): 45.2 ± 15.0 TC: 46.6 ± 16.1 CC: 53.8 ± 17.9	TT (Wt): 1 TC: 1.031 CC: 1.190	Subsample P = 7.9E-6 Total sample P = 3.1E-3	7/8		
	N/A rs10505337	Engelman et al., 2010		x										Hispanic	Mean ± SD [pmol/L] TT (Wt): 44.7 ± 14.7 TC: 46.3 ± 16.2 CC: 48.5 ± 15.3	TT (Wt): 1 TC: 1.036 CC: 1.085	Subsample P = 2.0E-5 Total sample P = 2.7E-3	7/8		
	N/A rs2486443	Engelman et al., 2010		x										Hispanic	Mean ± SD [pmol/L] GG (Wt): 45.7 ± 15.3 GA: 50.6 ± 18.2 AA: N/A	GG (Wt):1 GA: 1.107	Subsample P = 2.4E-5 Total sample P = 3.5E-4	7/8		
	N/A rs2154175	Engelman et al., 2010		x										Hispanic	Mean ± SD [pmol/L] GG (Wt): 44.0 ± 14.0 GT: 48.0 ± 16.3 TT: 52.7 ± 22.0	GG (Wt):1 GT: 1.091 TT: 1.198	Subsample P = 1.5E-5 Total sample P = 9.9E-4	7/8		

Footnotes
Effect directions refer to minor alleles; reference group: Wt
Absolute values apply to the total sample
These SNPs all were all significantly associated with Vit.D conc. In the study's GWA subsample (P < 1E-4, n= 229) and the entire cohort (P < 1E-2, n= 1190).
¹ rs9970802 and rs10889028 were in high LD with rs6680429 and were the only SNPs to meet Bonferroni corrected P-value cut off (P < 1.62E-7) in the GWA analysis.
Abbreviations: N/A, not applicable is indicated for a Gene if the SNP is intragenic; LD, linkage disequilibrium

Vitamin D	C10orf88 rs6599638	Ahn et al., 2010 ¹	x											Caucasian	Mean [nmol/L]	Mean [nmol/L]			6/8	
															ATBC AA (WT): 41.8 AG: 39.6 GG: 39.5 PLCQ AA (WT): 60.3 AG: 57.8 GG: 57.6 NHS-CGEMS AA (WT): 83.3 AG: 83.0 GG: 77.5	ATBC AA (WT): 1 AG: 0.947 GG: 0.945 PLCQ AA (WT): 1 AG: 0.959 GG: 0.955 NHS-CGEMS AA (WT): 1 AG: 0.996 GG: 0.930	ATBC P= 5.0E-4 PLCQ P= 2.3E-2 NHS-CGEMS P= 2.2E-3			

Footnotes
Effect directions refer to minor allele G ; reference group: AA (wt)
¹ Ahn et al (2020) analysed 5 GWAS and 3 case-control studies for associations between SNPs and 25(OH)D, the cohorts listed here include the GWAS that found significant results. Subjects include cases and controls.
Abbreviations: ATBC, Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study; PLCQ, Prostate, Lung, Colorectal, Ovarian Cancer Screening Trial; NHS-CGEMS, case-control studies of breast cancer (CGEMS) nested within the Nurses' Health Study (NHS)

Vitamin D	Gene and SNP	Source	Vitamin										Ancestry	Outcome				Risk of bias	Notes
			Vitamin D					Vit. B12	Vit. B9 (Folate)	Vit. B6 (PLP)	Hcy								
			Calcifediol (25(OH)D)	Calcitriol (1,25(OH)2D)	Ergocalciferol (D2)	VDPP	Vit.D deficiency		Red blood cell count	Folate / Folic acid	Serum / Plasma Folate								
	NADSYN1/DHCR7 rs3829251	Ahn et al., 2010 ^{1,2}	x									Caucasian	ATBC GG (Wt): 41.4 GA: 38.8 AA: 39.4 PLCO GG (Wt): 59.3 GA: 56.2 AA: 53.0 NHS-CGEMS GG (Wt): 83.3 GA: 77.8 AA: 81.3	ATBC GG (Wt): 1 GA: 0.944 AA: 0.969 PLCO GG (Wt): 1 GA: 0.948 AA: 0.894 NHS-CGEMS GG (Wt): 1 GA: 0.934 AA: 0.976	ATBC R(SE): -0.14 (0.06) PLCO R(SE): -0.22 (0.06) NHS-CGEMS R(SE): -0.28 (0.11)	ATBC P= 2.0E-2 PLCO P= 3.5E-4 NHS-CGEMS P= 9.2E-3	6/8		
		Lu et al., 2011 [†]	x									Asian (Chinese)			GLR Beijing: β (SE)= -0.066 (0.02) Shanghai: β (SE)= -0.029 (0.01) Conditional analysis Beijing: β (SE)= -0.080 (0.04)	P= 3.1E-5 P= 0.0434 Conditional analysis P= 0.0526		8/8	GLR Analyses performed under additive model with adjusting for covariates. Conditional analyses: incl. all variants, which were in the same locus, in one multiple regression model.
		Slow et al., 2020	x									Caucasian			Baseline 25(OH)D [nmol/L] β (95% CI): -7.30 (-12.35, -2.24) Baseline free 25(OH)D [pmol/L] β (95% CI): -3.76 (-6.46, -1.07) ¹	P= 0.005 P= 0.00658		12/13	¹ association remained significant after 2 mo of Vit. D3 supplementation

Footnotes
 Effect directions refer to minor allele A ; reference group: GG (wt)
 β = variation in serum 25(OH)D per risk allele. Lu et al.(2011) refer to changes in log-25(OH)D
¹ Statistical analyses in these studies were performed on log-transformed 25(OH)D values.
² Ahn et al (2020) analyzed 5 GWAS and 3 case-control studies for associations between SNPs and 25(OH)D, the cohorts listed here include the GWAS that found significant results. Subjects include cases and controls.
³ rs11234027 was r2=1 with NADSYN1 SNP rs3829251 in the HapMap CEU panel and significantly associated with 25(OH)D in one of the replication cohorts in Ahn et al., 2010 (cohort: HPFS)
 Abbreviations: ATBC, Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study; PLCO, Prostate, Lung, Colorectal, Ovarian Cancer Screening Trial; NHS-CGEMS, case-control studies of breast cancer (CGEMS) nested within the Nurses' Health Study (NHS)

Vitamin D	NADSYN1/DHCR7 rs12785878	Xu et al., 2015								Asian (Chinese) Kazak ethnic group				Odds for VDD OR(95%CI): 2.442 (1.224, 4.873) Allele Freq. VDD GG: 0.23 GT: 0.55 TT: 0.22 Control GG: 0.39 GT: 0.43 TT: 0.18	P = 0.011	8/8	VDD: 25(OH)D < 20ng/mL
		Wang et al., 2010 ^{1, 2}	x							Caucasian	Mean ± SE [nmol/L] 1958 British Birth Cohort Wt: 59.6 ± 0.31 het.: 56.3 ± 0.30 hom.: 55.7 ± 0.32	Wt: 1 het.: 0.945 Hom.: 0.935	Candidate gene analysis Discovery Cohort P = 1.27E-12 Replication Cohort P = 2.39E-16 Overall P = 2.12-27	8/8			
		Grant et al., 2022	x							Mixed		Adjusted Mean Difference (95%CI), [nmol/L] GG: Ref. (0.00) GT: 4.22 (1.74, 6.70) TT: 8.06 (5.42, 10.69)		Both P < 0.001	7/8		
		Slow et al., 2020	x							Caucasian			Baseline 25(OH)D [nmol/L] β (95% CI): -5.42 (-9.24, -1.59) Baseline free 25(OH)D [pmol/L] β (95% CI): -3.50 (-5.52, -1.47) ² SNP * Vit.D supplementation on free 25(OH)D [pmol/L] β (95% CI): -8.86 (-13.95, -3.76)	P= 0.00591 P= 0.00080 ³ P= 0.00071 ³	12/13	² association remained significant after 2 mo of Vit. D3 supplementation ³ remained signif. After Bonferroni correction	
		Kwak et al., 2018	x							Asian (Korean)			"found negative associations btw serum 25(OH)D level and the effect allele T"	P < 0.001	7/8		

Footnotes
 Effect directions refer to minor allele T; reference group: GG (wt)
 β = variation in serum 25(OH)D per risk allele
¹ Statistical analyses in these studies were performed on log-transformed 25(OH)D values.
² rs7944926 was a perfect proxy in this cohort (r2=1.0) and results can be found in their original paper

Table S11: Antioxidants parameter study

	Gene and SNP	Source	Antioxidant						Ancestry	Outcome				Notes
			Selenium	Selenoprotein P	Alpha-carotene	Beta-carotene	Alpha-tocopherol			Absolute values and Mean Difference	Effect size	Other	P-value	
Antioxidants	BCO1 rs6564851	Yabuta et al., 2016				x		Asian (Japanese)	Mean $\pm$ SD [μ g/dL] GG: 63.9 $\pm$ 52.6 GT+TT: 31.2 $\pm$ 23.4 MD $\pm$ SD: 32.7 $\pm$ 57.57	GG: 1 GT + TT: 0.488 Cohen's d = 0.568			0.0032	
		Ferruci et al., 2009				x		Caucasian		Effect (95%CI) InCHIANTI: 0.160 (0.112, 0.208) WHAS: 0.199 (0.116, 0.282) ATBC: 0.13 (0.092, 0.171) Meta-analysis: 0.149 (0.120, 0.177)	Standard error (SE) 0.024 0.042 0.020 0.015	9.7E-11 2.6E-6 1.1E-10 1.6E-24		Paper states that "Participants with a G allele had an average beta-carotene level 0.26 (0.18, 0.34) standard deviations higher than participants with a T allele."
					x					Effect (95%CI) InCHIANTI: 0.089 (0.035, 0.143) WHAS: 0.091 (0.003, 0.185) Meta-analysis: 0.089 (0.043, 0.136)	Standard error (SE) 0.027 0.048 0.024	0.001 0.057 0.0001		

Footnotes

Minor allele frequencies vary depending on ancestry.

Effect directions for Yabuta et al (2016) refer to minor allele T; reference genotype: GG (wt) while effect directions for Ferruci et al (2009) refer to minor allele G; reference genotype: TT (wt)

Effect sizes by Ferruci et al. (2009) were calculated with natural log-transformed concentrations.

Calculations to obtain Cohen's d are presented in the Calculations sheet

^a based on ATBC cohort

Antioxidants	BCO1 rs6420424	Ferruci et al., 2009				x		Caucasian	Effect (95%CI) InCHIANTI: 0.152 (0.103, 0.201) WHAS: 0.165 (0.082, 0.248) Meta-analysis: 0.155 (0.11, 0.198)	Standard error (SE) 0.025 0.042 0.022	1.9E-9 1.0E-4 6.5E-13		
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Footnotes

Effect directions refer to minor allele A; reference genotype: GG (wt)

Effect sizes were calculated with natural log-transformed concentrations.

rs6420424 failed genotyping in the ATBC study, therefore no values are presented for this cohort

Antioxidants	BCO1 rs8044334	Ferruci et al., 2009				x		Caucasian	Effect (95%CI) InCHIANTI: 0.161 (0.106, 0.216) WHAS: 0.169 (0.084, 0.255) ATBC: 0.07 (0.034, 0.114) Meta-analysis: 0.109 (0.079, 0.139)	Standard error (SE) 0.028 0.044 0.02 0.015	1.3E-8 1.1E-4 0.0003 9.3E-13		
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Footnotes

Effect directions refer to minor allele G; reference genotype: TT (wt)

Effect sizes were calculated with natural log-transformed concentrations.

Antioxidants	BCO1 rs11645428	Ferruci et al., 2009				x		Caucasian	Effect (95%CI) InCHIANTI: -0.118 (-0.165, -0.072) WHAS: -0.196 (-0.279, -0.113) ATBC: -0.12 (-0.160, 0.075) Meta-analysis: -0.129 (-0.159, -0.099)	Standard error (SE) 0.024 0.042 0.022 0.015	8.3E-7 3.7E-6 7.4E-8 1.5E-17		
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Footnotes

Effect directions refer to minor allele A; reference genotype: GG (wt)

Effect sizes were calculated with natural log-transformed concentrations.

Antioxidants	APOA rs12272004	Ferruci et al., 2009					x	Caucasian	Effect (95%CI) InCHIANTI: 0.11 (0.066, 0.15) WHAS: 0.121 (0.048, 0.194) ATBC: 0.047 (0.017, 0.077) Meta-analysis: 0.072 (0.049, 0.095) ^a	Standard error (SE) 0.022 0.038 0.015 0.012	3.9E-7 0.001 0.0019 7.8E-10		
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Footnotes

Effect directions refer to minor allele A; reference genotype: CC (wt)

Effect sizes were calculated with natural log-transformed concentrations.

^a Unadjusted values; values adjusted for TAG: Effect (95% CI): 0.055 (0.02, 0.091), P=0.002

Antioxidants	SELENOP rs3877899		x				NR		"SNP affected plasma Se conc. post-supplementation and 2 wk after Se withdrawal."	0.012 * 0.001 **		* after 6 weeks of 100 μ g Sodium selenite/day n ** 2 weeks after supplementation withdrawal
		Méplan et al., 2007		x			Caucasian & Asian	Mean $\pm$ SE [μ g/mL plasma] Women GG (Wt) : 5 GA: 4.7 Men GG (Wt): 4.2 GA: 5.1 MD $\pm$ SD by gender [μ g/mL] GA: -0.4 $\pm$ 2.79 GG: 0.8 $\pm$ 2.42	Comparison by gender GA Cohen's d = -0.14 GG Cohen's d = 0.33	Gender effect P = 0.028	Absolute values are estimated based on Figure 3A in Méplan et al. (2007)	
		Combs et al., 2011	x				NR	Geometric Mean (-1SD, + 1SD) [ng/mL] GG (Wt): 3.62 (2.75, 4.76) GA: 3.24 (2.44, 4.31) AA: 3.49 (2.91, 4.18)	GG (Wt): 1 GA: 0.895 AA: 0.964	NR	No P-value reported, but the difference between GG and GA was stated as significant in the text	
		Kopp et al., 2018 ^a		x			Caucasian	At week 26 MD (95%CI) CC vs. CT+TT [ng/mL] -4.68 (8.49, -0.871)		0.018	Model incl. unsupplemented control subjects: P = 0.048	
			x					At week 26 CC vs. CT+TT [ng/mL] MD (95%CI): -5.76 (-12.5, 1.01)		0.093		
		Batai et al., 2021	x				Caucasian		β (SE): -0.011 (0.004) ^b	0.002		

Footnotes

Effect directions refer to minor allele T (A on reverse DNA strand); reference genotype: CC (wt) (GG on reverse strand)

Calculations to obtain Cohen's d are presented in the Calculations sheet

Values reported as geometric mean with a 1 SD interval were logarithmically transformed to approximated normal distribution.

^a Supplementation: ca. 50.3 μ g selenium/day for 26wks^b Association significant at baseline, but not after 1 year of supplementing 200 μ g of selenized yeast/ day

Abbreviations: MD, mean difference; NR, Not reported; SE, standard error

Antioxidants	GPX1 rs1050450	Combs et al., 2011	x					NR	Mean $\pm$ SD [ng/mL] CC (Wt): 145.9 $\pm$ 24.3 CT: 139.5 $\pm$ 23.1 TT: 135.7 $\pm$ 19	CC (Wt): 1 CT: 0.956 TT: 0.930 CT Cohen's d = -0.191 TT Cohen's d = -0.330	NR		No P-value reported, but the difference between TT and CT was stated as significant in the text
		Batai et al., 2021	x					Caucasian		β (SE): 0.010 (0.003) ^a	0.004		

Footnotes

Effect directions refer to minor allele A (T on reverse DNA strand); reference genotype: GG (wt) (CC on reverse strand)

Calculations to obtain Cohen's d are presented in the Calculations sheet

^a Association significant at baseline, but not after 1 year of supplementing 200 μ g of selenized yeast/ day

Abbreviations: MD, mean difference; NR, Not reported

Cohen's d calculations

<i>rs3877899: Plasma SePP conc. - Méplan, 2007</i>	Genotype 1: GA women	Genotype 2: GA men
Mean Value (µg/mL)	4.7	5.1
n	42	33
Standard Error (SE) Formula	SD/ sqrt(n)	
SE	0.3	0.35
Standard Deviation (SD) Formula	SE x sqrt(n)	
SD	1.94422221	2.010596926
Mean SD Formula	Sqrt(SD1^2 + SD2^2)	
Mean SD	2.796873254	
Effect size Formula	(Mean 1-Mean 2)/Mean SD	
Effect size	<u>-0.143016849</u>	

<i>rs3877899: Plasma SePP conc. - Méplan, 2007</i>	Genotype 1: GG women	Genotype 2: GG men
Mean Value(µg/mL)	5	4.2
n	42	33
Standard Error (SE) Formula	SD/ sqrt(n)	
SE	0.3	0.25
Standard Deviation (SD) Formula	Sqrt(SD1^2 + SD2^2)	
SD	1.94422221	1.436140662
Mean SD Formula	(SD 1+ SD 2) / 2	
Mean SD	2.417126393	
Effect size Formula	(Mean 1-Mean 2)/Mean SD	
Effect size	<u>0.330971522</u>	

<i>rs1050450: plasma Se - Combs et al., 2011</i>	Genotype 1: CC	Genotype 2: CT
Mean Value (ng/mL)	145.9	139.5
n	119	113
Standard Error (SE) Formula	SD/ sqrt(n)	
SE		
Standard Deviation (SD) Formula	SE x sqrt(n)	
SD	24.3	23.1
Mean SD Formula	Sqrt(SD1^2 + SD2^2)	
Mean SD	33.52760057	
Effect size Formula	(Mean 1-Mean 2)/Mean SD	
Effect size	<u>-0.190887504</u>	

<i>rs1050450: plasma Se - Combs et al., 2011</i>	Genotype 1: TT	Genotype 2: CC
Mean Value (ng/mL)	135.7	145.9
n	28	119
Standard Error (SE) Formula	SD/ sqrt(n)	
SE		
Standard Deviation (SD) Formula	SE x sqrt(n)	
SD	19	24.3
Mean SD Formula	Sqrt(SD1^2 + SD2^2)	
Mean SD	30.84623154	
Effect size Formula	(Mean 1-Mean 2)/Mean SD	
Effect size	<u>-0.330672484</u>	

<i>rs6564851: B-carotene - Yabuta et al., 2016</i>	GT+TT	GG
Mean Value (µg/dL)	31.2	63.9
n	-	-
Standard Error (SE) Formula	SD/ sqrt(n)	
SE		
Standard Deviation (SD) Formula	SE x sqrt(n)	
SD	23.4	52.6
Mean SD Formula	Sqrt(SD1^2 + SD2^2)	
Mean SD	57.57013114	
Effect size Formula	(Mean 1-Mean 2)/Mean SD	
Effect size	<u>-0.568002875</u>	