Supplementary tables – diet review

Supplementary table 1 – Search strategy for systematic review of published reviews and meta-analyses

Category	Term
Diseases	1. Arthritis, Rheumatoid (mesh) (exp) (include all subheadings) 2. Inflammatory $arthritis 3. Undifferentiated arthritis 4. RA 5. Atrophic arthritis 6. Proliferative arthritis 7. Osteoarth$ 8. Arthrosis 9. Degenerative joint disease 10. Hypertrophic arthritis 11. Arthropathy 12. Polyarthritis 13. OA 14. Arthritis psoriatica 15. Arthropathic psoriasis 16. Psoriatic arthropathy 17. Arthritis, Psoriatic (mesh) (exp) (include all subheadings) 18. Psoria$ arthriti$ [have to uncheck “map team to subject heading”] 19. Psoria$ arthropath$ [have to uncheck “map team to subject heading”] 20. Undifferentiated oligoarthritis 21. Arthritic psoriasis 22. PsA 23. Ankylosing spondylitis (mesh) (exp) (include all subheadings) 24. Ankylosi$ 25. Spondyloarthr$ [have to uncheck “map team to subject heading”] 26. Spondylarthr$ [have to uncheck “map team to subject heading”] 27. Spondylitis (mesh) (exp) (include all subheadings) 28. Bechtere$ [have to uncheck “map team to subject heading”] 29. Marie-Strumpell 30. Spinal arthritis 31. Lupus erythematosus, systemic (mesh) (exp) (include all subheadings) 32. systemic lupus erythematosus 33. SLE 34. Libman-Sacks disease 35. Libman Sacks disease 36. Lupus erythematosus disseminatus 37. Disseminated lupus erythematosus 38. Lupus syndrome 39. Sclerosis, Systemic (mesh) (exp) (include all subheadings) 40. SSc ~~41. Scleros$~~ (removed because of ALS, multiple sclerosis etc.) 42. Thibierge-Weissenbach syndrome 43. Morphea 44. Gout (mesh) (exp) (include all subheadings) 45. Gout$

	46. Podagra 47. Tophus 48. Tophi 49. Tophaceous 50. Urate 51. Uric acid 52. Hyperurecemi$ [have to uncheck “map team to subject heading”] 53. Hyperurecaemi$ [have to uncheck “map team to subject heading”] 54. Hyperuricemia$ 55. Hyperuricaemi$ [have to uncheck “map team to subject heading”] 56. arthritis urica 57. Gout acute
Life-style exposures	58. Diet (mesh) (exp) (include all subheadings) 59. Nutrition 60. Food (mesh) (exp) (include all subheadings) 61. Food habit$ 62. Nutritional status (mesh) (exp) (include all subheadings) 63. Vitamin$ (mesh) (exp) (include all subheadings) 64. Antioxidant$ (mesh) (exp) (include all subheadings) 65. Fatty acid$ (mesh) (exp) (include all subheadings) 66. Carbohydrate$ (mesh) (exp) (include all subheadings) 67. Diet$ protein 68. Calcium 69. Fish oil$ (mesh) (exp) (include all subheadings) 70. Fruit (mesh) (exp) (include all subheadings) 71. Vegetable$ (mesh) (exp) (include all subheadings) 72. Micronutrient$ (mesh) (exp) (include all subheadings) 73. Nutriment$ 74. Neutraceutical$ 75. Exercis$ 76. Strength$ 77. Endurance 78. Cardiorespiratory 79. Aerobic 80. Aerobic training 81. Exercise program$ 82. Exercise therap$ [have to uncheck “map team to subject heading”] 83. Physical education 84. Physical training 85. Physical therapy 86. Physiotherapy 87. Muscle stretching 88. Sport (mesh) (exp) (include all subheadings) 89. Bod$y Weight (mesh) (exp) (include all subheadings) 90. Weight change 91. Weight loss (mesh) (exp) (include all subheadings) 92. Weight reduction 93. Weight gain 94. Anti obesity 95. Anti-obesity 96. Antiobesity

	97. Slimming 98. Smok$ 99. Smoking (mesh) (exp) (include all subheadings) 100. Tobacco (mesh) (exp) (include all subheadings) 101. Cigarette$ 102. Pipe$ 103. Cigar$ 104. Nicotine (mesh) (exp) (include all subheadings) 105. Water pipe 106. Hookah 107. Shisha 108. Paid work 109. Employment (mesh) (exp) (include all subheadings) 110. Work$ disability 111. Productivity 112. Employability 113. Work$ ability 114. Absenteeism (mesh) (exp) (include all subheadings) 115. Sick leave (mesh) (exp) (include all subheadings) 116. Presenteeism (mesh) (exp) (include all subheadings) 117. Sick$ absence 118. Work instability 119. Return to work (mesh) (exp) (include all subheadings) 120. Economic consequences 121. Occupational health 122. Labo$r
Systematic review terms	123. Systematic adj5 review 124. Narrative review 125. Meta-analysis (mesh) (exp) 126. Meta analysis 127. Meta adj5 analysis 128. Meta-synthesis 129. Meta synthesis 130. Meta adj5 synthesis 131. Literature review 132. Literature search 133. Meta-narrative review 134. Meta narrative review
Combining terms	135. RA – 1 OR 2 OR 3 OR 4 OR 5 OR 6 136. OA – 7 OR 8 OR 9 OR 10 OR 11 OR 12 OR 13 137. PSA – 14 OR 15 OR 16 OR 17 OR 18 OR 19 OR 20 OR 21 OR 22 138. AS – 23 OR 24 OR 25 OR 26 OR 27 OR 28 OR 29 OR 30 139. SLE – 31 OR 32 OR 33 OR 34 OR 35 OR 36 OR 37 OR 38 140. SSc – 39 OR 40 OR 41 OR 42 OR 43 141. Gout – 44 OR 45 OR 46 OR 47 OR 48 OR 49 OR 50 OR 51 OR 52 OR 53 OR 54 OR 55 OR 56 OR 57 142. Diseases – 136 OR 137 OR 138 OR 139 OR 140 OR 141 OR 142 143. Diet – 58 OR 59 OR 60 OR 61 OR 62 OR 63 OR 64 OR 65 OR 66 OR 67 OR 68 OR 69 OR 70 OR 71 OR 72 OR 73 OR 74 144. Exercise – 75 OR 76 OR 77 OR 78 OR 79 OR 80 OR 81 OR 82 OR 83 OR 84 OR 85 OR 86 OR 87 OR 88

	145. Weight – 89 OR 90 OR 91 OR 92 OR 93 OR 94 OR 95 OR 96 OR 97 146. Smoking - 98 OR 99 OR 100 OR 101 OR 102 OR 103 OR 104 OR 105 OR 106 OR 107 147. Work – 108 OR 109 OR 110 OR 111 OR 112 OR 113 OR 114 OR 115 OR 116 OR 117 OR 118 OR 119 OR 120 OR 121 OR 122 148. Exposures – 144 OR 145 OR 146 OR 147 OR 148 149. Systematic review terms - 123 OR 124 OR 125 OR 126 OR 127 OR 128 OR 129 OR 130 OR 131 OR 132 OR 133 OR 134 OR 135 150. 143 AND 149 AND 150

Supplementary table 2 – search strategy to identify published systematic reviews and meta-analyses on alcohol

The results from the first review of published systematic reviews and meta-analyses (supplementary table 1) were presented at a teleconference in January 2019. At this teleconference, it was decided to add alcohol as an exposure of interest for this taskforce. This led to a second systematic review of published reviews and meta-analyses. For completeness, the search strategy for this review is below. The results from this review are not reported in this systematic review on diet; they are published in a separate review on smoking and alcohol. However, these studies are included in the flow chart of figure 1, hence the inclusion of the search strategy here.

Category	Term
	1. Arthritis, Rheumatoid (mesh) (exp) (include all subheadings) 2. Inflammatory $arthritis 3. Undifferentiated arthritis 4. RA 5. Atrophic arthritis 6. Proliferative arthritis 7. Osteoarth$ 8. Arthrosis 9. Degenerative joint disease 10. Hypertrophic arthritis 11. Arthropathy 12. Polyarthritis 13. OA 14. Arthritis psoriatica 15. Arthropathic psoriasis 16. Psoriatic arthropathy 17. Arthritis, Psoriatic (mesh) (exp) (include all subheadings) 18. Psoria$ arthriti$ [have to uncheck “map team to subject heading”] 19. Psoria$ arthropath$ [have to uncheck “map team to subject heading”] 20. Undifferentiated oligoarthritis 21. Arthritic psoriasis 22. PsA 23. Ankylosing spondylitis (mesh) (exp) (include all subheadings) 24. Ankylosi$ 25. Spondyloarthr$ [have to uncheck “map team to subject heading”] 26. Spondylarthr$ [have to uncheck “map team to subject heading”] 27. Spondylitis (mesh) (exp) (include all subheadings) 28. Bechtere$ [have to uncheck “map team to subject heading”] 29. Marie-Strumpell 30. Spinal arthritis 31. Lupus erythematosus, systemic (mesh) (exp) (include all subheadings) 32. systemic lupus erythematosus 33. SLE 34. Libman-Sacks disease 35. Libman Sacks disease 36. Lupus erythematosus disseminatus 37. Disseminated lupus erythematosus

	38. Lupus syndrome 39. Sclerosis, Systemic (mesh) (exp) (include all subheadings) 40. SSc 41. Thibierge-Weissenbach syndrome 42. Morphea 43. Gout (mesh) (exp) (include all subheadings) 44. Gout$ 45. Podagra 46. Tophus 47. Tophi 48. Tophaceous 49. Urate 50. Uric acid 51. Hyperurecemi$ [have to uncheck “map team to subject heading”] 52. Hyperurecaemi$ [have to uncheck “map team to subject heading”] 53. Hyperuricemia$ 54. Hyperuricaemi$ [have to uncheck “map team to subject heading”] 55. arthritis urica 56. Gout acute
Exposure	57. Alcohol 58. Ethanol 59. Beer 60. Wine 61. Spirit$ 62. liquor
Systematic review terms	63. Systematic adj5 review 64. Narrative review 65. Meta-analysis (mesh) (exp) 66. Meta analysis 67. Meta adj5 analysis 68. Meta-synthesis 69. Meta synthesis 70. Meta adj5 synthesis 71. Literature review 72. Literature search 73. Meta-narrative review 74. Meta narrative review
Combining terms	75. RA – 1 OR 2 OR 3 OR 4 OR 5 OR 6 76. OA – 7 OR 8 OR 9 OR 10 OR 11 OR 12 OR 13 77. PSA – 14 OR 15 OR 16 OR 17 OR 18 OR 19 OR 20 OR 21 OR 22 78. AS – 23 OR 24 OR 25 OR 26 OR 27 OR 28 OR 29 OR 30 79. SLE – 31 OR 32 OR 33 OR 34 OR 35 OR 36 OR 37 OR 38 80. SSc – 39 OR 40 OR 41 OR 42 81. Gout – 43 OR 44 OR 45 OR 46 OR 47 OR 48 OR 49 OR 50 OR 51 OR 52 OR 53 OR 54 OR 55 OR 56 82. Alcohol – 57 OR 58 OR 59 OR 60 OR 61 OR 62 83. Systematic review terms - 63 OR 64 OR 65 OR 66 OR 67 OR 68 OR 69 OR 70 OR 71 OR 72 OR 73 OR 74 84. Disease – 75 OR 76 OR 77 OR 78 OR 79 OR 80 OR 81 85. 82 AND 83 AND 84

Supplementary table 3 – Search terms for diet review

Category	Term
Disease terms	1. Arthritis, Rheumatoid (mesh) (exp) (include all subheadings) 2. Inflammatory $arthritis 3. Undifferentiated arthritis 4. RA 5. Atrophic arthritis 6. Proliferative arthritis 7. Osteoarth$ 8. Arthrosis 9. Degenerative joint disease 10. Hypertrophic arthritis 11. Arthropathy 12. Polyarthritis 13. OA 14. Arthritis psoriatica 15. Arthropathic psoriasis 16. Psoriatic arthropathy 17. Arthritis, Psoriatic (mesh) (exp) (include all subheadings) 18. Psoria$ arthriti$ [have to uncheck “map team to subject heading”] 19. Psoria$ arthropath$ [have to uncheck “map team to subject heading”] 20. Undifferentiated oligoarthritis 21. Arthritic psoriasis 22. PsA 23. Ankylosing spondylitis (mesh) (exp) (include all subheadings) 24. Ankylosi$ 25. Spondyloarthr$ [have to uncheck “map team to subject heading”] 26. Spondylarthr$ [have to uncheck “map team to subject heading”] 27. Spondylitis (mesh) (exp) (include all subheadings) 28. Bechtere$ [have to uncheck “map team to subject heading”] 29. Marie-Strumpell 30. Spinal arthritis 31. Lupus erythematosus, systemic (mesh) (exp) (include all subheadings) 32. systemic lupus erythematosus 33. SLE 34. Libman-Sacks disease 35. Libman Sacks disease 36. Lupus erythematosus disseminatus 37. Disseminated lupus erythematosus 38. Lupus syndrome 39. Sclerosis, Systemic (mesh) (exp) (include all subheadings) 40. SSc 41. Thibierge-Weissenbach syndrome 42. Morphea 43. Gout (mesh) (exp) (include all subheadings) 44. Gout$ 45. Podagra 46. Tophus 47. Tophi 48. Tophaceous 49. Urate

	50. Uric acid 51. Hyperurecemi$ [have to uncheck “map team to subject heading”] 52. Hyperurecaemi$ [have to uncheck “map team to subject heading”] 53. Hyperuricemia$ 54. Hyperuricaemi$ [have to uncheck “map team to subject heading”] 55. arthritis urica 56. Gout acute 57. Inflammatory joint disease
Diet exposures	58. Diet (mesh) (exp) (include all subheadings) 59. Nutrition 60. Food (mesh) (exp) (include all subheadings) 61. Food habit$ 62. Nutritional status (mesh) (exp) (include all subheadings) 63. Vitamin$ (mesh) (exp) (include all subheadings) 64. Antioxidant$ (mesh) (exp) (include all subheadings) 65. Fatty acid$ (mesh) (exp) (include all subheadings) 66. Carbohydrate$ (mesh) (exp) (include all subheadings) 67. Diet$ protein 68. Calcium 69. Fish oil$ (mesh) (exp) (include all subheadings) 70. Fruit (mesh) (exp) (include all subheadings) 71. Vegetable$ (mesh) (exp) (include all subheadings) 72. Micronutrient$ (mesh) (exp) (include all subheadings) 73. Nutriment$ 74. Neutraceutical$ 75. Dietary supplement 76. Probiotic 77. Prebiotic 78. Functional food
Exclusions	79. Cross-sectional 80. Cross sectional 81. Children 82. Child 83. Juvenile 84. Adolescent 85. Teenager 86. Animal 87. Rat 88. Mouse 89. Case study 90. Case series 91. Systematic adj5 review 92. Narrative review 93. Meta-analysis (mesh) (exp) 94. Meta analysis 95. Meta adj5 analysis 96. Meta-synthesis 97. Meta synthesis 98. Meta adj5 synthesis 99. Literature review 100. Literature search

	101. Meta-narrative review 102. Meta narrative review 103. Septic arthritis
OA exclusions	104. Vitamin E 105. Bromelain 106. Glucosamine 107. Willow bark extract 108. Chondroitin 109. Artemisia annua extract 110. Green lipped muscle extract 111. Diacerin 112. Methylsulfonylmethane 113. Avocado adj3 unsaponifiables 114. Soybean adj3 unsaponifiables 115. Undenatured type II collagen 116. Undenatured type 2 collagen 117. L-carnitine 118. Curcumin 119. Pycnogenol 120. Boswellia serrata 121. Cucuma longa 122. Passion fruit 123. Collagen hydrolysate
RA exclusions	124. Marine oil 125. Omega-3 126. Omega 3 127. Probiotics 128. Vitamin D
Combining terms	129. RA – 1 OR 2 OR 3 OR 4 OR 5 OR 6 130. RA exclusions – 124 OR 125 OR 126 OR 127 OR 128 131. RA minus exclusions – 129 NOT 130 132. OA – 7 OR 8 OR 9 OR 10 OR 11 OR 12 OR 13 133. OA exclusions –104 OR 105 OR 106 OR 107 OR 108 OR 109 OR 110 OR 111 OR 112 OR 113 OR 114 OR 115 OR 116 OR 117 OR 118 OR 119 OR 120 OR 121 OR 122 OR 123 134. OA minus exclusions – 132 NOT 133 135. PSA – 14 OR 15 OR 16 OR 17 OR 18 OR 19 OR 20 OR 21 OR 22 136. AS – 23 OR 24 OR 25 OR 26 OR 27 OR 28 OR 29 OR 30 137. SLE – 31 OR 32 OR 33 OR 34 OR 35 OR 36 OR 37 OR 38 138. SSc – 39 OR 40 OR 41 OR 42 139. Gout – 43 OR 44 OR 45 OR 46 OR 47 OR 48 OR 49 OR 50 OR 51 OR 52 OR 53 OR 54 OR 55 OR 56 140. Diseases – 128 OR 131 OR 132 OR 133 OR 134 OR 135 OR 136 OR 57 141. Diet – 58 OR 59 OR 60 OR 61 OR 62 OR 63 OR 64 OR 65 OR 66 OR 67 OR 68 OR 69 OR 70 OR 71 OR 72 OR 73 OR 74 OR 75 OR 76 OR 77 OR 78 142. Exclusions – 79 OR 80 OR 81 OR 82 OR 83 OR 84 OR 85 OR 86 OR 87 OR 88 OR 89 OR 90 OR 91 OR 92 OR 93 OR 94 OR 95 OR 96 OR 97 OR 98 OR 99 OR 100 OR 101 OR 102 OR 103 143. 140 AND 141 144. 143 NOT 142

Supplementary table 4 – Included outcomes and examples of measures used to assess these outcomes

- Disease activity
  - OA
    - Western Ontario and McMaster Universities Arthritis Index [WOMAC]
  - RA
    - Acute phase reactants (i.e. C-reactive protein and erythrocyte sedimentation rate)
    - Swollen joint count
    - Tender joint count
    - Physician global assessment of disease activity (VAS)
    - Patient global health (VAS)
    - Disease activity composite measures (eg. Disease Activity Score [DAS28, DAS44], Rheumatoid arthritis Impact of Disease Score [RAID])
  - PsA [1]
    - Acute phase reactants (i.e. C-reactive protein and erythrocyte sedimentation rate)
    - Swollen joint count
    - Tender joint count
    - Physician global assessment of disease activity (VAS)
    - Patient global assessment of disease activity (VAS)
    - Dactylitis (e.g. Leeds dactylitis index)
    - Enthesitis (e.g. Mander/Newcastle Enthesitis Index, Leeds Enthesitis index)
    - Extent of psoriasis (e.g. Psoriasis Area and Severity Index [PASI])
    - Nail involvement (e.g. Nail Psoriasis Severity Index)
    - Disease activity composite measures (e.g. Composite Psoriatic Disease Activity Index [CPDAI], Disease Activity in Psoriatic Arthritis [DAPSA], clinical Disease Activity in Psoriatic Arthritis [cDAPSA], PsA Impact of Disease Score [PsAID] Psoriatic Arthritis Disease Activity Score [PASDAS])
  - AS [2]
    - Acute phase reactants (i.e. C-reactive protein and erythrocyte sedimentation rate)
    - Swollen joint count
    - Tender joint count
    - Disease activity composite measures (e.g. Ankylosing Spondylitis Disease Activity Score [ASDAS], Bath Ankylosing Spondylitis Disease Activity Index [BASDAI], Disease Activity Score [DAS44])
    - Enthesitis
    - Spinal mobility (e.g. Bath Ankylosing Spondylitis Metrology Index [BASMI])
    - Stiffness
  - SLE [3]
    - Disease activity composite measures (e.g. British Isles Lupus Assessment Group measure [BILAG], Systemic Lupus Erythematosus Disease Activity Index [SLEDAI])
    - Organ damage measures (e.g. Systemic Lupus International Collaborating Clinics (SLICC)/American College of Rheumatology Damage Index [SDI])
  - SSc [4]
    - Skin (e.g. Modified Rodnan skin score, visual analogue scale [VAS]/likert scale, Durometer reading)
    - Musculoskeletal (e.g. tender joint count, tender friction rubs assessed by doctor, serum creatinine)

        - Cardiac / pulmonary / renal / gastrointestinal involvement
        - Raynaud's phenomenon (e.g. Raynaud condition score, VAS raynauds)
        - Digital ulcers (e.g. activity digital tip ulcer count on volar surface, VAS digital ulcer)
        - Acute phase reactants (i.e. C-reactive protein and erythrocyte sedimentation rate)
    - Gout [5]
        - Serum urate
        - Gout flare recurrence
        - Tophus regression [6] / tophi number
        - Joint inflammation / tenderness score
- Physical functioning
    - OA
        - Physical function (e.g. the Knee Injury and Osteoarthritis Outcome Score [KOOS], Veterans Short Form 12 Health Survey [VR-12], Hip disability and Osteoarthritis Outcome Score [HOOS], WOMAC).
        - Objective measures (e.g. gait speed, grip strength)
        - Range of motion of effected joint
    - RA
        - Physical function (e.g. the Health Assessment Questionnaire [HAQ], Arthritis Impact Measurement Scale [AIMS], SF36-physical function)
        - Objective measures (e.g. gait speed, grip strength)
    - PsA
        - Physical function (e.g. the HAQ, Arthritis Impact Measurement Scale [AIMS], SF36-physical function)
        - Objective measures (e.g. gait speed, grip strength)
    - AS
        - Physical function (e.g. Health Assessment Questionnaire for the Spondylarthropathies [HAQ-S], Dougados Functional Index [DFI], Bath Ankylosing Spondyltitis Functional Index [BASFI])
        - Objective measures (e.g. gait speed, grip strength)
    - SLE [7]
        - Physical function (e.g. the HAQ, SF-36 physical function, Valued Life Activities Disability Scale)
        - Objective measures (e.g. gait speed, grip strength)
    - SSc
        - Physical function (e.g. the HAQ, SF-36).
        - Objective measures (e.g. gait speed, grip strength)
    - Gout
        - Physical function (e.g. HAQ [5;8], SF-36)
        - Objective measures (e.g. gait speed, grip strength)
- Pain
    - OA [9]
        - OARSI-OMERACT Initiative: New OA Pain Measure
        - Dallas Pain Questionnaire
        - Neck Pain and Disability Scale [NPAD]
        - WOMAC
        - Australian/Canadian Hand OA Index (AUSCAN)
    - RA
        - Patient pain rating (e.g. visual analogue scale)
    - PSA

        - Patient pain rating (e.g. visual analogue scale)
    - AS
        - Patient pain rating (e.g. visual analogue scale)
    - SLE
        - Patient pain rating (e.g. visual analogue scale)
    - SSc
        - Patient pain rating (e.g. visual analogue scale)
    - Gout
        - Patient pain rating (e.g. visual analogue scale / likert scale) [10]
- Fatigue
    - OA
        - Patient fatigue rating (e.g. visual analogue scale, other disease specific measure)
        - Generic fatigue questionnaire (e.g. Chalder Fatigue Scale)
    - RA
        - Patient fatigue rating (e.g. visual analogue scale, other disease specific measure)
        - Generic fatigue questionnaire (e.g. Chalder Fatigue Scale)
        - Bristol Rheumatoid Arthritis Fatigue – multidimensional questionnaire (BRAF-MDQ)
    - PSA
        - Patient fatigue rating (e.g. visual analogue scale, other disease specific measure)
        - Generic fatigue questionnaire (e.g. Chalder Fatigue Scale)
    - AS
        - Patient fatigue rating (e.g. visual analogue scale, other disease specific measure)
        - Generic fatigue questionnaire (e.g. Chalder Fatigue Scale)
    - SLE
        - Patient fatigue rating (e.g. visual analogue scale, other disease specific measure)
        - Generic fatigue questionnaire (e.g. Chalder Fatigue Scale)
    - SSc
        - Patient fatigue rating (e.g. visual analogue scale, other disease specific measure)
        - Generic fatigue questionnaire (e.g. Chalder Fatigue Scale)
    - Gout
        - Patient fatigue rating (e.g. visual analogue scale, other disease specific measure)
        - Generic fatigue questionnaire (e.g. Chalder Fatigue Scale)
- Erosions
    - Joint damage by X-ray (e.g. Sharp method, Larsen method, Lane Index, Wilke Index , Kellgren-Lawrence hand OA radiological index [9])
- Physical comorbidity
    - Major comorbidity
        - MACE (major adverse cardiac event)
        - Lung disease
        - Peptic ulcer disease
        - Liver disease
        - Renal disease
        - Tuberculosis / other serious infections

- Diabetes
- Hyperthyroidism
- Depression
- Cancer
- Fractures
- High cholesterol / dyslipidaemia

- Mental health
  - Mental health assessment questionnaires (e.g. Hospital Anxiety and Depression Scale (HADS), the AIMS, Mini-mental state examination)
- Quality of life (e.g. EQ-5D, SF-36)
  - Disease specific quality of life measures (e.g. RaQOL [11], ASQOL [12], PsAQoL [13])
- Work status
  - Categorical rating of work status (e.g. at work, retired, sick leave)
  - Number of days absent from work in a given time window

Supplementary table 5 – Description of reviews of animal products in OA

Table – Animal products, description of reviews

Authors (date)	Review type	Study type included	Type of OA	Exposure detail	Number of studies included	Funders
Liu (2018) [14]	MA	RCTs	Hip, knee or hand	Collagen hydrolysate Undenatured type II collagen Green lipped mussel extract	2 1 1	**Government** (NHMRC program grant, Department of education grant), **Industry** (PuraPharm postgrad scholarship), author disclosures (Flexion, Nestle, Merck)
Senftleber (2017) [15]	MA	RCTs	Knee or hip	Marine oil supplements	6	**Charity** (Oak Foundation [indirectly funded]), **Government** (National Institute of Arthritis and Musculoskeletal and Skin Diseases, NIH [individual fellowship of an author])

MA = meta-analysis, NHMRC = National Health and Medical Research Council, NIH = National Institutes of Health, OA = osteoarthritis, RCT = randomised controlled trial

Supplementary table 6 – Description of studies of animal products in OA

Table – Animal products (OA), description of included studies

Author (date) [country]	Study design	Type of OA	Inclusion criteria	Exposure detail	N	Age years, mean (SD)	N (%) female	Funders
Azidah (2017) [Malaysia] [16]	RCT	Knee	ACR OA criteria, radiological grade I-II, symptoms ≥3 months Exclusions: secondary knee OA, disability comorbidity (e.g. renal / liver disease, neoplasm, other rheumatic disease), severe knee pain, willingness to have surgery, history of joint lavage, arthroscopy, hyaluronic acid treatment in previous 6 months, intraarticular steroids in last 3 months, allergy to channa striatus	1) 1000mg/day channa striatus 2) 500mg/day channa striatus p) corn starch placebo	1) 39 2) 38 p) 39	1) 52.0 (5.8) 2) 52.9 (6.7) p) 52.8 (7.0)	1) 28 (70%) 2) 23 (57.5%) p) 34 (85.0%)	**University** (Universiti Sains Malaysia Research University)
Hill (2016) [Australia] [17]	RCT	Knee	Aged >40 years, ACR criteria for OA, VAS pain >20mm Exclusions: severe radiographic OA (Grade 3 – OARSI Atlas20), dementia or inability to give informed consent, pregnancy or lactation, planned knee replacement, high dose fish oil use for ≥6 months, contraindications to MRI	1) High dose fish oil containing 4.5g EPA+DHA per day 2) Low dose fish oil containing 0.45g EPA+DHA per day	1) 101 2) 101	1) 60.8 (10.4) 2) 61.1 (9.6)	1) 59 (58.4) 2) 40 (39.6)	**Government** (National Health and Medical Research Council of Australia), **Charity** (Arthritis Australia)
Chen (2016) [Australia] [18]	RCT	Knee	Aged >40 years, ACR criteria for OA, VAS pain >20mm Exclusions: severe radiographic OA (Grade 3 – OARSI Atlas20), dementia or inability to give informed consent, pregnancy or lactation, planned knee replacement, high dose fish oil use for ≥6 months, contraindications to MRI	1) High dose fish oil containing 4.5g EPA+DHA per day 2) Low dose fish oil containing 0.45g EPA+DHA per day	1) 101 2) 101	1) 60.8 (10.4) 2) 61.1 (9.6)	1) 59 (58.4) 2) 40 (39.6)	**Government** (National Health and Medical Research Council of Australia), **Charity** (Arthritis Australia)
Kumar (2015) [India] [19]	RCT	Knee	Age 30-65 years, KL grade 2-4, VAS ≥40 [type of VAS undefined]	1) Pork, 2) Beef, p1) placebo, p2) placebo 5g skin dissolved in 250ml water or milk in morning and night after food	1) 19 2) 18 p1) 11 p2) 10	not reported	1) 17 (89.4) 2) 11 (57.9) p1) 10 (90.9) p2) 7 (63.6)	Not reported
Schauss (2012) [USA] [20]	RCT	Knee or hip	Age: 40-70, Pain VAS (0-10) ≥4 for ≥3 months. Exclusions: serious/chronic medical conditions, pregnancy, RA / inflammatory arthritis, NSAID therapy / alternative therapy for OA for past 15 days	1) Capsules of hydrolysed chicken sternal cartilage extract composed of hydrolysed collagen type II p) Capsules of cellulose	1) 35 p) 33	1) 54.3 (8.69) p) 54.5 (9.79)	1) 23 (65.7) p) 18 (54.5)	**Industry** (BioCell technology)

ACR = American College of Rheumatology, DHA = docosahexaenoic acid, EPA = eicosapentaenoic acid, KL = Kellgren Lawrence, N = number, NSAID = non-steroidal anti-inflammatory drug, OA = osteoarthritis, P = placebo, RA = rheumatoid arthritis, RCT = randomised controlled trial, SD = standard deviation, USA = United States of America, VAS = visual analogue scale

Table – Animal products (OA) cont., description of included studies

Author (date) [country]	Study design	Type of OA	Inclusion criteria	Exposure detail	N	Age years, mean (SD)	N (%) female	Funders
Nagaoka (2010) [Japan] [21]	RCT	Knee	Aged 40-85 years, KL grade 0-3 Exclusion: any inflammatory bone/cartilage condition, previous knee surgery, known allergy to chicken, participant in clinical trial, women who are pregnant, nursing or of child bearing potential, treatment with intra-articular hyaluronic acid, steroids within 3 weeks, use of health foods, presence of significant clinical condition	1) Capsules of chicken comb extract p) Placebo pills containing cellulose	1) 9 p) 12	1) 62.4 (12.5) p) 63.3 (9.5)	1) 17 (81.0) P) 18 (81.8)	Not reported
Ruff (2009) [USA] [22]	RCT	Knee	Age >18 years, symptoms of OA, ACR functional grade I-III, persistent knee pain. Exclusions: receiving remission inducing drugs in past 4 months, other serious conditions, body weight >113.5kg, allergy to eggs, pregnant women	1) Capsules containing egg shell membrane p) Capsules contacting vegetarian placebo	1) 29 p) 31	not reported	not reported	**Industry** (ESM Technologies)
Kalman (2008) [USA] [23]	RCT	Knee	Aged >40 years, KL grade >2, pain for at least 15 of previous 20 days Exclusion: chicken/corn/potato/rice/cellulose allergy, inflammatory arthritis, MS or autoimmune disorder, oral steroids in past 4 weeks, intraarticular steroids in past 3 months, joint injury, other serious condition, pregnancy, renal dysfunction	1) Capsule of chicken comb extract p) matched placebo capsules	1) 11 p) 9	1) 57.7 (10.1) p) 54.6 (7.7)	1) 7 (63.6) p) 4 (44.4)	**Industry** (Biobérica)
Hesslink (2002) [India] [24]	RCT	Knee	ACR OA criteria	1) Capsules containing standard fish oil blend rich in Omega-3 p) Identical capsules of soy lecithin	1) 33 p) 31	1) 58.1 (6.3) p) 55.5 (6.8)	1) 11 (33.3) p) 14 (45.2)	**Industry** (Imagenetix, Inc.)
Stammers (1992) [UK] [25]	RCT	Not reported	Aged 49-87 years, NSAIDS for at least 2 weeks	1) 10ml cod liver oil – 786 mg of EPA p) 10ml olive oil	1) 44 p) 42	1) 67 p) 69	1) 29 (65.9) p) 33 (78.6)	**Industry** (Seven Seas Ltd)
Kilinc (2018) [Turkey][26]	Single arm int.	Knee	Bilateral knee pain ≥4cm on VAS, analgesic and anti-inflammatory medication discontinued 3 weeks before start of treatment, KL grade II-III	720mg promerim for 15 days, then 360mg promerim for next 15 days. Patients also received exercise program.	92	51.5 (7.1)	69 (75)	No funding
Lu (2014) [USA] [27]	Pros. Cohort	Knee	Age 45-79, OA initiative Exclusion: baseline KL grade = 4, primary lateral joint space narrowing, difference of rim distance from tibial plateau to tibial rim closest to femoral condyle between baseline and any follow ≥2 mm	Mean glasses of milk per week, coded as: none, ≤3, 4-6, ≥7	2148	62.4 (9.0	1260 (58.7%)	**Government** (National Heart, Lung and Blood Institute, NIH), **Industry** (OAI: Pfizer, Novartis, Merck, GSK)

ACR = American College of Rheumatology, EPA = eicosapentaenoic acid, GSK = GlaxoSmithKline, KL = Kellgren Lawrence, N = number, NSAID = non-steroidal anti-inflammatory drug, OA = osteoarthritis, P = placebo, RA = rheumatoid arthritis, RCT = randomised controlled trial, SD = standard deviation, USA = United States of America, VAS = visual analogue scale

Supplementary table 7 – Collagen and OA progression, results

Table – Collagen, results and quality assessment

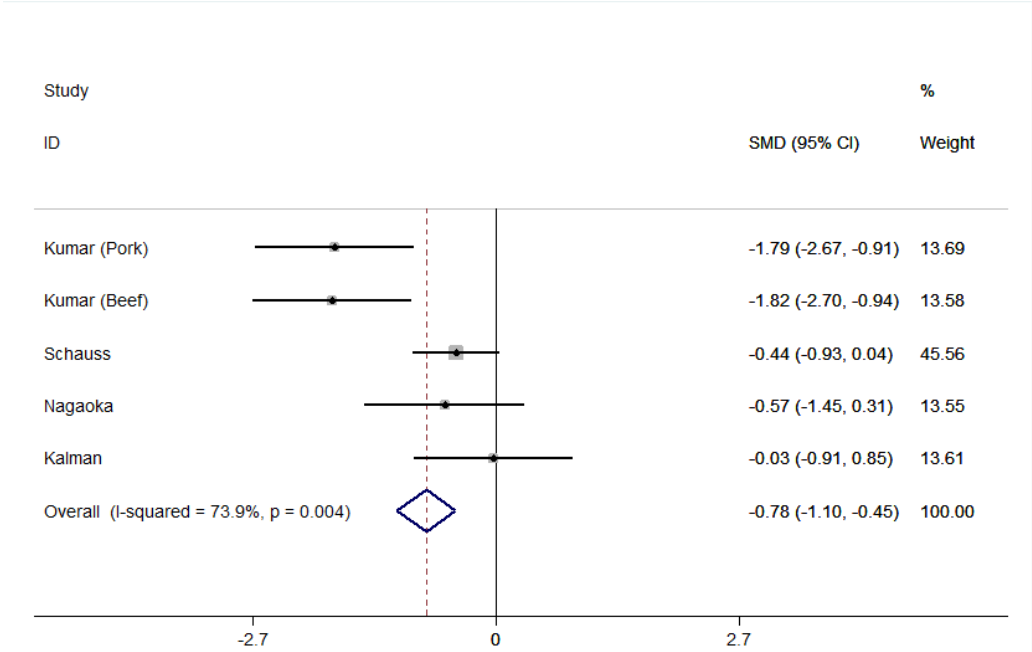
Outcome (outcome measure)	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	AMSTAR2 quality	Rand. Seq.	Alloc. Conc.	Blind. Part.	Blind. Asses.
Pain	Liu (2018) [MA] [14]	Undenatured type II collagen Short term: pooled SMD -0.67 (-1.01, -0.33); Collagen hydrolysate Medium term: pooled SMD -0.28 (-0.54, -0.02);		Moderate				
	Kumar (2015) [RCT] [19]	Pork collagen vs pork placebo at 91 days SMD -1.79 (-2.67, -0.91) Beef collagen vs beef placebo at 91 days SMD -1.83 (-2.75, -0.91)	Pain VAS, Baseline / 91 days, mean (SD) Pork collagen: 63.2 (10.6) / 31.1 (15.2) Beef collagen: 66.0 (12.3) / 28.0 (10.9) Pork placebo: 60.0 (6.3) / 57.3 (13.5) Beef placebo: 62.0 (14.0) / 55.0 (20.1)		L	H/UC	H/UC	H/UC
	Schauss (2012) [RCT] [20]	Collagen vs placebo at 70 days SMD -0.44 (-0.93, 0.04)	WOMAC pain, Baseline / 70 days, mean (SD) Collagen: 9.88 (2.93) / 6.13 (2.66) Placebo: 10.53 (2.71) / 7.48 (3.40)		L	L	L	L
	Nagaoka (2010) [RCT] [21]	Collagen vs placebo at 16 weeks SMD -0.57 (-1.45, 0.31)	Pain VAS, BL / 16 weeks, mean (SD) Collagen: 55.4 (8.6) / 12.6 (6.3) Placebo: 54.7 (8.5) / 22.2 (21.5)		H/UC	H/UC	H/UC	H/UC
	Kalman (2008) [RCT] [23]	Collagen vs placebo at 8 weeks SMD -0.03 (-0.91, 0.85)	WOMAC pain, Baseline / 8 weeks, mean (SD) Collagen: 10.4 (3.6) / 6.3 (4.0) Placebo: 10.4 (2.7) / 6.4 (2.7)		L	H/UC	L	H/UC
	Bespoke MA of: Kumar 2015 [beef] Kumar 2015 [Pork] Schauss 2012 Nagaoka 2010 Kalman 2008	Collagen vs placebo Meta-SMD -0.78 (-1.10, -0.45) I^2 = 74.0%						

Alloc. Conc. = allocation concealment, AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews, BL = baseline, Blind. Asses. = Blinded assessors, Blind. Part. = blinded participants, CI = confidence interval, H/UC = high / unclear risk of bias, L = low risk of bias, MA = meta-analysis, OA = osteoarthritis, Rand. Seq. = random sequence generation, RCT = randomised controlled trial, SD = standard deviation, SMD = Standardised mean difference, VAS = visual analogue scale, WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index

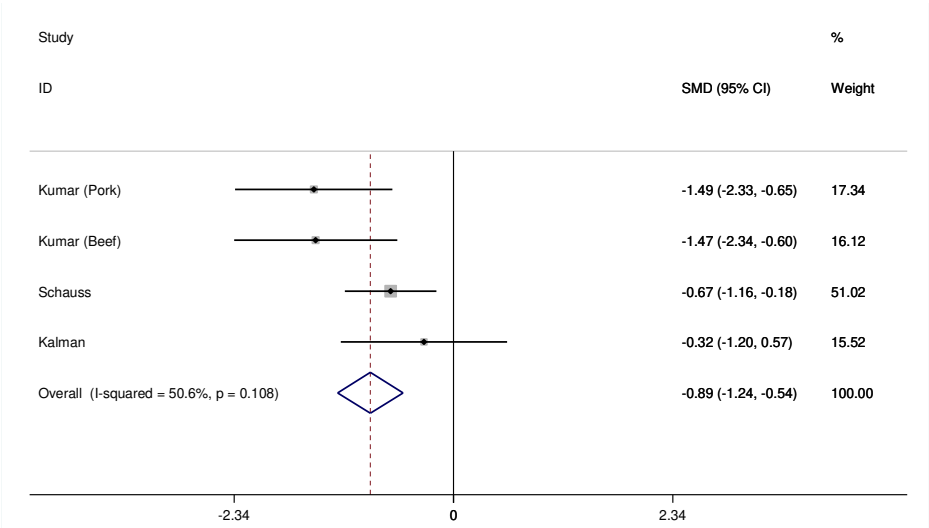
Table (cont.) – Collagen, results and quality assessment

Outcome (outcome measure)	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	AMSTAR2 quality	Rand. Seq.	Alloc. Conc.	Blind. Part.	Blind. Asses.
Function	Liu (2018) [MA] [14]	Undenatured type II collagen Short term: pooled SMD -0.55 (-0.94, -0.17); Collagen hydrolysate Short term: pooled SMD 0.11 (-0.57, 0.78)		Moderate				
	Kumar (2015) [RCT] [19]	Pork collagen vs pork placebo at 91 days SMD -1.49 (-2.33, -0.65) Beef collagen vs beef placebo at 91 days SMD -1.47 (-2.34, -0.60)	WOMAC function, Baseline / 91 days, mean (SD) Pork collagen: 47.2 (9.8) / 31.1 (9.8) Beef collagen: 50.3 (9.6) / 25.8 (11.3) Pork placebo: 47.3 (8.6) / 45.5 (9.4) Beef placebo: 50.1 (14.7) / 47.3 (19.4)		L	H/UC	H/UC	H/UC
	Schauss (2012) [RCT] [20]	Collagen vs placebo at 70 days SMD -0.67 (-1.16, -0.18)	WOMAC function, Baseline / 70 days, mean (SD) Collagen: 40.35 (8.51) / 26.65 (8.62) Placebo: 39.20 (8.75) / 32.90 (10.03)		L	L	L	L
	Kalman (2008) [RCT] [23]	Collagen vs placebo at 8 weeks SMD -0.32 (-1.20, 0.57)	WOMAC function, Baseline / 8 weeks, mean (SD) Collagen: 36.3 (7.7) / 23.1 (15.1) Placebo 37.4 (10.6) / 27.3 (10.7)		L	H/UC	L	H/UC
	Bespoke MA of: Kumar 2015 [beef] Kumar 2015 [Pork] Schauss 2012 Kalman 2008	Collagen vs placebo Pooled SMD -0.89 (-1.24, -0.54) I^2 = 47.7%						
Stiffness	Kalman (2008) [RCT] [23]	Collagen vs placebo at 8 weeks SMD 0.00 (-0.88, 0.88)	WOMAC stiffness, Baseline / 8 weeks, mean (SD) Collagen: 4.2 (1.0) / 2.9 (1.9) Placebo 4.5 (1.9) / 2.9 (1.0)		L	H/UC	L	H/UC
QoL	Kumar (2015) [RCT] [19]	Pork collagen vs pork placebo at 91 days SMD -1.57 (-2.42, -0.72) Beef collagen vs beef placebo at 91 days SMD -1.57 (-2.45, -0.69)	"QoL Score", Baseline / 91 days, mean (SD) Pork collagen: 53.4 (10.4) / 34.3 (10.8) Beef collagen: 56.9 (9.9) / 28.7 (11.4) Pork placebo: 53.3 (8.8) / 51.2 (10.7) Beef placebo: 56.3 (15.4) / 52.8 (20.9)		L	H/UC	H/UC	H/UC

Alloc. Conc. = allocation concealment, AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews, Blind. Asses. = Blinded assessors, Blind. Part. = blinded participants, CI = confidence interval, H/UC = high / unclear risk of bias, L = low risk of bias, MA = meta-analysis, OA = osteoarthritis, QoL = quality of life, Rand. Seq. = random sequence generation, RCT = randomised controlled trial, SD = standard deviation, SMD = Standardised mean difference, VAS = visual analogue scale, WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index



Supplementary figure 1 – Collagen, bespoke meta-analysis for pain (OA)



Supplementary Figure 2 – Collagen, bespoke meta-analysis for function (OA)

Supplementary table 8 – Milk and OA progression, results

Table – Collagen, results and quality assessment

Outcome (outcome measure)	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	Study Pop.	Attr.	Prog. Meas.	Outc. Meas.	Conf.	Stats.
Joint space width	Lu (2014) [Pros. Obs.] [27]		Decrease in joint space width, HR (95% CI) *Men* none: ref <=3: 0.77 (0.53, 1.13) 4-6: 0.92 (0.60, 1.40) >=7: 0.61 (0.39, 0.94); p=0.075 *Women*: none: ref <=3: 0.67 (0.50, 0.91) 4-6: 0.71 (0.50, 1.00) >=7: 0.56 (0.38, 0.81); p=0.008	L	L	M	L	L	L

Attr. = attrition, CI = confidence interval, Conf. = confounding, HR = hazard ratio, L = low risk of bias, M = moderate risk of bias, OA = osteoarthritis, Outc. Meas = outcome measurement, Prog. Meas. = prognostic factor measurement, Pros. Obs. = prospective observational, SMD = standardised mean difference, Stats. = statistical analysis, Study Pop. = study population

Supplementary table 9 – Egg shell membrane and OA progression, results

Table (cont.) – Egg-shell membrane, results and quality assessment

Outcome (outcome measure)	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	AMSTAR2 quality	Rand. Seq.	Alloc. Conc.	Blind. Part.	Blind. Asses.
Pain	Ruff (2009) [RCT] [22]	Egg-shall vs placebo at 60 days SMD -0.56 (-1.15, 0.04)	WOMAC pain, baseline / 60 days, mean (SD) Egg-shell: 44.0 (16.8) / 37.5 (25.2) Placebo: 50.6 (19.4) / 50.7 (22.2); p=0.038		L	L	L	L
Function	Ruff (2009) [RCT] [22]	Egg-shall vs placebo at 60 days SMD -0.48 (-1.08, 0.11)	WOMAC function, baseline / 60 days, mean (SD) Egg-shell: 48.1 (19.5) / 40.5 (27.1) Placebo: 55.2 (21.3) / 53.1 (24.9); p=0.076		L	L	L	L
Stiffness	Ruff (2009) [RCT] [22]	Egg-shall vs placebo at 60 days SMD -0.86 (-1.47, -0.24)	WOMAC stiffness, baseline / 60 days, mean (SD) Egg-shell: 50.5 (20.3) / 35.0 (25.8) Placebo: 59.3 (24.0) / 56.5 (24.3); p=0.005		L	L	L	L

Alloc. Conc. = allocation concealment, AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews, Blind. Asses. = Blinded assessors, Blind. Part. = blinded participants, CI = confidence interval, H/UC = high / unclear risk of bias, L = low risk of bias, OA = osteoarthritis Rand. Seq. = random sequence generation, RCT = randomised controlled trial, SD = standard deviation, SMD = Standardised mean difference, WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index

Supplementary table 10 – Channa Striatus extract and OA progression, results

Table – Channa Striatus (OA), results and quality assessment

Outcome	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	AMSTAR2 quality	Rand. Seq.	Alloc. Conc.	Blind. Part.	Blind. Asses.
Pain	Azidah (2017) [RCT] [16]	1000mg Channa striatus vs placebo at 6 months SMD -0.42 (-0.87, 0.03) 500mg Channa striatus vs placebo at 6 months SMD -0.31 (-0.76, 0.14)	WOMAC pain, 6 months, mean (SD*) Channa striatus 1000mg: 85.91 (96.94) Channa striatus 500mg: 96.65 (98.11) Placebo: 126.99 (96.86); p=0.139		L	L	L	L
Function	Azidah (2017) [RCT] [16]	1000mg Channa striatus vs placebo at 6 months SMD -0.56 (-1.01, -0.11) 500mg Channa striatus vs placebo at 6 months SMD -0.42 (-0.87, 0.03)	WOMAC function, 6 months, mean (SD*) Channa striatus 1000mg: 312.91 (329.36) Channa striatus 500mg: 358.15 (329.37) Placebo: 496.48 (329.36)		L	L	L	L
Stiffness	Azidah (2017) [RCT] [16]	1000mg Channa striatus vs placebo at 6 months SMD -0.51 (-0.96, -0.06) 500mg Channa striatus vs placebo at 6 months SMD -0.53 (-0.98, -0.07)	WOMAC stiffness, 6 months, mean (SD*) Channa striatus 1000mg: 35.12 (44.53) Channa striatus 500mg: 34.25 (44.52) Placebo: 57.76 (44.53); p=0.016		L	L	L	L

*calculated from 95% confidence interval reported in paper

Alloc. Conc. = allocation concealment, AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews, BL = baseline, Blind. Asses. = Blinded assessors, Blind. Part. = blinded participants, CI = confidence interval, H/UC = high / unclear risk of bias, L = low risk of bias, Rand. Seq. = random sequence generation, RCT = randomised controlled trial, SD = standard deviation, SMD = Standardised mean difference, WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index

Supplementary table 11 – Fish oil and OA progression, results

Table – Fish oil (OA), results and quality assessment

Outcome	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	AMSTAR2 quality	Rand. Seq.	Alloc. Conc.	Blind. Part.	Blind. Asses.
Pain	Senftleber (2017) [MA] [15]	Fish Oil vs control SMD -0.16 (-0.57, 0.24)		High				
	Hill (2016) [RCT] [17]		WOMAC pain, Mean difference (SE), high vs low dose 1 year: 2.3 (1.2) p = 0.06 2 years: 3.3 (1.3) p=0.009 [in favour of low dose]		L	L	L	L
	Hesslink (2002) [RCT] [24]	Fish oil vs placebo at 68 days SMD -0.61 (-1.12, -0.11)	LI pain, BL / day 68, mean (SD*) Fish oil: 6.0 (0.6) / 3.9 (1.7) Placebo: 6.1 (1.1) / 5.1 (2.2)		H/UC	H/UC	L	L
	Stammers (1992) [RCT] [25]	Fish oil vs placebo, change from baseline to 6 months SMD 0.21 (-0.21, 0.63)	VAS pain, change from bl to 6 months, mean (SD) Fish oil: 1 (20) Placebo: -3 (18)		H/UC	H/UC	H/UC	H/UC
Function	Senftleber (2017) [MA] [15]	Fish Oil vs control SMD 0.11 (-0.13, 0.35)		High				
	Hill (2016) [RCT] [17]		WOMAC function, Mean difference (SE), high vs low dose 1 year: 6.5 (3.7) p = 0.08 2 years: 8.5 (4.0) p=0.032 [in favour of low dose]		L	L	L	L
	Hesslink (2002) [RCT] [24]	Fish oil vs placebo at 68 days SMD -0.65 (-1.15, -0.14)	LI activities, BL / day 68, mean (SD*) Fish oil: 4.6 (1.1) / 3.1 (1.7) Placebo: 4.8 (1.1) / 4.2 (1.7)		H/UC	H/UC	L	L
	Stammers (1992) [RCT] [25]	Fish oil vs placebo, change from baseline to 6 months SMD 0.13 (-0.30, 0.55)	VAS disability, change from bl to 6 months, mean (SD) Fish oil: -2 (17) Placebo: -4 (15)		H/UC	H/UC	H/UC	H/UC
Bone mineral density	Chen (2016) [RCT] [18]		Bone mineral density, high vs low dose, regression coefficient (95% CI) [fully adjusted] Lumbar spine: 4.7 (-8.5, 17.9) Femoral neck: -3.8 (-12.5, 4.9)		L	L	L	L

*SD calculated from standard error in paper

Alloc. Conc. = allocation concealment, AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews, BL = baseline, Blind. Asses. = Blinded assessors, Blind. Part. = blinded participants, CI = confidence interval, H/UC = high / unclear risk of bias, L = low risk of bias, LI = Lequesne Index, MA = meta-analysis, OA = osteoarthritis, Rand. Seq. = random sequence generation, RCT = randomised controlled trial, SD = standard deviation, SE = standard error, SMD = Standardised mean difference, VAS = visual analogue scale, WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index

Supplementary table 12 – Green lipped mussel extract and OA progression, results

Table – Green-lipped mussel extract (OA), results and quality assessment

Outcome	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	AMSTAR2 quality	Rand. Seq.	Alloc. Conc.	Blind. Part.	Blind. Asses.
Pain	Liu (2018) [MA] [14]	Green-lipped mussel extract vs placebo SMD -0.37 (-0.81, 0.08)		Moderate				

Alloc. Conc. = allocation concealment, AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews, Blind. Asses. = Blinded assessors, Blind. Part. = blinded participants, CI = confidence interval, H/UC = high / unclear risk of bias, L = low risk of bias, MA = meta-analysis, OA = osteoarthritis, Rand. Seq. = random sequence generation, SMD = Standardised mean difference,

Supplementary table 13 – Promerim and OA progression, results

Table – Promerim (OA), results and quality assessment

Outcome	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	AMSTAR2 quality	Rand. Seq.	Alloc. Conc.	Blind. Part.	Blind. Asses.
Pain	Kilinc (2018) [Single arm][26]		VAS pain, pre / post intervention, mean (SD) 5.6 (1.1) / 2.6 (1.7) p<0.001					
WOMAC total	Kilinc (2018) [Single arm][26]		WOMAC total, pre / post intervention, mean (SD) 46.4 (8.2) / 72.1 (14.4) p<0.001 §					

§ The paper appears to have reversed the scale of the WOMAC, so that higher scores indicate improved health, although this is not certain.
Alloc. Conc. = allocation concealment, AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews, Blind. Asses. = Blinded assessors, Blind. Part. = blinded participants, CI = confidence interval, H/UC = high / unclear risk of bias, L = low risk of bias, OA = osteoarthritis, Rand. Seq. = random sequence generation, SD = standard deviation, SMD = Standardised mean difference, VAS = visual analogue scale, WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index

Supplementary table 14 – Description of reviews of experimental diets in OA

Table – Experimental diets (OA), description of reviews

Authors (date)	Review type	Study type included	Type of OA	Exposure detail	Number of studies included	Funders
Alrushud (2017) [28]	MA	RCTs	Knee	Caloric restriction + physical activity	5 (2 included in MA)	**University** (King Saud University, Saudi Arabia), **Government** (Saudi Arabian Cultural Bureau)

MA = meta-analysis, OA = osteoarthritis, RCT = randomised controlled trial

Supplementary table 15 – Description of studies of experimental diets in OA

Table – Experimental diets (OA), description of included studies

Author (date) [country]	Study design	Type of OA	Inclusion criteria	Exposure detail	N	Age, mean (SD) years	N (%) female	Funders
Dyer (2017) [UK] [29]	RCT	not reported	OA, aged 31-90 years Exclusions: comorbidity meaning they cannot follow diet, participating in other interventional research, prior involvement with Arthritis Action	1) Nutritional and dietary advice in line with Mediterranean diet given. Telephone support offered. p) Control followed no intervention	1) 50 p) 49	1) 66 (11) p) 60 (12)	1) 38 (76) p) 44 (88)	**Charity** (Arthritis Action)
Clinton (2015) [USA] [30]	RCT	not reported	OA, aged 18-70 years Exclusion: history of eating disorder, diabetes, inability to afford food, lack of control over food, pregnant or nursing, food allergies, following other medically prescribed diet	1) WFPB consists of fruits, vegetables, legumes and grains. No energy consumption restriction but encouraged to get at least 90% of calories from plants P) Control: ordinary diet	1) 19 p) 18	1) 56.1 (8.4) p) 60.0 (6.3)	1) 15 (78.9) p) 16 (88.9)	**Charity** (Blue Cross Blue Shield)
Riecke (2010) [Denmark] [31]	RCT	Knee	Obese (BMI>30), aged >50 years, ACR OA criteria Exclusions: previous/planned knee replacement, surgery or injections in knee in past 3 months, weight reducing drugs, lack of motivation to lose weight, inability to speak Danish	8 weeks of low calories: 1) 810 kcal per day 2) 415 kcal per day Both groups then had 8 more weeks of 1200 kcal per day	1) 96 2) 96	1) 63.3 (6.3) 2) 61.8 (6.4)	1) 77 (80.2) 2) 78 (81.3)	**Charity** (The Oak Foundation, The Velux Foundation, The Augustinus Foundation, The A.P. Møller Foundation, Erik Hørslev og hustru BirgitHørslevs Fond, Aase og Ejnar Danielsens fond and Bjarne Jensens Fond) **Industry** (Cambridge Weight Plan) **Professional body** (Danish Rheumatism Association)
Lopez-Gomez (2018) [Spain] [32]	Single arm int.	Knee	Obese, pending surgery, knee OA	Nutrition education + hypocaloric diet (diet structured into 6 meals – lunch and dinner replaced by “oral nutritional supplement”	75	62.2 (8.5)	75 (100)	Not reported

ACR = American College of Rheumatology, BMI = Body Mass Index, Int. = intervention, kcal = kilocalories, N = number, OA = osteoarthritis, RCT = randomised controlled trial, SD = standard deviation, UK = United Kingdom, USA = United States of America, WFPB = Whole Food Plant Based

Supplementary table 16 – Calorie restriction and OA progression, results

Table – Calorie restriction (OA), results and quality assessment

Outcome	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	AMSTAR2 quality	Rand. Seq.	Alloc. Conc.	Blind. Part.	Blind. Asses.
Pain	Alrushud (2017) [MA] [28]	Diet restriction vs exercise control at 18 months SMD -0.24 (-0.50, 0.02)	WOMAC pain, BL / 18 months, mean (SD) diet + exercise: 6.7 (3.4) / 3.7 (3.1) exercise control: 6.1 (2.9) / 4.4 (2.7) [1 study – Messier et al 2013 [33])	Moderate				
	Riecke (2010) [RCT] [31]	415 kcal vs 810 kcal at 16 weeks SMD -0.06 (-0.34, 0.22)	Pain VAS, change from BL – 16 weeks, mean (SD*) 810 kcal: -10.5 (17.93) 415 kcal: -11.6 (18.62); p=0.68		L	L	L	L
	Lopez-Gomez (2018) [single arm] [32]		WOMAC pain, BL / 3 months, mean (SD) Calorie restriction: 52.94 (26.08) / 45.25 (23.57) p<0.01					
Function	Alrushud (2017) [MA] [28]	Diet restriction vs exercise control at 18 months SMD -0.34 (-0.59, -0.08)	WOMAC function, BL / 18 months, mean (SD) diet + exercise: 24.6 (11.7) / 14.2 (10.4) exercise control: 23.1 (10.3) / 17.6 (9.8) [1 study – Messier et al 2013 [33])	Moderate				
	Riecke (2010) [RCT] [31]	415 kcal vs 810 kcal at 16 weeks SMD -0.08 (-0.37, 0.20)	Function VAS, change from BL – 16 weeks, mean (SD*) 810 kcal: -12.75 (18.91) 415 kcal: -14.44 (22.05); p0.57		L	L	L	L
	Lopez-Gomez (2018) [single arm] [32]		WOMAC function, BL / 3 months, mean (SD) Calorie restriction: 49.19 (27.01) / 40.16 (22.06 – 54.41) [sic] p<0.01					
Stiffness	Lopez-Gomez (2018) [single arm] [32]		WOMAC stiffness, BL / 3 months, median (IQR) Calorie restriction: 50 (25-75) / 25 (12.5-50); p=0.02					
6MWT	Alrushud (2017) [MA] [28]		Intervention vs exercise only control meta-mean difference: 15.05 (-11.77, 41.87) in favour of intervention	Moderate				
QoL	Riecke (2010) [RCT] [31]	415 kcal vs 810 kcal at 16 weeks SMD -0.03 (-0.32, 0.25)	KOOS QoL, change from BL – 16 weeks, mean (SD*) 810 kcal: 8.85 (15.68) 415 kcal: 8.31 (16.07); p=0.81		L	L	L	L

* calculated from standard error reported in paper

6MWT = six minute walk test, Alloc. Conc. = allocation concealment, AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews, BL = baseline, Blind. Asses. = Blinded assessors, Blind. Part. = blinded participants, CI = confidence interval, H/UC = high / unclear risk of bias, IQR = interquartile range, kcal = kilocalories, KOOS = Knee Injury and Osteoarthritis Outcome Score, L = low risk of bias, QoL = Quality of life, Rand. Seq. = random sequence generation, RCT = randomised controlled trial, SD = standard deviation, SMD = Standardised mean difference, WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index

Table – Calorie restriction, SF36 results, mean (SD)

Author (date) [BL]	PCS	MCS	GH	PF	RP	RE	SF	BP	V	MH
Lopez-Gomez (2018) [32] [BL]	-	-	41.49 (16.53)	25 (10-45) §	25 (0-100) §	69.13 (42.74)	75 (50-100) §	43.95 (23.68)	44.22 (23.68)	59.80 (27.40)
Lopez-Gomez (2018) [32] [FU]	-	-	48.79 (13.63)	75 (12.5-100) §	75 (12.5-100) §	81.85 (36.59)	87.5 (50-100) §	54.23 (27.76)	57.71 (54.34)	68.49 (22.98)
Riecke (2010) [810 kcal] †	6.07 (7.94 ‡)	1.32 (8.72 ‡)	-	-	-	-	-	-	-	-
Riecke (2010) [415 kcal] †	5.57 (8.13 ‡)	4.43 (8.03 ‡)	-	-	-	-	-	-	-	-

§ median (IQR)

† change from baseline to 16 weeks

‡ calculated from standard error in paper

BL = baseline, BP = bodily pain, FU = follow-up, GH = general health, IQR = interquartile range, MCS = mental component score, MH = mental health, PCS = physical component score, PF = physical function, RE = role emotional, RP = role physical, SD = standard deviation, SF = social functioning, V = vitality

Supplementary table 17 – Whole food, plant based diet and OA progression, results

Table – Whole food, plant based diet (OA), results and quality assessment

Outcome	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	AMSTAR2 quality	Rand. Seq.	Alloc. Conc.	Blind. Part.	Blind. Asses.
Pain	Clinton (2015) [RCT] [30]		Pain VAS, week 6, mean (SD not reported) WFPD: 2.21 Control: 2.38 p=NS		L	H/UC	H/UC	H/UC

Alloc. Conc. = allocation concealment, AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews, Blind. Asses. = Blinded assessors, Blind. Part. = blinded participants, CI = confidence interval, H/UC = high / unclear risk of bias, L = low risk of bias, OA = osteoarthritis, Rand. Seq. = random sequence generation, RCT = randomised controlled trial, SD = standard deviation, SMD = Standardised mean difference, VAS = visual analogue scale, WFPB = whole food plant based

Table – Whole food plant based diet (OA), SF36 results at final follow-up

Author (date) [study arm]	PCS	MCS	GH	PF	RP	RE	SF	BP	V	MH
Clinton (2015) [WFPB] [30] †	7.44	9.97	7.15	7.11	9.29	7.97	10.47	8.61	11.97	9.48
Clinton (2015) [Control] [30] †	1.31‡	6.87	2.01 ‡	1.02 ‡	2.65 ‡	5.05	5.08	5.41	5.49 ‡	6.46

† change from baseline to 6 weeks, T score

‡ p<0.05, WFPB vs control

BP = bodily pain, GH = general health, MCS = mental component score, MH = mental health, PCS = physical component score, PF = physical function, RE = role emotional, RP = role physical, SF = social functioning, V = vitality, WFPB = whole food plant based

Supplementary table 18 – Mediterranean diet and OA progression, results

Table – Mediterranean diet (OA), results and quality assessment

Outcome	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	AMSTAR2 quality	Rand. Seq.	Alloc. Conc.	Blind. Part.	Blind. Asses.
Function	Dyer (2017) [RCT] [29]	Med diet vs control at 4 months SMD -0.18 (-0.58, 0.22)	AIMS2 function, BL / 4 months, mean (SD) Med diet: 1.7 (1.5) / 1.6 (1.4) Control: 2.0 (1.9) / 1.9 (1.9)		H/UC	H/UC	H/UC	H/UC
Affect	Dyer (2017) [RCT] [29]	Med diet vs control at 4 months SMD -0.14 (-0.54, 0.25)	AIMS2 affect, BL / 4 months, mean (SD) Med diet: 2.7 (1.8) / 2.6 (2.0) Control: 3.4 (2.1) / 2.9 (2.2)		H/UC	H/UC	H/UC	H/UC

AIMS2 = Arthritis Impact and Measurement Scales 2, Alloc. Conc. = allocation concealment, AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews, BL = baseline, Blind. Asses. = Blinded assessors, Blind. Part. = blinded participants, CI = confidence interval, H/UC = high / unclear risk of bias, L = low risk of bias, med = Mediterranean, OA = osteoarthritis, Rand. Seq. = random sequence generation, RCT = randomised controlled trial, SD = standard deviation, SMD = Standardised mean difference

Supplementary table 19 – Description of studies of food components in OA

Table – Food components (OA), description of included studies

Author (date) [country]	Study design	Type of OA	Inclusion criteria	Exposure detail	N	Age, mean (SD) years	N (%) female	Funders
Dai (2017) [USA] [34]	Pros. Cohort	Knee	Osteoarthritis Initiative, aged 45-79 years, absence of inflammatory arthritis	Fibre intake from food frequency questionnaire (quartiles)	3703	Q1) 59.7 (9.0) Q2) 60.9 (9.1) Q3) 61.8 (9.1) Q4) 62.7 (9.1)	Q1: 1301 (58.1) Q2: 1296 (58.1) Q3: 1286 (57.5) Q4: 1296 (58.0)	**Government** (NIH), **Industry** (OAI: Pfizer, Novartis, Merck, GSK)
Lu (2017) [USA] [35]	Pros. Cohort	Knee	Osteoarthritis Initiative, aged 45-79 years, all have radiographic OA in at least one knee Exclusion: severe OA (KL grade = 4), difference of rim distance from tibial plateau to tibial rim closest to femoral condyle between baseline and any follow ≥2 mm	Fat intake from food frequency questionnaire (quartiles)	2092	Q1) 64.2 (8.7) Q2) 62.8 (9.0) Q3) 62.3 (9.1) Q4) 60.8 (8.8)	Q1) (60) Q2) (56.9) Q3) (59) Q4) 59.3)	**Government** (National Heart, Lung and Blood Institute, NIH), **Industry** (OAI: Pfizer, Novartis, Merck, GSK)

GSK = GlaxoSmithKline, KL = Kellgren Lawrence, N = number, NIH = National Institute for Health, OA = osteoarthritis, OAI = Osteoarthritis Initiative, pros. = prospective, Q1-4 = quartiles of fibre/fat intake, SD = standard deviation, USA = United States of America

Supplementary table 20 – Food components and OA progression, results

Table – Food components (OA), results and quality assessment

Outcome (outcome measure)	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	Study Pop.	Attr.	Prog. Meas.	Outc. Meas.	Conf.	Stats.
Pain	Dai (2017) [Pros. Obs.] [34]		Odds of being in mild / moderate / severe pain compared to no pain (95% CI) Fibre intake Q2 vs Q1: 1.16 (0.97, 1.39) / 0.92 (0.75, 1.13) / 0.65 (0.48, 0.89) Fibre intake Q3 vs Q1: 0.92 (0.77, 1.10) / 0.85 (0.70, 1.04) / 0.79 (0.59, 1.07) Fibre intake Q4 vs Q1: 1.05 (0.88, 1.26) / 0.76 (0.61, 0.93) / 0.56 (0.41, 0.78)	L	L	M	L	L	L
JSW loss	Lu (2017) [Pros. Obs.] [35]		JSW loss over follow-up, mean (SE) *Total fat* Q1: 0.26 (0.03); Q2: 0.27 (0.02) Q3: 0.31 (0.02); Q4: 0.35 (0.03), p for trend = 0.02 *Saturated fat* Q1: 0.25 (0.03); Q2: 0.26 (0.02) Q3: 0.33 (0.02); 0.37 (0.03) p for trend <0.01 *Monounsaturated fat* Q1: 0.36 (0.02); Q2: 0.29 (0.02); Q3: 0.32 (0.02); Q4: 0.32 (0.02) p for trend = 0.19 *Polyunsaturated fat* Q1: 0.34 (0.02); Q2: 0.31 (0.02); Q3: 0.26 (0.02); Q4: 0.28 (0.02) p for trend = 0.02	L	L	M	L	L	L

Attr. = attrition, CI = confidence interval, Conf. = confounding, JSW = joint space width, L = low risk of bias, M = moderate risk of bias, OA = osteoarthritis, Outc. Meas = outcome measurement, Prog. Meas. = prognostic factor measurement, Q1-4 = quartiles of fibre/fat intake, Rand. Seq. = random sequence generation, SE = standard error, SMD = Standardised mean difference, Stats. = statistical analysis, Study Pop. = study population

Supplementary table 21 – Description of reviews of fruits, vegetables and other plant based interventions in OA

Table – Fruits, vegetables and other plant based interventions (OA), description of reviews

Authors (date)	Review type	Study type included	Type of OA	Exposure detail	Number of studies included	Funders
Liu (2018) [14]	MA	RCTs	Hip, knee or hand	Artemisia Annua extract Avocado / soybean unsaponifiables Boswellia Serrata Bromelain Curcuma Longa Curcumin Passion fruit Pine tree extract	1 2 3 1 1 2 1 2	**Government** (NHMRC program grant, Department of education grant), **Industry** (PuraPharm postgrad scholarship), author disclosures (Flexion, Nestle, Merck)
Daily (2016) [36]	MA	RCTs	Knee	Turmeric extracts and its components	8	**Industry** (Korea Institute of Oriental Medicine), **Author disclosure** (lead author in president of a company that manufactures dietary supplements)
Cameron (2014) [37]	MA	RCTs	Hip, knee or hand	Avocado / soybean unsaponifiables Boswellia Serrata	6 5	**Universities** (Victoria University, University of Freiberg, Australian Catholic University, University of the Sunshine Coast), **Government** (National Center for Complementary and Alternative Medicine)
Percope de Andrade (2015) [38]	SR	RCTs, other reviews	Hip and knee	Avocado / soybean unsaponifiables	4 RCTs, 1 review	**Not reported**, One author disclosed support from Zimmer (medical device company)
McAlindon (2014) [39]	SR	RCTs, other reviews	Knee	Avocado / soybean unsaponifiables	1 meta-analysis	**Professional body** (OARSI)

MA = meta-analysis, NHMRC = National Health and Medical Research Council, OA = osteoarthritis, OARSI = Osteoarthritis Research Society International, RCT = randomised controlled trial , SR = systematic review

Supplementary table 22 – Description of studies of fruits, vegetables and other plant based interventions in OA

Table – Fruits, vegetables and other plant based interventions (OA), description of included studies

Author (date) [country]	Study design	Type of OA	Inclusion criteria	Exposure detail	N	Age, mean (SD) years	N (%) female	Funders
Hashempur (2018) [Iran] [40]	RCT	Knee	Aged 40-75 years, mild-moderate OA (ACR criteria), symptoms for 6 months Exclusions: Severe OA, ischemic heart disease, heart failure, hepatic and renal failure, pregnancy, lactation, history of gastrointestinal bleeding after NSAIDs, hypersensitivity or allergy to caffeine, alkaline drugs or warfarin use, recent initiation of joint protective activity, special diet for weight loss, recent change in physical activity, no ability to express pain.	1) Green tea extract tablets + diclofenac p) Diclofenac only	1) 20 p) 20	1) 56.7 (8.1) p) 53.1 (11.1)	1) 17 (85) p) 15 (75)	**University** (Shiraz University of Medical Sciences)
Salimzadeh (2018) [Iran] [41]	RCT	Knee	Mild to moderate OA, ACR OA criteria, women, aged 50-75 years, post-menopause, BMI 25-40 Exclusions: severe pain, scheduled surgery, intra-articular therapy in last 3 months, NSAIDs or other analgesia, allergic to garlic, diabetes, other chronic disorders, on weight-loss protocol, smokers, HRT, omega-3 supplements, warfarin or other anti-coagulants	1) Odourless garlic tablets, 2x 500mg per day p) Placebo tablets containing lactose	1) 39 p) 37	1) 58.9 (7.5) p) 58.5 (7.4)	1) 39 (100) p) 37 (100)	**University** (Tehran University of Medical Sciences and Health Services)
Essouiri (2017) [Morocco] [42]	RCT	Knee	ACR OA criteria Exclusions: OA due to inflammatory arthritis, microcrystalline aetiology, patient had knee surgery, cancer, KL grade IV	1) Agran oil, 30 ml per day for 8 weeks p) nothing (i.e. no placebo)	1) 51 p) 49	1) 58.2 (8.8) p) 58.9 (5.6)	1) 51 (92.7) p) 49 (94.2) [sic]	Not reported – authors declare to conflicts of interest
Karimifar (2017) [Iran] [43]	RCT	Knee	Aged 40-80 years, knee OA for ≥6 months based on ACR criteria, pain VAS >4cm, Lequesne pain and function index >7, CRP <10, ESR <20, KL grade II-III Exclusions: Liver, renal or cardiac dysfunction, intra-articular steroids or hyaluronic acid within last 3 months, all other bone and joint disorders, peptic ulcer disease, knee arthroscopic procedure within last 3 months, pregnancy, lactation	1) Elaeagnus angustifolia capsule 2) Elaeagnus angustifolia capsule and Boswellia Thurifera capsules p) Control	1) 23 2) 26 p) 26	1) 52.7 (11.1) 2) 52.0 (8.7) p) 53.0 (8.6)	1) 21 (91.3) 2) 23 (88.5) p) 22 (84.6)	**Industry** (Barij Essence Pharmaceutical Company)

ACR = American College of Rheumatology, BMI = body mass index, CRP = C-reactive protein, ESR = erythrocyte sedimentation rate, HRT = hormone replacement therapy, KL = Kellgren-Lawrence, ml = millilitre, N = number, NSAID = Non-steroidal anti-inflammatory drugs, OA = osteoarthritis, RCT = randomised controlled trial, SD = standard deviation, VAS = visual analogue scale

Table – Fruits, vegetables and other plant based interventions (OA), description of included studies

Author (date) [country]	Study design	Type of OA	Inclusion criteria	Exposure detail	N	Age, mean (SD) years	N (%) female	Funders
More (2017) [Germany] [44]	RCT	Knee	Aged 30-70 years, moderate pain (WOMAC 4-8) Exclusions: pregnancy, knee pain for other reasons, allergies to study materials, serious disease, ingestion of other supplements, treatment with cartilage protecting medicine, steroids, NSAIDs (other than ASA, diclofenac or paracetamol), cortisone treatment in last 3 weeks, opioids, medication/alcohol/drug abuse, Acute meniscus injuries, Rheumatoid arthritis, Infection-associated arthritis, bone injury in lower extremities in last 12 months, disc prolapse, arthroscopic surgery in last 6 months, magnetics, shockwave or acupuncture therapy, simultaneous participation in another study, relationship with sponsor or investigator	1) Rose-Canina mix (fruit puree, U. dioica L. leaf dry extract, H. procumbens (Burch.) DC. Ex Meisn. or H. zeyheri Decne. (both species can be used for devil's claw preparations [28]) root dry extract) in liquid form p) vegetable juice mix (olive oil, basil, vegetable juice concentrates)	1) 46 p) 44	1) 57.9 (8.3) p) 55.7 (9.3)	1) 34 (73.9) p) 33 (75.0)	**Industry** (Herbalist & Doc Gesundheitsgesellschaft mbH)
Rafraf (2017) [Iran] [45]	RCT	Knee	Women, aged 38-60 years, mild-moderate OA (ACR criteria), BMI 30-35 Exclusions: cardiovascular disease, diabetes, liver and kidney diseases, peptic or duodenal ulcer history, smoking, alcohol use, use of supplements (e.g. multivitamins, minerals) in past 4 weeks, allergy to pomegranate, use of NSAIDs	1) Dried pomegranate peel ground into powder and put into capsules p) Placebo capsules filled with rice flower	1) 30 p) 30	1) 48.7 (7.8) p) 52.2 (6.7)	1) 30 (100) p) 30 (100)	**University** (Tabriz University of Medical Sciences)
Ghoochani (2016) [Iran] [46]	RCT	Knee	ACR criteria, aged 30-80 years Exclusions: rheumatoid arthritis, diabetes, cardiovascular, liver or renal disease, cancer, consumption of antioxidants, pregnancy, treatment with oral/injectable steroids within 4 weeks or 6 months respectively	1) 200ml sugar and additive free pomegranate juice p) followed usual lifestyle	1) 19 p) 19	1) 56.7 (10.2) p) 53.8 (12.0)	1) 17 (89.5%) p) 17 (89.5%)	**University** (Ahvaz Jundishapur University of Medical Sciences)
Haghighian (2015) [Iran] [47]	RCT	Knee	Aged 50-70 years, mild to moderate OA (ACR crit) Exclusions: KL grade 1 or 4, BMI >35, cardiovascular disease, diabetes, liver or kidney disease, history of peptic or duodenal ulcers, smoking, alcohol use, use of supplements (e.g. multivitamins, minerals), allergy to sesame, using NSAIDs.	1) Sesame seed powder in 40g packs p) Placebo powder	1) 22 p) 23	1) 56.9 (6.4) p) 58.3 (7.8)	not reported	**University** (Tabriz University of Medical Sciences)

ACR = American College of Rheumatology, BMI = body mass index, KL = Kellgren-Lawrence, N = number, NSAID = non-steroidal anti-inflammatory drug, OA = osteoarthritis, RCT = randomised controlled trial, SD = standard deviation, WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index

Table – Fruits, vegetables and other plant based interventions (OA), description of included studies

Author (date) [country]	Study design	Type of OA	Inclusion criteria	Exposure detail	N	Age, mean (SD) years	N (%) female	Funders
Arjmandi (2014) [USA] [48]	RCT	Knee	Overweight or obese, aged 40-90 years, KL grade I-III Exclusions: history of liver / kidney disease or any other chronic or acute disease that might affect OA, allergy to shellfish or naproxen, knee surgery or significant injury in last 6 months, hyaluronan or cortisone injections in last 2 months	1) Capsules containing extracts of S. Baicalensis and A. Catechu p) Naproxen	1) 45 p) 34	1) 63.8 (2.1) p) 60.9 (1.8	1) 35 (77.7) p) 26 (76.5)	**Industry** (Unigen, Inc.)
Ebrahimi (2014) [Iran] [49]	RCT	Knee	Mild to moderate OA, ACR criteria, female, aged 40-70 years, BMI 25-34.9 Exclusions: Secondary OA, active synovitis, neurological disorder affecting movement, uncontrolled hypertension, diabetes, CVD, kidney disorder, liver disorder, taking supplements, smokers	Elaeagnus angustifolia (Russian Olive) 1) whole fruit powder 2) powder made just from medulla p) placebo made of corn starch	1) 26 2) 27 p) 25	1) 57.5 (7.2) 2) 54.5 (11.2) p) 57 (7.8)	1) 26 (100) 2) 27 (100) p) 25 (100)	**University** (Tabriz University)
Eftekhar Sadat (2013) [Iran] [50]	RCT	Knee	Aged 50-70 years, mild to moderate OA (ACR crit) Exclusions: BMI >30 or <18.5, cardiovascular disease, history of peptic or duodenal ulcers, smoking, alcohol use, use of supplements (e.g. multivitamins, minerals), allergy to sesame.	1) Sesame seed powder in 40g packs p) Standard drug therapy (no placebo)	1) 22 p) 23	not reported	81.82%	**University** (Tabriz University of Medical Sciences)
Paramdeep (2013) [India][51]	RCT (open label)	Knee	ACR Knee OA criteria, Knee pain 40-90mm on VAS Exclusions: cardiovascular disease, hypertension, gastroduodenal disorders, diabetes, hepatic or renal impairment, bleeding disorders, pregnancy	1) diclofenac + placebo (lactose tablet) 2) 750mg tablet of ginger + placebo 3) diclofenac + ginder	1) 20 2) 20 3) 20	1) 54.8 (9.7) 2) 52.9 (8.1) 3) 50.1 (11.3)	1) 14 (70%) 2) 12 (60%) 3) 14 (70%)	Not reported
Schumacher (2013) [USA] [52]	RCT (cross-over)	Knee	Aged >18 years, mild-moderate OA that meets ACR criteria Exclusions: systemic inflammatory conditions, chronic pain syndrome, steroid medication in last two months, hyaluronic acid injection in last 9 months, pregnancy, diabetes, inability to stop arthritis medication, food allergy, unstable medical conditions that would prevent completion	1) Cherry juice – prepared by mixing freshly prepared tart cherry juice with apple juice p) Placebo juice – unsweetened black cherry Kool-aid soft drink with water	58	57 (11)	14 (24.1)	**Industry** (CherryPharm)

ACR = American College of Rheumatology, BMI = body mass index, CVD = cardiovascular disease, KL = Kellgren-Lawrence, N = number, OA = osteoarthritis, RCT = randomised controlled trial, SD = standard deviation, USA = United States of America, VAS = visual analogue scale

Table – Fruits, vegetables and other plant based interventions (OA), description of included studies

Author (date) [country]	Study design	Type of OA	Inclusion criteria	Exposure detail	N	Age, mean (SD) years	N (%) female	Funders
Kuehl et al 2012 [USA] [53]	RCT	not reported	Aged 40-70 years, at least moderate OA pain (>40mm VAS), 1990 ACR OA criteria, ability to maintain intervention, willingness to take drug Exclusions: diabetes, not on stable pain medication, used non-pharmacological pain medication within last 30 days (e.g. acupuncture, ultrasound etc.)	1) Cherry juice – consumed two 10.5 oz bottles per day. 1 bottle = 50-60 cherries p) Placebo juice – unsweetened cherry flavoured drink mixed with water. Cherry syrup and lemon juice added to match tartness	1) 10 p) 10	1) 55.9 (9.1) p) 52.3 (14.2)	1) 10 (100) p) 10 (100)	**Industry** (Cherry Research Committee), **University** (Oregon Clinical and Translational Research)
Myers (2010) [Australia] [54]	RCT	Knee	Aged 18-65, COAT score 3-7, willing to stop OA treatment Exclusions: history of trauma with the affected joint, inflammatory joint conditions, steroid use in last 4 weeks, anti-inflammatory agents or anti-arthritic complementary therapy in last 3 weeks, liver function tests >3ULN, history of alcohol / substance abuse, lactating, pregnant, participated in another clinical trial in last 30 days, unwilling to have blood taken	1) 100mg of seaweed extracts 2) 1000mg of seaweed extracts Interventions also included vitamin B6, zinc sulphate and manganese sulphate in formulation	1) 5 2) 7	Women: 61.2 (9.0) Men: 57.1 (9.2)	6 (50)	**Industry** (Marinova Pty Ltd)
Frestedt (2009) [USA][55]	RCT	Knee	Ambulatory, aged 35-75, normal digestion, moderate-severe OA, met ACR criteria, WOMAC total ≤75, taking NSAIDs Exclusion: rheumatoid arthritis, gout, Paget's disease, seizure disorder, diabetes, hypertension, cardiovascular disease, hepatic or renal disease, active cancer, HIV, prescription pain medication, involved in another clinical trial in past 3 months, lactating or at risk of pregnancy, intramuscular / systematic steroids within 1 month, intra-articular steroids within 2 months, hyaluronic acid within 4 months	1) Capsules of aquamin p) Placebo capsules (maltodextran)	1) 8 p) 14	1) 62.5 (5.3) p) 62.9 (11.4)	1) 7 (88) p) 8 (57)	**Industry** (Marigot Ltd)
Oben (2009) [Cameroon] [56]	RCT	Knee	Aged 25-60 years, primary OA using ACR criteria Exclusions: BMI >40, rheumatoid arthritis, joint replacement in either knee, unable to walk without assistance, enrolment in another clinical study in last 6 months, pregnancy, active infection, autoimmune disease, AIDS, HIV, active hepatitis, active malignancy, diabetes requiring insulin	1) Tablets containing blend of phellodendron amurense extract and citrus sinensis (L.) Osbeck [Rutaceae] peel extract p) placebo capsules	1ov §) 20 1n §) 20 pov §) 20 pn §) 20	Not reported	not reported	**Industry** (Next Pharmaceuticals)

ACR = American College of Rheumatology, AIDS = acquired immune deficiency syndrome, BMI = body mass index, COAT = comprehensive arthritis test, HIV = human immunodeficiency virus, N = number, NSAID = non-steroidal anti-inflammatory drugs, OA = osteoarthritis, RCT = randomised controlled trial, SD = standard deviation, ULN = upper limit of normal, USA = United States of America, VAS = visual analogue scale, WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index

Table – Fruits, vegetables and other plant based interventions (OA), description of included studies

Author (date) [country]	Study design	Type of OA	Inclusion criteria	Exposure detail	N	Age, mean (SD) years	N (%) female	Funders
Rein (2004) [Denmark] [57]	RCT	Various joints	X-ray verified OA Exclusions: liver or kidney disease, allergies, drug/alcohol abuse, cancer, rheumatoid arthritis, fibromyalgia, gout, serious cardiovascular disease, asthma, any other disease that will reduce QoL, intra-articular hyaluroante, glucosamine sulphate, immunosuppressive drugs, steroids in past 6 weeks	1) Capsules of rose-canina fruit p) identical placebo capsules	1) 56 p) 56	1) 67.1 (11.6) p) 66.8 (11.8)	1) 37 (66.1) p) 34 (60.7)	**Industry** (Hyben Vital International)
Warholm (2003) [Norway] [58]	RCT	Knee and hip	Radiographic OA, symptom duration <12 months, pain for >6 months or on list for surgery Exclusions: Allergy to plant products, severe asthma, liver disease	1) capsules of powder produced from rose-canina fruit and seeds p) placebo capsules	1) 50 p) 50	1) 63.3 (9.9) p) 65.1 (12.2)	1) 31 (62.0) p) 34 (68.0)	**Industry** (Hyben Vital International)
Piscoya (2001) [Peru] [59]	RCT	Knee	Aged 45-75 years, KL grade II-III, ACR criteria, pain most days of last month, requiring NSAID treatment Exclusions: serious concomitant illness, secondary OA, hypersensitivity reactions to salicylates, intra-articular injection of steroids in last 3 months	1) Uncaria guianensis (Cat's Claw) extract in tablets p) Placebo tablets	1) 30 p) 15	1) 59.9 (8.4) p) 60.9 (6.5)	1) 0 (0) p) 0 (0)	**Government** (Seguro Social del Peru, NIH)
Hunt (2016) [New Zealand] [60]	Single arm int.	Hip or knee	Hip or knee OA	Artemisia annua	28	62 (range 45-75)	16 (47.1)	**Industry** (Promisia Ltd)

ACR = American College of Rheumatology, KL = Kellgren-Lawrence, N = number, NSAID = Non-steroid anti-inflammatory drugs, OA = osteoarthritis, QoL = quality of life, RCT = randomised controlled trial, SD = standard deviation

Supplementary table 23 – Aquamin and OA progression, results

Table – Aqumin (red mineral algae) (OA), results and quality assessment

Outcome	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	AMSTAR2 quality	Rand. Seq.	Alloc. Conc.	Blind. Part.	Blind. Asses.
Pain	Frestedt (2009) [RCT][55]	Aquamin vs placebo, change BL-12 weeks SMD 0.34 (-0.54, 1.21)	WOMAC pain, change from BL – 12 weeks, mean (SD*) Aquamin: 10.83 (23.48) Placebo: 5.38 (10.48); p=0.63		L	L	L	L
Function	Frestedt (2009) [RCT][55]	Aquamin vs placebo, change BL-12 weeks SMD 0.50 (-0.39, 1.38)	WOMAC function, change from BL – 12 weeks, mean (SD*) Aquamin: 14.72 (25.57) Placebo: 6.54 (8.08); p=0.43		L	L	L	L
Stiffness	Frestedt (2009) [RCT][55]	Aquamin vs placebo, change BL-12 weeks SMD 0.23 (-0.65, 1.10)	WOMAC stiffness, change from BL – 12 weeks, mean (SD*) Aquamin: 10.42 (35.84) Placebo: 4.81 (16.35); p=0.83		L	L	L	L
6MWT	Frestedt (2009) [RCT][55]	Aquamin vs placebo, change BL-12 weeks SMD 1.11 (0.17, 2.04)	6MWT, change from BL – 12 weeks, mean (SD*) Aquamin: 150 (135.76) Placebo: 12.5 (117.86); p=0.03		L	L	L	L

* Calculated from standard error reported in the paper; 6MWT = six minute walk test, Alloc. Conc. = allocation concealment, AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews, BL = baseline, Blind. Asses. = Blinded assessors, Blind. Part. = blinded participants, CI = confidence interval, H/UC = high / unclear risk of bias, L = low risk of bias, OA = osteoarthritis, Rand. Seq. = random sequence generation, RCT = randomised controlled trial, SD = standard deviation, SMD = Standardised mean difference, WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index

Supplementary table 24 – Argan oil and OA progression, results

Table – Argan oil (OA), results and quality assessment

Outcome	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	AMSTAR2 quality	Rand. Seq.	Alloc. Conc.	Blind. Part.	Blind. Asses.
Pain	Essouiri (2017) [RCT] [42]	Pain at 8 weeks SMD -0.28 (-0.67, 0.11)	WOMAC pain, BL / 8 weeks, mean (SD) Argan oil: 6.55 (4.17) / 4.86 (3.93) Control: 5.2 (3) / 5.84 (3); p<0.0001		L	H/UC	H/UC	H/UC
Function	Essouiri (2017) [RCT] [42]	Function at 8 weeks SMD -0.72 (-1.21, -0.31)	WOMAC function, BL / 8 weeks, mean (SD) Argan oil: 15.73 (7.62) / 11.71 (6.33) Control: 14 (6.41) / 16.2 (6.2); p<0.0001		L	H/UC	H/UC	H/UC
Stiffness	Essouiri (2017) [RCT] [42]	Stiffness at 8 weeks SMD -0.27 (-0.66, 0.13)	WOMAC stiffness, BL / 8 weeks, mean (SD) Argan oil: 3.86 (2.5) / 3.69 (3.46) Control: 3.82 (2.21) / 4.45 (2); p=0.1		L	H/UC	H/UC	H/UC

Alloc. Conc. = allocation concealment, AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews, BL = baseline, Blind. Asses. = Blinded assessors, Blind. Part. = blinded participants, CI = confidence interval, H/UC = high / unclear risk of bias, L = low risk of bias, OA = osteoarthritis, Rand. Seq. = random sequence generation, RCT = randomised controlled trial, SD = standard deviation, SMD = Standardised mean difference, WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index

Supplementary table 25 – Artemisia Annua and OA progression, results

Table – Artemisia Annua (OA), results and quality assessment

Outcome	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	AMSTAR2 quality	Rand. Seq.	Alloc. Conc.	Blind. Part.	Blind. Asses.
Pain	Liu (2018) [MA] [14]	Artemisia annua vs placebo SMD -0.37 (-1.03, 0.29)		Moderate				
	Hunt (2016) [Single arm] [60]		WOMAC pain, BL / 36 weeks, mean (SD) 8.6 (3.0) / 5.9 (4.0)					
Function	Liu (2018) [MA] [14]	Artemisia annua vs placebo SMD -0.15 (-0.81, 0.50)		Moderate				
	Hunt (2016) [Single arm] [60]		WOMAC function, BL / 36 weeks, mean (SD) 28.6 (21.2) / 21.9 (15.1)					
Stiffness	Hunt (2016) [Single arm] [60]		WOMAC stiffness, BL / 36 weeks, mean (SD) 3.9 (1.6) / 3.3 (7.2)					

Alloc. Conc. = allocation concealment, AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews, BL = baseline, Blind. Asses. = Blinded assessors, Blind. Part. = blinded participants, CI = confidence interval, H/UC = high / unclear risk of bias, L = low risk of bias, MA = meta-analysis, OA = osteoarthritis, Rand. Seq. = random sequence generation, SD = standard deviation, SMD = Standardised mean difference, WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index

Supplementary table 26 – Avocado / soybean unsaponifiables and OA progression, results

Table – Avocado / soybean unsaponifiables (OA), results and quality assessment

Outcome	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	AMSTAR2 quality	Rand. Seq.	Alloc. Conc.	Blind. Part.	Blind. Asses.
Pain	Liu (2018) [MA] [14]	ASU vs placebo Short term: SMD -0.57 (-0.95, -0.19)		Moderate				
	Cameron (2014) [MA] [37]	ASU vs placebo -8% (-16%, -1%) reduction		High				
	Percope de Andrade (2015) [SR] [38]		1/4 RCTs showed reductions in pain, 1 review did not support symptom modifying effect of ASU	Moderate				
	McAlindon (2014) [SR] [39]	ASU vs placebo 1 MA from 2008: SMD 0.39 (0.76, 0.01)		Moderate				
Function	Liu (2018) [MA] [14]	ASU vs placebo Short term: SMD -0.48 (-0.69, -0.28)		Moderate				
	Cameron (2014) [MA] [37]	ASU vs placebo -7% (-12%, -2%) reduction		High				

Alloc. Conc. = allocation concealment, AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews, ASU = Avocado / soybean unsaponifiables, Blind. Asses. = Blinded assessors, Blind. Part. = blinded participants, CI = confidence interval, H/UC = high / unclear risk of bias, L = low risk of bias, MA = meta-analysis, OA = osteoarthritis, Rand. Seq. = random sequence generation, RCT = randomised controlled trial, SMD = Standardised mean difference, SR = systematic review

Supplementary table 27 – Boswellia serrata and OA progression, results

Table – Boswellia Serrata (OA), results and quality assessment

Outcome	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	AMSTAR2 quality	Rand. Seq.	Alloc. Conc.	Blind. Part.	Blind. Asses.
Pain	Liu (2018) [MA] [14]	Boswellia serrata vs placebo Short term: SMD -1.61 (-2.10, -1.13)		Moderate				
	Cameron (2014) [MA] [37]	Boswellia serrata vs placebo Pain rated 17 points lower (8, 26) on 0-100 point scale		High				
Function	Liu (2018) [MA] [14]	Boswellia serrata vs placebo Short term: SMD -1.15 (-1.63, -0.68)		Moderate				
	Cameron (2014) [MA] [37]	Boswellia serrata vs placebo Function rated 8 points better (2, 14) on 100 point scale		High				

Alloc. Conc. = allocation concealment, AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews, Blind. Asses. = Blinded assessors, Blind. Part. = blinded participants, CI = confidence interval, H/UC = high / unclear risk of bias, L = low risk of bias, MA = meta-analysis, OA = osteoarthritis, Rand. Seq. = random sequence generation, SMD = Standardised mean difference

Supplementary table 28 – Bromelain and OA progression, results

Table – Bromelain (OA), results and quality assessment

Outcome	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	AMSTAR2 quality	Rand. Seq.	Alloc. Conc.	Blind. Part.	Blind. Asses.
Pain	Liu (2018) [MA] [14]	Bromelain vs placebo Short term: SMD -0.05 (-0.75, 0.64)		Moderate				
Function	Liu (2018) [MA] [14]	Bromelain vs placebo Short term: SMD -0.34 (-1.04, 0.36)		Moderate				

Alloc. Conc. = allocation concealment, AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews, Blind. Asses. = Blinded assessors, Blind. Part. = blinded participants, CI = confidence interval, MA = meta-analysis, OA = osteoarthritis, Rand. Seq. = random sequence generation, SMD = Standardised mean difference

Supplementary table 29 – Cherry juice and OA progression, results

Table – Cherry juice (OA), results and quality assessment

Outcome	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	AMSTAR2 quality	Rand. Seq.	Alloc. Conc.	Blind. Part.	Blind. Asses.
Pain	Schumacher (2013) [RCT] [52]	Cherry juice vs placebo at 6 weeks SMD -0.14 (-0.55, 0.27)	WOMAC pain, BL / 6 weeks, mean (SD) Cherry juice: 42.1 (22.9) / 36.3 (27) Placebo: 41.5 (24.4) / 40.0 (26.6); p=0.24		L	H/UC	L	L
Function	Schumacher (2013) [RCT] [52]	Cherry juice vs placebo at 6 weeks SMD -0.21 (-0.62, 0.20)	WOMAC function, BL / 6 weeks, mean (SD) Cherry juice: 46.9 (23.7) / 39.1 (25.9) Placebo: 46.7 (24.0) / 44.7 (27.2); p=0.13		L	H/UC	L	L
Stiffness	Schumacher (2013) [RCT] [52]	Cherry juice vs placebo at 6 weeks Cherry juice 1st: SMD -0.11 (-0.68, 0.47) Cherry juice 2nd: SMD -0.11 (-0.69, 0.47) [Comparing change scores of cherry juice first was significant in paper]	WOMAC stiffness, BL / 6 weeks, mean (SD) Cherry juice 1st: 51.1 (29.3) / 39.1 (30.1) Placebo: 39.5 (34.3) / 42.4 (32.8) ; p=0.048 Cherry juice 2nd: 48.3 (25.8) / 44.0 (28.5) Placebo: 55.1 (19.8) / 47.0 (26.8) § p=0.29		L	H/UC	L	L
CRP	Schumacher (2013) [RCT] [52]	Cherry juice vs placebo at 6 weeks SMD -0.92 (-1.35, -0.49)	CRP, BL / 6 weeks, mean (SD) Cherry juice: 2.38 (1.83) / 1.98 (1.73) Placebo: 2.99 (2.39) / 4.21 (2.98)		L	H/UC	L	L
	Kuehl (2012) [RCT]	Cherry juice vs placebo at 21 days SMD 0.05 (-0.82, 0.93)	CRP, BL / 21 days, mean (SD) Cherry juice: 7.19 (6.67) / 3.77 (4.57) Placebo: 2.61 (3.32) / 3.55 (3.56) change score p=0.016		H/UC	H/UC	L	L
	Bespoke MA of: Schumacher 2013 Kuehl 2012	Cherry juice vs placebo Meta-SMD -0.51 (-1.45, 0.43) I^2 73.6%						

§ stiffness in twice as the intervention x time interaction was significant (cross-over trial)

Alloc. Conc. = allocation concealment, AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews, BL = baseline, Blind. Asses. = Blinded assessors, Blind. Part. = blinded participants, CI = confidence interval, CRP = C-Reactive Protein, H/UC = high / unclear risk of bias, L = low risk of bias, MA = meta-analysis, OA = osteoarthritis, Rand. Seq. = random sequence generation, RCT = randomised controlled trial, SD = standard deviation, SMD = Standardised mean difference, WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index

Supplementary table 30 – Curcuma longa and OA progression, results

Table – Curcuma longa, results and quality assessment

Outcome	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	AMSTAR2 quality	Rand. Seq.	Alloc. Conc.	Blind. Part.	Blind. Asses.
Pain	Liu (2018) [MA] [14]	Curcuma longa vs placebo Short term: SMD -1.63 (-2.22, -1.03)		Moderate				
Function	Liu (2018) [MA] [14]	Curcuma longa vs placebo Short term: SMD -1.27 (-1.83, -0.70)		Moderate				

Alloc. Conc. = allocation concealment, AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews, Blind. Asses. = Blinded assessors, Blind. Part. = blinded participants, CI = confidence interval, H/UC = high / unclear risk of bias, L = low risk of bias, MA = meta-analysis, OA = osteoarthritis, Rand. Seq. = random sequence generation, SMD = Standardised mean difference

Supplementary table 31 – Curcumin and OA progression, results

Table – Curcumin (OA), results and quality assessment

Outcome	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	AMSTAR2 quality	Rand. Seq.	Alloc. Conc.	Blind. Part.	Blind. Asses.
Pain	Liu (2018) [MA] [14]	Curcumin vs placebo Short term: SMD -1.19 (-1.93, -0.45)		Moderate				
Function	Liu (2018) [MA] [14]	Curcumin vs placebo Short term: SMD -1.13 (-1.80, -0.46)		Moderate				

Alloc. Conc. = allocation concealment, AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews, Blind. Asses. = Blinded assessors, Blind. Part. = blinded participants, CI = confidence interval, MA = meta-analysis, OA = osteoarthritis, Rand. Seq. = random sequence generation, SMD = Standardised mean difference

Supplementary table 32 – Fruit powder and OA progression, results

Table – Fruit powder (OA), results and quality assessment

Outcome	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	AMSTAR2 quality	Rand. Seq.	Alloc. Conc.	Blind. Part.	Blind. Asses.
Pain	Ebrahimi (2014) [RCT] [49]	Whole fruit powder vs placebo at 8 weeks SMD -0.39 (-0.94, 0.17) Medulla powder vs placebo at 8 weeks SMD -0.51 (-1.06, 0.05)	WOMAC pain, BL / 8 weeks, mean (SD) Whole fruit: 9.08† (4.58) / 7.62 (4.67) Medulla: 9.75 (5.54) / 7.04 (4.92) Placebo: 9.95 (3.71) / 9.30 (3.93)		L	L	L	L
	Karimifar (2017) [RCT] [43]	Elaeagnus angustifoli vs control at 4 weeks SMD -0.37 (-0.94, 0.19) Elaeagnus angustifoli + Boswellia Thurifera vs control at 4 weeks SMD -0.25 (-0.80, 0.29)	Pain VAS, BL / 4 weeks, mean (SD) Elaeagnus angustifoli: 7.04 (1.15) / 4.65 (1.84) Elaeagnus angustifolia + Boswellia Thurifera: 7.03 (1.36) / 4.84 (1.96) Control: 7.01 (1.25) / 5.30 (1.66); p=0.304		H/UC	H/UC	H/UC	H/UC
Function	Ebrahimi (2014) [RCT] [49]	Whole fruit powder vs placebo at 8 weeks SMD -0.32 (-0.87, 0.24) Medulla powder vs placebo at 8 weeks SMD -0.67 (-1.23, -0.11)	WOMAC function, BL / 8 weeks, mean (SD) Whole fruit: 23.66 (13.82) / 20.9 (13.96) Medulla: 24.20 (12.12) / 17.78 (10.01) Placebo: 25.91 (10.17) / 24.91 (11.16)		L	L	L	L
	Karimifar (2017) [RCT] [43]	Elaeagnus angustifoli vs control at 4 weeks SMD -0.35 (-0.91, 0.22) Elaeagnus angustifoli + Boswellia Thurifera vs control at 4 weeks SMD -0.07 (-0.62, 0.47)	LPFI, BL / 4 weeks, mean (SD) Elaeagnus angustifoli: 12.47 (2.88) / 8.32 (3.25) Elaeagnus angustifolia + Boswellia Thurifera: 12.69 (3.35) / 9.09 (4.18) Control: 12.84 (2.73) / 9.34 (2.66); p=0.578		H/UC	H/UC	H/UC	H/UC
Stiffness	Ebrahimi (2014) [RCT] [49]	Whole fruit powder vs placebo at 8 weeks SMD -0.22 (-0.77, 0.33) Medulla powder vs placebo at 8 weeks SMD -0.24 (-0.78, 0.31)	WOMAC stiffness, BL / 8 weeks, mean (SD) Whole fruit: 3.21 (2.08) / 2.56 (2.14) Medulla: 4 (2.6) / 2.5 (2.34) Placebo: 3.66 (2.63) / 3.08 (2.61)		L	L	L	L
Patient global	Karimifar (2017) [RCT] [43]	Elaeagnus angustifoli vs control at 4 weeks SMD -0.24 (-0.80, 0.33) Elaeagnus angustifoli + Boswellia Thurifera vs control at 4 weeks SMD -0.64 (-1.20, -0.08)	Patient global VAS, BL / 4 weeks, mean (SD) Elaeagnus angustifoli: 1.44 (0.62) / 2.38 (0.43) Elaeagnus angustifolia + Boswellia Thurifera: 1.50 (0.68) / 2.17 (0.46) Control: 1.79 (0.64) / 2.50 (0.57); p=0.202		H/UC	H/UC	H/UC	H/UC

†written in the paper as 90.08 – assumed this was a missprint

Alloc. Conc. = allocation concealment, AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews, BL = baseline, Blind. Asses. = Blinded assessors, Blind. Part. = blinded participants, CI = confidence interval, H/UC = high / unclear risk of bias, L = low risk of bias, LPFI = Lequesne pain and function index, OA = osteoarthritis, Rand. Seq. = random sequence generation, RCT = randomised controlled trial, SD = standard deviation, SMD = Standardised mean difference, VAS = visual analogue scale, WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index

Supplementary table 33 – Garlic and OA progression, results

Table – Garlic (OA), results and quality assessment

Outcome	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	AMSTAR2 quality	Rand. Seq.	Alloc. Conc.	Blind. Part.	Blind. Asses.
Pain	Salimzadeh (2018) [RCT] [41]	Garlic vs placebo at 12 weeks SMD 0.03 (-0.43, 0.47)	WOMAC pain baseline / 12 weeks, mean (SD) Garlic: 8.3 (3.7) / (4.4) Placebo: 9.6 (3.1) / 6.9 (3.7); p=0.475		L	H/UC	L	H/UC
Function	Salimzadeh (2018) [RCT] [41]	Garlic vs placebo at 12 weeks SMD -0.17 (-0.62, 0.28)	WOMAC function at 12 weeks, mean (SD) Garlic: 27.7 (11.9) / 22.2 (12.4) Placebo: 27.8 (10.8) / 24.1 (10.2); p=0.221		L	H/UC	L	H/UC
Stiffness	Salimzadeh (2018) [RCT] [41]	Garlic vs placebo at 12 weeks SMD -0.63 (-1.09, -0.17)	WOMAC stiffness at 12 weeks, mean (SD) Garlic: 2.3 (1.6) / 1.4 (1.6) Placebo: 2.7 (1.9) / 2.5 (1.9); p=0.023		L	H/UC	L	H/UC

Alloc. Conc. = allocation concealment, AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews, Blind. Asses. = Blinded assessors, Blind. Part. = blinded participants, CI = confidence interval, H/UC = high / unclear risk of bias, L = low risk of bias, OA = osteoarthritis, Rand. Seq. = random sequence generation, RCT = randomised controlled trial, SD = standard deviation, SMD = Standardised mean difference, WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index

Supplementary table 34 – Ginger and OA progression, results

Table – Ginger (OA), results and quality assessment

Outcome	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	AMSTAR2 quality	Rand. Seq.	Alloc. Conc.	Blind. Part.	Blind. Asses.
Pain †	Paramdeep (2013) [RCT] [51]		Pain VAS, % improvement from BL to 12 weeks Diclofenac: 60.31% Ginger: 59.11% Ginger + diclofenac: 66.77%		H/UC	H/UC	H/UC	H/UC
WOMAC total	Paramdeep (2013) [RCT] [51]		WOMAC total, % improvement from BL to 12 weeks Diclofenac: 74.83% Ginger: 63.68% Ginger + diclofenac: 79.43%		H/UC	H/UC	H/UC	H/UC

† inclusion criteria states that the VAS used is a pain VAS, but for the rest of the paper the instrument is just referred to as the VAS – assuming that it is still measuring pain

Alloc. Conc. = allocation concealment, AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews, BL = baseline, Blind. Asses. = Blinded assessors, Blind. Part. = blinded participants, CI = confidence interval, H/UC = high / unclear risk of bias, L = low risk of bias, OA = osteoarthritis, Rand. Seq. = random sequence generation, RCT = randomised controlled trial, SMD = Standardised mean difference, VAS = visual analogue scale, WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index

Supplementary table 35 – Green tea extract and OA progression, results

Table – Green tea extract (OA), results and quality assessment

Outcome	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	AMSTAR2 quality	Rand. Seq.	Alloc. Conc.	Blind. Part.	Blind. Asses.
Pain	Hashempur (2018) [RCT] [40]	Green tea vs control at 1 month SMD 0.01 (-0.61, 0.63)	WOMAC pain, BL / 1 month, mean (SD) Green tea: 10.45 (4.87) / 6.70 (4.31) Control: 8.60 (3.42) / 6.65 (2.36); p=0.163		L	H/UC	H/UC	H/UC
Function	Hashempur (2018) [RCT] [40]	Green tea vs control at 1 month SMD -0.13 (-0.75, 0.49)	WOMAC function, BL / 1 month, mean (SD) Green tea: 31.15 (13.55) / 24.70 (13.94) Control: 24.15 (9.73) / 26.15 (7.52); p=0.004		L	H/UC	H/UC	H/UC
Stiffness	Hashempur (2018) [RCT] [40]	Green tea vs control at 1 month SMD -0.13 (-0.75, 0.49)	WOMAC function, BL / 1 month, mean (SD) Green tea: 2.30 (1.86) / 1.65 (1.75) Control: 1.85 (1.78) / 1.85 (1.38); p=0.150		L	H/UC	H/UC	H/UC

Alloc. Conc. = allocation concealment, AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews, BL = baseline, Blind. Asses. = Blinded assessors, Blind. Part. = blinded participants, CI = confidence interval, H/UC = high / unclear risk of bias, L = low risk of bias, OA = osteoarthritis, Rand. Seq. = random sequence generation, RCT = randomised controlled trial, SD = standard deviation, SMD = Standardised mean difference, WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index

Supplementary table 36 – Passion fruit and OA progression, results

Table – Passion fruit (OA), results and quality assessment

Outcome	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	AMSTAR2 quality	Rand. Seq.	Alloc. Conc.	Blind. Part.	Blind. Asses.
Pain	Liu (2018) [MA] [14]	Passion fruit vs placebo Short term : SMD -1.65 (-2.44, -0.86)		Moderate				
Function	Liu (2018) [MA] [14]	Passion fruit vs placebo Short term : SMD -1.55 (-2.33, -0.77)		Moderate				

Alloc. Conc. = allocation concealment, AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews, Blind. Asses. = Blinded assessors, Blind. Part. = blinded participants, CI = confidence interval, H/UC = high / unclear risk of bias, L = low risk of bias, MA = meta-analysis, Rand. Seq. = random sequence generation, SMD = Standardised mean difference

Supplementary table 37 – Pomegranate and OA progression, results

Table – Pomegranate (OA), results and quality assessment

Outcome	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	AMSTAR2 quality	Rand. Seq.	Alloc. Conc.	Blind. Part.	Blind. Asses.
Pain	Rafraf (2017) [RCT] [45]	Pomegranate vs placebo at 8 weeks SMD -0.55 (-1.07, -0.04) ‡	KOOS pain, BL / 8 weeks, mean (SD) † Pomegranate: 47.68 (21.87) / 60.74 (21.55) Placebo: 45.92 (23.47) / 48.14 (23.99); p=0.585		L	L	L	L
	Ghoochani (2016) [RCT] [46]	Pomegranate vs placebo at 6 weeks SMD -0.53 (-1.18, 0.11)	WOMAC pain, BL / 6 weeks, mean (SD) Pomegranate: 7.95 (4.99) / 7.32 (4.95) Placebo: 9.63 (5.37) / 10.05 (5.18); p=0.10		H/UC	H/UC	H/UC	H/UC
	Bespoke MA of: Rafraf 2017 Ghoochani 2016	Pomegranate vs placebo Meta-SMD -0.54 (-0.95, -0.14) I^2 = 0%						
Function	Rafraf (2017) [RCT] [45]	Pomegranate vs placebo at 8 weeks SMD -0.30 (-0.81, 0.21) ‡	KOOS ADL, BL / 8 weeks, mean (SD) † Pomegranate: 55.77 (19.31) / 69.17 (18.98) Placebo: 56.79 (19.87) / 63.53 (18.58); p=0.263		L	L	L	L
	Ghoochani (2016) [RCT] [46]	Pomegranate vs placebo at 6 weeks SMD -0.32 (-0.96, 0.32)	WOMAC function, BL / 6 weeks, mean (SD) Pomegranate: 27.74 (10.56) / 22.53 (11.19) Placebo: 25.47 (14.12) / 26.68 (14.35) p=0.32		H/UC	H/UC	H/UC	H/UC
	Bespoke MA of: Rafraf 2017 Ghoochani 2016	Pomegranate vs placebo Meta-SMD -0.31 (-0.71, 0.09) I^2 = 0%						
QoL	Rafraf (2017) [RCT] [45]	Pomegranate vs placebo SMD 0.18 (-0.32, 0.69) ‡ §	KOOS QoL, BL / 8 weeks, median (IQR) † Pomegranate: 18.75 (4.67 - 37.5) / 31.25 (6.25 - 50.0) Placebo: 37.5 (10.93 - 50.0) / 37.5 (12.5 - 56.25); p=0.548		L	L	L	L

† KOOS here = 0 (extreme problems) & 100 (no problems) – normally the other way round

‡ Effect size reversed here to fit into meta-analysis. Negative SMD = lower pain in treatment group compared to control

§ Mean and SD calculated from the median (IQR) using published formula[61]

ADL = activities of daily living, Alloc. Conc. = allocation concealment, AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews, BL = baseline, Blind. Asses. = Blinded assessors, Blind. Part. = blinded participants, CI = confidence interval, H/UC = high / unclear risk of bias, IQR = interquartile range, KOOS = Knee injury and Osteoarthritis Outcome Score, L = low risk of bias, MA = meta-analysis, OA = osteoarthritis, QoL = quality of life, Rand. Seq. = random sequence generation, RCT = randomised controlled trial, SD = standard deviation, SMD = Standardised mean difference, WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index

Supplementary table 38 – Rose canina mix and OA progression, results

Table – Rose-Canina mix (OA), results and quality assessment

Outcome	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	AMSTAR2 quality	Rand. Seq.	Alloc. Conc.	Blind. Part.	Blind. Asses.
Pain	More (2017) [RCT] [44]	Rose-Canaina vs placebo, change from baseline to 12 weeks SMD -2.49 (-3.04, -1.94)	WOMAC pain, change from BL to 12 weeks, mean (SD) Rose-Canina: -29.87 (10.36) Placebo: -10.23 (3.86); p<0.001		L	L	L	L
	Rein (2004) [RCT] [57]	Rose Canina vs placebo, change from baseline to 3 months Group 1 §: -0.62 (-1.00, -0.24) Group2 §: 0.20 (-0.17, 0.58)	Joint pain (0-4), change from baseline – 3 months, mean (SD) *Group 1 §:* Rose Canina: -1.91 (1.43) Placebo: -1.02 (1.45); p=0.0078 *Group 2 §:* Rose Canina: -1.45 (1.28) Placebo: -1.72 (1.37); p=0.6084		L	L	L	L
	Warholm (2003) [RCT] [58]		Joint pain, N(%) reporting some effect over 4 months Rose Canina: 31 (64.6%) Placebo: 27 (56.3%) p=0.035		L	H/UC	L	H/UC
Function	More (2017) [RCT] [44]	Rose-Canaina vs placebo, change from baseline to 12 weeks SMD -2.04 (-2.55, -1.53)	WOMAC function, change from BL to 12 weeks, mean (SD) Rose-Canina: -23.82 (9.17) Placebo: -9.17 (4.21)		L	L	L	L
Stiffness	More (2017) [RCT] [44]	Rose-Canaina vs placebo, change from baseline to 12 weeks SMD -1.75 (-2.24, -1.26)	WOMAC stiffness, change from BL to 12 weeks, mean (SD) Rose-Canina: -23.80 (11.84) Placebo: -7.73 (5.11)		L	L	L	L
	Rein (2004) [RCT] [57]	Rose Canina vs placebo, change from baseline to 3 months Group 1 §: -0.76 (-1.14, -0.38) Group2 §: 0.31 (-0.07, 0.67)	Joint stiffness (0-4), change from baseline – 3 months, mean (SD) *Group 1 §:* Rose Canina: -1.91 (1.25) Placebo: -0.91 (1.38); p=0.0025 *Group 2 §:* Rose Canina: -1.28 (1.35) Placebo: -1.71 (1.47); p=0.3850		L	L	L	L

§ Cross-over design: Group 1 received placebo and then active treatment, Group 2 received active treatment and then placebo

Alloc. Conc. = allocation concealment, AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews, BL = baseline, Blind. Asses. = Blinded assessors, Blind. Part. = blinded participants, CI = confidence interval, H/UC = high / unclear risk of bias, L = low risk of bias, OA = osteoarthritis, Rand. Seq. = random sequence generation, RCT = randomised controlled trial, SD = standard deviation, SMD = Standardised mean difference, WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index

Supplementary table 39 – S. Baicalensis and A. Catechu and OA progression, results

Table – S. Baicalensis and A. Catechu (OA), results and quality assessment

Outcome	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	AMSTAR2 quality	Rand. Seq.	Alloc. Conc.	Blind. Part.	Blind. Asses.
6MWT	Arjmandi (2014) [RCT] [48]	S. Baicalensis and A. Catechu vs control SMD 0.30 (-0.15, 0.75)	6MWT (m) at 1 week, mean (SD*) S. Baicalensis and A. Catechu: 434.2 (75.67) Control: 414.63 (47.29)		H/UC	H/UC	L	H/UC
CRP	Arjmandi (2014) [RCT] [48]	S. Baicalensis and A. Catechu vs control SMD 0.06 (-0.39, 0.51)	CRP at 1 week, mean (SD*) S. Baicalensis and A. Catechu: 3.11 (20.59) Control: 2.02 (13.76)		H/UC	H/UC	L	H/UC

* SD calculated from standard error in paper

6MWT = six minute walk test, Alloc. Conc. = allocation concealment, AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews, Blind. Asses. = Blinded assessors, Blind. Part. = blinded participants, CI = confidence interval, CRP = C-Reactive protein, H/UC = high / unclear risk of bias, L = low risk of bias, m= metres, OA = osteoarthritis, Rand. Seq. = random sequence generation, RCT = randomised controlled trial, SD = standard deviation, SMD = Standardised mean difference

Supplementary table 40 – Seaweed extract and OA progression, results

Table – Seaweed extract (OA), results and quality assessment

Outcome	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	AMSTAR2 quality	Rand. Seq.	Alloc. Conc.	Blind. Part.	Blind. Asses.
Pain	Myers (2010) [RCT] [54]	1000mg vs 100mg at 12 weeks SMD -0.83 (-2.04, 0.37)	COAT pain, BL / 12 weeks, mean (SD*) 100mg: 4.90 (1.79) / 3.83 (1.74) 1000mg: 4.79 (1.79) / 2.12 (2.24)		L	H/UC	H/UC	H/UC
Function	Myers (2010) [RCT] [54]	1000mg vs 100mg at 12 weeks SMD -0.77 (-1.96, 0.43)	COAT function, BL / 12 weeks, mean (SD*) 100mg: 3.81 (1.70) / 3.67 (1.66) 1000mg: 4.80 (2.07) / 2.40 (1.66)		L	H/UC	H/UC	H/UC
Stiffness	Myers (2010) [RCT] [54]	1000mg vs 100mg at 12 weeks SMD -0.75 (-1.95, 0.44)	COAT stiffness, BL / 12 weeks, mean (SD*) 100mg: 4.85 (1.73) / 3.61 (1.69) 1000mg: 4.72 (1.73) / 2.34 (1.69)		L	H/UC	H/UC	H/UC

* SD calculated from 95% CI in paper

Alloc. Conc. = allocation concealment, AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews, BL = baseline, Blind. Asses. = Blinded assessors, Blind. Part. = blinded participants, CI = confidence interval, COAT = Comprehensive Osteoarthritis Test, H/UC = high / unclear risk of bias, L = low risk of bias, OA = osteoarthritis, Rand. Seq. = random sequence generation, RCT = randomised controlled trial, SD = standard deviation, SMD = Standardised mean difference

Supplementary table 41 – Sesame powder and OA progression, results

Table – Sesame powder (OA), results and quality assessment

Outcome	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	AMSTAR2 quality	Rand. Seq.	Alloc. Conc.	Blind. Part.	Blind. Asses.
Pain	Eftekhar Sadat (2013) [RCT] [50]		Pain VAS at 2 months, median (IQR) Sesame: 3.5 (4.25) Control: 7 (3.00) § p=0.004		H/UC	H/UC	H/UC	H/UC
CRP	Haghighian (2015) [RCT] [47]	Sesame vs control at 2 months SMD -0.23 (-0.82, 0.35) †	CRP, BL / 2 months, mean (SD) Sesame: 1.45 (1.12) / 1.42 (1.32) Control: 1.64 (1.19) / 1.68 (0.87); p=0.06		H/UC	H/UC	H/UC	H/UC

§ Cannot convert to mean (SD) to calculate SMD using formula[61] as need 25th and 75th centile, but only the difference between those centiles is reported

† p value in paper is 0.06

Alloc. Conc. = allocation concealment, AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews, BL = baseline, Blind. Asses. = Blinded assessors, Blind. Part. = blinded participants, CI = confidence interval, CRP = C-reactive protein, H/UC = high / unclear risk of bias, IQR = interquartile range, L = low risk of bias, OA = osteoarthritis, Rand. Seq. = random sequence generation, RCT = randomised controlled trial, SD = standard deviation, SMD = Standardised mean difference, VAS = visual analogue scale

Supplementary table 42 – Tree bark extracts and OA progression, results

Table – Tree-bark extracts (OA), results and quality assessment

Outcome	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	AMSTAR2 quality	Rand. Seq.	Alloc. Conc.	Blind. Part.	Blind. Asses.
Pain	Liu (2018) [MA] [14]	Pine tree extract (pycnogenol) vs placebo Short term: SMD -1.21 (-1.53, -0.89)		Moderate				
	Karimifar (2017) [RCT] [43]	Elaeagnus angustifoli vs control at 4 weeks SMD -0.37 (-0.94, 0.19) Elaeagnus angustifoli + Boswellia Thurifera vs control at 4 weeks SMD -0.25 (-0.80, 0.29)	Pain VAS, BL / 4 weeks, mean (SD) Elaeagnus angustifoli: 7.04 (1.15) / 4.65 (1.84) Elaeagnus angustifolia + Boswellia Thurifera: 7.03 (1.36) / 4.84 (1.96) Control: 7.01 (1.25) / 5.30 (1.66); p=0.304		H/UC	H/UC	H/UC	H/UC
	Oben (2009) [RCT] [56]	Phellodendron vs placebo at 4 weeks [OV] SMD -2.83 (-3.72, -1.94) Phellodendron vs placebo at 4 weeks [n] SMD -1.87 (-2.62, -1.12)	LAI, BL / 8 weeks, mean (SD) Phellodendron [Ov]: 11.7 (1.5) / 6.3 (2.3) Phellodendron [n]: 11.4 (1.2) / 7.7 (1.4) Placebo [Ov]: 12.4 (1.3) / 11.8 (1.5) Placebo [n]: 11.7 (2.4) / 9.9 (0.9)		L	H/UC	L	H/UC
	Piscoya (2001) [RCT] [59]	Uncaria guianensis vs placebo at 4 weeks SMD -0.24 (-0.87, 0.38)	Pain, BL / 4 weeks, mean (SD*) Uncaria guianensis: 4.41 (2.63) / 3.42 (1.81) Placebo: 4.15 (2.98) / 3.94 (2.67)		H/UC	H/UC	L	L
Function	Liu (2018) [MA] [14]	Pine tree extract vs placebo SMD -1.84 (-2.32, -1.35)		Moderate				
	Karimifar (2017) [RCT] [43]	Elaeagnus angustifoli vs control at 4 weeks SMD -0.35 (-0.91, 0.22) Elaeagnus angustifoli + Boswellia Thurifera vs control at 4 weeks SMD -0.07 (-0.62, 0.47)	LPFI, BL / 4 weeks, mean (SD) Elaeagnus angustifoli: 12.47 (2.88) / 8.32 (3.25) Elaeagnus angustifolia + Boswellia Thurifera: 12.69 (3.35) / 9.09 (4.18) Control: 12.84 (2.73) / 9.34 (2.66); p=0.578		H/UC	H/UC	H/UC	H/UC
Patient global	Karimifar (2017) [RCT] [43]	Elaeagnus angustifoli vs control at 4 weeks SMD -0.24 (-0.80, 0.33) Elaeagnus angustifoli + Boswellia Thurifera vs control at 4 weeks SMD -0.64 (-1.20, -0.08)	Patient global VAS, BL / 4 weeks, mean (SD) Elaeagnus angustifoli: 1.44 (0.62) / 2.38 (0.43) Elaeagnus angustifolia + Boswellia Thurifera: 1.50 (0.68) / 2.17 (0.46) Control: 1.79 (0.64) / 2.50 (0.57); p=0.202		H/UC	H/UC	H/UC	H/UC
ESR	Oben (2009) [RCT] [56]	Phellodendron vs placebo at 4 weeks [OV] SMD -0.42 (-1.05, 0.20) Phellodendron vs placebo at 4 weeks [n] SMD 0.45 (-0.18, 1.08)	ESR, BL / 8 weeks, mean (SD) Phellodendron [Ov]: 12.7 (0.9) / 12.9 (1.6) Phellodendron [n]: 13.1 (1.2) / 13.3 (0.9) Placebo [Ov]: 13.6 (2.5) / 13.6 (1.7) Placebo [n]: 12.5 (1.4) / 12.8 (1.3)		L	H/UC	L	H/UC
CRP	Oben (2009) [RCT] [56]	Phellodendron vs placebo at 4 weeks [OV] SMD -1.97 (-2.74, -1.21) Phellodendron vs placebo at 4 weeks [n] SMD -0.11 (-0.73, 0.51)	CRP, BL / 8 weeks, mean (SD) Phellodendron [Ov]: 1.33 (0.2) / 0.68 (0.14) Phellodendron [n]: 1.15 (0.22) / 0.64 (0.50) Placebo [Ov]: 1.19 (0.26) / 1.08 (0.25) Placebo [n]: 0.76 (0.19) / 0.68 (0.18)		L	H/UC	L	H/UC

* standard deviation calculation from standard error in paper

Alloc. Conc. = allocation concealment, AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews, BL = baseline, Blind. Asses. = Blinded assessors, Blind. Part. = blinded participants, CI = confidence interval, CRP = C-reactive protein, ESR = erythrocyte sedimentation rate, H/UC = high / unclear risk of bias, L = low risk of bias, LAI = Lequesne Algofunctional Index, LPFI = Lequesne pain and function index, MA = meta-analysis, n = normal weight, OA = osteoarthritis, Ov = overweight, Rand. Seq. = random sequence generation, RCT = randomised controlled trial, SD = standard deviation, SMD = Standardised mean difference, VAS = visual analogue scale

Supplementary table 43 – Turmeric and OA progression, results

Table – Turmeric (OA), results and quality assessment

Outcome	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	AMSTAR2 quality	Rand. Seq.	Alloc. Conc.	Blind. Part.	Blind. Asses.
Pain	Daily (2016) [MA] [36]		Turmeric vs control meta-mean difference: -15.36 (-26.94, -3.77)	Low				

Alloc. Conc. = allocation concealment, AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews, Blind. Asses. = Blinded assessors, Blind. Part. = blinded participants, CI = confidence interval, H/UC = high / unclear risk of bias, L = low risk of bias, MA = meta-analysis, OA = osteoarthritis, Rand. Seq. = random sequence generation, SMD = Standardised mean difference

Supplementary table 44 – Description of reviews of minerals and supplements in OA

Table – Minerals and supplements (OA), description of reviews

Authors (date)	Review type	Study type included	Type of OA	Exposure detail	Number of studies included	Funders
Liu (2018) [14]	MA	RCTs	Hip, knee or hand	Chondroitin Glucosamine L-carnitine Methylsulfonylmethane	9 10 1 3	**Government** (NHMRC program grant, Department of education grant), **Industry** (PuraPharm postgrad scholarship), author disclosures (Flexion, Nestle, Merck)
Singh (2015) [62]	MA	RCTs	Hip, knee or hand	Chondroitin	43	**University** (University of Alabama at Birmingham, Minneapolis VA Medical Centre), **NGO** (Cochrane Complementary Medicine Field Bursary)
Gallagher (2015) [63]	SR	RCTs	Knee	Chondroitin	4	**No funding**
Percope de Andrade (2015) [38]	SR	RCTs, other reviews	Hip and knee	Chondroitin Glucosamine	1 MA 2 MA, 1 RCT	**Not reported**, One author disclosed support from Zimmer (medical device company)
McAlindon (2014) [39]	SR	RCTs, other reviews	Knee	Chondroitin Glucosamine	2 MA, 2 SR 2 MA, 3 SR	**Professional body** (OARSI)

MA = meta-analysis, NGO = non-governmental organisation, NHMRC = National Health and Medical Research Council, OA = osteoarthritis, OARSI = Osteoarthritis Research Society International, RCT = randomised controlled trial, SR = systematic review, VA = Veteran Affairs

Supplementary table 45 – Description of studies of minerals in OA

Table – Minerals and supplements (OA), description of included studies

Author (date) [country]	Study design	Type of OA	Inclusion criteria	Exposure detail	N	Age, mean (SD) years	N (%) female	Funders
Lei (2017) [China] [64]	RCT	Knee	Aged <80 years, ACR OA criteria, bilateral OA, degenerative primary knee OA with mild-moderate severity Exclusions: Using medications or food supplements in previous 6 months, OA secondary to trauma, rheumatoid arthritis, inflammatory disorders or haemophilia, candidate for joint replacement, active and generalised inflammatory comorbidity, mal-absorption disorders, presence of cardiac, renal or hepatic failure, using steroids >10mg/day, intra-articular injections during preceding 6 months, physically or mentally compromised	1) Skimmed milk containing Lactobacillus Casei Shirota p) Skimmed milk with no bacteria	1) 215 p) 218	1) 66.5 (5.2) p) 67.2 (4.8)	1) 120 (55.8) p) 121 (55.5)	**Government** (Food and Drug Administration of Hebei Province)
Neves (2011) [Brazil] [65]	RCT	Knee	Women, aged 50-65, ACR OA criteria Exclusions: participation in physical activity training during past year, BMI >35, cardiovascular disease, musculoskeletal disturbances which preclude exercise, vegetarian diet, previous use of creatine, glomerular filtration rate <30, KL grade I or IV, pain scale <2cm or >8 cm, use of NSAIDs during past 3 weeks, hyaluronic acid use in last 6 months, intraarticular steroid use in last 3 months	All patients underwent exercise regime 1) 20g creatine for 7 days and then 5g per day for next 11 weeks. Dissolved in juice. p) Dextrose dissolved in juice	1) 13 p) 11	1) 58 (3) p) 56 (3)	1) 13 (100) p) 11 (100)	**Charity** (Fundação de Amparo à Pesquisa do Estado de São Paulo), **Industry** (Ethika)
Scorei (2011) [Romania] [66]	RCT	Knee	Men / non-pregnant women, aged 40-85 years, primary knee OA (defined by the deterioration and abrasion of the articular cartilage (joint space narrowing) or by the formation of a new bone (osteophytes) at the knee joint surface) Exclusions: digestion problems, fever and/or under treatment with antibiotics, taking any pain killers and/or vitamin B6	2 capsules per day with meals 1) 2x 28.5mg 2) 2x 56.5mg 3) 2x 113mg p) fructose placebo	1) 19 2) 18 3) 17 p) 18	1) 68.2 (6.6) 2) 59.8 (8.8) 3) 64.8 (10) p) 67.6 (5.5)	1) 12 (63.2) 2) 8 (44.4) 3) 11 (64.7) p) 12 (66.7)	**Industry** (Natural Research, Ltd. (Romania))

ACR = American College of Rheumatology, BMI = body mass index, mg = milligram, N = number, NSAIDs = non-steroidal anti-inflammatory drugs, OA = osteoarthritis, RCT = randomised controlled trial, SD = standard deviation

Table – Minerals and supplements (OA), description of included studies

Author (date) [country]	Study design	Type of OA	Inclusion criteria	Exposure detail	N	Age, mean (SD) years	N (%) female	Funders
Roy (2005) [Canada] [67]	RCT	Knee	Primary OA, undergoing total knee replacement, no previous major knee surgery, not receiving workers' compensation benefits Exclusions: coronary artery disease, congestive heart failure, diabetes, renal failure, previous stroke or motor loss, hypertension, inability to give consent, COPD	1) 10g creatine for 10 days before surgery and 30 days after surgery p) Dextrose powder	1) 18 p) 19	1) 63.7 (10.0) p) 63.3 (10.2)	1) 9 (50.0) p) 11 (57.9)	**Industry** (Physician Services Inc), **NGO** (Canadian Foundation for Innovation), **Government** (Natural Sciences and Engineering Research Council of Canada, Hamilton Health Sciences)
Bansal (2014) [India] [68]	Single arm int.	Knee	Primary knee OA, aged >50 years, daily pain for 3 months, analgesic use at least once per week, <30 mins morning stiffness, WOMAC ≤75 in target knee, Brandt radiographic score I-II	Supplement with over 72 natural minerals in ionic form (e.g. boron, zinc, copper, selenium, magnesium, manganese, sulphur), taken twice daily for 6 months. Dose gradually increased to 40 drops	43	57.4	16 (37.2)	Not reported

COPD = chronic obstructive pulmonary disease, mg = milligram, N = number, NGO = non-governmental organisation, OA = osteoarthritis, RCT = randomised controlled trial, SD = standard deviation, WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index

Supplementary table 46 – Calcium fructobate and OA progression, results

Table – Calcium fructobate (OA), results and quality assessment

Outcome	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	AMSTAR2 quality	Rand. Seq.	Alloc. Conc.	Blind. Part.	Blind. Asses.
CRP	Scorei (2011) [RCT] [66]	28.5mg vs placebo at 2 weeks SMD -9.05 (-11.26, -6.83) § 56.5mg vs placebo at 2 weeks SMD -1.25 (-1.96, -0.53) 113mg vs placebo at 2 weeks SMD -2.33 (-3.20, -1.46)	CRP, BL / 2 weeks, mean (SD) 28.5mg: 0.78 (0.2) / 0.31 (0.02) [sic] 56.5mg: 0.75 (0.2) / 0.55 (0.24) 113mg: 0.57 (0.19) / 0.47 (0.17) Placebo: 0.73 (0.12) / 0.77 (0.07) [sic]		H/UC	H/UC	H/UC	H/UC
ESR	Scorei (2011) [RCT] [66]	28.5mg vs placebo at 2 weeks SMD -2.62 (-3.51, -1.73) 56.5mg vs placebo at 2 weeks SMD -2.06 (-2.87, -1.24) 113mg vs placebo at 2 weeks SMD -2.54 (-3.44, -1.63)	ESR, BL / 2 weeks, mean (SD) 28.5mg: 19.5 (3.5) / 17.5 (2.7) 56.5mg: 18.5 (6.4) / 16.3 (5.9) 113mg: 18.9 (2.3) / 17.3 (3.1) Placebo: 19.8 (3.2) / 27 (4.4)		H/UC	H/UC	H/UC	H/UC

§ Using the standard deviation in the published paper. Authors confirmed this was correct.

Alloc. Conc. = allocation concealment, AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews, BL = baseline, Blind. Asses. = Blinded assessors, Blind. Part. = blinded participants, CI = confidence interval, CRP = C-reactive protein, ESR = erythrocyte sedimentation rate, H/UC = high / unclear risk of bias, L = low risk of bias, OA = osteoarthritis, Rand. Seq. = random sequence generation, RCT = randomised controlled trial, SD = standard deviation, SMD = Standardised mean difference,

Supplementary table 47 – Chondroitin and OA progression, results

Table – Chondroitin (OA), results and quality assessment

Outcome	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	AMSTAR2 quality	Rand. Seq.	Alloc. Conc.	Blind. Part.	Blind. Asses.
Pain	Liu (2018) [MA] [14]	Chondroitin vs placebo Short term: SMD -0.34 (-0.49, -0.19)		Moderate				
	Singh (2015) [MA] [62]	Chondroitin vs placebo Short term: SMD -0.51 (-0.74, -0.28)		High				
	Gallagher (2015) [SR] [63]		Concluded that chondroitin resulted in no change in pain scores	Moderate				
	Percope de Andrade (2015) [SR] [38]		Identified one MA showing no evidence that chondroitin reduces pain	Moderate				
	McAlindon (2014) [SR] [39]		Reported large variation in pain estimates, ranging from SMD -0.13 (-0.27, 0.00) to SMD -0.75 (-0.99, -0.50)	Moderate				
Function	Liu (2018) [MA] [14]	Chondroitin vs placebo Short term: SMD -0.36 (-0.58, -0.13)		Moderate				
	Singh (2015) [MA] [62]	Chondroitin vs placebo Short term: SMD 0.11 (-0.47, 0.68)		High				
Structural progression	Gallagher (2015) [SR] [63]		3/4 studies reported a reduction in structural progression for chondroitin vs placebo	Moderate				

Alloc. Conc. = allocation concealment, AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews, Blind. Asses. = Blinded assessors, Blind. Part. = blinded participants, CI = confidence interval, H/UC = high / unclear risk of bias, L = low risk of bias, MA = meta-analysis, OA = osteoarthritis,Rand. Seq. = random sequence generation, SMD = Standardised mean difference, SR = systematic review

Supplementary table 48 – Creatine and OA progression, results

Table – Creatine (OA), results and quality assessment

Outcome	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	AMSTAR2 quality	Rand. Seq.	Alloc. Conc.	Blind. Part.	Blind. Asses.
Pain	Neves (2011) [RCT] [65]	Creatine vs placebo at 12 weeks SMD -0.80 (-1.64, 0.03)	WOMAC pain, BL / 12 weeks, mean (SD) Creatine: 5.8 (4.9) / 3.2 (2.0) Placebo: 8.0 (2.9) / 5.3 (3.2)		L	L	L	L
Function	Neves (2011) [RCT] [65]	Creatine vs placebo at 12 weeks SMD -0.82 (-1.66, 0.02)	WOMAC function, BL / 12 weeks, mean (SD) Creatine: 15.1 (13.9) / 9.0 (7.1) Placebo: 23.3 (10.8) / 15.9 (9.8)		L	L	L	L
Stiffness	Neves (2011) [RCT] [65]	Creatine vs placebo at 12 weeks SMD -1.22 (-2.10, -0.34)	WOMAC stiffness, BL / 12 weeks, mean (SD) Creatine: 2.7 (1.7) / 1.3 (1.1) Placebo: 3.2 (1.3) / 2.7 (1.2)		L	L	L	L
Grip strength	Roy (2005) [RCT] [67]	Creatine vs placebo at 30 days SMD 0.48 (-0.17, 1.14)	Grip strength at 30 days, mean (SD) Creatine: 38.2 (10.4) Placebo: 33.4 (9.6)		H/UC	L	L	L

Alloc. Conc. = allocation concealment, AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews, BL = baseline, Blind. Asses. = Blinded assessors, Blind. Part. = blinded participants, CI = confidence interval, H/UC = high / unclear risk of bias, L = low risk of bias, OA = osteoarthritis, Rand. Seq. = random sequence generation, RCT = randomised controlled trial, SD = standard deviation, SMD = Standardised mean difference, WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index

Supplementary table 49 – Glucosamine and OA progression, results

Table – Glucosamine (OA), results and quality assessment

Outcome	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	AMSTAR2 quality	Rand. Seq.	Alloc. Conc.	Blind. Part.	Blind. Asses.
Pain	Liu (2018) [MA] [14]	Glucosamine vs placebo SMD -0.28 (-0.52, -0.04)		Moderate				
	Percope de Andrade (2015) [SR] [38]		Identified one MA reporting no reduction, one Cochrane review reporting an relative risk [sic] of 0.47 (0.23, 0.72), 1 large RCT reporting no benefit	Moderate				
	McAlindon (2014) [SR] [39]		Reported large variation in pain estimates, ranging from SMD -0.17 (-0.05, -0.28) to SMD -0.47 (-0.72, -0.23)	Moderate				
Function	Liu (2018) [MA] [14]	Glucosamine vs placebo SMD -0.45 (-0.73, -0.17)		Moderate				

Alloc. Conc. = allocation concealment, AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews, Blind. Asses. = Blinded assessors, Blind. Part. = blinded participants, CI = confidence interval, MA = meta-analysis, OA = osteoarthritis, Rand. Seq. = random sequence generation, RCT = randomised controlled trial, SMD = Standardised mean difference, SR = systematic review

Supplementary table 50 – L-carnitine and OA progression, results

Table – L-carnitine (OA), results and quality assessment

Outcome	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	AMSTAR2 quality	Rand. Seq.	Alloc. Conc.	Blind. Part.	Blind. Asses.
Pain	Liu (2018) [MA] [14]	L-Carnitine vs placebo SMD -0.96 (-1.46, -0.46)		Moderate				
Function	Liu (2018) [MA] [14]	L-Carnitine vs placebo SMD -1.15 (-1.66, -0.64)		Moderate				

Alloc. Conc. = allocation concealment, AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews, Blind. Asses. = Blinded assessors, Blind. Part. = blinded participants, CI = confidence interval, H/UC = high / unclear risk of bias, L = low risk of bias, MA = meta-analysis, OA = osteoarthritis, Rand. Seq. = random sequence generation, SMD = Standardised mean difference

Supplementary table 51 – Lactobacillus Casei Shirota and OA progression, results

Table – Lactobacillus Casei Shirota (OA), results and quality assessment

Outcome	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	AMSTAR2 quality	Rand. Seq.	Alloc. Conc.	Blind. Part.	Blind. Asses.
Pain	Lei (2017) [RCT][64]	Probiotic vs placebo at 6 months SMD -0.93 (-1.12, -0.73)	WOMAC pain, BL / 6 months, mean (SD) Probiotic: 10.3 (4.5) / 6.2 (3.3) Placebo: 10.7 (5.3) / 9.7 (4.2); p=0.008		L	H/UC	L	L
Function	Lei (2017) [RCT][64]	Probiotic vs placebo at 6 months SMD -1.51 (-1.72, -1.29)	WOMAC function, BL / 6 months, mean (SD) Probiotic: 32.1 (13.4) / 16.1 (9.6) Placebo: 33.2 (12.9) / 31.9 (11.3); p<0.001		L	H/UC	L	L
Stiffness	Lei (2017) [RCT][64]	Probiotic vs placebo at 6 months SMD -0.49 (-0.68, -0.30)	WOMAC stiffness, BL / 6 months, mean (SD) Probiotic: 1.27 (1.14) / 0.22 (0.51) Placebo: 1.52 (1.31) / 0.47 (0.51); p=0.040		L	H/UC	L	L

Alloc. Conc. = allocation concealment, AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews, BL = baseline, Blind. Asses. = Blinded assessors, Blind. Part. = blinded participants, CI = confidence interval, H/UC = high / unclear risk of bias, L = low risk of bias, OA = osteoarthritis, Rand. Seq. = random sequence generation, RCT = randomised controlled trial, SD = standard deviation, SMD = Standardised mean difference, WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index

Supplementary table 52 – Methylsulfonylmethane and OA progression, results

Table – Methylsulfonylmethane (OA), results and quality assessment

Outcome	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	AMSTAR2 quality	Rand. Seq.	Alloc. Conc.	Blind. Part.	Blind. Asses.
Pain	Liu (2018) [MA] [14]	Methylsulfonylmethane vs placebo Short term: SMD -0.47 (-0.80, -0.14)		Moderate				
Function	Liu (2018) [MA] [14]	Methylsulfonylmethane vs placebo Short term: SMD -1.10 (-1.81, -0.38)		Moderate				

Alloc. Conc. = allocation concealment, AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews, Blind. Asses. = Blinded assessors, Blind. Part. = blinded participants, CI = confidence interval, H/UC = high / unclear risk of bias, L = low risk of bias, MA = meta-analysis, OA = osteoarthritis, Rand. Seq. = random sequence generation, SMD = Standardised mean difference

Supplementary table 53 – Multi-minerals and OA progression, results

Table – Multi-mineral (OA), results and quality assessment

Outcome	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	AMSTAR2 quality	Rand. Seq.	Alloc. Conc.	Blind. Part.	Blind. Asses.
Pain	Bansal (2014) [Single arm] [68]		WOMAC pain, change from BL to 1 year, mean -4.5					
Function	Bansal (2014) [Single arm] [68]		WOMAC function, change from BL to 1 year, mean -15					
Stiffness	Bansal (2014) [Single arm] [68]		WOMAC stiffness, change from BL to 1 year, mean -1.5					

Alloc. Conc. = allocation concealment, AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews, BL = baseline, Blind. Asses. = Blinded assessors, Blind. Part. = blinded participants, CI = confidence interval, OA = osteoarthritis, Rand. Seq. = random sequence generation, SMD = Standardised mean difference, WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index

Supplementary table 54 – Description of reviews of vitamins in OA

Table – Vitamin D, description of reviews

Authors (date)	Review type	Study type included	Type of OA	Exposure detail	Number of studies included	Funders
Liu (2018) [14]	MA	RCTs	Hip, knee or hand	Vitamin D Vitamin E	4 1	**Government** (NHMRC program grant, Department of education grant), **Industry** (PuraPharm postgrad scholarship), author disclosures (Flexion, Nestle, Merck)
Diao (2017) [69]	MA	RCTs	Knee	Vitamin D	4	Not reported – authors declare no conflicts of interest
Gao (2017) [70]	MA	RCTs	Knee	Vitamin D	4	None
Hussain (2017) [71]	SR	RCTs	Knee	Vitamin D	5	None
Bastick (2015) [72]	SR	Observational studies	Knee	Vitamin D	3	**Charity** (Dutch Arthritis Foundation)
Gallagher (2015) [63]	SR	RCTs	Knee	Vitamin D Vitamin E	1 1	**No funding**

MA = meta-analysis, NHMRC = National Health and Medical Research Council, OA = osteoarthritis, RCT = randomised controlled trial, SR = systematic review

Supplementary table 55 – Description of studies of vitamins in OA

Table – Vitamins (OA), description of included studies

Author (date) [country]	Study design	Type of OA	Inclusion criteria	Exposure detail	N	Age, mean (SD) years	N (%) female	Funders
Bischoff-Ferrari (2018) [Switzerland] [73]	RCT	Knee	Age ≥60 years, underwent total knee replacement, no plans for bilateral surgery for 2 years, willingness to stop current vitamin D / calcium supplement during trial, write in German, mini-mental state ≥24 Exclusions: inflammatory arthritis, inability to walk at least 3m with or without walking aid	1) 2000 IU vitamin D 2) 800 IU vitamin D	1) 137 2) 136	1) 70.2 (6.8) 2) 70.5 (6.0)	1) 69 (50.4) 2) 77 (56.6)	**Government** (Swiss National Science Foundation), **Charity** (Velux Stiftung, Baugarten Foundation)
Arden (2016) [UK] [74]	RCT	Knee	Aged >50 years, ambulatory, radiographic OA, KL grade II-III, joint space width >1mm, knee pain most days of last month	1) 800 IU of vitamin D p) matched placebo	1) 237 p) 237	1) 64 (8) p) 64 (8)	1) 144 (60.8) p) 145 (61.2)	**Charity** (Arthritis Research UK), **Government** (NIHR)
Jin (2016) [Australia] [75]	RCT	Knee	Aged 50-79 years, ACR criteria OA for ≥6 months, pain VAS 20-80mm, ACR functional class 1-3, physical likert good health score 0-2 (range 0-4), serum vitamin D level 12.5-60 nmol/l Exclusions: Grade 3 radiographic changes (Altman & Gold) severe knee pain on standing (≥80mm on VAS), contraindication to MRI, rheumatoid arthritis, psoriatic arthritis, lupus, cancer, severe cardiac or renal impairment, hypersensitivity to vitamin D, conditions affecting oral drug absorption, anticipated knee surgery in next 2 years, history of knee trauma, taking vitamin D or investigational drug in last 30 days	1) monthly capsule of 50,000 IU vitamin D p) inert placebo	1) 209 p) 204	1) 63.5 (6.9) p) 62.9 (7.2)	1) 106 (50.7) p) 102 (50.0)	**Government** (Australian National Health and Medical Research Council)
McAlindon (2013) [USA] [76]	RCT	Knee	Symptomatic knee OA, aged ≥45 years, KL grade II, ACR criteria for OA, mild pain on WOMAC Exclusions: supplemental intake of vitamin D >800 IU, serum calcium >10.5 mg/dl, hypercalcuria, use of supplements or medications with purported effects on cartilage, intraarticular therapy in last 3 months, chronic oral steroid use, lymphoma, sarcoidosis, tuberculosis, hyperparathyroidism, malabsorption disorders, glomerular filtration rate <30, history of inflammatory joint disease, pregnancy, any conditions precluding MRI	1) 2000 IU vitamin D p) placebo	1) 73 p) 73	1) 61.8 (7.7) p) 63.0 (9.3)	1) 49 (67.1) p) 40 (54.8)	**Government** (National Institute for Arthritis and Musculoskeletal Disorders, Office for Dietary Supplements, National Center for Research Resources)

ACR = American College of Rheumatology, AIDS = acquired immunodeficiency syndrome, HIV = human immunodeficiency virus, KL = Kellgren-Lawrence, pros = prospective, MRI = magnetic resonance imaging, N = number, NIHR = National Institutes for Health Research, OA = osteoarthritis, RCT = randomised controlled trial, SD = standard deviation, VAS = visual analogue scale, WOMAC = Western Ontario and McMaster Universities Arthritis Index

Table – Vitamins (OA), description of included studies

Author (date) [country]	Study design	Type of OA	Inclusion criteria	Exposure detail	N	Age, mean (SD) years	N (%) female	Funders
Medhi (2011) [India] [77]	RCT	Knee	Aged >40 years, knee OA Exclusions: history of knee trauma, joint deformity, previous joint surgery, neurological or vascular disease affecting joints, peptic ulcer, hepatic or renal insufficiency, prior intolerance or hypersensitivity to NSAIDs, anaemia, bleeding diasthesis, unstable medical condition (e.g. diabetes, heart failure), other concomitant medication	1) Vitamin C + Vitamin E + paracetamol p) paracetamol only	1) 50 p) 50	1) 54.8 (10.6) p) 52.8 (9.2)	1) 84% p) 64%	Not reported
Colker (2002) [USA] [78]	RCT	Knee	Age >35 years, knee OA diagnosed by physician, daily/almost daily pain, willing to avoid other dietary supplements Exclusions: rheumatoid arthritis, anti-inflammatory medication for OA, recent use of steroids/hyaluronic acid injections, pain prescription medication, allergy to milk, cancer, HIV, AIDS, congestive heart failure	1) Refrigerated beverage, milk based, fortified with vitamins B12, C, E and iron and zinc p) Refrigerated grape juice with no added vitamins	1) 16 p) 15	1) 51.5 (19.0) p) 59.0 (21.0)	1) 11 (68.8) p) 9 (60.0)	**Industry** (NuVim, Inc.)
Jonas (1996) [USA] [79]	RCT	Unspec-ified	Clinical and radiological OA (of ≥2 joints), daily use of anti-inflammatory medication, aged >40 years, symptom duration ≥5 years, joint pain requiring NSAID use Exclusions: pregnancy, morning stiffness lasting >30 minutes, palpable warmth of affected joints, severe liver disease, diabetes, gout, peptic or gastric ulcers, taking steroid medication, inability to understand questionnaire.	1) Niacinamide (vitamin B3) tablets 6x per day p) Placebo tablets	1) 31 p) 29	1) 64 (6.4) p) 65 (8.9)	1) 22 (71.0) p) 17 (58.6)	**Professional body** (American Academy of Family Practice)
Flynn (1994) [USA] [80]	RCT§	Hand	ARA OA criteria, hand OA diagnosed by chronic hand pain and stiffness signs of hypertrophic changes, subchondral sclerosis, non-uniform joint space narrowing	1) Vitamin B12 + folate p) folate only	26	Range: 52-82	23 (88.5)	**Charity** (Wallace Genetic Foundation), **University** (University of Missouri-Columbia)

§ Crossover design

ARA = American Rheumatism Association, AIDS = acquired immunodeficiency syndrome, HIV = human immunodeficiency virus, pros = prospective, N = number, NSAID = non-steroidal anti-inflammatory drugs, OA = osteoarthritis, RCT = randomised controlled trial, SD = standard deviation, USA = United States of America

Table – Vitamins (OA), description of included studies

Author (date) [country]	Study design	Type of OA	Inclusion criteria	Exposure detail	N	Age, mean (SD) years	N (%) female	Funders
Peregoy (2011) [USA] [81]	Pros. Cohort	Knee	Aged >40 years, KL grade >2 Exclusions: rheumatoid arthritis, systemic lupus erythematosus, ankylosing spondylitis, gout, disabling neuralgic disease, confined to wheelchair, mental incompetency, multivitamin use	Self-reported vitamin C supplementation	157	66.5 (8.7)	88 (56.1)	"Private funding"
Wilder (2009) [USA] [82]	Pros. Cohort	Knee	Aged ≥40 years Exclusions: rheumatoid arthritis, systemic lupus erythematosus, ankylosing spondylitis, gout, disabling neurological disease, confined to wheel chair, mental incompetency	Cumulative number of years of self-reported vitamin supplement use	217	65.9 (9.6)	133 (61.3)	**Not reported**
McAlindon (1996) [USA] [83]	Pros. cohort	Knee	Radiographic OA	Self-reported vitamin D intake (food frequency questionnaire)	62	70.3	37%	**University** (Boston University Arthritis Center), **Charity** (Arthritis and Rheumatism Council)

KL = Kellgren-Lawrence, pros = prospective, N = number, OA = osteoarthritis, RCT = randomised controlled trial, SD = standard deviation, USA = United States of America

Supplementary table 56 – Multi-vitamins and OA progression, results

Table – Multi-vitamin/vitamin supplementation (OA), results and quality assessment

Outcome	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	AMSTAR2 quality	Rand. Seq.	Alloc. Conc.	Blind. Part.	Blind. Asses.
Pain	Colker (2002) [RCT] [78]	Multivitamin vs placebo at 6 weeks SMD -0.26 (-0.97, 0.44)	Pain VAS, at 6 weeks, mean (SD*) Multivitamin: 3.17 (1.64) Placebo: 3.77 (2.79)		H/UC	H/UC	H/UC	H/UC
QoL	Colker (2002) [RCT] [78]	Multivitamin vs placebo at 6 weeks SMD -0.32 (-1.03, 0.39)	QoL KOOS, at 6 weeks, mean (SD*) Multivitamin: 50.4 (22.0) Placebo: 57.9 (25.17)		H/UC	H/UC	H/UC	H/UC

*SD calculated from standard error in paper

Alloc. Conc. = allocation concealment, AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews, Blind. Asses. = Blinded assessors, Blind. Part. = blinded participants, CI = confidence interval, H/UC = high / unclear risk of bias, KOOS = Knee Injury and Osteoarthritis Outcome Score, L = low risk of bias, OA = osteoarthritis, QoL = quality of life, Rand. Seq. = random sequence generation, RCT = randomised controlled trial, SD = standard deviation, SMD = Standardised mean difference, VAS = visual analogue scale

Table – Multi-vitamin/vitamin supplementation cont. (OA), results and quality assessment

Outcome (outcome measure)	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	Study Pop.	Attr.	Prog. Meas.	Outc. Meas.	Conf.	Stats.
Radiographic progression	Wilder (2009) [Pros. Obs.] [82]		Relative risk per year increase in supplementation (95% CI) Unadjusted: 0.88 (0.84, 0.93) Fully adjusted: 0.93 (0.87, 0.99)	L	L	M	L	M	L

Attr. = attrition, CI = confidence interval, Conf. = confounding, HR = hazard ratio, L = low risk of bias, M = moderate risk of bias, OA = osteoarthritis, Outc. Meas = outcome measurement, Prog. Meas. = prognostic factor measurement, Pros. Obs. = prospective observational, SMD = standardised mean difference, Stats. = statistical analysis, Study Pop. = study population

Supplementary table 57 – Vitamin B3 and OA progression, results

Table – Vitamin B3 (OA), results and quality assessment

Outcome	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	AMSTAR2 quality	Rand. Seq.	Alloc. Conc.	Blind. Part.	Blind. Asses.
Pain	Jonas (1996) [RCT] [79]		AIMS pain, change from BL to week 12, mean Vitamin B3: 0.10 Placebo: 0.82, p=0.1		L	L	L	L
ESR	Jonas (1996) [RCT] [79]		ESR, change from BL to week 12, mean Vitamin B3: -6.4 Placebo: 3.3, p=0.004		L	L	L	L

AIMS = Arthritis Impact Measurement Scales, Alloc. Conc. = allocation concealment, AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews, BL = baseline, Blind. Asses. = Blinded assessors, Blind. Part. = blinded participants, CI = confidence interval, ESR= erythrocyte sedimentation rate, H/UC = high / unclear risk of bias, L = low risk of bias, Rand. Seq. = random sequence generation, RCT = randomised controlled trial, SMD = Standardised mean difference,

Supplementary table 58 – Vitamin B12 and OA progression, results

Table – Vitamin B12 (OA), results and quality assessment

Outcome	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	AMSTAR2 quality	Rand. Seq.	Alloc. Conc.	Blind. Part.	Blind. Asses.
Pain	Flynn (1994) [RCT] [80]		Pain, mean score at end of cross-over phase Vitamin B12: 1.0 Placebo: 1.0		H/UC	H/UC	L	H/UC
Tender joint count	Flynn (1994) [RCT] [80]		Tender joint count, mean score at end of cross-over phase Vitamin B12: 3.4 Placebo: 3.7 p=0.02		H/UC	H/UC	L	H/UC
Patient global	Flynn (1994) [RCT] [80]		Patient global, mean score at end of cross-over phase Vitamin B12: 3.1 Placebo: 3.5		H/UC	H/UC	L	H/UC

Alloc. Conc. = allocation concealment, AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews, Blind. Asses. = Blinded assessors, Blind. Part. = blinded participants, CI = confidence interval, H/UC = high / unclear risk of bias, L = low risk of bias, OA = osteoarthritis, Rand. Seq. = random sequence generation, RCT = randomised controlled trial, SMD = Standardised mean difference

Supplementary table 59 – Vitamin C and OA progression, results

Table – Vitamin C (OA), results and quality assessment

Outcome (outcome measure)	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	Study Pop.	Attr.	Prog. Meas.	Outc. Meas.	Conf.	Stats.
Radiographic progression	Peregoy (2009) [Pros. Obs.] [81]		Relative risk per year increase in supplementation (95% CI) Unadjusted: 0.91 (0.79, 1.04) Fully adjusted: 0.94 (0.79, 1.12)	L	M	M	L	L	L

Attr. = attrition, CI = confidence interval, Conf. = confounding, L = low risk of bias, M = moderate risk of bias, OA = osteoarthritis, Outc. Meas = outcome measurement, Prog. Meas. = prognostic factor measurement, Pros. Obs. = prospective observational, SMD = standardised mean difference, Stats. = statistical analysis, Study Pop. = study population

Supplementary table 60 – Vitamin C + E and OA progression, results

Table – Vitamin C + E (OA), results and quality assessment

Outcome	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	AMSTAR2 quality	Rand. Seq.	Alloc. Conc.	Blind. Part.	Blind. Asses.
Pain	Medhi (2011) [RCT] [77]	Vitamin C + E vs placebo at 8 weeks SMD -0.46 (-0.86, -0.07)	Pain VAS at 8 weeks, mean (SD) Vitamin C + E: 4.12 (1.62) Placebo: 4.88 (1.66)		H/UC	H/UC	H/UC	H/UC

Alloc. Conc. = allocation concealment, AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews, Blind. Asses. = Blinded assessors, Blind. Part. = blinded participants, CI = confidence interval, H/UC = high / unclear risk of bias, L = low risk of bias, OA = osteoarthritis, Rand. Seq. = random sequence generation, SD = standard deviation, SMD = Standardised mean difference, VAS = visual analogue scale

Supplementary table 61 – Vitamin D and OA progression, results

Table – Vitamin D (OA), results and quality assessment

Outcome	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	AMSTAR2 quality	Rand. Seq.	Alloc. Conc.	Blind. Part.	Blind. Asses.
Pain	Liu (2018) [MA] [14]	Vitamin D vs placebo Long term: SMD -0.19 (-0.31, -0.06)		Moderate				
	Diao (2017) [MA] [69]	Vitamin D vs placebo SMD -0.32 (-0.63, -0.02)		Moderate				
	Gao (2017) [MA] [70]		Vitamin D vs placebo [WOMAC] MD -1.65 (-2.16, -1.14)	Low				
	Hussain (2017) [SR] [71]		1/4 studies reported a significant between group difference in pain scores	Moderate				
	Gallagher (2015) [SR] [63]		1 study reported no between group difference in pain	Moderate				
	Bischoff-Ferrari (2018) [RCT] [73]	2000 IU vitamin D vs 800 IU vitamin D at 24 months SMD -0.02 (-0.25, 0.22)	WOMAC pain, BL / 24 months, mean (SD*) 2000 IU vitamin D: 28.9 (11.0) / 6.2 (11.9) 800 IU vitamin D: 28.0 (11.3) / 6.4 (11.9)		L	L	L	L
	Arden (2016) [RCT] [74]		WOMAC pain, mean (95% CI) difference -0.79 (-2.31, 0.74)		L	L	L	L
	Jin (2016) [RCT] [75]	Vitamin D vs placebo at 24 months SMD -0.11 (-0.31, 0.08)	WOMAC pain, BL / 24 months, mean (SD) Vitamin D: 137.9 (88.8) / 87.0 (90.1) Placebo: 134.7 (83.4) / 97.2 (87.5); p=0.10		L	L	L	L
	McAlindon (2013) [RCT] [76]	Vitamin D vs placebo, change from BL – 2 years SMD -0.22 (-0.54, 0.11)	WOMAC pain, mean (SD*) change BL – 2 years Vitamin D: -2.31 (4.05) Placebo: -1.46 (3.77); p=0.17		L	L	L	L
Function	Liu (2018) [MA] [14]	Vitamin D vs placebo Long term: SMD -0.36 (-0.61, -0.11)		Moderate				
	Gao (2017) [MA] [70]		Vitamin D vs placebo [WOMAC] MD -1.87 (-2.58, -1.17)	Low				
	Hussain (2017) [SR] [71]		2/3 studies reported significant between group difference in function scores, final study p=0.07	Moderate				
	Bischoff-Ferrari (2018) [RCT] [73]	2000 IU vitamin D vs 800 IU vitamin D at 24 months SMD 0.04 (-0.20, 0.27)	WOMAC function, BL / 24 months, mean (SD*) 2000 IU vitamin D: 26.3 (10.5) / 7.0 (11.0) 800 IU vitamin D: 25.0 (10.4) / 6.6 (11.0)		L	L	L	L
	Arden (2016) [RCT] [74]		WOMAC function, mean (95% CI) difference -0.65 (-2.09, 0.79)		L	L	L	L
	Jin (2016) [RCT] [75]	Vitamin D vs placebo at 24 months SMD -0.18 (-0.37, 0.02)	WOMAC function, BL / 24 months, mean (SD) Vitamin D: 487.9 (318.1) / 306.4 (303.7) Placebo: 467.6 (292.8) / 361.8 (322.8); p=0.008		L	L	L	L
	McAlindon (2013) [RCT] [76]	Vitamin D vs placebo, change from BL – 2 years SMD -0.29 (-0.62, 0.04)	WOMAC function, mean (SD*) change BL – 2 years Vitamin D: -6.97 (12.16) Placebo: -3.82 (9.33); p=0.07		L	L	L	L

* SD calculated from 95% CI in paper; Alloc. Conc. = allocation concealment, AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews, BL = baseline, Blind. Asses. = Blinded assessors, Blind. Part. = blinded participants, CI = confidence interval, H/UC = high / unclear risk of bias, L = low risk of bias, MA = meta-analysis, MD = mean difference, OA = osteoarthritis, Rand. Seq. = random sequence generation, RCT = randomised controlled trial, SD = standard deviation, SMD = Standardised mean difference, SR = systematic review, WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index

Table [cont.] – Vitamin D (OA), results and quality assessment

Outcome	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	AMSTAR2 quality	Rand. Seq.	Alloc. Conc.	Blind. Part.	Blind. Asses.
Stiffness	Gao (2017) [MA] [70]		Vitamin D vs placebo [WOMAC] MD 0.03 (-0.17, 0.24)	Low				
	Arden (2016) [RCT] [74]		WOMAC stiffness, mean (95% CI) difference -1.52 (-3.24, 0.21)		L	L	L	L
	Jin (2016) [RCT] [75]	Vitamin D vs placebo at 24 months SMD -0.11 (-0.30, 0.09)	WOMAC stiffness, BL / 24 months, mean (SD) Vitamin D: 61.5 (41.5) / 41.1 (44.1) Placebo: 61.7 (40.1) / 45.7 (41.1); p=0.31		L	L	L	L
Structural progression	Bastick (2015) [SR] [72]		Moderate evidence that vitamin D is inversely associated with progression of knee OA (3/6 studies)	Moderate				
	Gallagher (2015) [SR] [63]		1 study reported no between group difference in structural progression	Moderate				

Alloc. Conc. = allocation concealment, AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews, BL = baseline, Blind. Asses. = Blinded assessors, Blind. Part. = blinded participants, CI = confidence interval, H/UC = high / unclear risk of bias, L = low risk of bias, MA = meta-analysis, OA = osteoarthritis,Rand. Seq. = random sequence generation, RCT = randomised controlled trial, SMD = Standardised mean difference, SR = systematic review, WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index

Table – Vitamin D (OA), results and quality assessment from observational studies

Outcome (outcome measure)	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	Study Pop.	Attr.	Prog. Meas.	Outc. Meas.	Conf.	Stats.
Radiographic progression	McAlindon (1996) [Pros. Obs.] [83]		Radiographic progression, OR (95% CI) Highest tertile of vitamin D intake: ref Middle tertile: 2.99 (1.06, 8.49) Lowest tertile: 4.05 (1.40, 11.6)	M	na.	M	L	L	L

Attr. = attrition, CI = confidence interval, Conf. = confounding, HR = hazard ratio, L = low risk of bias, M = moderate risk of bias, OA = osteoarthritis, OR = odds ratio, Outc. Meas = outcome measurement, Prog. Meas. = prognostic factor measurement, Pros. Obs. = prospective observational, SMD = standardised mean difference Stats. = statistical analysis, Study Pop. = study population

Supplementary table 62 – Vitamin E and OA progression, results

Table – Vitamin E (OA), results and quality assessment

Outcome	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	AMSTAR2 quality	Rand. Seq.	Alloc. Conc.	Blind. Part.	Blind. Asses.
Pain	Liu (2018) [MA] [14]	Vitamin E vs placebo SMD 0.01 (-0.44, 0.45)		Moderate				
	Gallagher (2015) [SR] [63]		1 study reported no between group difference in pain	Moderate				
Function	Liu (2018) [MA] [14]	Vitamin E vs placebo SMD -0.10 (-0.55, 0.35)		Moderate				
Structural progression	Gallagher (2015) [SR] [63]		1 study reported no between group difference in structural progression	Moderate				

Alloc. Conc. = allocation concealment, AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews, Blind. Asses. = Blinded assessors, Blind. Part. = blinded participants, CI = confidence interval, H/UC = high / unclear risk of bias, L = low risk of bias, MA = meta-analysis, OA = osteoarthritis, Rand. Seq. = random sequence generation, SMD = Standardised mean difference, SR = systematic review

Supplementary table 63 – Description of reviews of animal products in RA

Table – Animal products (RA), description of reviews

Authors (date)	Review type	Study type included	Exposure detail	Number of studies included	Funders
Gioxari (2018)[84]	MA	RCTs	Omega 3	20	**Government** (State Scholarship Foundation)
Senftleber (2017)[15]	MA	RCTs	Marine oil supplements	32	**Charity** (Oak Foundation [indirectly funded]), **Government** (National Institute of Arthritis and Musculoskeletal and Skin Diseases, NIH [individual fellowship of an author])
Cramp (2013)[85]	MA	RCTs	Omega 3	1	**Charity** (Arthritis Research UK)
Abdulrazaq (2017)[86]	SR	RCTs	Omega 3	18	Not reporting, authors declare no conflicts of interest

MA = meta-analysis, NIH = National Institutes of Health, RA = rheumatoid arthritis, RCT = randomised controlled trial, SR = systematic review

Supplementary table 64 – Description of studies of animal products in RA

Table – Animal products (RA), description of included studies

Author (date) [country]	Study design	Inclusion criteria	Exposure detail	N	Age, mean (SD) years	N (%) female	Funders
Lindqvist (2018) [Sweden][87]	RCT §	Aged 25-65 years, >2 years symptom duration, DAS28 >3.0	1) One meal a day replaced by intervention meal, with included blue mussels from Denmark p) Same as intervention but with meat instead of mussels	23	Median (IQR) 55 (46, 63)	23 (100)	**Charity** (Hakansson Foundation), **Government** (Swedish government under the ALF-funds)
Fu (2015) [China][88]	RCT	ACR criteria (no reference), symptom duration ≥6 months, ≥4 of the following: ≥4 swollen joints, ≥6 tender joints, ESR >28 mm/hr, morning stiffness last ≥45 mins, CRP >2 mg/dL	1) Capsules of hard-shelled mussel extract p) Placebo capsules	1) 18 p) 24	1) 56.6 (2.8) p) 58.3 (2.18)	1) 12 (66.7) p) 18 (75.0)	**Government** (National Natural Science Foundation of China, Ningbo Natural Science Foundation, PhD. Programs Foundation of Ministry of Education of China, National Basic Research Program of China)
Rajaei (2015) [Iran][89]	RCT	1987 RA criteria, RA diagnosed by two rheumatologists Exclusions: diagnosis >6 months, bone deformities, severe concomitant diseases (e.g. metabolic, gastrointestinal), functional class IV, use of omega 3 supplementation, digestive intolerance, severe infections, AST, ALT or creative >1.5x ULN, bilirubin >1.8mg/dL	1) 2 omega 3 capsules 3x per day p) placebo tablets	1) 30 p) 30	Not reported	1) 25 (83.3) p) 24 (80.0)	**University** (Ahvaz Jundishapur University of Medical Sciences)
Reed (2014) [Canada][90]	RCT	1987 RA, Functional Class I-III, aged 18-85, ≥3 swollen joints, ≥6 tender joints, ESR ≥28, stable DMARDs Exclusions: investigation drugs within one month of BL, already taking borage seed / fish oil ≥2000mg/d for 2 months before BL, intraarticular steroids within 6 months of BL, ALT/AST >1.5x ULN, bilirubin >1.8mg/dL	1) Fish oil 2) Borage seeds 3) Fish oil + Borage seeds	1) 53 2) 52 3) 45	1) 57.3 (12.3) 2) 60.3 (9.2) 3) 60.5 (13.0)	1) 46 (86.8) 2) 40 (76.9) 3) 36 (80.0)	Not reported, authors declare no conflicts of interest

§ Cross-over design

ACR = American College of Rheumatology, ALT = alanine aminotransferase, AST = Aspartate transaminase, BL = baseline, CRP = C-reactive protein, DAS28 = Disease Activity Score (28), DMARD = disease modifying anti-rheumatic drug, ESR = erythrocyte sedimentation rate, IQR = interquartile range, N = number, RA = rheumatoid arthritis, RCT = randomised controlled trial, SD = standard deviation, ULN = upper limit of normal

Table – Animal products (RA), description of included studies

Author (date) [country]	Study design	Inclusion criteria	Exposure detail	N	Age, mean (SD) years	N (%) female	Funders
Arborelius (1999) [Finland][91]	RCT	1987 RA criteria, aged >16 years, active disease (at least one of: ≥9 tender joints, ≥6 swollen joints, CRP ≥11) Exclusions: Pregnancy, wheel chair bound, functional class IV, participation in another clinical trial in which non-registered drugs are used, allergy to orange juice, glutein induced enteropathy	1) Collagen from pig skins – turned into powder and taken with orange juice p) Placebo made from wheat – powder almost identical to collagen	36§	57.0 (10)	26 (72.2)	**University** (Helsinki University Central Hospital), **Industry** (Extraco AB)
Skoldstam (1992) [Sweden][92]	RCT	1987 RA criteria, Functional Class II-III, Stable disease history and treatment for preceding three months	1) Fish oil capsules p) placebo capsules	1) 22 p) 21	1) 58 (range 40-73) p) 55 (range 28-70)	1) 18 (81.8) p) 14 (66.6)	**Government** (Swedish Council for Planning and Coordination of Research)
Tulleken (1990) [The Netherlands][93]	RCT	1958 RA criteria, stable treatment for 3 months	1) 4 fish oil capsules 3x per day p) Coconut oil with fish flavouring	1) 13 p) 14	1) 52 (range: 29, 66) p) 58 (range: 43, 68)	1) 12 (92.3) p) 12 (85.7)	**NGO** (Dutch League Against Rheumatism)
van der Tempel (1990) [The Netherlands][94]	RCT §	Classical or definite RA	1) Fish oil capsules p) Coconut oil with fish flavouring	16	53	9 (56.3)	**NGO** (Dutch League Against Rheumatism)
Cleland (1988) [Australia][95]	RCT	Classical or definite RA	1) Fish oil capsules p) Olive oil	1) 23 p) 23	1) 51 (range: 22-71) p) 50 (25-74)	1) 16 (69.5) p) 16 (69.5)	**Government** (National Health and Medical Research Council of Australia), **Charity** (Arthritis Fund of Australia, Royal Adelaide Hospital Research Fund, Queen Elizabeth Hospital Research Foundation)

§ Cross-over design

CRP = C-reactive protein, N = number, NGO = non-governmental organisation, RA = rheumatoid arthritis, RCT = randomised controlled trial, SD = standard deviation

Table – Animal products (RA), description of included studies

Author (date) [country]	Study design	Inclusion criteria	Exposure detail	N	Age, mean (SD) years	N (%) female	Funders
Magaro (1988) [Italy][96]	RCT	Classical or definite RA, active disease: morning stiffness ≥30 mins, ≥6 tender joints, ≥3 swollen joints, ≥30mm/h ESR Exclusion: systemic steroids or immunosuppressive drugs in three months before BL	1) Max EPA – high in unsaturated fatty acids p) diet high in saturated fatty acids	1) 6 p) 6	1) 36 (range 20-50) p) 37 (range 20 55)	1) 6 (100) p) 6 (100	Not reported
Kremer (1987) [USA][97]	RCT §	Classical or definite RA, Functional class I-III, had at least three of the following four criteria: morning stiffness of at least 30 minutes duration; ≥6 tender joints; ≥3 swollen joints; ≥28 ESR	1) Daily fish oil supplements p) Placebo supplement	33	56.8 (range 23-74)	25 (75.8)	**Government** (NIH, Research Service of the Veterans Administration)
Cleland (2006) [Australia][98]	NRT	Aged >18 years, 1987 RA criteria, symptoms <12 months	1) Bottle fish oil juice / capsules depending on preference p) Those not taking fish oil regularly	1) 18 p) 15	1) 61.8 (9.9) p) 51.1 (15.9)	1) 67% p) 76%	**Government** (National Health and Medical Research Council of Australia)

§ Cross-over design

BL = baseline, CRP = C-reactive protein, EPA = eicosapentaenoic acid, ESR = erythrocyte sedimentation rate, N = number, NIH = National Institutes of Health, NRT = non-randomised trial, RA = rheumatoid arthritis, RCT = randomised controlled trial, SD = standard deviation

Supplementary table 65 – Collagen and RA progression, results

Table – Collagen (RA), results and quality assessment

Outcome	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	AMSTAR2 quality	Rand. Seq.	Alloc. Conc.	Blind. Part.	Blind. Asses.
Pain	Arborelius (1999) [RCT][91]		Pain VAS, mean difference between intervention and control -0.69, p = NS		L	H/UC	L	H/UC
Function	Arborelius (1999) [RCT][91]		HAQ (0-24), mean difference between intervention and control -3.88, p=NS		L	H/UC	L	H/UC
Tender joints	Arborelius (1999) [RCT][91]		Ritchie Index, mean difference between intervention and control 1.51, p=NS		L	H/UC	L	H/UC
Swollen joints	Arborelius (1999) [RCT][91]		Swollen joint count (54), mean difference between intervention and control -1.6, p=NS		L	H/UC	L	H/UC
Disease activity	Arborelius (1999) [RCT][91]		DAS, mean difference between intervention and control -0.54, p=NS		L	H/UC	L	H/UC
Acute Phase Reactants	Arborelius (1999) [RCT][91]		CRP / ESR, mean difference between intervention and control 1.48, p=NS / -3.65, p=NS		L	H/UC	L	H/UC
Patient global	Arborelius (1999) [RCT][91]		Patient global VAS, mean difference between intervention and control -1.1, p=NS		L	H/UC	L	H/UC

Alloc. Conc. = allocation concealment, AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews, Blind. Asses. = Blinded assessors, Blind. Part. = blinded participants, CI = confidence interval, CRP = C-reactive protein, DAS = Disease Activity Score, ESR = erythrocyte sedimentation rate, H/UC = high / unclear risk of bias, HAQ = Health Assessment Questionnaire, L = low risk of bias, NS = non-significant, RA = rheumatoid arthritis, Rand. Seq. = random sequence generation, RCT = randomised controlled trial, SMD = Standardised mean difference, VAS = visual analogue scale

Supplementary table 66 – Fish oil / omega 3 and RA progression, results

Table – Fish oils / omega 3 (RA), results and quality assessment

Outcome	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	AMSTAR2 quality	Rand. Seq.	Alloc. Conc.	Blind. Part.	Blind. Asses.
Pain	Gioxari (2018) [MA][84]	Omega 3 vs placebo SMD -0.32 (-0.59, -0.05)		Moderate				
	Senftleber (2017) [MA][15]	Marine oil supplements vs placebo SMD -0.21 (-0.42, -0.00)		High				
	Abdulrazaq (2017) [SR][86]	10/18 studies reported reduction a in pain from omega-3. Of these 10, only 4 were compared to placebo and 6 were comparisons to baseline scores		Moderate				
	Rajaei (2015) [RCT][89]		Pain VAS, BL / 12 weeks, mean Omega 3: 9 / 4 Placebo: 8 / 8		H/UC	H/UC	L	H/UC
	Skoldstam (1992) [RCT][92]	Fish oil vs placebo, change BL-6 months SMD -0.21 (-0.81, 0.39)	Pain VAS, BL-6 months, mean (SD §) Fish oil: 0.02 (0.66) Placebo: 0.17 (0.78)		H/UC	H/UC	L	L
	Tulleken (1990) [RCT][93]	Fish oil vs placebo SMD -0.46 (-1.22, 0.31)	Pain VAS, BL / 3 months, mean (SD †) Fish oil: 3.7 (1.7) / 3.1 (2.2) Placebo: 4.6 (1.9) / 4.1 (2.2)		H/UC	H/UC	L	H/UC
	van der Tempel (1990) [RCT][94]	Fish oil vs placebo at 12 weeks SMD -0.53 (-1.24, 0.17)	Pain VAS, 12 weeks, mean (SD §) Fish oil: 2.7 (2.0) Placebo: 4 (2.8)		H/UC	H/UC	L	L
	Cleland (1988) [RCT][95]	Fish oil vs placebo at 3 months SMD -0.02 (-0.60, 0.56)	Pain VAS, BL / 3 months, mean (SD) Fish oil: 9.6 (5.8) / 7.0 (4.6) Placebo: 9.8 (4.6) / 7.1 (5.1)		H/UC	H/UC	L	H/UC
	Kremer (1987) [RCT][97]	Fish oil vs placebo, change BL-14 weeks SMD -0.28 (-0.77, 0.20)	Pain, change BL – 14 weeks, mean (SD*) Fish oil: -0.21 (0.91) Placebo: 0.0 (0.53)		H/UC	H/UC	L	L
	Bespoke meta-analysis [92-95;97]	Fish oil vs placebo SMD -0.27 (-0.54, 0.00), I^2 0%						
Function	Gioxari (2018) [MA][84]	Omega 3 vs placebo SMD -0.26 (-0.46, -0.06)		Moderate				
	Senftleber (2017) [MA][15]	Marine oil supplements vs placebo SMD 0.05 (-0.11, 0.21)		High				
	Skoldstam (1992) [RCT][92]	Fish oil vs placebo, change BL-6 months SMD -0.35 (-0.95, 0.26)	HAQ, BL-6 months, mean (SD §) Fish oil: -0.07 (0.42) Placebo: 0.06 (0.32)		H/UC	H/UC	L	L
	Cleland (2006) [NRT][98]	Fish oil vs control at 3 years SMD -0.86 (-1.61, -0.12)	mHAQ, BL / 3 years, mean (SD) Fish oil: 6.6 (3.2) / 1.2 (1.7) Control: 7.1 (4.2) / 3.3 (3.2)					

* Calculated from 95% CI in paper § Calculated from standard error in paper † Mean (SD) calculated from median (range) using published formula [61] Alloc. Conc. = allocation concealment, AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews, BL = baseline, Blind. Asses. = Blinded assessors, Blind. Part. = blinded participants, CI = confidence interval, H/UC = high / unclear risk of bias, HAQ = Health Assessment Questionnaire, L = low risk of bias, MA = meta-analysis, mHAQ = modified Health Assessment Questionnaire, NRT = non-randomised trial, RA = rheumatoid arthritis, Rand. Seq. = random sequence generation, RCT = randomised controlled trial, SD = standard deviation, SMD = Standardised mean difference, VAS = visual analogue scale

Table – Fish oils / omega 3 (RA), results and quality assessment

Outcome	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	AMSTAR2 quality	Rand. Seq.	Alloc. Conc.	Blind. Part.	Blind. Asses.
Disease activity	Rajaei (2015) [RCT][89]		DAS28, ≤3.2 / 3.2-5.1 / >5.1 at 12 weeks Omega 3: 20 / 5 / 0 Placebo: 0 / 24 / 0;		H/UC	H/UC	L	H/UC
	Reed (2014) [RCT][90]	Fish oil vs borage seed, change from BL to 18 months SMD 0.12 (-0.26, 0.50)	DAS28, change from BL to 18 months, mean (SD*) Fish oil: -1.28 (2.25) Borage seed: -1.53 (1.91) Fish oil + Borage seed: -1.45 (1.92)		H/UC	H/UC	L	L
	Cleland (2006) [NRT][98]	Fish oil vs control at 3 years SMD -1.27 (-2.06, -0.49)	DAS28, BL / 3 years, mean (SD) Fish oil: 5.0 (1.5) / 2.1 (0.9) Control: 5.7 (0.9) / 3.3 (1.0)					
Tender joints	Gioxari (2018) [MA][84]	Omega 3 vs placebo SMD -0.24 (-0.39, -0.095)		Moderate				
	Rajaei (2015) [RCT][89]		Tender joint count, BL / 12 weeks, mean Omega 3: 21 / 5 Placebo: 24 / 20; p<0.05		H/UC	H/UC	L	H/UC
	Skoldstam (1992) [RCT][92]	Fish oil vs placebo, change BL-6 months SMD -0.02 (-0.62, 0.58)	Ritchie Index, BL-6 months, mean (SD §) Fish oil: -2.6 (5.2) Placebo: -2.5 (6.0)		H/UC	H/UC	L	L
	Tulleken (1990) [RCT][93]	Fish oil vs placebo SMD 0.11 (-0.64, 0.87)	Ritchie Index, BL / 3 months, mean (SD †) Fish oil: 22 (13.7) / 15.3 (14.6) Placebo: 15.8 (6.4) / 14 (7.3)		H/UC	H/UC	L	H/UC
	Cleland (1988) [RCT][95]		Tender joint count, BL / 3 months, mean (range) Fish oil: 13 (4-41) / 9.5 (1-31) Placebo: 13 (3-36) / 12 (0-41)		H/UC	H/UC	L	H/UC
	Magaro (1988) [RCT][96]	Max EPA vs placebo at 30 days SMD -1.32 (-2.60, -0.05)	Ritchie index, 30 days, mean (SD §) Max EPA: 10.6 (8.5) Control: 21.4 (7.8)		H/UC	H/UC	H/UC	H/UC
	Kremer (1987) [RCT][97]	Fish oil vs placebo, change BL-14 weeks SMD -0.81 (-1.32, -0.31)	Tender joint count, change BL – 14 weeks, mean (SD*) Fish oil: -3.5 (5.0) Placebo: 0.01 (3.5)		H/UC	H/UC	L	L
	Cleland (2006) [NRT][98]	Fish oil vs control at 3 years SMD -1.06 (-1.82, -0.29)	Tender joint count, BL / 3 years, mean (SD) Fish oil: 6.4 (6.2) / 0.7 (1.1) Control: 8.8 (3.6) / 3.5 (3.9)					
	Bespoke MA[92;93;96;97]	Fish oil vs placebo SMD -0.42 (-1.01, 0.16), I^2 62.3%						

* Calculated from 95% CI in paper, § Calculated from standard error in paper, † Mean (SD) calculated from median (range) using published formula [61] Alloc. Conc. = allocation concealment, AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews, BL = baseline, Blind. Asses. = Blinded assessors, Blind. Part. = blinded participants, CI = confidence interval, DAS28 = Disease activity score 28, EPA = eicosapentaenoic acid, H/UC = high / unclear risk of bias, L = low risk of bias, MA = meta-analysis, NRT = non-randomised trial, RA = rheumatoid arthritis, Rand. Seq. = random sequence generation, RCT = randomised controlled trial, SD = standard deviation, SMD = Standardised mean difference

Table – Fish oils / omega 3 (RA), results and quality assessment

Outcome	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	AMSTAR2 quality	Rand. Seq.	Alloc. Conc.	Blind. Part.	Blind. Asses.
Swollen joints	Gioxari (2018) [MA][84]	Omega 3 vs placebo SMD -0.08 (-0.23, 0.07)		Moderate				
	Rajaei (2015) [RCT][89]		Swollen joint count, BL / 12 weeks, mean Omega 3: 10 / 3 Placebo: 7 / 5; p<0.05		H/UC	H/UC	L	H/UC
	Tulleken (1990) [RCT][93]	Fish oil vs placebo SMD -0.11 (-0.87, 0.64)	Swollen joint count, BL / 3 months, mean (SD †) Fish oil: 9 (7.2) / 5.8 (4.5) Placebo: 6.3 (3.2) / 6.3 (4.4)		H/UC	H/UC	L	H/UC
	van der Tempel (1990) [RCT][94]	Fish oil vs placebo at 12 weeks SMD -0.67 (-1.38, 0.04)	Joint swelling, 12 weeks, mean (SD §) Fish oil: 2 (4) Placebo: 8 (12)		H/UC	H/UC	L	L
	Cleland (1988) [RCT][95]		Swollen joint count, BL / 3 months, mean (range) Fish oil: 3.5 (0-12) / 3.6 (0-9) Placebo: 3.8 (0-8) / 3.5 (0-12)		H/UC	H/UC	L	H/UC
	Kremer (1987) [RCT][97]	Fish oil vs placebo, change BL-14 weeks SMD -0.41 (-0.90, 0.08)	Swollen joint count, change BL – 14 weeks, mean (SD*) Fish oil: -2.8 (4.4) Placebo: -1.0 (4.4)		H/UC	H/UC	L	L
	Cleland (2006) [NRT][98]	Fish oil vs control at 3 years SMD 0.42 (-0.30, 1.14)	Swollen joint count, BL / 3 years, mean (SD) Fish oil: 5.4 (5.5) / 0.9 (1.8) Control: 6.9 (4.7) / 0.3 (0.6)					
Inflammation	Senftleber (2017) [MA][15]	Marine oil supplements vs placebo SMD -0.20 (-0.42, 0.03)		High				

* Calculated from 95% CI in paper

§ Calculated from standard error in paper

† Mean (SD) calculated from median (range) using published formula [61]

Alloc. Conc. = allocation concealment, AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews, BL = baseline, Blind. Asses. = Blinded assessors, Blind. Part. = blinded participants, CI = confidence interval, H/UC = high / unclear risk of bias, L = low risk of bias, MA = meta-analysis, NRT = non-randomised trial, RA = rheumatoid arthritis, Rand. Seq. = random sequence generation, RCT = randomised controlled trial, SD = standard deviation, SMD = Standardised mean difference

Table – Fish oils / omega 3 (RA), results and quality assessment

Outcome	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	AMSTAR2 quality	Rand. Seq.	Alloc. Conc.	Blind. Part.	Blind. Asses.
Morning stiffness	Gioxari (2018) [MA][84]	Omega 3 vs placebo SMD -0.42 (-0.68, -0.16)		Moderate				
	Rajaei (2015) [RCT][89]		Morning stiffness, BL / 12 weeks, mean Omega 3: 128 / 40 Placebo: 116 / 94; p<0.05		H/UC	H/UC	L	H/UC
	Tulleken (1990) [RCT][93]	Fish oil vs placebo SMD -0.66 (-1.44, 0.12)	Morning stiffness, BL / 3 months, mean (SD †) Fish oil: 45 (17.9) / 45 (35.9) Placebo: 52.5 (35.1) / 75 (52.7)		H/UC	H/UC	L	H/UC
	van der Tempel (1990) [RCT][94]	Fish oil vs placebo at 12 weeks SMD -0.89 (-1.62, -0.16)	Morning stiffness, 12 weeks, mean (SD §) Fish oil: 15 (20) Placebo: 50 (52)		H/UC	H/UC	L	L
	Cleland (1988) [RCT][95]		Morning stiffness, BL / 3 months, mean (range) Fish oil: 48 (0-240) / 25 (0-120) Placebo: 63 (5-240) / 38 (0-180)		H/UC	H/UC	L	H/UC
	Magaro (1988) [RCT][96]	Max EPA vs placebo at 30 days SMD -0.61 (-1.77, 0.55)	Morning stiffness, 30 days, mean (SD §) Max EPA: 22 (20.7) Control: 36 (24.9)		H/UC	H/UC	H/UC	H/UC
	Kremer (1987) [RCT][97]	Fish oil vs placebo, change BL-14 weeks SMD -0.42 (-0.90, 0.07)	Morning stiffness (mins), change BL – 14 weeks, mean (SD*) Fish oil: -5.9 (48.9) Placebo: 49.4 (182.0)		H/UC	H/UC	L	L
	Bespoke MA [93;94;96;97]	Fish oil vs placebo SMD -0.59 (-0.93, -0.24), I^2 0%						

* Calculated from 95% CI in paper, § Calculated from standard error in paper, † Mean (SD) calculated from median (range) using published formula [61]

Alloc. Conc. = allocation concealment, AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews, BL = baseline, Blind. Asses. = Blinded assessors, Blind. Part. = blinded participants, CI = confidence interval, EPA = eicosapentaenoic acid, ESR = erythrocyte sedimentation rate, H/UC = high / unclear risk of bias, L = low risk of bias, MA = meta-analysis, RA = rheumatoid arthritis, Rand. Seq. = random sequence generation, RCT = randomised controlled trial, SD = standard deviation, SMD = Standardised mean difference

Table – Fish oils / omega 3 (RA), results and quality assessment

Outcome	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	AMSTAR2 quality	Rand. Seq.	Alloc. Conc.	Blind. Part.	Blind. Asses.
Fatigue	Gioxari (2018) [MA][84]	Omega 3 vs placebo SMD -0.10 (-0.55, 0.34)		Moderate				
	Cramp (2013) [MA][85]	Omega 3 vs placebo SMD 0.93 (0.47, 1.39) in favour of control						
	Kremer (1987) [RCT][97]	Fish oil vs placebo, change BL-14 weeks SMD 0.57 (0.08, 1.06)	Time to fatigue (mins), change BL – 14 weeks, mean (SD*) Fish oil: 176.8 (274.9) Placebo: 8.4 (314.5)		H/UC	H/UC	L	L
Patient global	Skoldstam (1992) [RCT][92]	Fish oil vs placebo, change BL-6 months SMD -0.53 (-1.13, 0.08)	Patient global, change BL-6 months, mean (SD §) Fish oil: 0.01 (0.66) Placebo: 0.40 (0.82)		H/UC	H/UC	L	L
	Kremer (1987) [RCT][97]	Fish oil vs placebo, change BL-14 weeks SMD -0.19 (-0.67, 0.30)	Patient global, change BL – 14 weeks, mean (SD*) Fish oil: -0.11 (0.70) Placebo: 0.0 (0.47)		H/UC	H/UC	L	L

* Calculated from 95% CI in paper, § Calculated from standard error in paper, † Mean (SD) calculated from median (range) using published formula [61]

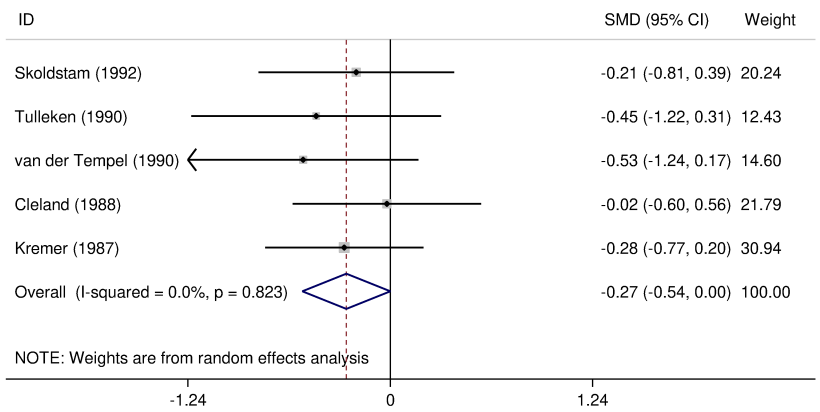
Alloc. Conc. = allocation concealment, AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews, BL = baseline, Blind. Asses. = Blinded assessors, Blind. Part. = blinded participants, C-reactive protein, CI = confidence interval, H/UC = high / unclear risk of bias, L = low risk of bias, MA = meta-analysis, RA = rheumatoid arthritis, Rand. Seq. = random sequence generation, RCT = randomised controlled trial, SD = standard deviation, SMD = Standardised mean difference

Table – Fish oils / omega 3 (RA), results and quality assessment

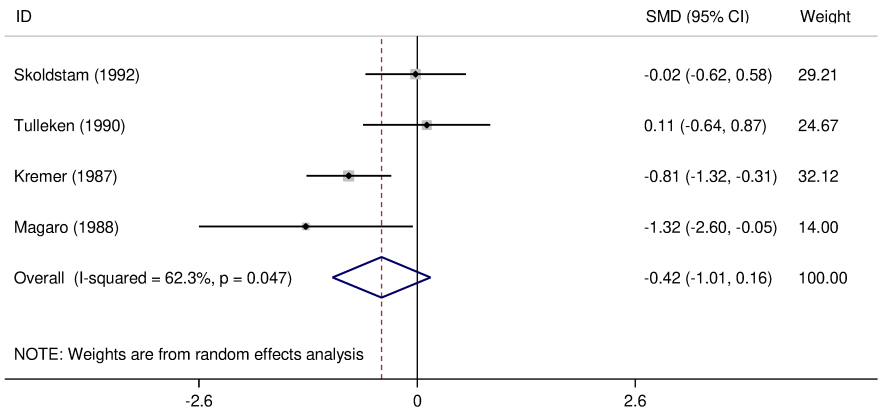
Outcome	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	AMSTAR2 quality	Rand. Seq.	Alloc. Conc.	Blind. Part.	Blind. Asses.
CRP	Gioxari (2018) [MA][84]	Omega 3 vs placebo SMD 0.44 (-0.13, 1.00)		Moderate				
	Skoldstam (1992) [RCT][92]	Fish oil vs placebo, change BL-6 months SMD -0.17 (-0.77, 0.43)	CRP, change BL-6 months, mean (SD §) Fish oil: 7 (18.8) Placebo: 12 (36.7)		H/UC	H/UC	L	L
	Tulleken (1990) [RCT][93]	Fish oil vs placebo SMD -0.63 (-1.41, 0.14)	CRP, BL / 3 months, mean (SD †) Fish oil: 18.3 (15.2) / 20.3 (15.2) Placebo: 42 (31.0) / 35 (28.7)		H/UC	H/UC	L	H/UC
	van der Tempel (1990) [RCT][94]	Fish oil vs placebo at 12 weeks SMD -0.16 (-0.86, 0.53)	CRP, 12 weeks, mean (SD †) Fish oil: 26.5 (18.7) Placebo: 29.5 (18.7)		H/UC	H/UC	L	L
	Cleland (2006) [NRT][98]		CRP, BL / 3 years, mean (range) Fish oil: 30.8 (1, 140) / 4.0 (0.3, 19) Control: 17.2 (4, 34) / 6.6 (3, 15)					
	Bespoke MA [92-94]	Fish oil vs placebo SMD -0.29 (-0.68, 0.11)						
ESR	Gioxari (2018) [MA][84]	Omega 3 vs placebo SMD -0.16 (0.32, -0.00)		Moderate				
	Rajaei (2015) [RCT][89]		ESR, BL / 12 weeks, mean Omega 3: 39 / 16 Placebo: 35 / 33; p<0.05		H/UC	H/UC	L	H/UC
	Skoldstam (1992) [RCT][92]	Fish oil vs placebo, change BL-6 months SMD 0.00 (-0.60, 0.60)	ESR, change BL-6 months, mean (SD §) Fish oil: 6 (14.1) Placebo: 6 (18.3)		H/UC	H/UC	L	L
	Tulleken (1990) [RCT][93]	Fish oil vs placebo SMD -1.10 (-1.92, -0.29)	ESR, BL / 3 months, mean (SD †) Fish oil: 38.5 (19.7) / 27.3 (15.8) Placebo: 56.5 (18.2) / 49.5 (23.4)		H/UC	H/UC	L	H/UC
	Kremer (1987) [RCT][97]	Fish oil vs placebo, change BL-14 weeks SMD 0.08 (-0.40, 0.56)	ESR, change BL – 14 weeks, mean (SD*) Fish oil: -0.8 (17.6) Placebo: -2.07 (14.1)		H/UC	H/UC	L	L
	Cleland (2006) [NRT][98]		ESR, BL / 3 years, mean (range) Fish oil: 43.1 (1, 91) / 8.5 (2, 34) Control: 36.5 (4, 80) / 21.5 (8, 46)					
	Bespoke meta-analysis[92;93;97]	Fish oil vs placebo SMD -0.27 (-0.91, 0.37), I^2 68.6%						

* Calculated from 95% CI in paper, § Calculated from standard error in paper, † Mean (SD) calculated from median (range) using published formula [61]

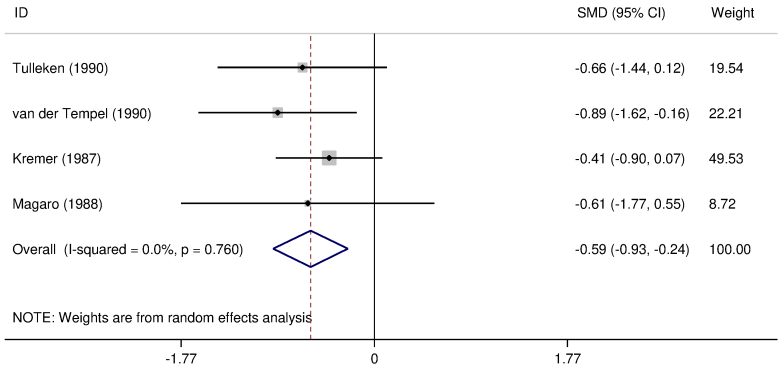
Alloc. Conc. = allocation concealment, AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews, BL = baseline, Blind. Asses. = Blinded assessors, Blind. Part. = blinded participants, CRP = C-reactive protein, CI = confidence interval, ESR = erythrocyte sedimentation rate, H/UC = high / unclear risk of bias, L = low risk of bias, MA = meta-analysis, NRT = non-randomised trial, RA = rheumatoid arthritis, Rand. Seq. = random sequence generation, RCT = randomised controlled trial, SD = standard deviation, SMD = Standardised mean difference



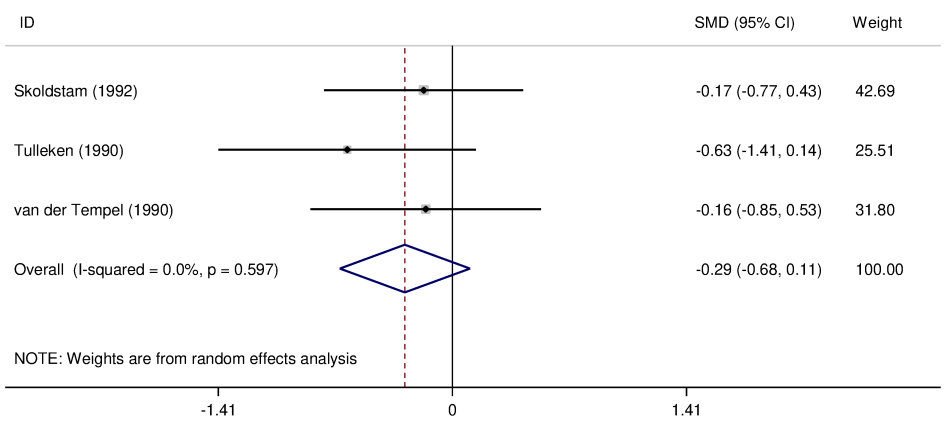
Supplementary figure 3 – Fish oil / omega 3 (RA), bespoke meta-



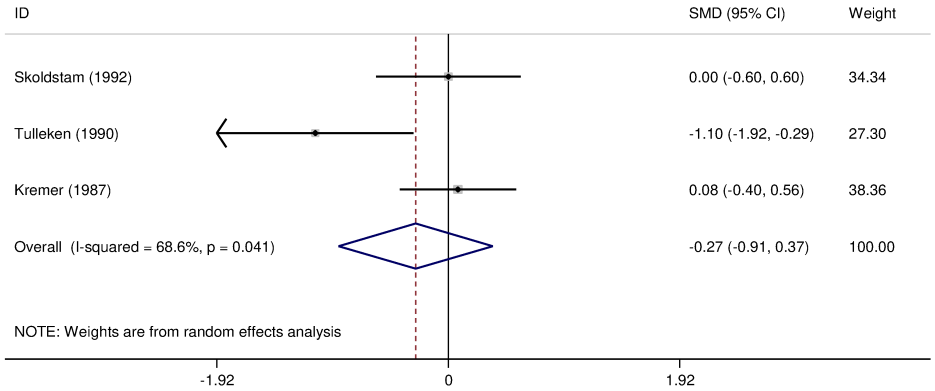
Supplementary figure 4 – Fish oil / omega 3 (RA), bespoke meta-analysis for tender joint count



Supplementary figure 5 – Fish oil / omega 3 (RA), bespoke meta-analysis for morning stiffness



Supplementary figure 6 – Fish oil / omega 3 (RA), bespoke meta-analysis for CRP



Supplementary figure 7– Fish oil / omega 3 (RA), bespoke meta-analysis for ESR

Supplementary table 67 – Mussel extracts and RA progression, results

Table – Mussels (RA), results and quality assessment

Outcome	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	AMSTAR2 quality	Rand. Seq.	Alloc. Conc.	Blind. Part.	Blind. Asses.
Pain	Lindqvist (2018) [RCT][87]	Mussels vs control at 11 weeks SMD -0.37 (-0.96, 0.21)	Pain VAS, BL / 11 weeks, mean (SD §) Mussels: 51 (33.2) / 31.3 (30.8) Control: 31.3 (30.8) / 44.3 (38.7)		L	H/UC	H/UC	H/UC
Function	Lindqvist (2018) [RCT][87]	Mussels vs control at 11 weeks SMD -0.20 (-0.78, 0.38)	HAQ, BL / 11 weeks, mean (SD §) Mussels: 0.93 (0.61) / 0.80 (0.91) Control: 0.95 (0.66) / 0.96 (0.70)		L	H/UC	H/UC	H/UC
Disease activity	Lindqvist (2018) [RCT][87]		DAS28, BL / 11 weeks, median (IQR) Mussels: 3.75 (3.15, 4.53) / 3.40 (2.41, 3.73) Control: 3.81 (3.16, 3.73 [sic]) / 3.77 (2.69, 4.22);		L	H/UC	H/UC	H/UC
	Fu (2015) [RCT][88]	Mussels vs control at 11 weeks SMD -0.94 (-1.58, -0.29)	DAS28, BL / 6 months, mean (SD*) Mussels: 5.80 (0.51) / 4.69 (0.51) Control: 5.71 (0.73) / 5.07 (0.69); p<0.01		L	H/UC	L	L
Tender joints	Lindqvist (2018) [RCT][87]	Mussels vs control at 11 weeks SMD -0.22 (-0.80, 0.36)	Tender joint count, BL / 11 weeks, mean (SD §) Mussels: 4.3 (4.0) / 2.7 (3.2) Control: 5.3 (8.7) / 3.7 (5.5)		L	H/UC	H/UC	H/UC
	Fu (2015) [RCT][88]	Mussels vs control at 11 weeks SMD -0.79 (-1.43, -0.16)	Tender joint count, BL / 6 months, mean (SD*) Mussels: 10.6 (1.7) / 5.1 (2.1) Control: 9.5 (2.9) / 6.9 (2.4); p<0.01		L	H/UC	L	L
Swollen joints	Lindqvist (2018) [RCT][87]	Mussels vs control at 11 weeks SMD -0.40 (-0.98, 0.19)	Swollen joint count, BL / 11 weeks, mean (SD §) Mussels: 2 (1.6) / 1 (1.6) Control: 2 (1.6) / 2 (3.2)		L	H/UC	H/UC	H/UC
	Fu (2015) [RCT][88]	Mussels vs control at 11 weeks SMD -0.46 (-1.08, 0.16)	Swollen joint count, BL / 6 months, mean (SD*) Mussels: 7.3 (3.0) / 4.1 (2.1) Control: 7.8 (3.6) / 5.3 (2.9); p=0.053		L	H/UC	L	L
Morning stiffness	Fu (2015) [RCT][88]	Mussels vs control at 11 weeks SMD -0.58 (-1.20, 0.04)	Morning stiffness, BL / 6 months, mean (SD*) Mussels: 69.7 (26.7) / 40.6 (29.7) Control: 72.7 (39.2) / 58.1 (32.3); p=0.016		L	H/UC	L	L
Fatigue	Lindqvist (2018) [RCT][87]	Mussels vs control at 11 weeks SMD -0.49 (-1.08, 0.10)	Fatigue VAS, BL / 11 weeks, mean (SD §) Mussels: 65.0 (26.1) / 46.3 (38.7) Control: 59.0 (30.8) / 61.3 (19.8)		L	H/UC	H/UC	H/UC
Patient global	Lindqvist (2018) [RCT][87]	Mussels vs control at 11 weeks SMD -0.51 (-1.10, 0.07)	Patient global VAS, BL / 11 weeks, mean (SD §) Mussels: 54.3 (25.3) / 33.0 (37.1) Control: 49.0 (26.9) / 47.0 (10.3)		L	H/UC	H/UC	H/UC
	Fu (2015) [RCT][88]	Mussels vs control at 11 weeks SMD 0.18 (-0.43, 0.79)	Patient global VAS, BL / 6 months, mean (SD*) Mussels: 53.5 (11.5) / 42.4 (9.8) Control: 47.9 (12.7) / 40.6 (10.3); p=0.135		L	H/UC	L	L

§ Calculated from median (IQR) using published formula

* Calculated from standard error in paper

Alloc. Conc. = allocation concealment, AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews, BL = baseline, Blind. Asses. = Blinded assessors, Blind. Part. = blinded participants, CI = confidence interval, DAS28 = Disease Activity Score 28, H/UC = high / unclear risk of bias, HAQ = Health Assessment Questionnaire, IQR = interquartile range, L = low risk of bias, RA = rheumatoid arthritis, Rand. Seq. = random sequence generation, RCT = randomised controlled trial, SD = standard deviation, SMD = Standardised mean difference, VAS = visual analogue scale

Table – Mussels (RA) [cont.], results and quality assessment

Outcome	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	AMSTAR2 quality	Rand. Seq.	Alloc. Conc.	Blind. Part.	Blind. Asses.
CRP	Lindqvist (2018) [RCT][87]	Mussels vs control at 11 weeks SMD 0.00 (-0.58, 0.58)	CRP, BL / 11 weeks, mean (SD §) Mussels: 2.7 (3.2) / 1.7 (1.6) Control: 1.7 (2.4) / 1.7 (2.4)		L	H/UC	H/UC	H/UC
	Fu (2015) [RCT][88]	Mussels vs control at 11 weeks SMD -0.48 (-1.10, 0.14)	CRP, BL / 6 months, mean (SD*) Mussels: 14.4 (7.2) / 11.4 (6.4) Control: 16.3 (9.8) / 14.9 (7.8); p0=0.273		L	H/UC	L	L
ESR	Lindqvist (2018) [RCT][87]	Mussels vs control at 11 weeks SMD -0.15 (-0.73, 0.43)	ESR, BL / 11 weeks, mean (SD §) Mussels: 14.3 (16.2) / 11.0 (11.5) Control: 14.0 (15.8) / 13.0 (15.0)		L	H/UC	H/UC	H/UC
	Fu (2015) [RCT][88]	Mussels vs control at 11 weeks SMD -0.22 (-0.83, 0.40)	ESR, BL / 6 months, mean (SD*) Mussels: 50.8 (27.2) / 34.7 (19.9) Control: 53.3 (29.9) / 38.9 (19.1); p=0.571		L	H/UC	L	L

§ Calculated from median (IQR) using published formula

* Calculated from standard error in paper

Alloc. Conc. = allocation concealment, AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews, BL = baseline, Blind. Asses. = Blinded assessors, Blind. Part. = blinded participants, CI = confidence interval, CRP = C-reactive protein, ESR = erythrocyte sedimentation rate, H/UC = high / unclear risk of bias, IQR = interquartile range, L = low risk of bias, RA = rheumatoid arthritis, Rand. Seq. = random sequence generation, RCT = randomised controlled trial, SD = standard deviation, SMD = Standardised mean difference

Table – Mussels (RA), SF36 results at final follow-up

Author (date)	PCS	MCS	GH	PF	RP	RE	SF	BP	V	MH
Lindqvist (2018) [Mussels][87]	39.3 (12.6)	51 (7.1)								
Lindqvist (2018) [Control][87]	38 (8.7)	47 (10.3)								

BP = bodily pain, GH = general health, MCS = mental component score, MH = mental health, PCS = physical component score, PF = physical function, RA = rheumatoid arthritis, RE = role emotional, RP = role physical, SF = social functioning, V = vitality

Supplementary table 68 – Description of reviews of experimental diets in RA

Table – Experimental diet (RA), description of reviews

Authors (date)	Review type	Study type included	Exposure detail	Number of studies included	Funders
Cramp (2013)[85]	MA	RCTs	Mediterranean diet	1	**Charity** (Arthritis Research UK)

MA = meta-analysis, RA = rheumatoid arthritis, RCT = randomised controlled trial

Supplementary table 69 – Description of studies of experimental diets in RA

Table – Experimental diets (RA), description of included studies

Author (date) [country]	Study design	Inclusion criteria	Exposure detail	N	Age, mean (SD) years	N (%) female	Funders
Podas (2007) [UK][99]	RCT	1987 RA criteria, active RA (≥3 of: ≥3 swollen joints, ≥6 tender joints, >45 mins morning stiffness, >28mm ESR), stable DMARDs for 6 weeks Exclusions: pregnancy, diabetes, other systemic illnesses	1) Liquid elemental diet E028 p) Oral steroids	1) 21 p) 9	1) 47 p) 48	1) 16 (76.2) p) 6 (66.7)	**Industry** (Scientific Hospital Supplies Ltd)
Skoldstam (2003) [Sweden][100]	RCT	1987 RA criteria, symptom duration >2 years, stable disease under adequate control Exclusions: DMARDs unchanged for >3 months, steroids for >4 weeks, and NSAIDs >0 days. Daily dose oral steroids not >12.5, DAS28 >2.0, no other comorbidities that demand active medical attention, vegetarians, those already eating Mediterranean-like diet	1) Mediterranean diet p) Continue regular diet	1) 26 p) 25	1) 58 (range: 33-73) p) 59 (range: 35-75)	1) 21 (80.8) p) 20 (80)	**University** (Faculty of Social Sciences of Umea University), **Public Foundation** (Swedish Foundation for Health Care Sciences and Allergy Research), **Government** (Health Research Council), **Charity** (Swedish Nutrition Foundation, the JC Kempe Memorial Scholarship Fund, the Borgerskapet i Umeå Fund, and the Uppsala Hemsysterskola Fund.
Hafstrom (2001) [Sweden][101]	RCT	1987 RA criteria, aged 20-69 years, symptom duration 2-10 years, not tried dietary manipulation, no history of food sensitivity, active disease, stable dose of DMARDs	1) Vegan diet with no gluten p) Non-vegan diet – well balanced	1) 38 p) 28	1) 49.5 (9.6) p) 50.8 (11.9)	Not reported	**Charity** (Axel and Margaret Ax:son Johnson Foundation, Swedish Rheumatism Association), **Government** (Swedish Medical Research Council)
Sarzi-Puttini (2000) [Italy][102]	RCT	1987 RA criteria, aged 25-70 years, Steinbrocker functional class I-II, stable therapy for 12 weeks, ≥4 of the following: ≥5 painful joints, ≥3 swollen joints, ≥4 pain VAS, ≥45 mins morning stiffness, ≥30 mm/hr ESR	1) Hypoallergenic diet (rice, cornmeal, cornbread, hydrolysed milk, fresh pineapple, cooked apple) with no: wheal meal, eggs, milk, strawberries and acid fruit, tomato, chocolate, crustacean, dried fruit. p) Same calorie content but containing allergenic food.	1) 22 p) 21	1) 49.56 (range: 32-64) p) 50.28 (range: 29-70)	1) 19 (76) p) 20 (80)	Not reported

* estimated from median and range in paper using published formula[61]

DAS28 = Disease Activity Score 28, DMARDs = disease modifying anti-rheumatoid drugs, ESR = erythrocyte sedimentation rate, hr = hour, mm = millimetres, N = number, NGO = non-governmental organisation, NSAID = non-steroidal anti-inflammatory drugs, RA = rheumatoid arthritis, RCT = randomised controlled trial, SD = standard deviation, UK = United Kingdom, VAS = visual analogue scale

Table – Experimental diets (RA), description of included studies

Author (date) [country]	Study design	Inclusion criteria	Exposure detail	N	Age, mean (SD) years	N (%) female	Funders
Holst-Jensen (1998) [Denmark][103]	RCT	1987 RA criteria, aged 18-75 years, symptom duration ≥6 months, active RA (at least three of: ≥3 swollen joints, ≥6 tender joints, ≥28mm/hr ESR, ≥45 mins morning stiffness), stable DMARDs for 3 months Exclusions: Signs or symptoms of any other severe disease, pacemaker, prosthetic joint, electrolyte derangement, edema	1) Liquid elemental diet, no solids p) Continue normal diet	1) 15 p) 15	Median (10^{th} / 90^{th} percentiles): 1) 46 (29/72) p) 56 (34/70)	1) 14 (93) p) 10 (67)	**NGO** (Danish Rheumatoid Association), **Industry** (Ferrosan Ltd.)
Nenonen (1998) [Finland][104]	RCT	1987 RA, Steinbrocker functional class II-III, >3 swollen joints or >5 tender joints, >20 ESR or >10 CRP	1) Uncooked, lactobacilli rich, vegan diet p) Continue normal diet	1) 19 p) 20	1) 49.1 (7.1) p) 55.6 (10.8)	1) 18 (94.7) p) 19 (95.0)	**Charity (**Juho Vainio Foundation)
Kavanagh (1995) [UK][105]	RCT	Definite RA Exclusions: Taking steroids / DMARDs	1) Liquid elemental diet E028 + chicken, fish, rice, carrots, runner beans and bananas p) E028 + normal diet (elemental diet to replace some drinks)	1) 24 p) 23	1) 42.8 (10.5) p) 48.5 (13.7)	1) 18 (75) p) 19 (82.6)	**Charity** (Arthritis Rheumatism Council)
Haugen (1994) [Norway][106]	RCT	1987 RA criteria, active RA (at least three of: : ≥3 swollen joints, ≥6 tender joints, ≥28mm/hr ESR, ≥45 mins morning stiffness), stable DMARDs for 3 months, steroid dose ≤7.5mg per day and stable for 4 weeks	1) Liquid elemental diet E028 P) Soup	1) 10 p) 7	1) 50.3 (13.3) * p) 53.5 (13.9) *	1) 9 (90) p) 5 (71.4)	**Charity** (The Norwegian Women's Public Health Association, Anders Jahres Legacy, Grethe Harbitz Legacy, Eckbo Legacy, Olga Imerslund legacy)
van de Laar (1992) [The Netherlands][107]	RCT	Met ≥6 ARA 1958 criteria (1 had to be RF+), ≥3 of the following: >28mm/h ESR, >45 mins morning stiffness, >5 tender joints, >2 swollen joints Exclusions: function class IV	1) Allergy / additive / preservative free diet 2) Allergy free other than milk allergens and azo colourings	1) 45 2) 49	1) 57.7 2) 58.6	1) 30 (66.7) p) 36 (73.5)	**Industry** (het Praeventiefonds)
Panush (1983) [USA][108]	RCT	Definite Stage I-III, RA after 16 years, stable medication regime, ≥3 of the following: ≥6 tender joints, ≥3 swollen joints, ≥45 minutes morning stiffness, >228mm/hr ESR	1) Diet consisting or little meat except fish and occasional fowl, no fruit, no herbs, no spices, no dairy products, no alcohol, no additives, no preservatives, supplemental iron and vitamins p) Placebo diet – excluded select items from food groups, but included those eliminated from experimental diet	1) 11 p) 15	1) 53.6 p) 56.3	1) 5 (45.5) p) 4 (26.7)	**Charity** (Arthritis Foundation), **Government** (Veterans Administration)

* estimated from median and range in paper using published formula[61]

ARA = American Rheumatism Association, CRP = C-reactive protein, DMARDs = disease modifying anti-rheumatoid drugs, ESR = erythrocyte sedimentation rate, hr = hour, mm = millimetres, N = number, NGO = non-governmental organisation, RA = rheumatoid arthritis, RCT = randomised controlled trial, RF = rheumatoid factor, SD = standard deviation, UK = United Kingdom, USA = United States of America

Table – Experimental diets (RA), description of included studies

Author (date) [country]	Study design	Inclusion criteria	Exposure detail	N	Age, mean (SD) years	N (%) female	Funders
Sundqvist (1982) [Sweden][109]	RCT	1958 RA criteria, Functional class I-II, stable medication for last 2 months	1) Fasted for 10 days then vegetarian diet with no alcohol, tobacco or coffee/tea p) Normal diet	1) 5 p) 5	Not reported	Not reported	**Charity** (Swedish National Association Against Rheumatism)
Skoldstam (1979) [Sweden][110]	RCT	1958 RA criteria, low-moderate inflammatory activity, functional classes I-II, taking NSAIDs, stable treatment in months preceding trial	1) Fasting for 7-10 days followed by lactovegetarian diet (no animal/fish, yoghurt ok by milk/cream discouraged p) No diet intervention	1) 16 p) 10	1) 52 (range: 35-66) p) 54 (range: 43-65)	1) 10 (62.5) p) 9 (90.0)	**Charity** (Swedish National Association Against Rheumatism)
Abendroth (2010) [Germany][111]	NRT	1987 RA criteria Exclusions: antibiotics in last 4 weeks, malnutrition, BMI <19 or >40, renal insufficiency, pregnancy, malignant disorders, mental inability to co-operate, participation in another study	1) Mediterranean diet 2) Fasting (800kcal per day)	1) 28 2) 22	1) 60.0 (12.1) 2) 55.7 (7.2)	1) 26 (92.9) 2) 21 (95.5)	Not reported (authors declare no conflicts)
McKellar (2007) [UK][112]	NRT	Aged 30-70	1) Went on Mediterranean diet cooking course and then given recipes and information on healthy eating p) Received freely available information on healthy eating only	1) 75 p) 55	Median (IQR) 1) 58 (47, 64) p) 52 (45, 61)	1) 75 (100) p) 55 (100)	**Professional body** (Scottish Society of Physicians)
Adam (2003) [Germany][113]	NRT	1987 RA, Stable medication for 4 weeks for NSAIDs and 8 weeks for DMARDs Exclusions: gastrointestinal or metabolic diseases, alcohol abuse, known allergies	1) Modified lactovegetarian diet (only plant derived fats and oils, no egg yolk, dairy products with reduced fat, limited meta intake) p) Western diet	1) 30 p) 30	1) 58.0 (12.5) p) 56.8 (13.3)	Adam (2003) [Germany][113]	**Government** (Governmental Ministry of Research and Technology of Germany)
Fraser (2000) [Norway][114]	NRT	1987 RA criteria	1) Ketogenic 2) Fasting (<865 kJ)	1) 13 2) 10	1) 44 (range: 25-69) 2) 49 (range: 31-65)	1) 12 (92) 2) 9 (90)	**Charity** (Norwegian Women's Public Health Association)
Denissov (1992) [Russia] [115]	NRT	Classical or definite RA, Stable treatment 6-12 months before trial	1) Hypoallergenic, anti-inflammatory diet p) Conventional therapy only	1) 68 p) 24	47.7 (1.3)	1) 65 (95.6) p) 20 (83.3)	Not reported
McDougall (2002) [USA][116]	Single Arm int.	Moderate to severe RA, Stable medication Exclusions: not following vegan / dairy free diet, diabetes, heart disease, high blood pressure, cancer, other chronic disease	Vegan diet, with no added fats or oils	24	56 (11)	22 (91.6)	**Charity** (Betty Wood Estate)
Kjeldsen-Kragh (1994) [Norway][117]	RCT - extension	Classic or definite RA	1) Vegetarian diet – responders 2) Vegetarian diet – non-responders p) Control	1) 10 2) 12 p) 21	1) 50 (range: 30-63) 2) 54 (range: 37-63) p) 55 (range: 38-78)	1) 9 (90.0) 2) 10 (83.3) p) 19 (95.0)	**Charity** (Norwegian Women's Public Health Association, The Anders Jahre's Fund for Promotion of Science, The Isberg's Legacy, The Grethe Harbitz Legacy and The Eckbo's Legacy.)

* estimated from median and range in paper using published formula[61], BMI = body mass index, DMARDs = disease modifying anti-rheumatoid drugs, ESR = erythrocyte sedimentation rate, hr = hour, kcal = kilocalories, kJ = kilojoules, mm = millimetres, N = number, NGO = non-governmental organisation, NRT = non-randomised trial, NSAID = non-steroidal anti-inflammatory drug, RA = rheumatoid arthritis, RCT = randomised controlled trial, SD = standard deviation, UK = United Kingdom

Supplementary table 70 – Elemental diet and RA progression, results

Table – Elemental diet (RA), results and quality assessment

Outcome	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	AMSTAR2 quality	Rand. Seq.	Alloc. Conc.	Blind. Part.	Blind. Asses.
Pain	Podas (2007) [RCT][99]	Elemental diet vs steroids at 2 weeks SMD 1.36 (0.51, 2.22) [in favour of steroids]	Pain VAS, BL / 2 weeks, mean* (SD*) Elemental diet: 6.90 (1.38) / 5.05 (1.85) Steroids: 4.35 (2.07) / 2.58 (1.71)		L	H/UC	H/UC	L
	Holst-Jensen (1998) [RCT][103]		Pain (0-30), BL / 6 months, median (10/90 centiles) Elemental diet: 17.0 (5.4, 23.6) / 17.0 (6.4, 22.4) Placebo: 15.0 (3.6, 23.6) / 14.0 (4.6, 22.4)		H/UC	H/UC	H/UC	L
Function	Podas (2007) [RCT][99]	Elemental diet vs steroids at 2 weeks SMD 0.49 (-0.30, 1.28)	HAQ, BL / 2 weeks, mean* (SD*) Elemental diet: 1.88 (0.66) / 1.68 (0.76) Steroids: 1.90 (0.40) / 1.30 (0.80)		L	H/UC	H/UC	L
	Holst-Jensen (1998) [RCT][103]		HAQ, BL / 6 months, median (10/90 centiles) Elemental diet: 1.00 (0.68, 2.03) / 1.00 (0.50, 2.20) Placebo: 1.19 (0.32, 1.88) / 1.19 (0.00, 2.19)		H/UC	H/UC	H/UC	L
	Kavanagh (1995) [RCT][105]	Elemental diet vs control at 4 weeks SMD -0.13 (-0.70, 0.44)	'Functional score', BL / 4 weeks, mean (SD) Elemental diet: 10.65 (5.66) / 9.7 (6.3) Control: 9.32 (4.92) / 10.5 (5.9)		H/UC	H/UC	H/UC	H/UC
Morning stiffness	Podas (2007) [RCT][99]	Elemental diet vs steroids at 2 weeks SMD 1.22 (0.37, 2.06) [in favour of steroids]	Morning stiffness, BL / 2 weeks, mean* (SD*) Elemental diet: 443 (373) / 414 (380) Steroids: 188 (151) / 23 (25) [sic]		L	H/UC	H/UC	L
	Holst-Jensen (1998) [RCT][103]		Morning stiffness, BL / 6 months, median (10/90 centiles) Elemental diet: 2.0 (1.0, 7.8) / 3.0 (1.0, 6.0) Placebo: 3.5 (1.0, 7.5) / 2.5 (1.0, 6.0)		H/UC	H/UC	H/UC	L
Tender joints	Podas (2007) [RCT][99]	Elemental diet vs steroids at 2 weeks SMD 0.52 (-0.27, 1.31)	Ritchie Index, BL / 2 weeks, mean* (SD*) Elemental diet: 31.5 (16.9) / 26 (16.9) Steroids: 29.8 (18.4) / 17.8 (12.4)		L	H/UC	H/UC	L
	Holst-Jensen (1998) [RCT][103]		Ritchie Index, BL / 6 months, median (10/90 centiles) Elemental diet: 9.5 (4.0, 21.5) / 10.0 (5.3, 16.4) Placebo: 12.5 (7.3, 33) / 10.0 (3.6, 23.0)		H/UC	H/UC	H/UC	L
	Haugen (1994) [RCT][106]	Elemental diet vs control change from baseline to 4 weeks SMD -0.32 (-1.30, 0.65)	Tender joint count, mean (SD) change baseline to 4 weeks § Elemental diet: -4.5 (5.72) Placebo: -2.4 (7.46)		H/UC	H/UC	H/UC	H/UC
	Kavanagh (1995) [RCT][105]	Elemental diet vs control at 4 weeks SMD -0.43 (-1.01, 0.15)	Ritchie Index, BL / 4 weeks, mean (SD) Elemental diet: 12.6 (6.8) / 10.3 (6.9) Control: 10.4 (7.2) / 14.1 (10.5)		H/UC	H/UC	H/UC	H/UC
	Bespoke MA of: Kavanagh (1995) Haugen (1994)	Elemental diet vs control SMD -0.40 (-0.90, 0.10) I^2 0%						

* Estimated from median and range in paper using published formula[61]; § Calculated by reviewers from data published in the paper; Alloc. Conc. = allocation concealment, AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews, BL = baseline, Blind. Asses. = Blinded assessors, Blind. Part. = blinded participants, CI = confidence interval, H/UC = high / unclear risk of bias, HAQ = Health Assessment Questionnaire, L = low risk of bias, MA = meta-analysis, RA = rheumatoid arthritis, Rand. Seq. = random sequence generation, RCT = randomised controlled trial, SD = standard deviation, SMD = Standardised mean difference

Table – Elemental diet (RA) [cont.], results and quality assessment

Outcome	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	AMSTAR2 quality	Rand. Seq.	Alloc. Conc.	Blind. Part.	Blind. Asses.
Swollen joints	Podas (2007) [RCT][99]	Elemental diet vs steroids at 2 weeks SMD -0.17 (-0.95, 0.61)	Swollen joint count, BL / 2 weeks, mean* (SD*) Elemental diet: 42 (22.8) / 41 (23.8) Steroids: 64.5 (31.5) / 45 (22.8)		L	H/UC	H/UC	L
	Holst-Jensen (1998) [RCT][103]		Swollen joint count, BL / 6 months, median (10/90 centiles) Elemental diet: 9.0 (5.2, 13.8) / 7.0 (5.0, 12.0) Placebo: 11.0 (5.8, 23.4) / 9.0 (3.4, 23.6)		H/UC	H/UC	H/UC	L
	Haugen (1994) [RCT][106]	Elemental diet vs control change from baseline to 4 weeks SMD -0.26 (-1.23, 0.71)	Swollen joint count, mean (SD) change baseline to 4 weeks § Elemental diet: -2.6 (3.86) Placebo: -1.7 (2.87)		H/UC	H/UC	H/UC	H/UC
CRP	Podas (2007) [RCT][99]	Elemental diet vs steroids at 2 weeks SMD 1.33 (0.47, 2.18) [in favour of steroids]	CRP, BL / 2 weeks, mean* (SD*) Elemental diet: 5.5 (3.8) / 6.4 (4.6) Steroids: 4.4 (1.6) / 1.2 (0.9)		L	H/UC	H/UC	L
	Holst-Jensen (1998) [RCT][103]		CRP, BL / 6 months, median (10/90 centiles) Elemental diet: 11 (5, 57) / 11 (4, 59) Placebo: 25 (10, 78) / 15 (4, 142)		H/UC	H/UC	H/UC	L
	Haugen (1994) [RCT][106]	Elemental diet vs control change from baseline to 4 weeks SMD 0.23 (-0.74, 1.20)	CRP, mean (SD) change baseline to 4 weeks § Elemental diet: 5.7 (25.43) Placebo: 1.14 (4.18)		H/UC	H/UC	H/UC	H/UC
	Kavanagh (1995) [RCT][105]	Elemental diet vs control at 4 weeks SMD 0.10 (-0.47, 0.67)	CRP, BL / 4 weeks, mean (SD) Elemental diet: 16.4 (18.7) / 12.3 (12.4) Control: 8.6 (8.3) / 11.4 (1.7 [sic])		H/UC	H/UC	H/UC	H/UC
	Bespoke MA of: Kavanagh (1995) Haugen (1994)	Elemental diet vs control SMD 0.13 (-0.36, 0.63) I^2 0%						

* estimated from median and range in paper using published formula[61]; § Calculated by reviewers from data published in the paper

Alloc. Conc. = allocation concealment, AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews, BL = baseline, Blind. Asses. = Blinded assessors, Blind. Part. = blinded participants, CI = confidence interval, CRP = C-reactive protein, H/UC = high / unclear risk of bias, L = low risk of bias, MA = meta-analysis, RA = rheumatoid arthritis, Rand. Seq. = random sequence generation, RCT = randomised controlled trial, SD = standard deviation, SMD = Standardised mean difference,

Supplementary table 71 – Hypoallergenic diet and RA progression, results

Table – Hypoallergenic diet (RA), results and quality assessment

Outcome	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	AMSTAR2 quality	Rand. Seq.	Alloc. Conc.	Blind. Part.	Blind. Asses.
Pain	Sarzi-Puttini (2000) [RCT][102]	Hypoallergenic diet vs control at 24 weeks SMD -0.16 (-0.76, 0.44)	Pain VAS, BL / 24 weeks, mean (SD) Hypoallergenic diet: 46.8 (16.1) / 37.6 (12.3) Control: 44.2 (18.7) / 40.4 (21.5)		H/UC	H/UC	H/UC	H/UC
	Denissov (1992) [non-randomised trial][115]		Pain (0-3), BL / 4 weeks, mean (SD/SE*) Hypoallergenic diet: 1.75 (0.1) / 1.1 (0.07) Control: 1.6 (0.13) / 1.0 (0.09)					
Tender joints	Sarzi-Puttini (2000) [RCT][102]	Hypoallergenic diet vs control at 24 weeks SMD -0.22 (-0.82, 0.38)	Ritchie Index, BL / 24 weeks, mean (SD) Hypoallergenic diet: 13.2 (4.4) / 9.2 (3.8) Control: 11.7 (4.3) / 10.1 (4.5)		H/UC	H/UC	H/UC	H/UC
	Denissov (1992) [non-randomised trial][115]		Ritchie Index, BL / 4 weeks, mean (SD/SE*) Hypoallergenic diet: 15.7 (1.2) / 10.6 (0.9) Control: 15.9 (1.7) / 10.1 (1.5)					
	van de Laar (1992) [RCT][107]	Hypoallergenic diet vs Hypoallergenic diet + milk, change from BL-12 weeks SMD 0.02 (-0.39, 0.42)	Ritchie Index, mean (SD) change BL-12 weeks Hypoallergenic diet: -1.9 (6.8) Hypoallergenic diet + milk: -2.0 (6.1)		H/UC	H/UC	H/UC	H/UC
Swollen joints	Sarzi-Puttini (2000) [RCT][102]	Hypoallergenic diet vs control at 24 weeks SMD -0.15 (-0.75, 0.45)	Swollen joint count, BL / 24 weeks, mean (SD) Hypoallergenic diet: 6.4 (3.1) / 5.1 (2.3) Control: 5.7 (2.7) / 5.5 (3.0)		H/UC	H/UC	H/UC	H/UC
Morning stiffness	Sarzi-Puttini (2000) [RCT][102]	Hypoallergenic diet vs control at 24 weeks SMD -0.14 (-0.74, 0.46)	Morning stiffness, BL / 24 weeks, mean (SD) Hypoallergenic diet: 62.5 (51.9) / 40.6 (34.2) Control: 51.4 (42.1) / 45.8 (40.3)		H/UC	H/UC	H/UC	H/UC
	van de Laar (1992) [RCT][107]	Hypoallergenic diet vs Hypoallergenic diet + milk, change from BL-12 weeks SMD 0.10 (-0.30, 0.51)	Morning stiffness, mean (SD) change BL-12 weeks Hypoallergenic diet: -23.4 (39.1) Hypoallergenic diet + milk: -27.3 (38.0)		H/UC	H/UC	H/UC	H/UC
	Denissov (1992) [non-randomised trial][115]		Morning stiffness (mins), BL / 4 weeks, mean (SD/SE*) Hypoallergenic diet: 115.4 (25.3) / 56.7 (19.4) Control: 89.2 (18.5) / 38.1 (13.9)					
Fatigue	van de Laar (1992) [RCT][107]	Hypoallergenic diet vs Hypoallergenic diet + milk, change from BL-12 weeks SMD -0.28 (-0.69, 0.12)	Fatigue VAS, mean (SD) change BL-12 weeks Hypoallergenic diet: 0.7 (1.3) Hypoallergenic diet + milk: 1.1 (1.5)		H/UC	H/UC	H/UC	H/UC
Patient global	van de Laar (1992) [RCT][107]	Hypoallergenic diet vs Hypoallergenic diet + milk, change from BL-12 weeks SMD -0.31 (-0.72, 0.10)	Patient global VAS, mean (SD) change BL-12 weeks Hypoallergenic diet: 0.7 (1.3) Hypoallergenic diet + milk: 1.1 (1.3)		H/UC	H/UC	H/UC	H/UC

* Unclear whether the paper reported standard deviations or standard errors – hence have not calculated an SMD

Alloc. Conc. = allocation concealment, AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews, BL = baseline, Blind. Asses. = Blinded assessors, Blind. Part. = blinded participants, CI = confidence interval, CRP = C-reactive protein, ESR = erythrocyte sedimentation rate, H/UC = high / unclear risk of bias, L = low risk of bias, RA = rheumatoid arthritis, Rand. Seq. = random sequence generation, RCT = randomised controlled trial, SD = standard deviation, SE = standard error, SMD = Standardised mean difference, VAS = visual analogue scale

Table – Hypoallergenic diet (RA) [cont.], results and quality assessment

Outcome	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	AMSTAR2 quality	Rand. Seq.	Alloc. Conc.	Blind. Part.	Blind. Asses.
CRP	van de Laar (1992) [RCT][107]	Hypoallergenic diet vs Hypoallergenic diet + milk, change from BL-12 weeks SMD 0.27 (-0.14, 0.68)	CRP, mean (SD) change BL-12 weeks Hypoallergenic diet: -1.7 (15.7) Hypoallergenic diet + milk: -5.5 (12.2)		H/UC	H/UC	H/UC	H/UC
ESR	Sarzi-Puttini (2000) [RCT][102]	Hypoallergenic diet vs control at 24 weeks SMD -0.08 (-0.67, 0.52)	ESR, BL / 24 weeks, mean (SD) Hypoallergenic diet: 36.2 (18.8) / 28.9 (18.9) Control: 33.1 (20.1) / 30.6 (25.8)		H/UC	H/UC	H/UC	H/UC
	van de Laar (1992) [RCT][107]	Hypoallergenic diet vs Hypoallergenic diet + milk, change from BL-12 weeks SMD 0.20 (-0.21, 0.61)	ESR, mean (SD) change BL-12 weeks Hypoallergenic diet: 2.0 (10.9) Hypoallergenic diet + milk: 0.2 (6.9)		H/UC	H/UC	H/UC	H/UC
Grip strength	van de Laar (1992) [RCT][107]	Hypoallergenic diet vs Hypoallergenic diet + milk, change from BL-12 weeks *Left* SMD 0.24 (-0.17, 0.64) *Right* SMD 0.22 (-0.19, 0.62)	Grip strength, mean (SD) change BL-12 weeks *Left* Hypoallergenic diet: 4.4 (7.1) Hypoallergenic diet + milk: 2.7 (7.2) *Right* Hypoallergenic diet: 2.5 (9.2) Hypoallergenic diet + milk: 0.8 (6.4)		H/UC	H/UC	H/UC	H/UC
Grip strength	Denissov (1992) [non-randomised trial][115]		Grip strength, BL / 4 weeks, mean (SD/SE*) *Left* Hypoallergenic diet: 210.6 (17.1) / 239.5 (15.0) Control: 114.9 (21.1) 134.9 (19.0) *Right* Hypoallergenic diet: 204.5 (16.0) / 247.3 (14.6) Control: 131.2 (20) / 147.1 (20.9)					

* Unclear whether the paper reported standard deviations or standard errors – hence have not calculated an SMD

Alloc. Conc. = allocation concealment, AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews, BL = baseline, Blind. Asses. = Blinded assessors, Blind. Part. = blinded participants, CI = confidence interval, CRP = C-reactive protein, ESR = erythrocyte sedimentation rate, H/UC = high / unclear risk of bias, L = low risk of bias, RA = rheumatoid arthritis, Rand. Seq. = random sequence generation, RCT = randomised controlled trial, SD = standard deviation, SE = standard error, SMD = Standardised mean difference

Supplementary table 72 – Ketogenic diet and RA progression, results

Table – Ketogenic diet (RA), results and quality assessment

Outcome	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	AMSTAR2 quality	Rand. Seq.	Alloc. Conc.	Blind. Part.	Blind. Asses.
Tender joints	Fraser (2000) [NRT][114]		Tender joint count (28), BL / day 7, median (95% CI) Ketogenic diet: 12 (6, 16) / 8 (5, 14) Fasting: 14 (8, 21) / 10 (2, 17)					
CRP	Fraser (2000) [NRT][114]		CRP, BL / day 7, median (95% CI) Ketogenic diet: 13 (5, 61) / 19 (9, 56) Fasting: 25 (13, 47) / 13 (7, 33)					
ESR	Fraser (2000) [NRT][114]		ESR, BL / day 7, median (95% CI) Ketogenic diet: 28 (20, 48) / 28 (16, 40) Fasting: 33 (22, 54) / 21 (10, 48)					

Alloc. Conc. = allocation concealment, AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews, BL = baseline, Blind. Asses. = Blinded assessors, Blind. Part. = blinded participants, CI = confidence interval, CRP = C-reactive protein, ESR = erythrocyte sedimentation rate, H/UC = high / unclear risk of bias, L = low risk of bias, NRT = non-randomised trial, RA = rheumatoid arthritis, Rand. Seq. = random sequence generation, SMD = Standardised mean difference,

Supplementary table 73 – Mediterranean diet and RA progression, results

Table – Mediterranean diet (RA), results and quality assessment

Outcome	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	AMSTAR2 quality	Rand. Seq.	Alloc. Conc.	Blind. Part.	Blind. Asses.
Pain	Skoldstam (2003) [RCT][100]	Mediterranean diet vs usual diet SMD -0.81 (-1.38, -0.23)	Pain VAS, BL / 12 weeks, mean (SD) Mediterranean diet: 32 (20) / 20 (13) Usual diet: 31 (20) / 34 (21); p=0.006		H/UC	H/UC	H/UC	H/UC
	McKellar (2007) [NRT][112]		Pain VAS, BL / 6 months, median Mediterranean diet: 50 / 50 Healthy eating info: 55 / 63, p=0.049					
Function	Skoldstam (2003) [RCT][100]	Mediterranean diet vs usual diet SMD -0.39 (-0.95, 0.16)	HAQ, BL / 12 weeks, mean (SD) Mediterranean diet: 0.7 (0.5) / 0.6 (0.4) Usual diet: 0.8 (0.6) / 0.8 (0.6); p=0.012		H/UC	H/UC	H/UC	H/UC
	Abendroth (2010) [NRT][111]	Mediterranean diet vs fasting SMD 0.58 (0.01, 1.15) in favour of fasting	HAQ, BL / 7 days, mean (SD) Mediterranean diet: 2.4 (0.8) / 2.2 (0.8) Fasting: 2.0 (0.6) / 1.8 (0.5); p=0.571					
	McKellar (2007) [NRT][112]		HAQ, BL / 6 months, median Mediterranean diet: 1.75 / 1.625 Healthy eating info: 1.75 / 1.875, p=NS					
Disease Activity	Skoldstam (2003) [RCT][100]	Mediterranean diet vs usual diet SMD -0.30 (-0.85, 0.26)	DAS28, BL / 12 weeks, mean (SD) Mediterranean diet: 4.4 (1.2) / 3.9 (1.2) Usual diet: 4.3 (1.4) / 4.3 (1.5); p=0.047		H/UC	H/UC	H/UC	H/UC
	McKellar (2007) [NRT][112]		DAS28, BL / 6 months, median Mediterranean diet: 4.7 / 4.4 Healthy eating info: 5.0 / 4.8					
SF36-physical	Abendroth (2010) [NRT][111]	Mediterranean diet vs fasting SMD 0.00 (-0.56, 0.56)	SF36-physical, BL / 7 days, mean (SD) Mediterranean diet: -2.0 (0.8) / -1.5 (0.9) Fasting: -2.1 (0.9) / -1.5 (1.1)					
Tender joints	Skoldstam (2003) [RCT][100]	Mediterranean diet vs usual diet SMD -0.28 (-0.83, 0.28)	Tender joint count, BL / 12 weeks, mean (SD) Mediterranean diet: 6.8 (5.9) / 4.5 (5.1) Usual diet: 6.9 (6.3) / 6.1 (6.4); p=0.212		H/UC	H/UC	H/UC	H/UC
	McKellar (2007) [NRT][112]		Tender joint count (28), BL / 6 months, median Mediterranean diet: 5 / 4 Healthy eating info: 6 / 6					
Swollen joints	Skoldstam (2003) [RCT][100]	Mediterranean diet vs usual diet SMD -0.43 (-0.98, 0.13)	Swollen joint count, BL / 12 weeks, mean (SD) Mediterranean diet: 7.0 (5.6) / 5.2 (5.1) Usual diet: 6.9 (5.0) / 7.5 (5.7); p=0.001		H/UC	H/UC	H/UC	H/UC
	McKellar (2007) [NRT][112]		Swollen joint count (28), BL / 6 months, median Mediterranean diet: 6 / 4 Healthy eating info: 6 / 5					

Alloc. Conc. = allocation concealment, AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews, BL = baseline, Blind. Asses. = Blinded assessors, Blind. Part. = blinded participants, CI = confidence interval, DAS28 = Disease Activity Score (28), H/UC = high / unclear risk of bias, HAQ = Health Assessment Questionnaire, L = low risk of bias, NRT = non-randomised trial, NS = non-significant, RA = rheumatoid arthritis, Rand. Seq. = random sequence generation, RCT = randomised controlled trial, SD = standard deviation, SMD = Standardised mean difference, VAS = visual analogue scale

Table – Mediterranean diet (RA) [cont.], results and quality assessment

Outcome	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	AMSTAR2 quality	Rand. Seq.	Alloc. Conc.	Blind. Part.	Blind. Asses.
Patient global	Skoldstam (2003) [RCT][100]	Mediterranean diet vs usual diet SMD -0.52 (-1.08, 0.04)	Patient global VAS, BL / 12 weeks, mean (SD) Mediterranean diet: 30 (22) / 18 (13) Usual diet: 28 (20) / 27 (21); p=0.061		H/UC	H/UC	H/UC	H/UC
	McKellar (2007) [NRT][112]		Patient global VAS, BL / 6 months, median Mediterranean diet: 50 / 45 Healthy eating info: 54 / 63 p=0.002					
Fatigue	Cramp (2013) [MA][85]	Mediterranean diet vs control SMD 0.37 (-0.18, 0.93)		High				
SF36-mental	Abendroth (2010) [NRT][111]	Mediterranean diet vs fasting SMD -1.18 (-1.79, -0.57)	SF36-mental, BL / 7 days, mean (SD) Mediterranean diet: -1.2 (1.1) / -1.1 (1.1) Fasting: -0.2 (1.1) / 0.1 (0.9)					
Morning stiffness	Skoldstam (2003) [RCT][100]	Mediterranean diet vs usual diet SMD -0.45 (-1.00, 0.11)	Morning stiffness, BL / 12 weeks, mean (SD) Mediterranean diet: 49 (42) / 44 (52) Usual diet: 64 (38) / 70 (64); p=0.367		H/UC	H/UC	H/UC	H/UC
	McKellar (2007) [NRT][112]		Morning stiffness (mins), BL / 6 months, median Mediterranean diet: 30 / 15 Healthy eating info: 60 / 30 p=0.041					
CRP	Skoldstam (2003) [RCT][100]	Mediterranean diet vs usual diet SMD -0.22 (-0.77, 0.33)	Morning stiffness, BL / 12 weeks, mean (SD) Mediterranean diet: 17 (20) / 12 (15) Usual diet: 15 (14) / 15 (12)		H/UC	H/UC	H/UC	H/UC
	Abendroth (2010) [NRT][111]	Mediterranean diet vs fasting SMD 0.53 (-0.04, 1.09) in favour of fasting	CRP, BL / 7 days, mean (SD) Mediterranean diet: 2.0 (2.7) / 1.6 (2.2) Fasting: 0.8 (1.0) / 0.7 (0.7)					
	McKellar (2007) [NRT][112]		CRP, BL / 6 months, median Mediterranean diet: 10 / 10 Healthy eating info: 8.5 / 8					
ESR	Skoldstam (2003) [RCT][100]	Mediterranean diet vs usual diet SMD 0.00 (-0.55, 0.55)	ESR, BL / 12 weeks, mean (SD) Mediterranean diet: 24 (15) / 25 (15) Usual diet: 23 (15) / 25 (19)		H/UC	H/UC	H/UC	H/UC
	McKellar (2007) [NRT][112]		ESR, BL / 6 months, median Mediterranean diet: 19 / 16 Healthy eating info: 19 / 16					
Grip strength	Skoldstam (2003) [RCT][100]	Mediterranean diet vs usual diet SMD -0.08 (-0.63, 0.47)	Grip strength, BL / 12 weeks, mean (SD) Mediterranean diet: 26 (13) / 23 (13) Usual diet: 23 (8) / 24 (11)		H/UC	H/UC	H/UC	H/UC

Alloc. Conc. = allocation concealment, AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews, BL = baseline, Blind. Asses. = Blinded assessors, Blind. Part. = blinded participants, CI = confidence interval, CRP = C-reactive protein, ESR = erythrocyte sedimentation rate, H/UC = high / unclear risk of bias, L = low risk of bias, MA = meta-analysis, NRT = non-randomised trial, NS = non-significant, RA = rheumatoid arthritis, Rand. Seq. = random sequence generation, RCT = randomised controlled trial, SD = standard deviation, SMD = Standardised mean difference, VAS = visual analogue scale

Table – Mediterranean diet, SF36 – results are mean change from baseline to 12 weeks

Author (date)	PCS	MCS	GH	PF	RP	RE	SF	BP	V	MH
Skoldstam (2003) [100] [Mediterranean diet]			5.7 (14.6)	2.5 (15.2)	16.3 (43.6)	9.0 (39.5)	4.8 (19.0)	4.5 (24.3)	11..3 (20.7)	6.5 (16.5)
Skoldstam (2003) [100] [Usual diet]			0.7 (21.7)	1.4 (13.4)	-11.0 (38.2)	1.4 (27.9)	-5.4 (18.8)	4.0 (20.1)	4.2 (16.3)	3.7 (12.9)

BP = bodily pain, GH = general health, MCS = mental component score, MH = mental health, PCS = physical component score, PF = physical function, RE = role emotional, RP = role physical, SF = social functioning, V = vitality

Supplementary table 74 – Vegetarian / vegan diet and RA progression, results

Table – Vegetarian / vegan diet (RA), results and quality assessment

Outcome	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	AMSTAR2 quality	Rand. Seq.	Alloc. Conc.	Blind. Part.	Blind. Asses.
ACR20	Hafstrom (2001) [RCT][101]		ACR20, N achieved (%) at 12 months Vegan diet: 12 (34.2%) Control: 1 (3.8%) p=0.005§		H/UC	H/UC	H/UC	H/UC
Pain	Skoldstam (1979) [RCT][110]	Lactovegetarian diet vs control, BL-12 weeks SMD -0.32 (-1.11, 0.48)	Pain VAS, BL / change from BL-12 weeks, mean (SD) Lactovegetarian diet: 3.5 (1.9) / -1.2 (3.2) Control: 2.7 (1.7) / -0.3 (2.1)		H/UC	H/UC	H/UC	H/UC
	Kjeldsen-Kragh (1994) [RCT-extension][117]		Pain VAS, 1 year, mean (SD*) Vegetarian – responders: 1.54 (1.33) Vegetarian – non-responders: 5.05 (2.49) Control: 5.84 (2.25)					
	McDougall (2002) [Single arm int.][116]		Pain, BL / 4 weeks, mean (SD) 49 (20) / 34 (20), p<0.004					
Function	Skoldstam (1979) [RCT][110]	Lactovegetarian diet vs control, BL-12 weeks SMD 0.18 (-0.62, 0.97)	Functional capacity (0-99), BL / change from BL-12 weeks, mean (SD) Lactovegetarian diet: 31 (3) / 1.2 (7.0) Control: 34 (14) / -1.0 (18.3)		H/UC	H/UC	H/UC	H/UC
	Kjeldsen-Kragh (1994) [RCT-extension][117]		HAQ, 1 year, mean (SD*) Vegetarian – responders: 0.56 (0.51) Vegetarian – non-responders: 1.16 (0.62) Control: 1.06 (0.60)					
	McDougall (2002) [Single arm int.][116]		Function, BL / 4 weeks, mean (SD) 47 (25) / 29 (22) p<0.001					
Disease activity	Nenonen (1998) [RCT][104]	Vegan diet vs control at 3 months SMD -0.47 (-1.10, 0.17)	DAS, BL / 3 months, mean (SD†) Vegan diet: 3.26 (0.83) / 3.13 (0.97) Control: 3.44 (1.14) / 3.56 (0.87)		H/UC	H/UC	H/UC	H/UC

§ Calculated by reviewer based on numbers in paper
* Calculated from standard error in the paper
† Calculated from 95% CI in paper
ACR20 = American College of Rheumatology 20 (composite measure of outcome), Alloc. Conc. = allocation concealment, AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews, BL = baseline, Blind. Asses. = Blinded assessors, Blind. Part. = blinded participants, CI = confidence interval, CRP = C-reactive protein, DAS = Disease Activity Score, H/UC = high / unclear risk of bias, HAQ = Health Assessment Questionnaire, int. = intervention, L = low risk of bias, N = number, NRT = non-randomised trial, NS = non-significant, RA = rheumatoid arthritis, Rand. Seq. = random sequence generation, RCT = randomised controlled trial, SD = standard deviation, SMD = Standardised mean difference, VAS = visual analogue scale

Table – Vegetarian / vegan diet (RA) [cont.], results and quality assessment

Outcome	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	AMSTAR2 quality	Rand. Seq.	Alloc. Conc.	Blind. Part.	Blind. Asses.
Tender joints	Panush (1983) [RCT][108]		Tender joint count, BL / 10 weeks, mean Experimental diet: 28 / 23 Placebo diet: 19 / 17, p=NS		H/UC	H/UC	H/UC	H/UC
	Sundqvist (1982) [RCT][109]	Experimental diet vs control at 10 weeks SMD 0.42 (-0.84, 1.68)	Tender joint count, BL / 10 weeks, mean (SD) Experimental diet: 19.8 (2.5) / 18.8 (3.0) control: 16.8 (2.5) / 17.6 (2.7)		H/UC	H/UC	H/UC	H/UC
	Skoldstam (1979) [RCT][110]	Lactovegetarian diet vs control, BL-12 weeks SMD -0.51 (-1.32, 0.29)	Ritchie Index, BL / change from BL-12 weeks, mean (SD) Lactovegetarian diet: 16 (8) / -2.5 (5.6) Control: 13 (5) / 0.2 (4.7)		H/UC	H/UC	H/UC	H/UC
	Kjeldsen-Kragh (1994) [RCT-extension][117]		Tender joint count, 1 year, mean (SD*) Vegetarian – responders: 13.5 (8.2) Vegetarian – non-responders: 22.6 (11.8) Control: 29.6 (9.8)					
	McDougall (2002) [Single arm int.][116]		Joint tenderness, BL / 4 weeks, mean (SD) 24 (12) / 17 (16) p<0.01					
Swollen joints	Panush (1983) [RCT][108]		Swollen joint count, BL / 10 weeks, mean Experimental diet: 12 / 9 Placebo diet: 13 / 10, p=NS		H/UC	H/UC	H/UC	H/UC
	Kjeldsen-Kragh (1994) [RCT-extension][117]		Swollen joint count, 1 year, mean (SD*) Vegetarian – responders: 5.3 (3.8) Vegetarian – non-responders: 9.5 (6.2) Control: 11.7 (7.8)					
	McDougall (2002) [Single arm int.][116]		Joint swelling, BL / 4 weeks, mean (SD) 27 (9) / 22 (8) p<0.02					
Morning stiffness	Panush (1983) [RCT][108]		Morning stiffness, BL / 10 weeks, mean Experimental diet: 80 / 91 Placebo diet: 114 / 91, p=NS		H/UC	H/UC	H/UC	H/UC
	Kjeldsen-Kragh (1994) [RCT-extension][117]		Morning stiffness, 1 year, mean (SD*) Vegetarian – responders: 0.77 (1.01) Vegetarian – non-responders: 2.31 (1.94) Control: 2.67 (1.70)					
	McDougall (2002) [Single arm int.][116]		Morning stiffness, BL / 4 weeks, mean (SD) 104 (71) / 99 (116), p>0.05					

* Calculated from standard error in the paper

† Calculated from 95% CI in paper

Alloc. Conc. = allocation concealment, AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews, BL = baseline, Blind. Asses. = Blinded assessors, Blind. Part. = blinded participants, CI = confidence interval, H/UC = high / unclear risk of bias, int. = intervention, L = low risk of bias, NS = non-significant, RA = rheumatoid arthritis, Rand. Seq. = random sequence generation, RCT = randomised controlled trial, SD = standard deviation, SMD = Standardised mean difference, VAS = visual analogue scale

Table – Vegetarian / vegan diet (RA) [cont.], results and quality assessment

Outcome	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	AMSTAR2 quality	Rand. Seq.	Alloc. Conc.	Blind. Part.	Blind. Asses.
Patient global	Panush (1983) [RCT][108]		Patient global VAS, BL / 10 weeks, mean Experimental diet: 2.6 / 3.1 Placebo diet: 2.6 / 2.7, p=NS		H/UC	H/UC	H/UC	H/UC
	Kjeldsen-Kragh (1994) [RCT-extension][117]		Patient global VAS, 1 year, mean (SD*) Vegetarian – responders: 1.7 (1.52) Vegetarian – non-responders: 0.2 (1.11) Control: -0.4 (1.01)					
CRP	Adam (2003) [NRT][113]	Lactovegetarian diet vs control at 3 months SMD -0.38 (-0.90, 0.13)	CRP, BL / 3 months, mean (SD) Lactovegetarian diet: 1.6 (1.5) / 1.5 (1.6) Control: 2.2 (2.5) / 2.4 (2.9)					
	McDougall (2002) [Single arm int.][116]		CRP, BL / 4 weeks, mean (SD) 2.08 (1.8) / 1.74 (1.7), p>0.05					

* Calculated from standard error in the paper

Alloc. Conc. = allocation concealment, AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews, BL = baseline, Blind. Asses. = Blinded assessors, Blind. Part. = blinded participants, CI = confidence interval, H/UC = high / unclear risk of bias, L = low risk of bias, NRT = non-randomised trial, NS = non-significant, RA = rheumatoid arthritis, Rand. Seq. = random sequence generation, RCT = randomised controlled trial, SD = standard deviation, SMD = Standardised mean difference, VAS = visual analogue scale

Supplementary table 75 – Description of reviews of fruits, vegetables and other plant based interventions in RA

Table – Fruits, vegetables and other plant based interventions (RA), description of reviews

Authors (date)	Review type	Study type included	Exposure detail	Number of studies included	Funders
Cramp (2013)[85]	MA	RCTs	Andrographis Paniculata	1	**Charity** (Arthritis Research UK)

MA = meta-analysis, RA = rheumatoid arthritis, RCT = randomised controlled trial

Supplementary table 76 – Description of studies of fruits, vegetables and other plant based interventions in RA

Table – Fruits, vegetables and other plant based interventions (RA), description of included studies

Author (date) [country]	Study design	Inclusion criteria	Exposure detail	N	Age, mean (SD) years	N (%) female	Funders
Dawczynski (2017) [Germany][118]	RCT §	2010 ACR/EULAR RA criteria, DAS28>2.4 Exclusions: gastrointestinal or metabolic disease, alcohol abuse, dietary supplement intake, known food allergy/intolerance	1) Intervention food projects (sausage, tomato spread, milk powder) enriched with microalgae oil p) Intervention products enriched with sunflower oil	38	61.3 (12.8)	32 (84.2)	**Government** (German Federal Ministry of Education and Research)
Ghavipour (2017) [Iran][119]	RCT	1987 RA criteria, aged ≥40, active RA Exclusions: diabetes, hyperlipidaemia, hypertension, liver disease, kidney disease, severe infections, food intolerance or allergies, alcohol abuse, daily intake of any other drugs or vitamins / mineral supplements	1) Pomegranate extract p) Placebo made from cellulose	1) 30 p) 25	1) 48.4 (11.4) p) 49.1 (12.2)	1) 20 (66.7) p) 20 (80.0)	**University** (Shiraz University of Medical Science)
Javadi (2017) [Iran][120]	RCT	1987 ACR RA criteria, aged 19-70 years Exclusions: acute heart, kidney, liver disease, not taking antioxidants, type and dose of medications change in month prior to study, smokers, pregnancy / lactating,	1) Quercetin capsules p) Placebo capsules	1) 20 p) 20	1) 46.6 (9.9) p) 48.0 (8.4)	1) 20 (100) p) 20 (100)	**Government** (Iran University of Medical Sciences)
Hemmati (2016) [Iran][121]	RCT	Aged ≥18 years, 2010 RA criteria, symptoms uncontrolled by DMARDs, prednisolone and hydroxychloroquine Exclusions: pregnancy, kidney or liver failure, using other drugs that may affect disease activity	1) Curcumex capsules containing ginger, curcumin and black pepper p) placebo	1) 30 p) 30	Not reported	Not reported	**University** (Ahvaz Jundishapur University of Medical Sciences)
Javadi (2014) [Iran][122]	RCT	1987 ACR RA criteria, aged 19-70 years, no changes in treatment Exclusions: other disease that require special treatment or increasing severity of arthritis, smoking, acute illnesses	1) Quercetin capsules p) Placebo capsules	1) 20 p) 20	1) 46.6 (9.9) p) 48.0 (8.4)	1) 20 (100) p) 20 (100)	**Government** (Iran University of Medical Sciences)
Willich (2010) [Denmark][123]	RCT	Aged >18 years, 1987 ACR RA criteria Exclusions: Lupus erythematosus, known allergies to plant products, kidney or liver disease, drug abuse, psychiatric disease, pregnancy	1) 10 capsules per day of 0.5g rose hip powder p) Placebo capsules of similar taste	1) 44 p) 45	1) 57.0 (10.6) p) 56.1 (12.0)	1) 86% p) 93%	**Industry** (Dansk Droge, Hyben Vital ApS)
Bae (2009) [South Korea][124]	RCT §	1987 ACR RA criteria	1) Quercetin 2) Alpha Lipoic acid p) Cornstarch	20	52.1 (10.3)	19 (95.0)	**University** (Sookmyung Women's University Research Grants)

§ Cross-over design

ACR = American College of Rheumatology, DAS28 = Disease Activity Score 28, DMARD = disease modifying anti-rheumatic drug, EULAR = European League Against Rheumatism, N = number, RA = rheumatoid arthritis, RCT = randomised controlled trial, SD = standard deviation

Table – Fruits, vegetables and other plant based interventions (RA) [cont.], description of included studies

Author (date) [country]	Study design	Inclusion criteria	Exposure detail	N	Age, mean (SD) years	N (%) female	Funders
Li (2007) [Hong Kong][125]	RCT	1987 ACR RA criteria, stable sDMARD dose for 3 months Exclusions: 18 years of age, pregnancy, use of intraarticular steroids within 4 weeks of study, any severe chronic or uncontrolled disease, wheelchair bound	1) G Lucidum and San Miao San tablets (Chinese herbal medicine) p) placebo tablets	1) 32 p) 33	1) 50 (10) p) 50 (13)	1) 27 (84.4) p) 29 (87.9)	Not reported
Gheita (2012) [Egypt][126]	NRT§	2010 ACR/EULAR criteria	500mg twice daily	40	42.8 (12.5)	40 (100)	Not reported, authors declare no conflicts of interest
Kamal (2018) [Sudan][127]	Single arm int.	Aged 18-70 years, RF and anti-CCP positive, clinical stable, stable treatment Exclusions: Abnormal values of complete blood count, liver function test, renal function test, hepatic disease, infectious or autoimmune liver disease, chronic kidney disease, chronic respiratory disease, malignancy, connective tissue disease	1) Gum Arabic powder mixed into 200ml water and consumed in the morning	40	Men: 47.8 (2.8) Women: 55 (2.8)	38 (95)	**University** (University of Khartoum)
Kumar (2015) [India][128]	Single arm int.	Aged 18-60 years, 1987 ACR RA criteria Exclusions: unstable angina, myocardial infarction, heart failure or stroke, uncontrolled hypertension, uncontrolled diabetes, ALT or AST >2x ULN, impaired renal function, pregnancy / lactation, patients taking other Ayurvedic drugs	1) Ashwagandha powder mixed with water for 3 weeks, then Sidh Makardhwag with honey for 4 weeks	78	Women: 45.7 (8.6) Men: 49.8 (7.9)	45 (52.3)	**Government** (Central Council for Research in Ayurveda and Sidha (CCRAS), Department of AYUSH, Ministry of Health and Family Welfare, Government of India)
Matsuno (2009) [Japan][129]	Single arm int.	1987 ACR RA criteria Exclusions: history of synovial fluid drainage, intra-articular steroid in previous 2 months before baseline	Quercetin, glucosamine and chondroitin together	22	58.0 (10.0)	20 (90.9)	Not reported

§ Cross-over design

ACR = American College of Rheumatology, ALT = alanine aminotransferase, Anti-CCP = anti-cyclic citrullinated peptide, AST = Aspartate transaminase, DMARD = disease modifying anti-rheumatic drug, EULAR = European League Against Rheumatism , N = number, NRT = non-randomised trial, RA = rheumatoid arthritis, RCT = randomised controlled trial, RF = rheumatoid factor, SD = standard deviation

Supplementary table 77 – Andrographis Paniculata and RA progression, results

Table – Andrographis Paniculata (RA), results and quality assessment

Outcome	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	AMSTAR2 quality	Rand. Seq.	Alloc. Conc.	Blind. Part.	Blind. Asses.
Fatigue	Cramp (2013) [MA][85]	Andrographis Paniculata vs placebo SMD -0.25 (-0.77, 0.27)		High				

Alloc. Conc. = allocation concealment, AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews, Blind. Asses. = Blinded assessors, Blind. Part. = blinded participants, CI = confidence interval, H/UC = high / unclear risk of bias, L = low risk of bias, MA = meta-analysis, RA = rheumatoid arthritis, Rand. Seq. = random sequence generation, SMD = Standardised mean difference,

Supplementary table 78 – Ginger / curcumin / black pepper and RA progression, results

Table – Ginger / curcumin / black pepper (RA), results and quality assessment

Outcome	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	AMSTAR2 quality	Rand. Seq.	Alloc. Conc.	Blind. Part.	Blind. Asses.
Disease activity	Hemmati (2016) [RCT][121]	Curcumex vs placebo at 8 weeks SMD -2.74 (-3.45, -2.03)	DAS28 at 8 weeks, mean (SD) Curcumex: 3.29 (0.89) Placebo: 5.51 (0.72); p<0.001		H/UC	H/UC	H/UC	H/UC
Tender joints	Hemmati (2016) [RCT][121]	Curcumex vs placebo at 8 weeks SMD -2.75 (-3.46, -2.03)	Tender joint count at 8 weeks, mean (SD) Curcumex: 2.27 (1.96) Placebo: 10.33 (3.66); p<0.001		H/UC	H/UC	H/UC	H/UC
Swollen joints	Hemmati (2016) [RCT][121]	Curcumex vs placebo at 8 weeks SMD -2.14 (-2.77, -1.50)	Swollen joint count at 8 weeks, mean (SD) Curcumex: 1.07 (1.17) Placebo: 7.13 (3.84); p<0.001		H/UC	H/UC	H/UC	H/UC
ESR	Hemmati (2016) [RCT][121]	Curcumex vs placebo at 8 weeks SMD -1.05 (-1.60, -0.51)	ESR at 8 weeks, mean (SD) Curcumex: 21.50 (12.67) Placebo: 38.47 (18.92); p<0.001		H/UC	H/UC	H/UC	H/UC

Alloc. Conc. = allocation concealment, AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews, Blind. Asses. = Blinded assessors, Blind. Part. = blinded participants, CI = confidence interval, DAS28 = Disease Activity Score 28, ESR = erythrocyte sedimentation rate, H/UC = high / unclear risk of bias, L = low risk of bias, RA = rheumatoid arthritis, Rand. Seq. = random sequence generation, RCT = randomised controlled trial, SD = standard deviation, SMD = Standardised mean difference

Supplementary table 79 – Gum Arabic and RA progression, results

Table – Gum Arabic (RA), results and quality assessment

Outcome	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	AMSTAR2 quality	Rand. Seq.	Alloc. Conc.	Blind. Part.	Blind. Asses.
Disease activity	Kamal (2018) [single arm int.][127]		DAS28, BL / 12 weeks, mean (SD) 5.43 (1.49) / 3.8 (1.26), p<0.01					
Tender joints	Kamal (2018) [single arm int.][127]		Tender joint count, BL / 12 weeks, mean (SD) 10.66 (9.6) / 2.97 (6.03), p<0.01					
Swollen joints	Kamal (2018) [single arm int.][127]		Swollen joint count, BL / 12 weeks, mean (SD) 5.4 (6.5) / 2.05 (4.7), p<0.01					
Patient global	Kamal (2018) [single arm int.][127]		Patient global VAS, BL / 12 weeks, mean (SD) 4.85 (2.17) / 2.1 (1.9) p<0.01					

Alloc. Conc. = allocation concealment, AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews, BL = baseline, Blind. Asses. = Blinded assessors, Blind. Part. = blinded participants, CI = confidence interval, DAS28 = Disease Activity Score 28, H/UC = high / unclear risk of bias, int. = intervention, L = low risk of bias, RA = rheumatoid arthritis, Rand. Seq. = random sequence generation, SD = standard deviation, SMD = Standardised mean difference, VAS = visual analogue scale

Supplementary table 80 – Herbal medicine and RA progression, results

Table – Herbal medicine (RA), results and quality assessment

Outcome	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	AMSTAR2 quality	Rand. Seq.	Alloc. Conc.	Blind. Part.	Blind. Asses.
Pain	Li (2007) [RCT][125]	Herbal medicine vs placebo at 6 months SMD -0.25 (-0.74, 0.24)	Pain VAS, BL / 6 months, mean (SD) Herbal medicine: 4.9 (2.3) / 3.9 (2.5) Placebo: 4.8 (2.4) / 4.5 (2.3)		L	L	L	L
	Kumar (2015) [single arm int.][128]		Pain VAS, BL / 7 weeks, mean (SD) Men: 6.2 (0.7) / 4.4 (0.4) Women: 6.2 (0.7) / 4.4 (0.5)					
Function	Li (2007) [RCT][125]	Herbal medicine vs placebo at 6 months SMD 0.14 (-0.34, 0.63)	HAQ, BL / 6 months, mean (SD*) Herbal medicine: 1.2 (0.8) / 1.3 (0.7) Placebo: 1.1 (0.8) / 1.2 (0.7)		L	L	L	L
	Kumar (2015) [single arm int.][128]		Disability index, BL / 7 weeks, mean (SD) Men: 3.3 (1.1) / 2.5 (0.9) Women: 3.3 (1.3) / 2.6 (0.9)					
Disease activity	Kumar (2015) [single arm int.][128]		DAS28, BL / 7 weeks, mean (SD) Men: 5.0 (0.4) / 4.3 (0.2) Women: 5.1 (0.3) / 4.3 (0.2)					
Tender joints	Li (2007) [RCT][125]	Herbal medicine vs placebo at 6 months SMD -0.08 (-0.56, 0.41)	Tender joint count, BL / 6 months, mean (SD*) Herbal medicine: 2.7 (3.1) / 2.0 (3.1) Placebo: 2.3 (0.8) / 2.3 (4.6)		L	L	L	L
	Kumar (2015) [single arm int.][128]		Tender joint count, BL / 7 weeks, mean (SD) Men: 6.6 (1.3) / 4.8 (0.8) Women: 6.6 (1.2) / 4.8 (0.6)					
Swollen joints	Li (2007) [RCT][125]	Herbal medicine vs placebo at 6 months SMD -0.18 (-0.67, 0.31)	Swollen joint count, BL / 6 months, mean (SD*) Herbal medicine: 3.3 (2.3) / 4.0 (3.1) Placebo: 3.7 (3.1) / 4.7 (4.6)		L	L	L	L
	Kumar (2015) [single arm int.][128]		Swollen joint count, BL / 7 weeks, mean (SD) Men: 3.4 (1.7) / 2.5 (1.0) Women: 3.9 (1.8) / 2.7 (1.0)					
Patient global	Li (2007) [RCT][125]	Herbal medicine vs placebo at 6 months SMD -0.04 (-0.53, 0.45)	Patient global VAS, BL / 6 months, mean (SD) Herbal medicine: 5.7 (2.5) / 4.7 (2.6) Placebo: 5.4 (2.3) / 4.8 (2.5)		L	L	L	L
	Kumar (2015) [single arm int.][128]		Patient global VAS, BL / 7 weeks, mean (SD) Men: 52.1 (11.1) / 35.2 (8.0) Women: 53.6 (11.5) / 34.4 (7.9)					

* mean (SD) calculated from median (IQR) using publish formula[61]

Alloc. Conc. = allocation concealment, AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews, BL = baseline, Blind. Asses. = Blinded assessors, Blind. Part. = blinded participants, CI = confidence interval, DAS28 = Disease Activity Score 28, H/UC = high / unclear risk of bias, HAQ = Health Assessment Questionnaire, L = low risk of bias, RA = rheumatoid arthritis, Rand. Seq. = random sequence generation, RCT = randomised controlled trial, SD = standard deviation, SMD = Standardised mean difference, VAS = visual analogue scale

Table – Herbal medicine (RA) [cont.], results and quality assessment

Outcome	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	AMSTAR2 quality	Rand. Seq.	Alloc. Conc.	Blind. Part.	Blind. Asses.
ESR	Li (2007) [RCT][125]	Herbal medicine vs placebo at 6 months SMD -0.44 (-0.93, 0.05)	ESR, BL / 6 months, mean (SD*) Herbal medicine: 37.3 (21.7) / 36.0 (28.7) Placebo: 46 (44.9) / 49.7 (33.3)		L	L	L	L
	Kumar (2015) [single arm int.][128]		ESR, BL / 7 weeks, mean (SD) Men: 28.8 (3.3) / 21.6 (1.9) Women: 31.2 (3.1) / 22.1 (1.4)					
CRP	Li (2007) [RCT][125]	Herbal medicine vs placebo at 6 months SMD -0.28 (-0.77, 0.21)	CRP, BL / 6 months, mean (SD*) Herbal medicine: 11.5 (14.9) / 9.9 (9.7) Placebo: 15.3 (23.2) / 13.0 (12.1)		L	L	L	L

* mean (SD) calculated from median (IQR) using publish formula[61]

Alloc. Conc. = allocation concealment, AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews, BL = baseline, Blind. Asses. = Blinded assessors, Blind. Part. = blinded participants, CI = confidence interval, CRP = C-reactive protein, ESR = erythrocyte sedimentation rate, H/UC = high / unclear risk of bias, IQR = interquartile range, L = low risk of bias, RA = rheumatoid arthritis, Rand. Seq. = random sequence generation, RCT = randomised controlled trial, SD = standard deviation, SMD = Standardised mean difference

Supplementary table 81 – Microalgae oil and RA progression, results

Table – Microalgae oil (RA), results and quality assessment

Outcome	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	AMSTAR2 quality	Rand. Seq.	Alloc. Conc.	Blind. Part.	Blind. Asses.
Function	Dawczynski (2017) [RCT][118]	Microalgae oil vs placebo at 10 weeks SMD -0.26 (-0.72, 0.19)	HAQ at 10 weeks, mean (SD) Microalgae oil: 1.07 (0.64) Placebo: 1.26 (0.79)		H/UC	H/UC	L	H/UC
Disease activity	Dawczynski (2017) [RCT][118]	Microalgae oil vs placebo at 10 weeks SMD -0.21 (-0.66, 0.24)	DAS28 at 10 weeks, mean (SD) Microalgae oil: 3.88 (1.17) Placebo: 4.13 (1.2)		H/UC	H/UC	L	H/UC
Tender joints	Dawczynski (2017) [RCT][118]	Microalgae oil vs placebo at 10 weeks SMD -0.42 (-0.87, 0.04)	Tender joint count (66) at 10 weeks, mean (SD) Microalgae oil: 6.00 (5.01) Placebo: 8.79 (8.05)		H/UC	H/UC	L	H/UC
Swollen joints	Dawczynski (2017) [RCT][118]	Microalgae oil vs placebo at 10 weeks SMD -0.08 (-0.53, 0.37)	Swollen joint count (66) at 10 weeks, mean (SD) Microalgae oil: 3.92 (3.49) Placebo: 4.21 (3.72)		H/UC	H/UC	L	H/UC
Morning stiffness	Dawczynski (2017) [RCT][118]	Microalgae oil vs placebo at 10 weeks SMD -0.25 (-0.70, 0.20)	Morning stiffness at 10 weeks, mean (SD) Microalgae oil: 27.2 (30.7) Placebo: 35.8 (37.1)		H/UC	H/UC	L	H/UC
Patient global	Dawczynski (2017) [RCT][118]	Microalgae oil vs placebo at 10 weeks SMD -0.27 (-0.72, 0.19)	Patient global VAS at 10 weeks, mean (SD) Microalgae oil: 42.8 (22.33) Placebo: 38.67 (20.31)		H/UC	H/UC	L	H/UC
CRP	Dawczynski (2017) [RCT][118]	Microalgae oil vs placebo at 10 weeks SMD 0.16 (-0.29, 0.61)	CRP at 10 weeks, mean (SD) Microalgae oil: 7.57 (7.62) Placebo: 6.51 (5.58)		H/UC	H/UC	L	H/UC
ESR	Dawczynski (2017) [RCT][118]	Microalgae oil vs placebo at 10 weeks SMD 0.05 (-0.40, 0.50)	ESR at 10 weeks, mean (SD) Microalgae oil: 26.9 (21.7) Placebo: 25.8 (20.7)		H/UC	H/UC	L	H/UC
Erosions	Dawczynski (2017) [RCT][118]	Microalgae oil vs placebo at 10 weeks SMD 0.00 (-0.45, 0.45)	erosions at 10 weeks, mean (SD) Microalgae oil: 2.78 (2.47) Placebo: 2.78 (2.58)		H/UC	H/UC	L	H/UC

Alloc. Conc. = allocation concealment, AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews, Blind. Asses. = Blinded assessors, Blind. Part. = blinded participants, CI = confidence interval, CRP = C-reactive protein, DAS28 = Disease Activity Score 28, ESR = erythrocyte sedimentation rate, H/UC = high / unclear risk of bias, HAQ = Health Assessment Questionnaire, L = low risk of bias, RA = rheumatoid arthritis, Rand. Seq. = random sequence generation, RCT = randomised controlled trial, SD = standard deviation, SMD = Standardised mean difference, VAS = visual analogue scale

Supplementary table 82 – Nigella Sativa oil and RA progression, results

Table – Nigella Sativa oil (RA), results and quality assessment

Outcome	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	AMSTAR2 quality	Rand. Seq.	Alloc. Conc.	Blind. Part.	Blind. Asses.
Pain	Gheita (2012) [NRT§][126]	Nigella Sativa oil vs placebo after each period SMD -0.47 (-0.91, -0.02)	Pain VAS, BL/after placebo/after intervention, mean (SD) 60.25 (12.71) / 60.25 (12.71) / 52.75 (18.81)					
Disease activity	Gheita (2012) [NRT§][126]	Nigella Sativa oil vs placebo after each period SMD -0.57 (-1.02, -0.12)	DAS28, BL/after placebo/after intervention, mean (SD) 4.98 (0.79) / 4.99 (0.72) / 4.55 (0.82)					
Tender joints	Gheita (2012) [NRT§][126]	Nigella Sativa oil vs placebo after each period SMD -0.53 (-0.97, -0.08)	Ritchie Index, BL/after placebo/after intervention, mean (SD) 6.58 (4.17) / 6.43 (3.88) / 4.68 (2.66)					
Swollen joints	Gheita (2012) [NRT§][126]	Nigella Sativa oil vs placebo after each period SMD -0.92 (-1.38, -0.46)	Swollen joint count, BL/after placebo/after intervention, mean (SD) 2.4 (1.17) / 2.3 (1.14) / 1.35 (0.92)					
Morning stiffness	Gheita (2012) [NRT§][126]	Nigella Sativa oil vs placebo after each period SMD -0.63 (-1.08, -0.18)	Morning stiffness, BL/after placebo/after intervention, mean (SD) 30.63 (28.04) / 30.63 (28.04) / 17.13 (11.6)					
ESR	Gheita (2012) [NRT§][126]	Nigella Sativa oil vs placebo after each period SMD -0.23 (-0.67, 0.21)	ESR, BL/after placebo/after intervention, mean (SD) 36.25 (18.43) / 36.48 (18.6) / 32.75 (13.38)					

§ The study design had all patients taking a placebo for 1 months followed by the intervention

Alloc. Conc. = allocation concealment, AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews, BL = baseline, Blind. Asses. = Blinded assessors, Blind. Part. = blinded participants, CI = confidence interval, DAS28 = Disease Activity Score 28, ESR = erythrocyte sedimentation rate, H/UC = high / unclear risk of bias, L = low risk of bias, NRT = non-randomised trial, RA = rheumatoid arthritis, Rand. Seq. = random sequence generation, SD = standard deviation, SMD = Standardised mean difference, VAS = visual analogue scale

Supplementary table 83 – Pomegranate and RA progression, results

Table – Pomegranate (RA), results and quality assessment

Outcome	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	AMSTAR2 quality	Rand. Seq.	Alloc. Conc.	Blind. Part.	Blind. Asses.
Pain	Ghavipour (2017) [RCT][119]	Pomegranate vs placebo, change from BL to 56 days SMD -0.15 (-0.68, 0.38)	Pain VAS, BL / change at 56 days, mean (SD*) Pomegranate: 59.3 (143.0) / -17.6 (136.4) Placebo: 51.0 (124.5) / -1.6 (51.0); p=0.003		L	L	L	L
Function	Ghavipour (2017) [RCT][119]	Pomegranate vs placebo, change from BL to 56 days SMD -0.16 (-0.69, 0.38)	HAQ, BL / change at 56 days, mean (SD*) Pomegranate: 1.2 (3.3) / -0.4 (2.2) Placebo: 1.3 (3.5) / -0.1 (1.5); p=0.007		L	L	L	L
Tender joints	Ghavipour (2017) [RCT][119]	Pomegranate vs placebo, change from BL to 56 days SMD -0.17 (-0.71, 0.35)	Tender joint count, BL / change at 56 days, mean (SD*) Pomegranate: 5.8 (21.2) / -2.1 (17.0) Placebo: 7.0 (27.0) / 0.9 (16.5); p=0.001		L	L	L	L
Swollen joints	Ghavipour (2017) [RCT][119]	Pomegranate vs placebo, change from BL to 56 days SMD -0.22 (-0.75, 0.31)	Swollen joint count, BL / change at 56 days, mean (SD*) Pomegranate: 5.7 (17.0) / -2.6 (14.8) Placebo: 4.4 (13.5) / 0.08 (8.0); p<0.001		L	L	L	L
CRP	Ghavipour (2017) [RCT][119]	Pomegranate vs placebo, change from BL to 56 days SMD -0.06 (-0.59, 0.47)	CRP, BL / change at 56 days, mean (SD*) Pomegranate: 8.0 (23.0) / -0.8 (17.0) Placebo: 6.6 (22.5) / 0.4 (23.5); p=0.6		L	L	L	L
ESR	Ghavipour (2017) [RCT][119]	Pomegranate vs placebo, change from BL to 56 days SMD -0.11 (-0.64, 0.42)	ESR, BL / change at 56 days, mean (SD*) Pomegranate: 29.0 (85.4) / -4.3 (60.2) Placebo: 30.6 (98.0) / 3.5 (79.5);p =0.03		L	L	L	L

* Calculated from standard error in paper. Concern that there is a miss-print in the paper and this is in fact the standard deviation.

Alloc. Conc. = allocation concealment, AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews, BL = baseline, Blind. Asses. = Blinded assessors, Blind. Part. = blinded participants, CI = confidence interval, CRP = C-reactive protein, ESR = erythrocyte sedimentation rate, H/UC = high / unclear risk of bias, HAQ = Health Assessment Questionnaire, L = low risk of bias, RA = rheumatoid arthritis, Rand. Seq. = random sequence generation, RCT = randomised controlled trial, SD = standard deviation, SMD = Standardised mean difference, VAS = visual analogue scale

Supplementary table 84 – Quercetin and RA progression, results

Table – Quercetin (RA), results and quality assessment

Outcome	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	AMSTAR2 quality	Rand. Seq.	Alloc. Conc.	Blind. Part.	Blind. Asses.
Pain	Javadi (2017) [RCT][120]	Quercetin vs placebo at week 8 SMD -0.85 (-1.50, -0.20)	Morning pain VAS, BL / 8 weeks, mean (SD) Quercetin: 36.7 (19.1) / 21.5 (15.9) Placebo: 35.1 (24.4) / 40.3 (27.0); p=0.01		L	L	L	L
	Bae (2009) [RCT][124]	Quercetin vs placebo at week 4 SMD -0.10 (-0.73, 0.52)	Pain VAS, BL / 4 weeks, mean (SD*) Quercetin: 28.75 (19.95) / 30.00 (31.91) Placebo: 32.25 (27.92) / 33.33 (31.91); p=0.34		H/UC	H/UC	L	H/UC
	Matsuno (2009) [single arm int.][129]		Pain, BL / 3 months, mean (SD) 32.5 (25.4) / 27.4 (20.9) p=0.32					
	Bespoke MA Javadi (2017)[120] Bae (2017)[124]	Quercetin vs placebo SMD -0.47 (-1.20, 0.26), I^2 62.1%						
Function	Javadi (2017) [RCT][120]	Quercetin vs placebo at week 8 SMD -0.94 (-1.60, -0.29)	HAQ, BL / 8 weeks, mean (SD) Quercetin: 0.59 (0.37) / 0.35 (0.28) Placebo:0.67 (0.42) / 0.68 (0.41); p=0.008		L	L	L	L
	Bae (2017) [RCT][124]	Quercetin vs placebo at week 4 SMD -0.43 (-1.06, 0.20)	KHAQ, BL / 4 weeks, mean (SD*) Quercetin: 0.42 (0.56) / 0.36 (0.40) Placebo: 0.47 (0.40) / 0.59 (0.64); p=0.25		H/UC	H/UC	L	H/UC
	Bespoke MA Javadi (2017)[120] Bae (2017)[124]	Quercetin vs placebo SMD -0.68 (-1.18, -0.18), I^2 17.4%						
Disease activity	Javadi (2017) [RCT][120]	Quercetin vs placebo at week 8 SMD -0.40 (-1.03, 0.23)	DAS28, BL / 8 weeks, mean (SD) Quercetin: 3.22 (0.93) / 2.65 (0.98) Placebo: 3.13 (1.10) / 3.11 (1.29); p=0.04		L	L	L	L
Tender joints	Javadi (2017) [RCT][120]	Quercetin vs placebo at week 8 SMD -0.40 (-1.02, 0.23)	Tender joint count, BL / 8 weeks, mean (SD*) Quercetin: 1.3 (2.2) / 0.3 (0.8) Placebo: 0.8 (1.6) / 0.8 (1.6); p=0.33		L	L	L	L
Swollen joints	Javadi (2017) [RCT][120]	Quercetin vs placebo at week 8 SMD -0.24 (-0.86, 0.39)	Swollen joint count, BL / 8 weeks, mean (SD*) Quercetin: 0.7 (1.6) / 0.3 (0.8) Placebo: 0.7 (0.8) / 0.6 (1.6); p=0.36		L	L	L	L
	Matsuno (2009) [single arm int.][129]		Joint swelling score, BL / 3 months, mean (SD) 46.1 (22.1) / 39.7 (25.3) p=0.35					
Morning stiffness	Javadi (2017) [RCT][120]		Morning stiffness, BL / 8 weeks, mean (SD*) Quercetin: 10.4 (18.9) / 0 (0) Placebo: 11.3 (18.9) / 8.2 (16.0)		L	L	L	L
	Matsuno (2009) [single arm int.][129]		Morning stiffness, BL / 3 months, mean (SD) 94.6 (168.4) / 89.4 (171.8) p=0.97					

* mean (SD) calculated from median (IQR) using published formula[61], Alloc. Conc. = allocation concealment, AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews, BL = baseline, Blind. Asses. = Blinded assessors, Blind. Part. = blinded participants, CI = confidence interval, DAS28 = Disease Activity Score 28, H/UC = high / unclear risk of bias, HAQ = Health Assessment Questionnaire, IQR = interquartile range, MA = meta-analysis, KHAQ = Korean Health Assessment Questionnaire, L = low risk of bias, RA = rheumatoid arthritis, Rand. Seq. = random sequence generation, RCT = randomised controlled trial, SD =standard deviation, SMD = Standardised mean difference, VAS = visual analogue scale

Table – Quercetin (RA) [cont.], results and quality assessment

Outcome	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	AMSTAR2 quality	Rand. Seq.	Alloc. Conc.	Blind. Part.	Blind. Asses.
CRP	Javadi (2014) [RCT][122]	Quercetin vs placebo at week 8 SMD -0.21 (-0.83, 0.41)	CRP, BL / 8 weeks, mean (SD) Quercetin: 2.9 (3.0) / 2.2 (2.3) Placebo: 3.3 (2.3) / 2.7 (2.4); p=NS		H/UC	H/UC	L	H/UC
	Bae (2009) [RCT][124]	Quercetin vs placebo at week 4 SMD -0.22 (-0.84, 0.40)	CRP, BL / 4 weeks, mean (SD*) Quercetin: 2.57 (4.96) / 1.63 (2.56) Placebo: 1.71 (2.97) / 2.33 (3.71)		H/UC	H/UC	L	H/UC
	Matsuno (2009) [single arm int.][129]		CRP, BL / 3 months, mean (SD) 2.8 (2.4) / 3.3 (2.7) p=0.30					
	Bespoke MA Javadi (2014)[122] Bae (2017)[124]	Quercetin vs placebo SMD -0.22 (-0.66, 0.22), I^2 0%						
ESR	Javadi (2017) [RCT][120]	Quercetin vs placebo at week 8 SMD -0.36 (-0.99, 0.26)	ESR, BL / 8 weeks, mean (SD) Quercetin: 19.0 (8.6) / 16.9 (9.6) Placebo: 21.1 (12.4) / 22.0 (17.5); p=0.35		L	L	L	L
	Matsuno (2009) [single arm int.][129]		ESR, BL / 3 months, mean (SD) 66.0 (27.7) / 69.2 (28.7); p=0.46					

* mean (SD) calculated from median (IQR) using published formula[61]

Alloc. Conc. = allocation concealment, AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews, BL = baseline, Blind. Asses. = Blinded assessors, Blind. Part. = blinded participants, CI = confidence interval, CRP = C-reactive protein, ESR = erythrocyte sedimentation rate, H/UC = high / unclear risk of bias, IQR = interquartile range, L = low risk of bias, MA = meta-analysis, RA = rheumatoid arthritis, Rand. Seq. = random sequence generation, RCT = randomised controlled trial, SD =standard deviation, SMD = Standardised mean difference

Supplementary table 85 – Rose hip and RA progression, results

Table – Rose hip (RA), results and quality assessment

Outcome	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	AMSTAR2 quality	Rand. Seq.	Alloc. Conc.	Blind. Part.	Blind. Asses.
Pain	Willich (2010) [RCT][123]	Rose hip vs placebo SMD -0.25 (-0.67, 0.17)	Pain VAS, BL / 6 months, mean (SD) Rose hip: 44.73 (22.75) / 39.82 (23.44) Placebo: 45.56 (21.98) / 45.71 (23.47)		L	H/UC	L	H/UC
Function	Willich (2010) [RCT][123]	Rose hip vs placebo SMD -0.18 (-0.60, 0.24)	HAQ, BL / 6 months, mean (SD) Rose hip: 1.13 (0.55) / 1.03 (0.58) Placebo: 1.11 (0.76) / 1.15 (0.74)		L	H/UC	L	H/UC
Disease activity	Willich (2010) [RCT][123]	Rose hip vs placebo SMD -0.36 (-0.78, 0.06)	DAS28, BL / 6 months, mean (SD) Rose hip: 4.82 (1.33) / 3.93 (1.56) Placebo: 4.71 (1.01) / 4.42 (1.17)		L	H/UC	L	H/UC
Patient global	Willich (2010) [RCT][123]	Rose hip vs placebo SMD -0.31 (-0.73, 0.11)	Patient global VAS, BL / 6 months, mean (SD) Rose hip: 47.55 (25.96) / 39.57 (25.01) Placebo: 47.13 (21.28) / 47.18 (24.13)		L	H/UC	L	H/UC
QoL	Willich (2010) [RCT][123]	Rose hip vs placebo SMD -0.13 (-0.55, 0.29)	RAQOL, BL / 6 months, mean (SD) Rose hip: 11.57 (6.36) / 10.18 (7.22) Placebo: 10.87 (6.68) / 11.09 (6.89)		L	H/UC	L	H/UC
Mental Health	Willich (2010) [RCT][123]	Rose hip vs placebo SMD -0.02 (-0.43, 0.40)	SF-12 Mental, BL / 6 months, mean (SD) Rose hip: 49.30 (10.44) / 48.46 (10.85) Placebo: 49.13 (9.34) / 48.64 (9.46)		L	H/UC	L	H/UC

Alloc. Conc. = allocation concealment, AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews, BL = baseline, Blind. Asses. = Blinded assessors, Blind. Part. = blinded participants, CI = confidence interval, DAS28 = Disease Activity Score 28, H/UC = high / unclear risk of bias, HAQ = Health Assessment Questionnaire, L = low risk of bias, QoL = Quality of life, RA = rheumatoid arthritis, RAQOL = Rheumatoid Arthritis Quality of Life Measure, Rand. Seq. = random sequence generation, RCT = randomised controlled trial, SMD = Standardised mean difference, VAS = visual analogue scale

Supplementary table 86 – Description of reviews of minerals and supplements in RA

Table – Minerals and supplements (RA), description of reviews

Authors (date)	Review type	Study type included	Exposure detail	Number of studies included	Funders
Aqaeinezhad Rudbane (2018) [Iran][130]	MA	RCTs	Probiotics	5	**University** (Shiraz University of Medical Sciences)
Mohammed et al (2017) [Egypt][131]	MA	RCTs	Probiotics	6	Not reported, authors declare no conflict of interest

MA = meta-analysis, RA = randomised controlled trial, RCT = randomised controlled trial, SR = systematic review

Supplementary table 87 – Description of studies of minerals and supplements in RA

Table – Minerals and supplements (RA), description of included studies

Author (date) [country]	Study design	Inclusion criteria	Exposure detail	N	Age, mean (SD) years	N (%) female	Funders
Zamani (2017) [Iran][132]	RCT	1987 ACR RA, symptom duration >6 months, DAS28>3.2, aged 25-70 years Exclusions: chronic renal failure, pregnancy / lactation, symptoms or history of cardiovascular disease, diabetes, consumption of antihyperglycaemic agents including metformin, unable to read numbers / mark scales, unlikely to come to follow-up, taking probiotics / synbiotics, antioxidants and/or anti-inflammatory supplements such as vitamin E, vitamin C, taking antibiotics	1) synbiotic supplements - Lactobacillus acidophilus, Lactobacillus casei and Bifidobacterium bifidum p) Placebo (starch)	1) 27 p) 27	1) 49.3 (11.0) p) 49.5 (12.9)	1) 22 (81.5) p) 24 (88.9)	**University** (Vice-chancellor for Research, KUMS and Iran)
Wilkinson (2016) [UK][133]	RCT	2010 ACR/EULAR RA criteria, aged ≥18 years, stable medication for 3 months, not cognitively impaired, free from cachectic conditions, have an eGFR ≥60, no anabolic supplementation, no regular high-intensity exercise, not pregnant	1) Drink containing creatine p) Drink containing placebo	1) 15 p) 20	1) 63.0 (10.0) p) 57.2 (10.4)	1) 10 (66.7) p) 14 (70.0)	**University** (Betsi Cadwaladr University Health Board Small Grants Committee)
Abdollahzad (2015) [Iran][134]	RCT	Aged 18-65 years, DAS28>3.2, 1987 ACR RA criteria Exclusions: liver, kidney, diabetes, RA symptom duration <6 months, consumption of other antioxidants or fatty acid supplements one month before BL, smoking, warfarin, pregnancy/lactation, oral contraceptives	1) Co-enzyme Q10 p) Wheat starch placebo	1) 22 p) 23	1) 48.8 (11.6) p) 50.6 (11.1)	1) 19 (86.4) p) 20 (87.0)	**University** (Tabriz University of Medical Sciences)
Mirtaheri (2015) [Iran][135]	RCT	2010 ACR/EULAR criteria, aged 20-50 years, DAS28<5.1, stable medication for 1 month, no anti-oxidants Exclusions: other rheumatic diseases, cancer, diabetes, endocrine disorders, thyroid disorders, vitamin/mineral deficiency, BMI>40, hypertension, renal failure, hepatic diseases, gastrointestinal disorders, other autoimmune/inflammatory diseases, pregnancy/lactation, postmenopause, hormore replacement therapy, oral contraceptives, smoking,	1) Alpha-lipoic acid before breakfast and dinner p) Maltodextrin	1) 33 p) 32	1) 36.1 (8.8) p) 38.3 (8.6)	1) 33 (100) p) 32 (100)	Not reported

ACR = American College of Rheumatology, N = number, RA = rheumatoid arthritis, SD = standard deviation, USA = United States of America

Table – Minerals and supplements (RA), description of included studies

Author (date) [country]	Study design	Inclusion criteria	Exposure detail	N	Age, mean (SD) years	N (%) female	Funders
Alavi (2011) [UK][136]	RCT	Aged ≥18 years, 1987 ACR RA criteria, stable medication for ≥2 months Exclusions: quiescent disease, acute severe RA or severe concomitant disease requiring immunosuppressive or immunomodifying drugs, pregnant, breastfeeding, herbal remedies	1) Ambrotose complex – contains aloe vera, arabinogalactan, gum ghatti, gum tragacanth, glucosamine p) identical placebo (rice flower)	1) 33 p) 36	Not reported §	Not reported §	**Industry** (Mannatech incorporated)
Bae (2009) [South Korea][124]	RCT §	1987 ACR RA criteria	1) Alpha-lipoic acid p) Cornstarch	20	52.1 (10.3)	19 (95.0)	**University** (Sookmyung Women's University Research Grants)
Aryaeian (2008) [Iran][137]	RCT	1987 ACR RA criteria for >2 years, aged 19-69 years Exclusions: abnormal renal/hepatic function, smoking, myocardial infarction, pregnancy, vitamins/mineral supplements, hyperlipidemia, taking thyroid hormones, estrogens, progesterone, diuretics or β-blockers	1) Linoleic acid capsules 2) Linoleic acid capsules + vitamin E p) Sunflower and corn oil	1) 22 2) 22 p) 22	1) 46.2 (2.4) 2) 43.8 (12.8 [sic]) p) 48.0 (2.4)	1) 19 (86.3) 2) 17 (77.2) p) 19 (86.3)	**University** (Tehran University of Medical Sciences)
Rastmanesh (2008) [Iran][138]	RCT	Women, aged 18-60 years, hypokalemic, 1987 ACR RA criteria, active disease: >4 swollen joints, >4 tender joints, ESR >30 or CRP >1, stable treatment for ≥2 months Exclusions: inflammatory bowel disease, atrophic gastritis, and stoma, malignancy, and use of dietary supplements containing fish oil and/or antioxidants. Individuals with pre-existing renal disease, hyperkalemia, acidosis or insulin deficiency, using potassium-sparing diuretics, beta-adrenergic blockers, angiotensin-converting enzyme inhibitors, and digitalis	1) Enriched white grape juice containing potassium p) Placebo grape juice	1) 18 p) 18	1) 49.5 (7.0) p) 47.8 (5.1)	1) 18 (100) p) 18 (100)	**Government** (Iranian National Nutrition and Food Technology Research Institute)
Nakamura (2007) [Japan][139]	RCT	1987 ACR RA criteria, stable medicine for 6 months, stable RA activity	1) Glucosamine tablets P Placebo tablets	1) 25 p) 26	1) 61.4 (41-81) p) 62.6 (43-81)§	1) 22 (88.0) p) 22 (84.6)	Not reported

ACR = American College of Rheumatology, N = number, RA = rheumatoid arthritis, SD = standard deviation, USA = United States of America

Table – Minerals and supplements (RA), description of included studies

Author (date) [country]	Study design	Inclusion criteria	Exposure detail	N	Age, mean (SD) years	N (%) female	Funders
Marcora (2005) [UK][140]	RCT	1987 ACR RA criteria, stable medication for 3 months Exclusions: any condition prevention safe participation of physical function tests or if an increase in nitrogen is contraindicated, cognitive impairment, presence of cachectic disease, taking drugs or nutritional supplements known to affect skeletal muscle mass (exception: steroids), participation in regular, intense exercise	1) Beta-hydroxy-beta-methylbutyrate, glutamine and arginine in a sachet – patients mixed powder with water p) Placebo = isonitrogenous and isocaloric mixture of other, nonessential amino acids	1) 20 p) 20	1) 54 (10) p) 57 (8)	1) 12 (60.0) p) 13 (65.0)	Not reported
Mattingly (1982) [UK][141]	RCT	Classical or definite RA, symptom duration >1 year Exclusions: receiving gold, D-penicillamine, chloroquine, levamisole and immunosuppressants	1) Zinc sulphate tablets (220mg) p) Placebo tablets	1) 14 p) 13	1) 51 p) 57	1) 11 (78.5) p) 10 (76.9)	Not reported
Simkin (1976) [USA][142]	RCT	Classical or definite RA, active disease	1) Zinc sulphate tablets (220mg) p) Placebo tablets	24	54.3 (11.2)	Not reported	**Government** (National Institute of Arthritis and Musculoskeletal and Skin Diseases), **Charity** (Arthritis Foundatoin)
Bepler (1957) [USA][143]	RCT	1958 ACR RA criteria – definite cases only	1) Manganese glycerophosphate capsules p) lactose placebo	1) 9 p) 9	1) 52.4 (range: 31-60) p) 52.5 (range: 40-70)	Not reported	Not reported
Rasker (1982) [The Netherlands][144]	Single arm int.	Severe RA who failed antimalarials, gold, d-penicillamine, azathioprine	Zinc sulphate tablets (220mg)	22	57.6 (10.8)	20 (80)	Not reported

ACR = American College of Rheumatology, N = number, RA = rheumatoid arthritis, SD = standard deviation, USA = United States of America

Supplementary table 88 – Alpha-lipoic acid and RA progression, results

Table – Alpha-lipoic acid (RA), results and quality assessment

Outcome	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	AMSTAR2 quality	Rand. Seq.	Alloc. Conc.	Blind. Part.	Blind. Asses.
Pain	Bae (2009) [RCT][124]	Alpha-lipoic acid vs placebo at week 4 SMD -0.12 (-0.74, 0.50)	Pain VAS, BL / 4 weeks, mean (SD*) Alpha-lipoic acid: 35.12 (31.91) / 30.00 (23.93) Placebo: 32.25 (27.92) / 33.33 (31.91)		H/UC	H/UC	L	H/UC
Function	Bae (2009) [RCT][124]	Alpha-lipoic acid vs placebo at week 4 SMD -0.30 (-0.93, 0.32)	KHAQ, BL / 4 weeks, mean (SD*) Alpha-lipoic acid: 0.49 (0.32) / 0.43 (0.39) Placebo: 0.47 (0.40) / 0.59 (0.64)		H/UC	H/UC	L	H/UC
CRP	Mirtaheri (2015) [RCT][135]	Alpha-lipoic acid vs placebo at week 8 SMD -0.21 (-0.70, 0.28)	CRP, BL / 8 weeks, mean (SD*) Alpha-lipoic acid: 4.7 (7.0) / 2.7 (3.3) Placebo: 4.6 (6.7) / 3.5 (4.2)		L	H/UC	L	H/UC
	Bae (2009) [RCT][124]	Alpha-lipoic acid vs placebo at week 4 SMD -0.32 (-0.94, 0.30)	CRP, BL / 4 weeks, mean (SD*) Alpha-lipoic acid: 1.75 (3.30) / 1.33 (2.40) Placebo: 1.71 (2.97) / 2.33 (3.71)		H/UC	H/UC	L	H/UC
	Bespoke MA Mirataheri[135] Bae[124]	Alpha-lipoic acid vs placebo SMD -0.25 (-0.64, 0.13) I^2 0.0%						

* mean (SD) calculated from median (IQR) using published formula[61]

Alloc. Conc. = allocation concealment, AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews, BL = baseline, Blind. Asses. = Blinded assessors, Blind. Part. = blinded participants, CI = confidence interval, DAS28 = Disease Activity Score 28, ESR = erythrocyte sedimentation rate, H/UC = high / unclear risk of bias, HAQ = Health Assessment Questionnaire, IQR = interquartile range, int. = intervention, KHAQ = Korean Health Assessment Questionnaire, L = low risk of bias, RA = rheumatoid arthritis, Rand. Seq. = random sequence generation, RCT = randomised controlled trial, SD =standard deviation, SMD = Standardised mean difference, VAS = visual analogue scale

Supplementary table 89 – Ambrotose and RA progression, results

Table – Ambrotose (RA), results and quality assessment

Outcome	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	AMSTAR2 quality	Rand. Seq.	Alloc. Conc.	Blind. Part.	Blind. Asses.
Pain	Alavi (2011) [RCT][136]	Ambrotose vs placebo, change BL-6 months SMD -0.44 (-0.92, 0.04)	SF36 – pain, mean change BL-6 months (SD) Ambrotose: -4.83 (19.38) Placebo: 4.28 (21.61)		L	L	L	L
Function	Alavi (2011) [RCT][136]	Ambrotose vs placebo, change BL-6 months SMD -0.11 (-0.58, 0.37)	SF36 – function, mean change BL-6 months (SD) Ambrotose: 2.17 (20.16) Placebo: 4.22 (18.97)		L	L	L	L
Disease activity	Alavi (2011) [RCT][136]		DAS28, mean difference at 6 months adjusted for baseline (SE) 0.63 (0.23) p=0.009		L	L	L	L
Patient global	Alavi (2011) [RCT][136]		Patient global VAS, mean difference at 6 months adjusted for baseline (SE) 10.5 (4.4) p=0.02		L	L	L	L
Fatigue	Alavi (2011) [RCT][136]	Ambrotose vs placebo, change BL-6 months SMD 0.02 (-0.45, 0.49)	SF36 – vitality, mean change BL-6 months (SD) Ambrotose: -15.75 (14.61) Placebo: -16.13 (20.14)		L	L	L	L
QoL	Alavi (2011) [RCT][136]	Ambrotose vs placebo, change BL-6 months SMD -0.03 (-0.50, 0.45)	WHO QoL, mean change BL-6 months (SD) Ambrotose: 1.41 (5.70) Placebo: 1.53 (3.86)		L	L	L	L
Anxiety	Alavi (2011) [RCT][136]	Ambrotose vs placebo, change BL-6 months SMD 0.15 (-0.33, 0.62)	HADS anxiety, mean change BL-6 months (SD) Ambrotose: 0.33 (2.32) Placebo: -0.06 (2.95)		L	L	L	L
Depression	Alavi (2011) [RCT][136]	Ambrotose vs placebo, change BL-6 months SMD 0.40 (-0.07, 0.88)	HADS Depression, mean change BL-6 months (SD) Ambrotose: 0.10 (1.58) Placebo: -0.64 (2.04)		L	L	L	L

Alloc. Conc. = allocation concealment, AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews, BL = baseline, Blind. Asses. = Blinded assessors, Blind. Part. = blinded participants, CI = confidence interval, H/UC = high / unclear risk of bias, HADS = Hospital Anxiety and Depression Scale, L = low risk of bias, QoL = Quality of Life, RA = rheumatoid arthritis, Rand. Seq. = random sequence generation, RCT = randomised controlled trial, SD = standard deviation, SE = standard error, SMD = Standardised mean difference, WHO = World Health Organisation

Supplementary table 90 – Co-enzyme Q10 and RA progression, results

Table – Co-enzyme Q10 (RA), results and quality assessment

Outcome	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	AMSTAR2 quality	Rand. Seq.	Alloc. Conc.	Blind. Part.	Blind. Asses.
CRP	Abdollahzad (2015) [RCT][134]	Co-enzyme Q10 vs placebo at 2 months SMD -0.43 (-1.02, 0.16)	CRP, BL / 2 months, mean (SD) Co-enzyme Q10: 19.9 (18.0) / 14.7 (11.7) Placebo: 24.3 (19.9) / 21.3 (18.2)		L	L	L	L

Alloc. Conc. = allocation concealment, AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews, BL = baseline, Blind. Asses. = Blinded assessors, Blind. Part. = blinded participants, CI = confidence interval, CRP = C-reactive protein, H/UC = high / unclear risk of bias, L = low risk of bias, RA = rheumatoid arthritis, Rand. Seq. = random sequence generation, RCT = randomised controlled trial, SD = standard deviation, SMD = Standardised mean difference,

Supplementary table 91 – Creatine and RA progression, results

Table – Creatine (RA), results and quality assessment

Outcome	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	AMSTAR2 quality	Rand. Seq.	Alloc. Conc.	Blind. Part.	Blind. Asses.
Function	Wilkinson (2016) [RCT][133]	Creatine vs placebo, change over 12 weeks SMD 0.00 (-0.67, 0.67)	mHAQ, change from BL-12 weeks, mean (SD) Creatine: -0.1 (0.1) Placebo: -0.1 (0.1); p=0.836		L	L	L	L
Disease activity	Wilkinson (2016) [RCT][133]	Creatine vs placebo, change over 12 weeks SMD 0.00 (-0.67, 0.67)	DAS28, change from BL-12 weeks, mean (SD) Creatine: -0.1 (0.2) Placebo: -0.1 (0.2); p=0.990		L	L	L	L

Alloc. Conc. = allocation concealment, AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews, Blind. Asses. = Blinded assessors, Blind. Part. = blinded participants, CI = confidence interval, DAS28 = Disease Activity Score 28, H/UC = high / unclear risk of bias, L = low risk of bias, mHAQ = modified Health Assessment Questionnaire, RA = rheumatoid arthritis, Rand. Seq. = random sequence generation, RCT = randomised controlled trial, SD = standard deviation, SMD = Standardised mean difference,

Supplementary table 92 – Glucosamine and RA progression, results

Table – Glucosamine (RA), results and quality assessment

Outcome	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	AMSTAR2 quality	Rand. Seq.	Alloc. Conc.	Blind. Part.	Blind. Asses.
CRP	Nakamura (2007) [RCT][139]	CRP vs placebo at 12 weeks SMD 0.03 (-0.52, 0.57)	CRP, BL / 12 weeks, mean (SD*) Glucosamine: 0.81 (4.5) / 1.07 (7.9) Placebo: 1.13 (6.9) / 0.91 (4.4)		H/UC	H/UC	H/UC	H/UC
ESR	Nakamura (2007) [RCT][139]	CRP vs placebo at 12 weeks SMD 0.00 (-0.55, 0.55)	ESR, BL / 12 weeks, mean (SD*) Glucosamine: 29.9 (71.5) / 30.4 (83.0) Placebo: 31.4 (109.6) / 30.5 (96.9)		H/UC	H/UC	H/UC	H/UC

* Calculated from standard error in paper

Alloc. Conc. = allocation concealment, AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews, Blind. Asses. = Blinded assessors, Blind. Part. = blinded participants, CI = confidence interval, H/UC = high / unclear risk of bias, L = low risk of bias, RA = rheumatoid arthritis, Rand. Seq. = random sequence generation, RCT = randomised controlled trial, SD = standard deviation, SMD = Standardised mean difference,

Supplementary table 93 – Linoleic acid and RA progression, results

Table – Linoleic acid (RA), results and quality assessment

Outcome	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	AMSTAR 2 quality	Rand. Seq.	Alloc. Conc.	Blind. Part.	Blind. Asses.
CRP	Aryaeian (2008) [RCT][137]	Linoleic acid vs placebo SMD -0.00 (-0.60, 0.59) Linoleic acid + vitamin E vs placebo SMD -0.49 (-1.08, 0.12)	CRP, BL / 12 weeks, mean (SD*) Linoleic acid: 7.18 (10.1) / 5.46 (5.5) Linoleic acid + vitamin E: 5.23 (6.4) / 3.17 (3.9) Placebo: 6.44 (7.9) / 5.48 (5.6)		H/UC	H/UC	H/UC	H/UC
ESR	Aryaeian (2008) [RCT][137]	Linoleic acid vs placebo SMD -0.52 (-1.12, 0.08) Linoleic acid + vitamin E vs placebo SMD -0.58 (-1.19, 0.02)	CRP, BL / 12 weeks, mean (SD*) Linoleic acid: 26.81 (11.2) / 19.14 (10.1) Linoleic acid + vitamin E: 28.45 (17.3) / 17.77 (12.2) Placebo: 28.36 (21.5) / 27.04 (18.9)		H/UC	H/UC	H/UC	H/UC

*SD calculated from standard error reporting in paper

Alloc. Conc. = allocation concealment, AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews, Blind. Asses. = Blinded assessors, Blind. Part. = blinded participants, CI = confidence interval, CRP = C-reactive protein, H/UC = high / unclear risk of bias, L = low risk of bias, RA = rheumatoid arthritis, Rand. Seq. = random sequence generation, RCT = randomised controlled trial, SD = standard deviation, SMD = Standardised mean difference,

Supplementary table 94 – Manganese and RA progression, results

Table – Manganese (RA), results and quality assessment

Outcome	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	AMSTAR2 quality	Rand. Seq.	Alloc. Conc.	Blind. Part.	Blind. Asses.
Disease severity	Bepler (1957) [RCT][143]		Number improved / got worse after 2 months 1) 5 / 4 p) 5 / 4		H/UC	H/UC	H/UC	H/UC

Alloc. Conc. = allocation concealment, AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews, Blind. Asses. = Blinded assessors, Blind. Part. = blinded participants, CI = confidence interval, H/UC = high / unclear risk of bias, L = low risk of bias, RA = rheumatoid arthritis, Rand. Seq. = random sequence generation, RCT = randomised controlled trial, SMD = Standardised mean difference,

Supplementary table 95 – Potassium and RA progression, results

Table – Potassium (RA), results and quality assessment

Outcome	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	AMSTAR2 quality	Rand. Seq.	Alloc. Conc.	Blind. Part.	Blind. Asses.
Pain	Rastmanesh (2008) [RCT][138]	Potassium vs placebo, change BL-28 days SMD -2.63 (-3.54, -1.73)	Pain VAS, change BL-28 days, mean (SD) Potassium: -27.5 (8.7) Placebo: -3.4 (9.6); p<0.01		L	L	L	L
Disease activity	Rastmanesh (2008) [RCT][138]	Potassium vs placebo, change BL-28 days SMD -2.98 (-3.94, -2.02)	DAS28, change BL-28 days, mean (SD) Potassium: -0.69 (0.23) Placebo: -0.10 (0.16); p<0.01		L	L	L	L
Tender joints	Rastmanesh (2008) [RCT][138]	Potassium vs placebo, change BL-28 days SMD -2.20 (-3.03, -1.36)	Tender joint count, change BL-28 days, mean (SD) Potassium: -3.1 (1.65) Placebo: -0.31 (0.70); p<0.01		L	L	L	L
Swollen joints	Rastmanesh (2008) [RCT][138]	Potassium vs placebo, change BL-28 days SMD -2.76 (-3.69, -1.84)	Swollen joint count, change BL-28 days, mean (SD) Potassium: -2.93 (1.12) Placebo: -0.43 (0.62); p<0.03		L	L	L	L
Patient global	Rastmanesh (2008) [RCT][138]	Potassium vs placebo, change BL-28 days SMD -0.86 (-1.55, -0.18)	Patient global VAS, change BL-28 days, mean (SD) Potassium: -6.2 (7.6) Placebo: -0.93 (4.1); p<0.02		L	L	L	L
CRP	Rastmanesh (2008) [RCT][138]	Potassium vs placebo, change BL-28 days SMD -0.80 (-1.48, -0.12)	CRP, change BL-28 days, mean (SD) Potassium: -3.25 (4.70) Placebo: -0.09 (3.00); p<0.02		L	L	L	L
ESR	Rastmanesh (2008) [RCT][138]	Potassium vs placebo, change BL-28 days SMD -1.93 (-2.73, -1.13)	ESR, change BL-28 days, mean (SD) Potassium: -14.30 (7.15) Placebo: -2.06 (5.40); p<0.001		L	L	L	L

Alloc. Conc. = allocation concealment, AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews, BL = baseline, Blind. Asses. = Blinded assessors, Blind. Part. = blinded participants, CI = confidence interval, DAS28 = Disease Activity Score 28, H/UC = high / unclear risk of bias, L = low risk of bias, RA = rheumatoid arthritis, Rand. Seq. = random sequence generation, RCT = randomised controlled trial, SD = standard deviation, SMD = Standardised mean difference, VAS = visual analogue scale

Supplementary table 96 – Probiotics and RA progression, results

Table – Probiotics (RA), results and quality assessment

Outcome	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	AMSTAR2 quality	Rand. Seq.	Alloc. Conc.	Blind. Part.	Blind. Asses.
Pain	Zamani (2017) [RCT][132]	Synbiotic vs placebo at 8 weeks SMD -0.41 (-0.95, 0.13)	Pain VAS, mean (SD) at 8 weeks Synbiotics: 27.0 (15.6) Control: 35.9 (26.8)		L	H/UC	L	L
Function	Aqaeinezhad Rudbane (2018) [MA][130]	Probiotics vs placebo SMD -0.30 (-0.89, 0.29)		Low				
	Mohammed (2017) [MA][131]	Probiotics vs placebo MD -0.11 (-0.23, 0.01)		Moderate				
Disease activity	Aqaeinezhad Rudbane (2018) [MA][130]	Probiotics vs placebo SMD -0.58 (-0.97, -0.19)		Low				
	Mohammed (2017) [MA][131]	Probiotics vs placebo MD 0.02 (-0.58, 0.63)		Moderate				
	Zamani (2017) [RCT][132]	Synbiotic vs placebo at 8 weeks SMD -0.65 (-1.20, -0.10)	DAS28, mean (SD) at 8 weeks Synbiotics: 2.6 (0.7) Control: 3.2 (1.1)		L	H/UC	L	L
Tender joints	Aqaeinezhad Rudbane (2018) [MA][130]	Probiotics vs placebo SMD -0.21 (-0.53, 0.11)		Low				
Swollen joints	Aqaeinezhad Rudbane (2018) [MA][130]	Probiotics vs placebo SMD -0.30 (-0.62, 0.02)		Low				
	Mohammed (2017) [MA][131]	Probiotics vs placebo MD 0.17 (-0.39, 0.73)		Moderate				
CRP	Aqaeinezhad Rudbane (2018) [MA][130]	Probiotics vs placebo SMD -0.32 (-0.65, 0.00)		Low				
	Mohammed (2017) [MA][131]	Probiotics vs placebo MD -1.40 (-4.06, 1.26)		Moderate				
	Zamani (2017) [RCT][132]	Synbiotic vs placebo at 8 weeks SMD -0.74 (-1.30, -0.19)	CRP, mean (SD) at 8 weeks Synbiotics: 4609.2 (2711.7) Control: 8474.1 (6829.7)		L	H/UC	L	L
ESR	Aqaeinezhad Rudbane (2018) [MA][130]	Probiotics vs placebo SMD -0.17 (-0.76, 0.42)		Low				

Alloc. Conc. = allocation concealment, AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews, Blind. Asses. = Blinded assessors, Blind. Part. = blinded participants, CI = confidence interval, CRP = C-reactive protein, DAS28 = Disease Activity Score 28, ESR = erythrocyte sedimentation rate, H/UC = high / unclear risk of bias, L = low risk of bias, MA = meta-analysis, RA = rheumatoid arthritis, Rand. Seq. = random sequence generation, SD = standard deviation, SMD = Standardised mean difference, VAS = visual analogue scale

Supplementary table 97 – Zinc and RA progression, results

Table – Zinc (RA), results and quality assessment

Outcome	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	AMSTAR2 quality	Rand. Seq.	Alloc. Conc.	Blind. Part.	Blind. Asses.
Pain	Mattingly (1982) [RCT][141]		Pain VAS (0-20), BL / 6 months, mean Zinc: 7.83 / 5.00 Placebo: 11.56 / 8.56		H/UC	H/UC	L	H/UC
Tender joints	Mattingly (1982) [RCT][141]		Ritchie Index, BL / 6 months, mean Zinc: 21.2 / 19.6 Placebo: 27.8 / 26.3		H/UC	H/UC	L	H/UC
	Simkin (1976) [RCT][142]		Tenderness, BL / 12 weeks, mean (SE) Zinc: 28 (5) / 24 (5) Placebo: 28 (5) / 29 (9)		H/UC	L	L	H/UC
Swollen joints	Simkin (1976) [RCT][142]		Swelling, BL / 12 weeks, mean (SE) Zinc: 27 (3) / 20 (3) Placebo: 14 (2) / 13 (3) p<0.02		H/UC	L	L	H/UC
Joint score	Rasker (1982) [Single arm int.] [144]		Joint score*, BL / 2 months, mean (SD) 17 (7) / 19 (8)					
Morning stiffness	Mattingly (1982) [RCT][141]		Morning stiffness, BL / 6 months, mean Zinc: 1.92 / 1.58 Placebo: 2.56 / 3.22		H/UC	H/UC	L	H/UC
	Simkin (1976) [RCT][142]		Stiffness, BL / 12 weeks, mean (SE) Zinc: 4.0 (0.4) / 3.0 (0.8) Placebo: 3.5 (0.4) / 3.6 (0.5)		H/UC	L	L	H/UC
Patient global	Mattingly (1982) [RCT][141]		Patient global VAS, BL / 6 months, mean Zinc: 2.92 / 3.42 Placebo: 2.67 / 3.11		H/UC	H/UC	L	H/UC
	Simkin (1976) [RCT][142]		Patient global VAS, BL / 12 weeks, mean (SE) Zinc: 3.3 (0.2) / 3.1 (0.3) Placebo: 3.1 (0.1) / 3.2 (0.2)		H/UC	L	L	H/UC
ESR	Mattingly (1982) [RCT][141]		ESR, BL / 6 months, mean Zinc: 49.4 / 44.7 Placebo: 61.2 / 64.3		H/UC	H/UC	L	H/UC
	Rasker (1982) [Single arm int.] [144]		ESR, BL / 2 months, mean (SD) 20.3 (28.9) / 53.8 (27.8)					
Grip strength	Mattingly (1982) [RCT][141]		Grip strength, BL / 6 months, mean Zinc: 367 / 411 Placebo: 300 / 337		H/UC	H/UC	L	H/UC
	Simkin (1976) [RCT][142]		Grip strength, BL / 12 weeks, mean (SE) Zinc: 100 (16) / 98 (14) Placebo: 85 (12) / 84 (11)		H/UC	L	L	H/UC

* Joint score from Rasker = Number of affected joints, counting MCP, PIP and MTP joints of each limb as one.

Alloc. Conc. = allocation concealment, AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews, Blind. Asses. = Blinded assessors, Blind. Part. = blinded participants, CI = confidence interval, ESR = erythrocyte sedimentation rate, H/UC = high / unclear risk of bias, int. = intervention, L = low risk of bias, MCP = metacarpophalangeal, MTP = metatarsophalangeal, PIP = proximal interphalangeal, RA = rheumatoid arthritis, Rand. Seq. = random sequence generation, RCT = Randomised Controlled Trial, SD = standard deviation, SE = standard error, SMD = Standardised mean difference, VAS = visual analogue scale

Supplementary table 98 – Combined supplements and RA progression, results

Table – Combined supplements (RA), results and quality assessment

Outcome	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	AMSTAR2 quality	Rand. Seq.	Alloc. Conc.	Blind. Part.	Blind. Asses.
Disease Activity	Marcora (2005) [RCT][140]	Supplements vs placebo at 12 weeks SMD -0.69 (-1.33, -0.05)	RADAI, BL / 12 weeks, mean (SD) Supplements: 2.8 (1.1) / 3.0 (1.2) Placebo: 3.8 (1.4) / 3.9 (1.4); p=0.00 [sic]		L	L	L	L
Function	Marcora (2005) [RCT][140]	Supplements vs placebo at 12 weeks SMD -0.50 (-1.13, 0.13)	mHAQ, BL / 12 weeks, mean (SD) Supplements: 1.5 (0.4) / 1.4 (0.4) Placebo: 1.5 (0.3) / 1.6 (0.4); p=0.03		L	L	L	L
Fatigue	Marcora (2005) [RCT][140]	Supplements vs placebo at 12 weeks SMD -0.86 (-1.51, -0.21)	Fatigue (0-10), BL / 12 weeks, mean (SD) Supplements: 3.9 (3.0) / 3.1 (2.7) Placebo: 5.2 (1.7) / 5.5 (2.9); p=0.06		L	L	L	L
Psychological status	Marcora (2005) [RCT][140]	Supplements vs placebo at 12 weeks SMD -0.39 (-1.02, 0.23)	Psychological status (1-4), BL / 12 weeks, mean (SD) Supplements: 1.6 (0.5) / 1.5 (0.4) Placebo: 1.6 (0.4) / 1.7 (0.6); p=0.02		L	L	L	L
ESR	Marcora (2005) [RCT][140]	Supplements vs placebo at 12 weeks SMD -0.13 (-0.75, 0.49)	ESR, BL / 12 weeks, mean (SD) Supplements: 27.4 (22.6) / 23.3 (19.4) Placebo: 22.7 (14.6) / 25.4 (12.1); p=0.07		L	L	L	L
Grip strength	Marcora (2005) [RCT][140]	Supplements vs placebo at 12 weeks SMD 0.43 (-0.20, 1.06)	Grip strength, BL / 12 weeks, mean (SD) Supplements: 169 (126) / 181 (116) Placebo: 142 (103) / 137 (87); p=0.01		L	L	L	L

Alloc. Conc. = allocation concealment, AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews, Blind. Asses. = Blinded assessors, Blind. Part. = blinded participants, CI = confidence interval, ESR = erythrocyte sedimentation rate, H/UC = high / unclear risk of bias, L = low risk of bias, mHAQ = modified Health Assessment Questionnaire, RA = rheumatoid arthritis, RADAI = Rheumatoid Arthritis Disease Activity Index, Rand. Seq. = random sequence generation, RCT = randomised controlled trial, SD =standard deviation, SMD = Standardised mean difference,

Supplementary table 99 – Description of reviews of vitamins in RA

Table – Vitamins (RA), description of reviews

Authors (date)	Review type	Study type included	Exposure detail	Number of studies included	Funders
Franco (2017)[145]	MA	RCT	Vitamin D	5	**Charity** (São Paulo Research Foundation, Federico Foundation), **Government** (National Council for Scientific and Technological Development)

MA = meta-analysis, RCT = randomised controlled trial

Supplementary table 100 – Description of studies of vitamins in RA

Table – Vitamins (RA), description of included studies

Author (date) [country]	Study design	Inclusion criteria	Exposure detail	N	Age, mean (SD) years	N (%) female	Funders
Batooei (2018) [Iran][146]	RCT	Aged 18-65 years, 2010 ACR/EULAR criteria, active RA, stable renal function, absence of liver disease, can take oral intervention Exclusions: other inflammatory disease, receiving anti-inflammatory or antioxidant medications in past month, pregnancy/breast feeding	1) 600mg N-acetylcysteine (antioxidant) as effervescent tablets twice a day p) Identical effervescent placebo	1) 27 p) 24	1) 53.2 (12.5) p) 51.6 (11.3)	1) 22 (81.5) p) 23 (95.8)	**University (**Hamadan University of Medical Sciences)
Huang (2010) [Taiwan][147]	RCT	1987 ACR RA criteria, adults Exclusions: Pregnant, anaemia, thrombocytopenia, abnormal liver function, renal insufficiency, diabetes, cancer	1) 100mg/day vitamin B6 + folic acid p) Folic acid only	1) 20 p) 15	1) 53.9 (2.0) p) 53.0 (2.0)	1) 17 (85.0) p) 13 (86.7)	**Government** (National Science Council, Taiwan)
Nourmohammadi (2010) [Iran][148]	RCT	1987 ACR RA criteria, "inactive RA" Exclusions: chronic diseases: renal, diabetes, hepatic, hypertension, dyslipidaemia, inflammatory diseases, infection, malnutrition, obesity, smoking, alcohol	1) 300mg vitamin C, 5mg zinc, 25000 IU vitamin A every other day for 12 weeks p) Conventional treatment only (no placebo)	1) 24 p) 25	1) 48.8 (12.6) p) 48.8 (12.7)	1) 20 (83.3) p) 21 (84.0)	**University** (Iran University of Medical Sciences)
Aryaeian (2008) [Iran][137]	RCT	1987 ACR RA criteria for >2 years, aged 19-69 years Exclusions: abnormal renal/hepatic function, smoking, myocardial infarction, pregnancy, vitamins/mineral supplements, hyperlipidemia, taking thyroid hormones, estrogens, progesterone, diuretics or β-blockers	1) Vitamin E 2) vitamin E + Linoleic acid capsules p) Sunflower and corn oil	1) 21 2) 22 p) 22	1) 46.2 (2.4) 2) 43.8 (12.8 [sic]) p) 48.0 (2.4)	1) 19 (86.3) 2) 17 (77.2) p) 19 (86.3)	**University** (Tehran University of Medical Sciences)
Chiang (2005) [USA][149]	RCT	Aged >18 years, 1987 ACR RA criteria, vitamin B6 deficient Exclusions: pregnancy, oral contraceptive use, anaemia , thrombocytopenia, renal insufficiency, diabetes, cancer	1) 50mg vitamin B6 p) Identical placebo tablet	1) 14 p) 14	1) 53.9 (12.6) p) 57.5 (11.0)	1) 12 (85.7) p) 9 (64.3)	**Government** (National Science Council, Taiwan, US Department of Agriculture), **Charity** (Arthritis Foundation)

ACR = American College of Rheumatology, DMARD = disease modifying anti-rheumatic drug, EULAR = European League Against Rheumatism, mg = milligrams, N = number, NRT = non-randomised trial, NSAID = non-steroidal anti-inflammatory drug, RA = rheumatoid arthritis, RF = rheumatoid factor, SD = standard deviation

Table – Vitamins (RA), description of included studies

Author (date) [country]	Study design	Inclusion criteria	Exposure detail	N	Age, mean (SD) years	N (%) female	Funders
Edmonds (1997) [UK][150]	RCT	1987 ACR RA criteria, aged 18-80 years, Ritchie index ≥6 or morning stiffness ≥1 hour, receiving NSAIDs or DMARDs Exclusions: already taking vitamin E, vitamin E hypersensitivity, pregnancy, malabsorption, malignancy	1) Vitamin E p) Identical placebo	1) 20 p) 19	1) 55.4 (15.1) p) 52.0 (10.3)	1) 16 (80.0) p) 15 (78.9)	**Not reported**
Helmy (2001) [Egypt][151]	NRT	1987 ACR RA criteria Exclusions: endocrine, hepatic or renal disorders, malignancy or overt infections	1) Selenium, medicinal yeast, vitamin A, ascorbic acid, vitamin E 2) Same as 1), plus high dose of vitamin E p) standard treatment only	1) 10 2) 10 p) 10	1) 37.1 (8.8) 2) 39.5 (1.1) [sic] p) 43.9 (12.9)	1) 8 (80.0) 2) 8 (80.0) p) 7 (70.0)	**Not reported**
Jalili (2014) [Iran][152]	Single arm int.	1987 ACR RA criteria, aged 40-60 years, stable treatment ≥2 months Exclusions: diabetes, hypertension, thyroid disorders, liver and kidney failure, Cushing syndrome, severe infection, gastric illness, smoking	1) "Selenplus" capsule - 50 µg selenium, 8 mg zinc, 400 µg vitamin A, 125 mg vitamin C, and 40 mg vitamin E.	39	52.6 (5.3)	39 (100)	No source of funding, no conflicts of interest
van Vugt (2008) [The Netherlands][153]	Single arm int.	RF+, 1987 ACR RA criteria, non-smokers, not obese, NSAID/DMARD therapy for ≥3 months	Antioxidant enriched margerine, The spread contained a mix of a-tocopherol (400 mg), lycopene (10 mg), palm oil carotenoids (5 mg; mainly α-carotene) and lutein (10 mg). Further, patients received vitamin C (200 mg daily) as a supplement.	8	Not reported	8 (100)	**Not reported**

ACR = American College of Rheumatology, DMARD = disease modifying anti-rheumatic drug, EULAR = European League Against Rheumatism, mg = milligrams, N = number, NRT = non-randomised trial, NSAID = non-steroidal anti-inflammatory drug, RA = rheumatoid arthritis, RF = rheumatoid factor, SD = standard deviation

Supplementary table 101 – Antioxidants and RA progression, results

Table – Antioxidants (RA), results and quality assessment

Outcome	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	AMSTAR2 quality	Rand. Seq.	Alloc. Conc.	Blind. Part.	Blind. Asses.
Pain	Batooei (2018) [RCT][146]	Antioxidants vs placebo at 12 weeks SMD -1.17 (-1.77, -0.57)	Pain VAS, BL / 12 weeks, mean (SD) Antioxidant: 77.6 (10.9) / 50 (7.8) Placebo: 77.9 (17.7) / 66.9 (19.4); p=0.001		H/UC	H/UC	L	L
Function	Batooei (2018) [RCT][146]	Antioxidants vs placebo at 12 weeks SMD -0.86 (-1.44, -0.28)	HAQ, BL / 12 weeks, mean (SD) Antioxidant: 22.6 (13.1) / 13.9 (9.6) Placebo: 28.7 (11.7) / 24.1 (14); p<0.01		H/UC	H/UC	L	L
Disease activity	Batooei (2018) [RCT][146]	Antioxidants vs placebo at 12 weeks SMD -0.26 (-0.81, 0.29)	DAS28, BL / 12 weeks, mean (SD) Antioxidant: 5.1 (1.2) / 4.35 (1.2) Placebo: 5.3 (1.1) / 4.7 (1.5); p=0.4		H/UC	H/UC	L	L
	Nourmohammadi (2018) [RCT][148]	Antioxidants vs control at 12 weeks SMD -0.85 (-1.43, -0.26)	RADAI, BL / 12 weeks, mean (SD) Antioxidants: 5.06 (1.32) / 2.59 (0.95) Control: 4.96 (1.23) / 3.52 (1.22); p=0.005		H/UC	H/UC	H/UC	H/UC
	Jalili (2014) [Single arm int.][152]		DAS28, BL / 12 weeks, mean (SD) Antioxidants: 2.71 (1.19) / 2.65 (1.17); p=0.019					
	van Vugt (2008) [Single arm int.][153]		DAS28, BL / 10 weeks, mean Antioxidants: 5.84 / 4.82					
Tender joints	Batooei (2018) [RCT][146]	Antioxidants vs placebo at 12 weeks SMD -0.11 (-0.66, 0.44)	Tender joint count, BL / 12 weeks, mean (SD) Antioxidant: 10.6 (7.7) / 6.9 (5.5) Placebo: 10.9 (7) / 7.6 (7.5); p=0.7		H/UC	H/UC	L	L
	Helmy (2001) [NRT][151]	Antioxidants vs Control at 2 months SMD -1.32 (-2.30, -0.35) Antioxidants + vit E vs Control at 2 months SMD -1.19 (-2.15, -0.30)	Ritchie Index, BL / 2 months, mean (SD) Antioxidants: 37.0 (11.6) / 7.0 (6.3) Antioxidants + vit E: 32.5 (1.4) [sic] / 8.5 (5.8) Control: 26.5 (17.6) / 20.0 (12.4)					
	Jalili (2014) [Single arm int.][152]		Tender joint count, BL / 12 weeks, median (range) Antioxidants: 1 (0-17) / 1 (0-14); p=0.839					
Swollen joints	Batooei (2018) [RCT][146]	Antioxidants vs placebo at 12 weeks SMD -0.15 (-0.71, 0.40)	Swollen joint count, BL / 12 weeks, mean (SD) Antioxidant: 8.4 (6.2) / 6.3 (4.9) Placebo: 9.1 (5.7) / 7.1 (5.5); p=0.4		H/UC	H/UC	L	L
	Jalili (2014) [Single arm int.][152]		Swollen joint count, BL / 12 weeks, median (range) Antioxidants: 0 (0-15) / 0 (0-14); p=0.736					
Patient global	Batooei (2018) [RCT][146]	Antioxidants vs placebo at 12 weeks SMD -0.70 (-1.26, -0.13)	Patient global VAS, BL / 12 weeks, mean (SD) Antioxidant: 31.7 (11.3) / 23.6 (15) Placebo: 37.7 (14.7) / 35.6 (19.5); p<0.01		H/UC	H/UC	L	L

Alloc. Conc. = allocation concealment, AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews, Blind. Asses. = Blinded assessors, Blind. Part. = blinded participants, CI = confidence interval, CRP = C-reactive protein, DAS28 = Disease Activity Score 28, ESR = erythrocyte sedimentation rate, H/UC = high / unclear risk of bias, HAQ = Health Assessment Questionnaire, L = low risk of bias, NRT = non-randomised trial, RA = rheumatoid arthritis, Rand. Seq. = random sequence generation, RCT = randomised controlled trial, SD = standard deviation, SMD = Standardised mean difference, VAS = visual analogue scale

Table – Antioxidants (RA) cont., results and quality assessment

Outcome	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	AMSTAR2 quality	Rand. Seq.	Alloc. Conc.	Blind. Part.	Blind. Asses.
Morning stiffness	Helmy (2001) [NRT][151]	Antioxidants vs Control at 2 months SMD -1.40 (-2.39, -0.42) Antioxidants + vit E vs Control at 2 months SMD -1.51 (-2.52, -0.50)	Morning stiffness (mins), BL / 2 months, mean (SD) Antioxidants: 67.5 (30.8) / 10.0 (12.5) Antioxidants + vit E: 41.0 (37.8) / 7.5 (13.2) Control: 54.5 (37.5) / 39.0 (26.4)					
CRP	Jalili (2014) [Single arm int.][152]		CRP, BL / 12 weeks, mean (SD) Antioxidants: 5.50 (0.5) / 4.20 (0.51); p=0.003					
ESR	Batooei (2018) [RCT][146]	Antioxidants vs placebo at 12 weeks SMD -0.12 (-0.67, 0.43)	ESR, BL / 12 weeks, mean (SD) Antioxidant: 31.4 (19.6) / 25.2 (19.8) Placebo: 29.2 (19.3) / 27.8 (23.7); p=0.6		H/UC	H/UC	L	L
	Helmy (2001) [NRT][151]	Antioxidants vs Control at 2 months SMD -1.52 (-2.53, -0.51) Antioxidants + vit E vs Control at 2 months SMD -1.11 (-2.06, -0.16)	ESR, BL / 2 months, mean (SD) Antioxidants: 63.0 (27.1) / 14.0 (7.0) Antioxidants + vit E: 71.5 (21.1) / 18.0 (15.3) Control: 54.5 (29.3) / 39.5 (22.7)					

Alloc. Conc. = allocation concealment, AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews, Blind. Asses. = Blinded assessors, Blind. Part. = blinded participants, CI = confidence interval, CRP = C-reactive protein, DAS28 = Disease Activity Score 28, ESR = erythrocyte sedimentation rate, H/UC = high / unclear risk of bias, HAQ = Health Assessment Questionnaire, L = low risk of bias, NRT = non-randomised trial, RA = rheumatoid arthritis, Rand. Seq. = random sequence generation, RCT = randomised controlled trial, SD = standard deviation, SMD = Standardised mean difference, VAS = visual analogue scale

Supplementary table 102 – Vitamin B6 and RA progression, results

Table – Vitamin B6 (RA), results and quality assessment

Outcome	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	AMSTAR2 quality	Rand. Seq.	Alloc. Conc.	Blind. Part.	Blind. Asses.
Disease activity	Huang (2010) [RCT][147]	Vitamin B6 vs control at 12 weeks SMD -0.33 (-1.01, 0.34)	DAS28, BL / week 12, mean (SD) Vitamin B6: 4.1 (0.3) / 4.2 (0.3) Control: 4.1 (0.2) / 4.3 (0.3)		H/UC	H/UC	H/UC	H/UC
Tender joints	Huang (2010) [RCT][147]	Vitamin B6 vs control at 12 weeks SMD -0.58 (-1.26, 0.10)	Tender joint count, BL / week 12, mean (SD) Vitamin B6: 12.3 (4.1) / 11.6 (2.8) Control: 9.2 (2.2) / 13.3 (3.1)		H/UC	H/UC	H/UC	H/UC
Swollen joints	Huang (2010) [RCT][147]	Vitamin B6 vs control at 12 weeks SMD 0.55 (-0.13, 1.23)	Swollen joint count, BL / week 12, mean (SD) Vitamin B6: 5.3 (2.6) / 3.3 (1.9) Control: 2.6 (0.8) / 2.4 (1.2)		H/UC	H/UC	H/UC	H/UC
CRP	Huang (2010) [RCT][147]	Vitamin B6 vs control at 12 weeks SMD 0.20 (-0.47, 0.87)	CRP, BL / week 12, mean (SD) Vitamin B6: 0.3 (0.4) / 0.4 (0.4) Control: 0.3 (0.2) / 0.3 (0.6)		H/UC	H/UC	H/UC	H/UC
	Chiang (2005) [RCT][149]		CRP, BL / 30 days, median (95% CI) Vitamin B6: 2.0 (0.1, 17.2) / 3.0 (0.6, 14.8) Placebo: 13.0 (19.4, 52.6) / 7.0 (4.4, 27.5); p<0.0001		H/UC	L	L	H/UC
ESR	Chiang (2005) [RCT][149]		ESR, BL / 30 days, median (95% CI) Vitamin B6: 27.5 (18.8, 41.6) / 31.0 (22.4, 38.9) Placebo: 31.0 (19.4, 52.6) / 32.0 (24.0, 49.7); p<0.0001)		H/UC	L	L	H/UC

Alloc. Conc. = allocation concealment, AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews, BL = baseline, Blind. Asses. = Blinded assessors, Blind. Part. = blinded participants, CI = confidence interval, CRP = C-reactive protein, DAS28 = Disease Activity Score 28, ESR = erythrocyte sedimentation rate, H/UC = high / unclear risk of bias, L = low risk of bias, RA = rheumatoid arthritis, Rand. Seq. = random sequence generation, RCT = randomised controlled trial, SD = standard deviation, SMD = Standardised mean difference,

Supplementary table 103 – Vitamin D and RA progression, results

Table – Vitamin D (RA), results and quality assessment

Outcome	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	AMSTAR2 quality	Rand. Seq.	Alloc. Conc.	Blind. Part.	Blind. Asses.
Pain	Franco (2017) [MA][145]		Pain MD 2.79 (-1.87, 7.44)	Moderate				
Disease Activity	Franco (2017) [MA][145]		DAS MD -0.31 (-0.86, 0.25)	Moderate				

Alloc. Conc. = allocation concealment, AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews, Blind. Asses. = Blinded assessors, Blind. Part. = blinded participants, CI = confidence interval, DAS = Disease Activity Score, H/UC = high / unclear risk of bias, L = low risk of bias, MA = meta-analysis, MD = mean difference, RA = rheumatoid arthritis, Rand. Seq. = random sequence generation, SMD = Standardised mean difference,

Supplementary table 104 – Vitamin E and RA progression, results

Table – Vitamin E (RA), results and quality assessment

Outcome	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	AMSTAR 2 quality	Rand. Seq.	Alloc. Conc.	Blind. Part.	Blind. Asses.
Pain	Edmonds (1997) [RCT][150]	Vitamin E vs placebo: pain in morning / evening / after chosen activity after 12 weeks SMD -0.82 (-1.47, -0.16) / -0.68 (-1.32, -0.03) / -0.56 (-1.20, 0.08)	Pain in morning / evening / after chosen activity, mean (SD) change from bl Vitamin E: -0.56 (1.53) / -0.56 (1.43) / -0.68 (1.52) Placebo: 0.54 (1.12) / 0.28 (1.00) / 0.09 (1.19)		H/UC	H/UC	L	H/UC
Tender joints	Edmonds (1997) [RCT][150]	Vitamin E vs placebo SMD 0.12 (-0.51, 0.75)	Ritchie Index, BL / 12 weeks, mean (SD) Vitamin E: 15.9 (7.7) / 15.3 (10.0) Placebo: 14.9 (8.8) / 14.0 (12.1)		H/UC	H/UC	L	H/UC
Swollen joints	Edmonds (1997) [RCT][150]	Vitamin E vs placebo SMD -0.06 (-0.69, 0.57)	Swollen joint count, BL / 12 weeks, mean (SD) Vitamin E: 9.2 (3.4) / 9.9 (5.0) Placebo: 9.8 (5.4) / 10.2 (5.6)		H/UC	H/UC	L	H/UC
Morning stiffness	Edmonds (1997) [RCT][150]		Morning stiffness, BL / 12 weeks, median Vitamin E: 45 / 30 Placebo: 30 / 20		H/UC	H/UC	L	H/UC
CRP	Aryaeian (2008) [RCT][137]	Vitamin E vs placebo SMD -0.28 (-0.88, 0.32) Linoleic acid + vitamin E vs placebo SMD -0.49 (-1.08, 0.12)	CRP, BL / 12 weeks, mean (SD*) Vitamin E: 9.06 (14.3) / 4.07 (4.5) Vitamin E + linoleic acid: 5.23 (6.4) / 3.17 (3.9) Placebo: 6.44 (7.9) / 5.48 (5.6)		H/UC	H/UC	H/UC	H/UC
ESR	Aryaeian (2008) [RCT][137]	Linoleic acid vs placebo SMD 0.25 (-0.35, 0.85) Linoleic acid + vitamin E vs placebo SMD -0.58 (-1.19, 0.02)	CRP, BL / 12 weeks, mean (SD*) Vitamin E: 40.43 (26.2) / 32.28 (23.0) Vitamin E + linoleic acid: 28.45 (17.3) / 17.77 (12.2) Placebo: 28.36 (21.5) / 27.04 (18.9)		H/UC	H/UC	H/UC	H/UC

*SD calculated from standard error reporting in paper

Alloc. Conc. = allocation concealment, AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews, Blind. Asses. = Blinded assessors, Blind. Part. = blinded participants, CI = confidence interval, CRP = C-reactive protein, H/UC = high / unclear risk of bias, L = low risk of bias, RA = rheumatoid arthritis, Rand. Seq. = random sequence generation, RCT = randomised controlled trial, SD = standard deviation, SMD = Standardised mean difference,

Supplementary table 105 – Description of reviews of animal products in SLE

Table – Animal products (SLE), description of reviews

Authors (date)	Review type	Study type included	Exposure detail	Number of studies included	Funders
Rodriguez Huerta (2016)[154]	SR	RCTs, observational	Omega 3 consumption	3	**Government** (Spanish Ministry of Health, Social Affairs and Equality)

RCT = randomised controlled trial, SLE = systemic lupus erythematosus, SR = systematic review

Supplementary table 106 – Description of studies of animal products in SLE

Table – Animal products (SLE), description of included studies

Author (date) [country]	Study design	Inclusion criteria	Exposure detail	N	Age, mean (SD) years	N (%) female	Funders
Curado Borges (2017) [Brazil][155]	RCT	Aged 18-60 years, SLE ACR criteria, stable medication for SLE over last three months Exclusions: pregnancy, disease duration <1 year, allergy to fish, fish oil or any omega-3 product, omega 3 use in the last 6 months, diabetes, liver disease, active nephritis, chronic renal failure, any type of infection	1) Two omega 3 tablets (540mg of EPA and 100mg of DHA) p) No intervention and no placebo	1) 22 p) 27	Median (IQR) 37 (29-48)	1) 22 (100) p) 27 (100)	**Government** (Fundac¸ão de Amparo à Pesquisa do Estadode Minas Gerais)
Arriens (2015) [USA][156]	RCT	Aged 18-64 years, 1997 ACR SLE criteria Exclusions: Allergy to fish or fish oil, fish oil use within last two months, warfarin or heparin use, pregnancy	1) 6 fish oil tablets, taken as one or two doses per day (2.25g EPA and 2.25g DHA) p) Olive oil	1) 18 p) 14	median (IQR) 1) 46.2 (36.8-49.1) P) 35.6 (26.3-42.7)	1) 14 (77.8) p) 11 (78.6)	**Government** (NIH)
Bello (2013) [USA][157]	RCT	Revised ACR SLE criteria Exclusions: pregnancy, pregnancy plans, nursing, warfarin or heparin use, liver enzymes >2x ULN, allergy to fish, fish oil or omega 3 products, omega 3 use in previous 6 months, established coronary artery disease	1) 3g of omega 3 (1.8g EPA, 1.2g DHA) p) Placebo made of corn starch	1) 42 p) 43	1) 48.9 (10.6) p) 45.5 (10.8)	1) 41 (97.6) p) 39 (90.7)	**Government** (NIAMS), **University** (Johns Hopkins University School of Medicine General Clinical Research Center)
Wright (2008) [UK][158]	RCT	ACR criteria for SLE Exclusions: diabetes, hypertension, significant pulmonary, hepatic or renal disease, typical angina or myocardial infarction, cerebrovascular disease, history of transient ischaemic attack, use of antihypertensive, oral hypoglycaemic or lipid lowering agents, steroids >10mg prednisolone equivalent, pregnant / lactating women	1) 4 capsules of omega 3 per day (1.8g EPA and 1.2g DHA p) Identical capsules containing olive oil	1) 30 p) 30	1) 48.5 (9.1) p) 47.6 (9.6)	1) 29 (96.7) p) 27 (90.0)	**Charity** (The Wellcome Trust, Lupus UK)

§ crossover design

ACR = American College of Rheumatology, ARA = American Rheumatism Association, DHA = docosahexaenoic acid, EPA = eicosapentaenoic acid, IQR = interquartile range, N = number, NIAMS = National Institute of Arthritis and Musculoskeletal and Skin Diseases, NIH = National Institutes of Health, NRT = non-randomised trial, RCT = randomised controlled trial, SD = standard deviation, SLE = systemic lupus erythematosus, UK = United Kingdom, USA = United States of America

Table – Animal products (SLE) cont., description of included studies

Author (date) [country]	Study design	Inclusion criteria	Exposure detail	N	Age, mean (SD) years	N (%) female	Funders
Duffy (2004) [UK][159]	RCT	Aged 18-80 years, active, stable SLE, SLE revised criteria Exclusions: ongoing treatment for potentially life threatening disease, >10mg steroids, immunosuppressive drugs, vitamin or mineral supplements, taking omega 3 or copper supplements in previous 6 months, allergy to fish or copper	1) Fish oil (180mg EPA, 120mg DHA) and copper 2) Fish oil and placebo copper 3) Copper and placebo fish oil p) Placebo fish oil and copper	1) 13 2) 14 3) 13 p) 12	1) 46 (13.17) 2) 50.7 (15.2) 3) 43.2 (15.8) p) 43.2 (10.8)	9:1 female to male ratio	**Not reported**
Westberg (1990) [Sweden][160]	RCT §	ARA SLE criteria, no immunosuppressive drugs in last 6 months Exclusions: no clinical signs of SLE	1) MaxEPA (omega 3) p) Placebo	17	44.2 (6.6)	15 (88.2)	**Industry** (Seven Seas provided intervention)
Lozovoy (2015) [Brazil][161]	NRT	1997 ACR SLE criteria, stable prednisone treatment for 4 months Exclusions: anti-hypertensive drugs	1) Fish oil p) No fish oil	1) 41 p) 21	median (IQR) 1) 43.0 (32.0-51.0) p) 42.5 (34.0-60.0)	1) 37 (90.2) p) 20 (95.2)	**Government** (National Council of Brazilian Research), **Charity** (Araucária Foundation from the state of Paraná)

§ crossover design

ACR = American College of Rheumatology, ARA = American Rheumatism Association, DHA = docosahexaenoic acid, EPA = eicosapentaenoic acid, IQR = interquartile range, N = number, NIAMS = National Institute of Arthritis and Musculoskeletal and Skin Diseases, NIH = National Institutes of Health, NRT = non-randomised trial, RCT = randomised controlled trial, SD = standard deviation, SLE = systemic lupus erythematosus, UK = United Kingdom, USA = United States of America

Supplementary table 107 – Fish oil / omega 3 and SLE progression, results

Table – Fish oil / omega 3 (SLE), results and quality assessment

Outcome	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	AMSTAR2 quality	Rand. Seq.	Alloc. Conc.	Blind. Part.	Blind. Asses.
Pain	Arriens (2015) [RCT][156]	Fish oil vs placebo at 6 months SMD -1.00 (-1.74, -0.26)	SF36 pain score, 6 months, mean (SD §) Fish oil: 37.5 (28.2) Placebo: 70.4 (38.1)		L	H/UC	L	H/UC
Function	Arriens (2015) [RCT][156]	Fish oil vs placebo at 6 months SMD -1.24 (-2.01, -0.48)	SF36 function score, 6 months, mean (SD §) Fish oil: 32.1 (29.2) Placebo: 74.2 (39.1)		L	H/UC	L	H/UC
Disease activity	Rodriguez Huerta (2016) [SR][154]		2/3 studies reported reductions in disease activity	Moderate				
	Bello (2013) [RCT][157]	Omega 3 vs placebo, change from BL-12 weeks SMD -0.34 (-0.76, 0.09)	SLEDAI, change BL-12 weeks, mean (SD) Omega 3: -0.17 (1.87) Placebo: 0.51 (2.18); p=0.1122		H/UC	H/UC	H/UC	H/UC
	Duffy (2004) [RCT][159]		SLAM-R Patients taking fish oil had a significant improvement in disease activity compared to those not taking fish oil		H/UC	H/UC	L	H/UC
	Westberg (1990) [RCT][160]	Omega 3 vs placebo at 3 months SMD -0.20 (-0.88, 0.47)	Clinical score†, BL / 3 months, mean (SD) Omega 3: 1.49 (1.03) / 1.36 (1.28) Placebo: 1.41 (0.943) / 1.64 (1.50)		L	L	H/UC	L
	Lozovoy (2015) [NRT][161]	Omega 3 vs control at 120 days SMD 0.00 (-0.53, 0.53)	SLEDAI, BL / 120 days, mean (SD §) Omega 3: 4.0 (7.7) / 2.0 (4.6) Control: 2.0 (3.2) / 2.0 (3.2)					
Fatigue	Arriens (2015) [RCT][156]	Fish oil vs placebo at 6 months SMD -0.49 (-1.20, 0.22)	SF36 fatigue score, 6 months, mean (SD §) Fish oil: 37.9 (29.2) Placebo: 52.5 (30.9)		L	H/UC	L	H/UC
Physician global	Bello (2013) [RCT][157]	Omega 3 vs placebo, change from BL-12 weeks SMD -0.29 (-0.71, 0.14)	Physician global assessment, change BL-12 weeks, mean (SD) Omega 3: 0.07 (0.54) Placebo: 0.21 (0.44); p=0.2914		H/UC	H/UC	H/UC	H/UC

§ Mean (SD) estimated from median (interquartile range) using published formula[61]

† Clinical score made up of fatigue, pain, comorbidities, joint involvement and morning stiffness

Alloc. Conc. = allocation concealment, AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews, Anti-dsDNA = anti double strand deoxyribonucleic acid, BL = baseline, Blind. Asses. = Blinded assessors, Blind. Part. = blinded participants, CI = confidence interval, CRP = C-reactive protein, ESR = erythrocyte sedimentation rate, H/UC = high / unclear risk of bias, L = low risk of bias, Rand. Seq. = random sequence generation, SLAM-R = Systemic lupus activity measure – revised, SLE = systemic lupus erythematosus, SLEDAI = systemic lupus erythematosus disease activity index, SMD = Standardised mean difference, SR = systematic review

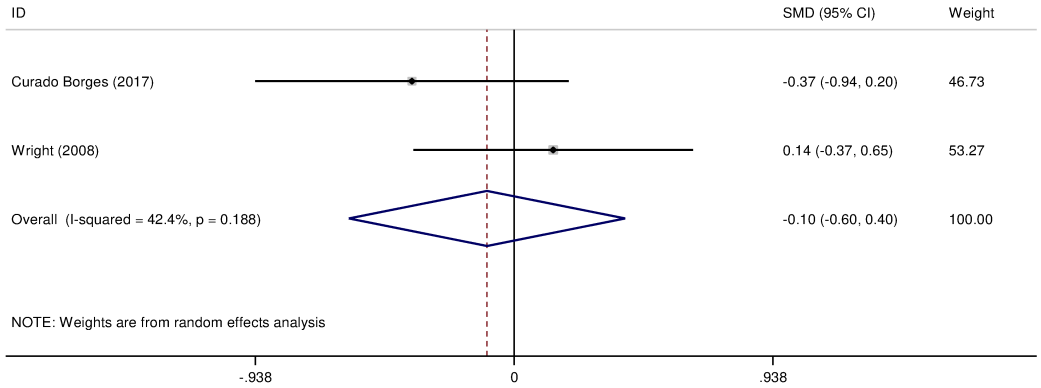
Table – Fish oil / omega 3 (SLE) cont., results and quality assessment

Outcome	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	AMSTAR2 quality	Rand. Seq.	Alloc. Conc.	Blind. Part.	Blind. Asses.
CRP	Curado Borges (2017) [RCT][155]	Omega 3 vs placebo at 12 weeks SMD -0.37 (-0.94, 0.20)	CRP, BL / 12 weeks, mean (SD §) Omega 3: 6.0 (2.5) / 5.7 (1.8) Control: 7.6 (5.2) / 7.2 (5.2); p=0.370		H/UC	H/UC	H/UC	H/UC
	Wright (2008) [RCT][158]	Omega 3 vs placebo at 24 weeks SMD 0.14 (-0.37, 0.65)	CRP, BL / 24 weeks, mean (SD) Omega 3: 9 (13) / 6 (6) Placebo: 5 (9) / 5 (8); p=0.988		H/UC	L	L	L
	Bespoke meta-analysis	Omega 3 vs placebo SMD -0.10 (-0.60, 0.40), I^2 = 42.4%						
ESR	Wright (2008) [RCT][158]	Omega 3 vs placebo at 24 weeks SMD 0.47 (-0.05, 0.98)	ESR, BL / 24 weeks, mean (SD) Omega 3: 33 (30) / 32 (31) Placebo: 19 (14) / 20 (19); p=0.868		H/UC	L	L	L
Anti-dsDNA	Wright (2008) [RCT][158]	Omega 3 vs placebo at 24 weeks SMD 0.03 (-0.47, 0.54)	Anti-dsDNA, BL / 24 weeks, mean (SD) Omega 3: 110 (75) / 126 (761) [sic] Placebo: 95 (55) / 108 (83); p=0.521		H/UC	L	L	L
	Lozovoy (2015) [NRT][161]	Omega 3 vs control at 120 days SMD -0.29 (-0.82, 0.24)	Anti-dsDNA, BL / 120 days, mean (SD §) Omega 3: 6.7 (15.4) / 1.7 (3.8) Control: 3.3 (8.0) / 3.3 (8.0)					

§ Mean (SD) estimated from median (interquartile range) using published formula[61]

† Clinical score made up of fatigue, pain, comorbidities, joint involvement and morning stiffness

Alloc. Conc. = allocation concealment, AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews, Anti-dsDNA = anti double strand deoxyribonucleic acid, BL = baseline, Blind. Asses. = Blinded assessors, Blind. Part. = blinded participants, CI = confidence interval, CRP = C-reactive protein, ESR = erythrocyte sedimentation rate, H/UC = high / unclear risk of bias, L = low risk of bias, Rand. Seq. = random sequence generation, SLE = systemic lupus erythematosus, SLEDAI = systemic lupus erythematosus disease activity index, SMD = Standardised mean difference, SR = systematic review



Supplementary figure 11 – Omega 3, bespoke meta-analysis for CRP [SLE]

Supplementary table 108 – Description of reviews of experimental diets in SLE

Table – Experimental diets (SLE), description of reviews

Authors (date)	Review type	Study type included	Exposure detail	Number of studies included	Funders
del Pino-Sedeno (2016)[162]	SR	RCTs, observational	Low glycaemic vs low calorie diet	1	**Government** (Spanish Ministry of Economy and Finance)
Rodriguez Huerta (2016)[154]	SR	RCTs, observational	Low glycaemic vs low calorie diet / dietary education program	2	**Government** (Spanish Ministry of Health, Social Affairs and Equality)
Yuen (2014)[163]	SR	RCTs	Low glycaemic vs low calorie diet	1	**Non reported** – authors declare no conflict of interest

RCT = randomised controlled trial, SLE = systemic lupus erythematosus, SR = systematic review

Supplementary table 109 – Description of studies of experimental diets in SLE

Table – Cholesterol lowering diet (SLE), description of included studies

Author (date) [country]	Study design	Inclusion criteria	Exposure detail	N	Age, mean (SD) years	N (%) female	Funders
Shah (2002) [USA][164]	RCT	Symptom duration >6 months, LDL cholesterol >100 mg/dl, able to read to 5th grade level Exclusions: pregnant, lactating, taking ≥20mg of prednisone per day, ≥20 units per week of alcohol, inadequate cognitive ability	1) Educated using the National Cholesterol Education Program via group counselling and telephone p) No dietary advice	1) 8 p) 8	1) 44.1 (9.3) p) 45.3 (11.7)	1) 8 (100) p) 8 (100)	**University** (University of Southwestern Medical Center)

N = number, SD = standard deviation, SLE = systemic lupus erythematosus, USA = United States of America

Supplementary table 110 – Experimental diets and SLE progression, results

Table – Cholesterol lowering diet (SLE), results and quality assessment

Outcome	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	AMSTAR2 quality	Rand. Seq.	Alloc. Conc.	Blind. Part.	Blind. Asses.
Disease activity	Rodriguez Huerta (2016) [SR][154]		No difference between diet and control	Moderate				
Fatigue	del Pino-Sedeno (2016) [SR][162]		Both diets reduced fatigue equally effectively, neither reduced fatigue more than the MCID	Moderate				
	Rodriguez Huerta (2016) [SR][154]		Both diets reduced fatigue equally effectively, neither reduced fatigue more than the MCID	Moderate				
	Yuen (2014) [SR][163]		Both diets reduced fatigue equally effectively, neither reduced fatigue more than the MCID	Low				
QoL	Shah (2002) [RCT][164]	Diet intervention vs control at 12 weeks SMD 1.04 (-0.01, 2.10)	QoL §, BL / 12 weeks, mean (SD) Diet intervention: 59.4 (7.8) / 68.4 (7.8) Control: 56.3 (15.1) / 53.8 (18.2)		H/UC	H/UC	H/UC	H/UC

§ Assessed using a VAS, higher scores = greater quality of life

Alloc. Conc. = allocation concealment, AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews, BL = baseline, Blind. Asses. = Blinded assessors, Blind. Part. = blinded participants, CI = confidence interval, H/UC = high / unclear risk of bias, L = low risk of bias, MCID = minimum clinically important difference, QoL = Quality of life, Rand. Seq. = random sequence generation, RCT = randomised controlled trial, SD = standard deviation, SLE = systemic lupus erythematosus, SMD = Standardised mean difference, SR = systematic review

Supplementary table 111 – Description of studies of food components in SLE

Table – Food elements (SLE), description of included studies

Author (date) [country]	Study design	Inclusion criteria	Exposure detail	N	Age, mean (SD) years	N (%) female	Funders
Minami (2011) [Japan][165]	Pros. Cohort	SLE	Various dietary components from the food frequency questionnaire	216	40.6 (13.3)	216 (100)	**Government** (Ministry of Education, Culture, Sports, Science and Technology, Japan)
Minami (2003) [Japan][166]	Pros. Cohort	1982 SLE criteria Exclusions: patients with serious symptoms (e.g. terminal symptoms and severe neuropsychiatric symptoms)	Various dietary components from the food frequency questionnaire	279	40.6 (13.7)	279 (100)	**Government** (Ministry of Health, Labour and Welfare, Japan
Karlson (1997) [USA][167]	Retro. Cohort	ACR criteria for SLE, all seen within 7 years of diagnosis	Adequacy of diet based on Food Frequency Questionnaire	200	52	186 (93.0)	**Government** (NIH), **Charity** (Arthritis Foundation)

N = number, SD = standard deviation, SLE = systemic lupus erythematosus

Supplementary table 112 – Food components and SLE progression, results

Table – Food elements (SLE), results and quality assessment

Outcome (outcome measure)	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	Study Pop.	Attr.	Prog. Meas.	Outc. Meas.	Conf.	Stats.
Active disease	Minami (2011) [Pros. Obs.] [165]		Risk of active disease, middle tertile / upper tertile [lower tertile = ref], HR (95% CI) Vitamin B6: 0.73 (0.35, 1.50) / 0.41 (0.18, 0.97) Vitamin B12: 1.21 (0.58, 2.52) / 1.06 (0.49, 2.33) Folate: 0.93 (0.45, 1.90) / 0.58 (0.25, 1.33) Total fibre: 0.86 (0.44, 1.71) / 0.29 (0.11, 0.78) Soluble fibre: 0.67 (0.33, 1.36) / 0.43 (0.18, 0.99) Insoluble fibre: 0.98 (0.49, 1.96) / 0.39 (0.15, 0.97)	L	L	M	M	M	L
	Minami (2003) [Pros. Obs.][166]		Risk of active disease, middle tertile / upper tertile [lower tertile = ref], RR (95% CI) total energy: 0.63 (0.30,1.32) / 0.84 (0.40, 1.76) total protein*: 0.89 (0.42,1.90) / 0.90 (0.43, 1.89) Total fat*: 1.86 (0.82, 4.24) / 1.49 (0.62, 3.58) Cholesterol: 1.57 (0.72, 3.42) / 1.29 (0.59, 2.84) Calcium: 0.97 (0.45, 2.12) / 1.07 (0.51, 2.27) Salt: 1.11 (0.54, 2.27) / 0.81 (0.37, 1.79) Crude fibre: 0.99 (0.49, 2.02) / 0.43 (0.18, 1.05) Vit A: 0.65 (0.32, 1.34) / 0.50 (0.22, 1.14) Retinol: 1.61 (0.74, 3.53) / 0.97 (0.43, 2.19) Carotene: 0.59 (0.27, 1.26) / 0.68 (0.32, 1.46) Vit B1: 1.00 (0.48, 2.07) / 0.59 (0.25, 1.36) Vit B2: 1.10 (0.53, 2.28) / 0.75 (0.34, 1.67) Niacin: 1.11 (0.53, 2.29) / 0.83 (0.37, 1.86) Vit C: 0.52 (0.25, 1.08) / 0.26 (0.10, 0.67) Vit D: 1.29 (0.60, 2.76) / 0.95 (0.43, 2.09) Vit E: 0.62 (0.30, 1.32) / 0.56 (0.25, 1.25)	L	L	M	M	M	L
Atherosclerotic vascular events	Minami (2011) [Pros. Obs.] [165]		Risk of atherosclerotic vascular events, middle tertile / upper tertile [lower tertile = ref], HR (95% CI) Vitamin B6: 1.04 (0.35, 3.10) / 0.41 (0.10, 1.72) Vitamin B12: 0.87 (0.23, 3.35) / 1.86 (0.60, 5.82) Folate: 0.56 (0.16, 1.99) / 0.83 (0.23, 2.99) Total dietary fibre: 1.69 (0.48, 6.02) / 0.89 (0.21, 3.74) Soluble dietary fibre: 1.61 (0.46, 5.66) / 0.83 (0.22, 3.15) Insoluble dietary fibre: 0.90 (0.28, 2.91) / 0.39 (0.10, 1.51)	L	L	M	M	M	L

Attr. = attrition, CI = confidence interval, Conf. = confounding, HR = hazard ratio, L = low risk of bias, M = moderate risk of bias, Outc. Meas = outcome measurement, Prog. Meas. = prognostic factor measurement, Pros. Obs. = prospective observational, RR = risk ratio, SLE = systemic lupus erythematosus, Stats. = statistical analysis, Study Pop. = study population

Supplementary table 113 – Poor nutrition and SLE progression, results

Table – Poor nutrition (SLE), results and quality assessment

Outcome (outcome measure)	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	Study Pop.	Attr.	Prog. Meas.	Outc. Meas.	Conf.	Stats.
Organ damage	Karlson (1997) [Retro. Cohort][167]		Organ damage Lower calorie intake: beta = 0.81, p=0.0018	L	na	M	L	L	L
Mental health	Karlson (1997) [Retro. Cohort][167]		Worse mental health lower % protein in diet: p=0.01, t=2.5	L	na	M	L	L	L

Attr. = attrition, CI = confidence interval, Conf. = confounding, HR = hazard ratio, L = low risk of bias, M = moderate risk of bias, Outc. Meas = outcome measurement, Prog. Meas. = prognostic factor measurement, Pros. Obs. = prospective observational, RR = risk ratio, SLE = systemic lupus erythematosus, Stats. = statistical analysis, Study Pop. = study population, t = t-statistic

Supplementary table 114 – Description of studies of fruits, vegetables and other plant based interventions in SLE

Table – F*ruits, vegetables and other plant based interventions (SLE), description of included studies*

Author (date) [country]	Study design	Inclusion criteria	Exposure detail	N	Age, mean (SD) years	N (%) female	Funders
Shamekhi (2017) [Iran][168]	RCT	Aged 15-55 years, 2012 ACR criteria Exclusions: any change in medication because of disease exacerbation or any other reason, pregnancy or lactation, smoking, alcohol and drug abuse, antioxidants or vitamin supplementation within last 6 months, engaged in heavy exercise or weight reduction programs, history of autoimmune disease	1) 1000mg green tea extract p) Starch	1) 32 p) 36	1) 38.9 (10.4) p) 39.3 (10.5)	1) 32 (100) p) 36 (100)	**University** (Ahvaz Jundishapur University of Medical Sciences)
Singgih Wahono (2017) [Indonesia][169]	RCT	SLE 1997 ACR criteria, SLEDAI >3, 25(OH)D level <30 Exclusions: Pregnant, taking supplements containing curcumin and vitamin D, had liver function disorders, impaired renal function, severe infections such as tuberculosis, pneumonia or HIV	1) Curcumin + vitamin D p) Placebo + vitamin D	1) 19 p) 20	1) 27.9 (7.9) p) 30.3 (10.0)	Not reported	Not reported – no conflicts of interest stated

ACR = American College of Rheumatology, HIV = human immunodeficiency virus, N = number, RCT = randomised controlled trial, SD = standard deviation, SLE = systemic lupus erythematosus, SLEDAI = systemic lupus erythematosus disease activity index

Supplementary table 115 – Curcumin and SLE progression, results

Table – Curcumin (SLE), results and quality assessment

Outcome	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	AMSTAR2 quality	Rand. Seq.	Alloc. Conc.	Blind. Part.	Blind. Asses.
Disease activity	Singgih Wahono (2017) [RCT][169]	Curcumin vs placebo at 3 months SMD 0.02 (-0.61, 0.64)	SLEDAI at 3 months, mean(SD) Curcumin: 9.2 (7.4) Placebo: 9.1 (5.6)		H/UC	H/UC	H/UC	H/UC

Alloc. Conc. = allocation concealment, AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews, Blind. Asses. = Blinded assessors, Blind. Part. = blinded participants, CI = confidence interval, H/UC = high / unclear risk of bias, L = low risk of bias, Rand. Seq. = random sequence generation, RCT = randomised controlled trial, SD = standard deviation, SLE = systemic lupus erythematosus, SLEDAI = systemic lupus erythematosus disease activity index, SMD = Standardised mean difference,

Supplementary table 116 – Green tea extract and SLE progression, results

Table – Green tea extract (SLE), results and quality assessment

Outcome	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	AMSTAR2 quality	Rand. Seq.	Alloc. Conc.	Blind. Part.	Blind. Asses.
Disease activity	Shamekhi (2017) [RCT][168]	Green tea extract vs placebo at 12 weeks SMD -0.03 (-0.50, 0.45)	SLEDAI, BL / 12 weeks, mean (SD) Green tea extract: 4.66 (3.32) / 2.78 (3.2) Placebo: 3.17 (3.21) / 2.86 (3.16); p=0.78		L	H/UC	L	L

Alloc. Conc. = allocation concealment, AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews, Blind. Asses. = Blinded assessors, Blind. Part. = blinded participants, CI = confidence interval, H/UC = high / unclear risk of bias, L = low risk of bias, Rand. Seq. = random sequence generation, RCT = randomised controlled trial, SD = standard deviation, SLE = systemic lupus erythematosus, SMD = Standardised mean difference,

Table – Green tea extract, SF12 results at final follow-up, mean (SD) / median (IQR)

Author (date)	PCS	MCS	GH	PF	RP	RE	SF	BP	V	MH
Shamekhi (2017)[168] – Green tea extract			54.3 (20.1)	89.8 (76.3, 0[sic])	69.8 (23.0)	55.6 (27.4)	54.6 (32.0, 78.4)	63.1 (44.8, 84.3)	81 (63.1, 95.5)	60.7 (24.9)
Shamekhi (2017)[168] - Placebo			37.9 (28.8)	55 (21.2, 86.4)	54.6 (30.4)	55.5 (27.8)	58.9 (33.6, 85.2)	35.9 (37.7, 79.6)	56.2 (28.1, 84.3)	58.7 (28.1)

BP = bodily pain, GH = general health, IQR = interquartile range, MCS = mental component score, MH = mental health, PCS = physical component score, PF = physical function, RE = role emotional, RP = role physical, SD = standard deviation, SF = social functioning, V = vitality

Supplementary table 117 – Description of studies of minerals and supplements in SLE

Table – Minerals and supplements (SLE), description of included studies

Author (date) [country]	Study design	Inclusion criteria	Exposure detail	N	Age, mean (SD) years	N (%) female	Funders
Duffy (2004) [UK][159]	RCT	Aged 18-80 years, active, stable SLE, SLE revised criteria Exclusions: ongoing treatment for potentially life threatening disease, >10mg steroids, immunosuppressive drugs, vitamin or mineral supplements, taking omega 3 or copper supplements in previous 6 months, allergy to fish or copper	1) Fish oil (180mg EPA, 120mg DHA) and copper 2) Fish oil and placebo copper 3) Copper and placebo fish oil p) Placebo fish oil and copper	1) 13 2) 14 3) 13 p) 12	1) 46 (13.17) 2) 50.7 (15.2) 3) 43.2 (15.8) p) 43.2 (10.8)	9:1 female to male ratio	**Not reported**
Al-Kushi (2018) [Saudi Arabia][170]	NRT	Exclusions: Patients who had malabsorption, renal and liver disease, chronic diarrheal illnesses and irritable bowel syndrome, antifungal or anticonvulsant medications, received vitamin D and / or calcium supplementation past 6 months	1) 1250mg calcium + 1400 IU vitamin D + steroids p1) no treatment and no supplementation p2) received steroids but no supplementation	1) 30 p1) 21 p2) 30	1) 37.7 (8.9) p1) 36.4 (7.6) p2) 35.2 (8.7)	66 (81.5)	No financial support

IU = International Units, mg = milligram, N = number, NRT = Non-randomised trial, SD = standard deviation, SLE = systemic lupus erythematosus

Supplementary table 118 – Calcium + vitamin D and SLE progression, results

Table – Calcium + vitamin D (SLE), results and quality assessment

Outcome	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	AMSTAR2 quality	Rand. Seq.	Alloc. Conc.	Blind. Part.	Blind. Asses.
Disease Activity	Al-Kushi (2018) [NRT][170]	Calcium + vitamin D vs no treatment no supplements at 6 months SMD -1.11 (-1.70, -0.51) Calcium + vitamin D vs steroids & no supplements at 6 months SMD 0.00 (-0.51, 0.51)	SLEDAI at 6 months, mean (SD) Calcium + vitamin D: 4.5 (0.5) No treatment, no supplementation: 5.1 (0.6) Steroids, no supplementation: 4.5 (0.6)					
ESR	Al-Kushi (2018) [NRT][170]	Calcium + vitamin D vs no treatment no supplements at 6 months SMD -0.68 (-1.26, -0.11) Calcium + vitamin D vs steroids & no supplements at 6 months SMD -0.09 (-0.60, 0.41)	ESR at 6 months, mean (SD) Calcium + vitamin D: 45.2 (16.5) No treatment, no supplementation: 56.7 (17.4) Steroids, no supplementation: 46.6 (13.7)					
Anti-dsDNA	Al-Kushi (2018) [NRT][170]	Calcium + vitamin D vs no treatment no supplements at 6 months SMD -0.15 (-0.71, 0.41) Calcium + vitamin D vs steroids & no supplements at 6 months SMD 0.00 (-0.51, 0.51)	Anti-dsDNA at 6 months, mean (SD) Calcium + vitamin D: 50.6 (28.8) No treatment, no supplementation: 55.2 (31.9) Steroids, no supplementation: 50.6 (22.4)					

Alloc. Conc. = allocation concealment, AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews, Anti-dsDNA = anti double strand deoxyribonucleic acid, Blind. Asses. = Blinded assessors, Blind. Part. = blinded participants, CI = confidence interval, ESR = erythrocyte sedimentation rate, H/UC = high / unclear risk of bias, L = low risk of bias, NRT = Non-randomised trial, Rand. Seq. = random sequence generation, SLE = systemic lupus erythematosus, SLEDAI = systemic lupus erythematosus disease activity index, SMD = Standardised mean difference,

Supplementary table 119 – Copper and SLE progression, results

Table – Copper (SLE), results and quality assessment

Outcome	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	AMSTAR2 quality	Rand. Seq.	Alloc. Conc.	Blind. Part.	Blind. Asses.
Disease Activity	Duffy (2004) [RCT][159]		SLAM-R at 24 weeks Copper vs no copper: no significant change		H/UC	H/UC	L	H/UC

Alloc. Conc. = allocation concealment, AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews, Blind. Asses. = Blinded assessors, Blind. Part. = blinded participants, CI = confidence interval, H/UC = high / unclear risk of bias, L = low risk of bias, Rand. Seq. = random sequence generation, SLAM-R = Systemic lupus activity measure – revised , SLE = systemic lupus erythematosus, SMD = Standardised mean difference,

Supplementary table 120 – Description of reviews of vitamins in SLE

Table – Vitamins (SLE), description of reviews

Authors (date)	Review type	Study type included	Exposure detail	Number of studies included	Funders
Franco (2017)[145]	MA	RCTs	Vitamin D	3	**Charity** (São Paulo Research Foundation, Federico Foundation), **Government** (National Council for Scientific and Technological Development)
Yuen (2014)[163]	SR	RCTs	Vitamin D	1	**Non reported** – authors declare no conflict of interest

MA = meta-analysis, RCT = randomised controlled trial, SLE = systemic lupus erythematosus

Supplementary table 121 – Description of studies of vitamins in SLE

Table – Vitamins (SLE), description of included studies

Author (date) [country]	Study design	Inclusion criteria	Exposure detail	N	Age, mean (SD) years	N (%) female	Funders
Karimzadeh (2017) [Iran][171]	RCT	Aged >18 years, fulfilled 4 of the ACR 1982 criteria, had vitamin D levels <30ng/ml Exclusions: history of any chronic systematic or inflammatory disease which affects vitamin D absorption, cirrhosis, myocardial infarction, malignancy, renal stones, hypercalcemia, hospitalisation due to complications of SLE	1) Vitamin D – 50,000 units/weekly for 12 weeks and then 50,000 units/month for 6 months p) No details	1) 45 p) 45	1) 33.8 (6.2) p) 35.7 (6.8)	1) 40 (88.9) p) 41 (91.1)	No financial support and no conflicts of interest
Andreoli (2015) [Italy][172]	RCT	Premenopause, 1997 SLE criteria, absence of disease flare, SLEDAI <6, no vitamin D supplements for 1 month	1) 300,000 IU vitamin D at baseline and 50,000 monthly thereafter p) 25,000 IU vitamin D monthly	1) 18 p) 16	Median (range) 1) 34 (24, 43) 2) 26 (19,44)	1) 18 (100) p) 16 (100)	**Government** (Government of Lombardy), **University** (University of Brescia)

N = number, RCT = randomised controlled trial, SD = standard deviation, SLE = systemic lupus erythematosus, SLEDAI = systemic lupus erythematosus disease activity index

Supplementary table 122 – Vitamin D and SLE progression, results

Table – Vitamin D (SLE), results and quality assessment

Outcome	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	AMSTAR2 quality	Rand. Seq.	Alloc. Conc.	Blind. Part.	Blind. Asses.
Disease activity	Franco (2017) [MA][145]		SLEDAI / ECLAM, mean Intervention: 3.00 / 1.80 Control: 5.4 / 2.75, p=0.06 / 0.121	Moderate				
	Karimzadeh (2017) [RCT][171]	Vitamin D vs control and 6 months SMD -0.18 (-0.60, 0.23)	SLEDAI BL / 6 months, mean (SD) Vitamin D: 3.09 (2.36) / 1.62 (1.25) Control: 3.09 (1.2) / 1.98 (2.47)		H/UC	H/UC	H/UC	H/UC
Fatigue	Yuen (2014) [SR][163]		One study reported a reduction in fatigue, but less than the MCID	Low				
Anti-dsDNA	Franco (2017) [MA][145]		Anti-dsDNA, risk difference -0.10 (-0.18, -0.03); p=0.005	Moderate				
	Andreoli (2015) [RCT][172]	High dose vitamin D vs low dose vitamin D at 1 year SMD 0.04 (-0.63, 0.72)	Anti-dsDNA, BL / 1 year, mean (SD §) High dose vitamin D: 12.2 (16.8) / 13.4 (19.9) Low dose vitamin D: 11.9 (14.7) / 12.6 (18.7)		H/UC	H/UC	H/UC	H/UC

§ mean (SD) estimated from median (interquartile range) using published forumla[61]

Alloc. Conc. = allocation concealment, AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews, Anti-dsDNA = anti double strand deoxyribonucleic acid, Blind. Asses. = Blinded assessors, Blind. Part. = blinded participants, CI = confidence interval, ECLAM = European Consensus Lupus Activity Measurement, H/UC = high / unclear risk of bias, L = low risk of bias, MA = meta-analysis, MCID = minimum clinically important difference, Rand. Seq. = random sequence generation, RCT = randomised controlled trial, SD = standard deviation, SLE = systemic lupus erythematosus, SLEDAI = systemic lupus erythematosus disease activity index, SMD = Standardised mean difference

Supplementary table 123 – Description of reviews of food components in AS

Table – Food components (AS), description of reviews

Authors (date)	Review type	Study type included	Exposure detail	Number of studies included	Funders
Macfarlane (2018)[173]	SR	RCTs, observational	Diet	16	**Charity** (National Ankylosing Spondylitis Society)

AS = ankylosing spondylitis, MA = meta-analysis, RCT = randomised controlled trial

Supplementary table 124 – Food components and AS progression , results

Table – Food components (AS), results and quality assessment

Outcome	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	AMSTAR2 quality	Rand. Seq.	Alloc. Conc.	Blind. Part.	Blind. Asses.
Disease activity	Macfarlane (2018) [SR][173]		BASDAI Alpha-linoleic acid = no association Carbohydrates = no association Fat = One study reported an association in females only, the other reported no association Linoleic acid = no association Long-chain omega 3 fatty acids = no association Polyunsaturated fatty acids = no association Protein = no association Saturated fatty acids = no association	Moderate				
CRP	Macfarlane (2018) [SR][173]		BASDAI Alpha-linoleic acid = no association Carbohydrates = no association Fat = no association Linoleic acid = no association Long-chain omega 3 fatty acids = no association Polyunsaturated fatty acids = no association Protein = no association Saturated fatty acids = no association	Moderate				
ESR	Macfarlane (2018) [SR][173]		BASDAI Alpha-linoleic acid = no association Carbohydrates = no association Fat = no association Linoleic acid = no association Long-chain omega 3 fatty acids = sign. association Polyunsaturated fatty acids = sign. association Protein = no association Saturated fatty acids = no association	Moderate				

Alloc. Conc. = allocation concealment, AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews, AS = ankylosing spondylitis, BASDAI = Bath Ankylosing Spondylitis Disease Activity Index, Blind. Asses. = Blinded assessors, Blind. Part. = blinded participants, CI = confidence interval, CRP = C-reactive protein, ESR = erythrocyte sedimentation rate, H/UC = high / unclear risk of bias, L = low risk of bias, Rand. Seq. = random sequence generation, SMD = Standardised mean difference,

Supplementary table 125 – Description of studies of minerals and supplements in AS

Table – Minerals and supplements (AS), description of included studies

Author (date) [country]	Study design	Inclusion criteria	Exposure detail	N	Age, mean (SD) years	N (%) female	Funders
Jenks (2010) [New Zealand][174]	RCT	European Spondylarthropathy Study Group criteria, BASDAI ≥3, BASFI ≥3, Maastricht Ankylosing Spondylitis Enthesitis Score ≥2 or peripheral joint count ≥2 Exclusions: Pregnant, <18 years of age, diagnosis of irritable bowel disease, severe immunosuppression or current gastrointestinal infection	1) Probiotic formulation containing 3 strains of bacteria p) Placebo powder	1) 32 p) 31	1) 45.5 (15) p) 41.1 (10)	1) 13 (40.6) p) 10 (32.3)	**Charity** (Arthritis New Zealand, Tony Hocken Research Scholarship)

AS = ankylosing spondylitis, BASDAI = Bath Ankylosing Spondylitis Disease Activity Index, BASFI = Bath Ankylosing Spondylitis Function Index, N = number, RCT = randomised controlled trial, SD = standard deviation

Supplementary table 126 – Probiotics and AS progression, results

Table – Probiotics (AS), results and quality assessment

Outcome	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	AMSTAR2 quality	Rand. Seq.	Alloc. Conc.	Blind. Part.	Blind. Asses.
Pain	Jenks (2010) [RCT][174]	Probiotic vs placebo at week 12 SMD 0.04 (-0.45, 0.54)	Pain VAS, BL / week 12, mean (SD) Probiotic: 2.9 (2.3) / 2.7 (2.5) Placebo: 3.0 (2.6) / 2.6 (2.2)		L	L	L	L
Function	Jenks (2010) [RCT][174]	Probiotic vs placebo at week 12 SMD -0.10 (-0.59, 0.40)	BASFI, BL / week 12, mean (SD) Probiotic: 3.5 (2.0) / 2.9 (1.9) Placebo: 3.6 (1.9) / 3.1 (2.2)		L	L	L	L
Disease activity	Jenks (2010) [RCT][174]	Probiotic vs placebo at week 12 SMD -0.33 (-0.82, 0.17)	BASDAI, BL / week 12, mean (SD) Probiotic: 4.2 (2.2) / 3.2 (2.1) Placebo: 4.5 (2.0) / 3.9 (2.2)		L	L	L	L
Tender joints	Jenks (2010) [RCT][174]	Probiotic vs placebo at week 12 SMD -0.34 (-0.84, 0.16)	TJC, BL / week 12, mean (SD) Probiotic: 2.0 (2.1) / 3.1 (3.9) Placebo: 2.6 (2.6) / 5.4 (8.8)		L	L	L	L
Swollen joints	Jenks (2010) [RCT][174]	Probiotic vs placebo at week 12 SMD 0.07 (-0.43, 0.56)	SJC, BL / week 12, mean (SD) Probiotic: 0.4 (0.9) / 0.25 (0.9) Placebo: 0.5 (1.1) / 0.2 (0.5)		L	L	L	L
Spinal mobility	Jenks (2010) [RCT][174]	Probiotic vs placebo at week 12 SMD -0.04 (-0.53, 0.46)	BASMI, BL / week 12, mean (SD) Probiotic: 2.7 (2.6) / 2.3 (2.3) Placebo: 2.7 (3.0) / 2.4 (3.0)		L	L	L	L

Alloc. Conc. = allocation concealment, AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews, AS = ankylosing spondylitis, ASQOL = Ankylosing Spondylitis Quality of Life, BASDAI = Bath Ankylosing Spondylitis Disease Activity Index, BASFI = Bath Ankylosing Spondylitis Function Index, BASMI = Bath Ankylosing Spondylitis Metrology Index, Blind. Asses. = Blinded assessors, Blind. Part. = blinded participants, CI = confidence interval, CRP = C-reactive protein, H/UC = high / unclear risk of bias, L = low risk of bias, MAF = Multidimensional Assessment of Fatigue, MASES = Maastricht Ankylosing Spondylitis Enthesitis Score, Rand. Seq. = random sequence generation, RCT = randomised controlled trial, SJC = swollen joint count, SMD = Standardised mean difference, TJC = tender joint count, VAS = visual analogue scale

Supplementary table 127 – Description of studies of animal products in PsA

Table – Animal products (PsA), description of included studies

Author (date) [country]	Study design	Inclusion criteria	Exposure detail	N	Age, mean (SD) years	N (%) female	Funders
Kristensen (2018) [Denmark][175]	RCT	CASPAR criteria for PsA, aged >18 years Exclusions: Pregnancy, treatment with bDMARD or oral steroids	1) 3g of n-3 polyunsaturated fatty acids (50% EPA and 50% DHA) per day p) olive oil placebo	1) 72 p) 71	1) 53.2 (11.4) p) 50.7 (11.5)	1) 40 (55.6) p) 43 (60.6)	**University** (Aalborg University Hospital Research Foundation), **Charity** (Medical Research Foundation of the Northern Denmark Region, Danish Rheumatism Association, Danish Psoriasis Foundation, Aage Bang Foundation, Abbvie Foundation, Heinrich Kopps Foundation, Jacob Madsen and wide Olga Madsen's Foundation)
Madland (2006) [Norway][176]	RCT	Polyarticular PsA (≥5 swollen joints in a patient with psoriasis and RF-)	1) Seal oil (containing polyunsaturated fatty acids – 2.4g EPA, 1.1g of DPA and 2.6g DHA) p) Soy oil placebo	1) 20 p) 20	1) 56.9 (11.5) p) 53.0 (10.6)	1) 10 (50) p) 12 (60)	**Charity** (The Foundation of Astri and Edvard Riisøen)
Veale (1994) [UK][177]	RCT	RF-, had joint involvement in at least 1 joint	1) Efamol oil (combination of fish oil and primrose oil) (240mg EPA, 132mg DHA) p) Liquid paraffin	1) 19 p) 19	Median (range) 1) 40 (18-76) p) 40 (25-58)	1) 12 (63.2) p) 12 (63.2)	**Industry** (Scotia Pharmaceuticals), Action Research

bDMARD = biologic disease modifying anti-rheumatic drugs, CASPAR = Classification Criteria for Psoriatic Arthritis, DHA = docosahexaenoic acid, DPA = docosapentaenoic acid, EPA = eicosapentaenoic acid, N = number, PsA = psoriatic arthritis, RCT = randomised controlled trial, RF = rheumatoid factor, SD = standard deviation, UK = United Kingdom

Supplementary table 128 – Marine animal oil / omega 3 and PsA progression, results

Table – Marine animal oil / omega 3 (PsA), results and quality assessment

Outcome	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	AMSTAR2 quality	Rand. Seq.	Alloc. Conc.	Blind. Part.	Blind. Asses.
Pain	Kristensen (2018) [RCT][175]		Pain VAS, mean at week 24 Fish oil: 30.12 Control: 34.45, p=0.36		L	L	L	L
	Madland (2006) [RCT][176]	Seal oil vs control at 6 weeks SMD 0.09 (-0.53, 0.71)	Pain VAS, BL / 6 weeks, mean (SD §) Seal oil: 50.3 (23.3) / 38.3 (22.2) Control: 41.5 (21.1) / 36.5 (18.5)		H/UC	H/UC	L	H/UC
Function	Kristensen (2018) [RCT][175]		HAQ, mean at week 24 Fish oil: 0.70 Control: 0.78, p=0.81		L	L	L	L
	Madland (2006) [RCT][176]	Seal oil vs control at 6 weeks SMD 0.61 (-0.02, 1.25)	MHAQ, BL / 6 weeks, mean (SD §) Seal oil: 1.73 (0.40) / 1.75 (0.48) Control: 1.58 (0.35) / 1.50 (0.32)		H/UC	H/UC	L	H/UC
Disease activity	Kristensen (2018) [RCT][175]		DAS28-CRP, mean at week 24 Fish oil: 2.34 Control: 2.71, p=0.20		L	L	L	L
	Kristensen (2018) [RCT][175]		ASDAS, mean at week 24 Fish oil: 1.95 Control: 2.26, p=0.96		L	L	L	L
	Kristensen (2018) [RCT][175]		BASDAI, mean at week 24 Fish oil: 11.29 Control: 14.37, p=0.42		L	L	L	L
Tender joints	Kristensen (2018) [RCT][175]		TJC, mean at week 24 Fish oil: 2.67 Control: 4.10, p=0.08		L	L	L	L
	Madland (2006) [RCT][176]	Seal oil vs control at 6 weeks SMD -0.03 (-0.65, 0.59)	TJC. BL / 6 weeks, mean (SD §) Seal oil: 13.8 (9.9) / 9.8 (7.8) Control: 13.0 (7.2) / 10.0 (7.0)		H/UC	H/UC	L	H/UC
	Veale (1994) [RCT][177]	Efamol oils vs control at 12 months SMD 0.29 (-0.35, 0.93)	Ritchie Index at 12 months, mean (SD §) Efamol oil: 12 (7.04) Control: 10.25 (4.61)		H/UC	H/UC	L	H/UC
	Bespoke meta-analysis	Marine oils vs control SMD 0.13 (-0.32, 0.57) I^2 0.0%						

§ Mean (SD) estimated from median (range) using published formula[61]

Alloc. Conc. = allocation concealment, AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews, ASDAS = Ankylosing Spondylitis Disease Activity Score, BASDAI = Bath Ankylosing Spondylitis Disease Activity Index, Blind. Asses. = Blinded assessors, Blind. Part. = blinded participants, CI = confidence interval, CRP = C-reactive protein, DAS28 = Disease Activity Score, ESR = erythrocyte sedimentation rate, H/UC = high / unclear risk of bias, HAQ = Health Assessment Questionnaire, L = low risk of bias, LEI = Leeds Enthesitis Index, PASI = Psoriasis Area and Severity Index, PsA = psoriatic arthritis, Rand. Seq. = random sequence generation, RCT = randomised controlled trial, SJC = swollen joint count, SMD = Standardised mean difference, SPARCC = Spondyloarthritis Research Consortium of Canada Enthesitis Index, TJC = tender joint count, VAS = visual analogue scale

Table – Marine animal oil / omega 3 (PsA), results and quality assessment

Outcome	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	AMSTAR2 quality	Rand. Seq.	Alloc. Conc.	Blind. Part.	Blind. Asses.
Swollen joints	Kristensen (2018) [RCT][175]		SJC, mean at week 24 Fish oil: 0.30 Control: 0.84, p=0.41		L	L	L	L
	Madland (2006) [RCT][176]	Seal oil vs control at 6 weeks SMD -0.67 (-1.31, -0.03)	SJC. BL / 6 weeks, mean (SD §) Seal oil: 3.8 (2.9) / 2.3 (1.6) Control: 3.5 (2.7) / 4.0 (3.2)		H/UC	H/UC	L	H/UC
Enthesitis	Kristensen (2018) [RCT][175]		LEI, mean at week 24 Fish oil: 0.83 Control: 0.84, p=0.94		L	L	L	L
	Kristensen (2018) [RCT][175]		SPARCC, mean at week 24 Fish oil: 1.85 Control: 1.94, p=0.89		L	L	L	L
Psoriasis severity	Kristensen (2018) [RCT][175]		PASI, mean at week 24 Fish oil: 1.61 Control: 2.04, p=0.47		L	L	L	L
Patient global	Madland (2006) [RCT][176]	Seal oil vs control at 6 weeks SMD 0.09 (-0.53, 0.71)	Patient global VAS. BL / 6 weeks, mean (SD §) Seal oil: 50.3 (23.3) / 38.3 (22.2) Control: 41.5 (21.1) / 36.5 (18.5)		H/UC	H/UC	L	H/UC
CRP	Veale (1994) [RCT][177]		"No significant difference"		H/UC	H/UC	L	H/UC
ESR	Madland (2006) [RCT][176]	Seal oil vs control at 6 weeks SMD -0.30 (-0.92, 0.32)	ESR. BL / 6 weeks, mean (SD §) Seal oil: 14.3 (10.2) / 15.8 (11.5) Control: 13.3 (8.3) / 20.0 (16.1)		H/UC	H/UC	L	H/UC
	Veale (1994) [RCT][177]		"No significant difference"		H/UC	H/UC	L	H/UC

§ Mean (SD) estimated from median (range) using published formula[61]

Alloc. Conc. = allocation concealment, AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews, ASDAS = Ankylosing Spondylitis Disease Activity Score, BASDAI = Bath Ankylosing Spondylitis Disease Activity Index, Blind. Asses. = Blinded assessors, Blind. Part. = blinded participants, CI = confidence interval, CRP = C-reactive protein, DAS28 = Disease Activity Score, ESR = erythrocyte sedimentation rate, H/UC = high / unclear risk of bias, HAQ = Health Assessment Questionnaire, L = low risk of bias, LEI = Leeds Enthesitis Index, PASI = Psoriasis Area and Severity Index, PsA = psoriatic arthritis, Rand. Seq. = random sequence generation, RCT = randomised controlled trial, SJC = swollen joint count, SMD = Standardised mean difference, SPARCC = Spondyloarthritis Research Consortium of Canada Enthesitis Index, TJC = tender joint count, VAS = visual analogue scale

Supplementary table 129 – Description of studies of minerals and supplements in PsA

Table – Minerals and supplements (PsA), description of included studies

Author (date) [country]	Study design	Inclusion criteria	Exposure detail	N	Age, mean (SD) years	N (%) female	Funders
Kharaeva (2009) [Russia][178]	RCT	Joint involvement, history of psoriasis, radiographic presentation of polyarthritis	1) Selenium, co-enzyme Q10 and vitamin E p) Soy based placebo	1) 15 p) 15	1) 43.1 (7.6) p) 44.0 (6.9)	1) 7 (46.7) p) 9 (60.0)	**Government** (Italian Ministry for Health)

N = number, PsA = psoriatic arthritis, RCT = randomised controlled trial, SD = standard deviation

Supplementary table 130 – Selenium / co-enzyme Q10 / vitamin E and PsA progression, results

Table – Selenium / coenzyme Q10 / vitamin E (PsA), results and quality assessment

Outcome	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	AMSTAR2 quality	Rand. Seq.	Alloc. Conc.	Blind. Part.	Blind. Asses.
Disease severity	Kharaeva (2009) [RCT][178]	Selenium / coenzyme Q10 / vitamin E vs control at 30 days SMD -8.03 (-10.25, -5.81)	Severity score §, day 30, mean (SD †) Selenium / coenzyme Q10 / vitamin E: 1.9 (0.39) Control: 6.8 (0.77)		H/UC	H/UC	H/UC	H/UC
Psoriasis severity	Kharaeva (2009) [RCT][178]	Selenium / coenzyme Q10 / vitamin E vs control at 30 days SMD -0.09 (-0.81, 0.62)	PASI, day 30, mean (SD †) Selenium / coenzyme Q10 / vitamin E: 16 (23.2) Control: 29 (38.7)		H/UC	H/UC	H/UC	H/UC

§ composite score of 4 point scales assessing desquamation of psoriatic plaques, hyperemia of psoriatic plaques, inflammation of psoriatic plaques, nail dystrophy and pain in joints
† calculated from standard error
Alloc. Conc. = allocation concealment, AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews, Blind. Asses. = Blinded assessors, Blind. Part. = blinded participants, CI = confidence interval, H/UC = high / unclear risk of bias, L = low risk of bias, PASI = Psoriasis Area and Severity Index, PsA = psoriatic arthritis, Rand. Seq. = random sequence generation, SMD = Standardised mean difference,

Supplementary table 131 – Description of studies of experimental diets in SSc

Table – Experimental diets (SSc), description of included studies

Author (date) [country]	Study design	Inclusion criteria	Exposure detail	N	Age, mean (SD) years	N (%) female	Funders
Doerfler (2017) [USA][179]	Single arm int.	Aged >18 years, referred from rheumatologist to a university affiliated gastroenterologist practice for GI symptoms and unintentional weight-loss Exclusions: Pregnant, deemed too ill to participate, unwilling to travel to study	1) individualised plan based on several themes (calorie and protein intake, modified textures, lifestyle modifications) intended to prevent further weight loss and address a spectrum of motility issues (e.g. gastroparesis, diarrhoea, dysphagia) and fatigue management	18	51.3 (11)	16 (88.9)	**Government** (National Cancer Institute, Cancer Education and Career Development Program), **Charity** (American Dietetic Association Foundation)
Ortiz-Santamaria (2014) [Spain][180]	Single arm int.	Aged ≥18 years, LeRoy and Medsger criteria for SSc, read Catalan/Castilian, ≥1 on MUST screening Exclusions: neoplastic process, other conditions that interfere with the nutritional status of the patient, mental or cognitive psychiatric impairment	Supplements for deficiencies (iron, vitamin D), met dietician to discuss diet, encouraged to eat healthily	9	62.6 (11.7)	8 (88.9)	Not reported – authors declare no conflicts of interest

int. = intervention, MUST = Malnutrition Universal Screening Tool, N = number, SD = standard deviation, SSc = systemic sclerosis, USA = United States of America

Supplementary table 132 – Medical nutrition therapy and SSc progression, results

Table – Medical nutrition therapy (SSc), results and quality assessment

Outcome	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	AMSTAR2 quality	Rand. Seq.	Alloc. Conc.	Blind. Part.	Blind. Asses.
Patient global	Doerfler (2017) [Single arm int.][179]		Abridged patient-generated subjective global assessment, BL / 6 weeks, mean (SD) 13.1 (7.2) / 7.6 (5.2), p=0.01					
Quality of life	Doerfler (2017) [Single arm int.][179]		HRQoL, BL / 6 weeks, mean (SD) 7.7 (6.6) / 6.6 (6.5), p=0.34					

Alloc. Conc. = allocation concealment, AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews, BL = baseline, Blind. Asses. = Blinded assessors, Blind. Part. = blinded participants, CI = confidence interval, H/UC = high / unclear risk of bias, HRQoL = Health related quality of life, L = low risk of bias, Rand. Seq. = random sequence generation, SD = standard deviation, SMD = Standardised mean difference, SSc = systemic sclerosis

Table – Medical nutrition therapy (SSc), SF36 results at BL / final follow-up

Author (date)	PCS	MCS	GH	PF	RP	RE	SF	BP	V	MH
Ortiz-Santamaria (2014)[180]	32.6 (6.9) / 38.3 (2.1)	38.4 (14.4) / 35.33 (18.4)	31.7 (8.4) / 33.0 (3.6)	31.6 (8.03) / 44.0 (6.6)	37.0 (11.2) / 30.3 (3.21)	35.8 (51.6) / 31.0 (12.1)	41.0 (15.1) / 32.0 (8.2)	37.6 (7.2) / 29.7 (5.77)	37.7 (10.5) / 29.7 (5.8)	33.1 (12.8) / 20.0 (3.6)

BL = baseline, BP = bodily pain, GH = general health, MCS = mental component score, MH = mental health, PCS = physical component score, PF = physical function, RE = role emotional, RP = role physical, SF = social functioning, SSc = systemic sclerosis, V = vitality

Supplementary table 133 – Description of studies of vitamins in SSc

Table – Vitamins (SSc), description of included studies

Author (date) [country]	Study design	Inclusion criteria	Exposure detail	N	Age, mean (SD) years	N (%) female	Funders
Ostojic (2011) [Serbia][181]	RCT	Early diffuse SSc, symptom duration <15 months, positive antibodies against topoisomerase, high skin thickness progression rate (≥12/year), decreased lung diffusing capacity (≤75%)	1) cyclophosphamide, and antioxidants (alpha-tocopherol [vitamin E] 400 IU / day and ascorbic acid [vitamin C] 1000 mg per day) p) cyclophosphamide only [All patients treated with prednisolone, metoclopramide, ranitidine and nifedipine	1) 6 p) 7	1) 51.3 (10.1) p) 46.6 (9.1)	1) 4 (66.7) p) 4 (57.1)	None declared – authors reported no conflicts of interest
Herrick (2000) [UK][182]	RCT§	Limited cutaneous SSc, 26 patients met the ARA SSc classification, other 7 all suffered Raynauds and were considered SSc on the following basis: (a) Sclerodactyly and abnormal nailfold microscopy (4 patients, 2 of whom were positive for anticentromere antibody); (b) Calcinosis, abnormal nail-fold microscopy and positive anticentromere antibody (1 patient); (c) Sclerodactyly and reduced peristalsis on barium swallow (1 patient); (d) Digital pitting, abnormal nail-fold microscopy and positive anticentromere antibody (1 patient). Exclusions: cigarette smokers, vitamin supplementation <10 weeks before study entry	1) 300mg selenium, 28.8mg beta-carotene, 188mg vitamin E, approx. 600mg vitamin C, approx. 1.6g methionine p) Matching placebo tablets	33	47 (range: 25-68)	30 (90.9)	**Charity** (Raynaud's and Sclerosis Association)
Hulshof (2000) [The Netherlands][183]	RCT	Morphea or SSc according to criteria Exclusion: use of any systemic or topical therapy for SSc <1 month prior to start of study, use of medication likely to interfere with safety of treatment, clinically relevant abnormalities, serological evidence of Borrelia Burgdorferi	1) Vitamin D – 0.75 µg/day calcitriol for 6 months and 1.25 µg/day for an additional 3 months p) Placebo	1) 10 p) 10	1) 41.8 (19.1) p) 55.5 (14.6)	1) 10 (100) p) 9 (90.0)	Not reported

§ Crossover design

N = number, RCT = randomised controlled trial, SD = standard deviation, SSc = systemic sclerosis, UK = United Kingdom

Supplementary table 134 – Antioxidants and SSc progression, results

Table – Antioxidants (SSc), results and quality assessment

Outcome	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	AMSTAR2 quality	Rand. Seq.	Alloc. Conc.	Blind. Part.	Blind. Asses.
Skin score	Ostojic (2011) [RCT][181]	Antioxidants vs control at 1 month SMD -1.07 (-2.25, 0.11)	Modified Rodnan Skin Score, BL / 1 month, mean (SD) Antioxidants: 15.7 (6.0) / 16.4 (4.1) Control: 17.9 (6.7) / 23.6 (8.3)		H/UC	H/UC	H/UC	H/UC
Raynaud's	Herrick (2000) [RCT][182]	Antioxidants vs control at 10 weeks SMD 0.05 (-0.44, 0.53)	Raynaud's attacks by 10 weeks, mean (SD §) Antioxidants: 143.7 (70.5) Control: 139 (130.19); p=0.88		H/UC	H/UC	L	L

§ Estimated from median (IQR) using published equation[61]

Alloc. Conc. = allocation concealment, AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews, Blind. Asses. = Blinded assessors, Blind. Part. = blinded participants, CI = confidence interval, H/UC = high / unclear risk of bias, L = low risk of bias, Rand. Seq. = random sequence generation, SMD = Standardised mean difference, SSc = systemic sclerosis

Supplementary table 135 – Vitamin D and SSc progression, results

Table – Vitamin D (SSc), results and quality assessment

Outcome	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	AMSTAR2 quality	Rand. Seq.	Alloc. Conc.	Blind. Part.	Blind. Asses.
Skin score	Hulshof (2000) [RCT][183]	Vitamin D vs placebo at 9 months SMD -2.50 (-4.65, -0.35)	Rodnan skin score, mean (SD) † at 9 months Vitamin D: 3.66 (5.51) Control: 21.75 (8.18)		H/UC	L	L	H/UC

† Calculated from results in paper to exclude patients with morphea (N=7)

Alloc. Conc. = allocation concealment, AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews, Blind. Asses. = Blinded assessors, Blind. Part. = blinded participants, CI = confidence interval, H/UC = high / unclear risk of bias, L = low risk of bias, MA = meta-analysis, Rand. Seq. = random sequence generation, SMD = Standardised mean difference, SSc = systemic sclerosis

Supplementary table 136 – Description of reviews of animal products in gout

Table – Animal products (gout), description of reviews

Authors (date)	Review type	Study type included	Exposure detail	Number of studies included	Funders
Andres (2014)[184]	SR	RCTs	Enriched skimmed milk powder	1	**Hospital** (Hospital General Universitario de Alicante, Hospital General Universitario de Elda, Cabrini Hospital), **University** (Columbia University Medical Center, Monash University, Universidad Camilo José Cela)
Moi et al (2013)[185]	SR	RCTs	Enriched skimmed milk powder	1	**Hospital** (The Royal Melbourne Hospital, Cabrini Hospital, Southampton General Hospital), **University** (Monash University)

MA = meta-analysis, RCT = randomised controlled trial, SR = systematic review

Supplementary table 137 – Enriched milk powder and gout progression, results

Table – Enriched milk powder (gout), results and quality assessment

Outcome	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	AMSTAR2 quality	Rand. Seq.	Alloc. Conc.	Blind. Part.	Blind. Asses.
Pain	Andres (2014) [SR][184] & Moi (2013)[185]		Pain, mean difference between intervention and placebo -1.03 (-1.89, -0.17)	High				
Function	Andres (2014) [SR][184] & Moi (2013)[185]		Function, mean difference between intervention and placebo -0.03 (-0.14, 0.08)	High				
Uric acid	Andres (2014) [SR][184] & Moi (2013)[185]		Serum uric acid, mean difference between intervention and placebo -0.01 (-0.04, 0.01)	High				
Gout flare	Andres (2014) [SR][184] & Moi (2013)[185]		Gout flare, mean difference between intervention and placebo -0.21 (-0.76, 0.34)	High				

Alloc. Conc. = allocation concealment, AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews, Blind. Asses. = Blinded assessors, Blind. Part. = blinded participants, CI = confidence interval, H/UC = high / unclear risk of bias, L = low risk of bias, Rand. Seq. = random sequence generation, SMD = Standardised mean difference

Supplementary table 138 – Description of studies of fruits, vegetables and other plant based intervention studies in gout

Table – Fruits, vegetables and other plant based intervention (gout), description of included studies

Author (date) [country]	Study design	Inclusion criteria	Exposure detail	N	Age, mean (SD) years	N (%) female	Funders
Yu (2018) [China][186]	RCT	Physician diagnosed gout, hyperuricemia (serum uric acid >420 micromol/L) aged 18-70 years, "dampness heat pouring downward pattern" (Chinese medicine) Exclusions: Pregnancy or lactation, allergic constitution, serum creatine >1.5mg/dL, ALT>2x upper limit of normal, severe deformity of stiffness of gouty arthropathy resulting in disability, arrhythmia of clinical significance, history of alcohol abuse, severe cerebrovascular, kidney, liver or hematopoietic system comorbidities, cancer, mental disorders, taking hypouricemic medications, azathioprine, 6-mercaptopurine, medications containing aspirin (>325mg) or salicylate, or had participated in other clinical trials with last 3 months	1) "Yellow-Dragon Wonderful Seed Formula" containing Earthworm, cardamon, Phellodendron bark, Atractylodes, sword-like attractylodes rhizome, Chinese atractylodes rhizome, Coix seeds, Job's tears, Cyathula, medicinal cyathula root 2) Same as 1) + gypsum p) allopurinol	1) 24 2) 24 p) 24	1) 45.3 (9.9) 2) 46.1 (10.8) p) 49.2 (9.5	1) 0 (0) 2) 0 (0) p) 0 (0)	**Government** (National TCM Clinical Research Base for Diabetes Mellitus)

N = number, SD = standard deviation, TCM = traditional Chinese medicine, USA = United States of America

Supplementary table 139 – Herbal medicine and gout progression, results

Table – Herbal medicine (gout), results and quality assessment

Outcome	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	AMSTAR2 quality	Rand. Seq.	Alloc. Conc.	Blind. Part.	Blind. Asses.
Uric acid	Yu (2018) [RCT][186]	Yellow-dragon Wonderful seed vs allopurinol at 4 weeks SMD 0.30 (-0.27, 0.87) Yellow-dragon Wonderful seed + gypsum vs allopurinol at 4 weeks SMD 0.48 (-0.09, 1.06)	Serum uric acid, BL / 4 weeks, mean (SD) Yellow-dragon Wonderful seed: 562.29 (108.30) / 526.29 (156.15) Yellow-dragon Wonderful seed + gypsum: 585.46 (100.06) / 566.29 (206.08) Allopurinol: 618.00 (114.27) / 480.83 (144.34)		L	L	H/UC	H/UC
CRP	Yu (2018) [RCT][186]	Yellow-dragon Wonderful seed vs allopurinol at 4 weeks SMD -0.18 (-0.74, 0.39) Yellow-dragon Wonderful seed + gypsum vs allopurinol at 4 weeks SMD 0.11 (-0.46, 0.68)	Serum uric acid, BL / 4 weeks, mean (SD) Yellow-dragon Wonderful seed: 13.13 (2.63) / 10.33 (4.34) Yellow-dragon Wonderful seed + gypsum: 14.03 (3.40) / 11.64 (4.62) Allopurinol: 13.15 (1.13) / 11.13 (4.77)		L	L	H/UC	H/UC

Alloc. Conc. = allocation concealment, AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews, BL = baseline, Blind. Asses. = Blinded assessors, Blind. Part. = blinded participants, CI = confidence interval, CRP = C-reactive protein, H/UC = high / unclear risk of bias, L = low risk of bias, Rand. Seq. = random sequence generation, SD = standard deviation, SMD = Standardised mean difference

Supplementary table 140 – Description of studies of vitamins in gout

Table – Vitamins (Gout), description of included studies

Author (date) [country]	Study design	Inclusion criteria	Exposure detail	N	Age, mean (SD) years	N (%) female	Funders
Stamp (2013) [New Zealand][187]	RCT	ACR gout criteria, serum uric acid >0.36 mmoles/litre Exclusions: taking over the counter vitamin supplements	1) Vitamin C, 500mg/day p) Allopurinol	1) 20 p) 20	1) 61.2 (range 39-86) p) 55 (range 27-78)	1) 18 (90.0) p) 18 (90.0)	**Government** (Health Research Council of New Zealand)
Azzeh (2017) [Saudi Arabia][188]	Single arm int.	Exclusions: aged <20 years, history of dialysis, alcohol consumption, pregnant/lactating women, mutli-vitamin supplements during last 3 months, diuretic drug and/or any uricosuric agent (e.g. allopurinol)	1) Vitamin C, 500mg/day	15	52.9 (11.4)	6 (40.0)	Not reported – authors declare no conflict of interest

int. = intervention, N = number, SD = standard deviation

Supplementary table 141 – Vitamin C and gout progression, results

Table – Vitamin C (gout), results and quality assessment

Outcome	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	AMSTAR2 quality	Rand. Seq.	Alloc. Conc.	Blind. Part.	Blind. Asses.
Uric acid	Stamp (2013) [RCT][187]	Vitamin C vs Allopurinol, mean change BL-8 weeks SMD 0.12 (-0.50, 0.74)	Serum uric acid, mean (SD) change BL-8 weeks Vitamin C: -0.014 (0.23) Allopurinol: -0.188 (1.98); p<0.001		H/UC	H/UC	H/UC	H/UC
	Azzeh (2017) [single arm int.][188]		Serum uric acid, BL / 8 weeks, mean (SD) 8.09 (1.09) / 8.4 (1.15)					

Alloc. Conc. = allocation concealment, AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews, BL = baseline, Blind. Asses. = Blinded assessors, Blind. Part. = blinded participants, CI = confidence interval, H/UC = high / unclear risk of bias, L = low risk of bias, Rand. Seq. = random sequence generation, SD = standard deviation, SMD = Standardised mean difference

Supplementary table 142 – Description of studies including more than one RMD

Table –Studies of more than one RMD, description of included studies

Author (date) [country]	Study design	Inclusion criteria	Exposure detail	N	Age, mean (SD) years	N (%) female	Funders
Jantti (1985) [Finland][189]	NRT	RA or spondyloarthritis, 1 reactive arthritis, two months prior to trial patients didn't receive DMARDs, 2 weeks before – no NSAIDs / paracetamol allowed.	1) Linoleic acid p) Olive oil	1) 6 p) 4	Not reported	Not reported	**Government** (Academy of Finland), **Charity** (Yrjo Jahnsson Foundation)
Bradley (1990) [USA][190]	Single arm int.	Obese patients	Powdered meal replacement consumed twice daily with one regular meal	30	64.6	25 (83.3)	Not reported

int. = intervention, OA = osteoarthritis, N = number, RA = rheumatoid arthritis, RMD = rheumatic and musculoskeletal disease, SD = standard deviation, USA = United States of America

Supplementary table 143 – Results of studies including more than one RMD

Table – Elemental diet (RA and OA), results and quality assessment

Outcome	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	AMSTAR2 quality	Rand. Seq.	Alloc. Conc.	Blind. Part.	Blind. Asses.
Function	Bradley (1990) [single arm int.][190]		50ft walk test (seconds), BL / 6 weeks, mean 12.0 / 9.7					

Alloc. Conc. = allocation concealment, AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews, Blind. Asses. = Blinded assessors, Blind. Part. = blinded participants, CI = confidence interval, H/UC = high / unclear risk of bias, int. = intervention, L = low risk of bias, OA = osteoarthritis, RA = rheumatoid arthritis, Rand. Seq. = random sequence generation, SMD = Standardised mean difference

Table – Linoleic acid (RA and AS), results and quality assessment

Outcome	Study (date) [study type]	Standardised result, SMD (95% CI) unless otherwise stated	Natural result	AMSTAR2 quality	Rand. Seq.	Alloc. Conc.	Blind. Part.	Blind. Asses.
Tender joints	Jantti (1985) [NRT][189]		Tender joint count, change from BL-21 days, mean (range) Linoleic acid: 3 (-1, 15) Placebo: 2 (-1, 5)					
Swollen joints	Jantti (1985) [NRT][189]		Swollen joint count, change from BL-21 days, mean (range) Linoleic acid: 1 (0, 2) Placebo: 0 (-1, 1)					
Morning stiffness	Jantti (1985) [NRT][189]		Morning stiffness, change from BL-21 days, mean (range) Linoleic acid: 10 (-60, 90) Placebo: -6 (-20, 0)					
Grip strength	Jantti (1985) [NRT][189]		Grip strength (left), change from BL-21 days, mean (range) Linoleic acid: -0.1 (-0.2, 0.1) Placebo: -0.1 (-0.2, 0.2) Grip strength (right), change from BL-21 days, mean (range) Linoleic acid: 0 (-0.2, 0.2) Placebo: 0 (-0.1, 0.1)					
ESR	Jantti (1985) [NRT][189]		ESR, change from BL-21 days, mean (range) Linoleic acid: -1 (-10, 7) Placebo: -2 (-12, 8)					

Alloc. Conc. = allocation concealment, AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews, BL = baseline, Blind. Asses. = Blinded assessors, Blind. Part. = blinded participants, CI = confidence interval, ESR = erythrocyte sedimentation rate, H/UC = high / unclear risk of bias, L = low risk of bias, NRT = nonrandomised trial, Rand. Seq. = random sequence generation, SMD = Standardised mean difference

Reference List

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