Appendix A. Technical Expert Panel and Peer Reviewers

Technical Expert Panel Members

Name	Organization
Timothy G. Beukelman, MD	University of Alabama at Birmingham (American College of Rheumatology)
Dennis Dietzen, PhD	Washington University School of Medicine, St. Louis, MO (American Association for Clinical Chemistry)
James N. Jarvis, M.D.	Oklahoma University Health Sciences Center, Oklahoma City (American Academy of Pediatrics)
Charles H. Spencer, M.D.	Ohio State University, Columbus (American Academy of Pediatrics)

Peer Reviewers

Name	Organization
TBD	

Appendix B. Literature Search Strings

Title: ANA RF Anti CCP Testing Search Strategies
Database: MEDLINE , 1950 - present
Search name: ANA RF Anti CCP Testing -MEDLINE -
Notes: limits: human, 1960-2009
Date searched: Jan 21, 2010
Results: 5389 (S116)

1. citrulline/	35. or/14-15,19-27,31-34
2. exp Peptides, Cyclic/	36. Arthritis/
3. 1 and 2	37. ($arthritis or ($articular adj arthritis)).ti,ab.
4. ((anti adj ccp) or (citrullinated adj peptide*)).mp.	38. or/36-37
5. ((citrulline adj antibod*) or (anti-citrulline adj antibod*)).ti,ab.	39. exp child/ or (adolesc* or early or juvenile).ti,ab.
6. exp Antibodies, Antinuclear/	40. (JIA or JRA).ti,ab.
7. ((antinuclear adj antibod*) or (antinuclear adj factor*)).ti,ab.	41. or/39-40
8. (ana adj titer).ti,ab.	42. 38 and 41
9. (ANA adj2 test*).ti,ab.	43. exp Arthritis, Juvenile Rheumatoid/
10. (FANA adj2 test*).ti,ab.	44. ((juvenile or early) adj (rheumatoid or idiopathic) adj arthritis).ti,ab.
11. exp Rheumatoid Factor/	45. or/42-44
12. (rheumatoid adj factor*).ti,ab.	46. or/14-15,19,21-27,31-34,45
13. or/3-12	47. incidence/
14. exp Lupus Erythematosus, Systemic/	48. prevalence/
15. (JSLE or SLE or "lupus erythematosus").ti,ab.	49. exp disease progression/
16. exp Pain/di, et	50. Natural History/
17. Growth/ph	51. natural history.ti,ab.
18. (grow* and (pain or pains)).ti,ab.	52. or/47-51
19. 16 and (17 or 18)	53. exp Mass Screening/
20. musculoskeletal diseases/ or arm/ or leg/ or extremities/	54. exp "referral and consultation"/
21. 16 and 20	55. (screen* or refer*).ti,ab.
22. Fibromyalgia/	56. or/53-55
23. fibromyalgia.ti,ab.	57. exp "Reproducibility of Results"/
24. exp arthralgia/	58. exp "Sensitivity and Specificity"/
25. arthralgia.ti,ab.	59. Predictive Value of Tests/
26. ((joint* adj pain*) or (limb* adj pain*)).ti,ab.	60. (di or bl or cl or im).fs.
27. limp*.ti,ab.	61. exp Diagnostic Errors/
28. benign.ti,ab.	62. early diagnosis/
29. exp Joint Instability/	63. exp delayed diagnosis/
30. (joint adj (instability or hypermobility)).ti,ab.	64. Diagnosis, Differential/
31. 28 and (29 or 30)	65. or/57-64
32. Patellofemoral Pain Syndrome/	66. (cost or costs or economic*).ti,ab.
33. (patellofemoral adj pain adj syndrome).ti,ab.	67. exp "Costs and Cost Analysis"/
34. exp Synovitis/ or synovitis.mp.	68. cost-benefit analysis/
71. exp demography/	69. ec.fs.
72. age factors/ or "age of onset"/	70. or/66-68
73. sex factors/	95. (Pubert* or Pubescen* or Prepubescen*).mp.
74. infection/ or infection*.ti,ab.	96. exp Pediatrics/
75. anxiety/ or (anxious* or anxiety).ti,ab.	97. (Pediatric* or Paediatric* or Peadiatric*).mp.
76. comorbidity/	98. exp Schools/
77. or/71-76	99. (Nursery school* or Kindergar* or Primary school* or Secondary school* or Elementary school* or High school* or Highschool*).mp.
78. exp Rheumatic Diseases/di, co, et, im, pa, pp	100. or/85-99
79. exp Connective Tissue Diseases/di, co, et, im, pa, pp	101. adolescent/ and adult/
80. exp arthritis/di, co, et, im, pa, pp	102. 100 not 101
81. arthritis, rheumatoid/di, co, et, im, pa, pp	103. (52 or 56) and 35 and 102
82. arthritis, juvenile rheumatoid/di, co, et, im, pa, pp	104. 13 and 102 and 65 and (84 or 46)
83. exp Lupus Erythematosus, Systemic/di, co, et, im, pa, pp	105. 13 and 46 and 102
	106. 13 and (56 or 65) and 46 and 102

84. or/78-83 85. exp infant/ 86. (Infant* or infancy or Newborn* or Baby* or Babies or Neonat* or Preterm* or Prematur* or Postmatur*).mp. 87. exp Child/ 88. (Child* or Schoolchild* or School age* or Preschool* or Kid or kids or Toddler*).mp. 89. exp Adolescent/ 90. Adoles*.mp. 91. (Teen* or Boy* or Girl*).mp. 92. exp Minors/ 93. minors*.mp. 94. exp Puberty/	107. 13 and 77 and 102 108. (13 or 84) and 70 109. 13 and (35 or 45) and 102 110. 77 and 65 and 13 and 102 111. (52 or 56) and (45 or 84) and 102 112. 13 and (56 or 65) and 70 113. 13 and 70 114. or/103-113 115. humans/ NOT (humans/ and animals/) 116. 114 AND 115

Topic: ANA RF Anti CCP Testing Search Strategies
Database: EMBASE, 1980 - present
Search name: ANA RF Anti CCP Testing - EMBASE-amy

Notes: limits of: english, human, 1980-2009
Date searched: Jan 21, 2010
Results: 4849 (S108)

1. cyclic citrullinated peptide/ 2. ((anti adj ccp) or (citrullinated adj peptide*)).mp. 3. ((citrulline adj antibod*) or (anti-citrulline adj antibod*)).ti,ab. 4. exp Antinuclear Antibody/ 5. ((antinuclear adj antibod*) or (antinuclear adj factor*)).ti,ab. 6. (ana adj titer).ti,ab. 7. (ANA adj2 test*).ti,ab. 8. (FANA adj2 test*).ti,ab. 9. exp Rheumatoid Factor/ 10. rheumatoid factor*.ti,ab. 11. or/1-10 12. exp Systemic Lupus Erythematosus/ 13. (JSLE or SLE or "lupus erythematosus").ti,ab. 14. (grow* and (pain or pains)).ti,ab. 15. musculoskeletal diseases/ or arm/ or leg/ or extremities/ 16. pain/di, et 17. 15 and 16 18. exp arthralgia/ 19. arthralgia.ti,ab. 20. ((joint* adj pain*) or (limb* adj pain*)).ti,ab. 21. limp*.ti,ab. 22. Fibromyalgia/ 23. fibromyalgia.ti,ab. 24. benign.ti,ab. 25. exp Joint Instability/ or Joint hypermobility/ 26. (joint adj (instability or hypermobility)).ti,ab. 27. 24 and (25 or 26) 28. Patellofemoral Pain Syndrome/ 29. patellofemoral joint/ and pain/ 30. (patellofemoral adj pain adj syndrome).ti,ab. 31. knee pain/ or ankle pain/ 32. exp Synovitis/ or synovitis.mp. 33. "complex regional pain syndrome"/ 34. or/12-23,27-33	37. or/35-36 38. exp child/ or (adolesc* or early or juvenile).ti,ab. 39. (JIA or JRA).ti,ab. 40. or/38-39 41. 37 and 40 42. exp Juvenile Rheumatoid Arthritis/ 43. ((juvenile or early) adj (rheumatoid or idiopathic) adj arthritis).ti,ab. 44. or/41-43 45. incidence/ or prevalence/ or seasonal variation/ 46. exp disease course/ 47. natural history.ti,ab. 48. or/45-47 49. exp mass screening/ or screening/ 50. exp "referral and consultation"/ 51. (screen* or refer*).ti,ab. 52. or/49-51 53. Differential Diagnosis/ 54. exp Reproducibility/ 55. exp "sensitivity and specificity"/ 56. Predictive Value of Tests/ 57. serodiagnosis/ 58. (di or bl or cl or im).fs. 59. exp Diagnostic Error/ 60. "diagnostic techniques and procedures"/ 61. diagnostic procedure/ 62. early diagnosis/ 63. Diagnostic Accuracy/ 64. physical examination/ 65. blood examination/ 66. "Pain Assessment"/ 67. or/53-66 68. (cost or costs or economic*).ti,ab. 69. exp economic aspect/ 70. cost-benefit analysis/ 71. ec.fs. 72. or/68-70

35. Arthritis/ 36. ($arthritis or ($articular adj arthritis)).ti,ab. 75. gender/ or sex difference/ 76. infection/ or infection*.ti,ab. 77. anxiety/ or (anxious* or anxiety).ti,ab. 78. comorbidity/ 79. or/73-78 80. exp newborn/ 81. (Infant* or infancy or Newborn* or Baby* or Babies or Neonat* or Preterm* or Prematur* or Postmatur*).mp. 82. exp Child/ 83. (Child* or Schoolchild* or School age* or Preschool* or Kid or kids or Toddler*).mp. 84. exp Adolescent/ 85. Adoles*.mp. 86. (Teen* or Boy* or Girl*).mp. 87. (minors* or juvenil*).mp. 88. exp Adolescence/ 89. (Pubert* or Pubescen* or Prepubescen*).mp. 90. exp Pediatrics/	73. exp demography/ or geographic distribution/ 74. age/ 91. (Pediatric* or Paediatric* or Peadiatric*).mp. 92. exp school/ or high school/ or kindergarten/ or middle school/ or nursery school/ or primary school/ 93. (Nursery school* or Kindergar* or Primary school* or Secondary school* or Elementary school* or High school* or Highschool*).mp. 94. or/80-93 95. (48 or 52) and 67 and 34 and 94 96. 11 and 94 and 67 and (34 or 44) 97. 11 and 94 and (34 or 44) 98. 11 and (67 or 52) and (34 or 44) and 94 99. 11 and 79 and 94 100. 11 and 79 and 67 101. 11 and 72 and (44 or 94) 102. 11 and 72 and (34 or 44) and 94 and 67 103. 11 and 94 and 67 104. or/95-103 105. adolescent/ and adult/ 106. 104 not 105 107. humans/ and animals/ 108. 106 not 107

Topic: ANA RF Anti CCP Testing Search Strategies
Database: CINAHL , 1960-present
Notes: limits of: english, human, 1980-2009
Date searched: Jan 21, 2010
Topic: ANA RF Anti CCP Testing Search Strategies
Database: Cochrane Library – CDSR and CENTRAL
Notes: limits: english only, human, 1960-2009
Date searched: Feb 2010
Results: 216

#1(citrulline OR anti-ccp) or (rheumatoid factor) or (citrullinated peptide) or (antinuclear AND (antibod* OR factor*)) or (ANA OR FANA) and test* in Cochrane Reviews and Clinical Trials
#2 (lupus) or (JSLE OR SLE) or (limb or grow*) AND pain or (fibromyalgia) or (arthralgia) in Cochrane Reviews and Clinical Trials
#3 (joint AND (instability OR hypermobility)) or (patellofemoral pain syndrome) or (synovitis) or (JRA OR JIA) or (juvenile OR early) AND (rheumatoid OR idiopathic) AND arthritis in Cochrane Reviews and Clinical Trials
#4 (#2 OR #3)
#5 (incidence OR prevalence) or (disease AND (progression OR history)) or (natural history) in Cochrane Reviews and Clinical Trials
#6 (mass screening) or (screen*) or (refer*) or (consultation) or (referral and consultation) in Cochrane Reviews and Clinical Trials
#7 (sensitivity OR specificity) or (diagnostic error*) or (early diagnosis) or (delayed diagnosis) or (differential diagnosis) in Cochrane Reviews and Clinical Trials
#8 (demography) or (age of onset) OR (age factors) or (sex factors) or (infection) or (anxiety OR anxious*) in Cochrane Reviews and Clinical Trials
#9 (child*) or (adolescen*) or (infant* OR infancy OR newborn* OR baby OR babies) or (pediatric* OR paediatric*) in Cochrane Reviews and Clinical Trials
#10 (#1 AND #4 AND #7 AND #9) 42 edit delete #11 (#1 AND #4 AND #9)
#12 (#1 AND #8 AND #9) 185 edit delete #13 (#1 AND #4 AND #6 AND #9)
#14 (#4 AND #6 AND #9) 642 edit delete #15 ((#5 OR #6) AND #4 AND #9)
#16 (#10 OR #11 OR #12 OR #13 OR #14 OR #15)
#17 (#16), from 1960 to 2009
#18 (#10 OR #11 OR #12 OR #13)
#19 (#10 OR #11 OR #12 OR #13), from 1960 to 2009

Topic: ANA RF Anti CCP Testing Search Strategies
Database: Web of Science (ISI): Science Expanded, Social Sciences Expanded
Notes: limits: english only, human, 1980
Date searched: 9Feb10
Results: 856 (line #17)a

#17= #14 OR #13 OR #12 OR #10 OR #8
Refined by: Languages=(ENGLISH)
Databases=SCI-EXPANDED, SSCI Timespan=1960-2009
# 16= #14 OR #13 OR #12 OR #10 OR #8
Databases=SCI-EXPANDED, SSCI Timespan=1960-2009

# 15= #14 OR #12 OR #10 OR #8
Databases=SCI-EXPANDED, SSCI Timespan=1960-2009

# 14= #7 AND #6 AND #5 AND #1
Databases=SCI-EXPANDED, SSCI Timespan=1960-2009

# 13= #7 AND #6 AND #1
Databases=SCI-EXPANDED, SSCI Timespan=1960-2009

# 12= #11 AND #7 AND #5 AND #2
Databases=SCI-EXPANDED, SSCI Timespan=1960-2009

# 11= #4 OR #3
Databases=SCI-EXPANDED, SSCI Timespan=1960-2009

# 10= #9 AND #7 AND #2 AND #1
Databases=SCI-EXPANDED, SSCI Timespan=1960-2009

# 9= #5 OR #4
Databases=SCI-EXPANDED, SSCI Timespan=1960-2009

# 8= #7 AND #5 AND #2 AND #1
Databases=SCI-EXPANDED, SSCI Timespan=1960-2009

# 7= Topic=(infant*) OR Topic=(child*) OR Topic=(adolescen*) OR Topic=(pediatric* OR paediatric*)
Databases=SCI-EXPANDED, SSCI Timespan=1960-2009

# 6= Topic=(demography) OR Topic=((age factor*) OR (age of onset)) OR Topic=(sex factor* OR gender) OR Topic=(infection*) OR Topic=(anxiety*) OR Topic=(comorbid*)
Databases=SCI-EXPANDED, SSCI Timespan=1960-2009

# 5= Topic=(early diagnos*) OR Topic=(differential diagnos*) OR Topic=(delayed diagnos*) OR Topic=(diagnostic error*)
Databases=SCI-EXPANDED, SSCI Timespan=1960-2009

# 4= Topic=(screen*) OR Topic=(referral OR refer*) OR Topic=(consultation OR consult*)
Databases=SCI-EXPANDED, SSCI Timespan=1960-2009
# 3= Topic=(incidence) OR Topic=(prevalence) OR Topic=(disease progression) OR Topic=(disease history) OR Topic=(natural history)
Databases=SCI-EXPANDED, SSCI Timespan=1960-2009

# 2= Topic=(JSLE OR SLE OR lupus OR JIA OR JRA) OR Topic=((limb pain) OR (grow* pain)) OR Topic=(fibromyalgia OR arthralgia) OR Topic=(joint AND (instability OR hypermobility)) OR Topic=((patellofemoral pain syndrome) OR synovitis) OR Topic=((juvenile OR early) AND (rheumatoid OR idiopathic) and arthritis)
Databases=SCI-EXPANDED, SSCI Timespan=1960-2009

1= Topic=(antinuclear AND (antibod* OR factor* OR test*)) OR Topic=(anti-ccp OR (citrullinated peptide)) OR Topic=((ANA OR FANA) AND (test*)) OR Topic=(rheumatoid factor*)

Databases=SCI-EXPANDED, SSCI Timespan=1960-2009

Topic: ANA RF Anti CCP Testing Search Strategies
Database: Academic Science Complete (EBSCO)
Notes: Limits: same as above
Date searched: 9Feb10
Results: 226

S20= S17 or S18 Limiters - Published Date from: 19600101-20091231
S19= S17 or S18
S18= S14 NOT S16
S17= S14 and S15
S16= Animal
S15= Human
S14= S8 or S9 or S10 or S11 or S12 or S13
S13= S2 and S5 and S7
S12= S2 and S4 and S7
S11= S1 and S2 and S4 and S7
S10= S1 and S2 and S7
S9= S1 and S3 and S6 and S8
S8= S1 and S2 and S3 and S7
S7= Children or Pediatric or Paediatric or Infant or Adolescent or Adolescence
S6= Demography or Gender or Anxiety or Infection
S5= Incidence or Prevalence or Natural history
S4= Screening or Referral or Consultation
S3= Diagnostic errors or Diagnosis
S2= Lupus or Rheumatoid arthritis or Fibromyalgia or Synovitis
S1= citrulline or anti-ccp or Rheumatoid factor

Database	Dates searched	Date search ran	Number of results
MEDLINE (OVID)	1960-2009	14Jan10	5389
EMBASE (OVID)	1980-2009	14Jan10	4849
CINAHL (EBSCO)	1960-2009	14Jan10	374
CDSR & CENTRAL (Cochrane)	1960-2009	9Feb10	216
Web of Science (ISI)	1960-2009	9Feb10	856
Academic Search Complete (EBSCO)	1960-2009	9Feb10	226
TOTAL RESULTS			**11910**

Search alerts:

1) PubMed
2) Web of Science
3) Scopus – Forward searching only

Appendix C. Inclusion/Exclusion Form

ANA, RF, and CCP Testing in Pediatric Populations

INCLUSION/EXCLUSION FORM

Reviewer's initial: Ref ID:

Criteria	Decision
1. **REPORT OF PRIMARY RESEARCH**	
2. **POPULATION** (at least two of the followings)	
a. Children and adolescents aged 18 years or younger	
AND (any of the followings)	
b1. Diagnosed with SLE or JIA/JRA/Still's disease	☐
b2. With undiagnosed limb pains	☐
b3. Given index test results	☐
3. **INDEX TEST** (any of the followings)	
a. Antinuclear antibody (ANA)*	☐
b. Rheumatoid factor (RF)†	☐
c. Cyclic-citrullinated peptide (CCP)	☐
EXCLUDE IF	
*Using non-human substrate for ANA or published before 1980	☐
†Testing for hidden RF	☐
4. **REFERENCE STANDARD**	
a. Clinical diagnosis of SLE or JIA/JRA/Still's disease	
5. **REPORT OF NUMERICAL DATA** (any of the following)	
a. Data sufficient to compute a 2x2 table	☐
b. Data on subsequent impacts due to test results	☐

Comments:

REVIEWER'S DECISION‡:

FINAL DECISION:

Foreign language (if applicable):

‡Reason for exclusion (if applicable):

Article excluded, but may inform the followings:

- ☐ Background
- ☐ KQ1a
- ☐ KQ1b
- ☐ KQ2

Appendix D. List of Excluded Studies

EXCLUDED STUDIES (N = 425)

The following studies failed to meet at least one of the pre-specified inclusion criteria.

Study design (N = 127)

The following studies were excluded because they were not reports of primary research.

1. Abbassian A. The limping child: a clinical approach to diagnosis. Br J Hosp Med 2007;68(5):246-50.
2. Agarwal V, Mahajan A. Laboratory tests in rheumatology: Rational utilization and interpretation. JK Science 2004;6(1):52-5.
3. Al-Mendalawi MD. Juvenile systemic lupus erythematosus in Bahrain. A tertiary referral center experience. Saudi Med J 2009;30(9):1240-1.
4. Ansell BA. Rheumatoid disease, laboratory data. CRC Crit Rev Clin Lab Sci 1972;3(2):193-201.
5. Ansell BM. Juvenile chronic arthritis, juvenile rheumatoid arthritis, and inflammatory arthropathies of childhood. Curr Opin Rheumatol 1990;2(5):799-803.
6. Ballardini P, Busachi CA, Amoresano A, et al. Prevalence of rheumatoid factors in juvenile rheumatoid arthritis. Clin Exp Rheumatol 2010;9(5):548.
7. Banerjee P, Crain B. 2-year-old girl with right leg weakness. Brain Pathol2008;18(4):608-10.
8. Baum J, Fink C. Juvenile rheumatoid arthritis in monozygotic twins: a case report and review of the literature. Arthritis Rheum 1968;11(1):33-6.
9. Bizzaro N, Wiik A. Appropriateness in anti-nuclear antibody testing: from clinical request to strategic laboratory practice. Clin Exp Rheumatol 2004;22(3):349-55.
10. Bloch-Michel H, Waltzing P, Brauner M, et al. The rosette rheumatoid test in seronegative juvenile-infantile polyarthritis [French]. Ann Med Interne (Paris) 1972;123(4):375-9.
11. Bodman-Smith MD, Fife MF, Wythe H, et al. Anti-BiP antibody levels in juvenile idiopathic arthritis (JIA). Rheumatology 2004;43(10):1305-6.
12. Bonagura VR, Ilowite NT, Hatam L, et al. Expression of the major rheumatoid factor cross-reactive idiotype in pediatric patients with systemic lupus erythematosus. Clin Immunol Immunopathol 1991;60(2):232-43.
13. Boone JE, Baldwin J, Levine C. Juvenile rheumatoid arthritis. Pediatr Clin North Am 1974;21(4):885-915.
14. Brady M. The child with a limp. J Pediatr Health Care 1993;7(5):226-8.
15. Bresnihan FP, Ansell BM. Effect of penicillamine treatment on immune complexes in two cases of seropositive juvenile rheumatoid arthritis. Ann Rheum Dis 1975;35(5):463-5.
16. Brizard J. Chronic inflammatory rheumatism in children [French]. Cahiers de Medecine 1972;13(3):167-79.
17. Brown RJ. Introduction to the special issue on medically unexplained symptoms: background and future directions. Clin Psychol Rev 2007;27(7):769-80.
18. Bruneau CD, Edmonds JP, Hughes GR, et al. Detection and characterization of DNA-anti-DNA complexes in a patient with systemic lupus erythematosus. Clin Exp Immunol 1977;28(3):433-6.
19. Buc M, Parnicka Z, Rovensky J, et al. Juvenile idiopatic arthritis an overview of current status in immunopathogenesis, immunogenetic, and immunotherapy [Slovak]. Rheumatologia 2006;20(4):209-14.
20. Carreno PL. Practical value of immunologic changes in juvenile chronic arthritis] [Spanish]. An Esp Pediatr 1993;39:Suppl-30.
21. Chamberlain MA. Referral of chronic arthritics. Br Med J (Clin Res Ed) 1984;288(6414):347-8.
22. Childhood SLE. S Afr Med J 2005;95(6):363.
23. Day NK, Geiger H, McLean R, et al. C2 deficiency. Development of lupus erythematosus. J Clin Invest 1973;52(7):1601-7.
24. Diagnosis, development and treatment principles of systemic lupus erythematosus [French]. Ann Dermatol Venereol 2000;127(SPEC.ISS. 1):A167-A173.
25. Dumas M, Loyau G. Diagnostic problems raised by polyarthritis of an inflammatory nature [French]. Sem Hop Ther 1972;48(9):645-8.
26. Gandon-Laloum S. Growth and limb pains [French]. Arch Pediatr 2006;13(6):550-2.
27. Ganley TJ, Gaugles RL, Moroz LA. Consultation with the specialist: patellofemoral conditions in childhood. Pediatr Rev 70 A.D.;27(7):264-9.
28. Gilbert NF, Deavers MT, Madewell JE, et al. A 16-year-old girl with pain and swelling in the medial clavicle. Clin Orthop Related Res 2008;466(12):3158-62.
29. Goeb V, Jouen F, Gilbert D, et al. Diagnostic and prognostic usefulness of antibodies to

citrullinated peptides. Am J Med 2009;76(4):343-9.
30. Goldenberg DL. Diagnosis and Differential Diagnosis of Fibromyalgia. Am J Med 2009;122(12 SUPPL.):S14-S21.
31. Gomez AP, Atrio AIS, Nieves AIT, et al. Differential diagnostic protocol of arthritis in infancy and adolescence [Spanish]. Medicine 2009;10(29):1972-5.
32. Gomez AP, Atrio AIS, Hernandez FA, et al. Juvenile idiopathic arthritis [Spanish]. Medicine 2009;10(29):1933-41.
33. Gottlieb BS, Ilowite NT. Systemic lupus erythematosus in children and adolescents. Pediatr Rev 2006;27(9):323-30.
34. Gough-Palmer A, McHugh K. Investigating hip pain in a well child. BMJ: Br Med J 2007;334(7605):1216-7.
35. Goumy L. Idiopathic juvenile polyarthritis [French]. Presse Med 2001;30(3):137-42.
36. Gregg S. Rheumatoid arthritis in childhood. Ariz Med 1971;28(8):577-85.
37. Gunther KP, Thielemann F, Bottesi M. Anterior knee pain in children and adolescents. Diagnosis and conservative treatment [German]. Orthopade 2003;32(2):110-8.
38. Gupta K, Chintu C, Raghu MB. Juvenile rheumatoid arthritis in Zambian children. East Afr Med J 1981;58(5):344-53.
39. Hanson V. The subtypes of juvenile rheumatoid arthritis and their significance. Ryumachi 1991;31(6):592-8.
40. Haustein UF, Sonnichsen N. Lupus erythematodes in childhood--a virus-induced autoimmune disease? [German]. Padiatr Grenzgeb 1974;13(2-3):163-76.
41. Hinze C, Brunner HI. Pediatric rheumatology - Its own specialty. Nat Clin Pract Rheumatol 2008;4(6):279.
42. Hull RG. Guidelines for management of childhood arthritis. Rheumatology 2001;40(11):1309-12.
43. Hunter PJ, Wedderburn LR. Pediatric rheumatic disease: Can molecular profiling predict the future in JIA? Nat Rev Rheumatol 2009;5(11):593-4.
44. Illei GG, Klippel JH. Why is the ANA result positive? Bull Rheum Dis 1999;48(1):1-4.
45. Irias JJ. Hydralazine-induced lupus erythematosus-like syndrome. Am J Dis Child 1975;129(7):862-4.
46. Iwata N, Mori M, Miyamae T, et al. Sjogren's syndrome associated with childhood-onset systemic lupus erythematosus [Japanese]. Nihon Rinsho Meneki Gakkai Kaishi 2008;31(3):166-71.
47. Jarvis JN. The unique clinical presentation of children with chronic arthritis: putting the pediatrics in pediatric rheumatology. Curr Probl Pediatr Adolesc Health Care 2006;36(3):80-2.
48. John M, John V, Oppermann J. Laboratorial findings in the case of juvenile chronic arthritis [German]. Z Klin Med 1985;40(19):1445-8.
49. Kallel-Sellami M, Baili-Klila L, Zerzeri Y, et al. Pediatric systemic lupus erythematosus with C1q deficiency. Ann N Y Acad Sci 2007;1108:193-6.
50. Kamoun M. Diagnostic performance and predictive value of anti-citrullinated peptide antibodies for diagnosis of rheumatoid arthritis: Toward more accurate detection? Clin Chem 2005;51(1):12-3.
51. Kanski JJ. Juvenile arthritis and uveitis. Surv Ophthalmol 1990;34(4):253-67.
52. Kashikar-Zuck S, Graham TB, Huenefeld MD, et al. A review of biobehavioral research in juvenile primary fibromyalgia syndrome. Arthritis Care Res2000;13(6):388-97.
53. Kaur S, Thami GP. Antinuclear antibody-negative systemic lupus erythematosus: revisited. Indian J Pediatr 2003;70(2):185-6.
54. Keren DF. Antinuclear antibody testing. Clin Lab Med 2002;22(2):447-74.
55. Klein-Gitelman M. Pediatric lupus versus adult lupus role of the laboratory. Clin Appl Immunol Rev 2004;4(5):333-50.
56. Kobayashi R, Mii S, Nakano T, et al. Neonatal lupus erythematosus in Japan: A review of the literature. Autoimmun Rev 2009;8(6):462-6.
57. Kolle G. Juvenile rheumatoid arthritis and related collagen diseases. Clinical aspects [German]. Monatsschr Kinderheilkd 1976;124(12):779-85.
58. Kornreich H, Malouf NN, Hanson V. Acute hepatic dysfunction in juvenile rheumatoid arthritis. J Pediatr 1971;79(1):27-35.
59. Laxer RM. Introduction. J Rheumol 1990;17(SUPPL. 26):1.
60. Leak AM. Autoantibody profile in juvenile chronic arthritis. Ann Rheum Dis 1988;47(3):178-82.
61. Leung AK, Lemay JF. The limping child. J Pediatr Health Care 2004;18(5):219-23.
62. Levinson JE. Juvenile rheumatoid arthritis. Postgrad Med 1972;51(6):88-94.
63. Lewis JG, Florkowski CM, Elder PA, et al. Rheumatoid factor and false positive sex-hormone binding globulin. Clin Chim Acta 2003;332(1-2):139-44.
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Population (N = 72)

The following studies were excluded because the study population was not consisted primarily of individuals ≤ 18 years with a diagnosis of JIA, SLE, or with undiagnosed MSK pain .

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Index test (N = 64)

The following studies were excluded because the index tests were not ANA, RF, and/or CCP.

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Reference standard (N = 7)

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Outcome data (N = 152)

The following studies were excluded because they did not report sufficient numeric data on test result.

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Appendix E. Evidence Tables

Study	Participants Characteristics	Index Test Characteristics
Andersson-Gare, B., 1994 (40) **Country (# centers):** Sweden (NR) **Funding:** Government **Study design:** Case control (Prospective) **Recruitment:** Epidemiological survey	**Inclusion criteria:** NR **Exclusion criteria:** NR **JIA patients** **$N_{analyzed}/N_{enrolled}$:** 271/271 **Mean/median age (range):** NR **Female:** NR **Median time since diagnosis (range):** 5.6yr (0.1-18.6yr) **Subtype:** Systemic (4.4%); Polyarticular (27.7%); Pauciarticular (36.9%); Monoarticular (24.7%); Juvenile ankylosing spondylitis (3.0%); Arthritis in connection with inflammatory bowel disease (0.4%); Juvenile psoriatic arthropathy (2.9%) **Reference standard for JIA diagnosis:** EULAR	**IgM-RF test** **Assay method:** Enzyme immunoassay **Source of antigen:** NR **Manufacturer (kit type):** Pharmacia Diagnostics, Uppsala, Sweden (RF IgM EIA) **Positive cutoff:** Mean of control group + 2 sd (= 7.34 AU/ml) **IgA-RF test** **Assay method:** Enzyme immunoassay **Source of antigen:** NR **Manufacturer (kit type):** Pharmacia Diagnostics, Uppsala, Sweden (RF IgA EIA) **Positive cutoff:** Mean of control group + 2 sd (= 3.58 AU/ml)

Results (Overall)

		Reference	
		+	-
Index test	+	29	4
	-	242	126

Disease group = JIA
Comparator = Healthy controls
Index = IgM-RF
Sensitivity = 10.7%
Specificity = 96.9%

Overall

		Reference	
		+	-
Index test	+	26	5
	-	245	124

Disease group = JIA
Comparator = Healthy controls
Index = IgA-RF
Sensitivity = 9.6%
Specificity = 96.1%

By subtype

		Reference	
		+	-
Index test	+	6	4
	-	111	126

Disease group = JIA (mono- and pauci-articular)
Comparator = Healthy controls
Index = IgM-RF
Sensitivity = 5.1%
Specificity = 96.9%

By subtype

		Reference	
		+	-
Index test	+	21	4
	-	102	126

Disease group = JIA (polyarticular)
Comparator = Healthy controls
Index = IgM-RF
Sensitivity = 17.1%
Specificity = 96.9%

By subtype

		Reference	
		+	-
Index test	+	1	4
	-	6	126

Disease group = JIA (systemic)
Comparator = Healthy controls
Index = IgM-RF
Sensitivity = 14.3%
Specificity = 96.9%

By subtype

		Reference	
		+	-
Index test	+	10	5
	-	107	124

Disease group = JIA (monoarticular and pauciarticular)
Comparator = Healthy controls
Index = IgA-RF
Sensitivity = 8.5%
Specificity = 96.1%

By subtype

		Reference	
		+	-
Index test	+	13	5
	-	110	124

Disease group = JIA (polyarticular)
Comparator = Healthy controls
Index = IgA-RF
Sensitivity = 10.6%
Specificity = 96.1%

By subtype

		Reference	
		+	-
Index test	+	0	5
	-	7	124

Disease group = JIA (systemic)
Comparator = Healthy controls
Index = IgA-RF
Sensitivity = 0%
Specificity = 96.1%

Study	Participants Characteristics	Index Test Characteristics
Avcin, T., 2002 (52) **Country (# centers):** Italy and Slovenia (4) **Funding:** Government **Study design:** Case control (Prospective) **Recruitment:** NR	**Inclusion criteria:** NR **Exclusion criteria:** NR **JIA patients** **$N_{analyzed}/N_{enrolled}$:** 109/109 **Mean age (range):** 8.7yr (0.6-20.3yr) **Female:** 72.5% **Mean time since diagnosis (range):** 3.6yr (0.3-15.6yr) **Subtype:** Polyarticular (47.7%); Oligoarticular (46.8%); Systemic (5.5%) **Reference standard for JIA diagnosis:** NR **SLE patients** **$N_{analyzed}/N_{enrolled}$:** 25/25 **Mean age (range):** NR **Female:** NR **Mean/median time since diagnosis (range):** NR **Reference standard for SLE diagnosis:** NR	**CCP test** **Assay method:** ELISA **Source of antigen:** NR **Manufacturer (kit type):** Euro-Diagnostica, Arnhem, The Netherlands (ImmunoScan RA anti-CCP test kit) **Positive cutoff:** 70 anti-CCP unit (AU)

Results (Overall)

		Reference	
		+	-
Index test	+	2	0
	-	107	30

Overall

		Reference	
		+	-
Index test	+	0	0
	-	25	30

By subtype

		Reference	
		+	-
Index test	+	1	0
	-	50	30

Disease group = JIA
Comparator = Healthy controls
Index = CCP
Sensitivity = 1.8%
Specificity = 100.%

By subtype

		Reference	
		+	-
Index test	+	1	0
	-	51	30

Disease group = JIA (polyarticular)
Comparator = Healthy controls
Index = CCP
Sensitivity = 1.9%
Specificity = 100.%

Disease group = SLE
Comparator = Healthy controls
Index = CCP
Sensitivity = 0.0%
Specificity = 100.%

By subtype

		Reference	
		+	-
Index test	+	0	0
	-	6	30

Disease group = JIA (systemic)
Comparator = Healthy controls
Index = CCP
Sensitivity = 0%
Specificity = 100.%

Disease group = JIA (oligoarticular)
Comparator = Healthy controls
Index = CCP
Sensitivity = 2.0%
Specificity = 100.%

Study	Participants Characteristics	Index Test Characteristics
Balogh, Z., 1980 (41) **Country (# centers):** Hungary (1) **Funding:** NR **Study design:** Case control (Prospective) **Recruitment:** Consecutive patients	**Inclusion criteria:** Healthy controls: Age- and sex-matched with JIA patients **Exclusion criteria:** JIA group: Juvenile ankylosing spondylitis, psoriatic arthritis, and arthritis associated with inflammatory bowel disease patients **JIA patients** **$N_{analyzed}/N_{enrolled}$:** 46/46 **Mean age (range):** 9.6yr (2.7-15.8yr) **Female:** 47.8% **Mean/median time since diagnosis (range):** NR **Subtype:** Pauciarticular (56.5%); Systemic (19.6%); Polyarticular (17.4%); Seropositive "adult-type" JCA (6.5%) **Reference standard for JIA diagnosis:** EULAR/WHO workshop, Oslo, 1978	**ANA test** **Assay method:** Immunofluorescence technique (Holborow and Johnson 1969) **Source of antigen:** Fluorescein-labeled anti-IgG (H+L) specific serum **Manufacturer (kit type):** Hyland (NR) **Positive cutoff:** Titre 1:10 **IgM-RF test** **Assay method:** Latex fixation test **Source of antigen:** NR **Manufacturer (kit type):** NR **Positive cutoff:** NR **RF test (unspecified isotype)** **Assay method:** Waaler-Rose test **Source of antigen:** NR **Manufacturer (kit type):** NR **Positive cutoff:** NR

Results (Overall)

		Reference	
		+	-
Index test	+	6	0
	-	40	10

Disease group = JIA
Comparator = Healthy controls
Index = ANA
Sensitivity = 13.0%
Specificity = 100.%

By subtype

Overall

		Reference	
		+	-
Index test	+	10	0
	-	36	10

Disease group = JIA
Comparator = Healthy controls
Index = IgM-RF (Latex)
Sensitivity = 21.7%
Specificity = 100.%

By subtype

By subtype

		Reference	
		+	-
Index test	+	7	0
	-	39	10

Disease group = JIA
Comparator = Healthy controls
Index = RF (Waaler-Rose)
Sensitivity = 15.2%
Specificity = 100.%

By subtype

		Reference	
		+	-
Index test	+	2	0
	-	24	10

Disease group = JIA (pauciarticular)
Comparator = Healthy controls
Index = ANA
Sensitivity = 7.7%
Specificity = 100.%

By subtype

		Reference	
		+	-
Index test	+	6	0
	-	20	10

Disease group = JIA (pauciarticular)
Comparator = Healthy controls
Index = IgM-RF (Latex)
Sensitivity = 23.1%
Specificity = 100.%

By subtype

		Reference	
		+	-
Index test	+	3	0
	-	23	10

Disease group = JIA (pauciarticular)
Comparator = Healthy controls
Index = RF (Waaler-Rose)
Sensitivity = 11.5%
Specificity = 100.%

		Reference	
		+	-
Index test	+	2	0
	-	6	10

Disease group = JIA (polyarticular)
Comparator = Healthy controls
Index = ANA
Sensitivity = 25.0%
Specificity = 100.%

By subtype

		Reference	
		+	-
Index test	+	0	0
	-	8	10

Disease group = JIA (polyarticular)
Comparator = Healthy controls
Index = IgM-RF (Latex)
Sensitivity = 0%
Specificity = 100.%

By subtype

		Reference	
		+	-
Index test	+	0	0
	-	8	10

Disease group = JIA (polyarticular)
Comparator = Healthy controls
Index = RF (Waaler-Rose)
Sensitivity = 0%
Specificity = 100.%

		Reference	
		+	-
Index test	+	0	0
	-	9	10

Disease group = JIA (systemic)
Comparator = Healthy controls
Index = ANA
Sensitivity = 0%
Specificity = 100.%

By subtype

		Reference	
		+	-
Index test	+	1	0
	-	8	10

Disease group = JIA (systemic)
Comparator = Healthy controls
Index = IgM-RF (Latex)
Sensitivity = 11.1%
Specificity = 100.%

By subtype

		Reference	
		+	-
Index test	+	1	0
	-	8	10

Disease group = JIA (systemic)
Comparator = Healthy controls
Index = RF (Waaler-Rose)
Sensitivity = 11.1%
Specificity = 100.%

Study	Participants Characteristics	Index Test Characteristics
Brunner, J., 2006 (53) **Country (# centers):** Germany (1) **Funding:** NR **Study design:** Case control (Prospective) **Recruitment:** NR	**Inclusion criteria:** ORG: With other autoimmunopathies such as Crohn's disease, reactive arthritis, diabetes mellitus type 1, uveitis, and myositis NRG: Undergoing interventional cardiac therapy. With non-autoimmunopathies such as infectious diseases, endocrinopathies, arthralgias, cystic fibrosis, galactosemia, hemophilia, ADD, epilepsy, Raynaud's phenomenon, osteochondroma, and fibromyalgia Healthy controls: Newborns with no known diseases **Exclusion criteria:** JIA: Written consent not obtained, bilateral anophthalmia, and insufficient blood volumes **JIA patients** **$N_{analyzed}/N_{enrolled}$:** 45/45 **Mean age (range):** 11.0yr (1.9-17.3yr) **Female:** 66.7% **Mean time since diagnosis (range):** 2.1yr (NR) **Subtype:** Polyarticular (15.6%); Systemic (6.7%); Oligoarticular (55.6%); Enthesitis-related arthritis (13.3%); Psoriatric (4.4%) **Reference standard for JIA diagnosis:** NR **SLE patients** **$N_{analyzed}/N_{enrolled}$:** 4/4	**CCP test** **Assay method:** ELISA **Source of antigen:** NR **Manufacturer (kit type):** Euroimmun lot 21122m, Germany (NR) **Positive cutoff:** 2.5 relative units (RU)

Mean age (range): NR

Female: NR

Mean time since diagnosis (range): NR

Subtype: NR

Reference standard for SLE diagnosis: NR

Results (Overall)

		Reference	
		+	-
Index test	+	2	0
	-	43	42

Disease group = JIA
Comparator = Healthy controls
Index = CCP
Sensitivity = 4.4%
Specificity = 100%

Overall

		Reference	
		+	-
Index test	+	2	5
	-	43	29

Disease group = JIA
Comparator = NRG
Index = CCP
Sensitivity = 4.4%
Specificity = 85.3%

Overall

		Reference	
		+	-
Index test	+	2	3
	-	43	34

Disease group = JIA
Comparator = ORG
Index = CCP
Sensitivity = 4.4%
Specificity = 91.9%

Overall

		Reference	
		+	-
Index test	+	1	0
	-	3	42

Disease group = SLE
Comparator = Healthy controls
Index = CCP
Sensitivity = 25.0%
Specificity = 100%

Overall

		Reference	
		+	-
Index test	+	1	5
	-	3	29

Disease group = SLE
Comparator = NRG
Index = CCP
Sensitivity = 25.0%
Specificity = 85.3%

Overall

		Reference	
		+	-
Index test	+	1	3
	-	3	34

Disease group = SLE
Comparator = ORG
Index = CCP
Sensitivity = 25.0%
Specificity = 91.9%

Study	Participants Characteristics	Index Test Characteristics
Egeskjold, E.M., 1981 (42) **Country (# centers):** Denmark (NR) **Funding:** Government **Study design:** Case control (Prospective) **Recruitment:** NR	**Inclusion criteria:** Healthy controls: Age- and sex-matched children without arthritis or chronic disease **Exclusion criteria:** NR **JIA patients** **$N_{analyzed}/N_{enrolled}$:** 48/48 **Mean/median age (range):** NR (1.0-16.0yr) **Female:** 68.8% **Mean/median time since diagnosis (range):** NR **Subtype:** Pauciarticular (52.1%); Polyarticular (29.2%); Systemic (18.8%) **Reference standard for JIA diagnosis:** ARA	**ANA test** **Assay method:** Immunofluorescence technique **Source of antigen:** NR **Manufacturer (kit type):** NR **Positive cutoff:** Titre 1:18 **RF test (IgM, IgG, IgA)** **Assay method:** IIF **Source of antigen:** Sheep red cell **Manufacturer (kit type):** DAKO (NR) **Positive cutoff:** Titre 1:9

Results (Overall)

		Reference	
		+	-
Index test	+	32	2
	-	16	46

Disease group = JIA
Comparator = Healthy controls
Index = ANA
Sensitivity = 66.7%
Specificity = 95.8%

Overall

		Reference	
		+	-
Index test	+	1	0
	-	47	48

Overall

		Reference	
		+	-
Index test	+	42	1
	-	6	47

Disease group = JIA
Comparator = Healthy controls
Index = IgG-RF
Sensitivity = 87.5%
Specificity = 97.9%

By subtype

		Reference	
		+	-
Index test	+	12	1
	-	4	47

Overall

		Reference	
		+	-
Index test	+	2	1
	-	46	47

Disease group = JIA
Comparator = Healthy controls
Index = IgM-RF
Sensitivity = 4.2%
Specificity = 97.9%

By subtype

		Reference	
		+	-
Index test	+	12	1
	-	2	47

Disease group = JIA
Comparator = Healthy controls
Index = IgA-RF
Sensitivity = 2.1%
Specificity = 100%

By subtype

		Reference	
		+	-
Index test	+	9	1
	-	0	47

Disease group = JIA (systemic)
Comparator = Healthy controls
Index = IgG-RF
Sensitivity = 100%
Specificity = 97.9%

Disease group = JIA (pauciarticular)
Comparator = Healthy controls
Index = IgG-RF
Sensitivity = 75.0%
Specificity = 97.9%

Disease group = JIA (polyarticular)
Comparator = Healthy controls
Index = IgG-RF
Sensitivity = 85.7%
Specificity = 97.9%

Study	Participants Characteristics	Index Test Characteristics
Egeskjold, E.M., 1982 (50) **Country (# centers):** Denmark (NR) **Funding:** Government **Study design:** Case control (NR) **Recruitment:** NR	**Inclusion criteria:** NR **Exclusion criteria:** NR **JIA patients** **$N_{analyzed}/N_{enrolled}$:** 13/13 **Mean/median age (range):** 7.1yr/ 7.0yr (2.0-15.0yr) **Female:** 69.2% **Mean time since diagnosis (range):** 3.5yr (0.6-6.4yr) **Subtype:** Pauciarticular (53.8%); Polyarticular (38.5%); Systemic (7.7%); Comorbid with chronical bilateral iridocyclitis (61.5%) **Reference standard for JIA diagnosis:** ARA	**ANA (IgM, IgG, IgA)** **Assay method:** IIF **Source of antigen:** Rat liver cryostat sections and leucocytes) **Manufacturer (kit type):** NR **Positive cutoff:** Maximum of peak 2 displacement beyond normal range **RF test (IgM, IgG, IgA)** **Assay method:** IIF **Source of antigen:** Sheep erythrocyte sensitized with rabbit IgG **Manufacturer (kit type):** NR **Positive cutoff:** Maximum of peak 2 displacement beyond normal range

Results (Overall)

		Reference	
		+	-
Index test	+	8	0
	-	5	3

Disease group = JIA
Comparator = Healthy controls
Index = IgM-ANA
Sensitivity = 61.5%
Specificity = 100.%

Overall

		Reference	
		+	-
Index test	+	2	0

Overall

		Reference	
		+	-
Index test	+	11	0
	-	2	3

Disease group = JIA
Comparator = Healthy controls
Index = IgG-ANA
Sensitivity = 84.676.9%
Specificity = 100.%

Overall

		Reference	
		+	-
Index test	+	10	0

Overall

		Reference	
		+	-
Index test	+	0	0
	-	13	3

Disease group = JIA
Comparator = Healthy controls
Index = IgA-ANA
Sensitivity = 0.0%
Specificity = 100.%

Overall

		Reference	
		+	-
Index test	+	0	0

	-	11	3

Disease group = JIA
Comparator = Healthy controls
Index = IgM-RF
Sensitivity = 15.4%
Specificity = 100.%

	-	3	3

Disease group = JIA
Comparator = Healthy controls
Index = IgG-RF
Sensitivity = 76.9%
Specificity = 100.%

	-	13	3

Disease group = JIA
Comparator = Healthy controls
Index = IgA-RF
Sensitivity = 0.0%
Specificity = 100.%

Study	Participants Characteristics	Index Test Characteristics
Eichenfield, A.H., 1986 (49) **Country (# centers):** U.S. (1) **Funding:** NR **Study design:** Cohort (Retrospective) **Recruitment:** Consecutive patients	**Inclusion criteria:** Cohort: Children's complaints were referable to the musculoskeletal system or as being of an "autoimmune" nature. RF test results must be available and measured between Jan 1981 and Dec 1982 **Exclusion criteria:** NR **Historical patient cohort** **$N_{analyzed}/N_{enrolled}$:** 437/437 **Mean/median age (range):** NR **Female:** NR **Mean/median time since diagnosis (range):** NR **Subtype:** NR **Reference standard for JIA diagnosis:** ARA	**IgM-RF test** **Assay method:** Latex fixation test **Source of antigen:** NR **Manufacturer (kit type):** Hyland Laboratories (RA-test) **Positive cutoff:** Titre 1:80

Results (Overall)

		Reference	
		+	-
Index test	+	5	6
	-	100	326

Disease group = JIA
Comparator = Non-JIA children with MSK complaints
Index = IgM-RF (Latex)
Sensitivity = 5.0%
Specificity = 98.2%

Study	Participants Characteristics	Index Test Characteristics
Fawcett, P.T., 1999 (30) **Country (# centers):** U.S. **Funding:** Government **Study design:** Case control (Prospective) **Recruitment:** NR	**Inclusion criteria:** ORG: Underwent elective orthopedic surgical procedures **Exclusion criteria:** NR **JIA patients** **$N_{analyzed}/N_{enrolled}$:** 178/178 **Mean/median age (range):** NR **Female:** NR **Mean/median time since diagnosis (range):** NR **Subtype:** Pauciarticular (49.4%); Polyarticular (38.2%); Systemic (12.4%) **Reference standard for JIA diagnosis:** ACR **SLE patients** **$N_{analyzed}/N_{enrolled}$:** 21/21 **Mean/median age (range):** NR **Female:** NR **Mean/median time since diagnosis (range):** NR **Reference standard for SLE diagnosis:** ACR	**ANA test** **Assay method:** IIF and ELISA (Immuno Concepts, Helix, Zeus) **Source of antigen:** IIF: HEp-2 cell line . Immuno Concepts : Sm, RNP, SSA, SSB, Scl-70, Jo-1. Helix : Sm, SmRNP, SSA, SSB, Scl-70, Jo-1, ds-DNA, histones, and centromere antigens. Zeus: Sm, RNP, SSA, SSB, Scl-70, Jo-1, and ds-DNA **Manufacturer (kit type):** IIF: Antibodies Incorporated, Davis, CA. ELISA: Immuno Concepts, Sacramento/CA, Helix, Sacramento/CA, Zeus, Raritan/NJ; IIF: IFA kit; IIF: Zeiss Axioplan microscope equipped for epifluorescence with excitation filters **Positive cutoff:** IIF: Positive if a clearly discernible fluorescence pattern appears at 1:40 serum dilution.

Results (Overall)

		Reference	
		+	-
Index test	+	110	4
	-	68	22

Overall

		Reference	
		+	-
Index test	+	16	0
	-	162	26

Overall

		Reference	
		+	-
Index test	+	73	5
	-	105	21

Disease group = JIA
Comparator = ORG
Index = ANA (IIF)
Sensitivity = 61.8%
Specificity = 84.6%

Overall

		Reference	
		+	-
Index test	+	119	7
	-	59	19

Disease group = JIA
Comparator = ORG
Index = ANA (ELISA – Zeus)
Sensitivity = 67.1%
Specificity = 73.1%

Overall

		Reference	
		+	-
Index test	+	20	5
	-	1	21

Disease group = SLE
Comparator = ORG
Index = ANA (ELISA – Helix)
Sensitivity = 95.2%
Specificity = 80.8%

By subtype

		Reference	
		+	-
Index test	+	5	0
	-	83	26

Disease group = JIA (pauciarticular)
Comparator = ORG
Index = ANA (ELISA – Immuno Concepts)
Sensitivity = 5.7%
Specificity = 100%

By subtype

Disease group = JIA
Comparator = ORG
Index = ANA (ELISA – Immuno Concepts)
Sensitivity = 9.0%
Specificity = 100.%

Overall

		Reference	
		+	-
Index test	+	21	4
	-	0	22

Disease group = SLE
Comparator = ORG
Index = ANA (IIF)
Sensitivity = 100%
Specificity = 84.6%

Overall

		Reference	
		+	-
Index test	+	20	7
	-	1	19

Disease group = SLE
Comparator = ORG
Index = ANA (ELISA – Zeus)
Sensitivity = 95.2%
Specificity = 73%

By subtype

		Reference	
		+	-
Index test	+	33	5
	-	55	21

Disease group = JIA (pauciarticular)
Comparator = ORG
Index = ANA (ELISA – Helix)
Sensitivity = 37.5%
Specificity = 80.8%

By subtype

Disease group = JIA
Comparator = ORG
Index = ANA (ELISA – Helix)
Sensitivity = 41.0%
Specificity = 80.8%

Overall

		Reference	
		+	-
Index test	+	16	0
	-	5	26

Disease group = SLE
Comparator = ORG
Index = ANA (ELISA – Immuno Concepts)
Sensitivity = 76.2%
Specificity = 100%

By subtype

		Reference	
		+	-
Index test	+	68	4
	-	20	22

Disease group = JIA (pauciarticular)
Comparator = ORG
Index = ANA (IIF)
Sensitivity = 77.3%
Specificity = 84.6%

By subtype

		Reference	
		+	-
Index test	+	56	7
	-	32	19

Disease group = JIA (pauciarticular)
Comparator = ORG
Index = ANA (ELISA – Zeus)
Sensitivity = 63.6%
Specificity = 73.1%

By subtype

		Reference	
		+	-
Index test	+	14	7
	-	8	19

Disease group = JIA (systemic)
Comparator = ORG
Index = ANA (ELISA – Zeus)
Sensitivity = 63.6%
Specificity = 73.1%

By subtype

		Reference	
		+	-
Index test	+	49	7
	-	19	19

Disease group = JIA (polyarticular)
Comparator = ORG
Index = ANA (ELISA - Zeus)
Sensitivity = 72.1%
Specificity = 73.1%

By subtype

		Reference	
		+	-
Index test	+	7	5
	-	15	21

Disease group = JIA (systemic)
Comparator = ORG
Index = ANA (ELISA – Helix)
Sensitivity = 31.8%
Specificity = 80.8%

		Reference	
		+	-
Index test	+	10	0
	-	58	26

Disease group = JIA (polyarticular)
Comparator = ORG
Index = ANA (ELISA – Immuno Concepts)
Sensitivity = 14.7%
Specificity = 100%

By subtype

		Reference	
		+	-
Index test	+	4	4
	-	18	22

Disease group = JIA (systemic)
Comparator = ORG
Index = ANA (IIF)
Sensitivity = 18.2%
Specificity = 84.6%

By subtype

		Reference	
		+	-
Index test	+	14	7
	-	8	19

Disease group = JIA (systemic)
Comparator = ORG
Index = ANA (ELISA – Zeus)
Sensitivity = 63.6%
Specificity = 73.1%

		Reference	
		+	-
Index test	+	33	5
	-	35	21

Disease group = JIA (polyarticular)
Comparator = ORG
Index = ANA (ELISA – Helix)
Sensitivity = 48.5%
Specificity = 80.8%

By subtype

		Reference	
		+	-
Index test	+	1	0
	-	21	26

Disease group = JIA (systemic)
Comparator = ORG
Index = ANA (ELISA – Immuno Concepts)
Sensitivity = 4.5%
Specificity = 100%

Study	Participants Characteristics	Index Test Characteristics
Ferreira, R.A., 2007 (43) **Country (# centers):** Brazil (3) **Funding:** NR **Study design:** Case control (Prospective) **Recruitment:** Random selection	**Inclusion criteria:** NR **Exclusion criteria:** NR **JIA patients** **$N_{analyzed}/N_{enrolled}$:** 91/91 **Mean age (range):** 10.5yr (2.1-22.7yr) **Female:** 64.8% **Mean time since diagnosis (range):** 5.2yr (0.2-17.3yr) **Subtype:** Polyarticular (27.5%); Pauciarticular (30.8%); Systemic (41.8%) **Reference standard for JIA diagnosis:** ACR	**IgM-RF test** **Assay method:** Latex fixation test **Source of antigen:** NR **Manufacturer (kit type):** RapiTex, Hoechst, Marburg, Germany (RF) **Positive cutoff:** 20 IU/ml **IgM-RF test** **Assay method:** ELISA **Source of antigen:** NR **Manufacturer (kit type):** Flow Laboratories, U.S. (Titertek Multiskan Plus) **Positive cutoff:** EI (absorbance of serum samples/cut off)> 1.0 **IgA-RF test** **Assay method:** ELISA **Source of antigen:** Mouse IgG **Manufacturer (kit type):** Flow Laboratories, U.S. (Titertek Multiskan Plus) **Positive cutoff:** EI> 1.0

Results (Overall)

		Reference	
		+	-
Index test	+	5	0
	-	86	45

Disease group = JIA
Comparator = Healthy controls
Index = IgM-RF (Latex)
Sensitivity = 5.5%

Overall

		Reference	
		+	-
Index test	+	30	3
	-	61	42

Disease group = JIA
Comparator = Healthy controls
Index = IgM-RF (ELISA)
Sensitivity = 33.0%

Overall

		Reference	
		+	-
Index test	+	40	7
	-	51	38

Disease group = JIA
Comparator = Healthy controls
Index = IgA-RF (ELISA)
Sensitivity = 44.0%

Specificity = 100.%

By subtype

		Reference	
		+	-
Index test	+	0	0
	-	28	45

Disease group = JIA (pauciarticular)
Comparator = Healthy controls
Index = IgM-RF (Latex)
Sensitivity = 0%
Specificity = 100%

By subtype

		Reference	
		+	-
Index test	+	5	0
	-	20	45

Disease group = JIA (polyarticular)
Comparator = Healthy controls
Index = IgM-RF (Latex)
Sensitivity = 20.0%
Specificity = 100%

By subtype

		Reference	
		+	-
Index test	+	0	0
	-	38	45

Disease group = JIA (systemic)
Comparator = Healthy controls
Index = IgM-RF (Latex)
Sensitivity = 0%
Specificity = 100%

Specificity = 93.3%

By subtype

		Reference	
		+	-
Index test	+	9	3
	-	19	42

Disease group = JIA (pauciarticular)
Comparator = Healthy controls
Index = IgM-RF (ELISA)
Sensitivity = 32.1%
Specificity = 93.3%

By subtype

		Reference	
		+	-
Index test	+	13	3
	-	12	42

Disease group = (polyarticular)
Comparator = Healthy controls
Index = IgM-RF (ELISA)
Sensitivity = 52.0%
Specificity = 93.3%

By subtype

		Reference	
		+	-
Index test	+	8	3
	-	30	42

Disease group = JIA (systemic)
Comparator = Healthy controls
Index = IgM-RF (ELISA)
Sensitivity = 21.1%
Specificity = 93.3%

Specificity = 84.4%

By subtype

		Reference	
		+	-
Index test	+	13	7
	-	15	38

Disease group = JIA (pauciarticular)
Comparator = Healthy controls
Index = IgA-RF (ELISA)
Sensitivity = 46.4%
Specificity = 84.4%

By subtype

		Reference	
		+	-
Index test	+	10	7
	-	15	38

Disease group = (polyarticular)
Comparator = Healthy controls
Index = IgA-RF (ELISA)
Sensitivity = 40.0%
Specificity = 84.4%

By subtype

		Reference	
		+	-
Index test	+	17	7
	-	21	38

Disease group = JIA (systemic)
Comparator = Healthy controls
Index = IgA-RF (ELISA)
Sensitivity = 44.7%
Specificity = 84.4%

Study	Participants Characteristics	Index Test Characteristics
Ferucci, E.D., 2005 (54) **Country (# centers):** U.S., throughout North America (NR) **Funding:** Government **Study design:** Case control (Prospective) **Recruitment:** Simplex patients were recruited among a local cohort in Cincinnatti; multiplex patients were recruited from the National Institute of Arthritis and Muscoloskeletal and Skin Diseases-supported JRA Affected Sibpair Registry. Siblings were selected randomly.	**Inclusion criteria:** Healthy controls: Children with increased risk of type I diabetes from the Diabetes and Autoimmunity Study in the Young (DAISY) **Exclusion criteria:** NR **JIA patients** **$N_{analyzed}/N_{enrolled}$:** 230/230 **Mean/median age (range):** 14.7yr (NR) **Female:** 73.9% **Mean/median time since diagnosis (range):** 9.7yr (NR) **Subtype:** Polyarticular (33.5%); Pauciarticular (60.4%); Systemic (6.1%) **Reference standard for JIA diagnosis:** ACR	**RF test (unspecified isotype)** **Assay method:** Nephelometry **Source of antigen:** NR **Manufacturer (kit type):** Dade-Behring, Newark, DE (NR) **Positive cutoff:** 15 IU/ml **CCP test** **Assay method:** ELISA **Source of antigen:** NR **Manufacturer (kit type):** Diastat; Axis-Shield Diagnostics, Dundee, Scotland, UK (NR) **Positive cutoff:** 5 units/ml

Results (Overall)

		Reference	
		+	-
Index test	+	25	23
	-	205	665

Disease group = JIA
Comparator = Healthy controls
Index = RF (unspecified isotype)
Sensitivity = 10.9%
Specificity = 96.7%

By subtype

		Reference	
		+	-
Index test	+	3	4

Overall

		Reference	
		+	-
Index test	+	13	4
	-	217	684

Disease group = JIA
Comparator = Healthy controls
Index = CCP
Sensitivity = 5.7%
Specificity = 99.4%

By subtype

		Reference	
		+	-
Index test	+	14	23

By subtype

		Reference	
		+	-
Index test	+	9	23
	-	130	665

Disease group = JIA (pauciarticular)
Comparator = Healthy controls
Index = RF (unspecified isotype)
Sensitivity = 6.5%
Specificity = 96.7%

By subtype

		Reference	
		+	-
Index test	+	10	4

	-	136	684

Disease group = JIA (pauciarticular)
Comparator = Healthy controls
Index = CCP
Sensitivity = 2.2%
Specificity = 99.4%

By subtype

		Reference	
		+	-
Index test	+	2	23
	-	12	665

Disease group = JIA (systemic)
Comparator = Healthy controls
Index = RF (unspecified isotype)
Sensitivity = 14.3%
Specificity = 96.7%

	-	63	665

Disease group = JIA (polyarticular)
Comparator = Healthy controls
Index = RF (unspecified isotype)
Sensitivity = 18.2%
Specificity = 96.7%

By subtype

		Reference	
		+	-
Index test	+	0	4
	-	14	684

Disease group = JIA (systemic)
Comparator = Healthy controls
Index = CCP
Sensitivity = 0%
Specificity = 99.4%

	-	67	684

Disease group = JIA (polyarticular)
Comparator = Healthy controls
Index = CCP
Sensitivity = 13.0%
Specificity = 99.4%

Study	Participants Characteristics	Index Test Characteristics
Habib, H.M., 2008 (55) **Country (# centers):** Eqypt (1) **Funding:** NR **Study design:** Case control (Prospective) **Recruitment:** NR	**Inclusion criteria:** NR **Exclusion criteria:** NR **JIA patients** **$N_{analyzed}/N_{enrolled}$:** 68/68 **Mean age (range):** 10.6yr (3.0-16.0yr) **Female:** 44.1% **Mean time since diagnosis (range):** 3.7yr (1.0-8.0yr) **Subtype:** Polyarticular (55.9%); Oligoarticular (29.4%); Systemic (14.7%) **Reference standard for JIA diagnosis:** ILAR **SLE patients** **$N_{analyzed}/N_{enrolled}$:** 14/14 **Mean age (range):** 12.1yr (NR) **Female:** 92.9% **Mean time since diagnosis (range):** 3.7yr (NR) **Reference standard for SLE diagnosis:** NR	**CCP test** **Assay method:** ELISA **Source of antigen:** Synthetic circular peptide containing citrulline **Manufacturer (kit type):** INOVA, San Diego, U.S. (Quanta LiteTM) **Positive cutoff:** 20 units/ml

Results (Overall)

		Reference	
		+	-
Index test	+	14	0
	-	54	20

Overall

		Reference	
		+	-
Index test	+	0	0
	-	14	20

By subtype

		Reference	
		+	-
Index test	+	0	0
	-	20	20

Disease group = JIA
Comparator = Healthy controls
Index = CCP
Sensitivity = 20.6%
Specificity = 100.%

By subtype

		Reference	
		+	-
Index test	+	14	0
	-	24	20

Disease group = SLE
Comparator = Healthy controls
Index = CCP
Sensitivity = 0.0%
Specificity = 100.%

By subtype

		Reference	
		+	-
Index test	+	0	0
	-	10	20

Disease group = JIA (oligoarticular)
Comparator = Healthy controls
Index = CCP
Sensitivity = 0%
Specificity = 100.%

Disease group = JIA (polyarticular)
Comparator = Healthy controls
Index = CCP
Sensitivity = 36.8%
Specificity = 100.%

Disease group = JIA (systemic)
Comparator = Healthy controls
Index = CCP
Sensitivity = 0%
Specificity = 100.%

Study	Participants Characteristics	Index Test Characteristics
Hanson, V., 1966 (39) **Country (# centers):** U.S. (1) **Funding:** NR **Study design:** Case control (NR) **Recruitment:** NR	**Inclusion criteria:** NR **Exclusion criteria:** NR **JIA patients** **$N_{analyzed}/N_{enrolled}$:** 45/58 **Mean/median age (range):** NR **Female:** NR **Mean/median time since diagnosis (range):** NR **Subtype:** NR **Reference standard for JIA diagnosis:** ARA **SLE patients** **$N_{analyzed}/N_{enrolled}$:** 14/14 **Mean/median age (range):** NR **Female:** 80% **Mean/median time since diagnosis (range):** NR **Subtype:** NR **Reference standard for SLE diagnosis:** Conformed to Cook et al, and Urbach, and also met the criteria by Bywaters (Weir et al.)	**IgM-RF test** **Assay method:** Latex titration test **Source of antigen:** NR **Manufacturer (kit type):** NR **Positive cutoff:** Titre 1:160

Results (Overall)

	Reference	
	+	-

Overall

	Reference	
	+	-

Overall

	Reference	
	+	-

Index test	+	10	0
	-	35	32

Disease group = JIA
Comparator = Healthy controls
Index = IgM-RF (Latex)
Sensitivity = 22.2%
Specificity = 100.%

Overall

		Reference	
		+	-
Index test	+	4	0
	-	10	32

Disease group = SLE
Comparator = Healthy controls
Index = IgM-RF (Latex)
Sensitivity = 28.6%
Specificity = 100.%

Index test	+	10	3
	-	35	30

Disease group = JIA
Comparator = ORG (other collagen diseases)
Index = IgM-RF (Latex)
Sensitivity = 22.2%
Specificity = 90.9%

Overall

		Reference	
		+	-
Index test	+	4	3
	-	10	30

Disease group = SLE
Comparator = ORG (other collagen diseases)
Index = IgM-RF (Latex)
Sensitivity = 28.6%
Specificity = 90.9%

Index test	+	10	1
	-	35	22

Disease group = JIA
Comparator = NRG (ulcerative collitis)
Index = IgM-RF (Latex)
Sensitivity = 22.2%
Specificity = 95.7%

Overall

		Reference	
		+	-
Index test	+	4	1
	-	10	22

Disease group = SLE
Comparator = NRG (ulcerative collitis)
Index = IgM-RF (Latex)
Sensitivity = 28.6%
Specificity = 95.7%

Study	Participants Characteristics	Index Test Characteristics
Haynes, D.C., 1986 (32) **Country (# centers):** U.S. (1) **Funding:** Government and non-commercial institution (NIH and House of St. Giles the Cripple) **Study design:** Case control (Prospective) **Recruitment:** NR	**Inclusion criteria:** NRG: Children with unspecified nonrheumatic disease. Age-matched with JIA patients **Exclusion criteria:** NR **JIA patients** **$N_{analyzed}/N_{enrolled}$:** 65/65 **Mean/median age (range):** NR (3.0-19.0yr) **Female:** NR **Mean/median time since diagnosis (range):** NR **Subtype:** Pauciarticular (35.3%); polyarticular (36.9%); systemic (27.7%) **Reference standard for JIA diagnosis:** ARA	**ANA test** **Assay method:** IIF **Source of antigen:** HEp-2 cell line **Manufacturer (kit type):** Breit Laboratories, Inc, Sacramento, CA (NR) **Positive cutoff:** A reading of 1+ or greater in fluorescence at 1:20 dilution **IgM-RF test** **Assay method:** ELISA **Source of antigen:** Human IgG **Manufacturer (kit type):** Sigma Chemical Co. (NR); Tago, Inc. (NR); and Pharmacia Fine Chemicals (NR) **Positive cutoff:** Mean of control group + 2 sd **IgG-RF test** **Assay method:** ELISA **Source of antigen:** Rabbit IgG **Manufacturer (kit type):** Sigma Chemical Co. (NR); Cappel Labs., Cochranville, PA (NR) **Positive cutoff:** Mean of control group + 2 sd

Results (Overall)

		Reference	
		+	-
Index test	+	33	1
	-	32	17

Overall

		Reference	
		+	-
Index test	+	23	0
	-	42	20

Overall

		Reference	
		+	-
Index test	+	4	0
	-	61	20

Disease group = JIA
Comparator = NRG (Unspecified)
Index = ANA
Sensitivity = 50.8%
Specificity = 94.4%

By subtype

		Reference	
		+	-
Index test	+	18	1
	-	6	17

Disease group = JIA
Comparator = NRG (Unspecified)
Index = IgM-RF
Sensitivity = 33.8%
Specificity = 100.%

By subtype

		Reference	
		+	-
Index test	+	12	1
	-	11	17

Disease group = JIA
Comparator = NRG (Unspecified)
Index = IgG-RF
Sensitivity = 6.2%
Specificity = 94.4%

By subtype

		Reference	
		+	-
Index test	+	3	1
	-	15	17

Disease group = JIA (pauciarticular)
Comparator = NRG (Unspecified)
Index = ANA
Sensitivity = 75.0%
Specificity = 94.4%

By subtype

		Reference	
		+	-
Index test	+	5	0
	-	19	20

Disease group = JIA (polyarticular)
Comparator = NRG (Unspecified)
Index = ANA
Sensitivity = 52.2%
Specificity = 94.4%

By subtype

		Reference	
		+	-
Index test	+	10	0
	-	13	20

Disease group = JIA (systemic)
Comparator = NRG (Unspecified)
Index = ANA
Sensitivity = 16.7%
Specificity = 94.4%

By subtype

		Reference	
		+	-
Index test	+	8	0
	-	10	20

Disease group = JIA (pauciarticular)
Comparator = NRG (Unspecified)
Index = IgM-RF
Sensitivity = 20.8%
Specificity = 100.%

By subtype

		Reference	
		+	-
Index test	+	1	0
	-	23	20

Disease group = JIA (polyarticular)
Comparator = NRG (Unspecified)
Index = IgM-RF
Sensitivity = 43.5%
Specificity = 100.%

By subtype

		Reference	
		+	-
Index test	+	2	0
	-	21	20

Disease group = JIA (systemic)
Comparator = NRG (Unspecified)
Index = IgM-RF
Sensitivity = 44.4%
Specificity = 100.%

By subtype

		Reference	
		+	-
Index test	+	1	0
	-	17	20

Disease group = JIA (pauciarticular)
Comparator = NRG (Unspecified)
Index = IgG-RF
Sensitivity = 4.2%
Specificity = 100.%

Disease group = JIA (polyarticular)
Comparator = NRG (Unspecified)
Index = IgG-RF
Sensitivity = 8.7%
Specificity = 100.%

Disease group = JIA (systemic)
Comparator = NRG (Unspecified)
Index = IgG-RF
Sensitivity = 5.6%
Specificity = 100.%

Study	Participants Characteristics	Index Test Characteristics
Jones, O.Y., 2006 (33) **Country (# centers):** More than one countries from North America (7) **Funding:** NR **Study design:** Case control (Retrospective) **Recruitment:** Random selection	**Inclusion criteria:** NRG: Records available in the Pediatric Rheumatology Disease Registry (1992-1995) **Exclusion criteria:** NR **JIA patients** **$N_{analyzed}/N_{enrolled}$:** 194/206 **Mean age (range):** 6.4yr (2.4-17.1yr) **Female:** 75.2% **Mean/median time since diagnosis (range):** NR **Subtype:** Pauciarticular (41.8%); Polyarticular (38.4%); Systemic (19.9%) **Reference standard for JIA diagnosis:** NR	**ANA test** **Assay method:** NR **Source of antigen:** NR **Manufacturer (kit type):** NR **Positive cutoff:** Titre 1:80

Results (Overall)

		Reference	
		+	-
Index test	+	66	6
	-	128	28

Disease group = JIA
Comparator = NRG (Acute lymphocytic leukemia)
Index = ANA
Sensitivity = 34.0%
Specificity = 82.4%

Study	Participants Characteristics	Index Test Characteristics
Kasapcopur, O., 2004 (56) **Country (# centers):** Turkey (1) **Funding:** Academic institution **Study design:** Case control (Prospective) **Recruitment:** Consecutive patients	**Inclusion criteria:** NR **Exclusion criteria:** NR **JIA patients** **$N_{analyzed}/N_{enrolled}$:** 122/122 **Mean age (range):** 8.8yr (1.2-19.3yr) **Female:** 59.0% **Mean time since diagnosis (range):** 4.3yr (NR) **Subtype:** Polyarticular (39.3%); Oligoarticular (29.5%); Systemic (23.0%); Enthsitis-related arthritis (5.7%); Juvenile psoriatic arthritis (2.5%) **Reference standard for JIA diagnosis:** ILAR **SLE patients** **$N_{analyzed}/N_{enrolled}$:** 19/19 **Mean age (range):** 13.6yr (5.3-18.0yr) **Female:** 89.5% **Mean time since diagnosis (range):** 4.5yr (NR) **Reference standard for SLE diagnosis:** NR	**CCP test** **Assay method:** ELISA **Source of antigen:** NR **Manufacturer (kit type):** Euroimmun, Germany (NR) **Positive cutoff:** 5 relative units

Results (Overall)

		Reference	
		+	-
Index test	+	3	0

Overall

		Reference	
		+	-
Index test	+	0	0

	-	119	15

Disease group = JIA
Comparator = Healthy controls
Index = CCP
Sensitivity = 2.5%
Specificity = 100.%

	-	19	15

Disease group = SLE
Comparator = Healthy controls
Index = CCP
Sensitivity = 0.0%
Specificity = 100.%

Study	Participants Characteristics	Index Test Characteristics
Kwok, J.S.Y., 2005 (58) **Country (# centers):** Hong Kong (1) **Funding:** Academic institution **Study design:** Case control (Retrospective) **Recruitment:** NR	**Inclusion criteria:** NR **Exclusion criteria:** NR **JIA patients** **$N_{analyzed}/N_{enrolled}$:** 59/59 **Mean age (range):** 15.0yr (2.4-24.0yr) **Female:** 40.7% **Mean time since diagnosis (range):** 4.3yr (0.4-16.0yr) **Subtype:** Oligoarticular (25.4%); Polyarticular (32.2%); Systemic (6.8%); Enthesitis-related (20.3%); Other arthritides (15.3%) **Reference standard for JIA diagnosis:** ILAR **SLE patients** **$N_{analyzed}/N_{enrolled}$:** 21/21 **Mean age (range):** NR **Female:** NR **Mean time since diagnosis (range):** NR **Reference standard for SLE diagnosis:** NR	**CCP test** **Assay method:** ELISA **Source of antigen:** NR **Manufacturer (kit type):** Inova Diagnostics Inc, San Diego, CA; QuantaLite CCP IgG ELISA kit; NR **Positive cutoff:** 20 AU

Results (Overall)

		Reference	
		+	-
Index test	+	6	1
	-	53	25

Overall

		Reference	
		+	-
Index test	+	0	1
	-	21	25

By subtype

		Reference	
		+	-
Index test	+	1	1
	-	14	25

Disease group = JIA
Comparator = NRG (allergy, idiopathic thrombocytopenia, and hepatitis C)
Index = CCP
Sensitivity = 10.2%
Specificity = 97.9%

By subtype

		Reference	
		+	-
Index test	+	4	1
	-	15	25

Disease group = SLE
Comparator = NRG (allergy, idiopathic thrombocytopenia, and hepatitis C)
Index = CCP
Sensitivity = 0.0%
Specificity = 96.2%

By subtype

		Reference	
		+	-
Index test	+	1	1
	-	3	25

Disease group = JIA (oligoarticular)
Comparator = NRG (allergy, idiopathic thrombocytopenia, and hepatitis C)
Index = CCP
Sensitivity = 6.7%
Specificity = 97.9%

Disease group = JIA (polyarticular)
Comparator = NRG (allergy, idiopathic thrombocytopenia, and hepatitis C)
Index = CCP
Sensitivity = 21.1%
Specificity = 97.9%

Disease group = JIA (systemic)
Comparator = NRG (allergy, idiopathic thrombocytopenia, and hepatitis C)
Index = CCP
Sensitivity = 25.0%
Specificity = 97.9%

Study	Participants Characteristics	Index Test Characteristics
Lipinska, J., 2008 (34) **Country (# centers):** Poland (NR) **Funding:** Academic institution **Study design:** Case control (Prospective) **Recruitment:** NR	**Inclusion criteria:** NRG: With functional cardio-vascular system dysfunction. Age- and sex-matched with JIA patients **Exclusion criteria:** NR **JIA patients** **$N_{analyzed}/N_{enrolled}$:** 96/96 **Mean/median age (range):** 12.8yr (3.0-18.0yr) **Female:** 61.5% **Mean/median time since diagnosis (range):** NR **Subtype:** Oligoarticular (37.5%); Polyarticular (51.0%); Systemic (11.5%) **Reference standard for JIA diagnosis:** ILAR	**ANA test** **Assay method:** IIF **Source of antigen:** NR **Manufacturer (kit type):** Euroimmun Polska Sp. z o.o. (NR) **Positive cutoff:** Titre 1:320 **IgM-RF test** **Assay method:** ELISA **Source of antigen:** NR **Manufacturer (kit type):** Biomedica Poland Sp. Z.o.o. (05-500 Piaseczno ELISA kit) **Positive cutoff:** 24 RU/ml **CCP test** **Assay method:** ELISA **Source of antigen:** NR **Manufacturer (kit type):** Euroimmun Polska Sp. z o.o. (52-219 Wroclaw) **Positive cutoff:** 5 RU/ml

Results (Overall)

		Reference	
		+	-
Index test	+	8	0
	-	88	22

Disease group = JIA
Comparator = NRG
Index = ANA
Sensitivity = 8.3%
Specificity = 100.%

Overall

		Reference	
		+	-
Index test	+	14	1
	-	82	21

Disease group = JIA
Comparator = NRG
Index = IgM-RF
Sensitivity = 14.6%
Specificity = 95.5%

Overall

		Reference	
		+	-
Index test	+	40	0
	-	56	22

Disease group = JIA
Comparator = NRG
Index = CCP
Sensitivity = 41.7%
Specificity = 100.%

By subtype

		Reference	
		+	-
Index test	+	2	1
	-	34	21

Disease group = JIA (oligoarticular)
Comparator = NRG
Index = IgM-RF
Sensitivity = 5.6%
Specificity = 95.5%

By subtype

		Reference	
		+	-
Index test	+	11	1
	-	38	21

Disease group = JIA (polyarticular)
Comparator = NRG
Index = IgM-RF
Sensitivity = 22.4%
Specificity = 95.5%

By subtype

		Reference	
		+	-
Index test	+	1	1
	-	10	21

Disease group = JIA (systemic)
Comparator = NRG
Index = IgM-RF
Sensitivity = 9.1%
Specificity = 95.5%

By subtype

		Reference	
		+	-
Index test	+	13	0
	-	23	22

Disease group = JIA (oligoarticular)
Comparator = NRG
Index = CCP
Sensitivity = 36.1%
Specificity = 100%

By subtype

		Reference	
		+	-
Index test	+	21	0
	-	28	22

Disease group = JIA (polyarticular)
Comparator = NRG
Index = CCP
Sensitivity = 42.9%
Specificity = 100%

By subtype

		Reference	
		+	-
Index test	+	6	0
	-	5	22

Disease group = JIA (systemic)
Comparator = NRG
Index = CCP
Sensitivity = 54.5%
Specificity = 100%

Study	Participants Characteristics	Index Test Characteristics
Mo, N., 2008 (57) **Country (# centers):** UK (1) **Funding:** NR **Study design:** Case control (Prospective) **Recruitment:** Random selection	**Inclusion criteria:** NR **Exclusion criteria:** NR **JIA patients** **$N_{analyzed}/N_{enrolled}$:** 43/43 **Mean/median age (range):** NR **Female:** NR **Mean/median time since diagnosis (range):** NR **Subtype:** NR **Reference standard for JIA diagnosis:** NR	**CCP test** **Assay method:** ELISA **Source of antigen:** Synthetic peptide **Manufacturer (kit type):** Invitrogen (cfc-1-cyc) **Positive cutoff:** NR **CCP test** **Assay method:** ELISA **Source of antigen:** NR **Manufacturer (kit type):** Axis-Shield (commercial anti-CCP2 kit) **Positive cutoff:** NR **CCP test** **Assay method:** ELISA **Source of antigen:** NR **Manufacturer (kit type):** Inova (commercial anti-CCP3 kit) **Positive cutoff:** NR

Results (Overall)

		Reference	
		+	-
Index test	+	6	0
	-	37	26

Disease group = JIA
Comparator = NRG (non-JIA)
Index = CCP (Invitrogen)
Sensitivity = 14.0%
Specificity = 100.%

Overall

		Reference	
		+	-
Index test	+	7	0
	-	36	26

Disease group = JIA
Comparator = NRG (non-JIA)
Index = CCP (Axis-Shield)
Sensitivity = 16.3%
Specificity = 100.%

Overall

		Reference	
		+	-
Index test	+	5	0
	-	38	26

Disease group = JIA
Comparator = NRG (non-JIA)
Index = CCP (Inova)
Sensitivity = 11.6%
Specificity = 100.%

By subtype

		Reference	
		+	-
Index test	+	1	0
	-	18	26

Disease group = JIA (oligoarticular)
Comparator = NRG (non-JIA)
Index = CCP (Axis-Shield)
Sensitivity = 5.3%
Specificity = 100.%

By subtype

		Reference	
		+	-
Index test	+	4	0
	-	12	26

Disease group = JIA (polyarticular)
Comparator = NRG (non-JIA)
Index = CCP (Axis-Shield)
Sensitivity = 25.0%
Specificity = 100.%

By subtype

		Reference	
		+	-
Index test	+	2	0
	-	6	26

Disease group = JIA (systemic)
Comparator = NRG (non-JIA)
Index = CCP (Axis-Shield)
Sensitivity = 25.0%
Specificity = 100.%

Study	Participants Characteristics	Index Test Characteristics
Nordal, E.B., 2009 (35) **Country (# centers):** Norway (5) **Funding:** Non-commercial institution **Study design:** Case control (Prospective) **Recruitment:** Consecutive patients	**Inclusion criteria:** JIA patients: Newly diagnosed cases NRG: Children undergoing elective outpatient procedures with no diagnosis of inflammatory diseases **Exclusion criteria:** NR **JIA patients** **$N_{analyzed}/N_{enrolled}$:** 100/174 **Mean/median age (range):** NR **Female:** 71.0% **Mean/median time since diagnosis (range):** NR (max: 1.0yr) **Subtype:** Oligoarticular (50.0%) **Reference standard for JIA diagnosis:** ILAR	**ANA test** **Assay method:** IIF **Source of antigen:** HEp-2 cell line **Manufacturer (kit type):** Immunoconcepts, Sacramento, CA (NR) **Positive cutoff:** Titre 1:80 **ANA test** **Assay method:** ELISA **Source of antigen:** Recombinant or purified native nuclear antigens **Manufacturer (kit type):** Pharmacia Diagnostics, Freiburg, Germany (Varelisa Recombi ANA screening test). **Positive cutoff:** Titre 1:101

Results (Overall)

		Reference	
		+	-
Index test	+	57	3
	-	43	55

Disease group = JIA
Comparator = NRG (no inflammatory diseases; undergoing elective surgery)
Index = ANA (IIF)
Sensitivity = 57.0%
Specificity = 94.8%

By comorbidity

	Reference	
	+	-

Overall

		Reference	
		+	-
Index test	+	4	0
	-	96	58

Disease group = JIA
Comparator = NRG (no inflammatory diseases; undergoing elective surgery)
Index = ANA (ELISA)
Sensitivity = 4.0%
Specificity = 100.%

By comorbidity

		Reference	
		+	-
Index test	+	13	N/A
	-	3	N/A

Disease group = JIA (with uveitis)
Comparator = NRG (no inflammatory diseases; undergoing elective surgery)
Index = ANA (IIF)
Sensitivity = 81.3%
Specificity = N/A

Index test	+	44	N/A
	-	40	N/A

Disease group = JIA (without uveitis)
Comparator = NRG (no inflammatory diseases; undergoing elective surgery)
Index = ANA (IIF)
Sensitivity = 52.4%
Specificity = N/A

Study	Participants Characteristics	Index Test Characteristics
Osborn, T.G., 1984 (36) **Country (# centers):** U.S. (1) **Funding:** Government **Study design:** Case control (Prospective) **Recruitment:** NR	**Inclusion criteria:** NR **Exclusion criteria:** NR **JIA patients** **$N_{analyzed}/N_{enrolled}$:** 217/217 **Mean/median age (range):** NR (0.2-16.0yr) **Female:** 66.4% **Mean/median time since diagnosis (range):** NR **Subtype:** Pauciarticular (46.5%); Systemic (12.9%); Polyarticular (40.6%) **Reference standard for JIA diagnosis:** ARA	**ANA test** **Assay method:** IIF **Source of antigen:** HEp-2 cell line **Manufacturer (kit type):** NR **Positive cutoff:** Titre 1:40

Results (Overall)

		Reference	
		+	-
Index test	+	131	3
	-	86	32

Disease group = JIA
Comparator = Healthy controls
Index = ANA
Sensitivity = 60.4%
Specificity = 91.4%

By subtype

		Reference	
		+	-
Index test	+	59	3
	-	29	32

Overall

		Reference	
		+	-
Index test	+	131	15
	-	86	16

Disease group = JIA
Comparator = ORG (other connective tissue diseases)
Index = ANA
Sensitivity = 60.4%
Specificity = 51.6%

By subtype

		Reference	
		+	-
Index test	+	9	3
	-	19	32

By subtype

		Reference	
		+	-
Index test	+	63	3
	-	38	32

Disease group = JIA (pauciarticular)
Comparator = Healthy controls
Index = ANA
Sensitivity = 62.4%
Specificity = 91.4%

By subtype

		Reference	
		+	-
Index test	+	63	15
	-	38	16

Disease group = JIA (polyarticular)
Comparator = Healthy controls
Index = ANA
Sensitivity = 67.0%
Specificity = 91.4%

By subtype

		Reference	
		+	-
Index test	+	59	15
	-	29	16

Disease group = JIA (systemic)
Comparator = Healthy controls
Index = ANA
Sensitivity = 32.1%
Specificity = 91.4%

By subtype

		Reference	
		+	-
Index test	+	9	15
	-	19	16

Disease group = JIA (pauciarticular)
Comparator = ORG (other connective tissue diseases)
Index = ANA
Sensitivity = 62.4%
Specificity = 51.6%

Disease group = JIA (polyarticular)
Comparator = ORG (other connective tissue diseases)
Index = ANA
Sensitivity = 67.0%
Specificity = 51.6%

Disease group = JIA (systemic)
Comparator = ORG (other connective tissue diseases)
Index = ANA
Sensitivity = 32.1%
Specificity = 51.6%

Study	Participants Characteristics	Index Test Characteristics
Permin, H., 1982 (44) **Country (# centers):** Denmark (NR) **Funding:** Non-commercial institution **Study design:** Case control (Prospective) **Recruitment:** Random selection	**Inclusion criteria:** NR **Exclusion criteria:** NR **JIA patients** **$N_{analyzed}/N_{enrolled}$:** 26/26 **Mean age (range):** 9.0yr (2.0-16.0yr) **Female:** 73.1% **Mean time since diagnosis (range):** 3.yr (0.5-15.0yr) **Subtype:** Polyarticular (42.3%); Pauciarticular (42.3%); Systemic (15.4%) **Reference standard for JIA diagnosis:** ARA	**IgM-RF test** **Assay method:** IIF **Source of antigen:** Formalin-fixed sheep red cell IgG **Manufacturer (kit type):** NR **Positive cutoff:** Titre 1:10 **IgG-RF test** **Assay method:** IIF **Source of antigen:** Formalin-fixed sheep red cell IgG **Manufacturer (kit type):** NR **Positive cutoff:** Titre 1:10 **IgA-RF test** **Assay method:** IIF **Source of antigen:** Formalin-fixed sheep red cell IgG **Manufacturer (kit type):** NR **Positive cutoff:** Titre 1:10 **IgE-RF test** **Assay method:** IIF **Source of antigen:** Formalin-fixed sheep red cell IgG **Manufacturer (kit type):** NR **Positive cutoff:** Titre 1:16
Results (Overall)	**Overall**	**Overall**

		Reference	
		+	-
Index test	+	1	0
	-	25	23

Disease group = JIA
Comparator = Healthy controls
Index = IgM-RF
Sensitivity = 3.9%
Specificity = 100.%

		Reference	
		+	-
Index test	+	22	0
	-	4	23

Disease group = JIA
Comparator = Healthy controls
Index = IgG-RF
Sensitivity = 84.6%
Specificity = 100.%

		Reference	
		+	-
Index test	+	0	0
	-	26	23

Disease group = JIA
Comparator = Healthy controls
Index = IgA-RF
Sensitivity = 0%
Specificity = 100.%

Overall

		Reference	
		+	-
Index test	+	0	0
	-	26	23

Disease group = JIA
Comparator = Healthy controls
Index = IgE-RF
Sensitivity = 0%
Specificity = 100.%

Study	Participants Characteristics	Index Test Characteristics
Roizenblatt, S., 1993 (45) **Country (# centers):** Brazil (1) **Funding:** NR **Study design:** Case control (Prospective) **Recruitment:** NR	**Inclusion criteria:** ORG: Hypermobile children. Matched age and sex. **Exclusion criteria:** NR **JIA patients** **$N_{analyzed}/N_{enrolled}$:** 24/24 **Mean age (range):** 9.0yr (2.3-15.0yr) **Female:** 54.2% **Mean/median time since diagnosis (range):** NR (Min: 0.5yr) **Subtype:** Polyarticular (37.5%); Pauciarticular (50.0%); Systemic (12.5%) **Reference standard for JIA diagnosis:** ACR	**IgM-RF test** **Assay method:** ELISA **Source of antigen:** Sheep erytrocyte **Manufacturer (kit type):** Dako Ab (NR) **Positive cutoff:** Mean of control group + 2 sd **IgG-RF test** **Assay method:** ELISA **Source of antigen:** NR **Manufacturer (kit type):** NR **Positive cutoff:** Mean of control group + 2 sd

Results (Overall)

		Reference	
		+	-
Index test	+	1	0
	-	23	26

Disease group = JIA
Comparator = ORG
Index = IgM-RF
Sensitivity = 4.2%
Specificity = 100.%

By subtype

		Reference	
		+	-
Index test	+	0	0
	-	9	26

Overall

		Reference	
		+	-
Index test	+	19	0
	-	5	26

Disease group = JIA
Comparator = ORG
Index = IgG-RF
Sensitivity = 79.2%
Specificity = 100.%

By subtype

		Reference	
		+	-
Index test	+	0	0
	-	3	26

By subtype

		Reference	
		+	-
Index test	+	1	0
	-	11	26

Disease group = JIA (pauciarticular)
Comparator = ORG
Index = IgM-RF
Sensitivity = 8.3%
Specificity = 100%

By subtype

		Reference	
		+	-
Index test	+	10	0
	-	2	26

Disease group = JIA (polyarticular)
Comparator = ORG
Index = IgM-RF
Sensitivity = 0%
Specificity = 100%

By subtype

		Reference	
		+	-
Index test	+	7	0
	-	2	26

Disease group = JIA (systemic)
Comparator = ORG
Index = IgM-RF
Sensitivity = 0%
Specificity = 100%

By subtype

		Reference	
		+	-
Index test	+	2	0
	-	1	26

Disease group = JIA (pauciarticular)
Comparator = ORG
Index = IgG-RF
Sensitivity = 83.3%
Specificity = 100%

Disease group = JIA (polyarticular)
Comparator = ORG
Index = IgG-RF
Sensitivity = 77.8%
Specificity = 100%

Disease group = JIA (systemic)
Comparator = ORG
Index = IgG-RF
Sensitivity = 66.7%
Specificity = 100%

Study	Participants Characteristics	Index Test Characteristics
Saulsbury F.T., 1990 (51) **Country (# centers):** U.S. (NR) **Funding:** Non-commercial institution **Study design:** Case control (NR) **Recruitment:** NR	**Inclusion criteria:** NR **Exclusion criteria:** NR **JIA patients** **$N_{analyzed}/N_{enrolled}$:** 50/50 **Mean/median age (range):** NR (1.0-18.0yr) **Female:** 78.0% **Mean/median time since diagnosis (range):** NR **Subtype:** Pauciarticular (56.0%); polyarticular (28.0%); systemic (16.0%) **Reference standard for JIA diagnosis:** Based on reference No. 7	**IgM-RF test** **Assay method:** ELISA **Source of antigen:** Latex beads coated with human IgG **Manufacturer (kit type):** Dynatech Laboratories, Alexandria, VA (NR) **Positive cutoff:** Titre 1:20 **IgG-RF test** **Assay method:** ELISA **Source of antigen:** Rabbit IgG **Manufacturer (kit type):** Gamma Biologicals, Inc. Houston, TX (NR) **Positive cutoff:** Titre 1:20 **IgA-RF test** **Assay method:** ELISA **Source of antigen:** Latex beads coated with human IgG **Manufacturer (kit type):** Dynatech Laboratories, Alexandria, VA (NR) **Positive cutoff:** Titre 1:20

Results (Overall)

		Reference	
		+	-
Index test	+	11	1
	-	39	38

Disease group = JIA
Comparator = Healthy controls
Index = IgM-RF

Overall

		Reference	
		+	-
Index test	+	2	0
	-	48	39

Disease group = JIA
Comparator = Healthy controls
Index = IgG-RF

Overall

		Reference	
		+	-
Index test	+	11	1
	-	39	38

Disease group = JIA
Comparator = Healthy controls
Index = IgA-RF

Sensitivity = 22.0%
Specificity = 97.4%

By subtype

		Reference	
		+	-
Index test	+	5	1
	-	23	38

Disease group = JIA (pauciarticular)
Comparator = Healthy controls
Index = IgM-RF
Sensitivity = 17.9%
Specificity = 97.4%

By subtype

		Reference	
		+	-
Index test	+	5	1
	-	9	38

Disease group = JIA (polyarticular)
Comparator = Healthy controls
Index = IgM-RF
Sensitivity = 35.7%
Specificity = 97.4%

By subtype

		Reference	
		+	-
Index test	+	1	1
	-	7	38

Disease group = JIA (systemic)
Comparator = Healthy controls
Index = IgM-RF
Sensitivity = 12.5%
Specificity = 97.4%

Sensitivity = 58.0%
Specificity = 94.9%

By subtype

		Reference	
		+	-
Index test	+	0	0
	-	28	39

Disease group = JIA (pauciarticular)
Comparator = Healthy controls
Index = IgG-RF
Sensitivity = 0%
Specificity = 100%

By subtype

		Reference	
		+	-
Index test	+	1	0
	-	13	39

Disease group = JIA (polyarticular)
Comparator = Healthy controls
Index = IgG-RF
Sensitivity = 7.1%
Specificity = 100%

By subtype

		Reference	
		+	-
Index test	+	1	0
	-	7	39

Disease group = JIA (systemic)
Comparator = Healthy controls
Index = IgG-RF
Sensitivity = 12.5%
Specificity = 100%

Sensitivity = 32.0%
Specificity = 97.4%

By subtype

		Reference	
		+	-
Index test	+	8	1
	-	20	38

Disease group = JIA (pauciarticular)
Comparator = Healthy controls
Index = IgA-RF
Sensitivity = 28.9%
Specificity = 97.4%

By subtype

		Reference	
		+	-
Index test	+	2	1
	-	12	38

Disease group = JIA (polyarticular)
Comparator = Healthy controls
Index = IgA-RF
Sensitivity = 14.3%
Specificity = 97.4%

By subtype

		Reference	
		+	-
Index test	+	1	1
	-	7	38

Disease group = JIA (systemic)
Comparator = Healthy controls
Index = IgA-RF
Sensitivity = 12.5%
Specificity = 97.4%

Study	Participants Characteristics	Index Test Characteristics
Siamopoulou-Mavridou, A., 1991 (37) **Country (# centers):** Greece (NR) **Funding:** NR **Study design:** Case control (Prospective) **Recruitment:** Consecutive patients	**Inclusion criteria:** Healthy controls: Age- and sex-matched children without rheumatic disease **Exclusion criteria:** NR **JIA patients** **$N_{analyzed}/N_{enrolled}$:** 69/69 **Mean age (range):** 8.6yr (1.0-15.0yr) **Female:** 59.4% **Mean/median time since diagnosis (range):** 5.7yr (1.0-9.0yr) **Subtype:** Pauciarticular (43.5%); Polyarticular (29.0%); Systemic (27.5%) **Reference standard for JIA diagnosis:** EULAR	**ANA test** **Assay method:** IIF **Source of antigen:** HEp-2 cell line **Manufacturer (kit type):** NR **Positive cutoff:** Titre 1:40 **IgM-RF test** **Assay method:** Latex fixation test **Source of antigen:** NR **Manufacturer (kit type):** Behringwerke AG (NR) **Positive cutoff:** Mean optical density (OD) of healthy controls + 3 sd

Results (Overall)

		Reference	
		+	-
Index test	+	41	2
	-	28	64

Disease group = JIA
Comparator = Healthy controls
Index = ANA
Sensitivity = 59.4%
Specificity = 97.0%

By subtype

		Reference	
		+	-
Index test	+	13	2
	-	7	64

Overall

		Reference	
		+	-
Index test	+	3	0
	-	66	66

Disease group = JIA
Comparator = Healthy controls
Index = IgM-RF
Sensitivity = 4.4%
Specificity = 100.%

By subtype

		Reference	
		+	-
Index test	+	7	2
	-	12	64

By subtype

		Reference	
		+	-
Index test	+	21	2
	-	9	64

Disease group = JIA (pauciarticular)
Comparator = Healthy controls
Index = ANA
Sensitivity = 70.0%
Specificity = 97.0%

By subtype

		Reference	
		+	-
Index test	+	0	0
	-	30	66

Disease group = JIA (polyarticular)
Comparator = Healthy controls
Index = ANA
Sensitivity = 65.0%
Specificity = 97.0%

By subtype

		Reference	
		+	-
Index test	+	3	0
	-	17	66

Disease group = JIA (systemic)
Comparator = Healthy controls
Index = ANA
Sensitivity = 36.8%
Specificity = 97.0%

By subtype

		Reference	
		+	-
Index test	+	0	0
	-	19	66

Disease group = JIA (pauciarticular)
Comparator = Healthy controls
Index = IgM-RF
Sensitivity = 0%
Specificity = 100%

Disease group = JIA (polyarticular)
Comparator = Healthy controls
Index = IgM-RF
Sensitivity = 15.0%
Specificity = 100%

Disease group = JIA (systemic)
Comparator = Healthy controls
Index = IgM-RF
Sensitivity = 0%
Specificity = 100%

Study	Participants Characteristics	Index Test Characteristics
Taseski, B., 1981 (46) **Country (# centers):** Yugoslavia (1) **Funding:** NR **Study design:** Case control (Prospective) **Recruitment:** NR	**Inclusion criteria:** NR **Exclusion criteria:** NR **JIA patients** **$N_{analyzed}/N_{enrolled}$:** 40/40 **Mean/median age (range):** NR (Max: 17.0yr) **Female:** NR **Mean/median time since diagnosis (range):** NR **Subtype:** Monoarthicular (25.0%); Systemic (15.0%); Polyarticular (60.0%) **Reference standard for JIA diagnosis:** NR **Reference standard for SLE diagnosis:** NR	**RF test (unspecified isotype)** **Assay method:** Photometrical latex test (PLT) **Source of antigen:** NR **Manufacturer (kit type):** NR **Positive cutoff:** Photometrically measured even at the lowest serum dilution **RF test (unspecified isotype)** **Assay method:** Standard sensitized sheep-cell test (SSC) **Source of antigen:** Sheep cell **Manufacturer (kit type):** NR **Positive cutoff:** Titre 1:64 **IgM-RF test** **Assay method:** Latex slide test (LST) **Source of antigen:** NR **Manufacturer (kit type):** NR **Positive cutoff:** Agglutination visually detected

Results (Overall)

		Reference	
		+	-
Index test	+	20	4
	-	20	20

Disease group = JIA
Comparator = Healthy controls
Index = RF (PLT)

Overall

		Reference	
		+	-
Index test	+	0	0
	-	40	24

Disease group = JIA
Comparator = Healthy controls
Index = IgM-RF (LST)

Overall

		Reference	
		+	-
Index test	+	1	0
	-	39	24

Disease group = JIA
Comparator = Healthy controls
Index = RF (SSC)

Sensitivity = 50.0%
Specificity = 83.3%

Overall

		Reference	
		+	-
Index test	+	9	4
	-	18	20

Disease group = JIA
Comparator = ORG (collagen diseases)
Index = RF (PLT)
Sensitivity = 33.3%
Specificity = 83.3%

Overall

		Reference	
		+	-
Index test	+	2	4
	-	0	20

Disease group = SLE
Comparator = Healthy controls
Index = RF (PLT)
Sensitivity = 100 %
Specificity = 100.%

Sensitivity = 0%
Specificity = 100.%

Overall

		Reference	
		+	-
Index test	+	1	0
	-	26	24

Disease group = JIA
Comparator = ORG (collagen diseases)
Index = IgM-RF (LST)
Sensitivity = 3.7%
Specificity = 100.%

Sensitivity = 2.5%
Specificity = 100.%

Overall

		Reference	
		+	-
Index test	+	3	0
	-	24	24

Disease group = JIA
Comparator = ORG (collagen diseases)
Index = RF (SSC)
Sensitivity = 11.1%
Specificity = 100.%

Study	Participants Characteristics	Index Test Characteristics
Varbanova, B.B., 1999 (47) **Country (# centers):** Bulgaria (NR) **Funding:** NR **Study design:** Case control (Prospective) **Recruitment:** NR	**Inclusion criteria:** NR **Exclusion criteria:** NR **JIA patients** **$N_{analyzed}/N_{enrolled}$:** 53/53 **Mean/median age (range):** NR (1.5-18.0yr) **Female:** NR **Mean/median time since diagnosis (range):** NR (Min: 1yr) **Subtype:** Pauciarticular (62.3%); Seronegative Polyarticular (37.7%) **Reference standard for JIA diagnosis:** EULAR **SLE patients** **$N_{analyzed}/N_{enrolled}$:** 22/22 **Mean/median age (range):** NR **Female:** NR **Mean/median time since diagnosis (range):** NR **Reference standard for SLE diagnosis:** NR	**IgM-RF test** **Assay method:** ELISA **Source of antigen:** Human gamma globulin **Manufacturer (kit type):** CLB-Amsterdam (NR) **Positive cutoff:** 6.25 IU **IgG-RF test** **Assay method:** ELISA **Source of antigen:** Rabbit IgG **Manufacturer (kit type):** NR **Positive cutoff:** Mean international unit (IU) of healthy controls + 2 sd **IgA-RF test** **Assay method:** ELISA **Source of antigen:** Rabbit IgG **Manufacturer (kit type):** NR **Positive cutoff:** Mean IU of healthy controls + 2 sd

Results (Overall)

		Reference	
		+	-
Index test	+	17	0
	-	36	58

Overall

		Reference	
		+	-
Index test	+	7	0
	-	46	58

Overall

		Reference	
		+	-
Index test	+	15	0
	-	38	58

Disease group = JIA
Comparator = Healthy controls
Index = IgM-RF
Sensitivity = 32.1%
Specificity = 100.%

Overall

		Reference	
		+	-
Index test	+	2	0
	-	20	58

Disease group = SLE
Comparator = Healthy controls
Index = IgM-RF
Sensitivity = 9.1%
Specificity = 100.%

By subtype

		Reference	
		+	-
Index test	+	6	0
	-	27	58

Disease group = JIA (pauciarticular)
Comparator = Healthy controls
Index = IgM-RF
Sensitivity = 18.2%
Specificity = 100%

By subtype

		Reference	
		+	-
Index test	+	3	0
	-	17	58

Disease group = JIA (polyarticular)
Comparator = Healthy controls
Index = IgG-RF
Sensitivity = 15.0%
Specificity = 100%

Disease group = JIA
Comparator = Healthy controls
Index = IgG-RF
Sensitivity = 13.2%
Specificity = 100.%

Overall

		Reference	
		+	-
Index test	+	3	0
	-	19	58

Disease group = SLE
Comparator = Healthy controls
Index = IgG-RF
Sensitivity = 13.6%
Specificity = 100.%

By subtype

		Reference	
		+	-
Index test	+	11	0
	-	9	58

Disease group = JIA (polyarticular)
Comparator = Healthy controls
Index = IgM-RF
Sensitivity = 55.0%
Specificity = 100%

By subtype

		Reference	
		+	-
Index test	+	7	0
	-	26	58

Disease group = JIA (pauciarticular)
Comparator = Healthy controls
Index = IgA-RF
Sensitivity = 21.2%
Specificity = 100%

Disease group = JIA
Comparator = Healthy controls
Index = IgA-RF
Sensitivity = 28.3%
Specificity = 100.%

Overall

		Reference	
		+	-
Index test	+	2	0
	-	20	58

Disease group = SLE
Comparator = Healthy controls
Index = IgA-RF
Sensitivity = 9.1%
Specificity = 100.%

By subtype

		Reference	
		+	-
Index test	+	4	0
	-	29	58

Disease group = JIA (pauciarticular)
Comparator = Healthy controls
Index = IgG-RF
Sensitivity = 12.1%
Specificity = 100%

By subtype

		Reference	
		+	-
Index test	+	8	0
	-	12	58

Disease group = JIA (polyarticular)
Comparator = Healthy controls
Index = IgA-RF
Sensitivity = 40.0%
Specificity = 100%

Study	Participants Characteristics	Index Test Characteristics
Wakhlu, A., 2003 (38) **Country (# centers):** India (1) **Funding:** Academic institution **Study design:** Case control (Prospective) **Recruitment:** NR	**Inclusion criteria:** NR **Exclusion criteria:** NR **JIA patients** **$N_{analyzed}/N_{enrolled}$:** 148/148 **Median age (range):** 14.0yr (2.0-26.0yr) **Female:** 43.2% **Mean/median time since diagnosis (range):** NR **Subtype:** Pauciarticular (36.5%); Polyarticular (43.2%); Systemic (20.3%) **Reference standard for JIA diagnosis:** ARA	**ANA test** **Assay method:** IIF **Source of antigen:** HEp-2 cell line **Manufacturer (kit type):** NR **Positive cutoff:** Titre 1:40

Overall

		Reference	
		+	-
Index test	+	2	0
	-	146	25

Disease group = JIA
Comparator = Healthy controls
Index = ANA
Sensitivity = 1.4%
Specificity = 100.%

By subtype

		Reference	
		+	-
Index test	+	0	0
	-	30	25

Disease group = JIA (systemic)

By subtype

		Reference	
		+	-
Index test	+	0	0
	-	54	25

Disease group = JIA (pauciarticular)
Comparator = Healthy controls
Index = ANA
Sensitivity = 0%
Specificity = 100.%

By subtype

		Reference	
		+	-
Index test	+	2	0
	-	62	25

Disease group = JIA (polyarticular)
Comparator = Healthy controls
Index = ANA
Sensitivity = 3.1%
Specificity = 100.%

Comparator = Healthy controls
Index = ANA
Sensitivity = 0%
Specificity = 100.%

Study	Participants Characteristics	Index Test Characteristics
Walker, S.M., 1990 (98) **Country (# centers):** U.S. (1) **Funding:** Supported in part by Arthritis Foundation (Southern California chapter) **Study design:** Case control (Prospective) **Recruitment:** Random selection	**Inclusion criteria:** NR **Exclusion criteria:** JIA patients: Exclude ankylosing spondylitis **JIA patients** **$N_{analyzed}/N_{enrolled}$:** 68/68 **Mean/median age (range):** NR **Female:** NR **Mean/median time since diagnosis (range):** NR **Subtype:** Polyarticular (35.3%); Systemic (39.7%); Pauciarticular (25.0%) **Reference standard for JIA diagnosis:** ARA	**IgA-RF test** **Assay method:** ELISA **Source of antigen:** Multiple (i.e.: rabbit IgG, human Fab fragment, and murine IgG) **Manufacturer (kit type):** Multiple such as Dynatech; Signma; Rockland; and Calbiochem (NR) **Positive cutoff:** Mean OD of healthy controls + 2 sd at 1:100 dilution

Results (Overall)

		Reference	
		+	-
Index test	+	15	0
	-	53	32

Disease group = JIA
Comparator = Healthy controls
Index = IgA-RF
Sensitivity = 22.1%
Specificity = 100.%

By subtype

		Reference	
		+	-
Index test	+	0	0
	-	27	32

Disease group = JIA (systemic)

By subtype

		Reference	
		+	-
Index test	+	1	0
	-	16	32

Disease group = JIA (pauciarticular)
Comparator = Healthy controls
Index = IgA-RF
Sensitivity = 5.9%
Specificity = 100.%

By subtype

		Reference	
		+	-
Index test	+	14	0
	-	10	32

Disease group = JIA (polyarticular)
Comparator = Healthy controls
Index = IgA-RF
Sensitivity = 58.3%
Specificity = 100.%

Comparator = Healthy controls
Index = IgA-RF
Sensitivity = 0.0%
Specificity = 100.%

Study	Participants Characteristics	Index Test Characteristics
Wananukul, S., 2005 (31) **Country (# centers):** Thailand (1) **Funding:** Non-commercial institution **Study design:** Case control (Prospective) **Recruitment:** NR	**Inclusion criteria:** NRG: Scheduled for elective surgery (adenotonsillectomy, herniorrhaphy or plastic surgery) **Exclusion criteria:** All participants: Exclude overt autoimmune disease, or conditions associated with abnormal ANA titers (infection, hepatitis and malignancy) or underwent treatment with certain drugs (procainamide, hydralazine, chlorpromazine, etc) All participants: Exclude children aged less than 6 months old **SLE patients** **$N_{analyzed}/N_{enrolled}$:** 46/52 **Mean/median age (range):** NR (5.0-15.0yr) **Female:** NR **Mean/median time since diagnosis (range):** NR **Subtype:** NR **Reference standard for SLE diagnosis:** 1997 revised criteria for the classification of SLE	**ANA test** **Assay method:** IIF **Source of antigen:** HEp-2 cell line **Manufacturer (kit type):** Diasarin, Stillwater, MN (ANAFAST kits) **Positive cutoff:** Titre ≥ 1:40

Results (Overall)

		Reference	
		+	-
Index test	+	42	15
	-	4	84

Disease group = SLE
Comparator = Healthy controls (elective

Overall

		Reference	
		+	-
Index test	+	42	17
	-	4	91

Disease group = SLE
Comparator = Healthy controls

surgery) Index = ANA **Sensitivity** = 91.3% **Specificity** = 84.8%	Index = ANA **Sensitivity** = 91.3% **Specificity** = 84.3%

Study	Participants Characteristics	Index Test Characteristics
Wernick, R., 1981 (48) **Country (# centers):** U.S. (NR) **Funding:** Government **Study design:** Case control (Prospective) **Recruitment:** NR	**Inclusion criteria:** NR **Exclusion criteria:** NR **JIA patients** **$N_{analyzed}/N_{enrolled}$:** 49/49 **Mean/median age (range):** NR **Female:** NR **Mean/median time since diagnosis (range):** NR **Subtype:** Polyarticular (22.4%); Pauciarticular (59.2%); Systemic (18.4%) **Reference standard for JIA diagnosis:** ARA **SLE patients** **$N_{analyzed}/N_{enrolled}$:** 7/7 **Mean/median age (range):** NR **Female:** NR **Mean/median time since diagnosis (range):** NR **Reference standard for SLE diagnosis:** ARA	**IgM-RF test** **Assay method:** Solid phase radioimmunoassay **Source of antigen:** Rabbit and human IgG **Manufacturer (kit type):** Signma Chemical Co., St. Louis, MO (Cohn Fraction II) **Positive cutoff:** Mean of normal controls + 2 SD **IgG-RF test** **Assay method:** Solid phase radioimmunoassay **Source of antigen:** Rabbit and human IgG **Manufacturer (kit type):** Signma Chemical Co., St. Louis, MO (Cohn Fraction II) **Positive cutoff:** Mean of normal controls + 2 SD

Results (Overall)

		Reference	
		+	-
Index test	+	2	2
	-	47	30

Overall

		Reference	
		+	-
Index test	+	4	1
	-	45	32

Overall

		Reference	
		+	-
Index test	+	0	1
	-	7	32

Disease group = JIA
Comparator = NRG (Scoliosis and neurologic diseases)
Index = IgM-RF
Sensitivity = 4.1%
Specificity = 93.8%

Overall

		Reference	
		+	-
Index test	+	1	2
	-	6	30

Disease group = SLE
Comparator = NRG (Scoliosis and neurologic diseases)
Index = IgG-RF
Sensitivity = 14.3%
Specificity = 93.8%

By subtype

		Reference	
		+	-
Index test	+	0	2
	-	9	30

Disease group = JIA (systemic)
Comparator = NRG (Scoliosis and neurologic diseases)
Index = IgM-RF
Sensitivity = 0%
Specificity = 93.8%

By subtype

		Reference	
		+	-
Index test	+	1	1
	-	8	32

Disease group = JIA (systemic)
Comparator = NRG (Scoliosis and neurologic diseases)
Index = IgG-RF
Sensitivity = 11.1%

Disease group = JIA
Comparator = NRG (Scoliosis and neurologic diseases)
Index = IgG-RF
Sensitivity = 8.2%
Specificity = 90.6%

By subtype

		Reference	
		+	-
Index test	+	1	2
	-	28	30

Disease group = JIA (pauciarticular)
Comparator = NRG (Scoliosis and neurologic diseases)
Index = IgM-RF
Sensitivity = 3.4%
Specificity = 93.8%

By subtype

		Reference	
		+	-
Index test	+	2	1
	-	27	32

Disease group = JIA (pauciarticular)
Comparator = NRG (Scoliosis and neurologic diseases)
Index = IgG-RF
Sensitivity = 6.9%
Specificity = 97.0%

Disease group = SLE
Comparator = NRG (scoliosis and neurologic diseases)
Index = IgM-RF
Sensitivity = 0%
Specificity = 97.0%

By subtype

		Reference	
		+	-
Index test	+	1	2
	-	10	30

Disease group = JIA (polyarticular)
Comparator = NRG (Scoliosis and neurologic diseases)
Index = IgM-RF
Sensitivity = 9.1%
Specificity = 93.8%

By subtype

		Reference	
		+	-
Index test	+	1	1
	-	10	32

Disease group = JIA (polyarticular)
Comparator = NRG (Scoliosis and neurologic diseases)
Index = IgG-RF
Sensitivity = 9.1%
Specificity = 97.0%

Specificity = 90.6%

Appendix F. Subgroup analyses by onset-type of juvenile idiopathic arthritis

Subgroup analysis of studies examining antinuclear antibody test for juvenile idiopathic arthritis (Figures 9-11)

Figure 1. Forest plot of sensitivity and specificity of antinuclear antibody test for pauci- or oligo-articular juvenile idiopathic arthritis

Study	TP	FP	FN	TN	Sensitivity	Specificity
Fawcett 1999 (ORG)	68	4	20	22	0.77 [0.67, 0.86]	0.85 [0.65, 0.96]
Haynes 1986 (NRG)	18	1	6	17	0.75 [0.53, 0.90]	0.94 [0.73, 1.00]
Osborn 1984 (healthy)	63	18	38	48	0.62 [0.52, 0.72]	0.73 [0.60, 0.83]
S-Mavridou 1991 (healthy)	21	2	9	64	0.70 [0.51, 0.85]	0.97 [0.89, 1.00]
Wakhlu 2003 (healthy)	0	0	54	25	0.00 [0.00, 0.07]	1.00 [0.86, 1.00]

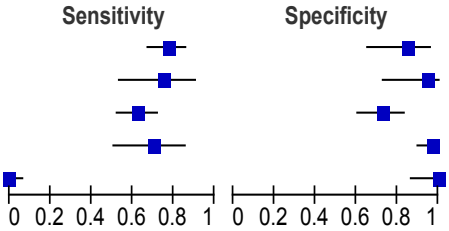


Figure 2. Forest plot of sensitivity and specificity of antinuclear antibody test for polyarticular juvenile idiopathic arthritis

Study	TP	FP	FN	TN	Sensitivity	Specificity
Fawcett 1999 (ORG)	38	4	30	22	0.56 [0.43, 0.68]	0.85 [0.65, 0.96]
Haynes 1986 (NRG)	12	1	11	17	0.52 [0.31, 0.73]	0.94 [0.73, 1.00]
Osborn 1984 (healthy)	59	18	29	48	0.67 [0.56, 0.77]	0.73 [0.60, 0.83]
S-Mavridou 1991 (healthy)	13	2	7	64	0.65 [0.41, 0.85]	0.97 [0.89, 1.00]
Wakhlu 2003 (healthy)	2	0	62	25	0.03 [0.00, 0.11]	1.00 [0.86, 1.00]

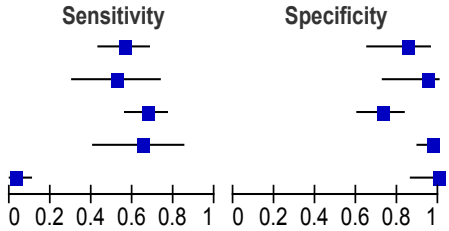
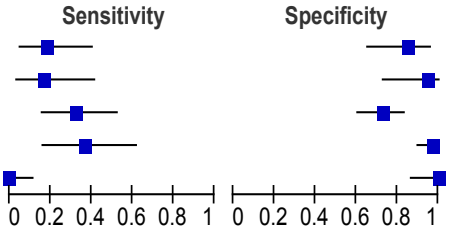


Figure 3. Forest plot of sensitivity and specificity of antinuclear antibody test for systemic juvenile idiopathic arthritis

Study	TP	FP	FN	TN	Sensitivity	Specificity
Fawcett 1999 (ORG)	4	4	18	22	0.18 [0.05, 0.40]	0.85 [0.65, 0.96]
Haynes 1986 (NRG)	3	1	15	17	0.17 [0.04, 0.41]	0.94 [0.73, 1.00]
Osborn 1984 (healthy)	9	18	19	48	0.32 [0.16, 0.52]	0.73 [0.60, 0.83]
S-Mavridou 1991 (healthy)	7	2	12	64	0.37 [0.16, 0.62]	0.97 [0.89, 1.00]
Wakhlu 2003 (healthy)	0	0	30	25	0.00 [0.00, 0.12]	1.00 [0.86, 1.00]



Subgroup analysis of studies examining IgM-RF test for juvenile idiopathic arthritis (Figures 12-14)

Figure 4. Forest plot of the sensitivity and specificity of IgM-rheumatoid factor test for pauci- or oligo-articular juvenile idiopathic arthritis

Study	TP	FP	FN	TN	Sensitivity	Specificity
Andersson-Gare 1994 (healthy)	6	4	111	126	0.05 [0.02, 0.11]	0.97 [0.92, 0.99]
Ferreira 2007 (healthy)	9	3	19	42	0.32 [0.16, 0.52]	0.93 [0.82, 0.99]
Haynes 1986 (NRG)	5	0	19	20	0.21 [0.07, 0.42]	1.00 [0.83, 1.00]
Lipinska 2008 (NRG)	2	1	34	21	0.06 [0.01, 0.19]	0.95 [0.77, 1.00]
Roizenblatt 1983 (ORG)	1	0	11	26	0.08 [0.00, 0.38]	1.00 [0.87, 1.00]
Saulsbury 1990 (healthy)	5	1	23	38	0.18 [0.06, 0.37]	0.97 [0.87, 1.00]
Varbanova 1999 (healthy)	6	0	27	58	0.18 [0.07, 0.35]	1.00 [0.94, 1.00]
Wernick 1981 (NRG)	1	2	28	30	0.03 [0.00, 0.18]	0.94 [0.79, 0.99]

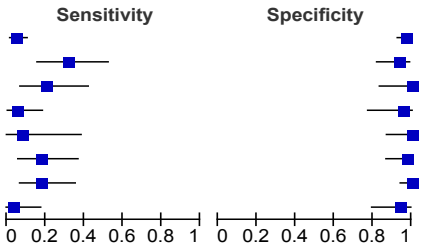


Figure 5. Forest plot of the sensitivity and specificity of IgM-rheumatoid factor test for polyarticular juvenile idiopathic arthritis

Study	TP	FP	FN	TN	Sensitivity	Specificity
Andersson-Gare 1994 (healthy)	21	4	102	126	0.17 [0.11, 0.25]	0.97 [0.92, 0.99]
Ferreira 2007 (healthy)	13	3	12	42	0.52 [0.31, 0.72]	0.93 [0.82, 0.99]
Haynes 1986 (NRG)	10	0	13	20	0.43 [0.23, 0.66]	1.00 [0.83, 1.00]
Lipinska 2008 (NRG)	11	1	38	21	0.22 [0.12, 0.37]	0.95 [0.77, 1.00]
Roizenblatt 1983 (ORG)	0	0	9	26	0.00 [0.00, 0.34]	1.00 [0.87, 1.00]
Saulsbury 1990 (healthy)	5	1	9	38	0.36 [0.13, 0.65]	0.97 [0.87, 1.00]
Varbanova 1999 (healthy)	11	0	9	58	0.55 [0.32, 0.77]	1.00 [0.94, 1.00]
Wernick 1981 (NRG)	1	2	10	30	0.09 [0.00, 0.41]	0.94 [0.79, 0.99]

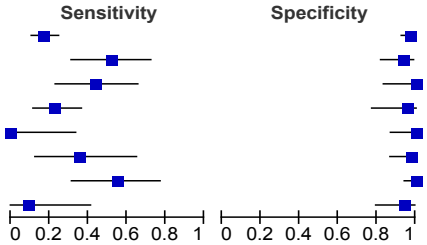
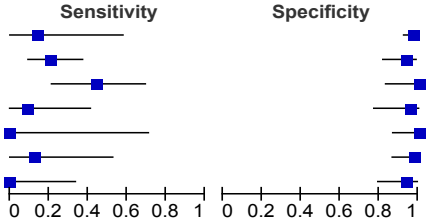


Figure 6. Forest plot of the sensitivity and specificity of IgM-rheumatoid factor test using the enzyme-linked immunosorbent assay method for systemic juvenile idiopathic arthritis

Study	TP	FP	FN	TN	Sensitivity	Specificity
Andersson-Gare 1994 (healthy)	1	4	6	126	0.14 [0.00, 0.58]	0.97 [0.92, 0.99]
Ferreira 2007 (healthy)	8	3	30	42	0.21 [0.10, 0.37]	0.93 [0.82, 0.99]
Haynes 1986 (NRG)	8	0	10	20	0.44 [0.22, 0.69]	1.00 [0.83, 1.00]
Lipinska 2008 (NRG)	1	1	10	21	0.09 [0.00, 0.41]	0.95 [0.77, 1.00]
Roizenblatt 1983 (ORG)	0	0	3	26	0.00 [0.00, 0.71]	1.00 [0.87, 1.00]
Saulsbury 1990 (healthy)	1	1	7	38	0.13 [0.00, 0.53]	0.97 [0.87, 1.00]
Wernick 1981 (NRG)	0	2	9	30	0.00 [0.00, 0.34]	0.94 [0.79, 0.99]



Subgroup analysis of studies examining CCP test for juvenile idiopathic arthritis (Figures 15-17)

Figure 7. Forest plot of sensitivity and specificity of cyclic-citrullinated peptide test for pauci- or oligo-articular juvenile idiopathic arthritis

Study	TP	FP	FN	TN	Sensitivity	Specificity
Avcin 2002 (healthy)	1	0	50	30	0.02 [0.00, 0.10]	1.00 [0.88, 1.00]
Ferucci 2005 (healthy)	3	4	136	684	0.02 [0.00, 0.06]	0.99 [0.99, 1.00]
Habib 2008 (healthy)	0	0	20	20	0.00 [0.00, 0.17]	1.00 [0.83, 1.00]
Kwok 2005 (NRG)	1	1	14	25	0.07 [0.00, 0.32]	0.96 [0.80, 1.00]
Lipinska 2008 (NRG)	13	0	23	22	0.36 [0.21, 0.54]	1.00 [0.85, 1.00]
Mo 2008 (NRG)	1	0	18	26	0.05 [0.00, 0.26]	1.00 [0.87, 1.00]

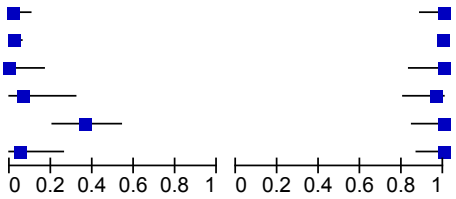


Figure 8. Forest plot of sensitivity and specificity of cyclic-citrullinated peptide test for polyarticular juvenile idiopathic arthritis

Study	TP	FP	FN	TN	Sensitivity	Specificity
Avcin 2002 (healthy)	1	0	51	30	0.02 [0.00, 0.10]	1.00 [0.88, 1.00]
Ferucci 2005 (healthy)	10	4	67	684	0.13 [0.06, 0.23]	0.99 [0.99, 1.00]
Habib 2008 (healthy)	14	0	24	20	0.37 [0.22, 0.54]	1.00 [0.83, 1.00]
Kwok 2005 (NRG)	4	1	15	25	0.21 [0.06, 0.46]	0.96 [0.80, 1.00]
Lipinska 2008 (NRG)	21	0	28	22	0.43 [0.29, 0.58]	1.00 [0.85, 1.00]
Mo 2008 (NRG)	4	0	12	26	0.25 [0.07, 0.52]	1.00 [0.87, 1.00]

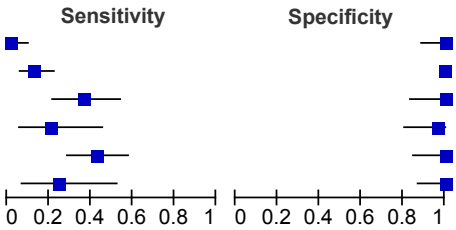
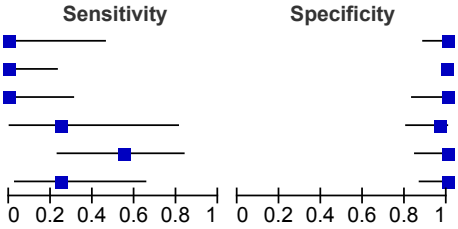


Figure 9. Forest plot of sensitivity and specificity of cyclic-citrullinated peptide test for systemic juvenile idiopathic arthritis

Study	TP	FP	FN	TN	Sensitivity	Specificity
Avcin 2002 (healthy)	0	0	6	30	0.00 [0.00, 0.46]	1.00 [0.88, 1.00]
Ferucci 2005 (healthy)	0	4	14	684	0.00 [0.00, 0.23]	0.99 [0.99, 1.00]
Habib 2008 (healthy)	0	0	10	20	0.00 [0.00, 0.31]	1.00 [0.83, 1.00]
Kwok 2005 (NRG)	1	1	3	25	0.25 [0.01, 0.81]	0.96 [0.80, 1.00]
Lipinska 2008 (NRG)	6	0	5	22	0.55 [0.23, 0.83]	1.00 [0.85, 1.00]
Mo 2008 (NRG)	2	0	6	26	0.25 [0.03, 0.65]	1.00 [0.87, 1.00]