Supplementary file I. Details on search strategy following the PRISMA 2009 checklist http://www.prisma-statement.org

1) Description of information sources:
    1.1 Pubmed search:
        First search upon 28th of February 2015
        Second search upon 28th of February 2016

    1.2 Cochrane database:
        First search upon February 28th of 2015
        Second search upon February 28th of 2016

    1.3 Biomed Central search:
        Search upon 28th of February 2015
        (Second search was not performed since Biomed Central search builder was unavailable due to working.)

2) Full electronic search strategy
      - on **Pubmed**
    Combination of two searches:
    - ("scleroderma, systemic"[MeSH Terms] OR "scleroderma"[All Fields])

    AND ("disease activity score"[All Fields] OR "disease activity" OR "response index")

    - ("scleroderma, systemic"[MeSH Terms] OR "scleroderma"[All Fields]) AND ("disease activity score"[All Fields] OR "disease activity" OR "index") AND ("truth" OR "discrimination" OR "feasibility" OR "validity" OR "sensitivity to change" OR "reliability" OR OMERACT)

    Language limits were added after reviewing title selection.

    Duplicates were manually removed.

    Titles without abstract or full texts were excluded.

    No date limits were used in the first search. In the search update the limits from 1st March 2015 upon 28th February 2016 were added.

    - on **Biomed Central:** ("systemic sclerosis" [All Fields]) AND ("disease activity" [All Fields]) AND (validity, OMERACT, truth, discrimination, reliability [Any word, All Fields])

    - on **Cochrane library:** ("scleroderma, systemic"[MeSH Terms]) AND ("disease activity " OR "disease activity index" OR "response index")

3) Results with reasons for full text exclusions (n=55).
    a. Not about the topic.
        i. Opinions/reviews/editorials, n=8
        ii. About Disease severity index, n=1
        iii. About criteria of Fiocco, n=3
        iv. About self assessment questionnaire, n=1
    b. Disease activity was measured based on another activity outcome (other than a disease activity index), n=28.
    c. Disease activity index was mentioned in article, but the article did not fulfil the inclusion criteria (content did not concern the development of DAI, did not discuss about the validation status of DAI, neither used a DAI in their analysis), n=6.
    d. No full text available, n=8.

Supplementary file 2. Overview of studies assessing an association between the Disease Activity Score (DAS), determined by the European Scleroderma Study Group (EScSG) activity index, and variable constructs (n=45).

Study	Country	Population	Assessed associations (method)	Results (univariate analysis, except when otherwise specified)
Yalcinkaya et al. 2015 (1)	Turkey	59 with SSc	Association of presence of DU* and DAS (Pearson's Chi square test)	DU positive: DAS 1.9 ± 2.1 vs DU negative: DAS 1.2 ± 2.0 (p=0.11)
			Association of severity of PVI$^\Delta$ and DAS (Pearson's Chi square test)	PVI severe: DAS 2.1 ± 2.4 vs PVI non severe: DAS 1.3 ± 1.9 (p=0.19)
			In DU* positive groups: correlation of scores of ramification and disorganisation with DA	R=0.396, **p=0.041;** R=0.702, **p<0.001**
			In DU* negative groups: correlation of scores of capillary loss, ramifications, disorganisation and microangiopathy with DA (Mann-Whitney U-test)	R=0.427, **p=0.015;** R=0.750, **p<0.001;** R=0.370, **p=0.037;** R=0.673, **p<0.001**
Favoino et al. 2015 (2)	Italy	77 with SSc	Association of HLA-G‡ and DAS (Mann-Whitney U-test)	HLA-G positive: DAS 1.48 ± 1.23 vs HLA-G negative: DAS 2 ± 1.69 (p=0.373)
			Association of HLA-G‡ negative patients and active disease	OR 0.34, **p=0.046**
Koca et al. 2014 (3)	Turkey	37 with SSc	Correlation Galectin-3 level and DAS (Pearson correlation)	No correlation found
			Association Galectin-3 level and active disease	Active: Gal-3 4.6 ± 5.8 vs Inactive: Gal-3 1.3 ± 1.1 ng/ml (**p=0.015**)
Rosato et al. 2014 (4)	Italy	40 patients with SSc, 20 controls	Correlation pulmonary vasculopathy (VE/VCO2 slope$^¥$) and DAS (Spearman's rank correlation)	R=0.59, **p<0.001**
Tomcik et al. 2014 (5)	Czech-republic	33 patients with SSc, 20 controls	Correlation S100A4 level and DAS	R=0.750, **p=0.0001**
Keck et al. 2014 (6)	Multinational	86 men with SSc	Association abnormal nailfold capillaroscopy and median DAS	**p=0.02**
Soydinc et al. 2014 (7)	Turkey	76 with SSc and 45 controls	Correlation mean MPV· and DAS	R=-0.310, **p=0.006**
Lambrecht et al. 2014 (8)	Belgium	119 with SSc and 29 controls	Correlation GDF15$^\parallel$ level and DAS	R=0.338, **p<0.001**
Tedeschini et al. 2014 (9)	Italy	78 with SSc	Association of depressive symptoms (BDI¶) and DAS (Pearson's Chi square test)	BDI<10: DAS 1.7 ± 1.2 vs BDI≥10: DAS 2.8 ± 1.9 (**p=0.003**).
Lanteri et al. 2014 (10)	France	134 with SSc and 401 controls	Correlation sFLC level** and DAS (Spearman's rank correlation) Correlation clinical and biological parameters and DAS$	R=0.28, **p=0.0009**
Sambataro et al. 2014 (11)	Italy	107 patients with SSc	Correlation Nailfold videocapillaroscopic determinants and DAS (Spearman's rank correlation): - NEMO$ - GC score$ - Cs score$	R=0.65, **p<0.0001** R=0.47, **p<0.0001** R=-0.27, **p=0.004**
Sariyildiz et al. 2013 (12)	Turkey	48 with SSc and 42 controls	Correlation sleep quality (Pittsburgh Sleep Quality Index) and DAS (Spearman's rank correlation)	No correlation found
Giovannetti et al. 2013 (13)	Italy	30 with SSc	Correlation antiERα-antibody level§ and DAS (Spearman's rank correlation)	R=0.3, **p=0.003**
		71 with SSc and 90 controls	Association between presence of antiERα-antibodies and DAS	**p=0.001**
Perrot et al. 2013 (14)	France	82 with SSc	Correlation pain (VAS†) and DAS (Pearson correlation)	No correlation found

Study	Country	Population	Assessed associations (method)	Results (univariate analysis, except when otherwise specified)
Golemati *et al.* 2013 (15)	Greece	85 patients with SSc, 120 controls	Association psychological wellbeing and active disease Depression (CES-D[‡]>16) Negative life events (LES[‡]>2) Positive reappraisal (WoC[‡]>2)	OR 2.761 (95% CI 1.131–6.739), **p=0.029** OR 3.677 (95% CI 1.217–11.110), **p=0.026** OR 0.348 (95% CI 0.142–0.854), **p=0.028**
Dunne *et al.* 2013 (16)	Canada	26 patients with lcSSc, 14 patients with dcSSc	Correlation Ang2/Tie2 ratio[#] and DAS (Spearman's rank correlation)	- lcSSc: R=0.50, **p=0.0157** - dcSSc: R=0.60, **p=0.0317**
Budulgan *et al.* 2013 (17)	Turkey	30 patients with SSc, 30 controls	Association leptin level and active disease Association leptin level/BMI and active disease	Active: leptin 1.92 ± 2.90 vs Inactive: leptin 7.02 ± 7.65 ng/ml (**p=0.02**). Active: 0.07 ± 0.11 vs Inactive 0.26 ± 0.28 (**p=0.02**).
Perosa *et al.* 2013 (18)	Italy	121 patients with SSc 75 ACA-positive patients with SSc	Association ACA-positivity[Δ] and DAS (Mann-Whitney U-test) Association anti-FOXE3p53-62 Ab negativity[ΔΔ] and DAS (Mann-Whitney U-test) Association anti-FOXE3p53-62 Ab negativity[ΔΔ] and active disease	No association found **p=0.038** **p=0.045**
Muangchan *et al.* 2012 (19)	Canada	1043 patients with SSc	Correlation elevated CRP level (>8mg/L) and DAS (Spearman's rank correlation)	R=0.229, **p<0.0001**
Caporali *et al.* 2012 (20)	Italy	160 patients with SSc	Correlation malnutrition and DAS (multiple regression analysis)	OR 3.72 (95%CI 1.84-7.52), **p<0.001**
Martin *et al.* 2012 (21)	Brazil	18 patients with SSc, 10 controls	Correlation collagen V deposition in skin and DAS (Spearman's rank correlation)	R=0.45, **p=0.03**
Deuschle *et al.* 2011 (22)	Germany	101 patients with SSc	Correlation 6 minutes' walk distance and DAS (Spearman's rank correlation)	R=-0.321, **p<0.01**
Bonella *et al.* 2011 (23)	Italy	25 patients with SSc	Correlation with DAS (Spearman's rank correlation) - serum level of KL-6 - serum level of Anti-Scl-70[◊] - serum level of SP-D[ł]	R=0.73, **p<0.0001** R=0.42, **p=0.03** No correlation found
Müller *et al.* 2011 (24)	Brazil	96 patients with SSc	Association ATA-1/anti-PolIII[◊] antibodies and active disease	**p<0.01/p=0.05**
Michalska-Jakubus *et al.* 2011 (25)	Poland	47 patients with SSc, 27 controls	Correlation Ang2 level and active disease (multivariate regression analysis) Correlation Ang2 level and DAS (Spearman's rank correlation)	ß=0.305, **p=0.038** R=0.403, **p<0.01**
Walker *et al.* 2010 (26)	Canada	326 patients with SSc	Association SSc subset (dcSSc vs lcSSc) and DAS (in patients with the same disease duration and depression scores) Association disease duration and DAS Association depression score (CES-D[‡]) and DAS (overdispersed Poisson regression model)	**RR=1.42 (95% CI 1.21-1.65)** **RR=0.88 (95% CI 0.82-0.95)** **RR=1.22 (95% CI 1.14-1.31)**
Minier *et al.* 2010 (27)	Hungary	80 patients with SSc	Correlation cost of illness (total costs) and DAS (Spearman's rank correlation)	R=0.28, **p<0.05**
Cuomo *et al.* 2010 (28)	Italy	46 patients with SSc	Correlation exercise performance (maximum oxygen uptake) and DAS (Spearman's rank correlation)	No correlation found
Vettori *et al.* 2010 (29)	Italy	50 patients with SSc, 41 controls	Association atherosclerosis (IMT[□□]) and DAS (multiple regression analysis)	No association found

Study	Country	Population	Assessed associations (method)	Results (univariate analysis, except when otherwise specified)
Minier et al. 2010 (30)	Hungary	131 patients with SSc	Correlation serum markers and DAS at both time points (Y0,Y1) Correlation clinical outcome measures and DAS (CATPCA[†])	**Correlation** with albumin, VEGF, vWF, PSGL-1 and CRP **Correlation** with HAQ-DI, ulcer score, mRSS, the 17-area thickness score, number of joint contractures and the hand anatomic index
Slobodin et al. 2010 (31)	Israel	10 patients with SSc, 10 controls	Correlation numbers of Tregulatory cells (expressed as patient-to-control ratio) and DAS (Spearman's rank correlation)	R=0.71, $p=0.034$
Fan et al. 2010 (32)	Canada	520 with SSc	Correlation PGA[¥¥] and DAS (Pearsons correlation)	R=0.375, $p<0.001$
Allanore et al. 2010 (33)	Multinational	7073 with SSc	Association left ventricular dysfunction (ejection fraction <55%) and active disease (multiple regression analysis)	OR=1.42 (95% CI 1.09-1.86), $p<0.011$
Vacca et al. 2009 (34)	Italy/France	156 patients with SSc	Correlation vitamin D level and DAS (Spearman's rank correlation)	R=–0.17, $p=0.04$
Vanthuyne et al. 2009 (35)	Belgium	156 patients with SSc	Correlation manual ability and active disease	R=-0.4, $p<0.001$
Hanke et al. 2009 (36)	Germany	266 patients with SSc	Correlation signal strength Anti-topoI (with LIA··) and DAS (Spearman's rank correlation)	R=0.234, $p=0.01$
Volpe et al. 2009 (37)	Italy	65 with SSc	Correlation antiCENP-B[Δ]/antiScl70 and DAS (Pearson's correlation)	No correlation found
Cuomo et al. 2008 (38)	Italy	302 with SSc	Association hypocomplementemia and DAS	$p<0.0003$
Nevskaya et al. 2008 (39)	Russia	40 patients with SSc, 24 controls	Association EPC level[‖] (median % of positive cells) and active disease	Active: EPC 0.02 ± 0.024 vs Inactive: EPC 0.009 ± 0.008, $p<0.05$
Allanore et al. 2007 (40)	France	32 patients with SSc	Association EPC level[‖] (median % of positive cells) and active disease	Active: EPC 1.49 (0.38-3.04) vs Inactive: EPC 0.62 (0.31-1.8), $p<0.05$
Sfrent-Cornateanu et al. 2006 (41)	Romania	20 patients with SSc, 26 controls	Association homozygotes/ heterozygotes promotor gen of IL6 and DAS (Mann Whitney test)	5.0 ± 3.3 vs 2.4 ± 3.6, $p<0.05$
Volpe et al. 2006 (42)	Italy	28 patients with SSc, 28 controls	Correlation FVIIa level and active disease (Kendall's rank correlation)	No correlation found
Volpe et al. 2006 (43)	Italy	43 patients with SSc	Correlation urinary level of isoprostane and DAS	No correlation found
Danieli et al. 2005 (44)	Italy	76 patients with SSc	Correlation HR-QOL[¶¶] (by SF-36) and DAS (Spearman's rank correlation)	Poor correlation (only vitality and social functioning dimensions were correlated [$p<0.05$])
La Montagna et al. 2004 (45)	Italy	44 patients with SSc, 20 controls	Correlation prolactin level and DAS (Spearman's rank correlation)	No correlation found

DAS: Disease Activity Score, determined by the European Scleroderma Study Group activity index; Active disease is DAS ≥ 3; DA: disease activity; *DU: digital ulcers; [Δ]PVI: peripheral vascular involvement; [‡]HLA-G: Human Leucocyte Antigen-G; [¥] VE/VCO₂ slope: minute ventilation over CO_2 ventilation, which is an indirect sign of ventilation perfusion mismatch when elevated (>34); ·MPV: mean platelet volume; [‖]GDF: growth differentiation factor; [¶]BDI: Beck Depression Inventory; **sFLC: serum Free Light Chains of immunoglobulins, marker of B-cell activity; [$]NEMO: number of micro-haemorrhages; [$]GC scores: giant capillaries scores; [$]Cs scores: mean number of capillaries; [§] antiERα: anti-estrogen receptor alfa; [†]VAS: visual analogue scale; [‡]CES-D: Centre for Epidemiologic Studies–Depression Scale; [‡]LES: life experiences survey; [‡]WoC: ways of coping; [#]Ang2/Tie2: Angiopoietin2 and its receptor Tie2; [Δ]ACA: anti-centromere protein antibody; [ΔΔ]anti-FOXE3p53-62 Ab: FOXE3-derived peptide; [◊]anti-Scl-70, ATA-1: antitopoisomerase-1 antibody; [↓]SP-D: surfactant protein D; [◊]Anti-polIII: anti-RNA polymerase III antibody; [‡‡]IMT: intima-media thickness of carotid arteries; [†]CATPCA: categorical principal component analysis; [¥¥]PGA: physian's global assessment of disease activity; ··LIA: line immuno-assay; [Δ]anti-CENP-B: Anti-centromere proteinB antibody; [‖]EPC level: endothelial progenitor cells, estimate of the number of functional EPC in bloodstream on the expression of CD34+ and/or CD133+; [¶¶]HR-QOL: health related-quality of life, measured by Short Form-36. $ See Supplemental Table in Lanteri et al.
Significant associations/correlations in bold

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