Supplementary Table S1. PICOs? developed to drive the literature review.

Research Question	*Q1: How has ASSD been defined in the available literature?*	*Q2: What is the accuracy of the different definitions for diagnosing ASSD?*
Population	People with suspected ASSD (adults) Patients with confirmed ASSD (adults)	People with suspected ASSD (adults) Patients with confirmed ASSD (adults)
Interventions	Definition of ASSD by clinical, laboratory, imaging, instrumental testing, and histology features (alone or combined)	Definition of ASSD by clinical, laboratory, imaging, instrumental testing, and histology features (alone or combined)
Comparators (if applicable – not required for inclusion)	Other definitions of ASSD	Diagnosis of ASSD by expert opinion
Outcomes	N/A	Sensitivity Specificity Positive and negative predictive values Positive and negative likelihood ratios Diagnostic Odds Ratio
Study type	Systematic literature reviews, meta-analyses, RCTs, controlled trials, non-controlled trials, diagnostic accuracy studies, cohort studies, cross-sectional studies, and case-control studies	Systematic literature reviews, meta-analyses, RCTs, controlled trials, non-controlled trials, diagnostic accuracy studies, cohort studies, cross-sectional studies, and case-control studies

ASSD: anti-synthetase syndrome; RCT: randomised clinical trial; N/A: not applicable.

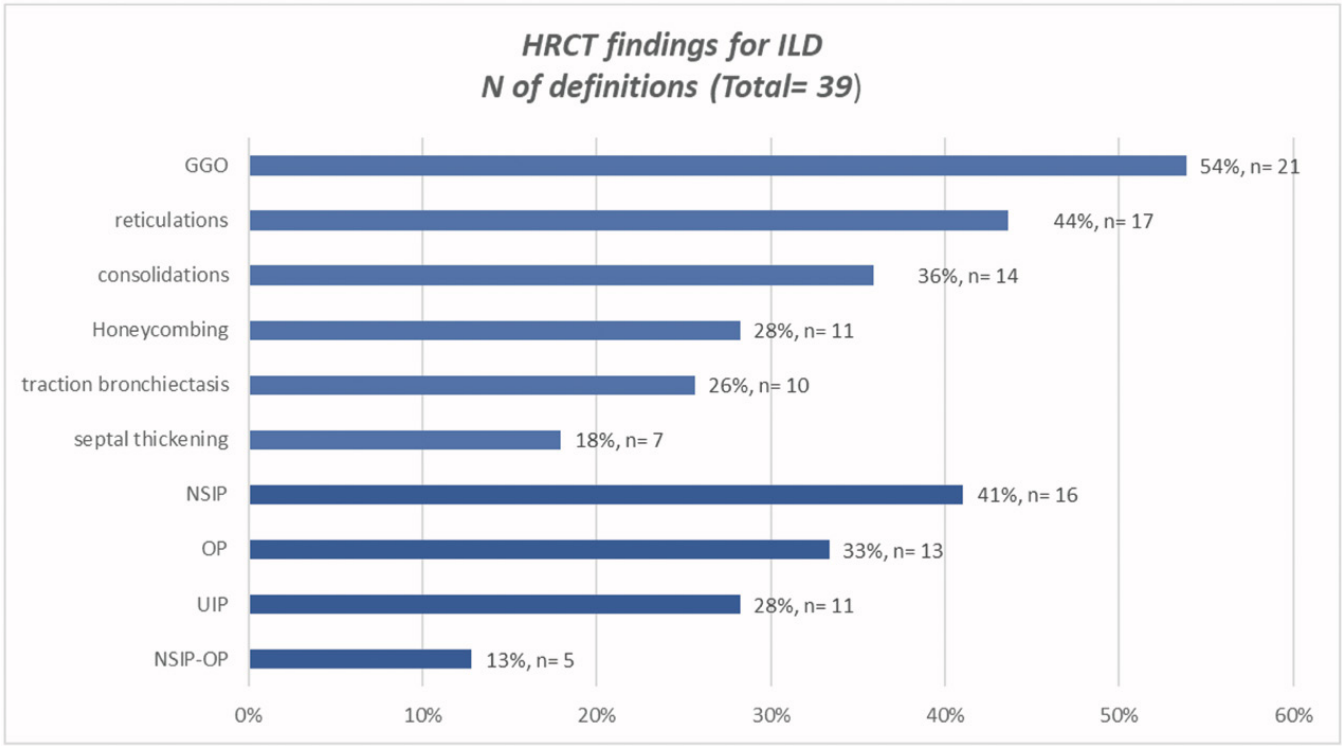
Supplementary Table S2. Search strategies for the SLR.

PubMed	#1. antisynthetase syndrome [supplementary concept] OR "Antisynthetase syndrome" OR ASSD OR "antisynthetase antibodies" OR "antisynthetase antibody" OR "antiaminoacyl-tRNA synthetase antibodies" OR "anti-aminoacyl-tRNA synthetase antibody" #2. "Myositis/complications"[Majr] #3. "Lung Diseases, Interstitial/complications"[Majr] OR "interstitial pneumonia with autoimmune features" OR IPAF #4. "Anti jo1" OR "Anti SSA/RO 52" OR "Anti OJ" OR "Anti EJ" OR "Anti PL 12" OR "Anti PL 7" OR "Anti KS" OR "Anti Zo" OR "Anti Ha") #5. #1 OR #2 OR #3 OR #4 #6. #5 NOT "Case reports"[Publication Type] Filters: Publication date from 1984/01/01 to 2018/11/06; English; French; Italian; Spanish
Embase	#1. 'antisynthetase syndrome'/exp OR 'Antisynthetase syndrome' OR ASSD OR 'antisynthetase antibod*' OR 'anti aminoacyl-tRNA synthetase antibod*' #2. 'Myositis'/mj AND complications/lnk #3. 'Interstitial Lung Disease'/mj AND 'complications'/lnk #4. 'interstitial pneumonia with autoimmune features' OR IPAF #5. 'Anti jo1' OR 'Anti SSA/RO 52' OR 'Anti OJ' OR 'Anti EJ' OR 'Anti PL 12' OR 'Anti PL 7' OR 'Anti KS' OR 'Anti Zo' OR 'Anti Ha' #6. (#1 OR #2 OR #3 OR #4 OR #5) #6 NOT 'case report'/exp #7. AND [1984-2018]/py AND ([english]/lim OR [french]/lim OR [italian]/lim OR [spanish]/lim)

Supplemetary Table S3. Muscle biopsy variables retrieved by the SLR and number of studies including them.

	N studies using variable for definition (Q1)	N studies using assessing variable performance (Q2)	Total (n= 11)
NECROSIS/REGENERATION			
Perifascicular necrosis	2	3	5
Diffuse necrosis	3	2	5
perimysial necrosis/regeneration	0	1	1
perivascular necrosis/regeneration	0	1	1
perifascicular mitochondrial disfunction	0	1	1
INFLAMMATION			
perimysial inflammation	1	3	4
perivascular inflammation	0	2	2
endomysial inflammation	1	3	4
ATROPHY/FRAGMENTATION			
perimysial fragmentation	0	4	4
perifascicular atrophy	0	6	6
diffuse atrophy	0	1	1
MHC/C5B-9 EXPRESSION			
MHC I diffuse expression	1	3	4
MHC I perifascicular expression	0	1	1
MHC II diffuse expression	0	1	1
C5b-9 diffuse expression	1	2	3
C5b-9 perifascicular expression	0	2	2
OTHER FINDIGNS			
microinfarcts	0	1	1
ischemic myosinolisis*	0	1	1
actin filament inclusion	0	1	1
mitochondrial disfunction	0	3	3
MxA sarcoplasmic expression	0	1	1
RIG-1 expression	0	1	1

*defined as punched-out vacuoles or myofibrillar rarefaction areas, corresponding to foci of myosin filament proteolysis.



Supplementary Fig. S1. Histogram of HRCT findings used in ASSD definition.

Supplementary Table S4. Summary of findings – Q1 How has ASSD been defined in the available literature?
RoB: risk of bias; DM: dermatomyositis; PM: polymyositis; GGO: ground glass opacification; NSIP: nonspecific interstitial pneumonia; OP: organizing pneumonia; ILD: interstitial lung disease; HRCT: high resolution computed tomography; PFT: pulmonary function test; ARS: aminoacyl tRNA synthetase; ATS: American thoracic society; UIP: usual interstitial pneumonia; LIP: lymphocytic interstitial pneumonia; CK: creatinine kinase; RP: Raynaud's phenomenon; MH: mechanic's hands; EMG: electromyography; MRI: magnetic resonance imaging.
The Risk of Bias was evaluated by the Newcastle-Ottawa Scale for cohort studies or case-control studies, according to study design. S: Selection Items; C: comparability items; O: Outcome items. The symbol "*" indicates the score for each component of the scale. §: risk of bias assessed by QUADAS-2.

Study	Number of pts	Population	Study design	Index test (variables)	RoB
La Corte 2006 (1)	21	Patients with ASSD from a single Rheumatology centre in Italy	Retrospective cross-sectional cohort	• Anti Jo1 • Myositis ◦ Bohan and Peter criteria for probable or definite DM/PM ◦ EMG*	S ** C O**
Marie 2013 (2)	91	Anti Jo1 patients from 4 academic centres	Retrospective, longitudinal cohort	• Anti Jo1 • myositis ◦ Bohan and Peter criteria for PM/DM	S ** C ** O **
Debray 2014 (3)	33	ASSD from 4 tertiary centres specialised in rare lung diseases without any previous immunosuppressive therapy	Retrospective, longitudinal cohort	• Anti Jo1 • Anti PL 12 • Anti PL7 • ILD ◦ HRCT • GGO • Reticulations • Bronchiectasis • Consolidations • Honeycombing • NSIP • NSIP-OP • OP	S ** C O **
Aguilera Cros 2018 (4)	27	ASSD from a single centre	Retrospective, cross-sectional cohort	• Jo-1 • PL-12 • PL-7 • Myositis • arthritis • ILD HRCT ◦ NSIP ◦ UIP ◦ OP • Fever • Raynaud's phenomenon • mechanic's hand	S ** C O
Hervier 2016 (5)	33	ASSD from a single centre	Cross sectional cohort	• Jo-1 (22/33) • PL-12 (6/33) • PL-7 (3/33) • EJ (1/33) • OJ (1/33) • Myositis • ILD • rheumatic symptoms	S ** C O
Sasano 2016 (6)	12	Consecutive patients with ASSD from a single centre	Retrospective, longitudinal cohort	• Anti EJ • ILD ◦ HRCT • GGO • Reticulations • Consolidations • Septal thickening • HC • Emphysema ◦ Biopsy • Cellular NSIP • fibrosing NSIP • unclassifiable • myositis • arthritis • fever • RP • MH	S * C O **
Andersson 2015 (7)	22	ASSD patients from single centre register	Retrospective, longitudinal cohort	• Anti Jo-1 • PL-12 • PL-7 • ILD ◦ HRCT • GGO • Septal thickening • Consolidations reticulations ◦ PFT • myositis ◦ B&P criteria for PM/DM • CPK • Weakness (MMT-8)	S * C O **

Study	Number of pts	Population	Study design	Index test (variables)	RoB
Cobo-Ibanez 2018 (8)	50	Consecutive ASSD patients from urope ntre registry???	Retrospective longitudinal cohort	• Jo-1 • PL-7 • Pl-12 • myositis ◦ Bohan and Peter ◦ Tanimoto criteria for PM/DM	S ** C ** O **
Bachmeyer 2007 (9)	7	ASSD from single centre registry	Retrospective longitudinal cohort	• anti Jo-1 • ILD ◦ Cough ◦ dyspnoea • arthritis • Myositis	S * C O **
Marie 2013 (10)	5	Patients with anti PL12 antibodies from a single centre	Retrospective longitudinal cohort	• Anti PL-12	S * C O **
Uruha 2016 (11)	50	Patients with ARS positivity and myositis	Cross sectional cohort	• Anti Jo-1 • Anti Pl-7 • Anti PL-12 • Anti-EJ • Anti-OJ • Anti-KS • Myositis ◦ Biopsy (Perifascicular necrosis/atrophy)	S * C O
Pinal-Fernandez 2015 (12)	21	ASSD patients from a single Rheumatology centre cohort	Cross sectional cohort	• Anti Jo1 • Anti PL7 • Anti PL12 • ILD ◦ HRCT • GGO ◦ PFT ◦ Clinical* ◦ Biopsy* • Myositis • Arthritis • Raynaud's phenomenon • Mechanic's Hands • fever	S ** C O
Rojas-Serrano 2015 (13)	43	ASSD patients from a single pneumology centre in Europe	Longitudinal cohort	• Jo1 • EJ • OJ • PL 7 • PL 12 • ILD ◦ PFT ◦ HRCT • GGO • Consolidations • reticulations • Myositis ◦ Bohan and Peter • Fever • Mechanic's hands • arthritis	S * C * O **
Hervier 2013 (14)	203	ASSD patients from 9 French university hospitals	Retrospective longitudinal cohort	• Anti Jo-1 • Anti PL-7 • Anti PL-12 • Anti EJ • Anti OJ • myositis by Bohan and Peter criteria • ILD ◦ HRCT • NSIP • UIP • OP ◦ PFT • arthritis	S * C ** O **
Andersson 2016 (15)	68	ASSD patients from a single centre cohort in Europe	Cross sectional	• Anti Jo-1 • Anti PL-7 • Anti PL-12 • ILD ◦ PFT ◦ HRCT • GGO • Reticulation • UIP • Opacities • Emphysema • Subpleural curvilinear lines and parenchymal bands • Wedge shaped • Myositis ◦ Probable or definite PM/DM (Bohan and Peter)	S ** C O **

Study	Number of pts	Population	Study design	Index test (variables)	RoB
Schneider 2018 (16)	12	Anti PL 12 patients from a single centre myositis register from US	Retrospective cross-sectional cohort	• Anti PL-12 • Myositis ◦ Probable or definite PM/DM (Bohan and Peter)	S * C O**
Schneider 2014 (17)	4	Anti EJ patients from a single centre myositis register from US	Retrospective cross-sectional cohort	• Anti-EJ • Myositis ◦ Probable or definite PM/DM (Bohan and Peter)	S * C O **
Doyle 2018 (18)	25	Consecutive ASSD patients from 2 US centres	Retrospective longitudinal cohort	• Jo-1 • PL-7 • PL-12 • ILD ◦ PFT ◦ HRCT • NSIP • Fibrotic NSIP/UIP • NSIP/OP • DAD	S * C O **
Bauhammer 2016 (19)	61	Anti Jo1 patients from 2 Rheumatology centres in Europe	Retrospective longitudinal cohort	• Anti Jo1 positivity • Myositis ◦ Bohan and Peter's criteria for PM/DM	S ** C O**
Marie 2012 (20)	7	patients with ASSD and ILD from a single centre in France	Retrospective longitudinal cohort	• Anti Jo1 • Myositis ◦ Bohan and Peter's criteria for definite PM/DM	S * C O **
Sem 2009 (21)	11	Patients with ASSD and ILD from a tertiary centre in Europe	Retrospective longitudinal cohort	• Anti Jo-1 • Anti PL-12 • ILD ◦ HRCT • GGO • Reticulations • Consolidations • HC ◦ PFT	S * C O **
Couture 2018 (22)	10	Patients with ASSD and diagnosis of sarcoidosis from 10 French university hospitals	Longitudinal cohort	• Anti jo1 • Anti PL12 • Anti PL 7 • ILD ◦ HRCT • NSIP • NSIP/OP • emphysema • myositis	S ** C O **
Lefevre 2015 (23)	73	ASSD patients from a multicentric French cohort	Retrospective longitudinal cohort	• Anti Jo1 • Anti PL7 • Anti PL12 • Anti EJ • ILD ◦ HRCT ◦ PFT* • Myositis ◦ CPK ◦ EMG ◦ biopsy • arthritis	S * C O **
Marie 2012 (24)	89	Consecutive anti Jo1 patients from 4 French academic centres	Longitudinal cohort	• Anti Jo1 • Myositis ◦ Bohan and Peter's criteria for PM/DM	S ** C O **
Noguchi 2017 (25)	51	ASSD from all over Japan	Cross sectional	• Anti Jo1 • Anti PL7 • Anti PL12 • Anti OJ • Anti EJ • Anti KS • Myositis ◦ weakness ◦ EMG ◦ MRI ◦ Biopsy* • Perifascicular necrosis • Diffuse necrosis • Perimysial inflammation • HLA ABC deposition • C5b-9 expression	S ** C O **
Gofrit 2018 (26)	15	ARS positive patients from a medical centre database	Cross sectional	• Anti Jo1 • anti PL7 • anti PL12 • myositis • ILD • RP • Skin rash • Arthritis/arthralgia	S * C O *

Study	Number of pts	Population	Study design	Index test (variables)	RoB
Lilleker 2018 (27)	512	ASSD from Euromyositis register	Multicentric cross sectional cohort	• Anti Jo1 • Anti PL7 • Anti PL12 • Anti OJ • Anti EJ • Anti KS • Anti Zo • Myositis ◦ Bohan and Peter's criteria • Arthritis • ILD ◦ HRCT ◦ X rays ◦ PFTs • mechanic's hands • Raynaud's phenomenon • fever	S ** C * O **
Späth 2004 (28)	12	antiJo1 patients from a Neurology department	Longitudinal cohort	• Myositis ◦ CPK elevation ◦ Clinical weakness (NA) • Anti Jo1	S * C O **
Yousem 2014 (29)	8	PL7 patients from a single centre in US	Retrospective longitudinal cohort	• Anti PL7 • CTD diagnosis	S * C O **
Braillard Poccard 2018 (30)	10	ASSD from one Argentinian university hospital	Retrospective cross-sectional cohort	• Arthritis • Raynaud's phenomenon • mechanic hands • myositis ◦ elevated CK ◦ muscle weakness • ILD • antisynthetase antibodies	S ** C O
Carrasco Cubero 2018 (31)	5	Anti Jo1 ASSD from a single centre in Spain	Retrospective cross-sectional study	• myositis • anti Jo1 • fever • arthritis • Raynaud's phenomenon • mechanic's hands • ILD ◦ HRCT • NSIP • UIP • Respiratory bronchiolitis interstitial lung disease (RB-ILD)	S * C O **
Casal-Dominguez (32)	16	ASSD patients from a single centre in Spain	Cross sectional	• Anti Jo1 • Anti PL7 • Anti PL12 • Myositis ◦ Probable or definite PM/DM by Bohan and Peter	S ** C ** O
Araujo 2018 (33)	42	ASSD patients from a single centre in Brazil	Cross sectional	• Anti Jo1 • Anti EJ • Anti OJ • Anti PL7 • Anti PL12 • Myositis ◦ PM/DM by Bohan and Peter's criteria • ILD ◦ HRCT • GGO • Incipient pneumonia • fibrosis ◦ dyspnoea • Arthritis • RP • MH • fever	S *** C O
Hervier 2012 (34)	233	ASSD patients from 8 centres in France	longitudinal	• anti Jo1 • anti PL7 • anti PL12 • ILD ◦ HRCT ◦ PFT • myositis ◦ CK elevation ◦ Muscle weakness ◦ EMG ◦ Muscle biopsy (diffuse myofiber necrosis/regeneration) • Arthritis/arthralgia	S * C O **
Marie 2013 (35)	86	consecutive anti-Jo1 patients with ASS reviewed in 4 academic centresl	ongitudinal	• Myositis ◦ PM/DM by Bohan and Peter • Anti Jo1	S * C O**

Study	Number of pts	Population	Study design	Index test (variables)	RoB
Allenbach 2015 (36)	10	ASSD patients from 4 French adult internal medicine departments enrolled for a Phase II trial	open-label, prospective, multicentre phase II study	• myositis ◦ proximal weakness ◦ EMG ◦ biopsy • muscle fibre necrosis and regeneration • inflammatory cell infiltrate • anti-Jo-1 • anti-PL-7 • anti-PL-12	S * C O **
Lepri 2016 (37)	15	ASSD from 8 centres in Europe	multicentre retrospective longitudinal	• anti-synthetase antibodies • ILD ◦ HRCT • GGO • Reticulations • honeycombing	S ** C O **
Marie 2012 (38)	95	ASSD patients from a single centre in France	Retrospective longitudinal	• myositis ◦ PM/DM by Bohn and Peter • Anti Jo1 • Anti PL7 • Anti PL12	S * C O **
Cavagna 2015 (39)	225	anti Jo1 patients from 24 centres in Europe	Retrospective longitudinal	• Anti Jo1 • ILD ◦ PFT ◦ HRCT • Myositis ◦ CK elevation ◦ EMG ◦ Biopsy • Arthritis	S ** C O **
Gomard-Mennesson 2007 (40)	14	ASSD patients from a monocentric cohort of anti Jo1 subjects	Retrospective cross sectional	• Anti Jo1 • Myositis ◦ CPK ◦ EMG • ILD ◦ PFT ◦ HRCT • RP • arthritis	S ** C * O
Shi 2017 (41)	124	Consecutive ASSD patients from a single centre	Retrospective longitudinal	• Anti Jo1 • Anti PL7 • Anti PL12 • Anti EJ • Myositis ◦ DM/PM diagnosis according to Bohan and Peter • ILD ◦ HRCT • UIP • NSIP • OP • Arthritis • RP • MH	S * C ** O **
Kalluri 2009 (42)	31	Anti PL 12 patients from a multicentric cohort in US	Cross sectional	• Anti PL12 • Myositis ◦ DM/PM diagnosis according to Bohan and Peter • ILD ◦ PFT ◦ HRCT • GGO • Septal thickening • HC ◦ Biopsy • UIP • NSIP • OP • Arthritis • RP • MH • fever	S * C O
Hervier 2010 (43)	17	anti PL12 patients from three university hospitals	longitudinal	• Anti PL12 • ILD ◦ Cough ◦ dyspnoea ◦ HRCT • NSIP • OP ◦ Biopsy* ◦ BAL* • Myositis ◦ Clinical ◦ EMG	S * C O **

Study	Number of pts	Population	Study design	Index test (variables)	RoB
				◦ CK ◦ Biopsy* • Fever • RP • MH • Weight loss • Oesophageal involvement • PH	
Marie 2013 (44)	15	anti PL 7 patients from 5 university hospitals in France	Retrospective longitudinal	• Anti PL7 • myositis ◦ DM/PM according to Bohan and Peter ◦ Sontheimer criteria for ADM	S * C O **
Trallero-Araguas 2016 (45)	148	anti Jo1 patients from 18 Spanish centres	Retrospective longitudinal	• Anti Jo1 • Myositis ◦ DM/PM according to Bohan and Peter • ILD ◦ HRCT ◦ PFT • arthritis	S * C O **
Bartoloni 2017 (46)	165	anti Jo1 patients from a multicentric European cohort	Retrospective longitudinal	• Anti Jo1 • Arthritis • ILD ◦ PFT ◦ HRCT • GGO • Fibrosis • Myositis ◦ CK elevation ◦ aldolase ◦ EMG ◦ Biopsy*	S * C O **
Cen 2013 (47)	134	Patients with IIM, diagnosis based on the criteria of the ENMC workshop, and anti JO1	Retrospective cross-sectional study	• Anti Jo1 • Myositis • ILD ◦ HRCT • Arthritis	S ** C * O
Pinal-Fernandez 2017 (48)	292	IIM testing positive for anti-synthetase antibodies	Retrospective cross-sectional study	• Anti Jo1 • Anti PL7 • Anti PL12 • Anti EJ • Anti OJ • Anti Ro52 • myositis	S ** C O *
Chartrand 2016 (49)	33	ASSD suspected based on multi-disciplinary assessment	Retrospective cross-sectional study	• ILD ◦ PFT* ◦ HRCT • NSIP • NSIP-OP • OP • UIP • Anti Jo1 • Anti PL7 • Anti PL12 • Anti EJ • Anti OJ	S ** C O *
Cerbelli 2018 (50)	18	Cases: Consecutive patients with anti ARS antibodies and suspected myositis referred for histological evaluation. Controls: DM according to the ENMC criteria.	Case-control	• Anti Jo1 • Anti Pl7 • Myositis ◦ ENMC 2004 proposed criteria • Weakness • CPK • EMG • MRI ◦ biopsy • Necrosis • Regeneration • Atrophy • Endomysial infiltrates • Perimysial inflammation+ • Perimysial fragmentation • MHC enhancement • C5B9 sarcolemmal positivity • COX deficient fibers	S ** C O *
Shinjo 2010 (51)	18	ASSD with anti Jo1	Retrospective cross-sectional study	• Myositis ◦ PM/DM by Bohan and Peter • Anti Jo1	S * C O **
Labirua-Iturburu 2012 (52)	18	ASSD with anti PL7	Retrospective cross-sectional study	• Anti PL7 • Myositis ◦ PM/DM by Bohan and Peter ◦ Sontheimer criteria for ADM	S ** C O **

Study	Number of pts	Population	Study design	Index test (variables)	RoB
Fischer 2007 (53)	9	Consecutive patients with ILD suspicious for ASSD with negative anti Jo1 antibodies	Prospective cohort	• ILD ◦ HRCT • GGO • Reticulations • Consolidations • Bronchiectasis • NSIP • OP ◦ PFTs • Anti PL7 • Anti PL12	S ** C O**
Targoff 1992 (54)	5	Patients with available serum samples, PM/DM criteria and positive anti EJ antibodies	Retrospective cross-sectional study	• Myositis ◦ PM/DM by Bohan and Peter • ILD ◦ Chest X rays ◦ PFTs • Anti EJ	S ** C O **
Cavagna 2010 (55)	12	Patients with anti Jo1 positive ASSD	Cross-sectional cohort	• Anti Jo1 • ILD ◦ HRCT ◦ PFT • Myositis • MH • arthritis	S * C O **
Hervier 2011 (56)	12	Patients testing twice positive for anti PL7 with one or more symptoms of ASSD	Retrospective cross-sectional study	• ILD ◦ Dyspnea ◦ Cough ◦ HRCT • GGO • Bronchiectasis • Consolidations • NSIP • OP • Obliterative bronchiolitis • Myositis • Anti PL7	S * C O **
Mumm 2010 (57)	6	New onset inflammatory polyarthritis and anti-synthetase autoantibodies	Retrospective Case series	• Arthritis • Anti Jo1 • Anti OJ • Anti PL12	S C O **
Stanciu 2012 (58)	48	Anti Jo1 antibodies with at least 1 year of follow-up	Retrospective cohort	• Anti Jo1	S ** C O *
Dieval 2012 (59)	14	ASSD with positive anti-synthetase autoantibodies	Retrospective Case series	• Anti Jo1 • Anti PL7 • Anti PL12 • Myositis • ILD • Arthritis • RP • MH	S * C O **
Maturu 2016 (60)	9	Patients retrieved from the medical record database of a single tertiary centre	Retrospective cohort	• Anti Jo1 • ILD ◦ HRCT • NSIP • UIP • OP ◦ PFTs* • Myositis ◦ PM/DM by Bohan and Peter ◦ Weakness* ◦ CPK* ◦ EMG* ◦ Biopsy* • Arthritis	S * C O **
Zamarron 2017 (61)	11	Patients with pulmonary involvement and anti-synthetase antibodies positivity	Prospective cohort	• Anti Jo1 • Anti PL12 • ILD ◦ HRCT • GGO • Reticulations • Bronchiectasis ◦ PFTs	S * C O **
Waseda 2016 (62)	64	Patients with ILD and anti-synthetase antibodies positivity	Retrospective cross-sectional study	• ILD ◦ GGO ◦ reticulations ◦ consolidations ◦ septal thickening ◦ HC ◦ NSIP ◦ OP ◦ NSIP/OP	S * C O **

Study	Number of pts	Population	Study design	Index test (variables)	RoB
				◦ UIP • Anti JO1 • Anti EJ • Anti PL7 • Anti PL12 • Anti OJ • Anti KS	
Labirua-Itruburu 2013 (63)	15	Patients with ASSD and ILD, treated with calcineurin inhibitors	Retrospective cohort	• ILD ◦ HRCT • GGO • RETICULATIONS • Septal thickening • HC ◦ PFTs • Anti Jo1 • Anti PL12 • myositis ◦ PM/DM by Bohan and Peter	S * C O **
Vancsa 2009 (64)	27	Patients with IIM and anti Jo1	Retrospective cohort	• Myositis ◦ PM/DM by Bohan and Peter • Anti Jo1	S ** C O **
Karadimitrakis 2009 (65)	17	Patients with IIM and anti Jo1	Retrospective cohort	• Myositis ◦ PM/DM by Bohan and Peter • Anti Jo1	S * C O **
Hirakata 2007 (66)	8	Patients with PM/DM, with likely IM, with ILD without any other cause and anti-KS antibodies	Cross-sectional cohort	• Myositis ◦ PM/DM by Bohan and Peter ◦ weakness • ILD ◦ Chest X rays ◦ PFTs • Anti KS	S ** C O **
Johnson 2014 (67)	41	PM/DM, presence of ILD and at least 6 months of follow-up	Retrospective cohort	• Myositis ◦ PM/DM by Bohan and Peter • ILD ◦ PFTs ◦ biopsy ◦ HRCT • GGO • Reticulations/fibrosis • Anti Jo1 • Anti PL7 • Anti PL 12 • Anti EJ • Anti OJ	S ** C* O *
Koreeda 2010 (68)	14	Patients with ILD and anti-synthetase antibodies positivity	Prospective cohort	• ILD ◦ HRCT • GGO • Septal thickening • Bronchiectasis • Consolidations • HC • Anti Jo1 • Anti PL12 • Anti EJ • Anti OJ • Anti KS	S ** C O *
Yura 2017 (69)	38	Patients with interstitial pneumonia of unknown cause not fulfilling classification criteria	Retrospective cohort	• ILD ◦ HRCT • Reticulations • HC • Bronchiectasis • GGO • Consolidations • Septal thickening • UIP • OP • NSIP • DAD • Anti Jo1 • Anti PL12 • Anti PL7 • Anti OJ • Anti EJ • Anti KS	S ** C O **
Lecouffe-Despret 2018 (70)	9	Patients with a request for myositis specific autoantibodies	Retrospective cross-sectional study	• myositis • ARS ◦ jo1 ◦ pl12	S * C O **

Study	Number of pts	Population	Study design	Index test (variables)	RoB
Vuillard 2018 (71)	28	Patients admitted to the ICU for acute respiratory failure	Retrospective cohort	• Anti Jo1 • Anti PL7 • Anti PL12 • Anti EJ • ILD ◦ Clinical (acute respiratory failure)	S * C O **
Zamora 2016 (72)	104	ASSD with positive anti Jo1 and ILD	Retrospective cohort	• Anti JO1 • myositis • ILD ◦ GGO ◦ HC ◦ Reticulations ◦ Bronchiectasis ◦ Consolidations ◦ UIP ◦ NSIP ◦ OP ◦ NSIP/OP • Biopsy* ◦ NSIP ◦ OP ◦ UIP ◦ DAD • PFT*	S * C * O **
Ben- Salem 2018 (73)	9	Patients with ASSD and ILD	Retrospective cohort	• Anti Jo1 • Anti Pl12 • ILD	S * C O **
Aouizerate 2014 (74)	33	Patients with myositis and ARS positivity	Case-control	• Anti Jo1 • Anti Pl12 • Anti Pl7 • Anti EJ • Myositis	§
Stenzel 2015 (75)	21	Patients with myositis and ARS positivity	Case-control	• Myositis • Anti Jo1 • Anti Pl12 • Anti Pl7	§
Lega 2014 (76)	1462	Patients with diagnosis of CTD and ARS positivity	Systematic review	• Anti Jo1 • Anti PL7 • Anti Pl12 • Anti KS • Anti OJ • Anti EJ • CTD diagnosis • ILD	§
Pinal-Fernandez 2015 (77)	20	Patients with definite or probable DM/PM by B&P + anti Jo1	Cross-sectional study	• myositis ◦ PM/DM diagnosis according with Bohan and Peter • Anti Jo1	§
Mescam-Mancini 2015 (78)	19	Anti Jo1 patients	diagnostic accuracy studies	• Anti Jo1 • myositis	§
Uruha 2018 (79)	30	Patients with myositis and ARS positivity	Case-control	• Myositis • Anti EJ • Anti OJ • Anti KS	§
Andersson 2017 (80)	66	Patients with ARS positivity, ILD or myositis	Case-control	• anti Jo1 • Anti Pl12 • Anti Pl7 • ILD ◦ HRCT ◦ PFTs • Myositis ◦ PM/DM by Bohan and Peter	§
Watanabe 2011 (81)	13	Patients with ILD and ARS positivity	Retrospective longitudinal	• Anti Jo1 • anti Pl12 • anti Pl7 • anti EJ • anti OJ • anti KS • ILD ◦ HRCT • Septal thickening • GGO • Reticulations • Bronchiectasis • Consolidations	§
Mozaffar 2000 (82)	11	Anti Jo1 + myositis	Case-control	• Anti Jo1 • myositis	§

Supplementary Table S5. *Summary of findings – Q2 What is the accuracy of the different definitions for diagnosing ASSD?*
Summary of findings of studies included in research question 2. ARS anti-RNA synthetase, ASSD anti synthetase syndrome, CTD connective tissue disease, DM dermatomyositis, GGO ground glass opacity, HRCT high resolution computed tomography, IBM inclusion body myositis, ILD interstitial lung disease, IMNM immune-mediated necrotizing myopathy, MH mechanic's hands, NSIP nonspecific interstitial pneumonia, OP organising pneumonia, PFT pulmonary function tests, PM polymyositis, RP Raynaud's phenomenon, UIP usual interstitial pneumonia.

Study	Number of pts	Population	Controls	Study design	Reference standard	Index test (variables)	Diagnostic performance
Aouizerate 2014 (74)	33 cases 27 controls	Patients with myositis and ARS positivity	17 patients with DM 10 patients with fibromyalgia	Case-control	ASSD diagnosed by Myositis AND ARS positivity	HLA-DR myofiber expression	HLA-DR myofiber expression Sensitivit 84.21% 95%CI (72.13-92.52%) Specificity 79.49% 95%CI (63.54-90.7%) PPV 85.71% 95%CI (76.2-91.83%) NPV 77.5% 95%CI (64.94-86.5%) DOR 20.67 95%CI (7.2-59.3) P < 0.0001 LR+ 4.11 95%CI (2.19-7.69) LR- 0.2 95%CI (0.11-0.37)
						C5b-9 deposition on non-necrotic myofibers	C5b-9 deposition on non-necrotic myofibers Sensitivity 53.12% 95%CI (34.74-70.91%) Specificity 81.25% 95%CI (54.53-95.95%) PPV 85% 95%CI(66-94.3%) NPV 46.43% 95%CI (35.88-57.31%) DOR 4.91 95%CI (1.169-20.61) P = 0.0297 LR+ 2.83 95%CI (0.97-8.27) LR- 0.58 95%CI (0.37-0.89)
						Perimysial connective tissue fragmentation	Perimysial connective tissue fragmentation Sensitivity 78.8% 95%CI (61.1-91%) Specificity 17.65% 95%CI (3.8-43.3%) PPV 65% 95%CI (58.34-71.13%) NPV 30% 95%CI (11.24-59.2%) DOR 0.79 95%CI (0.177-3.57) p= 0.7656 LR+ 0.96 95%CI (0.72-1.27) LR- 1.2 95%CI (0.36-4.07)
						Perifascicular atrophy	Perifascicular atrophy Sensitivity 45.45% 95%CI (28.11-63.65%) Specificity 47.06% 95%CI (22.98-72.2%) PPV 62.5% 95%CI (48.18-74.9%) NPV 30.77% 95%CI (19.72-44.56%) DOR 0.741 95%CI (0.23-2.4) p= 0.6161 LR+ 0.86 95%CI (0.48-1.54) LR- 1.16 95%CI (0.64-2.1)
						Microinfarcts	MICROINFARTS Sensitivity 6.06% 95%CI (0.74-20.23%) Specificity 58.82% 95%CI (32.92%-81.56%) PPV 22.22% 95%CI (6.23-55.13%) NPV 24.39% 95%CI (17.68-32.64%) DOR 0.092 95%CI (0.0164-0.518) p= 0.0068 LR+ 0.15 95%CI (0.03-0.63) LR- 1.6 95%CI (1.06-2.4)
						Ischaemic myosinolisis (punched out vacuoles)	Ischaemic myosinolisis Sensitivity 6.06% 95%CI (0.74-20.23%) Specificity 64.71% 95%CI (38.33-85-8%) PPV 25% 95%CI (7-60%) NPV 26.19% 95%CI (19.82-33.75%) DOR 0.118 95%CI (0.021-0.674) p= 0.0163 LR+ 0.17 95%CI (0.04-0.76) LR- 1.45 95%CI (1.01-2.08)
						HLA-ABC expression	HLA-ABC Sensitivity 93.94% 95%CI (79.77-99.26%) Specificity 37.04% 95%CI (19.4-57.63%) PPV 64.58% 95%CI (62.58-66.54%) NPV 83.33% 95%CI (54.46-95.43%) DOR 9.12 95%CI (1.79-46.51) p=0.0078 LR+ 1.49 95%CI (1.1-2.02) LR- 0.16 95%CI (0.04-0.68)
Stenzel 2015 (75)	21 case patient 53 controls	Patients with myositis and ARS positivity	14 DM 14 NAM 14 IBM 11 nonspecific myositis	Case-control	ARS antibody + Clinically significant myositis	presence of myonuclear actin filament inclusions	Sensitivity 80.95% 95%CI (58.09-94.55%) Specificity 100% 95%CI (93.28-100%) PPV 100% NPV 92.98% 95%CI (84.58-96.97%) DOR 416.1 p= 0.0001 95% CI(21.32-8120.8) LR+ LR- 0.19 95%CI (0.08-0.46)
Lega 2014 (76)	1462 case 559 controls	Patients with diagnosis of CTD and ARS positivity	154 Mi2 144 SRP 116 PM-Scl 226 U1RNP 61 Ku	Meta-analysis	Diagnosis of CTD anti ARS positivity	Arthralgia	Arthralgia Sensitivity 61.97% 95%CI (59.43-64.47%) Specificity 64.05% 95%CI (60.37-67.61%) PPV 78.24% 95%CI (76.37-80%) NPV 44.68% 95%CI (42.57-46.81%) DOR 2.9 95%CI (2.4-3.5) LR+ 1.72 95%CI (1.55-1.92) LR- 0.59 95%CI (0.54-0.65)

Study	Number of pts	Population	Controls	Study design	Reference standard	Index test (variables)	Diagnostic performance
						ILD	ILD Sensitivity 69.97% 95%CI (67.55-72.31%) Specificity 85.16% 95%CI (82.31-87.71%) PPV 90.77% 95%CI (89.14-92-18%) NPV 57.63% 95%CI (55.56-59.67%) DOR 13.37 95%CI (10.56-16.94) LR+ 4.72 95%CI (3.94-5-65) LR- 0.35 95%CI (0.32-0.38)
						Fever	Fever Sensitivity 43.02% 95%CI (40.47-45.61%) Specificity 64.19% 95%CI (60.52-67.75%) PPV 71.48% 95%CI (69.07-73.77%) NPV 35.07% 95%CI (33.47-36.71%) DOR 1.35 95%CI (1.12-1.63) LR+ 1.2 95%CI (1.07-1.35) LR- 0.89 95%CI (0.83-0.95)
						RP	RP Sensitivity 46.99% 95%CI (44.41-49.59%) Specificity 55.35% 95%CI (51.58-59.07%) PPV 68.7% 95%CI (66.54-70.78%) NPV 33.36% 95%CI (31.56-35.21%) DOR 1.098 95%CI (0.917-1.317) LR+ 1.05 95%CI (0.95-1.16) LR- 0.96 95%CI (0.88-1.04)
						MH	MH Sensitivity 27.98% 95%CI (25.69-30.35%) Specificity 97.57% 95%CI (96.15-98.58%) PPV 96.01% 95%CI (93.72-97.48%) NPV 39.38% 95%CI (38.57-40.19%) DOR 15.63 95%CI (9.53-25.63) LR+ 11.54 95%CI (7.16-18.58) LR- 0.74 95%CI (0.71-0.76)
						DM rash	DM rash Sensitivity 32.01% 95%CI (29.62-34.47%) Specificity 45.93% 95%CI (42.2-49.71%) PPV 55.25% 95%CI (52.74-57.74%) NPV 24.47% 95%CI (22.88-26.12%) DOR 0.4 95%CI (0.33-0.48) LR+ 0.59 95%CI (0.54-0.66) LR- 1.48 95%CI (1.36-1.62)
						Sclerodactyly	Sclerodactyly Sensitivity 11.97% 95%CI (10.35-13.74%) Specificity 59.91% 95% CI (56.18-63.57%) PPV 38.38% 95%CI (34.54-42.37%) NPV 24.6% 95%CI (23.45-25.8%) DOR 0.2 95%CI (0.16-0.25) LR+ 0.3 95%CI (0.25-0.35) LR- 1.47 95%CI (1.38-1.57%)
						cancer	cancer Sensitivity 9.03% 95%CI (7.61-10.62%) Specificity 92.44% 95%CI (90.23-94.29%) PPV 71.35% 95%CI (64.72-77.18%) NPV 32.76% 95%CI (32.18-33.35%) DOR 1.21 95%CI (0.87-1.69) LR+ 1.19 95%CI (0.88-1.62) LR- 0.98 95%CI (0.96-1.01)
Pinal-Fernandez 2015 (77)	20 patients 78 controls	Patients with definite or probable DM/PM by B&P + anti **Jo**	25 Anti–TIF1-γ 17 NXP2 12 Mi2 15 MDA5 9 PM-Scl 22 Ro52 15 seronegative myositis	Cross-sectional study	Expert opinion (definite or probable DM/PM by B&P + anti Jo1)	Perivascular inflammation	Perivascular inflammation Sensitivity 75% 95%CI (50.9-91.34%) Specificity 39.74% 95%CI (28.83-51.46%) PPV 24.19% 95%CI (18.96-30.33%) NPV 86.11% 95%CI (73.45-93.29%) DOR 1.98 95%CI(0.64-6) p= 0.2278 LR+ 1.24 95%CI (0.91-1.7) LR- 0.63 95%CI (0.28-1.41)
						Perifascicular atrophy	Perifascicular atrophy Sensitivity 60% 95%CI (36.05-80.88%) Specificity 51.3% 95%CI (39.69-62.77%) PPV 24% 95%CI (17.12-32.55%) NPV 83.33% 95%CI (73.71-89.92%) DOR 1.58 95%CI (0.58-4.3) p= 0.37 LR+ 1.23 95%CI (0.81-1.88) LR- 0.78 95%CI (0.44-1.39)
						Primary inflammation (endomysial inflammation)	Primary inflammation Sensitivity 40% 95%CI (19.12-63.95%) Specificity 78.21% 95%CI (67.41-86.76%) PPV 32% 95%CI (19.22-48.2%) NPV 83.56% 95%CI (77.72-88.11%) DOR 2.4 95%CI (0.83-6.78) p=0.1014 LR+ 1.84 95%CI (0.93-3.63) LR- 0.77 95%CI (0.53-1.12) Accuracy 70.4% 95%CI (60.34-79.21%)

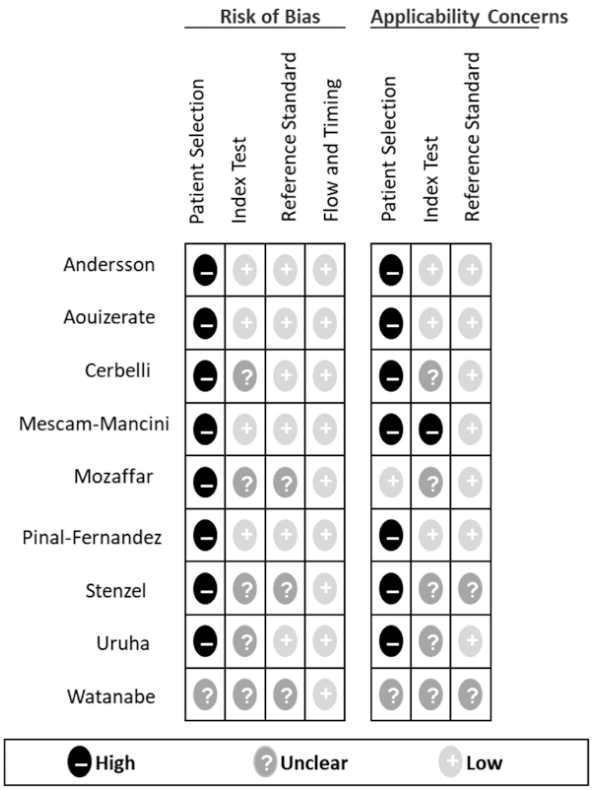
Study	Number of pts	Population	Controls	Study design	Reference standard	Index test (variables)	Diagnostic performance
						Necrotizing myopathy	Necrotizing myopathy Sensitivity 10% 95%CI (1.23-31.7%) Specificity 83.33% 95%CI (73.2-90.8%) PPV 13.33% 95%CI (3.64-38.55%) NPV 78.13% 95%CI (75.16-81.16%) DOR 0.55 95%CI (0.115-2.7) p= 0.4652 LR+ 0.6 95%CI (0.15-2.45) LR- 1.08 95%CI (0.91-1.29)
						Mitochondrial disfunction	Mitochondrial disfunction Sensitivity 20% 95%CI (5.73-43.66%) Specificity 70.51% 95%CI (59.11-80.3%) PPV 14.81% 95%CI (6.35-30.83%) NPV 77.46% 95%CI (72.57-81.71%) DOR 0.6 95%CI (0.18-1.98) p= 0.4 LR+ 0.68 95%CI (0.26-1.74) LR- 1.13 95%CI (0.87-1.47)
Mescam-Mancini 2015 (78)	19 cases 63 controls	Anti Jo1 patients	20 DM 21 IMNM 22 IBM	diagnostic accuracy studies	Expert opinion (anti Jo1 AND clinical manifestation of ASSD including ILD or myositis or arthritis/arthralgia)	myofibre necrosis	myofibre necrosis Sensitivity 89.47% 95%CI (66.86-98.7%) Specificity 17.46% 95%CI (9.05-29.01%) PPV 24.64% 95%CI (21.26-28.36%) NPV 84.62% 95%CI (57.15-95.78%) DOR 1.8 95%CI (0.37-8.92) p=0.473 LR+ 1.08 95%CI (0.9-1.31) LR- 0.6 95%CI (0.15-2.49)
						perifascicular necrosis	perifascicular necrosis Sensitivity 78.95% 95%CI (54.43-93.95%) Specificity 85.71% 95%CI (74.61-93.25%) PPV 62.50% 95%CI (46.58-76.11%) NPV 93.10% 95%CI (84.89-97.01%) DOR 22.5 95%CI (6.0747-83.34) p<0.0001 LR+ 5.53 95%CI (2.89-10.56) LR- 0.25 95%CI (0.10-0.59)
						myofiber atrophy	myofiber atrophy Sensitivity 84.21% 95%CI (60.42-96.62%) Specificity 3.17% 95%CI (0.39-11%) PPV 20.78% 95%CI (17.68-24.26%) NPV 40% 95%CI (10.72-78.73%) DOR 0.175 95%CI (0.027-1.137) p=0.0679 LR+ 0.87 95%CI (0.71-1.06) LR- 4.97 95%CI (0.9-27.61)
						perifascicular atrophy	perifascicular atrophy Sensitivity 63.16% 95%CI (38.36-83.71%) Specificity 71.43% 95%CI (58.65-82.11%) PPV 40.00% 95%CI (28.38-52.86%) NPV 86.54% 95%CI (77.76-92.20%) DOR 4.29 95%CI (1.45-12.63) p=0.0083 LR+ 2.21 95%CI (1.31-3.72) LR- 0.52 95%CI (0.28-0.95)
						perimysial fragmentation	perimysial fragmentation Sensitivity 73.68% 95%CI (48.80-90.85%) Specificity 73.02% 95%CI (60.35-83.43%) PPV 45.16% 95%CI (33.60-57.27%) NPV 90.20% 95%CI (81.30-95.20%) DOR 7.58 95%CI (2.37-24.24) p= 0.0006 LR+ 2.73 95%CI (1.68-4.44) LR- 0.36 95%CI (0.17-0.78)
						perimysial inflammation	perimysial inflammation Sensitivity 100% 95%CI (82.35-100%) Specificity 38.10% 95%CI (26.15-51.20%) PPV 32.76% 95%CI (28.64-37.16%) NPV 100% DOR 24.19 95%CI (1.4-419.04) p=0.0286 LR+ 1.62 95%CI (1.33-1.96) LR- 0
						perimysial inflammation with extension to endomysium	perimysial inflammation with extension to endomysium Sensitivity 73.68% 95%CI (48.80-90.85%) Specificity 33.33% 95%CI (21.95-46.34%) PPV 25.00% 95%CI (19.48-31.47%) NPV 80.77% 95%CI (64.69-90.59%) DOR 1.4 95%CI (0.44-4.41) p= 0.5655 LR+ 1.11 95%CI (0.80-1.52) LR- 0.79 95%CI (0.34-1.81)
						MHC I diffuse positivity	MHC I diffuse positivity Sensitivity 94.74% 95%CI (73.97-99.87%) Specificity 25.40% 95%CI (15.27-37.94%) PPV 27.69% 95%CI (24.26-31.41%) NPV 94.12% 95%CI (69.39-99.12%) DOR 6.13 95%CI (0.76-49.64) p= 0.0894 LR+ 1.27 95%CI (1.06-1.52) LR- 0.21 95%CI (0.03-1.46)

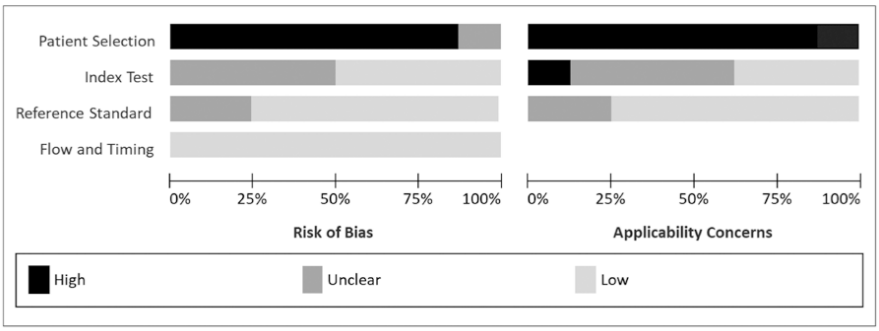
Study	Number of pts	Population	Controls	Study design	Reference standard	Index test (variables)	Diagnostic performance
						MHC CLASS I in perifascicular regions	MHC CLASS I in perifascicular regions Sensitivity 78.95% 95%CI (54.43-93.95%) Specificity 71.43% 95%CI (58.65-82.11%) PPV 45.45% 95%CI (34.60-56.76%) NPV 91.84% 95%CI (82.28-96.46%) DOR 9.375 95%CI (2.74-32.11) p= 0.0004 LR+ 2.76 95%CI (1.75-4.35) LR- 0.29 95%CI (0.12-0.71)
						C5b-9 sarcolemmal immunoreactivity	C5b-9 sarcolemmal immunoreactivity Sensitivity 84.21% 95%CI (60.42-96.62%) Specificity 25.40% 95%CI (15.27-37.94%) PPV 25.40% 95%CI (21.09-30.25%) NPV 84.21% 95%CI (63.47-94.24%) DOR 1.82 95%CI (0.47-7.05) p= 0.39 LR+ 1.13 95%CI (0.89-1.44) LR- 0.62 95%CI (0.20-1.91)
						C5b-9 perifascicular	C5b-9 perifascicular Sensitivity 26.32% 95%CI (9.15-51.20%) Specificity 19.05% 95%CI (10.25-30.91%) PPV 8.93% 95%CI (4.38-17.36%) NPV 46.15% 95%CI (32.52-60.38%) DOR 0.084 95%CI (0.025-0.28) p= 0.0001 LR+ 0.33 95%CI (0.15-0.70) LR- 3.87 95%CI (2.18-6.88)
Uruha 2018 (79)	30 ASSD 78 controls	Patients with myositis and ARS positivity	10 anti TIF1-gamma 13 anti NXP2 6 anti Mi-2 10 anti MDA5 1 anti SAE 17 antibody negative DM	Case-control study	Expert opinion (ARS and myositis)	sarcoplasmic myxovirus resistance protein A (MxA) expression	sarcoplasmic myxovirus resistance protein A (MxA) expression Sensitivity 0 Specificity 43.6% 95%CI(32.39% to 55.30%) PPV 0 NPV 53.12% 95%CI(46.82-59.33%) DOR 0.0127 95%I(0.0008 to 0.2153) LR+ 0 LR- 2.29 95%CI(1.78-2.95)
						RIG-1 expression	RIG-1 expression Sensitivity 0 Specificity 89.74% 95%CI(80.79% to 95.47%) PPV 0 NPV 70% 95%CI(68.40% to 71.55%) DOR 0.136 95%CI(0.0076 to 2.4311) LR+ 0 LR- 1.11 95%CI(1.03 to 1.20)
						perifascicular atrophy	perifascicular atrophy Sensitivity 20% 95%CI(7.71% to 38.57) Specificity 57.69% 95%CI(45.98% to 68.81%) PPV 15.38% 95%CI(7.83% to 28.02%) NPV 65.22% 95%CI(59.09% to 70.88%) DOR 0.34 95%CI(0.1253 to 0.9277)(1) LR+ 0.47 95%CI(0.22 to 1.01) LR- 1.39 95%CI(1.07 to 1.80)
Andersson 2017 (80)	66 ASSD 67 controls	Patients with ARS positivity, ILD or myositis	Healthy matched control	Case control	Expert opinion (ARS positivity + ILD and/or PM/DM diagnosis)	MRI Muscle edema	Muscle edema Sensitivity 37.88% 95%CI (26.22 to 50.66%) Specificity 88.06%95%CI (77.82%to 94.70%) PPV 75.76% 95%CI(60.34% to 86.52%) NPV 59% 95%CI(53.89% to 63.92%) DOR 4.4970 95%CI(1.8461 to 10.9542) LR+ 3.17 95%CI(1.54 to 6.52) LR- 0.71 95%CI(0.57 to 0.87)
						MRI Fascial edema	Fascial edema Sensitivity 28.79% 95%CI(18.30% to 41.25%) Specificity 92.54% 95%CI(83.44% to 97.53%) PPV 79.17% 95%CI(60.12% to 90.55%) NPV 56.88% 95%CI(52.73% to 60.94%) DOR 5.0128 95%CI(1.7444 to 14.4046) LR+ 3.86 95%CI(1.53 to 9.72) LR- 0.77 95%CI(0.65 to 0.91)
						MRI Fatty replacement	Fatty replacement Sensitivity 42.42% 95%CI(30.34% to 55.21%) Specificity 95.52% 95%CI(87.47% to 99.07%) PPV 90.32% 95%CI(74.88% to 96.69%) NPV 62.75% 95%CI(57.64% to 67.59%) DOR 16.46 95%CI(4.6891 to 57.7517) LR+ 9.47 95%CI(3.03 to 29.66) LR- 0.6 95%CI(0.49 to 0.75)
						MRI Muscle volume reduction	Muscle volume reduction Sensitivity 13.64% 95%CI(6.43% to 24.31%) Specificity 92.54% 95%CI(83.44% to 97.53%) PPV 64.29% 95%CI(38.91% to 83.57%) NPV 52.1% 95%CI(49.16% to 55.02%) DOR 1.958 95%CI(0.6194 to 6.1888) LR+ 1.83 95%CI(0.65 to 5.16) LR- 0.93 95%CI(0.83 to 1.05)

Study	Number of pts	Population	Controls	Study design	Reference standard	Index test (variables)	Diagnostic performance
Watanabe 2011 (81)	13 ASSD 185 controls	Patients with ILD and ARS positivity	Patients with ILD without ARS	Retrospective longitudinal	Expert opinion (IIP + ARS positivity)	Fever (>38 °C)	Fever Sensitivity 15.38% 95%CI(1.92% to 45.45%) Specificity 94.87 % 95%CI(90.77% to 97.51%) PPV 16.67% 95%CI(4.65% to 45.05%) NPV 94.39 % 95%CI(93.01% to 95.51%) DOR 3.1818 95%CI(0.6197 to 16.3356) LR+ 3 95%CI(0.73 to 12.30) LR- 0.89 95%CI(0.71 to 1.13)
						Body weight loss	Body weight loss Sensitivity 7.69% 95%CI(0.19% to 36.03%) Specificity 95.14 % 95%CI(90.97% to 97.75%) PPV 10% 95%CI(1.50% to 44.79%) NPV 93.62 % 95%CI(92.59% to 94.51%) DOR 1.6296 95%CI(0.1904 to 13.9508) LR+ 1.58 95%CI(0.22 to 11.54) LR- 0.97 95%CI(0.83 to 1.14)
						Dyspnoea	Dyspnoea Sensitivity 92.31% 95%CI(63.97% to 99.81%) Specificity 16.76 % 95%CI(11.68% to 22.93%) PPV 7.23% 95%CI(6.17% to 8.45%) NPV 96.88 % 95%CI(82.11% to 99.52%) DOR 2.4156 95%CI(0.3029 to 19.2621) LR+ 1.11 95%CI(0.94 to 1.31) LR- 0.46 95%CI(0.07 to 3.10)
						Cough	Cough Sensitivity 38.46% 95%CI(13.86% to 68.42%) Specificity 61.62% 95%CI(54.20% to 68.66%) PPV 6.58% 95%CI(3.34% to 12.55%) NPV 3.44 % 95%CI(90.13% to 95.69%) DOR 1.0035 95%CI(0.3159 to 3.1884) LR+ 1 95%CI(0.49 to 2.04) LR- 1 95%CI(0.64 to 1.56)
						Other respiratory symptoms	Other respiratory symptoms Sensitivity 7.69% 95%CI(0.19% to 36.03%) Specificity 95.14 % 95%CI(90.97% to 97.75%) PPV 10% 95%CI(1.50% to 44.79%) NPV 93.62% 95%CI(92.59% to 94.51%) DOR 1.6296 95%CI(0.1904 to 13.9508) LR+ 1.58 95%CI(0.22 to 11.54) LR- 0.97 95%CI(0.83 to 1.14)
						Fine crackles	Fine crackles Sensitivity 92.31% 95%CI(63.97% to 99.81%) Specificity 9.73% 95%CI(5.87% to 14.94%) PPV 6.70% 95%CI(5.75% to 7.80%) NPV 94.74% 95%CI(72.25% to 99.20%) DOR 1.2934 95%CI(0.1588 to 10.5325) LR+ 1.02 95%CI(0.87 to 1.20) LR- 0.79 95%CI(0.11 to 5.47)
						Clubbed fingers	Clubbed fingers Sensitivity 7.69% 95%CI(0.19% to 36.03%) Specificity 81.62 % 95%CI(75.28% to 86.92%) PPV 2.86% 95%CI(0.43% to 16.54%) NPV 92.64 % 95%CI(91.38% to 93.72%) DOR 0.3701 95%CI(0.0465 to 2.9438) LR+ 0.42 95%CI(0.06 to 2.82) LR- 1.13 95%CI(0.95 to 1.34)
						Arthralgia or joint deformity	Arthralgia or joint deformity Sensitivity 15.38% 95%CI(1.92% to 45.45%) Specificity 97.84% 95%CI(94.56% to 99.41%) PPV 33.33% 95%CI(9.16% to 71.27%) NPV 94.27 % 95%CI(92.88% to 95.41%) DOR 8.2273 95%CI(1.3556 to 49.9334) LR+ 7.12 95%CI(1.43 to 35.30) LR- 0.86 95%CI(0.69 to 1.09)
						Raynaud's phenomenon	Raynaud's Phenomenon Sensitivity 7.69% 95%CI(0.19% to 36.03%) Specificity 97.84% 95%CI(94.56% to 99.41%) PPV 20.00% 95%CI(2.92% to 67.52%) NPV 93.78% 95%CI(92.79% to 94.64%) DOR 3.7708 95%CI(0.3904 to 36.4227) LR+ 3.56 95%CI(0.43 to 29.58) LR- 0.94 95%CI(0.81 to 1.11)
						Cutaneous symptoms	CUTANEOUS SYMPTOMS Sensitivity 30.77% 95%CI(9.09% to 61.43%) Specificity 98.38% 95%CI(95.33% to 99.66%) PPV 7.14% 95%CI(24.98% to 84.22%) NPV 95.29 % 95%CI(93.36% to 96.67%) DOR 26.963 95%CI(5.2314 to 138.9684) LR+ 18.97 95%CI(4.74 to 75.98) LR- 95.29 95%CI(93.36% to 96.67%)

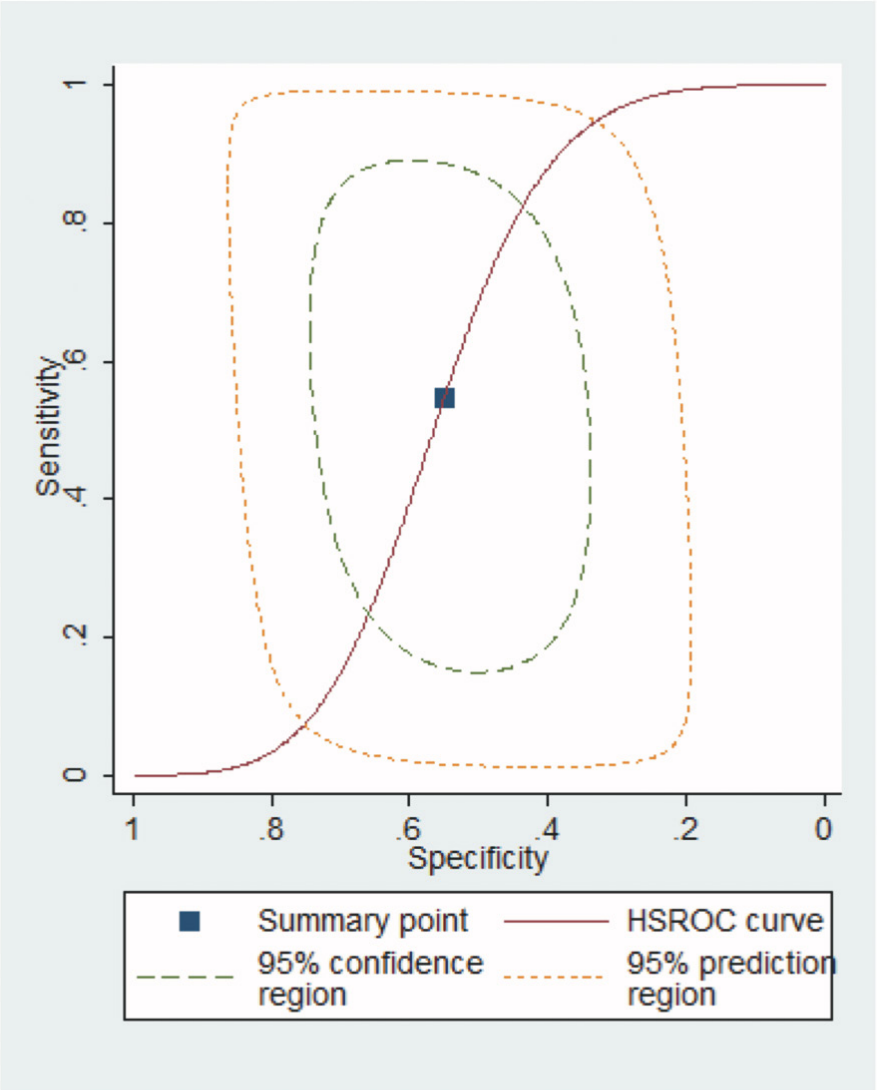
Study	Number of pts	Population	Controls	Study design	Reference standard	Index test (variables)	Diagnostic performance
Cerbelli 2018 (50)	18	Consecutive patients with anti ARS antibodies and suspected myositis referred for histological evaluation.	DM according to the ENMC criteria	Case-control	Expert opinion + antiJo1 or PL7	Perifascicular Necrosis	Sensitivity 66% 95%CI (34% to 90%) Specificity 57% 95%CI (18% to 90%) PPV 72% 95%CI (50% to 87%) NPV 50% 95%CI (26% to 73%) LR+ 0.61 95%CI (0.61 to 4) LR- 0.58 95%CI (0.21 to 1.63)
						Perifascicular Regeneration	Sensitivity 66% 95% CI (34% to 90%) Specificity 28% 95% CI (3% to 70%) PPV 61% 95% CI (46% to 74%) NPV 33% 95% CI (10% to 67%) LR+ 0.93 95% CI (0.46 to 0.74) LR- 1.17 95% CI (0.28 to 4.82)
						Perifascicular Atrophy	Sensitivity 36% 95% CI (10% to 69%) Specificity 0% 95% CI (0% to 40%) PPV 36% 95% CI (20% to 55%) LR+ 0.36 (0.17 to 0.79)
						Endomysial infiltrates (inflammation)	Sensitivity 72% 95% CI (39% to 93%) Specificity 28% 95% CI (3% to 70%) PPV 61% 95% CI (35% to 82%) NPV 40% 95% CI (12% to 75%) LR+ 1.02 95% CI (0.56 to 1.84) LR- 0.95 95% CI (0.21 to 4.35)
						Perimysial inflammation	Sensitivity 54% 95% CI (23% to 83%) Specificity 14% 95% CI (0.3% to 57%) PPV 5% 95% CI (35% to 82%) NPV 16% 95% CI (2% to 57%) LR+ 0.64 95 % CI (0.34 to 1.18) LR- 3.18 95% CI (0.46 to 21.85)
						Perimysial fragmentation	Sensitivity 81% 95% CI (48% to 97%) Specificity 28% 95% CI (3% to 70%) PPV 64% 95% CI (51% to 75%) NPV 50% 95% CI (15% to 84%) LR+ 1.15 95% CI (0.66 to 1.98) LR- 0.64 95 % CI (0.11 to 3.54)
						MHC I enhancement	Sensitivity 54% 95% CI (23% to 83%) Specificity 14% 95% CI (0.3% to 57%) PPV 050% 95% CI (35% to 64%) NPV 16% 95% CI (2% to 57%) LR+ 0.64 95% CI (0.34,1.18) LR- 3.18 95% CI (0.46,21.85)
						C5B9 sarcolemmal positivity	Sensitivity 72% 95% CI (39% to 93%) Specificity 14% 95% CI (3.6% to 57%) PPV 57% 95% CI (45% to 68%) NPV 25% 95% CI (4% to 72%) LR+ 0.85 95% CI (0.53 to 1.36) LR- 1.91 95% CI (0.24 to 14.91)
						COX deficient fibers	Sensitivity 0% 95% CI (0% to 28%) Specificity 0% 95% CI (0% to 40%)
Mozaffar 2000 (82)	11	Patients who underwent muscle biopsy for myositis	26 DM 27 PM 8 IBM 5 fasciitis	Case-control	Myositis + anti Jo1	Perifascicular atrophy	Perifascicular atrophy Sensitivity 100% (CI 71.5%-100%) Specificity 59% (CI 46.3-71%) PPV 28.95% (CI 23.36-35.25%) NPV 100% AUC DOR LR+ 2.44 (CI 1.83-3.27) LR- 100
						Perifascicular necrosis/regeneration	Perifascicular necrosis/regeneration Sensitivity 90.91% (CI 58.72-99.77%) Specificity 71.21% (CI 58.75-81.7%) PPV 34.48% (CI 25.64-44.55%) NPV 97.92% (CI 87.82-99.67%) AUC DOR LR+ 3.16 (2.07-4.82) LR- 0.13 (0.02-0.83)
						Perimysial Inflammation	Perimysial inflammation Sensitivity 100% (CI 71.51-100%) Specificity 71.21% (CI 58.75-81.7%) PPV 36.67% (CI 28.37-45.83%) NPV 100% AUC DOR LR+ 3.47 (CI 2.38-5.08) LR- 0

Study	Number of pts	Population	Controls	Study design	Reference standard	Index test (variables)	Diagnostic performance
						Endomysial Inflammation	Endomysial inflammation Sensitivity 18.18% (CI 2.28-51.78%) Specificity 48.48% (CI 35.99-61.12%) PPV 5.56% (CI 1.62-17.39%) NPV 78.05% (CI 70.99-83.78%) AUC DOR LR+ 0.35 (CI 0.1-1.26) LR- 1.69 (CI 1.16-2.45)
						Perivascular inflammation	Perivascular inflammation Sensitivity 9.09% (CI 0.23-41.28%) Specificity 39.39% (CI 27.58-52.19%) PPV 2.44% (CI 0.38-14.06%) NPV 72.22% (CI 64.63-78.72%) AUC DOR LR+ 0.15 (CI 0.02-0.98) LR- 2.31 (CI 1.62-3.28)
						Perimysial fragmentation	Perimysial fragmentation Sensitivity 100% (CI 71.51-100%) Specificity 84.84% (CI 73.9-92.49%) PPV 52.38% (CI 38.33-66.07%) NPV 100% AUC DOR LR+ 6.6 (CI 3.73-11.68) LR- 0
						ALP Perimysial staining	ALP perimysial staining Sensitivity 90.91% (CI 58.72-99.77%) Specificity 59.09% (CI 46.29-71.05%) PPV 27.01% (CI 20.78-34.34%) NPV 97.5% (CI 85.62-99.61%) AUC DOR LR+ 2.22 (CI 1.57-3.14) LR- 0.15 (CI 0.02-1.01)
						ALP Small vessel staining	ALP small vessels staining Sensitivity 9.09% (CI 0.23-41.28%) Specificity 60.61% (CI 47.81-72.42%) PPV 3.7% (CI 0.58-20.33%) NPV 80% (CI 75.33-83.97%) AUC DOR LR+ 0.23 (CI 0.03-1.53) LR- 1.5 (1.15-1.96)
						Perifascicular COX deficiency (mitochondrial dysfunction)	Perifascicular COX deficiency Sensitivity 0% (CI 0-28.49%) Specificity 75.76% (CI 63.64-85.46%) PPV 0 NPV 81.97% (CI 79.86-83.9%) AUC DOR LR+ 0 LR- 1.32 (CI 1.15-1.51)
						Scattered COX deficiency	Scattered COX deficiency Sensitivity 0% (CI O-28.49%) Specificity 78.79% (CI 66.98-87.89%) PPV 0 NPV 82.54% (CI 80.66-84.27%) AUC DOR LR+ 0 LR- 1.27 (1.12-1.44)





Supplementary Fig. S2. Risk of bias for studies included in Q2, assessed by QUADAS -2.



- Pooled sensitivity (95% CI) 0.55 (0.3,0.77)
- Pooled specificity (95% CI) 0.55 (0.44,0.65)
- Pooled LR + (95%CI) 1.21 (0.68,2.14)
- Pooled LR- (95% CI) 0.82 (0.44,1.54)

Supplementary Fig. S3. Hierarchical summary ROC for perifascicular necrosis/atrophy.