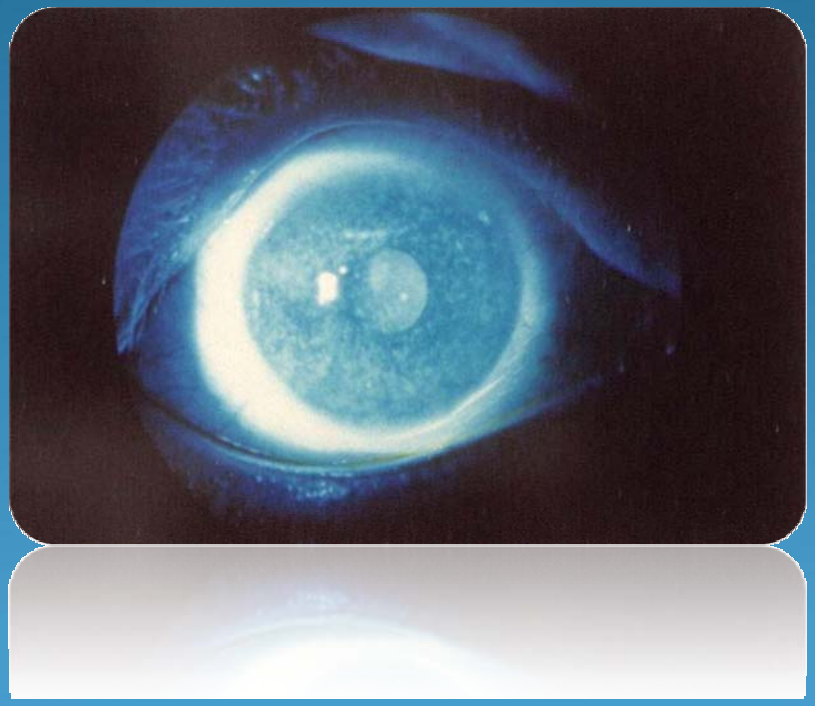
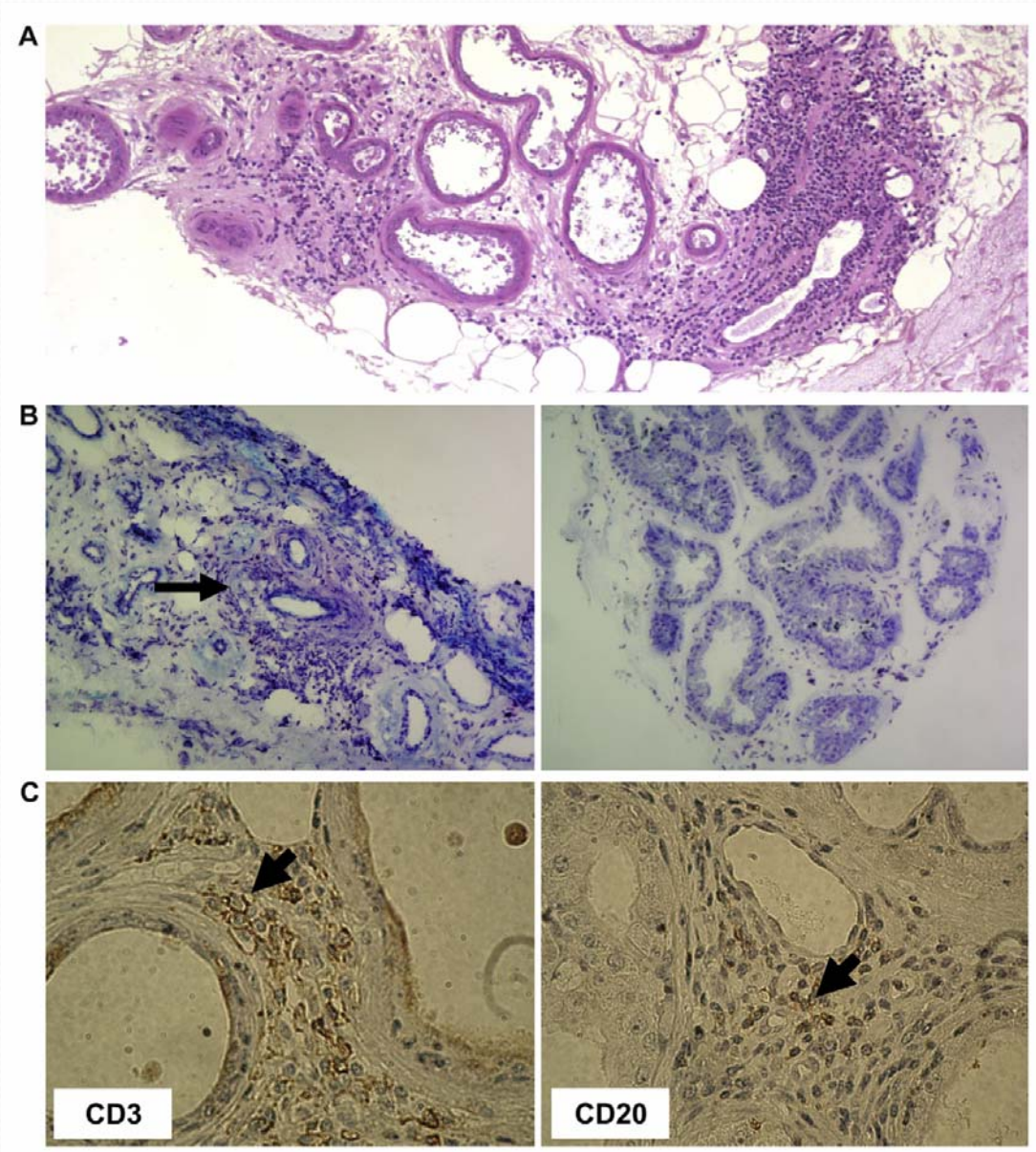
Síndrome de Sjögren



TOP FIVE ARTICLES 2010

Fig. 1. Pathological changes in the cutaneous tissue of patients with primary Sjögren's syndrome (SS). A. Epidermis infiltrated with mononuclear cells (MNCs) stained with hematoxylin-and-eosin. B. Toluidine blue-staining reveals MNCs (arrow) in the sweat glands of the skin biopsy of a patient with primary SS on the left, but not in those of the skin biopsy from a healthy volunteer on the right (x10). C. Immunohistochemical analysis of a skin specimen from an individual suspected of primary SS shows CD3-positive T lymphocytes on the left, and CD20-positive B lymphocytes on the right (x40).



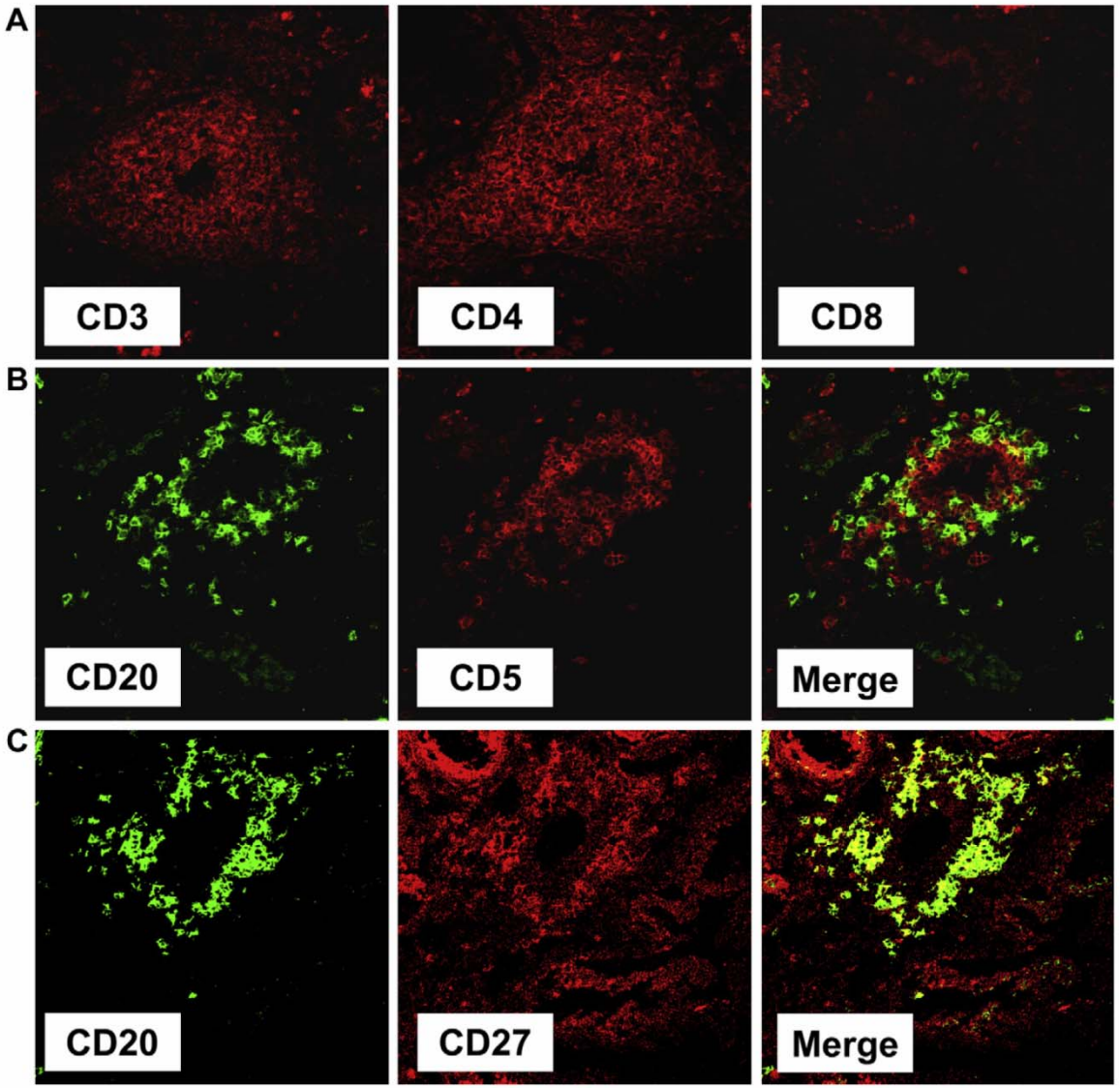
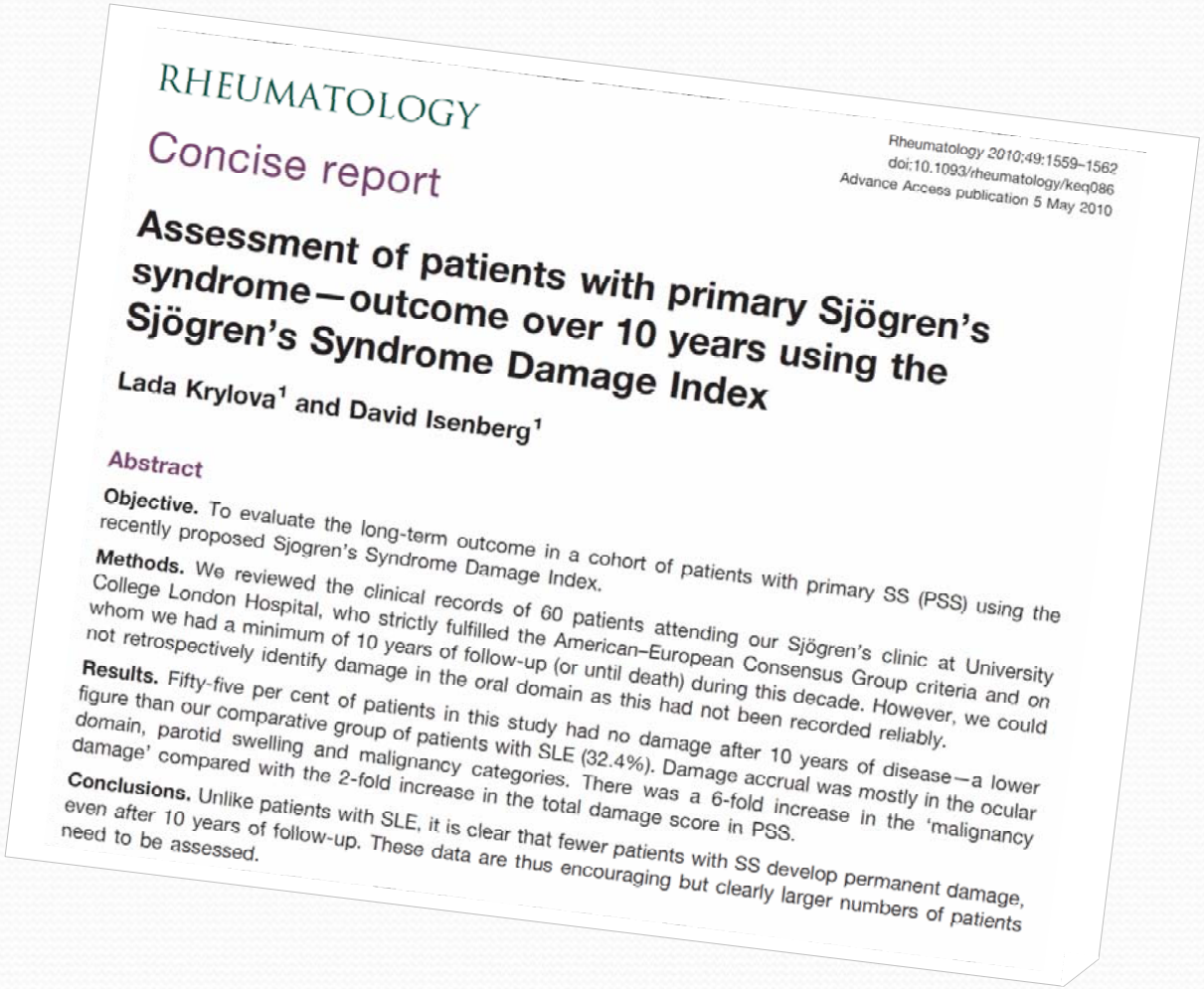


Fig. 2. Phenotype analysis of cutaneous B lymphocytes from patients with primary Sjögren's syndrome. B cells, as defined by the expression of CD20 (left panels) stained green with fluorescein isothiocyanate-conjugated anti-CD20 antibody (Ab). The overlay of this green with tetramethyl rhodamine isothiocyanate-generated red-stain anti-CD5, anti-CD27, anti-IgD and anti-CD24 Abs (is seen yellow). A. B lymphocytes, defined as CD20-positive (left panel), are negative for CD5 (middle panel), as confirmed by the absence of overlay in the left panel (one green arrow points to B cells, and another red to CD5). B. These CD20-positive B cells are positive for CD27. The overlay is seen yellow (arrowed in yellow in the right panel). C- The B cells are negative for IgD. D- Some of them are positive for CD24.



RHEUMATOLOGY

Concise report

Rheumatology 2010;49:1559–1562
doi:10.1093/rheumatology/keq086
Advance Access publication 5 May 2010

Assessment of patients with primary Sjögren's syndrome—outcome over 10 years using the Sjögren's Syndrome Damage Index

Lada Krylova[1] and David Isenberg[1]

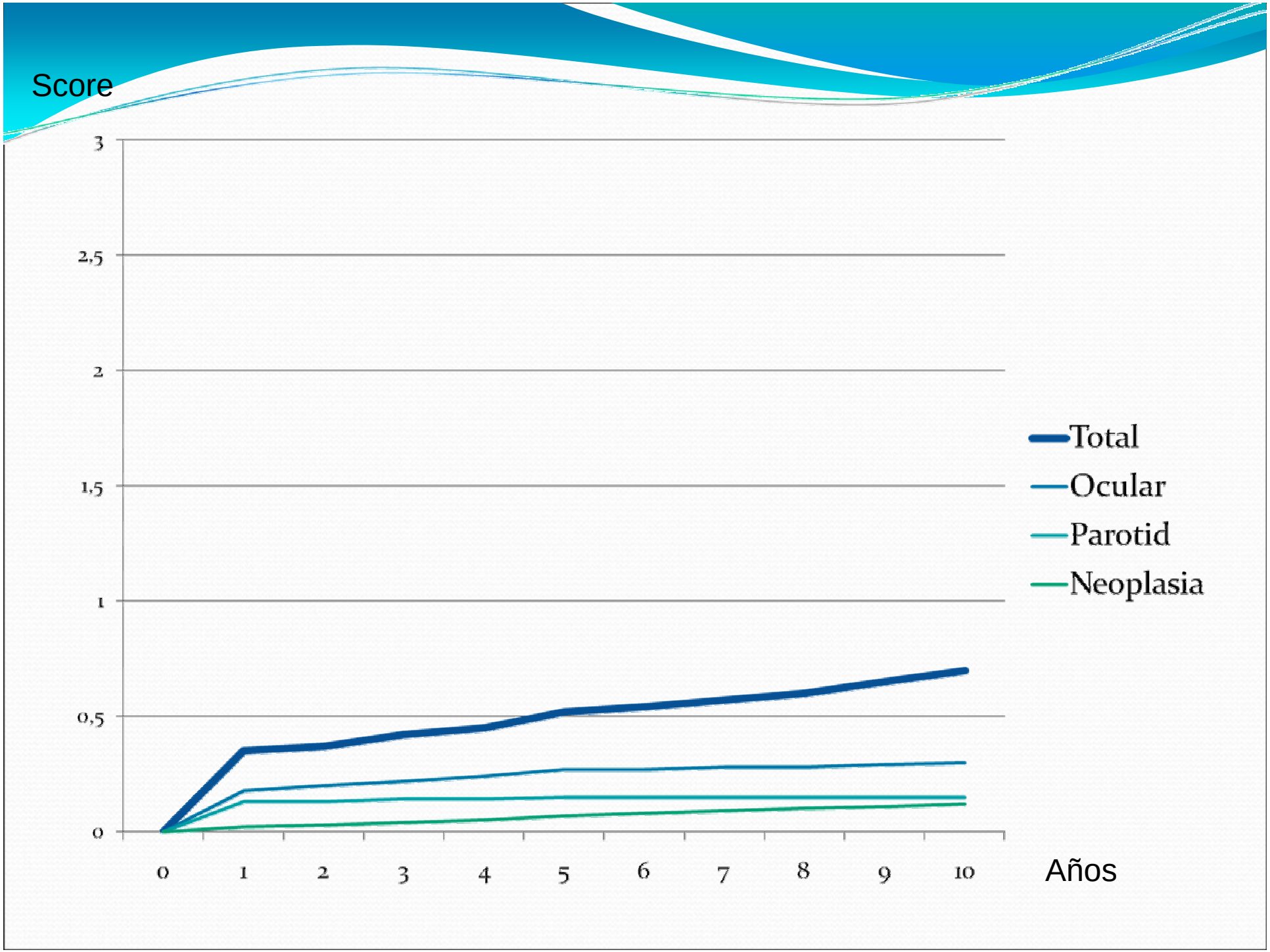
Abstract

Objective. To evaluate the long-term outcome in a cohort of patients with primary SS (PSS) using the recently proposed Sjogren's Syndrome Damage Index.

Methods. We reviewed the clinical records of 60 patients attending our Sjögren's clinic at University College London Hospital, who strictly fulfilled the American–European Consensus Group criteria and on whom we had a minimum of 10 years of follow-up (or until death) during this decade. However, we could not retrospectively identify damage in the oral domain as this had not been recorded reliably.

Results. Fifty-five per cent of patients in this study had no damage after 10 years of disease—a lower figure than our comparative group of patients with SLE (32.4%). Damage accrual was mostly in the ocular domain, parotid swelling and malignancy categories. There was a 6-fold increase in the 'malignancy damage' compared with the 2-fold increase in the total damage score in PSS.

Conclusions. Unlike patients with SLE, it is clear that fewer patients with SS develop permanent damage, even after 10 years of follow-up. These data are thus encouraging but clearly larger numbers of patients need to be assessed.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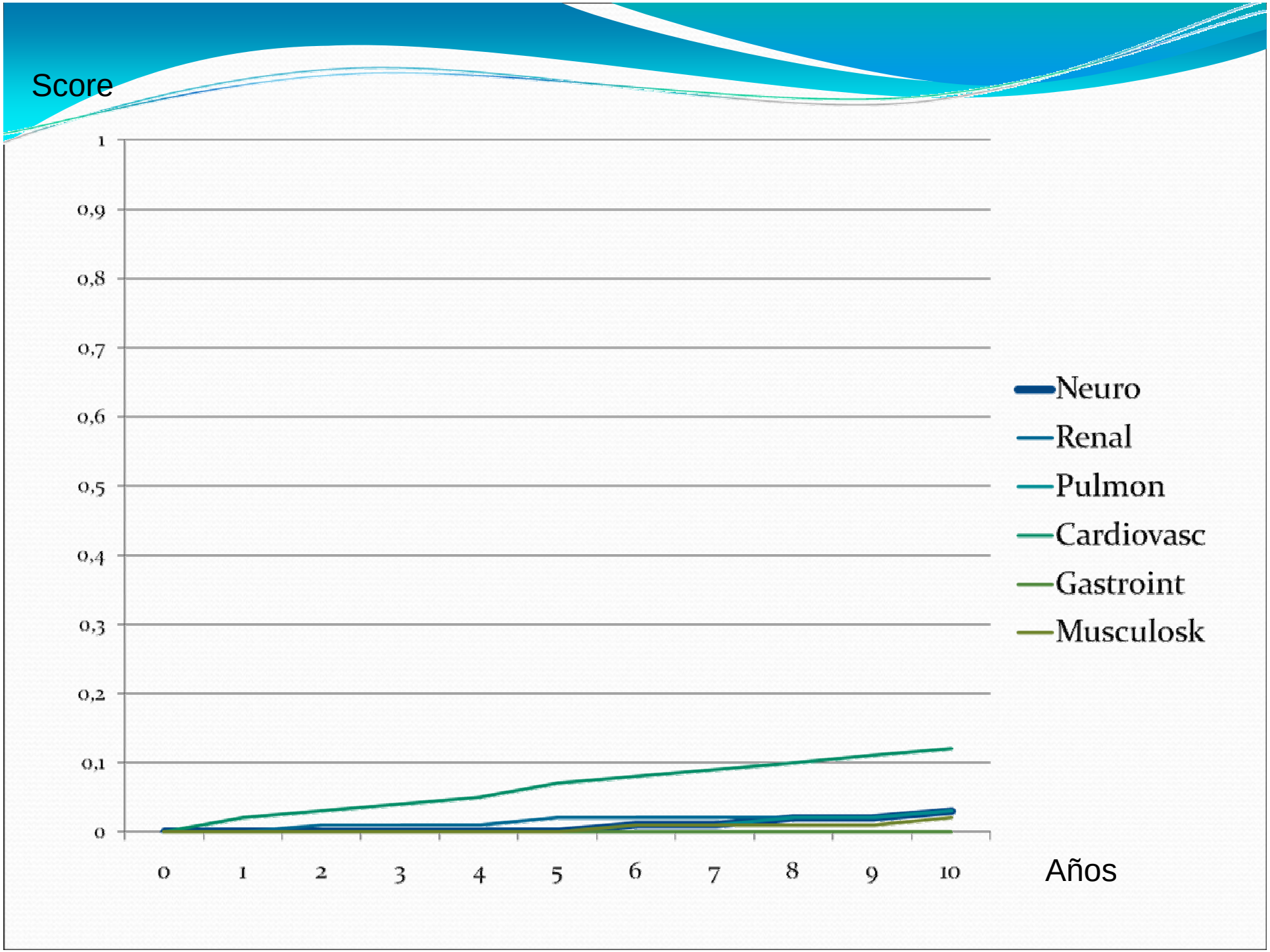
Total
Ocular
Parotid
Neoplasia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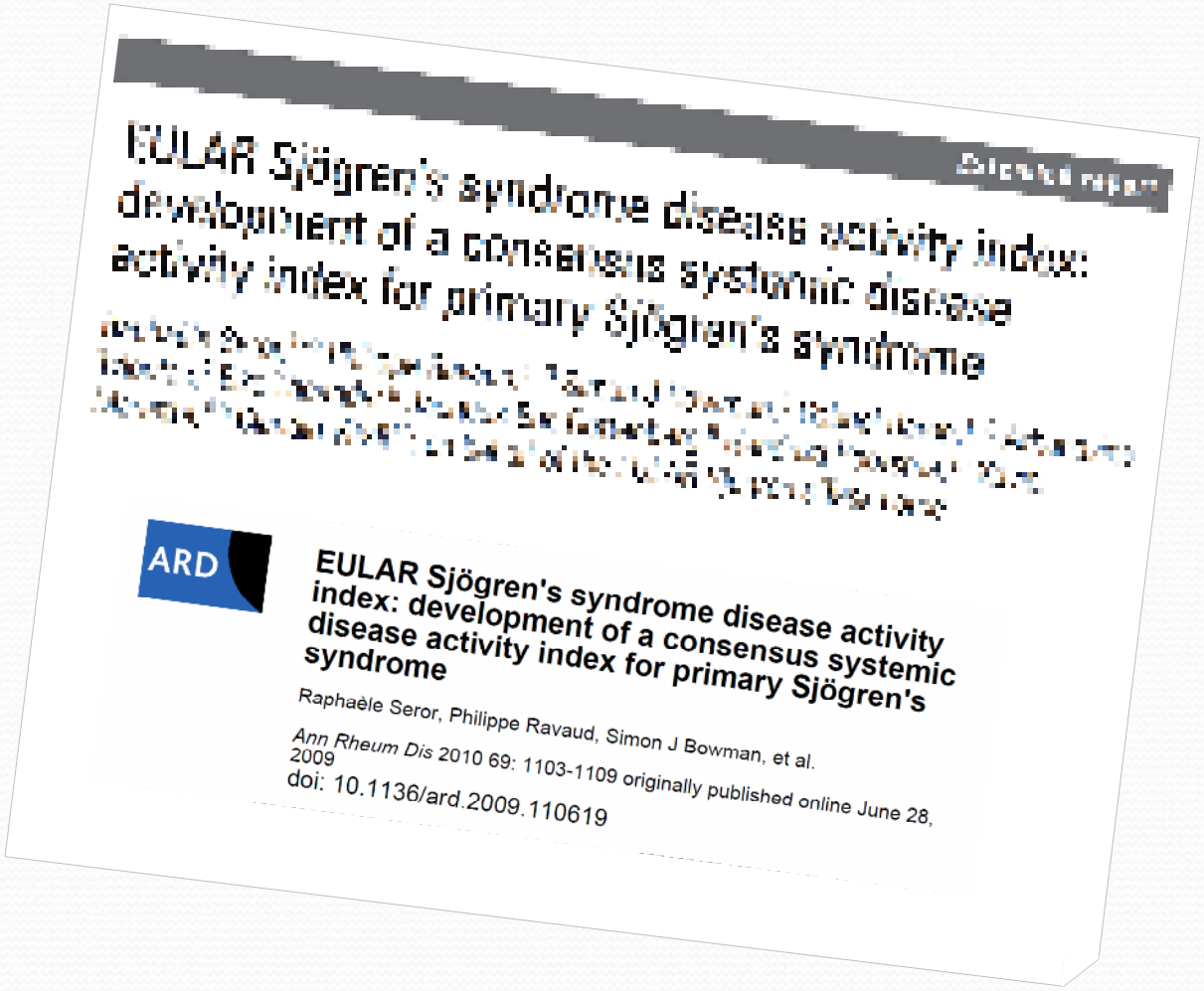

EULAR Sjögren's syndrome disease activity index: development of a consensus systemic disease activity index for primary Sjögren's syndrome

Raphaèle Seror, Philippe Ravaud, Simon J Bowman, et al.

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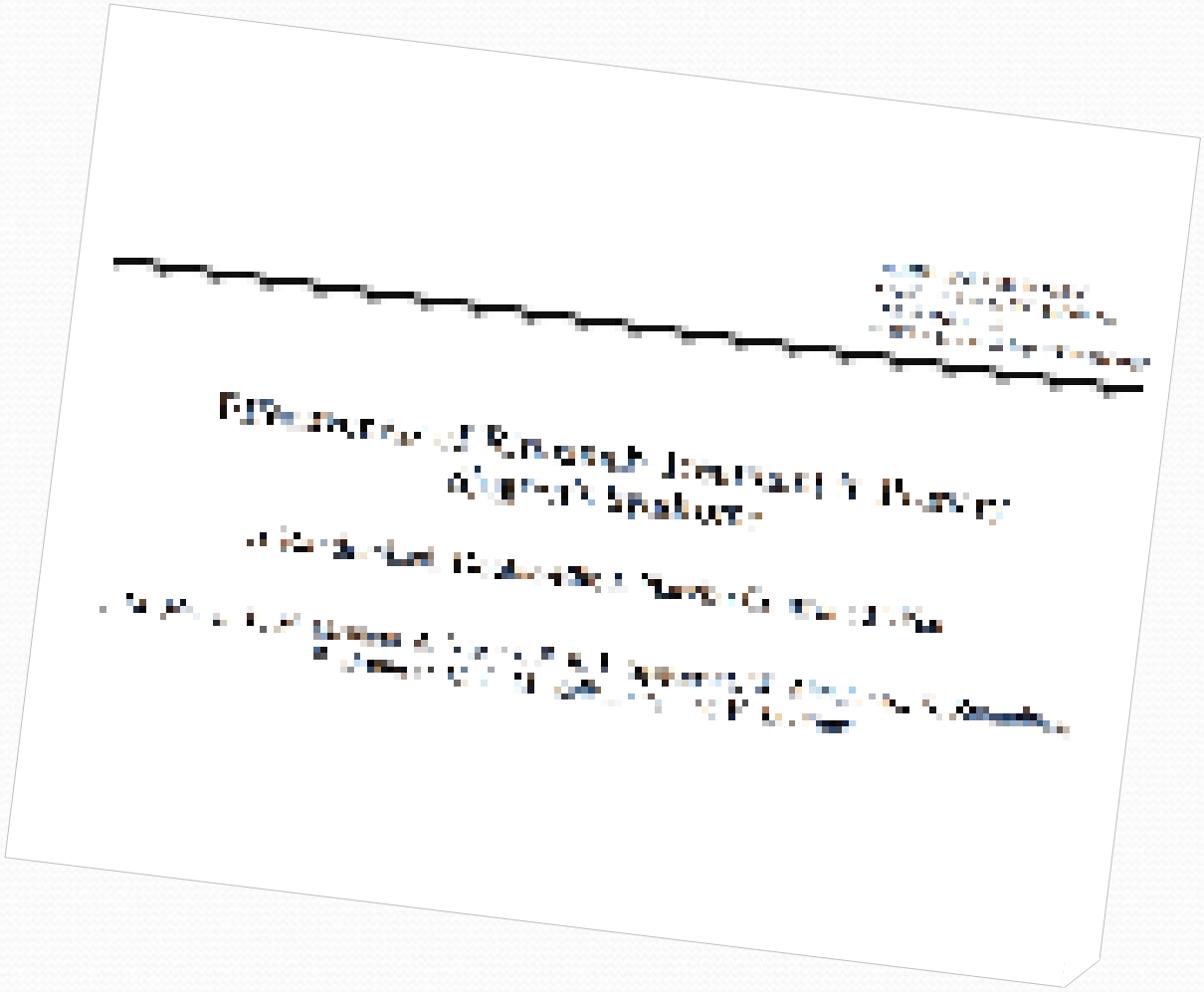
Table 3 The EULAR Sjögren's syndrome disease activity index (ESSDAI): domain and item definitions and weights

Domain [weight]	Activity level	Description
Constitutional [3] Exclusion of fever of infectious origin and voluntary weight loss	No = 0	Absence of the following symptoms
	Low = 1	Mild or intermittent fever (37.5–38.5°C)/night sweats and/or involuntary weight loss of 5–10% of body weight
	Moderate = 2	Severe fever (>38.5°C)/night sweats and/or involuntary weight loss of >10% of body weight
Lymphadenopathy [4] Exclusion of infection	No = 0	Absence of the following features
	Low = 1	Lymphadenopathy ≥1 cm in any nodal region or ≥2 cm in inguinal region
	Moderate = 2	Lymphadenopathy ≥2 cm in any nodal region or ≥3 cm in inguinal region, and/or splenomegaly (clinically palpable or assessed by imaging)
	High = 3	Current malignant B-cell proliferative disorder
Glandular [2] Exclusion of stone or infection	No = 0	Absence of glandular swelling
	Low =1	Small glandular swelling with enlarged parotid (≤3 cm), or limited submandibular or lachrymal swelling
	Moderate = 2	Major glandular swelling with enlarged parotid (>3 cm), or important submandibular or lachrymal swelling
Articular [2] Exclusion of osteoarthritis	No = 0	Absence of currently active articular involvement
	Low = 1	Arthralgias in hands, wrists, ankles and feet accompanied by morning stiffness (>30 min)
	Moderate = 2	1–5 (of 28 total count) synovitis
	High = 3	≥6 (of 28 total count) synovitis
Cutaneous [3] Rate as 'no activity' stable long-lasting features related to damage	No = 0	Absence of currently active cutaneous involvement
	Low =1	Erythema multiforma
	Moderate = 2	Limited cutaneous vasculitis, including urticarial vasculitis, or purpura limited to feet and ankle, or subacute cutaneous lupus
	High = 3	Diffuse cutaneous vasculitis, including urticarial vasculitis, or diffuse purpura, or ulcers related to vasculitis
Pulmonary [5] Rate as 'no activity' stable long-lasting features related to damage, or respiratory involvement not related to the disease (tobacco use, etc)	No =0	Absence of currently active pulmonary involvement
	Low = 1	Persistent cough or bronchial involvement with no radiographic abnormalities on radiography Or radiological or HRCT evidence of interstitial lung disease with no breathlessness and normal lung function test
	Moderate = 2	Moderately active pulmonary involvement, such as interstitial lung disease shown by HRCT with shortness of breath on exercise (NHYA II) or abnormal lung function tests restricted to 70%>DL_{CO}≥40% or 80%>FVC≥60%
	High = 3	Highly active pulmonary involvement, such as interstitial lung disease shown by HRCT with shortness of breath at rest (NHYA III, IV) or with abnormal lung function tests DL_{CO}<40% or FVC<60%
Renal [5] Rate as 'no activity' stable long-lasting features related to damage and renal involvement not related to the disease. If biopsy has been performed, please rate activity based on histological features first	No = 0	Absence of currently active renal involvement with proteinuria <0.5 g/day, no haematuria, no leucocyturia, no acidosis, or long-lasting stable proteinuria due to damage
	Low = 1	Evidence of mild active renal involvement, limited to tubular acidosis without renal failure or glomerular involvement with proteinuria (between 0.5 and 1 g/day) and without haematuria or renal failure (GFR ≥60 ml/min)
	Moderate = 2	Moderately active renal involvement, such as tubular acidosis with renal failure (GFR <60 ml/min) or glomerular involvement with proteinuria between 1 and 1.5 g/day and without haematuria or renal failure (GFR ≥60 ml/min) or histological evidence of extra-membranous glomerulonephritis or important interstitial lymphoid infiltrate
	High = 3	Highly active renal involvement, such as glomerular involvement with proteinuria >1.5 g/day or haematuria or renal failure (GFR <60 ml/min), or histological evidence of proliferative glomerulonephritis or cryoglobulinaemia-related renal involvement



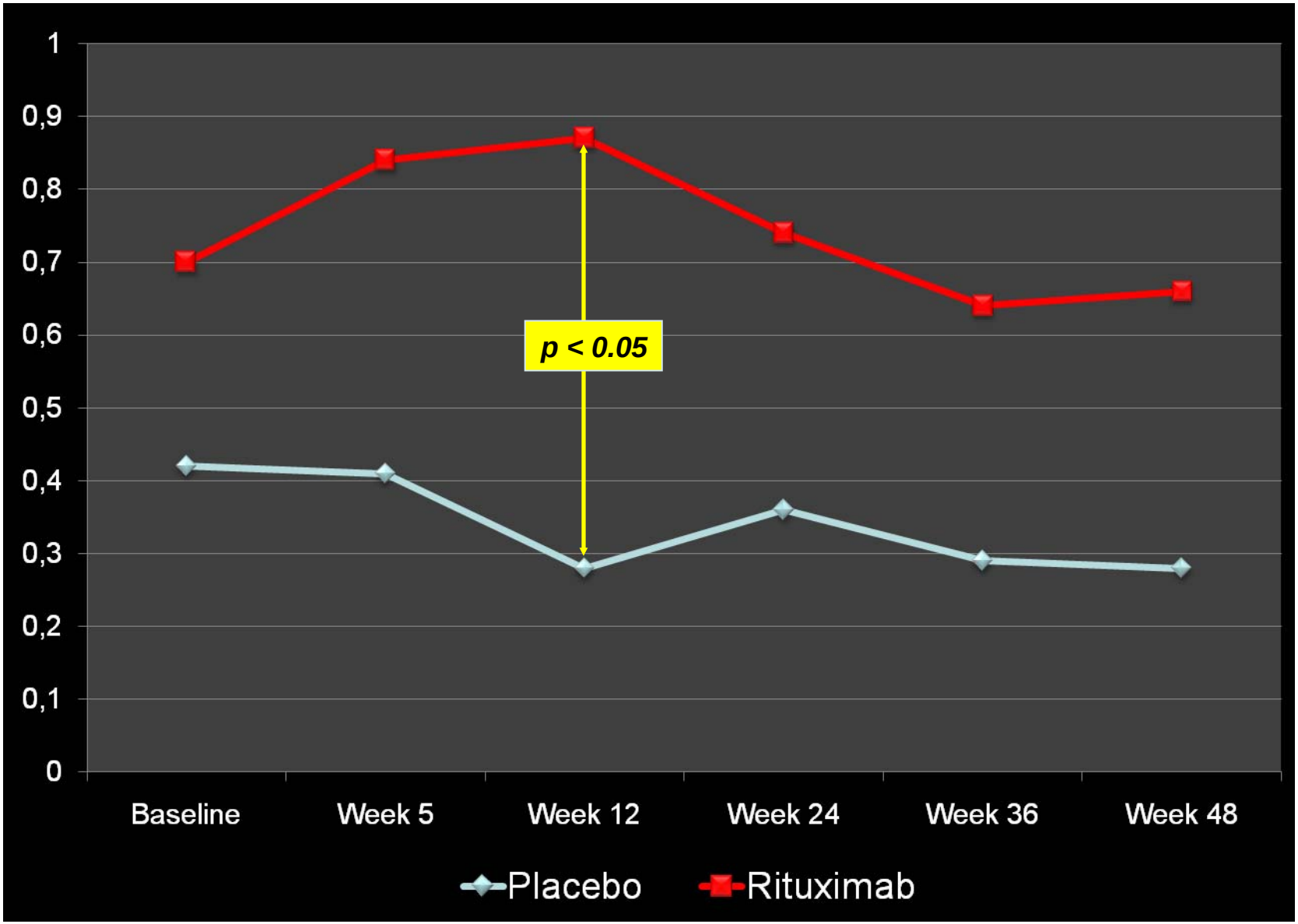
In conclusion, the results of this study indicate that rituximab could be an effective and safe treatment strategy for patients with primary SS. B cell depletion resulted in improvement of the primary end point, the rate of stimulated whole saliva secretion. Explorative analyses also showed improvements, of at least 6–9 months' duration, in the objective and subjective secondary end points of disease activity. Since primary SS has a great impact on health-related quality of life, employment, and disability (1), it is worthwhile to further explore the role of rituximab in a large-size, randomized, controlled trial.

Table 1. Baseline characteristics of the patients in the rituximab and placebo treatment groups*

Variable	Placebo (n = 10)	Rituximab (n = 20)
Age, mean ± SD years	43 ± 17	43 ± 11
No. female/no. male	10	19/1
Disease duration, mean ± SD months	67 ± 63	63 ± 50
IgG, mean ± SD gm/liter	21 ± 7	23 ± 8
IgM-RF, mean ± SD IU/ml	221 ± 245	102 ± 79
Anti-Ro/SSA positive	10 (100)	20 (100)
Anti-La/SSB positive	8 (80)	14 (70)
Parotid gland swelling	10 (100)	17 (85)
Whole saliva flow, ml/minute		
Unstimulated	0.06 ± 0.09	0.17 ± 0.19†
Stimulated	0.42 ± 0.26	0.70 ± 0.57
Extraglandular manifestation		
Arthralgia	5 (50)	15 (75)
Arthritis	0 (0)	6 (30)
Renal involvement	0 (0)	2 (10)
Esophageal involvement	1 (10)	0 (0)
Peripheral polyneuropathy	0 (0)	1 (5)
Raynaud's phenomenon	6 (60)	11 (55)
Tendomyalgia	8 (80)	17 (85)
Vasculitis	3 (30)	6 (30)
Thyroid dysfunction	0 (0)	1 (5)
Use of artificial tears	8 (80)	14 (70)
Use of artificial saliva	2 (20)	2 (10)

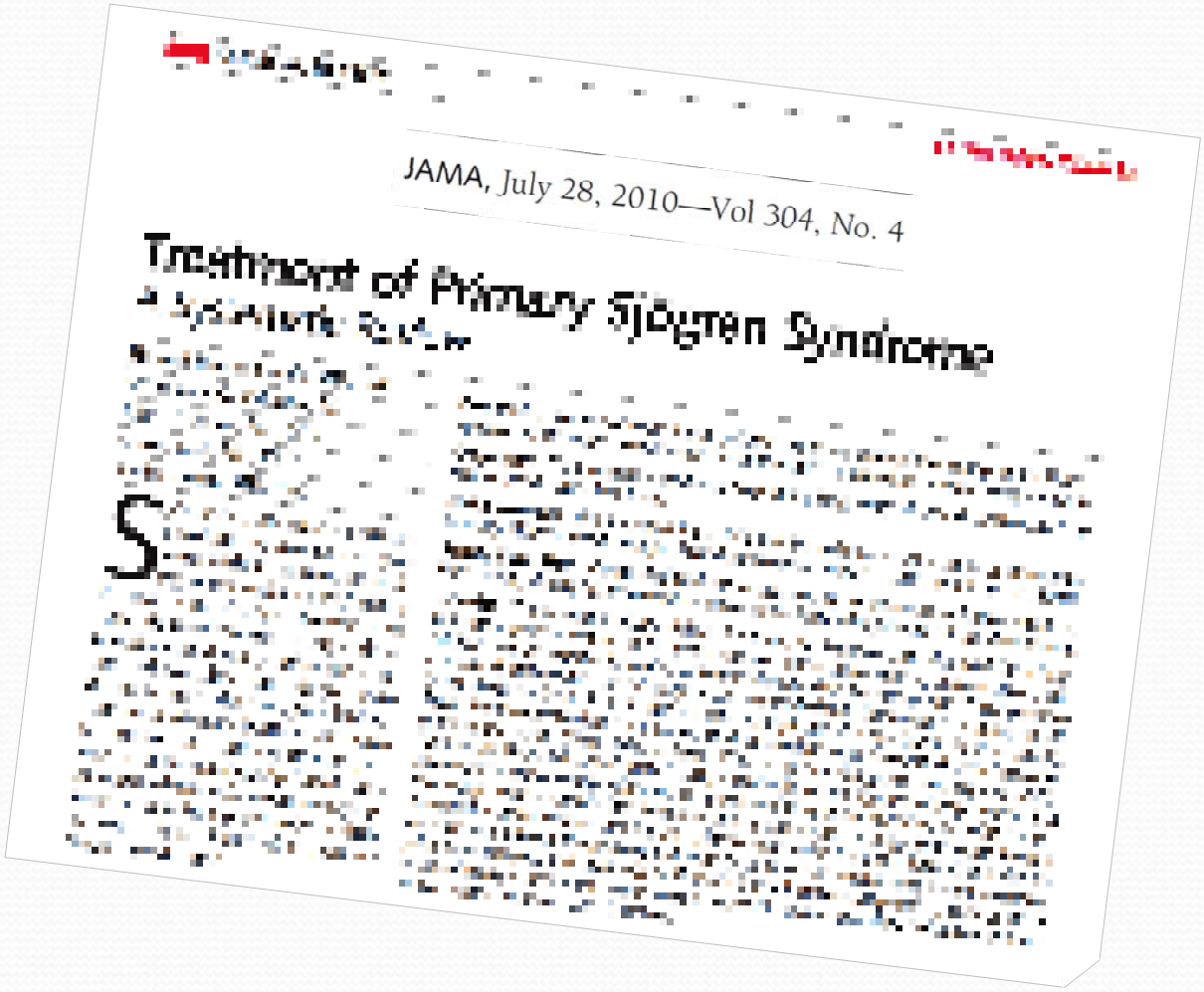
* Except where indicated otherwise, values are the number (%) of patients. RF = rheumatoid factor.
† $P < 0.05$ versus placebo.

Stimulated whole salivary flow, mean (ml(minute)



ROLE OF THE STUDY SPONSOR

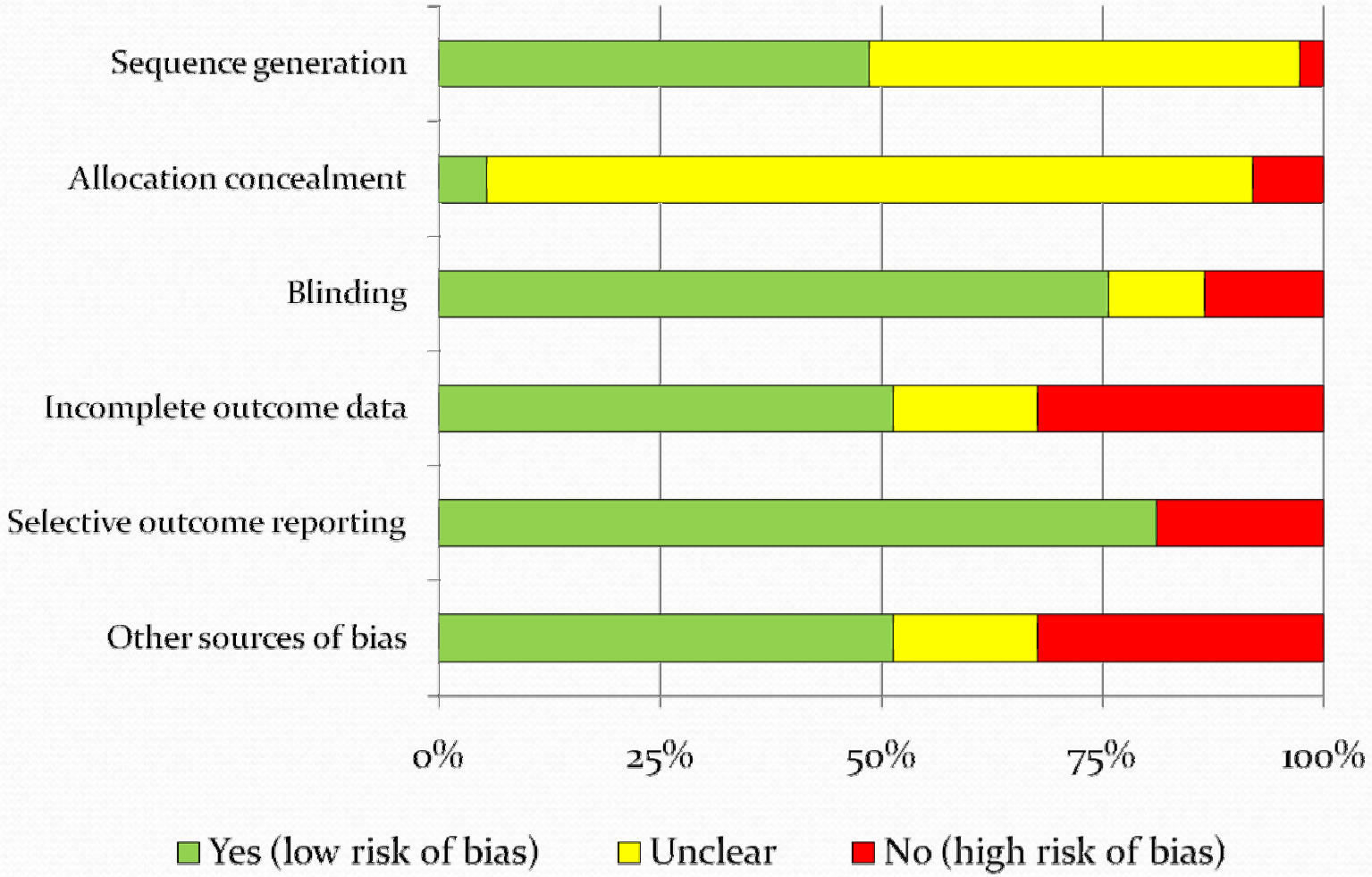
This trial was an investigator-driven study that was financially supported by Roche (Woerden, The Netherlands), which also supplied the study medication. There was no involvement of the study sponsor in the study design, patient recruitment, data collection, analysis and interpretation of the data, or writing of the report. Statistical analyses were performed by staff at the statistical department of Xendo Drug Development BV (Groningen, The Netherlands), which is an independent contract research organization. Medical writing support was provided by staff at Adelphi Communications (supported by F. Hoffmann-La Roche, Ltd.) during the final preparation of the article.



JAMA, July 28, 2010—Vol 304, No. 4

Treatment of Primary Sjögren Syndrome

Metodología (PRISMA, PICOTS, Cochrane)



Ensayos clínicos randomizados

Ciclosporina A tópica	Primary endpoint
Pilocarpina	Primary endpoint
Cevimelina	Primary endpoint

1. Pape del SSp

2. Ler stémica

3. Import /cronicidad

4. R nar

5. Escaso niv tratamiento