Supplementary Materials

Supplementary Table 1. Study PubMed search strategy	
#1.	(((((biomarkers[MeSH Terms]) OR (biomarkers)) OR (biomark*)) OR (marker*)) OR (biological marker*)) OR (biological signature*)
#2.	((((metabolite marker*) OR (metabolomics)) OR (metabolism)) OR (metabolome)) OR (metabolomics[MeSH Terms])
#3.	(((((((proteomic[MeSH Terms]) OR (genomics[MeSH Terms])) OR (transcriptomics)) OR (proteomics)) OR (genomics)) OR (transcriptome)) OR (proteome)) OR (genome)) OR (omics)
#4.	Molecular
#5.	((histology[MeSH Terms]) OR (histology)) OR (histological)
#6.	(physiological) OR (physiology)
#7.	(((((inflammation[MeSH Terms]) OR (inflam*)) OR (proinflam)) OR (metabo*)) OR (cytokin*)) OR (interleukin*)) OR (chemokin*)
#8.	**#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7**
#9.	osteoarthritis[MeSH Terms] OR osteoarthritides[MeSH Terms] OR osteoarthritis OR osteoa* OR osteoarthrosis OR polyosteoarthritis OR gonarthrosis OR OA OR KOA OR HOA
#10.	(((lower extremity[MeSH Terms]) OR (lower extremities[MeSH Terms])) OR (lower extremit*)) OR (lower extremity)
#11.	(knee) OR (knees)
#12.	(leg) or (legs)
#13.	(hip) OR (hips)
#14.	ankle*
#15.	(foot) OR (feet)
#16.	(ankle) OR (ankles)
#17.	(thigh) OR (shank)
#18.	(lower limb) OR (lower limbs)
#19.	**#10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18**
#20.	(muscle) OR (muscle*)
#21.	Strength
#22.	Function
#23.	Quality
#24.	((((activation) OR (co-activation)) OR (coactivation)) OR (cocontraction)) OR (co-contraction)
#25.	(((cross-sectional area) OR (anatomical cross-sectional area)) OR (CSA)) OR (ACSA)
#26.	(intramuscular fat) OR (intra-muscular fat)
#27.	Gait OR Timed-up-and-go OR timed up and go OR sit-to-stand OR sit to stand OR STS OR TUG OR stairs
#28.	**#20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27**
#29.	**#8 AND #9 AND #19 AND #28**

Supplementary Table 2: Study characteristics of papers, including lower limb muscle measure and a biological marker, not reporting correlations.

Author	Study Design	Total Sample Size	OA subgroup	OA location	OA subgroup sample size	Age (years)	Number of females (%)	K&L Grade	ACR	Lower limb muscle measure	Biological marker
Aguiar, Do Nascimento (1) *Brazil*	INV	22	Whole group	Knee	22	59 ± 6	18 (82)	3 (median)	No	Thigh circumference, training load, rang of motion	IL-6, TNF-α, sTNFR1, sTNFR2
Apparao, S (2) *Chennai, India*	OBS	20	Whole group	Knee	20	36 to 65	N/A	1 and 2	Yes	Handheld dynamometer, knee extensors and flexion strength	sCOMP
Armagan, Serin (3)	RCT	50	Group 1	Knee	30	63 ± 6	30 (100)	2 and 3	Yes	20 m walking time	CTX-II, IL-1β, MMP-3 levels, Nitric oxide
Turkey			Group 2	Knee	20	60 ± 7	20 (100)	2 and 3	Yes		
Arden, Cro (4)	RCT	474	Vitamin D	Knee	237	64 ± 8	144 (61)	0 to 4	No	Get-up and go, muscle strength, handgrip strength, Time to walk 10m	20(OH)D3
UK			Placebo	Knee	237	64 ± 8	145 (61)	0 to 4	No		
Azukizawa, Ito (5) *Japan*	INV	42	Whole group	Knee	42	59 ± 6	42 (100)	0/1 (n =32) 2/3 (n=10)	No	3-minute walk, 30 sec sit-to-stand, timed up and go	sCOMP, sPiiCP, uC2C, uCTX-II
Barker, Henriksen (6)	OBS	56	Vitamin D deficient	Knee	17	51 (3)	8 (47)	>2	No	Symptomatic acceleration knee extension, flexion, average power knee flexion, deceleration knee flexion, speak torque knee flexion, total work knee flexion,	25(OH)D, Ascorbic acid, Calcium, GM-CSF, Hs-CRP, IFN-γ, IL-1 β, IL-10, IL-12, IL-13, IL-2, IL-4, IL-5, IL-6, IL-7, IL-8, iPTH, Lutein, Rheumatoid factor, TNF-α, Uric acid, Zeaxanthin, α-Carotene, α-Tocopherol, β-Carotene,
USA			Vitamin D insufficient	Knee	21	48 (2)	12 (57)	>2	No		
			Vitamin D sufficient	Knee	18	47 (3)	11 (61)	>2	No		

Bischoff-Ferrari, Orav (7)	RCT	273	Whole group	Knee	273	70 ± 6	146 (54)	0 to 4	No	Gait speed 4 m, repeated sit-to-stand test	25(OH)D, iPTH
Switzerland			2000IU vitamin D	Knee	137	70 ± 7	69 (50)	0 to 4	No		
			800 IU vitamin D	Knee	136	71 ± 6	77 (57)	0 to 4	No		
Bolognesi, Belcaro (8)	INV	54	Standard management	Knee	26	53 ± 2	10 (39)	No	No	Pain free walking distance, total walking distance	CRP, ERS, Fibrinogen, Plasmatic reactive oxygen metabolites, sVCAM-1
Italy			Standard management and movardol	Knee	28	52 ± 4	10 (36)	No	No		
Chen, Wang (9)	OBS	18	Symptomatic	Knee	18	54 ± 5	18 (100)	2 and 3	No	Leg extension 1RM, 30% 1RM leg extension, 70% 1RM leg extension, leg curl 1RM, 30% 1RM leg curl, 70% 1RM leg curl	IGF-1, growth hormone, blood lactate, testosterone
China											
Chen, Han (10)	OBS	5318	OA	N/A	698	49 ± 9	419 (60)	No	No	Appendicular Lean Mass, handgrip strength	BUN, calcium, phosphorus, triglycerides, total cholesterol, creatinine, uric acid
USA											
Coppock, McNulty (11)	RCT	59	OA	N/A	39	69 ± 6	30 (77)	No	No	6-minute walk, 8ft up and go, 10 chair stands, SPPB, handgrip strength	Adiponectin, sCOMP, CRP, IL-6, TNF-α
USA											
Cornish and Peeler (12)	RCT	18	Creatine	Knee	9	58 ± 8	4 (44)	2 and 3	No	Knee extension at 0°, 45°, 90°, knee flexion at 0°, 45° and 90°	CRP, IL-1B, IL-6, s100 A8/A9, sCOMP, TNF-a
Canada			Placebo	Knee	9	57 ± 7	4 (44)	2 and 3	No		
Cuellar, Blizzard (13)	RCT	217	Vitamin D	knee	104	64 ± 7	49 (47)	No	No	External oblique (contracted) thickness	25(OH)D
Australia			Placebo	knee	113	63 ± 7	55 (49)	No	No		
de Almeida, Aily (14)	RCT	61	Circuit training	Knee	20	56 ± 5	15 (75)	2 (n=16) 3 (n=4)	Yes	30 sec chair tests, 40 m walk test, knee MVIC extension, knee	Fasting glucose, Glycemia, HDL, LDL, Total cholesterol, triglycerides
Brazil			Strength training	Knee	21	55 ± 7	16 (76)	2 (n=15) 3 (n=6)	Yes		

			Educational protocol	Knee	20	54 ± 8	16 (80)	2 (n=15) 3 (n=5)	Yes	MVIC flexion, lean mass, stair climb	
Edd, Favre (15) *Australia*	OBS	N/A	Pre-OA	Knee	52	44 ± 11	30 (58)	No	No	Speed	TNFα
Erhart-Hledik, Chehab (16) *USA*	Cohort	25	Whole group	Knee	25	59 ± 11	8 (32)	1.7 + 1.1 (0-4)	No	Walking speed, knee adduction moment (first peak), knee adduction moment (impulse)	sCOMP
Germanou, Chatzinikolaou (17) *Greece*	OBS	20	Patients	Knee	10	59 ± 6	10 (100)	>2	Yes	Knee extensor at 90°, 120°, 150°, knee flexibility, knee flexor at 90°, 120°, 150°, knee ROM	Catalase activity, Creatine kinase activity, CRP, Exercise lactate, GPX, GSH/GSSG, IL-6, LDH, Leukocytes, LPH, Oxidized GSH, Protein carbonyls, Reduced glutathione, Resting lactate, TBARS, TAC, Uric acid
Gibson, Morrison (18)	OBS	14	OA	Knee	7	67 ± 10	N/A	N/A	No	Joint extension, joint flexion, quad (fatiguability 100hz 30hz,10/50hz, 20/50hz), quad force loss, quad relaxation rates (sf50, sf95), quadricep MVC, total CSA, type i diameter and total fibres, type iia diameter and total fibres, type iib diameter and total fibres	Alkali soluble muscle protein, muscle protein, synthesis; muscle protein synthesis rate, RNA, DNA, muscle protein synthesis/RNA, RNA/DNA.
Scotland			Control		7	64 ± 10	N/A	N/A	No		
Gomes, Lacerda (19) *Brazil*	OBS	15	Whole group	Knee	15	67 ± 4	15 (100)	N/A	Yes	Physical function, 6MWT, $V0_{2max}$	IL-6, TNF, sTNFR1, sTNFR2

Gudbergsen, Boesen (20) *Denmark*	OBS	192	Whole group	Knee	192	63 ± 6	155 (81)	3	Yes	Quadriceps muscle strength, hamstrings muscle strength	CRP
Hagio and Aikawa (21) *Japan*	OBS	30	Whole Group	Hip	30	66 ± 9	25 (83)	N/A	No	TUG, 10m walk time	Creatine Kinase, CRP, myoglobin
Han, Zeng (22)	RCT	180	Study	Knee	90	51 ± 3	41 (46)	N/A	Yes	Muscle strength, ROM	IL-7, TNF-a
China			Control	Knee	90	51 ± 3	44 (46)	N/A	Yes		
Heidari, Javadian (23) *Iran*	OBS	67	Whole group	Knee	67	50 ± 7	58 (87)	4	Yes	Quadriceps muscle strength	25(OH)D
Jianda, Yuxing (24)	INV	75	MMA with pre-emptive analgesia group	Knee	38	68 ± 7	26 (72)	N/A	No	2MWT, 6MWT, ROM	CRP
China			MMA without pre-emptive analgesia group	Knee	37	69 ± 7	24 (65)	N/A	No		
Khan and Williams (25)	RCT	64	Etodolac	Knee	32	60 ± 8	19 (59)	N/A	No	Knee flexion, time to walk 15m	eosinophils, ESR, lymphocytes, Monocytes, neutrophils, platelet count, prothrombin time, red cell count, total white cell count
UK			Diclofenac	Knee	32	64 ± 8	22 (69)	N/A	No		
Kim, Lee (26)	RCT	41	Intervention	Knee	22	66 ± 6	14 (64)	1 to 3	Yes	Cadence, gait cycle time, gait velocity, knee varus/valgus ROM	COMP, CRP, IGF-1, IL-1β, IL-6, IL-8, TGF-β, TNF-α, YKL-40
Republic of Korea			Control	Knee	19	65 ± 9	17 (90)	1 to 3	Yes		
Kim, Hsu (27)	RCT	43	Intervention	Knee	20	67 ± 6	10 (50)	N/A	No	SPPB balance, SPPB chair stand, SPPB gait speed	CRP, IL-6, TNFa
USA			Standard care	Knee	23	67 ± 6	9 (39)	N/A	No		
Kuhi, Tamm (28) *Estonia*	OBS	86	Whole group	Knee	86	60 ± 5	43 (50)	2 to 4	No	30 m fast-paced walk test, 30 s chair STS, TUG	uC2C/Creatinine
Laslett, Quinn (29)	RCT	133	4Jointz	Knee	64	64 ± 10	35 (55)	0 to 2	Yes	Leg strength	IL-6, CTX-II
Australia			Placebo	Knee	69	66 ± 8	25 (36)	0 to 2	Yes		

Lee, Ro (30) *Korea*	OBS	4924	OA	Knee	821	68 ± 8	641 (78)	≥2	No	SMI, muscle mass	25(OH)D
Levinger, Begg (31) *Australia*	OBS	24	Whole Vitamin D insufficient Vitamin D sufficient	Knee Knee Knee	24 7 17	69 ± 6 70 ± 9 68 ± 5	12 (50) 4 (57.1) 8 (47)	N/A N/A N/A	Yes Yes Yes	Isokinetic knee extension 180°, isokinetic knee extension 90°, isometric knee extension, knee absorption power, knee negative work, lower limb muscle mass, muscle quality at isokinetic 180°, muscle quality at isokinetic 90°, muscle quality at isometric°	25(OH)D
Li, Wang (32)	INV	112	OA Control	Knee Knee	58 54	53 ± 12 52 ± 12	31 (54) 23 (43)	2 or 3 2 or 3	No No	Step length, gait speed, gait frequency	IL-1β, IL-6, IL-17,
Lim, Cicuttini (33)	RCT	304	Atorvastatin Placebo	Knee Knee	151 153	56 ± 7 56 ±8	92 (61) 77 (50)	0 to 2 0 to 2	Yes Yes	Quadricep muscle strength, vastus medialis CSA	Creatinine kinases, ALT, AST
Magrans-Courtney, Wilborn (34) *USA*	RCT	30	Glucosamine, chondroitin sulphate, methyl sulfonyl methane Placebo	Knee Knee	16 14	52 ± 10 57 ± 7	16 (100) 14 (100)	N/A N/A	No No	Bench press 1RM, circumference, fatigue index extension - 10 reps at 180°, 15 reps at 300°, 5 reps at 60°, fatigue index flexion - 10 reps at 180°, 15 reps at 300°, 5 reps at 60°, forward lunge knee function - contact time, distance, force impulse, impact index, peak torque extension - 10 reps at 180°, 15 reps at 300°, 5 reps at 60°, peak torque	ALT, AST, BUN, BUN/Creatinine Ratio, Cholesterol, creatine kinase, Cortisol, CRP, Creatinine, GGT, Glucose, Glucose/Insulin Ratio, HDL, $HOMA_{IR}$, IL-6, Insulin, LDL, Leptin, TNF-a, Triglycerides, Uric Acid

										flexion - 10 reps at 180°, 15 reps at 300°, 5 reps at 60°, ROM extension, ROM flexion, STS function - rising index, sway velocity, weight transfer, step up and over knee function - impact index, lift-up index, movement time, upper body endurance	
Manoy, Yuktanandana (35) *Thailand*	RCT	175	Whole group	Knee	175	65	158 (90)	No	Yes	Handgrip strength, knee extensor strength, timed-up and go, sit-to-stand, 6MWT	FBG, Insulin, HOMA-IR, total cholesterol, HDL, Triglycerides, LDL, 25(OH)D, calcium, phosphorus, PTH, hsCRP, IL-6, leptin, protein carbonyls
Marriott, Chopp-Hurley (36) *Canada*	RCT	17	Exercise No exercise	Knee Knee	10 7	65 ± 7 72 ± 11	10 (100) 7 (100)	1 to 4 1 to 4	Yes Yes	Power, strength	IL-6, CRP, TNFa
McAlindon, Lavalley (37) *USA*	RCT	146	Vitamin D Placebo	Knee Knee	73 73	62 ± 8 63 ± 9.3	49 (67) 40 (54)	2 to 4 2 to 4	Yes Yes	Chair stand, 20m walk test	25(OH)D
Messier, Loeser (38) *USA*	RCT	24	Exercise Exercise and diet	Knee Knee	11 13	69 ± 5 67 ± 4	7 (64) 10 (77)	N/A N/A	No No	6MWT, ambulation frequency, ambulation intensity, ankle maximum plantarflex velocity, ankle mean velocity, ankle ROM, cadence, knee maximum extension velocity, knee mean velocity, knee ROM, loading rate-least affected knee, loading	IL-l β

										rate-most affected knee, maximum braking, maximum propulsive, mean concentric extension, mean concentric flexion, stair climb, stance time, stride length, transfer frequency, transfer intensity, vertical propulsive peak, vertical impact peak, walking velocity	
Miller, Nicklas (39)	RCT	316	Healthy lifestyle	Knee	76	69 ± 6	51 (67)	N/A	No	Walking speed	Leptin
USA			Dietary weight loss	Knee	80	68 ± 6	57 (71)	N/A	No		
			Exercise	Knee	79	69 ± 7	60 (76)	N/A	No		
			Diet and exercise	Knee	74	69 ± 7	55 (74)	N/A	No		
Mundermann, King (40) *USA*	OBS	83	OA	Knee	42	61 ± 9	22 (52)	1 to 4	Yes	30-min walking exercise – distance, number of steps, walking speed, peak ankle dorsiflexion moment, eversion moment, peak external knee adduction moment, peak hip adduction moment, peak hip flexion moment, peak knee flexion moment, post-exercise rest - cadence, distance, number of steps	COMP
Nicklas, Mychaleckyj (41)	INV	214	Whole	Knee	214	69 ± 6	151 (70)	2.23 ± 0.82	No	Stair-climb time, walking distance	IL-6 174 G/C_CC, _CG, _GG, TNFa 238

USA											G/A_AG, _GG, TNFa 308 G/A_AA, AG, _GG, TNFR1 +36 A/G_AA, _AG, _GG, TNFR2 +1663 A/G_AA, _AG, _GG, TNFR2 +676 T/G_GG, _GT, _TT
Ngarmukos, Tanavalee (42)	OBS	94	2 PRP injections	Knee	51	67	47 (92)	1 to 4	Yes	Tug, 3m walking test, 5 x STS, ROM	IA-17A, Il-10, IL-13, IL-1B, IL-1RA, IL-4, IL-6, PDGF-AA, PDGF-BB, TGF-B1, TNFa, VEGF
Thailand			4 PRP injections	Knee	43	66	40 (93)	1 to 4	Yes		
Okoro, Stewart (43)	OBS	14	Males	Hip	8	65 ± 9	0 (0)	N/A	No	30 sec STS, 6MWT, leg lean mass, MVC quadriceps, TUG	CAPN2, CTSL2, CTSL2, FOS, IL-6, LPL, PPARG, PSMA7, TNFa,
UK			Females	Hip	6	61 ± 12	6 (100)	N/A	No		
Ostlind, Eek (44)	RCT	91	Whole group	Hip or knee	91	56 ± 6	74 (81)	N/A	No	Steps/day	CRP, ARGS, C2C, COMP
Sweden											
Park, Min (45)	RCT	81	Control	Knee	25	68 ± 4	25 (100)	1 or 2	No	Isokinetic torque 60º/s, skeletal muscle mass	IL-6, CRP, Resistin, TNFa
South Korea			Isometric exercise	Knee	25	67 ± 5	25 (100)	1 or 2	No		
			Isometric exercise and electro-myo-stimulation	Knee	25	66 ± 3	25 (100)	1 or 2	No		
Peker, Peker (46)	OBS	96	OA	Knee	48	54 ± 9	48 (100)	>2	No	Leg skeletal muscle mass index, leg muscle mass index	Neutrophil/lymphocytes, triglycerides, LDL, HDL, triglycerides/ HDL, monocytes/ lymphocytes
Turkey			Control	Knee	48	43 ± 9	48 (100)	>2	No		
Pérez-Piñero, Muñoz-Carrillo (47)	RCT	55	Experimental	Knee	29	51 ± 9	N/A	N/A	Yes	Muscle mass, TUG, knee flexor, extensor isokinetic 60º, 180º peak torque, relative	IL-1β, MMP-3, COMP
Spain			Control	Knee	26	50 ± 9	N/A	N/A	Yes		

										peak torque, total work, total work for 1 rep maximum, knee flexor, extensor isometric 90º peak torque, relative peak torque, total work, total work for 1 rep maximum, average power	
Perruccio, Zahid (48) *Canada*	OBS	6098	OA	Hip, knee, hands	3049	63	1701 (55.8)	N/A	No	TUG	CRP, HDL, triglycerides, total cholesterol, HbA1/c
Perry, Levinger (49) *Australia*	OBS	36	OA	Knee	19	70 ± 7	10 (53)	N/A	No	Voluntary maximal knee extensor torque - peak, voluntary maximal knee extensor torque	3Houabain binding site content, NKA α1, NKA α2 NKA α3, NKA β1, NKA β2, NKA β3
Petersen, Saxne (50)	RCT	36	Glucosamine	Knee	12	62 ± 3	7 (58)	2.5 ± 0.8	Yes	Knee extension 5RM, leg press 5RM	COMP, uCTX-II
Denmark			Ibuprofen	Knee	11	62 ± 5	7 (64)	2.3 ± 1	Yes		
			Placebo	Knee	12	63 ± 5	7 (58)	2.2 ± 1	Yes		
Pinsornsak, Kanokkangsadal (51)	RCT	66	Sahastara	Knee	31	60 ± 7	28 (90)	1 to 3	Yes	100m walk time test	BUN, ALP, ALT, AST, creatinine
Thailand			Diclofenac	Knee	30	58 ± 8	27 (90)	1 to 3	Yes		
Raut, Bichile (52)	RCT	93	Glucosamine sulphate (GS)	Knee	26	59 ± 7	21 (60)	N/A	Yes	50-feet walking	CTX II, ALP, Bilirubin, BUN, Creatinine, SGOT, SGPT, Haemoglobin, leucocytes count, Platelet count, TNFa-SRI, TNFa-SRII, Uric acid
India			AmrutBhallatak (ABFN02)	Knee	33	58 ± 9	30 (77)	N/A	Yes		
			ABFNO2 + GS	Knee	34	55 ± 8	27 (72)	N/A	Yes		
Roy, de Beer (53)	RCT	37	Placebo	Knee	19	63 ± 10	11 (58)	N/A	N/A	Ankle dorsiflexion strength, handgrip strength, knee	Creatine, phosphocreatine, total creatine, adenosine
Canada			Creatine	Knee	18	64 ± 10	9 (56)	N/A	N/A		

										extension strength, muscle fibre area, timed 30-ft walk, timed 4-step climb	triphosphate, creatinine
Samut, Dincer (54)	RCT	42	Isokinetic exercise	Knee	15	63 ± 8	14 (90)	2 to 3	Yes	30-sec STS, 6MWT, peak torque isokinetic	CRP, IL-6, TNF-a
Turkey			Aerobic exercise	Knee	14	58 ± 6	13 (90)	2 to 3	Yes	5 maximal reciprocal concentric extension contractions for each angular velocity of 180°/s to body weight, peak torque isokinetic 5 maximal reciprocal concentric extension contractions for each angular velocity of 60°/s to body weight, peak torque isokinetic 5 maximal reciprocal concentric flexion contractions for each angular velocity of 180°/s to body weight, peak torque isokinetic 5 maximal reciprocal concentric flexion contractions for each angular velocity of 60°/s to body weight	
			Control	Knee	13	61 ± 9	12 (90)	2 to 3	Yes		
Sanchez-Ramirez, van der Leeden (55) *Amsterdam*	OBS	186	Whole	Knee or hip	186	61 ± 7	127 (68)	>2	Yes	Knee muscle strength isokinetic - quadriceps - 60°, knee muscle strength isokinetic - hamstrings - 60°	CRP, ESR
Sarsan, Akkaya (56)	RCT	27	Mud packs	Knee	15	52 ± 5	N/A	2 to 3	Yes	6MWT	IGF-1, IL-6, TNFa
Turkey			Hot packs	Knee	12	54 ± 8	N/A	2 to 3	Yes		
Schumacher, Pullman-Mooar (57)	RCT	58	Whole	Knee	58	57 ± 11	14 (24)	2 to 3	Yes	Walking time	Creatinine, hsCRP, Urate

USA											
Shea, Loeser (58)	Cohort	1069	< phylloquinone <Vitamin D	Knee	257	75 ± 3	172 (67)	N/A	No	400m walk, 5-STS, chair stands time,	Triglycerides, Vitamin D, Vitamin K
USA			< phylloquinone > Vitamin D	Knee	459	75 ± 3	247 (54)	N/A	No	SPPB, usual 20m gait speed	
			> phylloquinone < Vitamin D	Knee	120	74 ± 3	87 (73)	N/A	No		
			> phylloquinone > Vitamin D	Knee	233	74 ± 3	134 (58)	N/A	No		
			< Vitamin K < Vitamin D	Knee	1351	61 ± 10	543 (40)	N/A	No		
			< Vitamin K > Vitamin D	Knee	236	61 ± 7	122 (52)	N/A	No		
			> Vitamin K < Vitamin D	Knee	2259	62 ± 9	1446 (64)	N/A	No		
			> Vitamin K > Vitamin D	Knee	629	61 ± 8	503 (80)	N/A	No		
Velangi, Mandalika (59)	RCT	100	Vitamin D3	Knee	25	30 to 65	0 (0)	1 to 2	No	6MWT	25(OH)D, CRP, ESR, s-COMP
India			Vitamin D3	Knee	25	30 to 65	25 (100)	1 to 2	No		
			Vitamin D3 and virgin coconut oil	Knee	25	30 to 65	0 (0)	1 to 2	No		
			Vitamin D3 and virgin coconut oil	Knee	25	30 to 65	25 (100)	1 to 2	No		
Wallis, Webster (60)	RCT	46	Walking	Knee	23	68 ± 8	9 (39)	3 to 4	No	30 sec chair test, 40 m walk test, steps per day	Fasting glucose, HDL, LDL, total cholesterol, triglycerides
Australia			Usual care	Knee	23	67 ± 7	11 (48)	3 to 4	No		
Wang, Yang (61)	RCT	99	Whole body vibration exercise + quadriceps resistance exercises	Knee	49	61 ± 10	36 (73.5)	2 or 3	Yes	6-minute walk distance, active knee extension and flexion, knee extension and flexion strength, timed up and go	COMP, CTX-II, Liquesce index
China			Quadriceps resistance exercises	Knee	50	62 ± 9	35 (70)	2 or 3	Yes		

Wasser, Hendershot (62) *USA*	OBS	38	OA	Knee	12	37 ± 7	0 (0)	>1	No	Cadence, continuous relative phase (frontal/sagittal/transverse), continuous relative phase var (frontal/sagittal/transverse), gait speed, KAM impulse, KAM loading rate,), knee flexion moment, knee flexion ROM, peak ankle dorsiflexion, peak knee flexion, peak pelvic anterior tilt, peak pelvic drop (contralateral), peak pelvic drop (prosthetic), pelvic tilt ROM, pelvis ROM (frontal/sagittal/transverse), stride length, stride width, trunk ROM (frontal/sagittal/transverse), trunk-pelvis (frontal/sagittal/transverse)	C2C, COMP, CCL-11, CCL-4, CCL-5, CCL-2, CXCL-10, CTX-1, HA, IL-18, IL-1a, IL-7, INF-a, MMP-2, MMP-12, MMP-13, MMP-3, MMP-7, MMP-8, MMP-9, NTX-1, PIIANP, SDF-1, TIMP-1, TNF-a,
Zertuche, Rabasa (63) *USA*	OBS	777	Radiographic OA	Knee	258	61 ± 8	158 (61)	>2	No	Mean quadriceps strength	Alkyl resorcinol - 17, - 19, - 21, - 23, - 25, - sum
			Symptomatic OA	Knee	260	63 ± 8	164 (63)	>2	No		

1RM: 1 repetition maximum; **S100 A8/A9:** calprotectin: **25(OH)D:** vitamin D; **25(OH)D3:** vitamin D3; **6MWT:** 6 minute walk test; **ALP:** alkaline phosphatase; **ALT:** alanine aminotransferase; **ARGS:** alanine-arginine-glycine-serine; **AST:** aspartate aminotransferase; **BUN:** blood urea nitrogen; **sC2C:** cleavage of type ii collagen by collagenases; **CAPN2:** calpain 2; **CCL-2:** chemokine (C-C Motif) ligand 2; **CCL-4:** chemokine (C-C Motif) ligand 4; **CCL-5:** chemokine (C-C Motif) ligand 5; **CCL-11:** chemokine (C-C Motif) ligand 11; s**COMP:** serum cartilage oligomeric matrix protein; **CSA:** cross-sectional area; **hs-CRP:** high-sensitivity c-reactive protein; **CRP**: c-reactive protein; **CTSL2:** cathepsin L2; **CTX-I:** c-terminal telopeptide type I collagen; **uCTX-II:** urinary c-terminal telopeptide type II collagen; **CXCL-10:** chemokine (C-X-C Motif) Ligand 10; **DNA:** deoxyribonucleic acid; **ESR:** erythrocyte sedimentation rate; **FBG:** fasting blood glucose; **FOS:** immediate early response gene; **GGT:** gamma glutamyl transferase; **GPX:** glutathione peroxidase activity; **GSH:** oxidised glutathione; **GSSG:** reduced glutathione; **GSH/GSSG:** oxidised/reduced glutathione; **HA:** hyaluronic acid; **HbA1c:** haemoglobin A1c; **HDL:** high-density lipoprotein; **$HOMA_{IR}$:** homeostatic

model assessment of insulin resistance; **IGF-1:** insulin-like growth factor-1; **IL-1α:** interleukin 1 alpha; **IL-1β:** interleukin 1 beta; **IL-1RA:** interleukin 1 receptor antagonist protein; **IL-10:** interleukin 10; **IL-12:** interleukin 12; **IL-13:** interleukin 13; **IL-17:** interleukin 17; **IL-18:** interleukin 187; **IL-2:** interleukin 2; **IL-4:** interleukin 4; **IL-5:** interleukin 5; **IL-6:** interleukin 6; **IL-7:** interleukin 7; **IL-8:** interleukin 8; **INF-α:** Interferon alpha; **INV:** intervention; **iPTH:** serum parathyroid hormone intact; **KAM:** knee adduction moment; **LDL:** low-density lipoprotein; **LDH:** lactate dehydrogenase; **LPH:** lipid hydroperoxides; **LPL:** lipoprotein lipase; **MMP-12:** serum matrix metalloproteinase 12; **MMP-13:** serum matrix metalloproteinase 13; **MMP-2:** serum matrix metalloproteinase 2; **MMP-3:** serum matrix metalloproteinase 3; **MMP-7:** serum matrix metalloproteinase 7; **MMP-8:** serum matrix metalloproteinase 8; **MMP-9:** serum matrix metalloproteinase 9; **MVIC:** maximum voluntary isometric contraction; **NKA:** sodium-potassium transporter Na-K^+-APT pump; **NTX-1:** N-telopeptide of type I collagen; **OA:** osteoarthritis; **OBS:** observational study; **PDGF-AA:** platelet derived growth factor subunit A; **PDGF-BB:** platelet derived growth factor subunit A; **PIIANP:** N-propeptide of collagen IIA; **sPiiCP:** cartilage type ii procollagen carboxy pro-peptide; **PPARAG:** peroxisome proliferated activated receptor gamma; **PSMA7:** 20s proteasome alpha subunit 7; **PTH:** parathyroid hormone; **RCT:** randomised controlled trial; **RNA:** ribonucleic acid; **ROM:** range of motion; **SDF-1:** Stromal-cell derived factor -1; **SPPB:** short physical performance battery; **SGOT:** Glutamic Oxaloacetic Transaminase; **SGPT:** Glutamic Pyruvic Transaminase; **STS:** sit-to-stand; **TAC:** total antioxidant capacity; **TBARS:** Thio barbituric acid-reactive substances; **TGF-β:** transforming growth factor beta; **TGF-β1:** transforming growth factor beta 1; **TIMP-1:** Tissue inhibitor matrix metalloproteinase 1; **TNF-α:** tumour necrosis factor alpha; **TNF:** tumour necrosis factor; **sTNFR1:** soluble forms tumour necrosis factor alpha receptor 1; **sTNFR2:** soluble forms tumour necrosis factor alpha receptor 2; **TUG:** Timed-up and go; **sVCAM-1:** serum vascular cell adhesion molecule-1; **VEGF:** vascular endothelial growth factor; **VO_{2max}:** maximum oxygen consumption; **YKL-40:** or chitinase-3-like protein.

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PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	Pg 1
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	Pg 2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	Pg 3
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	Pg 3
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	Pg 4
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	Pg 4
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	Supp Material
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	Pg 4
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	Pg 4
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	Pg 5
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	Pg 5
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	Pg 4
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	Pg 5
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	Pg 5
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	Pg 5
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	Pg 5
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	Pg 5
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	Pg 5
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	Pg 5
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	Pg 5
Certainty	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	N/A

PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
assessment			
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	Fig 1 / Pg 6
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	Fig 1 / Pg 6
Study characteristics	17	Cite each included study and present its characteristics.	Table 3
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	Table 2
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	Fig 2 / Table 4
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	Fig 2 / Pg 6
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	Fig 2 / Pg 6/7
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	N/A
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	N/A
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	N/A
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	N/A
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	Pg 8-11
	23b	Discuss any limitations of the evidence included in the review.	Pg 8-11
	23c	Discuss any limitations of the review processes used.	Pg 8-11
	23d	Discuss implications of the results for practice, policy, and future research.	Pg 8-11
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	Pg 4
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	Pg 4
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	N/A
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	Pg 11
Competing interests	26	Declare any competing interests of review authors.	Pg 11
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	Pg 11

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71

PRISMA 2020 Checklist

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