システマティックレビュー（SR）の進捗状況-2
（12月2日現在）

CQ番号	作成したCQ	SR担当者	SR進捗状況					SRレポート
			一次スクリーニング	二次スクリーニング	個々の研究エビデンスの評価	エビデンス総体の評価		
						定性的SR	定量的SR	
			テンプレート					
			4-1、4-2	4-2、4-3	4-5、4-6	4-7	4-9	4-8、4-10
14	非ステロイド性抗炎症薬は ASDに対して有用か	近藤裕也（筑波大学膠原病内科）	○	○	○	○	○	○
15	副腎皮質ステロイド全身投与はASDに対して有用か	武井修治（鹿児島大学） 岡本奈美（大阪医科大学）	○	○				
16	ステロイドパルス療法は ASDに対して有用か		○	○				
17	メトトレキサートは ASDに対して有用か		○	○				
18	シクロスポリンは ASDに対して有用か		○	○				
19	疾患修飾性抗リウマチ薬（disease modifying anti-rheumatic drugs）はASDの関節炎に対して有用か		○	○				
20	TNF阻害薬は ASDに対して有用か用か	高崎芳成（順天堂大学） 舟久保ゆう（埼玉医科大学）	○					
21	IL-6阻害薬は ASDに対して有用か		○					
22	IL-1阻害薬は ASDに対して有用か		○					
23	TNF阻害薬、IL-6阻害薬、IL-1阻害薬以外にASDに対して有用な生物学的製剤は存在するか		○					
24	ASDの第一選択薬は何か		○					
25	ステロイドパルス療法は全身型若年性特発性関節炎に対して有用かか	西本憲弘（東京医科大学） 三森明夫（国立国際医療センター）						
26	全身型若年性特発性関節炎において有用な免疫抑制剤はあるか							
27	全身型若年性特発性関節炎において有用な生物学的製剤はあるか							

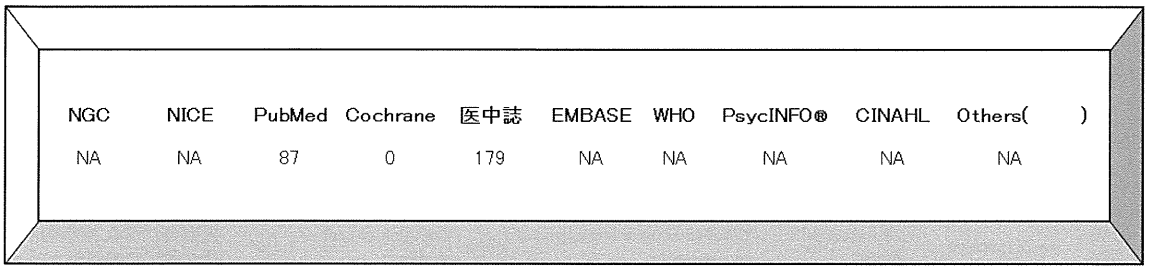
ASD CQ2のPICOと検索キーワード

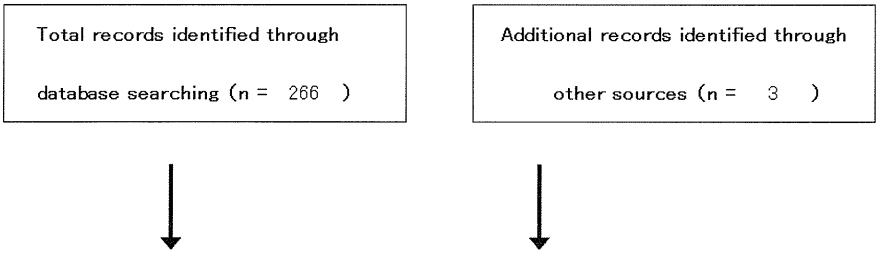
CQ14	P				I/C		O				作成者
	性別	年齢	疾患	病態	I	C	リスト	内容	益/害	重要度	採択可否	
ASDに特徴的な皮膚所見はあるか	指定なし	指定なし	ASD	皮疹	性状 出現部位 出現時期 自覚症状	プラセボ	O1	ASD診断感度上昇	益	7	○	川口
							O2	ASD診断特異度上昇	益	7	○	
							O3	症状による苦痛	害	3	×	藤本

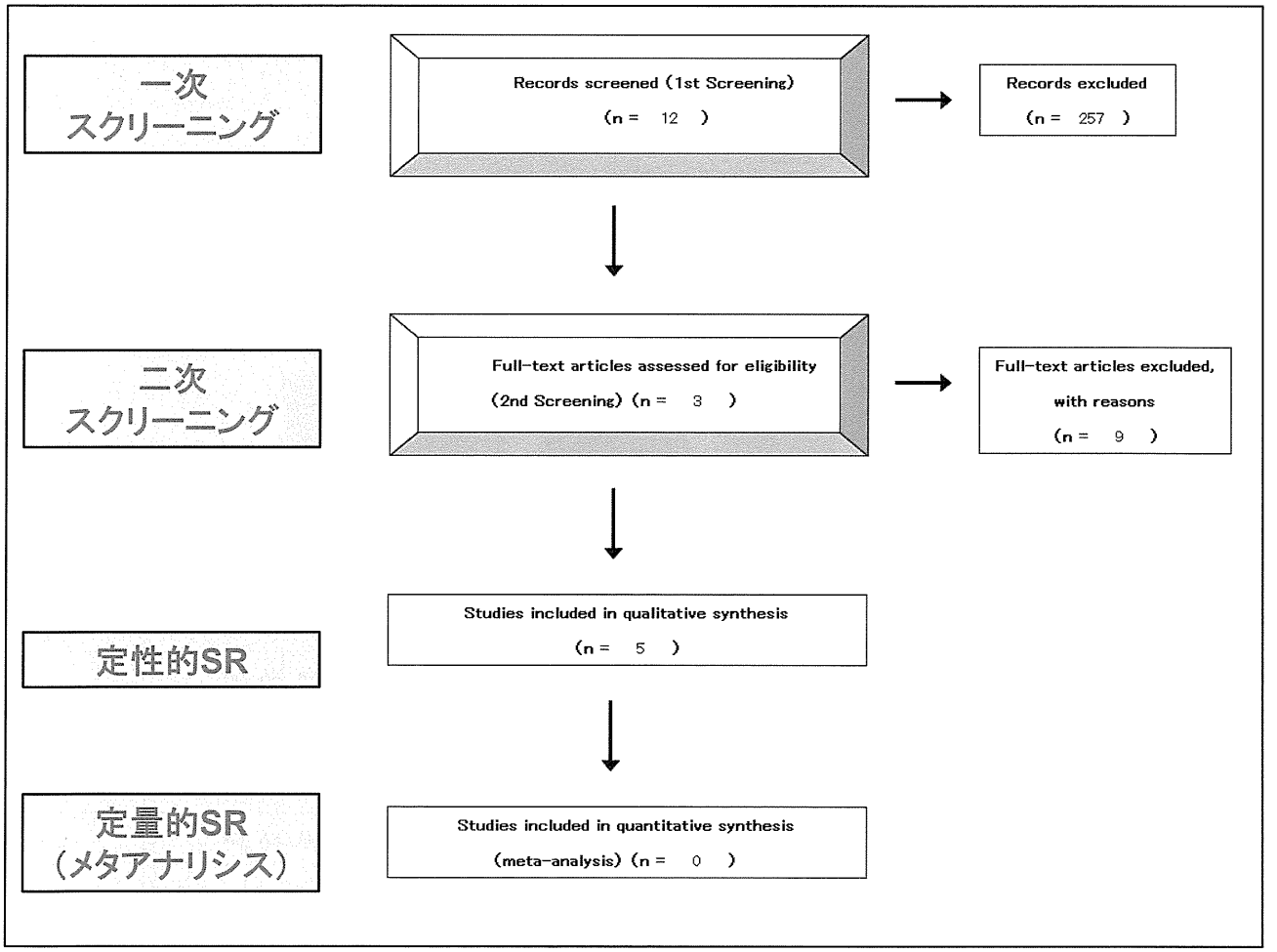
疾患：ASD		
SR担当者： 近藤裕也 岩本雅弘		
CQ番号 2	ASDに特徴的な皮膚所見はあるか	
キーワード	日本語	英語
1	成人スティル病	Adult Still's disease
2	皮疹	rash, eruption
3	性状	property, condition, state
4	持続期間	duration
5	出現部位	site, face, body, extremity, thigh, arm
6	出現時期	time
7	感度、特異度	sensitivity, specificity
8	自覚症状	complaint

文献検索フローチャート(データベース＋追加論文)
ASD CQ2

【4-2 文献検索フローチャート】 PRISMA声明を改変







【4-3：ASD CQ14　二次スクリーニング後の一覧表】

文献	研究デザイン	P	I	C	O	除外	コメント
Lee JY, Semin Arthritis Rheum 2012	retrospective	36 cases with AOSD	clinical records, clinical photos, and pathologic slides	none	clinicopathological features in skin lesion		
Yamamoto T, Rheumatol Int 2012	review					✔	systematic reviewではないため除外
Kong XD, Clin Rheumatol 2010	retrospective	104 cases with AOSD	relevant clnical details	none	clnical manifestations	✔	対照群がなく、皮疹の詳細な評価が無いため除外
Fortna RR, J Cuan Pathol 2010	retrospective	2 cases with AOSD and one case with juvenile Still's disease	clnical and histopathological examinations of skin eruptions	none	clnical and histopathlogical findings	✔	少数例報告のため除外
Zeng T, et al. J Rheumatol 2009	retrospective	61 cases with AOSD	relavent clnical details	none	common clnical features	✔	対照群がなく、皮疹の詳細な評価が無いため除外
Mohrpoor G, Mod Rheumatol 2008	retrospective	28 cases with AOSD	detailed history and physical examinations	none	common clnical findings	✔	対照群がなく、皮疹の詳細な評価が無いため除外
Singh S, Clin Rheumatol 2008	retrospective	14 cases with AOSD	clnical features	none	clnical manifestations	✔	対照群がなく、皮疹の詳細な評価が無いため除外
Uppal SS, Clin Rheumatol 2007	retrospective	22 cases with AOSD	sytemic and articular manifestations	none	clnical features	✔	対照群がなく、皮疹の詳細な評価が無いため除外
Lee JY, J Am Acad Der 2005	retrospective	11 patients with AOSD	clnical data and pathologic examinations	none	clnical and pathological form of skin eruptions		
Vanderschueren S, Clin Exp Rheumatol 2012	retrospective	22 cases with AOSD and 422 cases with classical FUO	clinical manifestations	none	clinical characteristics, treatment, and outocome		
Jiang L, J Rheumatol 2011	retrospective	70 cases with AOSD and 140 cases with fever	clinical and laboratory measures	none	diagnostic effecacy of clnical and laboratory measures		
Crispin JC, Medicine (Baltimore) 2005	retrospective	26 cases with AOSD and 135 cases with FUO	clnical characteristcs and laboratory parameters	none	clinical characteristics		

【4-6 評価シート 観察研究】

診療ガイドライン	ASD CQ2 ASDに特徴的な皮膚所見はあるか
対象	ASDの皮疹
介入	性状　出現部位　出現時期 自覚症状
対照	無

*バイアスリスク、非直接性
　各ドメインの評価は"高(-2)"、"中/疑い(-1)"、"低(0)"の3段階
　まとめは"高(-2)"、"中(-1)"、"低(0)"の3段階でエビデンス総体に反映させる
** 上昇要因
　各項目の評価は"高(+2)"、"中(+1)"、"低(0)"の3段階
　まとめは"高(+2)"、"中(+1)"、"低(0)"の3段階でエビデンス総体に反映させる
各アウトカムごとに別紙にまとめる

アウトカム	O2：ASD診断感度上昇

個別研究		バイアスリスク*							上昇要因**				非直接性*					リスク人数(アウトカム率)								
研究コード	研究デザイン	選択バイアス	実行バイアス	検出バイアス	症例現象バイアス	その他		まとめ	量反応関係	効果減弱交絡	効果の大きさ	まとめ	対象	介入	対照	アウトカム	まとめ	対照群母	対照群子	(%)	介入群母	介入群子	(%)	効果指標(種類)	効果指標(値)	信頼区間
		背景因子の差	ケアの差	不適切なアウトカム測定	不完全なフォローアップ	不十分な交絡の調整	その他のバイアス																			
Lee JY. 2012	症例集積	0	0	-1	0	-2	0	-2	0	0	0	0	0	0	0	-2	-2	NA	NA	NA	NA	NA	NA	NA	NA	
Lee JY. 2005	症例集積	0	-1	-2	0	-2	0	-2	0	0	0	0	-1	-1	0	-2	-2	NA	NA	NA	NA	NA	NA	NA	NA	
Vanderschueren S. 2012	症例対照研究	-1	0	-2	0	-2	0	-2	0	0	0	0	0	-1	0	-1	-1	NA	NA	NA	NA	NA	NA	NA	NA	
Jiang L. 2011	症例対照研究	-1	0	-2	0	-2	0	-2	0	0	0	0	0	-1	0	0	-1	NA	NA	NA	NA	NA	NA	NA	NA	
Crispin JC. 2005	症例対照研究	-1	0	-2	0	-2	0	-2	0	0	0	0	0	-1	0	0	-1	NA	NA	NA	NA	NA	NA	NA	NA	

【4-6 評価シート 観察研究】

診療ガイドライン	ASD CQ2 ASDに特徴的な皮膚所見はあるか
対象	ASDの皮疹
介入	性状 出現部位 出現時期 自覚症状
対照	無

*バイアスリスク、非直接性
各ドメインの評価は"高(-2)"、"中/疑い(-1)"、"低(0)"の3段階
まとめは"高(-2)"、"中(-1)"、"低(0)"の3段階でエビデンス総体に反映させる
** 上昇要因
各項目の評価は"高(+2)"、"中(+1)"、"低(0)"の3段階
まとめは"高(+2)"、"中(+1)"、"低(0)"の3段階でエビデンス総体に反映させる
各アウトカムごとに別紙にまとめる

アウトカム	O1:ASD診断特異度上昇

個別研究		バイアスリスク*							上昇要因**				非直接性*					リスク人数(アウトカム率)								
		選択バイアス	実行バイアス	検出バイアス	症例現象バイアス	その他																				
研究コード	研究デザイン	背景因子の差	ケアの差	不適切なアウトカム測定	不完全なフォローアップ	不十分な交絡の調整	その他のバイアス	まとめ	量反応関係	効果減弱交絡	効果の大きさ	まとめ	対象	介入	対照	アウトカム	まとめ	対照群分母	対照群分子	(%)	介入群分母	介入群分子	(%)	効果指標(種類)	効果指標(値)	信頼区間
Lee JY. 2012	症例集積	0	0	-1	0	-2	0	-2	0	0	0	0	0	0	0	-2	-2	NA	NA	NA	NA	NA	NA	NA	NA	
Lee JY. 2005	症例集積	0	-1	-2	0	-2	0	-2	0	0	0	0	-1	-1	0	-2	-2	NA	NA	NA	NA	NA	NA	NA	NA	
Vandersc hueren S. 2012	症例対照研究	-1	0	-2	0	-2	0	-2	0	0	0	0	0	-1	0	-1	-1	NA	NA	NA	NA	NA	NA	NA	NA	
Jiang L. 2011	症例対照研究	-1	0	-2	0	-2	0	-2	0	0	0	0	0	-1	0	0	-1	NA	NA	NA	NA	NA	NA	NA	NA	
Crispin JC. 2005	症例対照研究	-1	0	-2	0	-2	0	-2	0	0	0	0	0	-1	0	0	-1	NA	NA	NA	NA	NA	NA	NA	NA	

【4-7 評価シート エビデンス総体】

診療ガイドライン	ASD CQ2 ASDに特徴的な皮膚所見はあるか
対象	ASDの皮疹
介入	性状 出現部位 出現時期 自覚症状
対照	無

エビデンスの強さはRCTは"強(A)"からスタート、観察研究は弱(C)からスタート
* 各ドメインは"高(-2)"、"中/疑い(-1)"、"低(0)"の3段階
** エビデンスの強さは"強(A)"、"中(B)"、"弱(C)"、"非常に弱(D)"の4段階
*** 重要性はアウトカムの重要性(1～9)

エビデンス総体

								リスク人数(アウトカム率)											
アウトカム	研究デザイン/研究数	バイアスリスク*	非一貫性*	不精確*	非直接性*	その他(出版バイアスなど)**	上昇要因(観察研究)**	対照群分母	対照群分子	(%)	介入群分母	介入群分子	(%)	効果指標(種類)	効果指標統合値	信頼区間	エビデンスの強さ**	重要性***	コメント
ASD診断感度上昇	症例集積/2、症例対照研究/3	-2	-1	-1	-1	-1	0	NA	NA	NA	NA	NA	NA	NA	NA	NA	非常に弱(D)	7	ASDにおける皮疹の有無は診断感度を上昇させる可能性がある
ASD診断特異度上昇	症例集積/2、症例対照研究/3	-2	-1	-1	-1	-1	0	NA	NA	NA	NA	NA	NA	NA	NA	NA	非常に弱(D)	7	ASDにおける皮疹の有無は診断特異度を上昇させる可能性がある

【4-8 定性的システマティックレビュー】

CQ	2	ASDに特徴的な皮膚所見はあるか
P	ASDの皮疹	
I	性状 出現部位 出現時期 自覚症状	
C	無	
臨床的文脈		ASDの臨床症状

O1	ASD診断感度上昇
非直接性のまとめ	2つの症例集積研究では非直接性は高く、3つの症例対照研究では中等度であった。
バイアスリスクのまとめ	2つの症例集積研、3つの症例対照研究でバイアスリスクは高度であった。
非一貫性その他のまとめ	2つの症例集積研、3つの症例対照研究で非一貫性は中等度であった。
コメント	3つの症例対照研究の結果から、ASDにおける皮疹の有無は診断感度を上昇させる可能性がある

O2	ASD診断特異度上昇
非直接性のまとめ	2つの症例集積研究では非直接性は高く、3つの症例対照研究では中等度であった。
バイアスリスクのまとめ	2つの症例集積研、3つの症例対照研究でバイアスリスクは高度であった。
非一貫性その他のまとめ	2つの症例集積研、3つの症例対照研究で非一貫性は中等度であった。
コメント	3つの症例対照研究の結果から、ASDにおける皮疹の有無は診断特異度を上昇させる可能性があり、特に一過性、Still病に特徴的皮疹は、特異性が高い可能性がある

【4-10 SRレポートのまとめ】

5本の観察研究(3本の症例対照研究、2本の症例集積研究)を対象にSRを実施した。
3本の症例対照研究において、ASD以外の発熱性疾患を対照とした場合に皮疹の有無が診断感度を上昇させる可能性が示唆された(エビデンスの強さ:D)。
3本の症例対照研究において、ASD以外の発熱性疾患を対照とした場合に皮疹の有無が診断特異度を上昇される可能性が示唆され、特に一過性、ASDに典型的な皮疹はASDに特異性が高い所見であることが示唆された(D)。
皮疹の性状に関しては、症例対照研究では明示されていないが、2本の症例集積研究の結果からASDの経過中に一過性紅斑と同様に顔面、頸部、体幹、四肢伸側などに持続性紅斑が高頻度(64-78%)に認められ、病理学的には一過性紅斑が表在血管周囲の炎症細胞浸潤であるのに対して、持続性紅斑は角化上皮細胞の壊死巣と周囲の炎症細胞浸潤であることが報告されている。
以上の結果、エビデンスは弱いが、皮疹の有無はASDの診断感度、特異度を上昇させる可能性がある。

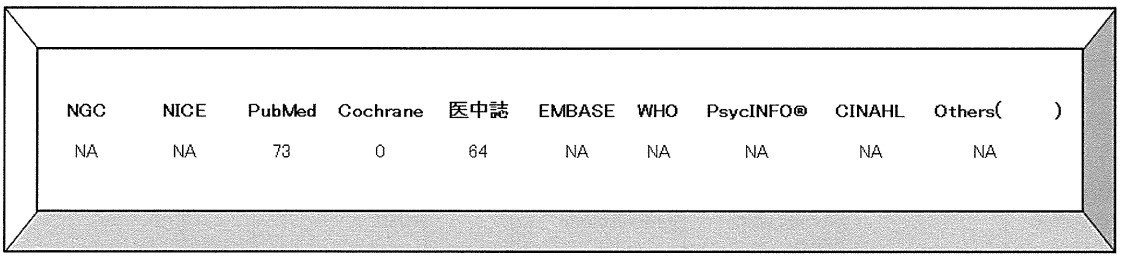
ASD CQ14のPICOと検索キーワード

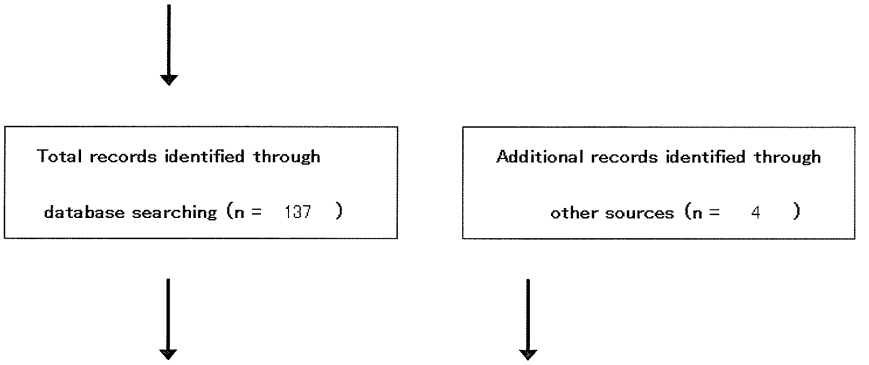
CQ14	P				I/C		O					作成者
	性別	年齢	疾患	病態	I	C	リスト	内容	益/害	重要度	採択可否	
非ステロイド性抗炎症薬はASDに対して有用か	指定なし	指定なし	ASD	発熱 関節症状 全身炎症 臓器障害	非ステロイド性抗炎症薬	プラセボ	O1	症状の改善	益	5	○	高崎 舟久保
							O2	病態の改善	益	4	○	
							O3	再発抑制	益	4	○	
							O4	薬剤による消化管障	害	4	○	
							O5	薬剤による腎障害	害	4	○	
							O6	薬剤アレルギー	害	6	○	

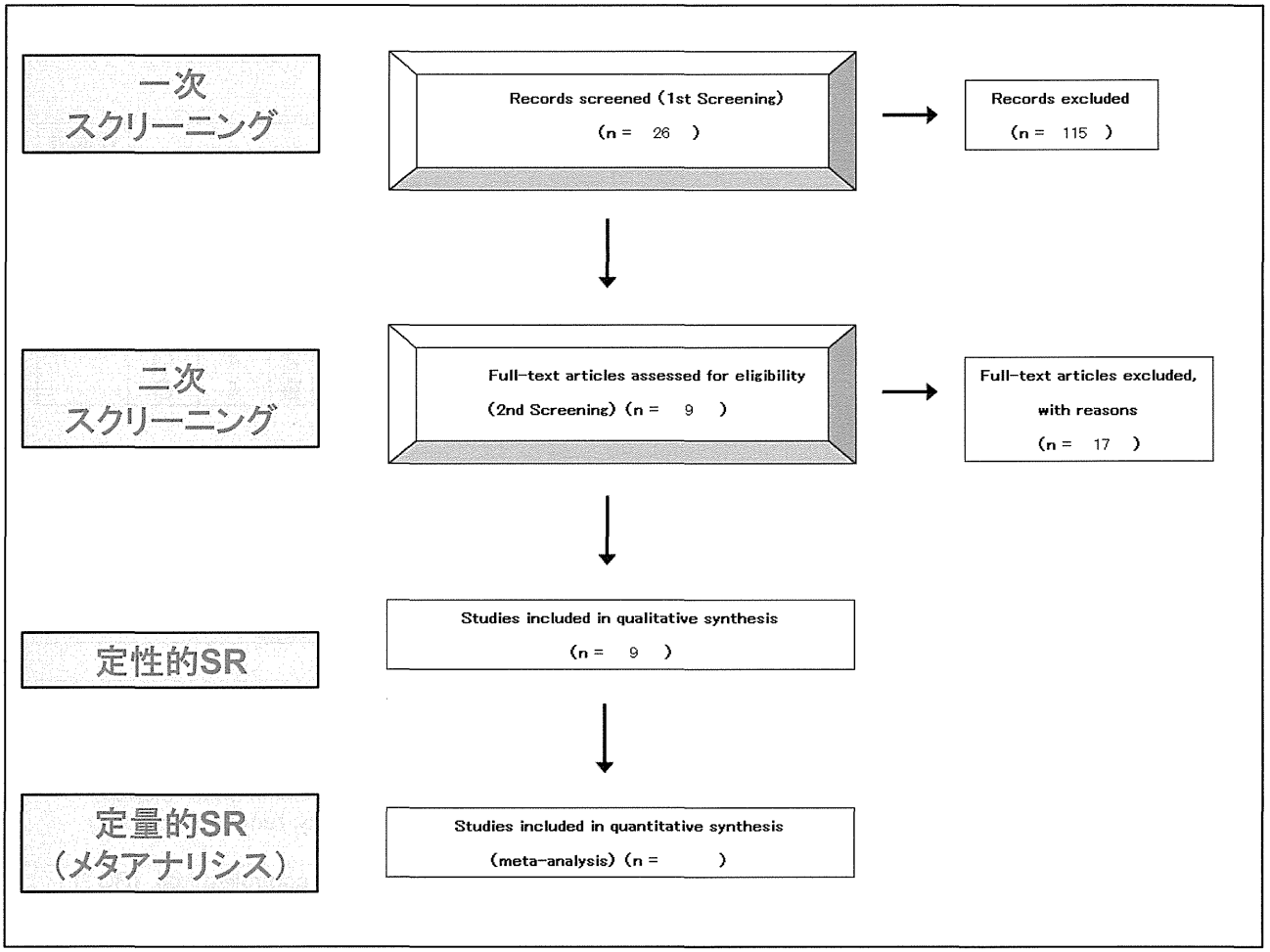
疾患：ASD		
SR担当者： 近藤裕也		
CQ番号 14	非ステロイド性抗炎症薬はASDに対して有用か	
キーワード	日本語	英語
1	成人スティル病	adult Still's disease
2	発熱、関節症状、全身炎症、臓器障害	fever, joint symptom, arthritis, arthropathy, systemic inflammation, organ dysfunction
3	非ステロイド性抗炎症薬	non steroidal anti-inflammatory drug, NSAIDs
4	症状、病態、再発抑制、消化管障害、腎障害、薬剤アレルギー	symptom, pathology, inhibition of relapse, gastrointestinal toxicity, renal toxicity, drug allergy
5	プラセボ、無作為化比較対照試験	placebo, randomized controlled trial (RCT)

文献検索フローチャート（データベース＋追加論文）
ASD CQ14

【4-2 文献検索フローチャート】 PRISMA声明を改変 ASD CQ14







【4-3：ASD CQ14　二次スクリーニング後の一覧表】

文献	研究デザイン	P	I	C	O	除外	コメント
Reddy Munagala VV. Int J Rheum Dis 2012	retrospective, case series	25 patients with AOSD	medicines used for the treatment	none	disease course, and outocome		
Iliou C. Clin Exp Rheumatol 2013	retrospective, case series	44 patients with AOSD	medications used response to treatment	none	treatment modalities applied and outcome		
Zhang XH. Int J Clin Exp Pthol 2012	case report	23-year -old woman with AOSD	methylpredonisolone and loxoprofen sodium	none	HPS secondary to AOSD		
Fukuda R. Tokai J Exp Clin Med 2010	case report	61-year-old man with AOSD	loxoprofen sodium and prednisolone	none	AOSD complicated with SIADH	✔	case reportのため除外
Kim HA. Rheumatol Int 2012	retrospective, case series	54 patients with AOSD	treatment	none	therapeutic response and prognostic factor		
Rajabally MN. J Crohns Colitis 2010	case report	30-year-old woman with AOSD complicated with crohn's colitis	NSAID and predonisolone	none	disease course of AOSD	✔	case reportのため除外
Lahiri M. Int J Rheum Dis 2010	case report	40-year-old woman with AOSD	NSAIDs and other therapies	none	disease course of AOSD	✔	case reportのため除外
Franchini S. Arthrritis Rheum 2010	retrospective, case series	45 cases with AOSD	drugs used for the treatment	none	outcome of therapy		
Gianella S. Am J Hematol 2008	case report	20-year old patient with AOSD	ibprofen and other thrapies	none	disease course of AOSD	✔	case reportのため除外
Singh S. Clin Rheumatol 2008	retrospective, case series	14 patients with AOSD	treatment	none	disease course and outcome		
Efthimiou P. Semin Arthritis Rheum 2006	review	AOSD	treatment	none	disease outcome	✔	systematic reviewではないため除外
Aarntzen EH. AnnRheum Dis 2005	case report	22-year-old patients with AOSD	NSAIDs	none	hypersensitivity		

【4-3：ASD CQ14　二次スクリーニング後の一覧表】

文献	研究デザイン	P	I	C	O	除外	コメント
常松 令. 臨床消化器内科 2012	case report	30代男性　AOSD	NSAID and steroid	none	disease course of AOSD	✔	case reportのため除外
Sari Aysegul. Mod Rheumatol 2010	case report	44-year-old woman with AOSD	NSAIDs and methylpredonisolone	none	disease course of AOSD	✔	case reportのため除外
根本 育恵. 臨床皮膚科 2006	case report	22歳女性　AOSD	NSAIDs屯用など	none	disease course of AOSD	✔	case reportのため除外
松清 大. 日本臨床外科学会誌 2004	case report	28歳女性　AOSD	NSAIDs	none	disease course of AOSD	✔	case reportのため除外
新井 幸宏. 臨床血液 2004	case report	17歳女性　AOSD	NSAIDsなど	none	disease course of AOSD	✔	case reportのため除外
Hagiyama H. Mod Rheumatol 2003	case report	24-year-old woman and 20-year-old man with AOSD	NSAIDsなど	none	disease course of AOSD	✔	case reportのため除外
藤永 洋.　中部リウマチ　2001	case report	46歳女性　AOSD	NSAIDsなど	none	disease course of AOSD	✔	case reportのため除外
竹内 俊彦　八千代病院紀要　2000	case report	64歳女性　AOSD	NSAIDsなど	none	disease course of AOSD	✔	case reportのため除外
Pay S. Clin Rheumatol 2006	retrospective, case series	95 patients with AOSD	treatment	none	disease course and outcome		
Masson C. Rev Rheum Engl Ed 1995	prospective	65 patients with AOSD	treatment	none	disease course and outcome		
Pouchot J. Medicine (Baltimore) 1991	retrospective, case series	62+C23 patients with AOSD	treatment	none	disease course and outcome	✔	AOSDの診断がYamaguchi's criteriaではないため（Medsger and Christy criteria）、除外
Wouters JM. Q J Med 1986	retrospective, case series	45 patients with AOSD	treatment	none	disease course and outcome	✔	AOSDの診断がYamaguchi's criteriaではないため（ARA criteria for sJIA）、除外

【4-6　評価シート　観察研究】

診療ガイドライン	ASD CQ14 非ステロイド性抗炎症薬は ASDに対して有用か
対象	ASDの症状、病態
介入	非ステロイド性抗炎症薬
対照	無治療

*バイアスリスク、非直接性
　各ドメインの評価は"高(−2)"、"中/疑い(−1)"、"低(0)"の3段階
　まとめは"高(−2)"、"中(−1)"、"低(0)"の3段階でエビデンス総体に反映させる
** 上昇要因
　各項目の評価は"高(+2)"、"中(+1)"、"低(0)"の3段階
　まとめは"高(+2)"、"中(+1)"、"低(0)"の3段階でエビデンス総体に反映させる
各アウトカムごとに別紙にまとめる

アウトカム	O1：症状の改善

個別研究		バイアスリスク*							上昇要因**				非直接性*					リスク人数（アウトカム率）								
研究コード	研究デザイン	選択バイアス	実行バイアス	検出バイアス	症例現象バイアス	その他		まとめ	量反応関係	効果減弱交絡	効果の大きさ	まとめ	対象	介入	対照	アウトカム	まとめ	対照群分母	対照群分子	(%)	介入群分母	介入群分子	(%)	効果指標(種類)	効果指標(値)	信頼区間
		背景因子の差	ケアの差	不適切なアウトカム測定	不完全なフォローアップ	不十分な交絡の調整	その他のバイアス																			
Reddy Munagala VV. 2012	症例集積	−1	−2	−2	−2	−2	0	−2	0	0	0	0	0	−2	−2	−2	−2	NA	NA	NA	25	0	0	NA	NA	NA
Iliou C. 2013	症例集積	−1	−2	−2	−2	−2	0	−2	0	0	0	0	0	−2	−2	−2	−2	NA	NA	NA	NA	NA	13.6	NA	NA	NA
Zhang XH. 2012	その他	−2	−1	−2	−1	−2	0	−2	0	0	0	0	0	−2	−2	−2	−2	NA	NA	NA	NA	NA	NA	NA	NA	NA
Kim HA. 2012	症例集積	−1	−2	−2	−2	−2	0	−2	0	0	0	0	0	−2	−2	−2	−2	NA	NA	NA	42	0	0	NA	NA	NA
Franchini S. 2010	症例集積	−1	−2	0	0	−1	0	−1	0	0	0	0	0	−1	−2	−1	−1	NA	NA	NA	25	4	16	NA	NA	NA
Singh S. 2008	症例集積	−1	−2	−2	−2	−2	0	−2	0	0	0	0	0	−2	−2	−2	−2	NA	NA	NA	14	0	0	NA	NA	NA
Aarntzen EH. 2005	その他	−2	−1	−2	−1	−2	0	−2	0	0	0	0	0	−1	−2	−2	−2	NA	NA	NA	1	1	100	NA	NA	NA
Pay S. 2006	症例集積	−1	−2	−2	−2	−2	0	−2	0	0	0	0	0	−2	−2	−2	−2	NA	NA	NA	NA	1	NA	NA	NA	NA
Masson C. 1995	症例集積	−1	−2	−2	−2	−2	0	−2	0	0	0	0	0	−2	−2	−2	−2	NA	NA	NA	65	8	12	NA	NA	NA

【4-6 評価シート 観察研究】

診療ガイドライン	ASD CQ14 非ステロイド性抗炎症薬は ASDに対して有用か
対象	ASDの症状、病態
介入	非ステロイド性抗炎症薬
対照	無治療

*バイアスリスク、非直接性
各ドメインの評価は"高(-2)"、"中/疑い(-1)"、"低(0)"の3段階
まとめは"高(-2)"、"中(-1)"、"低(0)"の3段階でエビデンス総体に反映させる
** 上昇要因
各項目の評価は"高(+2)"、"中(+1)"、"低(0)"の3段階
まとめは"高(+2)"、"中(+1)"、"低(0)"の3段階でエビデンス総体に反映させる
各アウトカムごとに別紙にまとめる

アウトカム	O4:薬剤による消化管障害

個別研究		バイアスリスク*							上昇要因**				非直接性*					リスク人数(アウトカム率)								
		選択バイアス	実行バイアス	検出バイアス	症例現象バイアス	その他			量反応関係	効果減弱交絡	効果の大きさ	まとめ	対象	介入	対照	アウトカム	まとめ	対照群分母	対照群分子	(%)	介入群分母	介入群分子	(%)	効果指標(種類)	効果指標(値)	信頼区間
研究コード	研究デザイン	背景因子の差	ケアの差	不適切なアウトカム測定	不完全なフォローアップ	不十分な交絡の調整	その他のバイアス	まとめ																		
Reddy Munagala VV. 2012	症例集積	-1	-2	-2	-2	-2	0	-2	0	0	0	0	0	-2	-2	-2	-2	NA	NA	NA	25	NA	NA	NA	NA	NA
Iliou C. 2013	症例集積	-1	-2	-2	-2	-2	0	-2	0	0	0	0	0	-2	-2	-2	-2	NA	NA	NA	NA	NA	NA	NA	NA	NA
Zhang XH. 2012	その他	-2	-1	-2	-1	-2	0	-2	0	0	0	0	0	-2	-2	-1	-1	NA	NA	NA	1	1	100	NA	NA	NA
Kim HA. 2012	症例集積	-1	-2	-2	-2	-2	0	-2	0	0	0	0	0	-2	-2	-2	-2	NA	NA	NA	42	NA	NA	NA	NA	NA
Franchini S. 2010	症例集積	-1	-2	-2	0	-1	0	-1	0	0	0	0	0	-1	-2	-2	-2	NA	NA	NA	25	NA	NA	NA	NA	NA
Singh S. 2008	症例集積	-1	-2	-2	-2	-2	0	-2	0	0	0	0	0	-2	-2	-2	-2	NA	NA	NA	14	NA	NA	NA	NA	NA
Aarntzen EH. 2005	その他	-2	-1	-2	-1	-2	0	-2	0	0	0	0	0	-1	-2	-2	-2	NA	NA	NA	1	NA	NA	NA	NA	NA
Pay S. 2006	症例集積	-1	-2	-2	-2	-2	0	-2	0	0	0	0	0	-2	-2	-2	-2	NA	NA	NA	NA	NA	NA	NA	NA	NA
Masson C. 1995	症例集積	-1	-2	-2	-2	-2	0	-2	0	0	0	0	0	-2	-2	-2	-2	NA	NA	NA	65	NA	NA	NA	NA	NA

【4-7 評価シート エビデンス総体】

診療ガイドライン	ASD CQ14 非ステロイド性抗炎症薬は ASDに対して有用か
対象	ASDの症状、病態
介入	非ステロイド性抗炎症薬
対照	無治療

エビデンスの強さはRCTは"強(A)"からスタート、観察研究は弱(C)からスタート
* 各ドメインは"高(-2)"、"中/疑い(-1)"、"低(0)"の3段階
** エビデンスの強さは"強(A)"、"中(B)"、"弱(C)"、"非常に弱(D)"の4段階
*** 重要性はアウトカムの重要性(1～9)

エビデンス総体

								リスク人数(アウトカム率)											
アウトカム	研究デザイン/研究数	バイアスリスク*	非一貫性*	不精確*	非直接性*	その他(出版バイアスなど)**	上昇要因(観察研究)**	対照群分母	対照群分子	(%)	介入群分母	介入群分子	(%)	効果指標(種類)	効果指標統合値	信頼区間	エビデンスの強さ**	重要性***	コメント
症状の改善	症例集積7/症例報告2	-2	-1	-2	-1	-1	0	NA	NA	NA	NA	NA	NA	NA	NA	NA	非常に弱(D)	5	NSAIDsによる症状改善効果をプラセボと比較した研究結果は無いが、無効である可能性が高い
病態の改善	症例集積7/症例報告2	-2	-1	-2	-1	-1	0	NA	NA	NA	NA	NA	NA	NA	NA	NA	非常に弱(D)	4	NSAIDsによる病態改善効果をプラセボと比較した研究結果は無いが、無効である可能性が高い
再発抑制	症例集積7/症例報告2	-2	-2	-2	-2	-1	0	NA	NA	NA	NA	NA	NA	NA	NA	NA	非常に弱(D)	4	NSAIDsによる再発抑制効果は不明
薬剤による消化管障害	症例集積7/症例報告2	-2	-2	-2	-2	-1	0	NA	NA	NA	NA	NA	NA	NA	NA	NA	非常に弱(D)	4	1つの症例報告でNSAIDs治療後に胃潰瘍を合併したとの報告があるのみ
薬剤による腎障害	症例集積7/症例報告2	-2	-2	-2	-2	-1	0	NA	NA	NA	NA	NA	NA	NA	NA	NA	非常に弱(D)	4	NSAIDsもよる腎障害は不明
薬剤アレルギー	症例集積7/症例報告2	-2	-2	-2	-2	-1	0	NA	NA	NA	NA	NA	NA	NA	NA	NA	非常に弱(D)	6	1つの症例報告でNSAIDs治療後に薬剤過敏による兼官性浮腫を合併したとの報告があるのみ

【4-8 定性的システマティックレビュー】

CQ	14
P	ASDの発熱、関節症状、全身炎症、臓器障害
I	非ステロイド性抗炎症薬
C	無治療
臨床的文脈	ASDの治療

O1	症状の改善
非直接性のまとめ	1つの症例集積研究では非直接性は中等度であり、その他の研究では高度であった。
バイアスリスクのまとめ	1つの症例集積研究ではバイアスリスクは中等度であり、その他の研究では高度であった。
非一貫性その他のまとめ	7つの症例集積研で非一貫性は中等度であった。
コメント	NSAIDsによる症状改善効果をプラセボと比較した研究結果は無いが、症例集積研究の結果からは無効である可能性が高い

O2	病態の改善
非直接性のまとめ	1つの症例集積研究では非直接性は中等度であり、その他の研究では高度であった。
バイアスリスクのまとめ	1つの症例集積研究ではバイアスリスクは中等度であり、その他の研究では高度であった。
非一貫性その他のまとめ	7つの症例集積研で非一貫性は中等度であった。
コメント	NSAIDsによる病態改善効果をプラセボと比較した研究結果は無いが、症例集積研究の結果からは無効である可能性が高い

O3	再発抑制
非直接性のまとめ	全ての研究で非直接性は高度であった。
バイアスリスクのまとめ	全ての研究でバイアスリスクは高度であった。
非一貫性その他のまとめ	全ての研究で非一貫性は高度であった。
コメント	NSAIDsによる再発抑制効果は不明である

【4-8 定性的システマティックレビュー】

CQ	14
P	ASDの発熱、関節症状、全身炎症、臓器障害
I	非ステロイド性抗炎症薬
C	無治療
臨床的文脈	ASDの治療

O4	薬剤による消化管障害
非直接性のまとめ	全ての研究で非直接性は高度であった。
バイアスリスクのまとめ	全ての研究でバイアスリスクは高度であった。
非一貫性その他のまとめ	全ての研究で非一貫性は高度であった。
コメント	1つの症例報告でNSAIDs治療後に胃潰瘍を合併したとの報告があるのみであり、因果関係は不明である

O5	薬剤による腎障害
非直接性のまとめ	全ての研究で非直接性は高度であった。
バイアスリスクのまとめ	全ての研究でバイアスリスクは高度であった。
非一貫性その他のまとめ	全ての研究で非一貫性は高度であった。
コメント	NSAIDsによる腎障害に関しては不明である

O6	薬剤アレルギー
非直接性のまとめ	全ての研究で非直接性は高度であった。
バイアスリスクのまとめ	全ての研究でバイアスリスクは高度であった。
非一貫性その他のまとめ	全ての研究で非一貫性は高度であった。
コメント	1つの症例報告でNSAIDs治療後に薬剤アレルギーによる血管性浮腫を合併したとの報告があるのみであり、因果関係は不明である

【4-10　SRレポートのまとめ】

7本の症例集積研究、2本の症例報告を対象にSRを実施した。
7本の症例集積研究において、ASDに対するNSAIDsの有効性は0-13.6%と報告されており、無治療群と比較した研究結果は無いが、ASDの症状、病態に対してNSAIDsの有効性は低いことが示唆された(エビデンスの強さ:D)。
本SRにおいては、NSAIDsによるASDの再発抑制効果は明らかにならなかった。
NSAIDsによる消化管障害、腎障害、薬剤アレルギーについて、無治療と比較した研究結果はないが、消化管障害、薬剤アレルギーに関する症例報告が認められた。
以上の結果、エビデンスは弱いが、NSAIDsはASDの症状、病態の改善効果は低いことが示唆された。

IV　研究成果の刊行に関する一覧表

雑誌

発表者氏名	論文タイトル名	発表誌名	巻号	ページ	出版年
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V　研究成果刊行物・別刷

EXTENDED REPORT

Defining disease activity states and clinically meaningful improvement in primary Sjögren's syndrome with EULAR primary Sjögren's syndrome disease activity (ESSDAI) and patient-reported indexes (ESSPRI)

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ABSTRACT

Objectives To define disease activity levels, minimal clinically important improvement (MCII) and patient-acceptable symptom state (PASS) with the primary Sjögren's syndrome (SS) disease activity indexes: European League Against Rheumatism (EULAR) SS disease activity index (ESSDAI) and EULAR SS patient-reported index (ESSPRI).

Methods For 790 patients from two large prospective cohorts, ESSDAI, physician evaluation of disease activity, ESSPRI and patients' satisfaction with their current health status were recorded. Receiver operating characteristic curve analyses and anchoring methods were used to estimate disease activity levels of ESSDAI and the PASS of ESSPRI. At follow-up visit, patients and physicians assessed, respectively, whether symptoms and disease activity have improved or not. An anchoring method based on this evaluation was used to estimate MCII of ESSDAI and ESSPRI.

Results Low-activity (ESSDAI<5), moderate-activity (5≤ESSDAI≤13) and high-activity (ESSDAI≥14) levels were defined. MCII of ESSDAI was defined as an improvement of at least three points. The PASS estimate was defined as an ESSPRI<5 points and MCII as a decrease of at least one point or 15%.

Conclusions This study determined disease activity levels, PASS and MCII of ESSDAI and ESSPRI. These results will help designing future clinical trials in SS. For evaluating systemic complications, the proposal is to include patients with moderate activity (ESSDAI≥5) and define response to treatment as an improvement of ESSDAI at least three points. For addressing patient-reported outcomes, inclusion of patients with unsatisfactory symptom state (ESSPRI≥5) and defining response as an improvement of ESSPRI at least one point or 15% seems reasonable.

Primary Sjögren's syndrome (SS) is a systemic disorder primarily characterised by lymphocytic infiltration of exocrine glands, resulting in functional impairment of salivary and lachrymal glands. The inflammatory process however extends beyond the exocrine glands and can potentially affect any organ.

As a result, clinical features can be divided into two facets for which two disease activity indexes have been recently developed by the European League Against Rheumatism (EULAR) SS task force: the EULAR SS disease activity index (ESSDAI)[1] for systemic features and the EULAR SS patient-reported index (ESSPRI)[2] for patients' symptoms. These indexes have been developed to be used as outcome measures in clinical trials and improve clinical research in the field of primary SS. Both indexes have been validated. They have been shown to be valid, reliable and sensitive to change.[3 4] Sensitivity to change was, however, better for ESSDAI than ESSPRI.

This study aimed at defining disease activity levels of ESSDAI, patient-acceptable symptom state (PASS) with ESSPRI and minimal clinically important improvement (MCII) of these two disease activity indexes. The objective was also to help determine the most effective way of conducting clinical trials for evaluation of new treatments in primary SS and to suggest thresholds to be used as entry criteria and response criteria.

PATIENTS AND METHODS

PATIENTS

EULAR cohort

Between 2009 and 2011, 395 patients with primary SS, according to the American-European

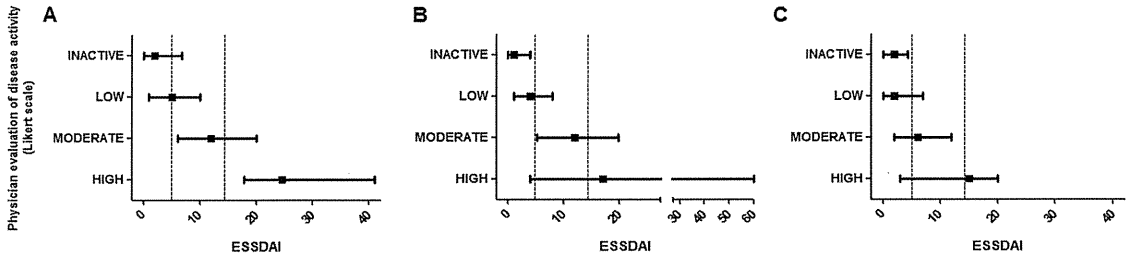

Figure 1 Distribution of European League Against Rheumatism Sjögren's syndrome disease activity index (ESSDAI) score according to disease activity levels. In patients from European League Against Rheumatism (EULAR) cohort at inclusion (A), at 6 months (B) and in the Assessment of Systemic Signs and Evolution of SS (ASSESS) cohort (C). Vertical dot lines represents disease activity thresholds of moderate activity (ESSDAI=5) and high activity (ESSDAI=14). ESSDAI score distribution is represented with mean value (square) and IQR, in each subgroups of activity as assessed by the physicians.

Consensus Group (AECG) criteria,[5] from 14 countries were prospectively included by 30 experienced investigators participating in this international EULAR collaborative project (project code CLI 010). This 6-month study aimed to validate ESSDAIs.[3] Investigators were asked to include approximately half of patients with systemic features, and therapeutic management was left to their discretion. This study was conducted with the approval of the institutional review board of GHU Paris Nord (n°IRB0006477). In each country, local ethical requirements have been observed.

ASSESS cohort

Between 2009 and 2011, 395 patients with primary SS according to AECG were included from 15 centres of Rheumatology and Internal Medicine in France in the 'Assessment of Systemic Signs and Evolution of SS' (ASSESS) 5-year prospective observational cohort that aim to identify predictive factors of systemic complications.[6 7] Therapeutic management was left to the discretion of treating physician. Data from baseline and the first year were analysed in the present study. Both cohorts included the same number of patients by chance.

MEASUREMENT

All specific questions are provided in online supplementary file 1.

Disease activity indexes

Status measures

At enrolment, physicians assessed systemic disease activity of each patient with a 4-point Likert scale (inactive, low, moderate or high) and a 0–10 numerical scale. They also completed ESSDAI. ESSDAI theoretically ranges from 0 to 123 but observed values rarely exceed 40. To remind them to distinguish between activity and patients symptoms, they were asked also to separately assess patients' symptoms with a 0–10 numerical scale. They also determined whether their patients were in minimal disease activity (MDA) state. A definition of MDA was provided, according to that used for rheumatoid arthritis.[8 9] In the EULAR cohort, all these scales were reassessed at 6 months.

Measures of change

At follow-up visit, physicians evaluated the change in disease activity according to a five-point Likert scale (much worse, worse, the same, better and much better).

Patient-centred measures

Status measures

At enrolment and at follow-up visit, all patients completed ESSPRI. ESSPRI ranges from 0 to 10. At the 6-month visit in the EULAR cohort, the patient's acceptability/satisfaction of its current state (taking account of his symptoms: dryness, fatigue and pain) was also recorded.

Measures of change

In the EULAR cohort at the follow-up visit, patients evaluated the change in their state according to a five-point Likert scale (very importantly improved, importantly improved, slightly improved, no change, worsened). To detect improvement, patients also assessed whether their current health status has importantly improved with a binary question.

STATISTICAL ANALYSES

Quantitative data are presented as mean±SD or median with IQRs. The 95% CIs for quantiles (median, upper quartile) were calculated based on a method that is distribution-free that uses order statistics (ranks) to compute the confidence limits as described by Hahn and Meeker.[10]

The following analyses aimed at defining disease activity levels of ESSDAI, PASS of ESSPRI and MCII of ESSDAI and ESSPRI. Analyses were performed in the two cohorts. If the results were reasonably similar, the estimates were integrated to obtain the final criteria. These final criteria were then tested for different aspects of external validity on data of all clinical trials[11–16] where ESSDAI and/or ESSPRI have been measured, whatever their positive and negative results. The aim was to assess their ability to discriminate between placebo and treated arms.

Definition of disease activity levels with ESSDAI

This step involved two distinct statistical methods.

Receiver operating characteristic curve analysis

Physicians' evaluation of disease activity was used as an external standard to determine the activity levels. For each cut-off, we computed a separate receiver operating characteristic (ROC) curve and calculated its sensitivity and specificity. For determining the cut-off of low-disease activity, we looked for the ESSDAI score that better discriminated between patients with inactive or low activity versus those with moderate or high activity. For the cut-off of high-disease activity, we looked for the ESSDAI score that better discriminated between patients with high activity compared with all other patients. For each cut-off, we selected the ESSDAI score having the maximal Youden index.[17]

Anchoring method according to MDA status

Two groups of patients were considered: those in MDA (MDA group), and those not (non-MDA group). For each group, we then identified the 75th centile of the ESSDAI values. This upper quartile determined the threshold between low and

moderate activity in the MDA group and the threshold between moderate and high activity in the non-MDA group.[18]

External validation

The threshold of moderate activity was foreseen to be used as an entry criterion in randomised control trials (RCTs) evaluating immunosuppressants or biologics. We then estimated, from these two cohorts[3 6] and from clinical trials,[11–16] the number of patients that would have been eligible according to the obtained thresholds. We retained the one sufficiently discriminating to select patients with active disease, but not too restrictive, so as not to limit recruitment for RCTs.

Determination of minimal clinically important improvement (MCII) with ESSDAI

MCII was estimated using an anchoring method based on the physician's assessment of evaluation of change in disease activity. MCII was estimated in the population of patients considered as 'better'. MCII was computed both as absolute and relative change of ESSDAI. MCII estimates were defined as the median value of the change in ESSDAI score in the population judged as improved.[19 20] To assess whether MCII estimates were above measurement error, we also calculated the minimal detectable change (MDC) with 95% confidence level using the following formula ($MDC=1.96*\sqrt{2}*SEM$). MDC provides another threshold that helps interpretation, that is, when a score change exceeds this level, there is reasonable certainty that it is true signal, and not just noise or error.[21]

External validation

In an RCT, MCII may be used as response criteria. We examined, using the different MCII estimates, what would have been the response rates in the placebo and active treatment arms of clinical trial.[11–16] Among them, we retained the minimal threshold having the best ability to discriminate between placebo and treated arms.

Definition of PASS with ESSPRI

PASS is defined as the value beyond which patients consider themselves well. The concept of PASS for patients' measures of symptoms is similar to the concept of low-disease activity for systemic disease activity measures.[22–24] However, they did not necessarily overlap, particularly in pSS where patients' symptoms and disease activity did not correlate.[7]

This step comprised also two distinct methods, performed in the two cohorts.

ROC curve analysis

ROC curves were computed for various cut-offs of ESSPRI score to calculate the sensitivity and specificity. To determine PASS, we looked for the ESSPRI score that better discriminated between patients who considered themselves in a satisfactory state and those not. We selected the optimal cut-off of ESSPRI as the one having the maximal Youden index.[17]

Anchoring method

Two groups of patients were determined: those considering their current health status as satisfactory (PASS group) and those not (non-PASS group). PASS was defined as the 75th centile of ESSPRI distribution in the PASS group.[23]

Final criteria and external validation

PASS threshold of ESSPRI might be used as entry criteria in RCTs evaluating symptomatic treatments. We estimated, from these two cohorts[3 6] and recent trials,[11–16 25] the number of patients that would have been eligible using the estimated cut-offs. We retained the one that correctly classified the highest number of patients.

Determination of MCII with ESSPRI

To estimate MCII, an anchoring method based on the patient's assessment of evaluation of change in symptom state was used. MCII was estimated by focusing on the population of patients who were considered as being 'importantly and slightly improved'. MCII was computed both as absolute and relative change of ESSPRI. MCIIs estimates were defined as the median value of the change (absolute or relative) in ESSPRI score in this target population. We performed the same analyses in the patients that answered to the binary question that they considered their current health status as importantly improved.

External validation

To assess the relevance of the obtained MCII estimates as response criteria and to assess whether a rounded value performed the same as a precise estimate, we examined for each threshold what would have been the response rates in placebo and treated arms of previous trials.[11–16] We finally retained the MCII thresholds based on their ability to discriminate between placebo and treated arms and its ease of use.

All statistical analyses involved the use of SAS release V.9.3 (SAS Institute, Cary, North Carolina, USA) and R release V.2.2.7 (The R Foundation for Statistical Computing, Vienna, Austria) statistical software packages.

RESULTS

Patients' characteristics

The EULAR cohort (table 1) included 395 patients with a median ESSDAI score of 6 (IQR=2–12) and a median ESSPRI score of 6 (IQR=4.3–7.3). A total of 350 patients (88.6%) have been followed until the 6-month visit. The ASSESS cohort (table 1) included 395 patients with a median ESSDAI score of 2 (IQR=0–7) and a median ESSPRI score of 5.7 (IQR=4.0–7.0), of whom 371 (93.9%) have been followed until the 1-year visit.

Definition of disease activity levels with ESSDAI

Using both anchoring method and ROC curve analysis, in the ASSESS cohort and at the 6-month visit in the EULAR cohort, the estimates of low-disease activity were similar (ESSDAI<5) (table 2). However, this threshold was higher at the baseline visit of the EULAR cohort due to the inclusion of patients with more active disease. The threshold of 5 was therefore retained. Except for the JOQUER trial and for the ASSESS cohort that included principally patients with low-disease activity, we estimated that 60.0–93.3% of the patients from all recent trials and from the EULAR cohort had an ESSDAI score ≥5 at inclusion (table 3).

The estimates of high-disease activity were similar (ESSDAI≥14) in both cohorts and at each visit, whatever the method used. According to this threshold, a high disease activity was found in 23.9% (92/385) and 10.2% (39/383) of the patients of the EULAR and ASSESS[6] cohorts, respectively, and 35/122 (28.7%), none, 10/119 (8.4%), 4/30 (13.3%) and 5/15 (33.3%) of the patients from TEARS,[12] rituximab trial from the Netherlands,[14] JOQUER,[13] BELISS[16] and ASAP trials,[15] respectively.

Thus low-activity, moderate-activity and high-activity levels were defined by an ESSDAI<5, between 5 and 13 and ≥14, respectively (figure 1).

Table 1 Characteristics of primary Sjögren's syndrome patients

	EULAR cohort (N=395)	ASSESS cohort (N=395)
Age (years)	57.5 [46–66]	58 [51–67]
Sex (female)	378 (95.7%)	370 (93.6%)
Disease duration (years)	6 [2–12]	5 [2–9]
Decrease in salivary flow	286 (72.6%)	162/327 (47.9%)
Positive salivary gland biopsy (focus score ≥1)	250/259 (96.5%)	318/352 (87.8%)
Autoantibodies		
Anti-SSA	313 (79.4%)	234 (59.2%)
Anti-SSB	202 (51.3%)	132 (33.5%)
Current or previous systemic involvement	251 (63.7%)	135 (65.0%)
Current systemic involvement	145 (36.8%)	122 (30.9%)
Present salivary gland swelling	87 (22.9%)	45 (11.4%)
Current treatment		
Corticosteroids	96 (24.3%)	94 (23.7%)
Hydroxychloroquine	115 (29.1%)	121 (23.7%)
Azathioprine	13 (3.3%)	6 (1.5%)
Methotrexate	16 (4.1%)	20 (5.1%)
Rituximab	12 (3.0%)	4 (1.0%)
Disease activity indexes		
ESSDAI	6 [2–12]	2 [0–7]
ESSPRI	6 [4.3–7.3]	5.7 [4–7]

Results are expressed as median [IQR] and mean±SD or number (%).
ASSESS, Assessment of Systemic Signs and Evolution of SS; EULAR, European League Against Rheumatism; ESSDAI, EULAR Sjögren's syndrome disease activity index; ESSPRI, EULAR Sjögren's syndrome patient-reported index.

Determination of MCII in disease activity with ESSDAI

In each cohort, MCII estimates were obtained for the whole cohort and in the population of patients having at least moderate activity at inclusion (table 5). From these results, three thresholds were considered: improvement of two, three or four points of ESSDAI. Since relative estimates were not concordant between the two cohorts, only absolute changes were retained. For each threshold, we estimated from data from recent trials the response rate in the placebo and treated arms (table 4). MDC was 4.4 and 2.7 in the EULAR and ASSESS cohorts, respectively. These thresholds were just below those of MCII estimates in each cohort. We finally retained an improvement of at least three points of ESSDAI as MCII since this threshold was the one that better discriminated between placebo and treated arms.

Definition of PASS with ESSPRI

The PASS estimates (table 2) were similar across cohorts whatever the method used. The two estimates of 5 and 6 were tested to assess how they discriminated between PASS and non-PASS groups. The threshold of 5 was the one that classified the higher number of patients (see online supplementary table S1). Even less specific, this threshold was more sensitive and less restrictive for inclusion of patients in clinical trial. This threshold was particularly sensitive to identify patients from the non-PASS group and identify 76.1–81.8% of these patients. Thus PASS was defined as an ESSPRI<5.

Determination of MCII in patients' symptoms with ESSPRI

MCII estimates were obtained from the EULAR cohort: in the whole cohort and in the population of patients having ESSPRI≥5 at baseline (table 4). In these two populations, MCII estimates were, respectively, 0.67 and 1 point, whatever the question and answer modality used; and relative MCII estimates were 10% and 15% of the baseline value, respectively. Both estimates differentiated similarly between placebo and active treatment arms. We finally retained an improvement of ESPPRI of at least one point for its ease of use, and the corresponding relative estimate of decrease of at least 15% of the baseline value as MCII (table 5).

Table 2 Tentative cut-off of disease activity levels with ESSDAI and PASS with ESSPRI

	EULAR cohort		ASSESS cohort
	At baseline	At 6 months	
ESSDAI cut-off			
Low vs moderate			
ROC curve analysis	9	5	5
AUC	0.826	0.809	0.709
Sensitivity/specificity	78.6%%/69.7%	70.3%/76.6%	72.3%/58.3%
Anchoring method			
75th centile of the distribution in MDA group	9 [7 to 11]	6 [5 to 8]	6 [5 to 8]
Moderate vs high			
ROC curve	14	15	14
AUC	0.951	0.866	0.823
Sensitivity/specificity	85.0%/100%	89.3%/75.0%	93.3%/66.7%
In non-MDA group			
75th centile of the distribution	17 [15 to 20]	16 [12 to 19]	12.5 [10 to 15]
ESSPRI: PASS estimating method			
Anchoring method			
75th centile of the distribution in the PASS group	6.33 [5.67 to 6.67]		6 [5.67 to 7.00]
ROC curve analysis	6.33		5.33
AUC	AUC=0.750		AUC=0.704
Sensitivity/specificity	71.5%/66.3%		64.7%/66.7%

ASSESS, Assessment of Systemic Signs and Evolution of SS; AUC, area under the curve; EULAR, European League Against Rheumatism; ESSDAI, EULAR Sjögren's syndrome disease activity index; ESSPRI, EULAR Sjögren's syndrome patient-reported index; MDA, minimal disease activity; PASS, patient-acceptable symptom state; ROC, receiver operating characteristic.