Supplementary file

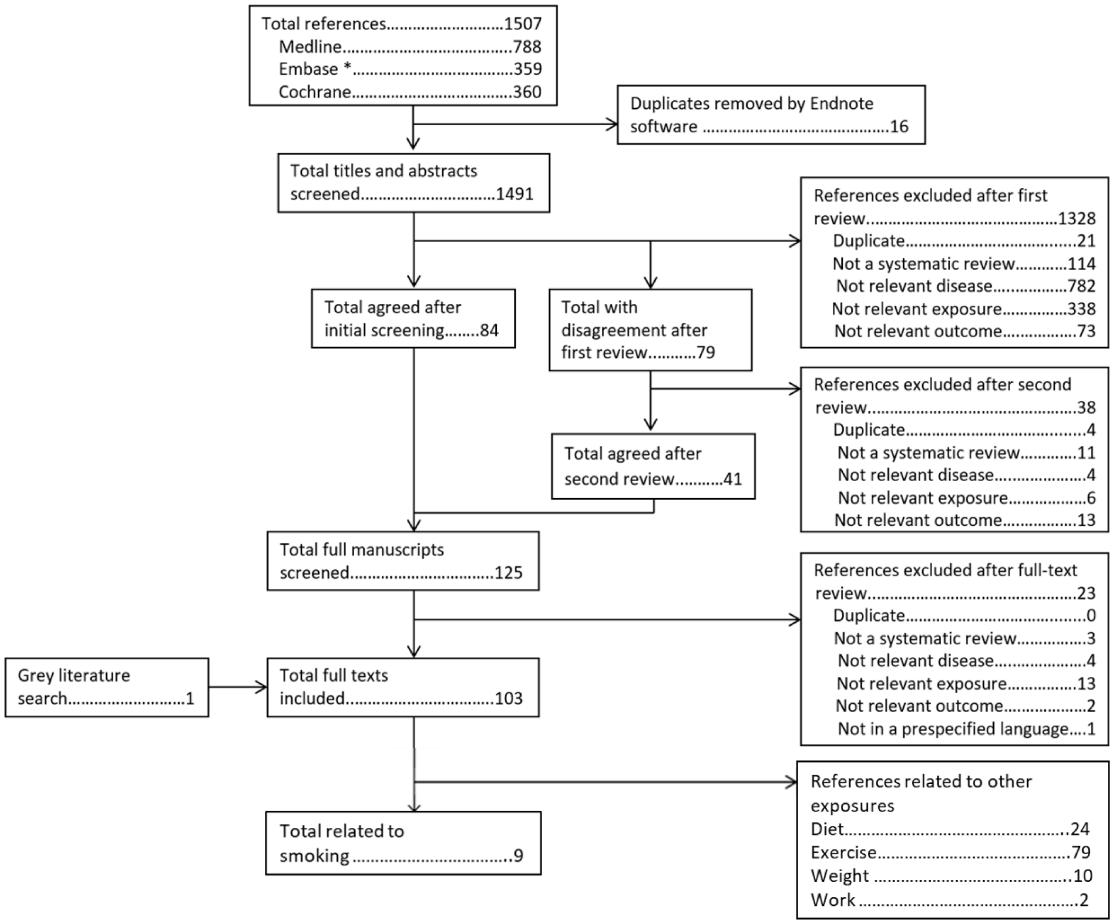

Figure S1. Flow chart of the selection of existing reviews and meta-analyses included in the systematic review

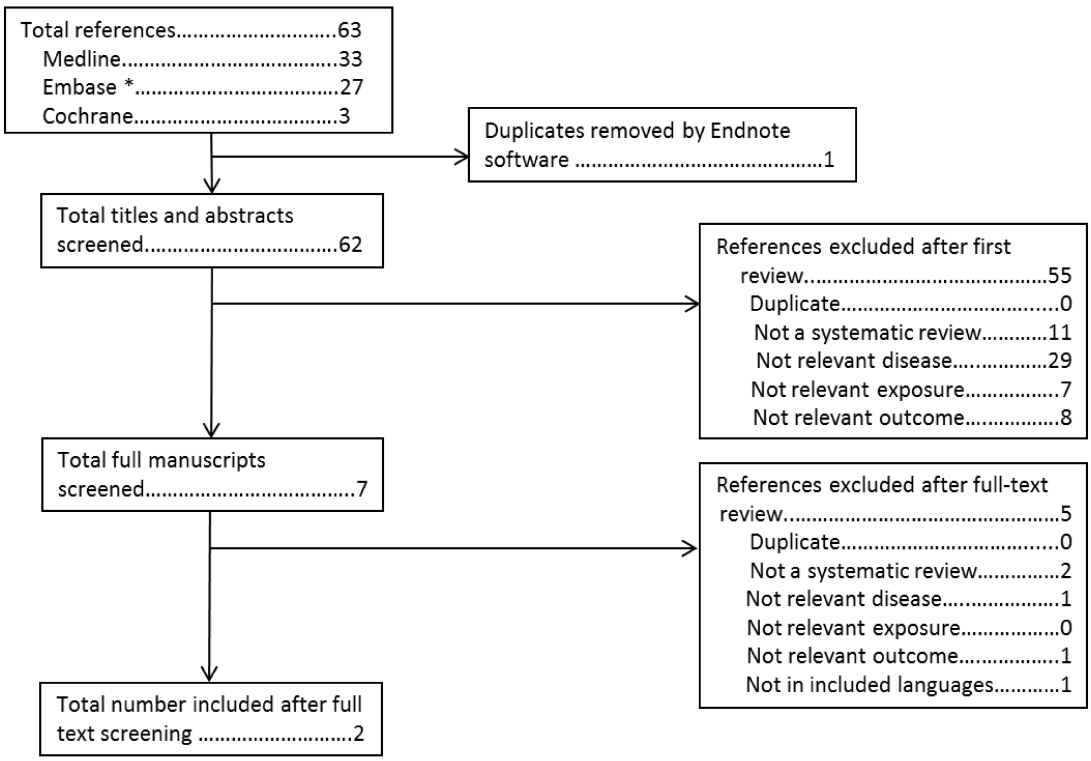

Figure S2. Flow chart of the selection of existing reviews and meta-analyses on alcohol included in the systematic review

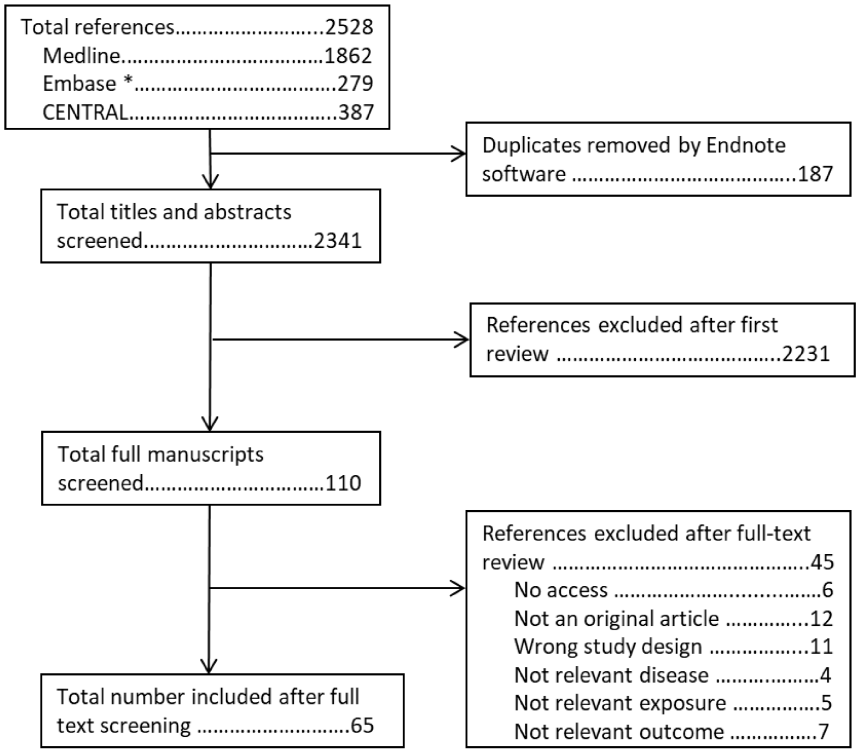

Figure S3. Flow chart of the selection of individual studies on smoking included in the systematic review

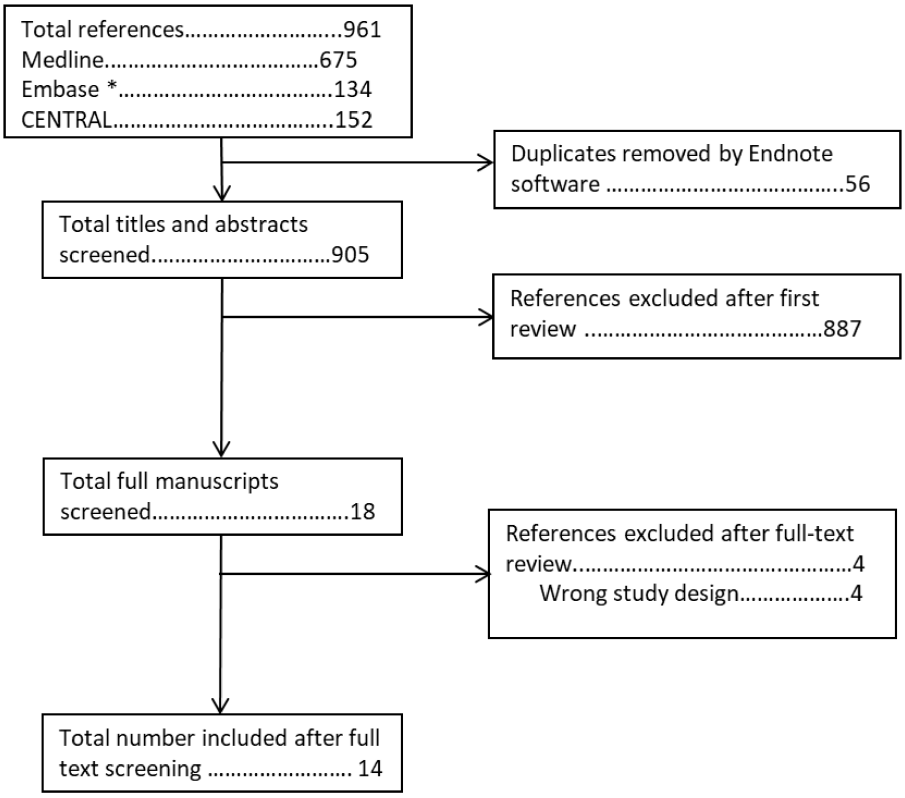

Figure S4. Flow chart of the selection of individual studies on alcohol included in the systematic review

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. Scleroderma, 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 for systematic review of original articles focusing on smoking in RMDs

Category	Term
Disease	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. Scleroderma, 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. Hyperurecemi$ [have to uncheck “map team to subject heading”] 50. Hyperurecaemi$ [have to uncheck “map team to subject heading”] 51. Hyperuricemia$ 52. Hyperuricaemi$ [have to uncheck “map team to subject heading”] 53. arthritis urica 54. Gout acute 55. Inflammatory joint disease
Exposure	56. Smok$ 57. Smoking (mesh) (exp) (include all subheadings) 58. Tobacco (mesh) (exp) (include all subheadings) 59. Cigarette$ 60. Pipe$ 61. Cigar$ 62. Nicotine (mesh) (exp) (include all subheadings) 63. Water pipe 64. Hookah 65. Shisha 66. E-cigarette 67. vaping
Exclusions	68. Cross-sectional 69. Cross sectional 70. Children 71. Child 72. Juvenile 73. Adolescent 74. Teenager 75. Animal 76. Rat 77. rats 78. Mouse 79. Case study 80. Case series 81. Systematic adj5 review 82. Narrative review 83. Meta-analysis (mesh) (exp) 84. Meta analysis

	85. Meta adj5 analysis 86. Meta-synthesis 87. Meta synthesis 88. Meta adj5 synthesis 89. Literature review 90. Literature search 91. Meta-narrative review 92. Meta narrative review
Combining terms	93. RA – 1 OR 2 OR 3 OR 4 OR 5 OR 6 94. OA – 7 OR 8 OR 9 OR 10 OR 11 OR 12 OR 13 95. PSA – 14 OR 15 OR 16 OR 17 OR 18 OR 19 OR 20 OR 21 OR 22 96. AS – 23 OR 24 OR 25 OR 26 OR 27 OR 28 OR 29 OR 30 97. SLE – 31 OR 32 OR 33 OR 34 OR 35 OR 36 OR 37 OR 38 98. SSc – 39 OR 40 OR 41 OR 42 99. 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 56 100. Diseases – 92 OR 93 OR 94 OR 95 OR 96 OR 97 OR 98 101. Smoking – 57 OR 58 OR 59 OR 60 OR 61 OR 62 OR 63 OR 64 OR 65 OR 66 OR 67 102. Exclusions –68 OR 69 OR 70 OR 71 OR 72 OR 73 OR 74 OR 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 OR 89 OR 90 OR 91 OR 92 103. 99 AND 100 104. 102 NOT 101

Supplementary table 3 – 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.

Category	Term
Disease	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. Scleroderma, 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 4 – Search strategy for systematic review of original articles focusing on alcohol in RMDs

Category	Term
Disease	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. Scleroderma, 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. Beer 59. Wine 60. Spirit$ 61. Liquor 62. Alcoholic drinking (mesh) (explode) (include subheadings) 63. Alcoholic beverages
Exclusions	64. Cross-sectional 65. Cross sectional 66. Children 67. Child 68. Juvenile 69. Adolescent 70. Teenager 71. Animal 72. Rat 73. Mouse 74. Case study 75. Case series 76. Systematic adj5 review 77. Narrative review 78. Meta-analysis (mesh) (exp) 79. Meta analysis 80. Meta adj5 analysis 81. Meta-synthesis 82. Meta synthesis 83. Meta adj5 synthesis 84. Literature review 85. Literature search

	86. Meta-narrative review 87. Meta narrative review 88. Case-control
Combining terms	89. RA – 1 OR 2 OR 3 OR 4 OR 5 OR 6 90. OA – 7 OR 8 OR 9 OR 10 OR 11 OR 12 OR 13 91. PSA – 14 OR 15 OR 16 OR 17 OR 18 OR 19 OR 20 OR 21 OR 22 92. AS – 23 OR 24 OR 25 OR 26 OR 27 OR 28 OR 29 OR 30 93. SLE – 31 OR 32 OR 33 OR 34 OR 35 OR 36 OR 37 OR 38 94. SSc – 39 OR 40 OR 41 OR 42 95. 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 96. Diseases –89 OR 90 OR 91 OR 92 OR 93 OR 94 OR 95 OR 96 97. Alcohol – 57 OR 58 OR 59 OR 60 OR 61 OR 62 OR 63 98. Exclusions –64 OR 65 OR 66 OR 67 OR 68 OR 72 OR 73 OR 74 OR 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 99. 96 AND 97 100. 99 NOT 98

Supplementary table 5 – 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])
  - AxSpA [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)
  - AxSpA
    - 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)
    - AxSpA
        - 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)
    - AxSpA
        - 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 6 – Oxford Centre for Evidence-Based Medicine Levels of Evidence

Level	Therapy/prevention/aetiology/harm
1a	Systematic review with homogeneity of RCTs
1b	Individual RCT (with narrow confidence interval)
1c	All or none
2a	Systematic review with homogeneity of cohort studies
2b	Individual cohort study (including low quality RCT; e.g. <80% follow-up)
2c	'Outcomes' research; ecological studies
3a	Systematic review (with homogeneity) of case-control studies
3b	Individual case-control study
4	Case-series (and poor quality cohort and case-control studies)
5	Expert opinion without explicit critical appraisal, or based on physiology, bench research or "first principles"

From Oxford Centre for Evidence-based Medicine Levels of Evidence. March 2009.
http://www.cebm.net/?o=1116

Supplementary table 7 – Osteoarthritis and smoking: evidence from meta-analyses and systematic reviews

Author (date)	Type of review	Study type included	Type of OA	Outcomes	Smoking negatively associated with outcome	Key findings	AMSTAR2
Pearce et al., 2013[1]	MA	CC, cohorts	All sites	Radiographic progression	Radiographic progression: ×	Overall, no association between smoking and radiographic progression of OA (OR 0.92, 95% CI 0.83, 1.02)	Moderate
de Rooij et al., 2016[2]	SR	Prospective cohorts	Knee	Pain, function	Pain: × Function: ✓	Pain: inconsistent evidence (1/2 low quality studies reported an association) function: strong evidence (2/2 high quality studies reported an association)	Moderate
Bastick et al., 2015[3]	SR	CC, cohorts	Knee	Radiographic progression	Radiographic progression: ×	Reported that 3/3 comparisons did not find as association between smoking and radiographic progression	Moderate

AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews 2, CC = case-control studies, CI = confidence interval, MA = meta-analysis, OA = osteoarthritis, OR = odds ratio, SR = systematic review

Supplementary table 8 – Osteoarthritis and smoking: evidence from individual studies

Author	Exposure	Study design	Inclusion criteria	Outcomes	Adjustment variables	Nb participants	Follow-up length	Age	Gender	Key findings
Amin et al., 2007 [4]	Cigarette smoking assessed with a standard questionnaire 2 groups: current smokers at baseline vs non-smokers	Prospective cohort study	-presence of osteophyte present on radiographs of the symptomatic knee -be able to walk, with or without the aid of a cane -be willing to participate in the longitudinal study -meet the American College of Rheumatology criteria for symptomatic knee osteoarthritis -men -minimum age of entry of 45 years	cartilage loss, knee pain (visual analog scale)	Age, body mass index and baseline cartilage scores Other potential confounders: knee pain and physical activity at baseline, and alignment.	159	30 months	Mean (SD), years: 68 (9)	159 (100%) men	Current smokers: increased risk for cartilage loss at the medial compartment of the tibiofemoral joint: OR=2.3 (1.0 to 5.4) and patellofemoral joint: OR=2.5 (1.1 to 5.7) compared with men who were not current smokers No increased risk for cartilage loss at the lateral compartment: OR=1.2 (0.3 to 4.2) Adjusted change in knee-specific VAS pain scores over follow-up not significantly different between men who were and were not current smokers (20.3, 95% CI 214.9 to 14.3 vs 21.0, 95% CI 26.0 to 4.0, respectively)
Kalichman et al., 2005 [5]	Smoking (yes vs no)	Prospective cohort study	Chuvashians (Caucasians of European origin) who live in many small villages in the Chuvasha Autonomy of the Russian Federation	Progression rate of hand OA between two evaluations of OA to investigate the rate of hand OA progression in different joint rows, as well as in all joints	age, age^2, body weight, stature, and body mass index	273	8 years	Men: 45.3 (16.1) years Women: 49.7 (15.3) years	Men: N=137 Women: N = 136	Influences of life-style factors on rate of hand OA progression: no significant associations or group differences in relation to smoking
Nishimura et al., 2011[6]	Cigarette smoking (yes vs no)	Prospective cohort study	-age ≥65 years of age in Miyagawa, a mountain village located in the centre of Mie Prefecture, Japan	Progression of radiographic osteoarthritis of the knee (KL grade)	-	360	4 years	Mean (SD): 71.0 (4.7) years	Men: N=119 Women: N=241	Cigarette smoking: OR=0.732 (95%CI: 0.087–6.151), p= 0.7742 No significant association

Supplementary table 9 – Osteoarthritis and smoking: methodological quality of individual studies

Authors	Study participation	Study attrition	Prognostic factor measurement	Outcome measurement	Study confounding	Statistical analysis and reporting	Quality
Amin et al., 2007 [4]	Low risk of bias	Moderate risk of bias	Low risk of bias	Low risk of bias	Moderate risk of bias	Low risk of bias	Moderate
Kalichman et al., 2005 [5]	Low risk of bias	High risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Moderate risk of bias	Low
Nishimura et al., 2011[6]	Low risk of bias	High risk of bias	Low risk of bias	Low risk of bias	Moderate risk of bias	Low risk of bias	Low

Supplementary table 10 – Rheumatoid arthritis and smoking: evidence form meta-analyses and systematic reviews

Author (date)	Type of review	Study type included	Outcomes	Smoking associated with worse outcome	Key findings (negative MD/SMD favours intervention)	AMSTAR2
Baghdadi et al., 2015 [7]	MA	Observational studies	Cardiovascular morbidity	Cardiovascular morbidity: ✓	Cardiovascular morbidity: meta-RR 1.50 (1.15, 1.84) vs non-smokers; smoking associated with worse cardiovascular morbidity	Moderate
Daien et al., 2017 [8]	SR	Observational studies	Treatment response	Treatment response: ✓	Smoking associated with lower odds of response to first-line DMARD with positive predictive value ranging from 38% to 71%	Low

AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews 2, MA = meta-analysis, RCTs = randomized controlled trials, RR = relative risk, SR = systematic review

Supplementary table 11 – Early rheumatoid arthritis and smoking: evidence from individual studies

Author	Exposure detail	Study design	Inclusion criteria	Outcomes	Adjustment variables	Nb participants	Follow-up length	Age	Gender	Key findings
Andersson et al., 2012 [9]	Cigarette smoking Never smokers, current smokers, previous smokers	Prospective cohort study	-early RA -disease duration of less or equal 2 years at inclusion -age over 18 years	-EULAR response -Functional status (HAQ) -Pain (visual analog scale) -CRP levels -Disease activity (DAS28)	-	1460	8 years	Mean: 56 years (min 47-max 65)	Women: 70%	-No clear differences in disease activity between never-smokers, current smokers, and patients who had stopped smoking — in HAQ, in VAS pain, in DAS28 -Significant difference in CRP levels at 2 years of follow-up (p=0.03) non-smokers: 10 units smokers: 11 units patients having stopped smoking before inclusion: 11 units patients having stopped smoking < 2 years after inclusion: 12 units -No statistical differences in EULAR response between the different smoking categories
Andersson et al., 2017 [10]	Cigarette smoking Non-smokers, current smokers, previous smokers	Prospective cohort study	-early RA -disease duration of less or equal 2 years at inclusion -age over 18 years	- Functional status (HAQ)	Sex, age, RF, and DMARD at baseline	1938	8 years	Cohort 1 : 53(14) / Cohort 2 : 56(15)	Cohort1 : women 68% / Cohort 2 : women : 70%	No differences in HAQ change over time, short- or long-term, among non-smokers, current smokers, and previous smokers
Bird et al., 2017 [11]	Smoking Never smokers, ex-smokers, current smokers	Prospective cohort study	All newly presented patients with RA whose date of clinical onset was < 12 months from their initial presentation at the clinic, were -18 years of age or older -be treated at a participating clinic -DAS28-ESR recorded in the time up to 24	DAS28-ESR remssion	Age and sex	1017	2 years	Mean (SD): 60.4 (14.7)	Women: 70%	Multivariate OR (95% CI) Current versus ex-smokers: 0.86 (95% CI: 0.50 - 1.46), p = 0.567 Current versus never smokers: 1.00 (95% CI: 0.60 - 1.67), p= 0.990 Ex-smokers versus never smokers: 1.17 (95% CI: 0.83 - 1.67), p= 0.372 No significant association

			months from the date of first consultation with the treating rheumatologist for RA							
Manfredsdottir et al., 2006 [12]	Tobacco smoking Current smokers, former smokers, never smokers	Prospective cohort study	- patients who fulfilled the 1987 ACR criteria for RA	-Disease activity -Pain score (VAS) -Radiographic progression (Sharp/ van der Heije score)	-	100	2 years	Mean (SD): 53.4 (17.9) years	Women: 57%	-Current smokers had the highest and the never smokers the lowest disease activity (P<0.001 and P= 0.02, respectively) No association between disease activity and the number of pack-years of tobacco smoking -CRP levels: no significant difference in CRP levels at any time point between the groups -Overall VAS pain score for the three groups: statistically significant differences (P = 0.005) Never smokers had significantly lower VAS pain score only at entry (P = 0.04) -No significant influence of smoking status on radiographic progression and no correlation between number of pack-years of tobacco smoking and radiological score
McWilliams et al., 2012 [13]	Smoking Never smokers, ever smokers	Prospective cohort study	All patients who had attended the 22 outpatient centers of the Early Rheumatoid Arthritis Network and provided appropriate data	Pain (SF-36)	NSAID, DMARD, and regular corticosteroid usage	1189	1 year	58 years (min: 47-max: 68)	Women: 68%	Ever smoked (vs never smoked): OR=1.03 (95% CI 0.68 -1.57), p= 0.915 Non-significant association
Nyhall-Wahlin et al., 2009 [14]	Smoking Non-smokers, smokers, ex-smokers, never smokers	Prospective cohort study	-Symptoms of arthritis (swollen joints) for 12 months -At least four of seven items from the 1987 ACR classification criteria for RA	Severe extra-articular manifestations (including pericarditis, pleuritis, interstitial lung disease, Felty's syndrome, neuropathy, scleritis, episcleritis,	Current smoking at baseline and glucocortico-steroids treatment	40	2 years	Mean (SD): 58.5 (11.6) years	Women: 72%	Current smoking at disease onset increased the risk for extra-articular manifestations OR=2.84 (1.15 - 6.98) for current vs non-smokers OR=4.11 (1.18 - 14.30) for current vs never smokers No increased risk for former smokers: OR=1.69 (0.52 - 5.46) vs never smokers

				glomerulonephritis , major cutaneous vasculitis)						
Papadopoulos et al., 2005 [15]	Cigarette smoking Current smokers, never smokers, ex-smokers Numbers of pack years	Prospective cohort study	- American College of Rheumatology criteria for RA -disease duration of less than one year -no prior treatment of disease modifying anti-rheumatic drugs or steroids	Disease expression, activity and severity: number of total joint count with tenderness and swelling, disease activity (DAS-28) and Larsen's score	Age, sex, DAS-28 score at baseline, Larsen's score at baseline, RF IgM, RF IgA and follow-up duration at the end of the study	293	Max mean follow-up: 46.8 months	NA	Women: 69,7%	All parameters studied differ significantly among the three groups, and current smokers present more active and severe disease than ex-smokers, and never smokers as evaluated by tender and swollen joint count, DAS-28, CRP, ESR (all p-values < 0.001) Ex-smokers: higher levels than the never smokers for all these parameters At last follow-up: Non-significant associations between the numbers of pack years and disease activity and radiological damage (Larsen score)
Ruiz-Esquide et al., 2011 [16]	Ever smokers, past smokers (smoking cessation ≥ 1 year before disease onset), current smokers at disease onset, and non-smokers	Prospective cohort study	-Consecutive outpatients attending the rheumatology units of the Hospital Clinic, Barcelona, and Hospital Parc Taulí, Sabadell, Spain -American College of Rheumatology RA criteria -symptoms duration < 24 months	-Clinical disease activity (28-joint Disease Activity Score) - EULAR response -Radiographic progression (Erosion Joint Count (EJC) and Larsen scores)	-	156	2 years	Mean (SD): 54.4 (14.9)	Women: 130 (83.3%)	Clinical disease activity at 12 and 24 months: similar in non-smokers vs current smokers Similar results when comparisons between ever-smokers and nonsmokers, current heavy smokers and nonsmokers Association with Larsen scores : Smoking (past vs nonsmoker) beta = 0.486 (-4.52, 5.49) p = 0.848 Smoking (current vs nonsmoker) beta = 4.274 (0.49, 8.05), p = 0.027 Similar results were obtained when EJC was used as the measure of radiographic damage. Smoking (past vs nonsmoker) beta = –0.065 (-0.8, 0.67), p = 0.861 Smoking (current vs nonsmoker) beta = 0.603 (0.05, 1.16), p = 0.034
Saevarsdottir et al., 2015 [17]	Current, past or never cigarette smokers Current smokers versus non-smokers, pooling past and never	Prospective cohort study	-RA according to the 1987 revised American College of Rheumatology criteria -Age ≥18 years - Symptom duration <1 year	radiographic prooression (increase in total Sharp-van der Hejde score of ≥5 after 1 year)	Gender, symptom duration, baseline erosions and HAQ	311	1 year	Median (IQR: 57 (46–64)	Men: 87 (28%)	Predictors of rapid radiographic progression Current vs never smokers: OR (95% CI) = 2.25 (1.12 to 4.54) Past vs never smokers: OR = 0.75 (0.38 to 1.48) Current smokers vs non- smokers: OR = 2.67 (1.44 to 4.95)

	smokers in the latter group		-28-joint disease activity score >3.2,no previous -disease modifying antirheumatic drug treatment -stable prednisolone dose, if present, for ≥4 weeks before entry and throughout the study of ≤10 mg/day							Predictors of radiographic progression (SHS score increase >1) Current vs never smokers: OR = 2.31 (1.18 to 4.54) Past vs never smokers: OR = 0.92 (0.52 to 1.65) Current smokers vs non-smokers: OR = 2.42 (1.33 to 4.42)
Vesperini et al., 2013 [18]	Patients' smoking habits Current smokers (active smoking) Ex-smokers (all patients who had stopped smoking before the first examination at inclusion) Non-smokers (no history of smoking at any time)	Prospective cohort study	-Age 18–70 years -inflammatory arthritis of at least 2 swollen joints lasting for 6 weeks to 6 months and with potential to evolve into RA -no disease-modifying antirheumatic drugs or steroids -2010 American College of Rheumatology /European League Against Rheumatism criteria for RA	-Risk of structural progression (change in the modified Sharp/van der Heijde score >=1) -Functional status (HAQ) -EULAR response -Rate of remission	Age, sex, joint erosion at inclusion, educational level, positivity for rheumatoid factor or anti–cyclic citrullinated peptide 2 antibodies, and shared HLA–DRB1 epitope	641	1y	Mean (SD): 48.43 (12.2) years	Women: 77.8%	Current smokers: decreased risk of radiographic disease progression as compared with non-smokers OR = 0.50 (0.27–0.91), p=0.024 No association between smoking status and HAQ, EULAR response or rate of DAS28 remission (p > 0.05) Effect of discontinuing smoking: this group did not differ in disease activity or severity scores from current smokers
Hetland et al., 2009 [19]	Ever smokers, never smoker	Prospective cohort study (data from patients included in a RCT)	- American College of Rheumatology 1987 revised criteria for RA -DMARD naïve -active disease of 6 months' duration with at least two swollen joints -age 18–75	Radiographic progression (change in Sharp/van der Heijde Score)	-	130	2 years	Median (IQR): 53.2 (43.5 – 62.7)	Women: 65%	Ever smoker (vs never smoker) Univariate analysis: Coefficient = -0.10 (-1.98 to 1.78), p= 0.92 Multivariate analysis: Coefficient = -0.43 (-3.17 to 2.32), p=0.76

Levitsky et al., 2017 [20]	Current smokers, non-current smokers	Prospective cohort study (data from patients included in a RCT)	-SWEFOT patients -available baseline BMI	EULAR non-remission (DAS28 ≥2.6)	Age, current smoking, disease duration, baseline erosions, HAQ and ESR	403	2 years	Median (IQR): 56 (45–64)	Women: 285 (71%)	Predictors of non-remission at 24 months Current smokers (vs non-current smokers): OR=2.6 (1.1–6.3)
Andersson et al., 2013 [21]	Snuff (smokeless tobacco) Questionnaire (''Do you use snuff? (yes/no).'') Patients used snuff only all along or previous smokers who had stopped smoking for at least 2 years before being included in the study and had continued to use snuff after stopping smoking	Nested case-control study	-early RA -disease duration of less or equal 2 years at inclusion -over 18 years old	-Disease activity (DAS-28) -Functional status (HAQ) -EULAR response	Disease duration, number of previous DMARDs and biologics (grouped together), and socio-economic status	51 patients and 145 controls	5 years	Median: 55 (44-61)	Men: 75%	Snuff users compared with never smokers (adjusted analyses): - DAS28: significantly lower DAS28 scores in snuff users at 3 months of follow-up (2.0 vs. 3.7, p= 0.001) and at 6 months (2.1 vs. 3.2, p = 0.003) - HAQ: only significant difference at 2 years but no differences in HAQ levels at any other time point (snuff users, 0.4 vs. 0.3 for never smokers; p = 0.03) - EULAR response (calculated from the DAS28 scores): no differences between snuff users and never smokers up to 1 year of follow-up Snuff users compared with previous smokers (adjusted analyses): - DAS28: significantly lower DAS28 values in snuff users at 3 months, 6 months, and 2 years - HAQ: no differences in HAQ values at any time point - EULAR response: no differences between snuff users and previous smokers up to 1 year of follow-up

Supplementary table 12 – Early rheumatoid arthritis and smoking: methodological quality of individual studies

Authors	Study participation	Study attrition	Prognostic factor measurement	Outcome measurement	Study confounding	Statistical analysis and reporting	Quality
Andersson et al., 2012 [9]	Low risk of bias	Low risk of bias	Low risk of bias risk of bias	Low risk of bias	Moderate risk of bias	Low risk of bias	Moderate
Andersson et al., 2017 [10]	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Moderate risk of bias	High
Bird et al., 2017 [11]	Low risk of bias	High risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low
Manfredsdottir et al., 2006 [12]	Low risk of bias	High risk of bias	Low risk of bias	Low risk of bias	Moderate risk of bias	Low risk of bias	Low
McWilliamset al., 2012 [13]	Low risk of bias	High risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias risk of bias	Low
Nyhall-Wahlin et al., 2009 [14]	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Moderate risk of bias	Low risk of bias	Moderate
Papadopoulos et al., 2005 [15]	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	High
Ruiz-Esquide et al., 2011 [16]	Low risk of bias	Moderate risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Moderate
Saevarsdottir et al., 2015 [17]	Low risk of bias	Moderate risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Moderate
Vesperini et al., 2013 [18]	Low risk of bias	High risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low
Hetland et al., 2009 [19]	Low risk of bias	Moderate risk of bias	Low risk of bias	Low risk of bias	Moderate risk of bias	Low risk of bias	Moderate
Levitsky et al., 2017 [20]	Moderate risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Moderate
Andersson et al., 2013 [21]	Low risk of bias	Moderate risk of bias	Low risk of bias risk of bias	Low risk of bias risk of bias	Low risk of bias	Moderate risk of bias	Moderate

Supplementary table 13 – Rheumatoid arthritis and smoking: evidence from individual studies

Author	Exposure detail	Study design	Inclusion criteria	Outcomes	Adjustment variables	Nb participants	Follow-up length	Age	Gender	Key findings
Crowson et al., 2018 [22]	Smoking status Current smokers, Former smokers, never smokers	Prospective cohort study	-patients with RA (based on physician diagnosis of RA and/or fulfillment of 1987 or 2010 American College of Rheumatology criteria for RA) -no prior CVD	Fatal/non-fatal CVD events including acute coronary syndrome (ST-elevation and non-ST elevation myocardial infarction and unstable angina pectoris), chronic ischemic heart disease (stable angina pectoris), coronary revascularization (e.g., percutaneous coronary intervention and coronary artery bypass grafting), CVD death, cerebrovascular events (ischemic cerebrovascular accident and transient ischemic attack) and peripheral vascular events (with and without revascularization procedures, peripheral artery disease)	Age, CVD risk factors and RA characteristics	5638	mean follow-up of 5.8	Mean (SD): 55.3 (14.0) years	76% women	Smoking: strong predictors of CVD overall and among both sexes, even after adjustment for all other CVD risk factors Adjusted hazard ratios for cardiovascular disease Former vs never smokers: Overall: HR = 1.43 (1.12, 1.83) Women: HR = 1.36 (1.01, 1.82) Men: HR = 1.75 (1.10, 2.79) Current vs never smokers: Overall: HR = 1.98 (1.52, 2.58) Women: HR = 1.79 (1.28, 2.50) Men: HR = 2.50 (1.56, 4.03)

Finckh et al., 2007 [23]	Smokers or non-smokers based on current smoking status (patient's self-reported questionnaire) Patients discontinuing smoking or starting smoking during the observation period: categorised as smokers -''heavy smokers'' (more than one pack/day) vs ''moderate smokers'' (one pack/day or less)	Prospective cohort study	- diagnosis of RA by a rheumatologist and at least two consecutive sets of radiographs	-progression of radiographic joint damage (Ratingen scores) -progression of functional disability	Baseline damage scores, disease activity (DAS28), functional disability (HAQ), use of DMARDs and glucocorticoids, presence of rheumatoid factor, gender, age, disease duration and education level	2004	3,1 years	Mean (SD) Non smokers : 56(13) years Moderate smokers : 52(13) years Heavy smokers : 51(10) years	Non smokers: 22% men Moderate smokers: 32% men Heavy smokers: 40% male	No evidence for more rapid progression of radiographic joint damage was seen among smokers compared to non-smokers: 2.79% (2.59–3.02) in non-smokers vs 2.51% (2.14–2.89) in smokers (p=0.26) Radiographic erosions evolved significantly more slowly in heavy smokers than in non-smokers (p< 0.001) Erosive disease in moderate smokers progressed at a rate similar to that in non-smokers (p=0.65) Average progression of 1.21% (0.23–2.25) in heavy smokers, 2.71% (2.35–3.06) in moderate smokers and 2.86% (2.65–3.07) in non-smokers -Evolution of HAQ scores did not differ significantly between smokers and non-smokers (p=0.35) Heavy smokers tended to have more favourable HAQ scores than non-smokers, although the difference did not reach significance At 2 years, heavy smokers improved their functional scores on average by – 0.16 (–0.05;–0.27), moderate smokers by –0.10 (–0.06;–0.14) and non-smokers by –0.11 (–0.09;– 0.13)
Kim et al., 2018 [24]	Passive smokers were defined as patients who were exposed to tobacco smoke that was exhaled by a smoker at home or in the workplace, according to their answer to	Prospective cohort study	-female RA patients who meet the revised criteria for RA	disease activity measures (swollen joint count (SJC), tender joint count (TJC), patient global estimate visual analog scale (VAS, mm), erythrocyte sedimentation rate (ESR,	-	191	17.3 months	Mean (SD): 59.1 (12.5) years	Women: 100%	ΔDAS28-ESR and ΔDAS28-CRP: significantly different between never and passive smokers (p=0.019 and p=0.023, respectively) No significant differences of changes in disease activity indexes such as SJC, TJC, patient VAS, ESR, CRP, DAS28-ESR, and DAS28-CRP between passive smokers and current smokers (p>0.05 of all) Disease activity of passive smokers not significantly changed (3.6±1.2 vs.

	the question "Have you spent time with one or more people who have smoked indoors at home or in your workplace?" Smoking status: current, never, passive, and ex-smoking			mm/hour), and C-reactive protein level (CRP, mg/L)), EULAR response						3.7±1.5, p=0.830 for DAS28-ESR and 2.9±1.2 vs. 3.0±1.6, p=0.897 for DAS28-CRP, respectively) No significant difference in treatment response based on EULAR response between never and passive smokers (p=0.171)
Kremers et al., 2008 [25]	Current, former or never smokers	Retrospective cohort study	All RA subjects fulfilled the 1987 American College of Rheumatology (ACR) criteria for RA	Combined CV outcome comprised coronary revascularization procedures, silent or non-fatal myocardial infarctions (MI), heart failure (HF) and CV deaths	CV risk factors	553 RA subjects and 574 matched non-RA subjects	14.7 years for RA subjects and 16.1 years for non-RA subjects	Mean: 57 years	Women: 73%	Increased absolute risk for CV events in RA subjects compared with non-RA subjects apparent across all age groups and risk factor categories Smoker 40-49 year old person: absolute risk of CV= 2.9% among non-RA subjects and 5.1% among RA subjects
Lu et al., 2014 [26]	Current, past or never smokers, More or less than 10 pack-years	Prospective cohort study	RA patients who had HLA-SE genotype, and have been followed up annually, up to 7 years	-disease activity (DAS28-CRP3) -functional status (modified HAQ)	baseline DAS28-CRP3 or MHAQ, gender, age, race, education, seropositivity (anti-CCP antibody and/or rheumatoid factor positive), disease duration and body mass index, current drug treatments (corticosteroids, NSAIDs), non-biologic and biologic DMARDs	662	4 years (median)	Mean (SD) Never smokers: 54.6 (14.3) Past smokers: 61.2 (11.0) Current smokers: 54.5 (11.4)	Women: Never smokers: 83.0% Past smokers: 82.4% Current smokers: 78.6%	No significant associations between current smoking and DAS28-CRP3 Current smoking: increased MHAQ compared to never smoking in seropositive RA (0.46±0.04 vs. 0.37±0.02, p=0.05) Consistent results were observed using pack-years to measure cumulative smoking

Quintana-Duque et al., 2017 [27]	Smoking status 2 categories based in the patient's self-reported questionnaire: Ever smokers (current and former smokers combined) and never smokers Never smokers: had smoked < 100 cigarettes in their lifetime and were not current smokers Former smokers: had to have quit at least 1 month before the study Current smokers: continued to smoke or quit less than 1 month before the study.	Prospective cohort study	-disease duration < 12 months -2010 American College of Rheumatology criteria for RA	-disease activity, (DAS-28) -disability (HAQ) -radiographic progression (Sharp van der Heije score)	Age, gender, HLA typification and anti-cyclic citrullinated peptide antibodies positivity	129	3 years	Mean (SD): Never smokers: 45.5 (14.7) years Ever smokers: 51.6 (13.6) years	Never smokers: 86 women (81.9%) Ever smokers: 15 women (62.5%)	Ever smokers: less risk of disability (HAQ ≥ 0.5) than never smokers at 36 month Ever vs. Never smokers: OR for HAQ ≥ 0.5 = 0.25 (0.06-0.97), p = 0.04 No evidence for more rapid progression of radiographic joint damage among smokers compared to non-smokers: OR = 1.4 (0.5-3.9) At the end of follow-up, no significant statistical difference on disease activity between never and ever smokers: OR = 0.63 (0.26–1.51) When excluding former smokers, never smokers compared to current smokers: higher disease activity according to DAS28 score Current vs. never smokers: OR for DAS28 > 2.6 = 0.33 (0.1–0.99), p = 0.04
Soderlin et al., 2011 [28]	Never smokers, previous smokers, current smokers	Prospective cohort study	-≥ 18 years of age -disease duration ≤ 1 year -1987 American College of Rheumatology RA classification criteria	-disease activity (DAS-28) -functional status (HAQ) -EULAR response	-	1587	1 year	Mean (SD): 58 (15)	Women: 68%	Current smoking at inclusion in the study: independent negative prognostic factor for EULAR response Current smokers (vs never smokers)At 3 months: OR=0.56 (0.41–0.77), p= 0.0001 At 6 months: 0.56 (0.41–0.77), p = 0.0001 At 1 year: OR = 0.69 (0.51–0.95), p= 0.02

										Smokers: no significant improvement in change from baseline to 12 months in all of the individual components of the DAS28 (swollen joints, p = 0.33; tender joints, p = 0.53; ESR, p = 0.22; and VAS global, p = 0.52) Previous smokers: no significant improvement in change from baseline to 12 months in tender joints and VAS global when plotted against disease duration (tender joints, p = 0.07; VAS global, p = 0.05) Never-smokers: significant changes from baseline to 12 months plotted against disease duration for all the individual variables of the DAS28 (swollen joints, p = 0.001; tender joints, p = 0.0001; ESR, p = 0.0001; VAS global, p = 0.0001) Significant correlation between disease duration and difference from baseline in HAQ at 12 months for never-smokers and previous smokers, but not for current smokers (never-smokers, p = 0.0001; previous smokers, p = 0.004 ; and current smokers, p = 0.62)
Soderlin et al., 2011 [29]	Never smokers, previous smokers, current smokers	Prospective cohort study	- ≥ 18 years of age -disease duration ≤ 1 year -1987 American College of Rheumatology RA classification criteria	-disease activity (DAS-28) -functional status (HAQ) -EULAR response	-	1787	1 year	Mean: 58 years	Women: N=1207 (68%)	Current smokers (vs never and previous smokers): significantly less improvement in mean DAS28 from baseline to 12 months : p = 0.0001 no significant differences in change for the mean values of CRP, pain, and HAQ: p = 0.202, 0.19, and 0.38, respectively At 12 months, significantly higher disease activity in current smokers (vs never smokers and previous smokers): 18% vs. 11% and 12%, respectively, p = 0.005

										At 12 months, current smoking at baseline was an independent predictor of a poor EULAR response: OR = 0.69 (0.50-0.93), p = 0.02 Similar data were obtained at 3 months (OR = 0.64, (0.47–0.87), p = 0.004) and 6 months (OR = 0.66, (0.48–0.91), p = 0.011)
Westhoff et al., 2008 [30]	Smoking behaviour: age at the beginning of regular smoking, intermission and total years smoked as well as the average daily number of cigarettes currently smoked and in the past	Prospective cohort study	-recent onset RA (according to the revised ACR criteria) -age ≥ 18 years -disease duration <24 months	-disease activity (ESR (mm/1 h), CRP (mg/l) and the 28-joint disease activity score (DAS28)) -radiographic joint damage (Ratingen score)	Age, sex, baseline DAS28 and RF	896	3 years	Mean (SD): 56.5 (13)	Women: N (%) 630 (70.3)	At 3 years, current smokers of both serological groups had slightly worse outcomes than never smokers of the same serological group (p=0.635 for RF+ patients and p = 0.003 for RF – patients) No significant difference in CRP levels (p=0,211 for RF+ and p= 0,421 for RF- patients) No influence of smoking on radiographic outcome (no matter which cut-off was chosen as dependent variable (RS >3 to >10) or how smoking was calibrated as an independent variable (current vs never smokers; past vs never smoker); or a combination of smoking status and PYs: former smokers </>20 PYs, current smokers </>20 PYs vs never smokers) in all serological groups
Gonzalez et al., 2008 [31]	Cigarette smoking status Current, former, never smokers Use of other tobacco products (eg, pipe, cigar) was not considered	Retrospective cohort study	-1987 American College of Rheumatology criteria for RA -between 1 January 1955 and 1 January 1995 among Rochester, Minnesota -residents >18 years of age	Risk of developing selected CV events (myocardial infarction (MI), heart failure (HF) and CV death)	Age, sex, and calendar year	603 subjects with RA and 603 non-RA subjects	The RA and non-RA subjects were followed for a mean of 15 and 17 years	Mean: 58 years	Women: 73% in both groups	Current smoking associated with a higher risk of developing a CV outcome HR = 1.32 (0.97-1.81)

Joseph, M et al., 2017 [32]	Smoking status was defined as periods of never, former and current smoking and could vary throughout follow-up. For former smokers, the number of years of cessation was defined. This value was reset to 0 at the start of each new period of former smoking	Retrospective cohort study	- first diagnosed with RA within the study window -aged 16 years or over at RA diagnosis	hospitalisations for cardiovascular events and respiratory infection	Gender, age, Townsend score, use of immunosuppressant disease-modifying antirheumatic drugs, use of oral glucocorticoids, use of non-steroidal anti-inflammatory drugs, type2 diabetes, use of cardiovascular drugs, use of aspirin/antiplatelet drugs, use of lipid regulators and body mass index	5079	13 years max	Median age (IQR): 61.0 (50.9, 70.9)	Women: 68.7%	Risk of hospitalisations for CVE Current smokers (vs never smokers): HR = 2.23 (1.46-3.40) Current smokers (vs former smokers): HR = 1.51 (1.04-2.19) Former smokers (vs never smokers): HR = 1.47 (1.04-2.08) Effect on smoking cessation on risk of hospitalisations for CVE Per year since cessation, light smoker : HR = 0.77 (0.66-0.91) Per year since cessation, heavy smoker : HR = 0.73 (0.62-0.87) Heavy vs light smoker (at the time of cessation): 1.80 (0.79-4.10)
Miyake et al., 2009 [33]	Smoker vs non-smoker	Retrospective cohort study	RA outpatients on NSAID medication for at least 3 months	development of peptic ulcers	-	196	39 months	Mean (SD): 61.9 (0.7) years	Women: N=173	Smoking status associated with development of peptic ulcers in rheumatoid arthritis patients on long-term NSAIDs treatment Smoker (vs non-smoker): OR = 2.71 (1.13–6.53), p=0.026
Baganz et al., 2018 [34]	Tobacco use Current, former or never smokers	Prospective cohort study	CAPEA: DMARD-naıve RA patients starting the 1st csDMARD - RABBIT: bDMARD-naıve RA patients switching either to a 2nd csDMARD or to a TNFi after one previous csDMARD failure - Both: at least moderate disease activity at baseline, defined by the disease activity score with	Achievement of low disease activity (DAS28 < 3.2) or remission (DAS28 < 2.6) within six months	Age, disease duration in years, DAS28>5.1, HAQ≥1.2, RF/ACPA positivity, erosions, BMI>30 kg/m2 and number of comorbidities (none, 1,≥2)	A total of 713 patients starting the 1st csDMARD (CAPEA), 1613 patients switching to the 2nd csDMARD therapy (RABBIT) and 388 patients switching to the 1st TNFi (RABBIT)	NA	Mean (SD): CAPEA: 57.1 (13.9) RABBIT: 58.9 (12.7) RABBIT: 55.6 (14.6)	Women: N(%) 442 (62) 1193 (74) 249 (64.2)	Achievement of low disease activity within six months: Current smoking: OR= 0.71 (0.48-1.04) / 0.85 (0.66-1.10) / 1.04 (0.55-1.94) Achievement of remission within six months: Current smoking: OR= 0.67 (0.46-1.00) / 0.72 (0.53-0.97) / 0.75 (0.39-1.46)

Doran et al., 2002 [35]	Ever smokers vs never smokers	Prospective cohort study	28 joints (DAS28) 3.2 and with at least one follow up visit - computerized diagnostic index of the Rochester Epidemiology Project for any diagnosis of arthritis (excluding degenerative arthritis or osteoarthritis) -≥18 years of age -diagnosis was confirmed or rejected based on the American College of Rheumatology 1987 diagnostic criteria for RA	Infection	-	609	Mean follow-up: 12.7 years	Mean age at RA incidence: 58.0 years	Women: N(%) 445 (73.1)	Smoking: predictor of objectively confirmed infections (univariate analysis) HR = 1.42 (1.10-1.84), p= 0.008 Non-predictor of infections requiring hospitalization (univariate analysis) HR = 1.29 (0.98-1.70), p= 0.071
Mantel et al., 2015 [36]	Never, current, past, non-regular smokers	Nested case-control study	- patients with incident RA between 18 and 70 years of age	Risk of acute coronary events	Linear and quadratic effect of age	Cases (138) / Controls (624)	NA	Mean (SD) age at diagnosis : Case 60.8 (7.3) / Control 51.6 12.7	Women: N(%) case 59 (42.8) / control 277 (44.4)	Current smoking (vs never smoking): OR = 1.45 (0.78–2.70) Past smoking (vs never smoking): OR = 1.77 (0.99–3.20) Non-regular smoking (vs never smoking): OR = 1.71 (0.67–4.32)
McWilliams et al., 2019 [37]	Ex-, current, never smokers	Prospective cohort study	-RA diagnostic by a consultant rheumatologist	Pain (SF-36)	-	ERAN: 683 + BSRBR BIOLOGICS 7,090 + BSRBR NONBIOLOGICS 1720	3 years	Mean (SD) 57 (13) 57 (11) 61 (12)	Women: 66% 77% 75%	ERAN Persistent pain (vs low pain) Current smokers: OR = 1.16 (0.52−2.56), p=0.717 Ex-smokers: OR = 4.65 (1.73−12.50), p=0 .002 ERAN Persistent pain (vs resolving pain) Current smokers: OR = 1.83 (1.05−3.18), p= 0.032 Ex-smokers: OR = 1.52 (0.86−2.67), p= 0.146 BSRBR Biologics Persistent pain (vs resolving pain) Current smokers: OR = 1.72 (1.41−2.11), p<.001

										Ex-smokers: OR = 1.17 (1.00−1.37), p= 0.045 BSRBR Nonbiologics Persistent pain (vs resolving pain) Current smokers: OR = 1.34 (0.89−2.02), p=0.156 Ex-smokers: OR = 1.64 (1.18−2.28), p= 0.003
Nannini et al., 2013 [38]	Ever vs never smokers	Prospective cohort study	-RA first diagnosed between January 1, 1955 and January 1, 1994, among Rochester, Minnesota residents -≥ 18 years of age -1987 American College of Rheumatology classification criteria for RA	Development of obstructive lung disease	-	Patients with RA (N=594) Subjects without RA (N=596)	Mean (SD): Patients with RA 16.3 (10.5) years Subjects without RA: 19.4 (11.1) years	Age at RA diagnosis/index date, mean (SD RA: 57.8 (15.2) No RA: 58.2 (15.3)	Women : N (%) RA: 435 (73.2%) No RA: 438 (73.5%)	Smoking (ever) (vs never): HR = 4.38 (2.14-8.99)
Rydell et al., 2018 [39]	Current, previous and never smokers	Prospective cohort study	-RA diagnosed by a specialist in rheumatology -1987 American College of Rheumatology classification criteria for RA -duration of symptoms ≤ 12 months at the time of inclusion	Risk of rapid radiographic progression (increase of ≥ 5 points in Sharp–van der Heijde score per year)	RF and presence of erosions	233	5 years	Median (IQR) age at inclusion: 62 (52–70) years	Women: N(%) 114 (70)	Current smokers (vs never smokers): OR = 2.92 (1.00-8.56) Ever smokers (vs never smokers): OR = 2.69 (1.01-7.18) Previous smoker (vs never smokers): OR = 2.50 (0.83-7.55)
Kiely et al., 2019 [40]	Ever vs never smokers	Prospective cohort study	ERAS: <2 years disease duration, no prior csDMARD therapy ERAN. <3 years disease duration	Development of interstitial lung disease (RA-ILD)	-	2701	ERAS: median follow-up 10 years ERAN: median follow-up 6 years	Age of RA onset <55: 1146 (42.4%) 56–64: 728 (27.0%) 65+: 827 (30.6%)	Female 1808 66.9%	RA-ILD onset after any conventional synthetic disease-modifying antirheumatic drugs exposure Smoking (ever): OR = 2.21 (1.21-4.03), p= 0.01 RA-ILD onset prior to any conventional synthetic disease-modifying antirheumatic drugs exposure Smoking (ever): OR = 1.91 (1.13-3.25), p= 0.016

Verstappen et al., 2013 [41] *	Never, past and current smokers	Prospective cohort study	Consecutive patients aged over 16 years with early IP from the Norfolk Arthritis Register (NOAR) recruited between 1990 and 1994	abnormal lung function	Age and gender	421	15 years	Mean (SD): 62 (13)	Women: 68%	Current smoking at baseline: predictor of obstructive lung disease Obstructive lung disease (OLD) Current smokers (vs never) OR = 15.25 (3.14-73.99) Past smokers (vs never) OR = 4.59 (0.99-21.33) Restrictive lung disease (RLD) Current smokers (vs never) OR = 1.45 (0.59-3.56) Past smokers (vs never) OR = 0.64 (0.28-150) Association with OLD at 15 y: Current smoking at 15 y: OR = 15.91 (3.00-84.3) Past smoking: OR = 5.90 (1.32-26.4) Association with RLD at 15 y: Current smoking at 15 y: OR = 2.01 (0.74-5.50) Past smoking: OR = 0.68 (0.30-1.51) In patients who stopped smoking between baseline and the 15-year follow-up visit: non-significant reduced risk of having OLD with longer cessation time (OR = 0.98, 95% CI 0.94 -1.02)

*Inflammatory polyarthritis

Supplementary table 14 – Rheumatoid arthritis and smoking: methodological quality of individual studies

Authors	Study participation	Study attrition	Prognostic factor measurement	Outcome measurement	Study confounding	Statistical analysis and reporting	Quality
Crowson et al., 2018 [22]	Moderate risk of bias	High risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low
Finckh et al., 2007 [23]	Low risk of bias	Moderate risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Moderate
Kim et al., 2018 [24]	Low risk of bias	Moderate risk of bias	Low risk of bias	Low risk of bias	High risk of bias	Low risk of bias	Low
Kremers et al., 2008 [25]	Low risk of bias	Moderate risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Moderate
Lu et al., 2014 [26]	Low risk of bias	Moderate risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Moderate
Quintana-Duque et al., 2017 [27]	Low risk of bias	High risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low
Soderlin et al., 2011 [28]	Low risk of bias	High risk of bias	Low risk of bias	Low risk of bias	moderate risk of bias	Low risk of bias	Low
Soderlin et al., 2011 [29]	Low risk of bias	High risk of bias	Low risk of bias	Low risk of bias	moderate risk of bias	Low risk of bias	Low
Westhoff et al., 2008 [30]	Low risk of bias	Moderate risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Moderate
Gonzalez et al., 2008 [31]	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	moderate risk of bias	Low risk of bias	Moderate
Joseph, M et al., 2017 [32]	Low risk of bias	Moderate risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Moderate
Miyake et al., 2009 [33]	Moderate risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Moderate risk of bias	Low risk of bias	Moderate
Baganz et al., 2018 [34]	Moderate risk of bias	Moderate risk of bias	Moderate risk of bias	Moderate risk of bias	Moderate risk of bias	Low risk of bias	Moderate
Doran et al., 2002 [35]	Low risk of bias	High risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low
Mantel et al., 2015 [36]	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	High
McWilliams et al., 2019 [37]	Moderate risk of bias	High risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low
Nannini et al., 2013 [38]	Low risk of bias	High risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low
Rydell et al., 2018 [39]	Low risk of bias	Moderate risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Moderate
Kiely et al., 2019 [40]	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Moderate risk of bias	Low risk of bias	Moderate
Verstappen et al., 2013 [41]	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	High

Supplementary table 15 – Systemic lupus erythematosus and smoking: evidence from systematic reviews

Author (date)	Type of review	Study type included	Outcomes	Smoking associated with worse outcome	Key findings (negative MD/SMD favours intervention)	AMSTAR2
Andrades et al., 2017 [42]	SR	Observational	Cardiovascular risk factors	Cardiovascular risk factors: ✓	Cardiovascular risk factors: smoking cessation is recommended, although further research is needed to study the association between smoking and cardiovascular risk factors	Moderate
Montes et al., 2016 [43]	SR	Observational	SLEDAI	SLEDAI:✗	SLEDAI: 2 cross-sectional studies assessed the association between smoking and SLEDAI, 1 reported an association. Authors conclude that the evidence is not strong enough to make conclusions	Moderate
Rodriguez Huerta et al., 2016 [44]	SR	Observational	SLEDAI, Rash, SF-36	SLEDAI: ✓ Rash: ✓ SF-36: ✓	SLEDAI: 3/4 studies reported an association between smoking and worse SLEDAI. Also higher duration/intensity associated with worse SLEDAI Rash: active smokers had increased risk of rash SF-36: 1 study reported smokers had worse scores on mental and physical components	Moderate

AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews 2, MA = meta-analysis, RR = relative risk, SLEDAI = systemic lupus erythematosus disease activity index, SR = systematic review

Supplementary table 16 – Systemic lupus erythematosus and smoking: evidence from individual studies

Author	Exposure detail	Study design	Inclusion criteria	Outcomes	Adjustment variables	Nb participants	Follow-up length	Age	Gender	Key findings
Bengtsson et al., 2012 [45]	Smoking habits Ever smokers, non-smokers	Prospective cohort study	- at least 4 of the 1982 SLE ACR classification criteria -being willing and able to be assessed clinically and by laboratory analyses for disease activity according to the SLE Disease Activity Index (SLEDAI) and for organ damage with the SLICC/ACR-DI	Cardiovascular events (myocardial infarction and/or stroke)	myocardial infarction and/or angina pectoris with intervention	774	7 years	Mean: 49 years	Women: 85%	Smoking, ever (vs non-smoking) Unadjusted HR = 1.14 (0.52–2.51) Adjusted HR = 0.65 (0.27–1.55)
Bernatsky et al., 2008 [46]	Ever, never smokers	Nested case-control study	SLE patients	Cancer risk	Age, sex, race/ethnicity, calendar year at cohort entry, and geographical residence	246 cancer cases and 538 controls without cancer	NA	Cancer group: median=47 years Control group: median=46	Women: N (%) Cancer group: 49 (96.08) Control group: 192 (94.12)	Adjusted hazard ratio (HR) estimates for cancer occurrence: Tobacco use (ever vs never smoker): HR = 0.81 (0.56-1.18) Adjusted Hr estimates for haematological cancer occurrence: Tobacco use (ever vs never smoker): HR = 0.79 (0.54–1.15)
Bernatsky et al., 2018 [47]	Ever smoker or not	Prospective cohort study	- lung cancers occurring after entry into the SLE cohort and up to the time of cohort exit	Lung cancer risk	time-dependent cumulative disease activity, any prior record of pulmonary fibrosis	4987	NA	Mean: 38 years	Men: 9%	Hazard ratio estimates for lung cancer: Unadjusted HR = 6.92 (2.87-16.7) Adjusted HR = 6.35 (2.43-16.6)
Bertoli et al., 2009 [48]	Current smoking: yes vs no	Prospective cohort study	- American College of	Arterial vascular events (myocardial infarction, angina	-	N=1333 Northwestern University	NA	Mean (SD): 35.7 (12.3)	Women: % 90.4%	Univariate analysis: Current smoking: HR = 2.06 (1.39-3.05), p < 0.001

			Rheumatology (ACR) -16 years of age or older -disease duration ≤10 years	pectoris and/or a vascular procedure for myocardial infarction (coronary artery bypass graft), cerebral vascular accident and claudication lasting ≥ six months and/or evidence of gangrene or significant tissue loss (loss of a digit or a limb)		(N=175), Johns Hopkins University (N=528), The University of Alabama at Birmingham (N=299), The University of Texas Health Science Center at Houston (N=229), and The University of Puerto Rico (N=102).				Multivariate analysis: Current smoking: HR = 2.20 (1.40-3.46), p < 0.001
Burgos et al., 2010 [49]	Current smoking or not (self reporting)	Prospective cohort study	- ACR criteria for the classification of SLE -disease duration of 45 years -16 years of age -defined ethnicity -living in the geographic recruitment area of the participating centres	Thrombotic events (arterial [myocardial infarction, angina, stroke, intermittent claudication or peripheral arterial thrombosis (or both)] or venous [visceral or peripheral (or both)])	-	643	Mean: 4.6 (3.5) years .	Mean: 36.4 years	Women: 90%	Smoking: Univariate OR = 1.80 (1.04-3.11), p= 0.036 Multivariate OR = 1.85 (1.01-3.40), p= 0.048
Calvo-Alen, G. et al., 2006 [50]	Current smoking or not	Prospective cohort study	Patients with SLE of Hispanic, African American, and Caucasian ethnicity from LUMINA, a multiethnic, longitudinal study	Vascular events (cardiovascular, cerebrovascular, peripheral vascular)	-	400	Patients who had a vascular event: 4,6 years Those who had not vascular event: 3.8 years	Mean (SD): 37.0 (12.4) years	Women: 90%	Patients with vascular event: more likely to be smokers 25.0% vs 13.1%; p = 0.0274

Ho et al., 2005 [51]	Smokers: yes, no	Prospective cohort study	- four of the American College of Rheumatology criteria for the classification of SLE - disease duration of 5 years at baseline - live within the catchment areas of the participating institutions	Thrombotic events (myocardial infarction, angina, stroke, intermittent claudication and/or peripheral arterial thrombosis)	-	442	Mean follow-up 88.4 months	NA	NA	Patients with thrombotic event: more likely to be smokers OR = 2.642 (1.248–5.593), p= 0.0112 Adjusted OR = 2.777 (1.317–5.852), p= 0.0073
Legge et al., 2016 [52]	Current, past, never smoking	Prospective cohort study	- American College of Rheumatology classification criteria for SLE	Time to first change in SDI score (progression of cumulative organ damage)	-	273	Mean (SD): 7.3 (4.3) years	Mean (SD): 44.1 (14.6) years	Women: 87.2%	Past or current smoking (vs never): Unadjusted HR = 2.07 (1.37-2.98), p< 0.001 Adjusted HR = 1.69 (1.1-2.6), p= 0.02
Turchin et al., 2009 [53]	Current smoking (i.e., whether or not the subject smoked at the time of the last clinic assessment)	Prospective cohort study	- revised American College of Rheumatology criteria for SLE	Cutaneous damage (alopecia; extensive scarring; and skin ulceration) (SLICC/ACR DI) Cutaneous features of active lupus (rash, oral ulcers, alopecia) (SLEDAI-2K)	age, sex, race, lupus disease duration, antimalarial or immunosuppressant use, and anti-DNA and anti-SSA antibody status	276	NA	Mean (SD): 45.1 (15.0) years	Women: 92%	Current smoking & SLICC/ACR DI: Total cutaneous: OR = 2.73 (1.10-6.81) Alopecia: OR = 1.95 (0.75-5.06) Scarring: OR = 4.70 (1.04-21.18) Current smoking & SLEDAI-2K: Total cutaneous OR=1.83 (0.69-4.89) Alopecia: OR = 1.08 (0.27-4.38) Rash: OR = 6.18 (1.63-23.40)
Enomoto et al., 2019 [54]	Current, ex, never smokers	Retrospective cohort study	Patients with SLE and thoracic diseases who had been treated in respiratory departments and thoroughly evaluated those with SLE-related	Systemic lupus erythematosus-related interstitial pneumonia	Age	55	Mean observation period: 85 months	Median age at the diagnosis (IQR): 54 (13, 79)	Men/women: 13/42	Current smokers (vs ex and never): significantly worse prognoses (log-rank, p = 0.001) Current smoker: HR = 6.689 (No CI available), p = 0.018 HR adjusted for age: Current smoker: HR = 6.105, p = 0.027

			interstitial pneumonia							
Rua-Figueroa et al., 2017 [55]	Tobacco use	Retrospective cohort study	Patients from the RELESSER-registry who met at least 4 ACR-97 SLE criteria	Severe infections	-	3658	Mean follow-up (SD): 120.2 (787.6) months	Median age: 32.9 years	Women: 90%	Bivariate analysis Tobacco smoking (any history) RR = 1.35(1.06–1.73), p=0.018 Multivariate analysis Tobacco (any use): HR= 1.332 (1.121-1.583)
Toloza et al., [56]	NA	Prospective cohort study	Patients with SLE according to the American College of Rheumatology criteria - disease duration of 5 years - defined ethnicity (all 4 grandparents of the same ethnicity as the patient) - live in the geographic catchment areas of the participating institutions	Cardiovascular (myocardial infarction and/or definite or classic angina and/or the undergoing of a vascular procedure for myocardial infarction [coronary artery bypass graft]), cerebrovascular (stroke) and peripheral vascular (arterial claudication and/or gangrene or significant tissue loss and/or arterial thrombosis in peripheral arteries) events	-	546	Median follow-up: 73.8 months	Mean (SD): 36.5 (12.3) years	Women: 89.6%	Predictors of the occurrence of vascular events (multivariable logistic regression analyses) Smoking: OR = 3.731 (1.391–10.000), p= 0.009 Predictors of the occurrence of vascular events (multivariable Cox proportional hazards regression analyses) Smoking: HR = 2.596 (1.043–6.463), p = 0.0404
Gustafsson et al., 2009 [57]	Ever vs never smoking	Prospective cohort study	All SLE patients at the Department of Rheumatology, Karolinska University Hospital who fulfilled four or more of the 1982 revised American College of Rheumatology	Coronary artery disease (angina pectoris, myocardial infarction, or cardiac sudden death)	Age	182	8 years	Median (IQR): 45 (31-53) years	Men: 10%	Baseline smoking status: predictor of the first ever cardiovascular event (age-adjusted Cox regression models) Smoking, ever: HR= 2.62 (1.11-7.03), p=0.03

			Criteria for classification of SLE during the inclusion period (1995-99)							
Julian, C et al., 2011 [58]	Current, ever, never smoker	Prospective cohort study	SLE diagnosis confirmed by medical chart review prior to enrolment, using American College of Rheumatology criteria	Depression (CES-D)	-	663	1 year	Age 20-39 195 (29%) Age 40-59 347 (52%) Age 60+ 121 (18%)	Women N(%): 589 (90)	Univariate analysis: History of smoking OR=1.1 (0.8-1.5) Model with traditional cardiovascular risk factors + demographics and depressive symptoms: OR = 1.2 (0.9-1.7) Model with SLE-specific characteristics + demographics + depressive symptoms and traditional cardiovascular risk and disease related factors: OR = 1.3 (0.9-1.8)
Petri et al. 1992 [59]	Ever, never smokers	Prospective cohort study	- clinical diagnosis of SLE by a faculty (board-certified) rheumatologist - four or more of the revised criteria of the American Rheumatism Association for the classification of SLE	Coronary artery disease (CAD) (angina pectoris, myocardial infarction, or cardiac sudden death)	-	229	NA	Mean (SD) at entry into cohort CAD+: 47.1 (11.8) CAD-: 34.7 (11.2)	Men CAD+: 21% CAD-: 7.6%	Smoking, ever OR = 0.9 (0.3-2.2)
Urowitz et al., 2016 [60]	Ever, nerver smokers	Prospective cohort study	- SLE diagnosis within the last 15 months - four or more American College of Rheumatology criteria for the	Early myocardial infarction	-	1848	Mean follow-up: 8.9 years	Mean (SD) at diagnosis: 34.7 (13.3) years	Women N(%): 1640 (88.8)	Univariate analysis: Smoking, ever: OR = 6.85 (2.53-18.52) Multivariable analysis Smoking, ever: OR = 7.50 (2.38-23.57)

			classification of SLE							
Dey et al., 2018 [61]	Smoking: yes, no	Prospective cohort study	- pre-existing confirmed clinical diagnosis of SLE	Fracture risk	Age	150	NA	Age at scan: 50.1 years	Women: 141	Crude Smoking: OR= 2.484 (1.17-5.32), p= 0.012 Adjusted Smoking: OR = 2.770 (1.34-5.72), p= 0.006

Supplementary table 17 – Systemic lupus erythematosus and smoking: methodological quality of individual studies

Authors	Study participation	Study attrition	Prognostic factor measurement	Outcome measurement	Study confounding	Statistical analysis and reporting	Quality
Bengtsson et al., 2012 [45]	Moderate risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Moderate risk of bias	Moderate
Bernatsky et al., 2008 [46]	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Moderate risk of bias	Low risk of bias	Moderate
Bernatsky et al., 2018 [46]	Moderate risk of bias	High risk of bias	Moderate risk of bias	Moderate risk of bias	Low risk of bias	Low risk of bias	Low
Bertoli et al., 2009 [48]	Low risk of bias	High risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low
Burgos et al., 2010 [49]	Low risk of bias	High risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low
Calvo-Alen, G. et al., 2006 [50]	Low risk of bias	High risk of bias	Low risk of bias	Low risk of bias	High risk of bias	Low risk of bias	Low
Ho et al., 2005 [51]	Low risk of bias	High risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low
Legge et al., 2016 [52]	Low risk of bias	Moderate risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Moderate
Turchin et al., 2009 [53]	Moderate risk of bias	High risk of bias	Moderate risk of bias	Moderate risk of bias	Low risk of bias	Low risk of bias	Low
Enomoto et al., 2019 [54]	Moderate risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Moderate
Rua-Figueroa et al., 2017 [55]	Moderate risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Moderate
Toloza et al., [56]	Low risk of bias	HIgh risk of bias	Low risk of bias	Low risk of bias	Moderate risk of bias	Low risk of bias	Low
Gustafsson et al., 2009 [57]	Low risk of bias	HIgh risk of bias	Low risk of bias	Low risk of bias	Moderate risk of bias	Low risk of bias	Low
Julian, C et al., 2011 [58]	Low risk of bias	High risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low
Petri et al. 1992 [59]	Low risk of bias	High risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low
Urowitz et al., 2016 [60]	Low risk of bias	High risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low
Dey et al., 2018 [61]	Moderate risk of bias	High risk of bias	Low risk of bias	Low risk of bias	Moderate risk of bias	Low risk of bias	Low

Supplementary table 18 – Axial spondyloarthritis and smoking: evidence from systematic reviews

Author (date)	Type of review	Study type included	Outcomes	Smoking associated with worse outcome	Key findings (negative MD/SMD favours intervention)	AMSTAR2
Villaverde-Garcia et al., 2017 [62]	SR	X-sectional, case-control, cohort	Pain, function, morning stiffness, disease activity, structural damage, QoL	Pain: ✓ Function: ✓ Morning stiffness: ✖ Disease activity: ✓ Structural damage: ✓ QoL: ✓	Pain: 2/3 X-sectional studies reported higher pain in smokers compared to never smokers Function: Current smoking associated with higher disability and ever smoking was associated with higher disability in 5/10 studies Morning stiffness: 1 X-sectional study reported no significant difference Disease activity: 8/8 X-sectional studies reported high BASDAI for smokers compared to non-smokers; 1 cohort study reported the same Structural damage: 6/7 studies reported smoking was associated with more damage QoL: 4/5 studies reported smoking was associated with worse QoL	Moderate

AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews 2, QoL = quality of life, , RR = relative risk, SR = systematic review

Supplementary table 19 – Axial spondyloarthritis and smoking – evidence from individual studies

Author	Exposure detail	Study design	Inclusion criteria	Outcomes	Adjustment variables	Nb participants	Follow-up length	Age	Gender	Key findings
Maas et al., 2017 [63]	Smoking duration	Prospective cohort study	-AS patients fulfilling the modified New York criteria enrolled in the Groningen Leeuwarden AS cohort between November 2004 and December 2012 -available lateral radiographs of the thoracic and lumbar spine at baseline and after 2 years of follow-up. -consecutive axial SpA outpatients irrespective of treatment regimen	prevalence and incidence of radiographic vertebral fractures	-	292	2 years	Mean (SD): 42.8 (12.5)	Men:70%	Median smoking duration (yrs) Prevalent fractures: Present 17 (0–29) Absent 10 (0–23) , p= 0.043 Incident fractures: Present 17 (IQR=5-30) Absent 12 (IQR 0-24) p=0.205 AS patients with a smoking duration of ≥20 years had a 2 times higher risk of having radiographic vertebral fractures than nonsmokers and patients with shorter smoking duration (approx. 30% vs 10–15%)
Ward et al., 2002 [64]	Current smokers, non-smokers	Prospective cohort study	- diagnosis of AS by the modified New York criteria16 -be age 18 or older -be able to read English	Functional disability (HAQ)	-	212	Median of 5 years (range 1.0 to 7.5)	47.8 (13.6)	Men: N(%) 149 (70.3)	Rate of progression of the HAQ-S: increased by an additional 0.025 units/yr (IC95% 0.0071, 0.0429) among current smokers compared to non-smokers p=0.007
Deminger et al., 2018 [65]	Ever smokers, current smokers, never smokers	Prospective cohort study	- AS according to the modified New York criteria	spinal radiographic progression (modified Stoke Ankylosing Spondylitis Spine Score)	-	204	5 years	50 (13)	89 Men 77 Women	Univariate logistic regression analyses for progression of ≥ 2 mSASSS units over 5 years Total group Ever-smoker: OR = 1.74 (0.88-3.44), p= 0.11 Current smoker: OR = 1.44 (0.50-4.14), p= 0.50 Men Ever-smoker: OR = 3.53 (1.42-8.77), p= 0.007 Current smoker: OR = 3.33 (0.74-15.00), p= 0.12 Women Ever-smoker: OR = 0.47 (0.14-1.65), p= 0.24 Current smoker: OR = 0.48 (0.06-4.18), p= 0.51 Smoking: predictor of progression of ≥ 2 modified Stoke Ankylosing Spondylitis Spine Score units over 5 years in men Ever smokers: OR=3.52 (1.29-9.58)

Poddubnyy et al., 2012 [66]	Current smoking, present vs. absent	Prospective cohort study	- definite clinical diagnosis of axial SpA according to the treating rheumatologist - fulfillment of the modified New York criteria -duration of symptoms was restricted to 10 years at the time of inclusion Non radiographic AxSpA: - fulfillment of the European Spondyloarthropathy Study Group criteria with minor modifications -maximum duration of symptoms was 5 years.	-spinal radiographic progression (defined as worsening of the mean modified Stoke Ankylosing Spondylitis Spine Score by >2 units over 2 years)	baseline CRP levels, time-averaged CRP levels , baseline ESR, time-averaged ESR	210	2 years	Mean (SD): 37.1 (10.6)	Men: N(%) 107 (51.0)	Current smoking significantly associated with an increase of 2 mSASSS units after 2 years OR = 2.75 (1.25-6.05), p= 0.012 4 models adjusted on baseline CRP levels, time- averaged CRP levels , baseline ESR, time-averaged ESR OR = 2.52 (1.06 5.99), p= 0.037 OR = 2.41 (1.01-5.76), p=0.048 OR = 2.54 (1.06-6.09), p= 0.037 OR = 2.31 (0.96-5.51); p = 0.060
Ward et al., 2001 [67]	Current, former, never smokers	Retrospective cohort study	- diagnosis of AS by the modified New York criteria -be age 18 or older -be able to read English	Work disability (standardised questionnaire)	-	234	NA	Mean (SD) age at onset of AS: 27.4 (11.0)	Men, n (%) 165 (70.5)	Current or former smoker (vs never) HR = 1.31 (0.54-3.14), p= 0.55
Wendling et al., 2017 [68]	NA	Prospective cohort study	- early inflammatory back pain of more than3 months and less than 3 years of duration -symptoms suggestive of SpA according to the local investigator's assessment	Remission (according 2 definitions: ASDAS-CRP < 1.3 or BASDAI < 3.6)	-	706	2 years	mean age (SD) is 33.8 (8.6) years	Men: 46%	ASDAS < 1.3 At baseline: Smoking: OR = 0.22 (0.08-0.56) At 2 year: Smoking: OR = 0.34 (0.13-0.87) BASDAI < 3.6 At baseline: Smoking: OR = 0.39 (0.16-0.95) At 2 years: Smoking: OR = 0.31 (0.15-0.63)

Supplementary table 20 – Axial spondyloarthritis and smoking: methodological quality of individual studies

Author	Study participation	Study attrition	Prognostic factor measurement	Outcome measurement	Study confounding	Statistical analysis and reporting	Quality
Maas et al., 2017 [63]	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	High
Ward et al., 2002 [64]	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	High
Deminger et al., 2018 [65]	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	High
Poddubnyy et al., 2012 [66]	Low risk of bias	High risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low
Ward et al., 2001 [67]	Low risk of bias	High risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low
Wendling et al., 2017 [68]	Moderate risk of bias	High risk of bias	Low risk of bias	Low risk of bias	Moderate risk of bias	Low risk of bias	Low

Supplementary table 21 – Psoriatic arthritis and smoking: evidence from individual studies

Author	Exposure detail	Study design	Inclusion criteria	Outcomes	Adjustment variables	Nb participants	Follow-up length	Age	Gender	Key findings
Tillett et al., 2013 [69]	Current, ever, never smokers	Prospective cohort study	Patients selected from the longitudinal cohort of PsA patients at the Royal National Hospital for Rheumatic Diseases, Bath, UK 98.2% of the cohort fulfil the Classification for Psoriatic Arthritis (CASPAR) criteria and disease duration >10 years	Physical function (HAQ)	-	267 patients	unclear	Age at diagnosis ≤50 years: 210 (79%) >50 years: 57 (21%)	Women (%): 47.2	Effect of smoking (current or ever vs never) on HAQ (difference from baseline): 0.23 p = 0.02

Supplementary table 22 – Psoriatic arthritis and smoking: methodological quality of individual studies

Author	Study participation	Study attrition	Prognostic factor measurement	Outcome measurement	Study confounding	Statistical analysis and reporting	Quality
Tillett [69]	Moderate risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	moderate risk of bias	Low risk of bias	Moderate

Supplementary table 23 – Systemic sclerosis and smoking: evidence from individual studies

Author	Exposure detail	Study design	Inclusion criteria	Outcomes	Adjustment variables	Nb participants	Follow-up length	Age	Gender	Key findings
Sakr et al., 2018 [70]	smoking history and number of pack-years smoked	Prospective cohort study	- at least 18 years of age -diagnosis of SSc confirmed by a participating rheumatologist - be fluent in either English or French -meet the 2013 ACR/EULAR (American College of Rheumatology/European League Against Rheumatism) classification criteria for SSc	Risk of lung cancer	-	1560	max 11y	Mean (SD): Lung cancer: 58.8 (11.2) No lung cancer; 55.2 (12.3)	Women: N(%): Lung cancer: 12 (66.7%) No lung cancer: 1321 (86.1%)	Smoking vs non-smoking (multivariate analysis) <10 pack-years: HR = 2.36 (0.51-10.97) 10–20 pack-years: HR = 5.04 (1.11-22.85) 20–30 pack-years: HR = 3.54 (0.55-23.00) >30 pack-years: HR = 6.17 (1.29-29.49)
Khimdas et al., 2011 [71]	Never, ever smokers (past or present)	Prospective cohort study	- diagnosis of SSc by a physician - informed and signed consent	digital ulcers	-	938	NA	Mean (SD): 55.4 (0.34)	Female: N(%) 807 (86.0)	Smoking OR=0.984 p=0.909 (univariate analysis)
Kwakkenbos et al., 2018 [72]	NA	Prospective cohort study	- classified by a physician as having SSc according to the 2013 ACR/EULAR classification criteria -be at least 18 years of age -have the ability to give informed consent -be fluent in English, French or Spanish -have access and be able to respond to questionnaires via the internet	Hand function (Cochin Hand Function Scale, higher scores indicate more difficulty)	-	1193	NA	Mean (SD): 55.1 (12.3)	Women: N(%) 1047 (88)	Relationship between current smoking and hand function Standardised coefficient regression (beta) = 0.07 P = 0.004

Supplementary table 24 – Systemic sclerosis and smoking: methodological quality of individual studies

Author	Study participation	Study attrition	Prognostic factor measurement	Outcome measurement	Study confounding	Statistical analysis and reporting	Quality
Sakr et al., 2018 [70]	Low risk of bias	Moderate risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Moderate
Khimdas et al., 2011 [71]	Moderate risk of bias	High risk of bias	Low risk of bias	Low risk of bias	Moderate risk of bias	Moderate risk of bias	Low
Kwakkenbos et al., 2018 [72]	Low risk of bias	high risk of bias	Low risk of bias	Low risk of bias	Moderate risk of bias	Low risk of bias	Low

Supplementary table 25 – Gout and smoking: evidence from individual studies

Author	Exposure detail	Study design	Inclusion criteria	Outcomes	Adjustment variables	Nb participants	Follow-up length	Age	Gender	Key findings
Alvarez-Nemegyei et al., 2005 [73]	Smoking habit	Nested case-control study	- diagnosis of gouty arthritis based on Wallace criteria	Musculoskeletal disability (American College of Rheumatology functional class) -chronic renal failure (glomerular filtration rate < 60 ml/min/1.73 m2)	-	90	NA	Mean (SD): 54 (12) years (range 22–81)	88 men (98%)	33% of smokers in patients with disability vs 40% in patients without disability, p=0.44 36% of smokers in patients with renal failure vs 37% in patients without renal failure, p=0.92
Su et al., 2008 [74]	Tobacco use	Retrospective cohort study	-male primary gout subjects -meet criteria for clinically defined gout	Renal function deterioration (based on creatinine levels)	-	318	Subjects with renal function deterioration: 81.20 (53.29) months Subjects without renal function deterioration: 92.41 (46.72) months	Subjects with renal function deterioration: 57.21 (13.02) Subjects without renal function deterioration: 62.5 (14.98)	318 men	26.4% of smokers in patients with renal function deterioration vs 18.2% in patients without renal function deterioration, p=0.488 (univariate)

Supplementary table 26 – Gout and smoking: Methodological quality of individual studies

Author	Study participation	Study attrition	Prognostic factor measurement	Outcome measurement	Study confounding	Statistical analysis and reporting	Quality
Alvarez-Nemegyei et al., 2005 [73]	Low risk of bias	High risk of bias	Low risk of bias	Low risk of bias	Moderate risk of bias	Moderate risk of bias	Low
Su et al., 2008 [74]	Moderate risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Moderate risk of bias	Low risk of bias	Moderate

Supplementary table 27 – Summary of cut-offs used for alcohol exposure in the individual studies

Authors	Level of evidence	Methodological quality	Details on alcohol consumption
Vandenberg et al., 1994 [75]	2B	Low	Chronic alcoholics vs Reformed alcoholics (abstained for 2 years) vs Non-alcoholics
Jonsen et al., 2007 [76]	2B	Moderate	Alcohol intake ≤15 g/month vs > 15 g/month
Kim et al., 2008 [77]	2B	Low	≥ 1 drink per week vs < 1 drink per week *The questionnaire used did not define specific alcohol quantities or volumes that constituted a given alcoholic beverage*
Su et al., 2008 [74]	2B	Low	Regular vs social drinker
Nissen et al., 2010 [78]	2B	Low	Occasional drinkers, daily drinkers (consumption of alcoholic beverages on 1 occasion per day), and heavy drinkers (consumption of alcoholic beverages on several occasions per day)
Davis et al., 2013 [79]	2B	Low	<15 drinks per month vs ≥15 drinks per month *The questionnaire used did not define specific alcohol quantities or volumes that constituted a given alcoholic beverage*
Lu et al., 2014 [26]	2B	Low	None, 0.1–5.0, 5.1–10.0 and >10 grams per day
Neogi et al., 2014 [80]	2B	Low	Seven categories: no alcohol consumption, >0–1 drink, >1–2, >2–4, >4–6, >6–8, and more than 8 drinks Moderate alcohol intake : no more than 2 drinks per day for men and no more than 1 drink per day for women *One typical drink is approximately 15 grams of alcohol*
Hanvivadhanakul et al., 2015 [81]	2B	Low	Yes vs No
Bird et al., 2017 [11]	2B	Low	Never, Rare, Mild (< 30 g), Moderate (30–40 g/day) or Heavy (> 40 g)
Humphreys et al., 2017 [82]	2B	Moderate	Weekly alcohol consumption (units) : 0, Mild (1–7), Moderate (8–14), Moderate High (15–21), High (>21) *A unit of alcohol represents 10 mL or 8 g of pure alcohol*
Sageloli et al., 2018 [83]	2B	High	Abstinent, moderate consumption (≤ 20 g/day for women and ≤ 30 g/day for men), abuse (> 20 g/day for women and > 30 g/day for men)

Supplementary table 28 – RMDs and alcohol: summary of evidence from systematic review

Author (date)	Type of review	RMD	Study type included	Outcomes	Alcohol associated with worse outcome	Key findings (negative MD/SMD favours intervention)	AMSTAR2
Buirs et al., 2016 [84]	SR	OA	Observational	Function	×	Two studies reported on association between alcohol consumption and functional ability post total hip replacement, both finding no association	Moderate
Nielsen et al., 2018 [85]	SR	Gout	Guidelines	-	✓	12/15 guidelines recommended reducing alcohol intake for gout patients. Of these, 5 guidelines rated the evidence as moderate/low quality, 7 rated the evidence as very low quality	Low

AMSTAR2 = Assessing the Methodological Quality of Systematic Reviews 2, OA = osteoarthritis, SR = systematic review

Supplementary table 29 – Rheumatoid arthritis and alcohol: evidence from individual studies

Author	Exposure detail	Study design	Inclusion criteria	Outcomes	Adjustment variables	Nb participants	Follow-up length	Age	Gender	Key findings
Bird et al., 2017 [11]	Alcohol consumption categorised as daily, heavy, moderate, mild, rare and never	Prospective cohort study	- newly diagnosed patients <12 months from initial presentation at clinic -date of onset <24 months from their initial presentation -≥18 years old -treated in a participating centre -6 months of follow-up data -had a DAS28-ESR at 24 months	DAS28-ESR remission (remission cut-off not defined)	Age and sex	1017	24 months	Mean (SD): 60.4 (14.7)	Women: N(%) 708 (70%)	Multivariable OR (95% CI) daily, moderate and heavy consumption vs never: 3.51 (1.68-7.34) mild consumption vs never: 1.25 (0.65-2.40) rare consumption vs never: 1.64 (0.99-2.70)
Davis et al., 2013 [79]	Current, past alcohol use, no alcohol use Those who used alcohol: asked to estimate the number of alcoholic drinks consumed in an average month	Prospective cohort study	-African American -ACR 1987 criteria -≤2 years disease duration at baseline	Radiographic progression (Sharp/van der Heijde score)	Age, sex, disease duration, follow-up time	166	3 years after symptom onset (1-3 years after enrollment)	Mean (SD): 51 (13)	Women: 86%	Sharp score, multivariable beta (95% CI) < 15 drinks per month: -0.005 (-0.041, 0.031) ≥ 15 drinks per month: 0.007 (0.001, 0.013)

Doran et al., 2002 [35]	Baseline alcoholism	Prospective cohort study	-RA diagnosis from 1955-1994 - aged ≥18 years -diagnosis confirmed using ACR 1987 criteria	Infections	-	609	Mean: 12.7 years	58.0 years	Women: 73.1%	Infection, hazard ratio (95% CI) Univariable: 1.91 (1.23, 2.99) Multivariable: 1.67 (1.16, 2.41) Hospitalised Infection, hazard ratio (95% CI) Univariable: 2.00 (1.27, 3.16) Multivariable: 1.85 (1.25, 2.74)
Humphreys et al., 2017 [82]	Alcohol consumption: yes/no + units of alcohol consumed per week 1 unit of alcohol = 10 mL or 8 g of pure alcohol and is used in the UK to make comparisons of alcohol consumption across different beverages.	Prospective cohort study	All patients with RA starting MTX after 1987	Episode of transaminitis (defined as alanine transaminase or aspartate aminotransferase levels of three times the upper limit of normal or higher)	Age and gender	11 839	max 30 years	Mean (SD): 61 (13.9)	Women: N(%) 8401 (71%)	Mild alcohol consumption (1-7 units per week) vs nondrinkers: HR (95% CI) = 1.02 (0.82-1.28) Moderate alcohol consumption (8-14 units per week) vs nondrinkers: HR= 0.98 (0.71-1.35) Statistically significant increase in rates of transaminitis for patients consuming over 21 units per week compared with non-drinkers: HR =1.85 (1.17 -2.93) Each increased unit of alcohol consumed was associated with a higher risk of transaminitis: HR =1.01 (1.00-1.02)
Kim et al., 2008 [77]	Alcohol consumers (alcohol consumption ≥ 1 drink per week) and nonconsumers	Retrospective cohort study	- American College of Rheumatology 1987 revised criteria for the classification of RA	Extraarticular manifestations (pericarditis, pleuritis, Felty's syndrome, cutaneous	-	405	NA	Mean (SD): 56.0 (11.74)	Women: N (%) 365 (90.1)	Occurrence of overall EAM: negative association with alcohol consumption OR=0.43 (0.21-0.91), p = 0.023

	(alcohol consumption <1 drink per week)			vasculitis, polyneuropathy, ocular involvement (e.g., scleritis, episcleritis, retinal vasculitis), glomerulonephritis, vasculitis involving other organs, amyloidosis, xerostomia, keratoconjunctivitis sicca, secondary Sjögren syndrome, pulmonary fibrosis, cervical myelopathy, and rheumatoid nodules irrespective of the sites involved)						Multivariate analysis: alcohol consumption carried a lower risk for occurrence of EAM OR=0.22 (0.09-0.54)
Lu et al., 2014 [26]	Alcohol consumption (none, 0.1–5.0, 5.1–10.0 and >10 grams per day, or gm/day). Alcohol consumption was initially measured as drinks per day and then translated into grams per day.	Prospective cohort study	RA patients with HLA-SE	-disease activity (DAS28-CRP3) -functional health status (Modified HAQ)	baseline DAS28-CRP3 or MHAQ, gender, age, race, education, seropositivity (anti-CCP antibody and/or rheumatoid factor positive), disease duration and body mass index, current drug treatments	662	4 years	Mean (SD) Alcohol Intake, gm/day : None (N=205) 60.2 (13.1) 0.1–5.0 gm/d (N=239): 55.0 (12.7) 5.1–10.0 gm/d (N=63): 52.0 (4.1) >10 gm/d (N=108): 60.0 (13.0)	Women (%) Alcohol Intake, gm/day : None (N=205) 87.3% 0.1–5.0 gm/d (N=239): 85.4% 5.1–10.0 gm/d (N=63): 81.0% >10 gm/d (N=108): 70.4%	Weak relationship with DAS28- CRP3 in seropositive RA Patients with alcohol consumption of 5.1–10.0 grams/day vs no alcohol use: lower level of Modified HAQ (MHAQ) one year later in all RA (0.34±0.02 vs. 0.40±0.02, p=0.02), as well as in seropositive (0.38±0.03 vs. 0.44±0.02, p=0.04) and seronegative RA (0.22±0.04 vs. 0.31±0.04, p=0.04) Moderate alcohol consumption: tended to reduce MHAQ only in HLA-SE positive

										patients, but not in HLA-SE negative patients
Nissen et al., 2010 [78]	Drinkers or non-drinkers of alcoholic beverages, based on the self-reported drinking status in the patient questionnaire. Patients who discontinued drinking alcohol and those who started drinking during the observation period were categorized as drinkers. Occasional drinkers, daily drinkers (consumption of alcoholic beverages on 1 occasion per day), and heavy drinkers (consumption of alcoholic beverages on several occasions per day)	Prospective cohort study	- confirmed diagnosis of RA by a rheumatologist -known alcohol consumption status, -at least 2 consecutive sets of radiographs of the hands and feet	-progression of radiographic joint damage (Ratingen score) -progression of functional disability (HAQ)	Rheumatoid factor (RF), age, sex, education level, Disease Activity Score in 28 joints (DAS28), HAQ status, DMARD therapy	2 908	3.9 years	Mean Non-drinkers: 55.7 years Alcohol drinkers: 53.9 years	Men (%) : Non-drinkers: 12 Drinkers: 32	Progression of radiographic joint damage at 1 year: in the drinkers: mean of 0.99% (0.89-1.09) in the occasional consumers: 0.99% (0.89-1.11) in the daily consumers: 0.92% (0.70-1.13) in the heavy consumers: 1.29% (0.82-1.76) in the nondrinkers: mean of 1.13% (1.01-1.26) Adjusted evolution of radiographic damage: -significantly less in occasional drinkers compared with nondrinkers (P=0.01) and in daily drinkers compared with nondrinkers (P=0.001) -significantly worse in heavy drinkers compared with occasional and daily drinkers (P<0.001) Progression of functional disability: more favorable evolution in the drinkers Increase in HAQ scores at 5 years of 0.36

										(0.32-0.41) in the drinkers vs 0.41 (0.35-0.46) in the nondrinkers No significant effect modification in HAQ scores by the quantity of alcohol consumption
Sageloli et al., 2018 [83]	Self-declared consumption of alcohol (grams/day) 3 categories according to the French recommendations of consumption thresholds [abstinent; moderate consumption, defined as ≤ 20 g/day for women and ≤ 30 g/day for men; and abuse, i.e. > 20 g/day for women and > 30 g/day for men]	Prospective cohort study	Patients with at least two joints affected by synovitis for more than 6 weeks and less than 6 months at baseline, and not undergoing treatment with synthetic or biological disease-modifying anti-rheumatic drugs (bDMARDs) at inclusion	Occurrence of radiological disease progression (increase to 5 points of the Sharp/van der Heijde score)	age, baseline erosion, rheumatoid factor, anti-citrullinated peptide antibody, smoking status, body mass index, and treatment with leflunomide or methotrexate and biologics	596	60 months	Median (IQR) Non-consumers: 50.1 (38.9; 56.9) / Moderate consumers: 53.7 (44.7; 59.4) / Abusers: 56.1 (51.5; 57.0)	Women: N (%) Non-consumers: 399 (80.9) Moderate consumers: 50 (62.5) Abusers: 13 (56.5)	No significant difference in radiological progression according to the different drinker groups (abstinent, moderate, abuse) at 12 and 36 months At 36 months, radiological progression in female consumers: OR = 1.17 (0.72-1.91), p = 0.532 in male consumers: OR = 0.57 (0.26-1.24), p = 0.159 At 60 months: Significant deleterious effect of moderate consumption in women: OR = 1.73 (1.01-2.96), p = 0.045 Trend towards a protective effect of moderate consumption in men: OR = 0.50 (0.21-1.16), p = 0.106

Supplementary table 30 – Rheumatoid arthritis and alcohol: methodological quality of individual studies

Authors	Study participation	Study attrition	Prognostic factor measurement	Outcome measurement	Study confounding	Statistical analysis and reporting	Quality
Bird et al., 2017 [11]	Low risk of bias	High risk of bias	Low risk of bias	Low risk of bias	Moderate risk of bias	Low risk of bias	Low
Davis et al., 2013 [79]	Low risk of bias	High risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low
Doran et al., 2002 [35]	Low risk of bias	High risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low
Humphreys et al., 2017 [82]	Low risk of bias	Moderate risk of bias	Low risk of bias	Low risk of bias	Moderate risk of bias	Low risk of bias	Moderate
Kim et al., 2008 [77]	Low risk of bias	High risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low
Lu et al., 2014 [26]	Low risk of bias	High risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low
Nissen et al., 2010 [78]	Low risk of bias	High risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low
Sageloli et al., 2018 [83]	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	High

Supplementary table 31 – Systemic lupus erythematosus and alcohol: evidence from individual studies

Author	Exposure detail	Study design	Inclusion criteria	Outcomes	Adjustment variables	Nb participants	Follow-up length	Age	Gender	Key findings
Jonsen et al., 2007 [76]	Alcohol intake 3 groups: 1) patients with an intake of 15 g alcohol per month, 2) patients with an intake of 15 g per month but 150 g per week, and 3) patients with an intake of 150 g alcohol per week	Prospective cohort study	Patients with at least four ACR classification criteria for SLE - clinical diagnosis of SLE, with at least two manifestations characteristic of SLE together with anti-nuclear antibodies	Cerebrovascular, cardiovascular and peripheral arterial organ damage (SLICC/ACR-DI), susceptibility to infections	-	138	Median follow-up time: 14 years (range 0–40)	Median age at diagnosis: 40 years (range 10–83)	121 women	Alcohol intake > 15 g/month: inversely correlated to development of cerebrovascular, cardiovascular and peripheral arterial organ damage (CPAD), p=0.007 Significant association between presence of CPAD and alcohol intake > 15 g/month: OR= 0.29 (0.096–0.870) No association between severe infection and alcohol intake

Supplementary table 32 – Systemic lupus erythematosus and alcohol: methodological quality of individual studies

Authors	Study participation	Study attrition	Prognostic factor measurement	Outcome measurement	Study confounding	Statistical analysis and reporting	Quality
Jonsen et al., 2007 [76]	Low	Moderate	Low	Low	Low	Low	Moderate

Supplementary table 33 – Gout and alcohol: evidence from individual studies

Author	Exposure detail	Study design	Inclusion criteria	Outcomes	Adjustment variables	Nb participants	Follow-up length	Age	Gender	Key findings
Alvarez-Nemegyei et al., 2005 [73]	history of alcoholism	Observational study (prospective cohort)	Primary gout based on Wallace criteria Exlcusions: secondary gout, no classification of renal failure on MSK disability	MSK physical disability defined as either ACR functional class >2 or >0.5 on HAQ Renal failure was defined as moderately or severely diminished glomerular filtration rate (GFR; < 60 ml/min/1.73 m2), based on the National Kidney Foundation criteria19,20.	-	90	unclear	54 (12)	2 (2.2%) female	alcoholism , N(%) 41/42 patients with MSK disability had history of alcoholism, whereas 44/48 patients with no MSK disability had history of alcoholism p=0.22 Renal failue, N(%) 24/25 patients with renal failure had history of alcoholism, whereas 52/55 patients without renal failure had history of alcoholism p=0.78
Hanvivadhanakul et al., 2015 [81]	Alcohol intake	Retrospective case note review	-ICD10 code M10.0	Achieved American College of Rheumatology recommended uric acid concentration within 6 months	-	139	6 months	Mean (SD): 61 (13.06)	Men: N (%) 108 (77%)	Number (%) of alcohol consumers in the responders/no response groups: Responders: 0 (0) No response: 12 (12.9), p=0.015

Neogi et al., 2014 [80]	Alcohol intake over the prior 24 hours and type of alcoholic beverage Alcohol intake included the number of servings of wine, beer (including light beer, ciders, and malt beverages), or liquor (either straight or in a mixed drink) consumed during the prior 24-hour period for control and hazard periods. Total amount of alcohol intake (grams/day) estimated based on number of servings reported in a 24-hour period Total amount of alcohol consumption: seven categories: no alcohol consumption, >0–1 drink, >1–2, >2–4, >4–6, >6–8, and more than 8 drinks. Moderate alcohol intake is considered to be no more than 2 drinks per day for men and no more than 1 drink per day for women.22 We grouped the daily consumption of each specific alcoholic beverage into the following categories based on their distribution: for wine, no wine consumption,	Prospective cohort study	-reported gout attack within the previous year -age 18 years or older -residents of the US -informed consent - American College of Rheumatology (ACR) Preliminary Classification Criteria for Gout	Gout attacks	diuretic use, purine intake, gout-related medication use (allopurinol, colchicine, NSAIDs, other urate-lowering therapies), and water intake	724	1 year	Mean (SD): 54.5 (12.5) year	Male: N (%) 568 (78.5)	Having up to one drink in a 24-hour period (vs no alcohol intake): OR=1.13 (0.80-1.58) Consuming >1-2 drinks in a 24-hour period (vs no alcohol intake) : OR=1.36 (1.00-1.88) Moderate alcohol consumption (i.e., up to 2 drinks/day for men and up to 1 drink/day for women) (vs any alcohol in the prior 24-hour period): Men: OR=1.41 (1.00–2.01) Women: OR=1.06 (0.49–2.30) Each type of alcoholic beverage intake associated with an increased risk of recurrent gout attacks Consuming 0–1 servings of wine over the prior 24 hours: OR= 1.25 (0.87-1.80) > 1–2 OR= 2.38 (1.57-3.62) > 2 OR= 1.41 (0.86–2.32) Consuming > 0–2 servings of beer over the prior 24 hours: OR= 1.29 (0.91-1.83) > 2–4 OR= 1.75 (1.19-2.59) > 4–6

	>0–1, >1–2, and >2 servings; for beer and for liquor, no consumption, >0–2, >2–4, >4–6, and >6 servings.									OR= 2.60 (1.40-4.81) > 6 OR= 2.32 (1.25-4.31) Consuming > 0–2 servings of hard liquor over the prior 24 hours: OR= 0.92 (0.62-1.37) > 2–4 OR= 1.67 (1.00-2.78) > 4–6 OR= 1.56 (0.95-2.57) > 6 OR= 2.79 (1.26-6.16)
Su et al., 2008 [74]	Tobacco use	Retrospective cohort study	-male primary gout subjects -meet criteria for clinically defined gout	Renal function deterioration (based on creatinine levels)	-	318	Subjects with renal function deterioration: 81.20 (53.29) months Subjects without renal function deterioration: 92.41 (46.72) months	Subjects with renal function deterioration: 57.21 (13.02) Subjects without renal function deterioration: 62.5 (14.98)	318 men	Association between alcohol consumption & deterioration of renal function: p= 0.17 (univariate analysis)
Vandenberg et al., 1994 [75]	Current chronic alcoholics, alcoholics who stated they had abstained for 2 years or longer, non alcoholics	Prospective cohort study	All consultations for acute gouty arthritis received by the Rheumatology section at MacGuire VA Medical Center for March 1990, throughJuly 1991	Levels of serum urate during acute gout flares	-	53	2 years	Chronic alcoholics: 61.9 Reformed alcoholics: 68.28 Non-alcoholics: 67.3	NA	Levels of serum urate during attack were significantly lower in patients with chronic alcoholism compared with non-alcoholic patients (p<0.015) Chronic alcoholics : 7.7 ± 1.3 mg/dL Reformed alcoholics : 8.7 ± 1.4 mg/dL Non-alcoholics : 10.1 ± 1.3 mg/dL

Supplementary table 34 – Gout and alcohol: methodological quality of individual studies

Authors	Study participation	Study attrition	Prognostic factor measurement	Outcome measurement	Study confounding	Statistical analysis and reporting	Quality
Alvarez-Nemegyei et al., 2005 [73]	Moderate risk of bias	High risk of bias	Low risk of bias	Low risk of bias	Moderate risk of bias	Low risk of bias	Low
Hanvivadhanakul et al., 2015 [81]	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	High risk of bias	Low risk of bias	Low
Neogi et al., 2014 [80]	Low risk of bias	High risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	Low
Su et al., 2008 [74]	Low risk of bias	High risk of bias	Low risk of bias	Low risk of bias	Moderate risk of bias	Low risk of bias	Low
Vandenberg et al., 1994 [75]	Low risk of bias	Low risk of bias	Low risk of bias	Low risk of bias	High risk of bias	Low risk of bias	Low

Supplementary table 35 – PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	1
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	4
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	5
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	5
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	6
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	5-6
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	Tables S1-S5
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	6-7
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	6-7
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	6-7 + Table S5
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	6-7
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	6
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	7
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	6-7
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	NA
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	NA
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	6-7

Section and Topic	Item #	Checklist item	Location where item is reported
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	NA
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	NA
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	NA
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	7 + table S6
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	7 + Fig S1-S4
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	Fig S1-S4
Study characteristics	17	Cite each included study and present its characteristics.	7-13 + Suppl. tables
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	7-13 + Suppl. tables
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	7-13 + Suppl. tables
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	7-13
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	NA
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	NA
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	NA
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	NA
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	7-13 + Suppl. tables
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	13-15
	23b	Discuss any limitations of the evidence included in the review.	14-15
	23c	Discuss any limitations of the review processes used.	14-15
	23d	Discuss implications of the results for practice, policy, and future research.	14-15
OTHER INFORMATION			
Registration and	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	NA

Section and Topic	Item #	Checklist item	Location where item is reported
protocol	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	NA
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	NA
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	16
Competing interests	26	Declare any competing interests of review authors.	16
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	NA

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