ANMAR
Associazione Nazionale
Malati Reumatici
Onlus

A.T.Ma.R

"La gestione clinica e organizzativa delle malattie reumatiche"

Importanza della diagnosi precoce

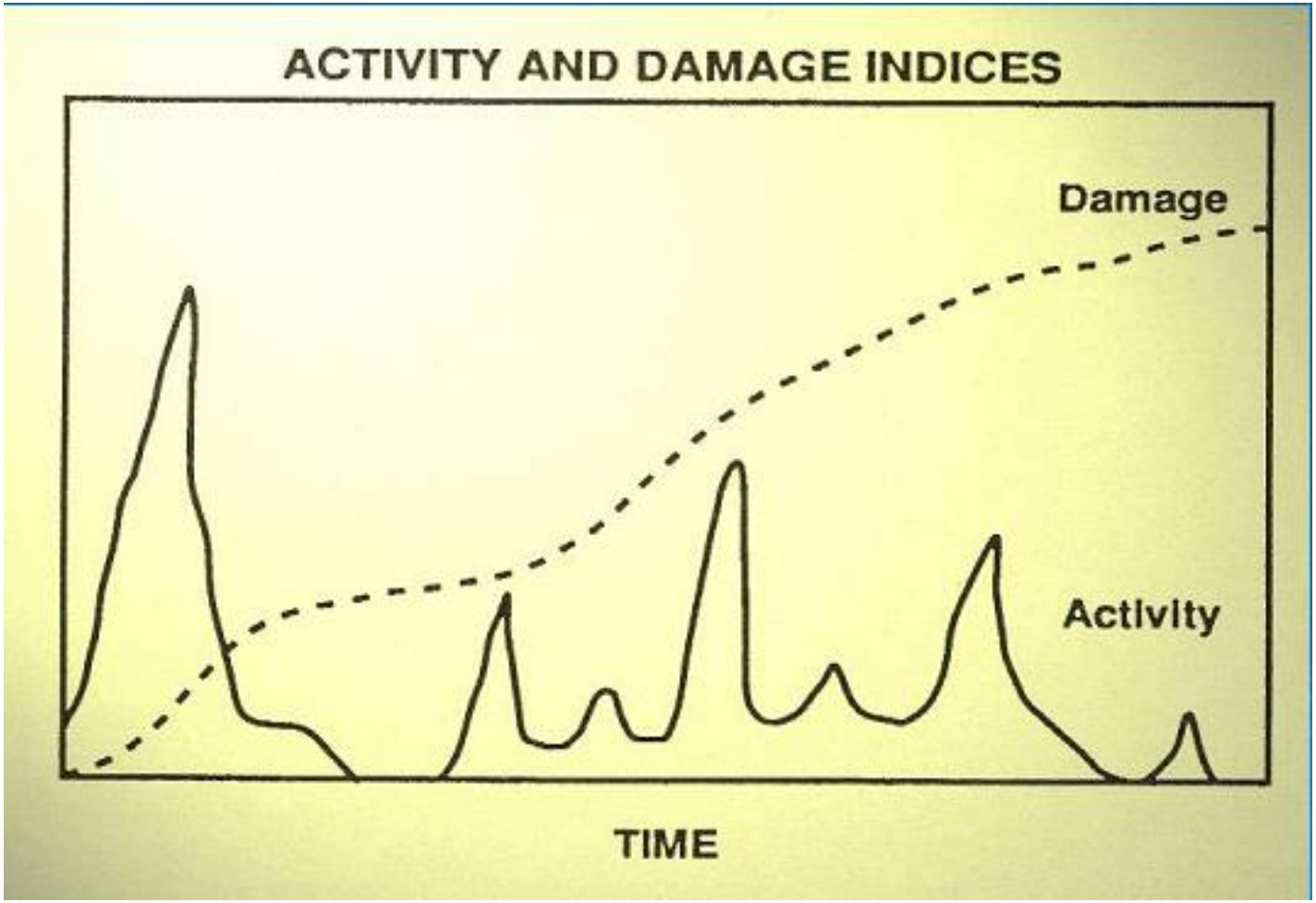
Chiara Baldini

U.O. Reumatologia, Università di Pisa

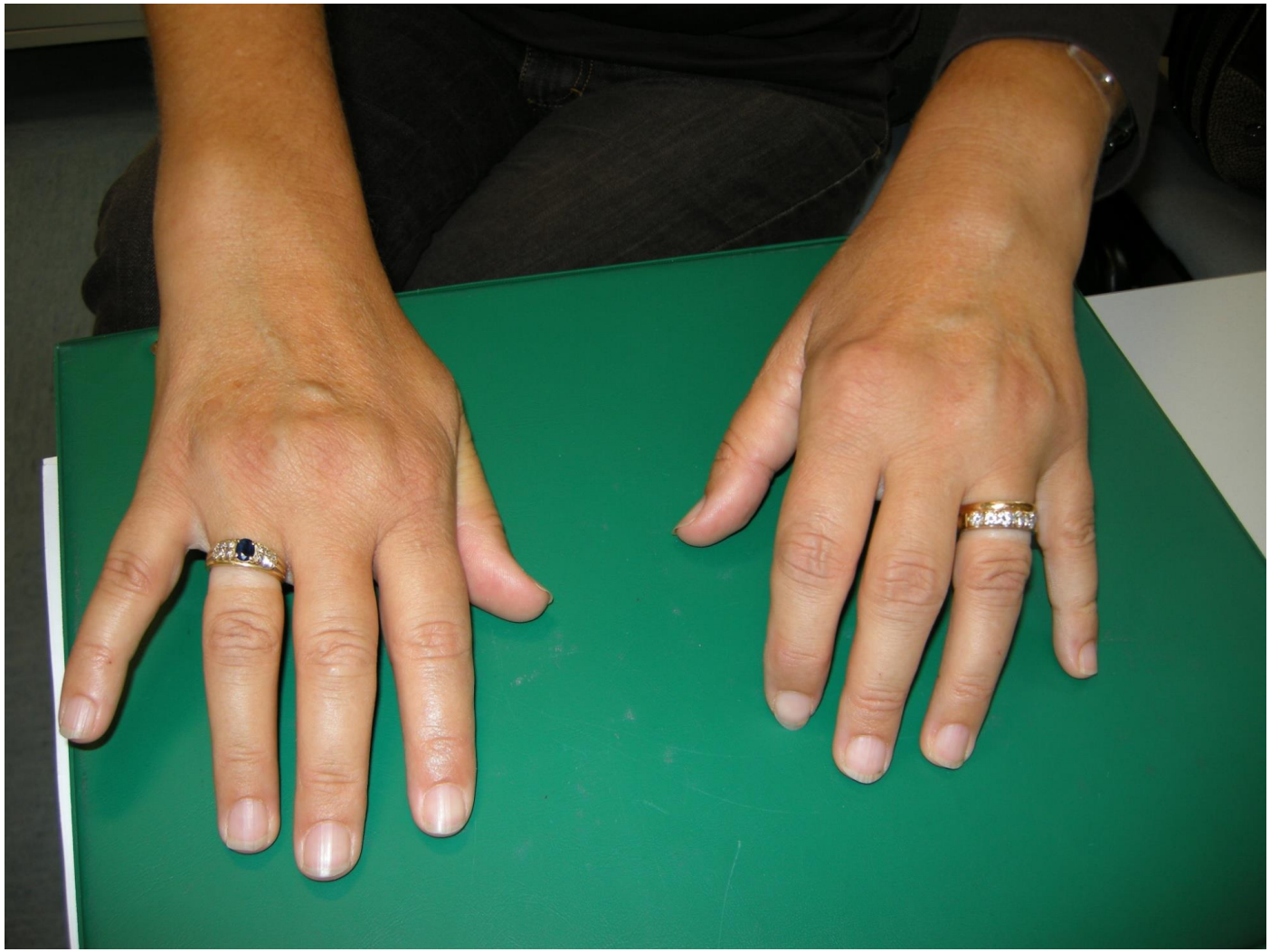
Agenda

- Diagnosi precoce:
  - Razionale patogenetico
  - Razionale clinico
- Il ritardo diagnostico: l'esperienza delle Early Clinics
- Prospettive future per la diagnosi precoce

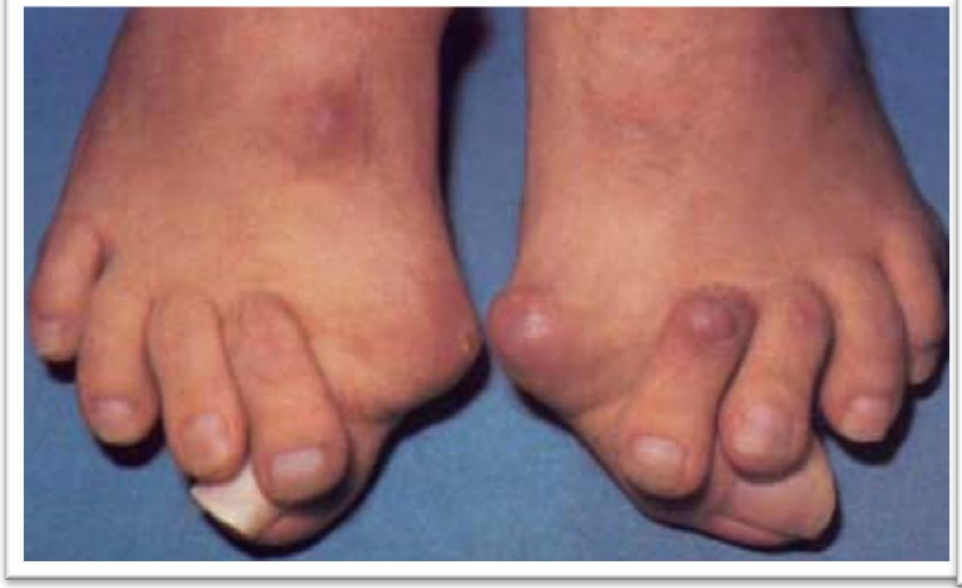
Malattie reumatiche: dall'infiammazione al danno

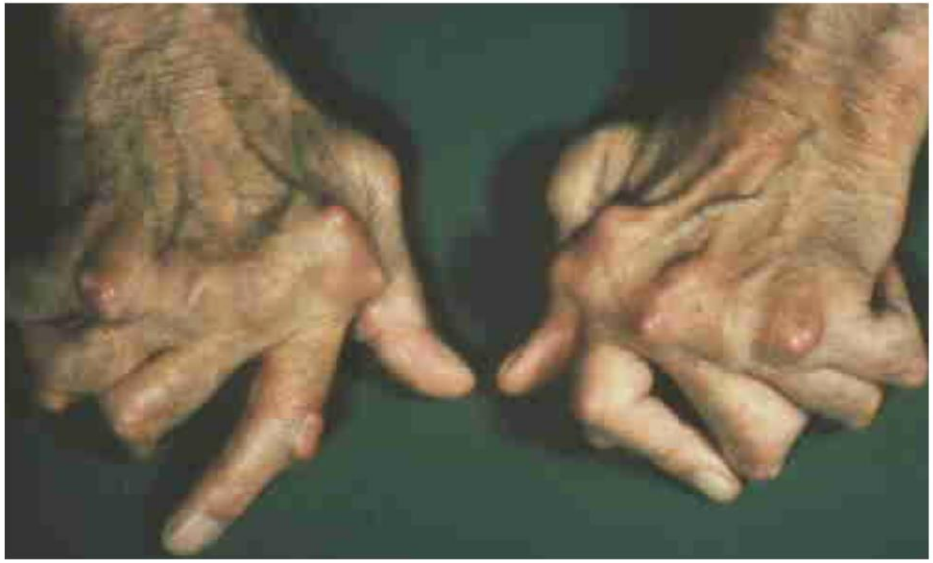


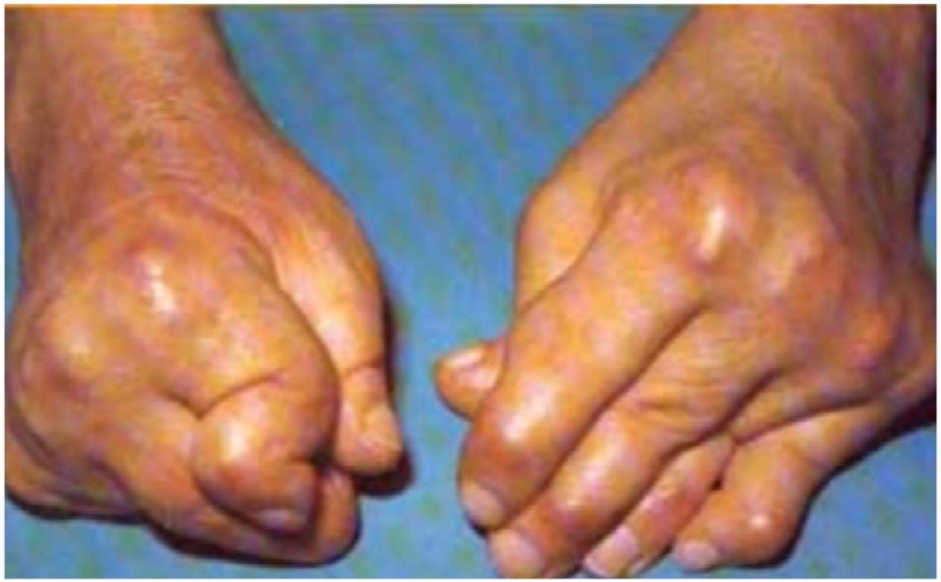
Artrite reumatoide: evoluzione dall'infiammazione …



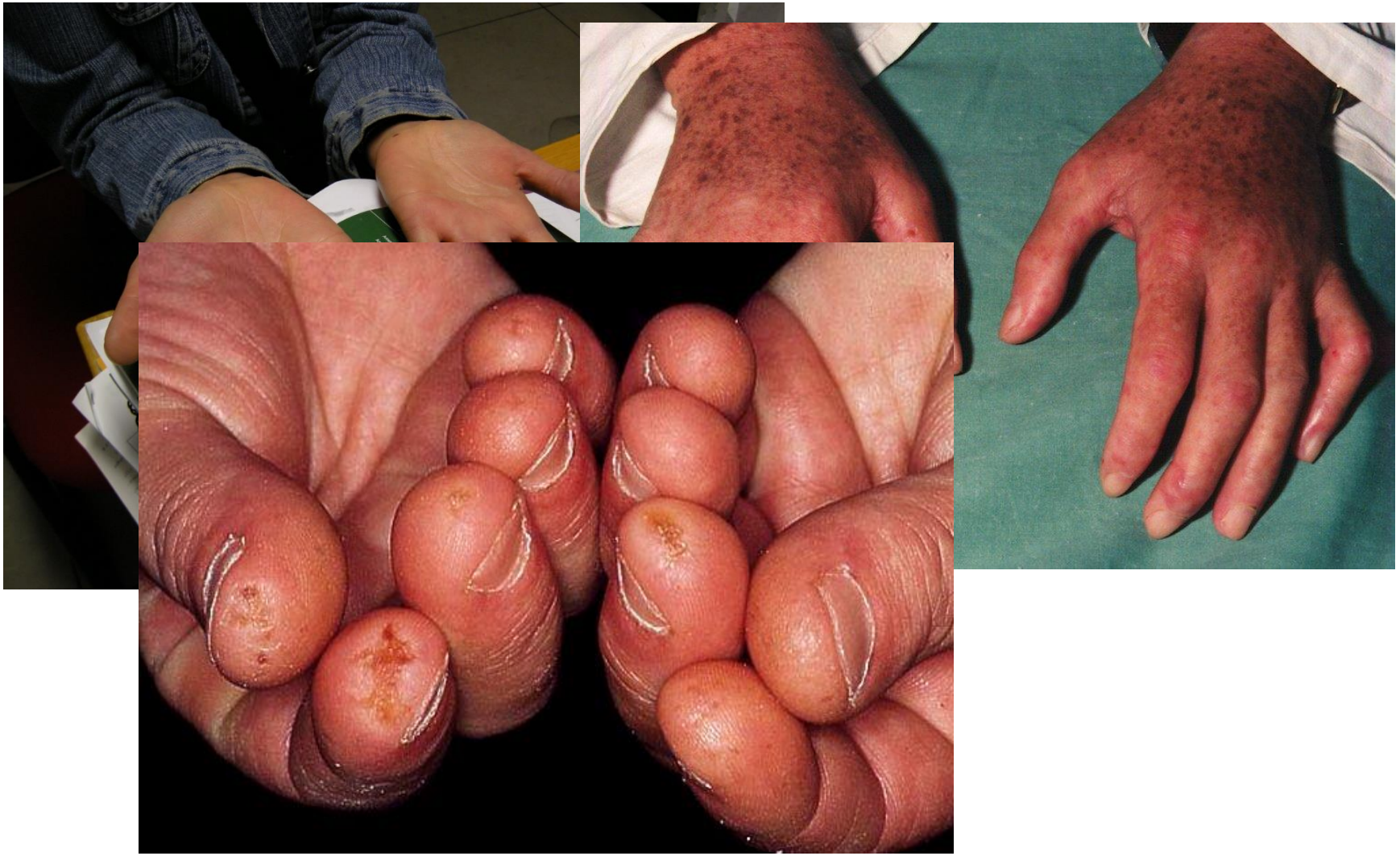
Artrite reumatoide: dall'infiammazione … al danno

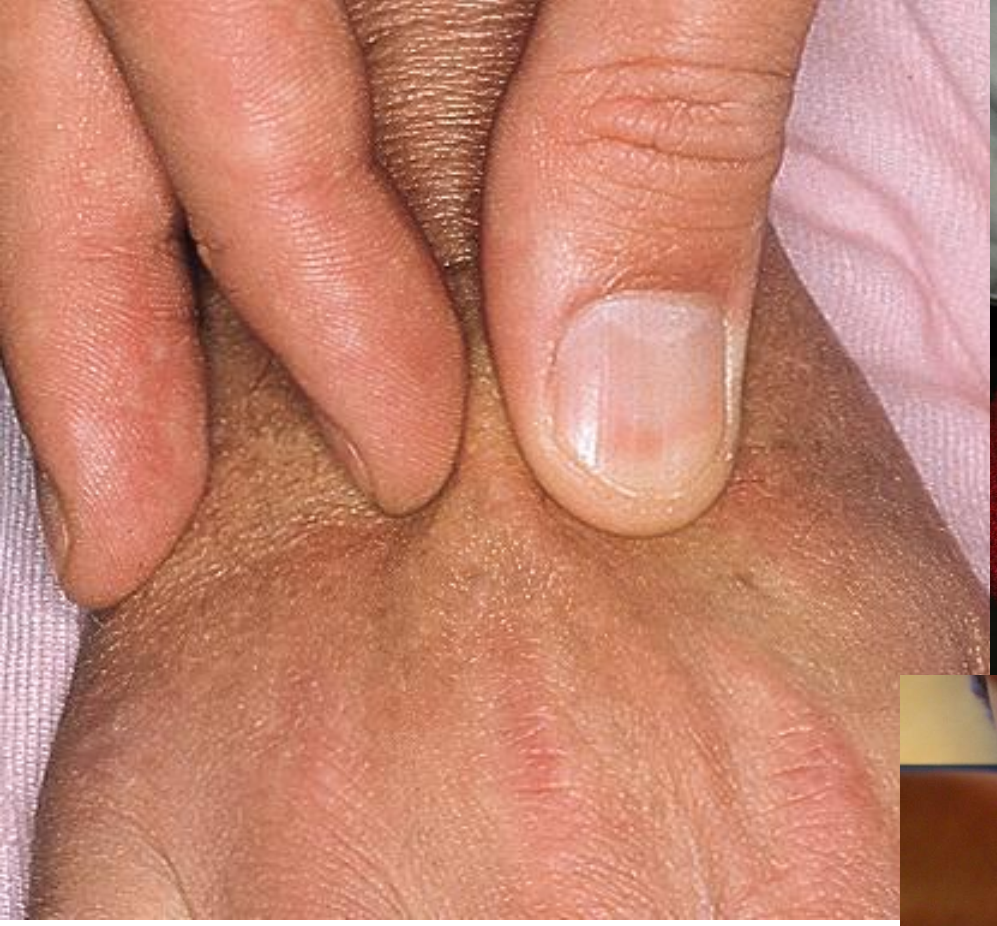


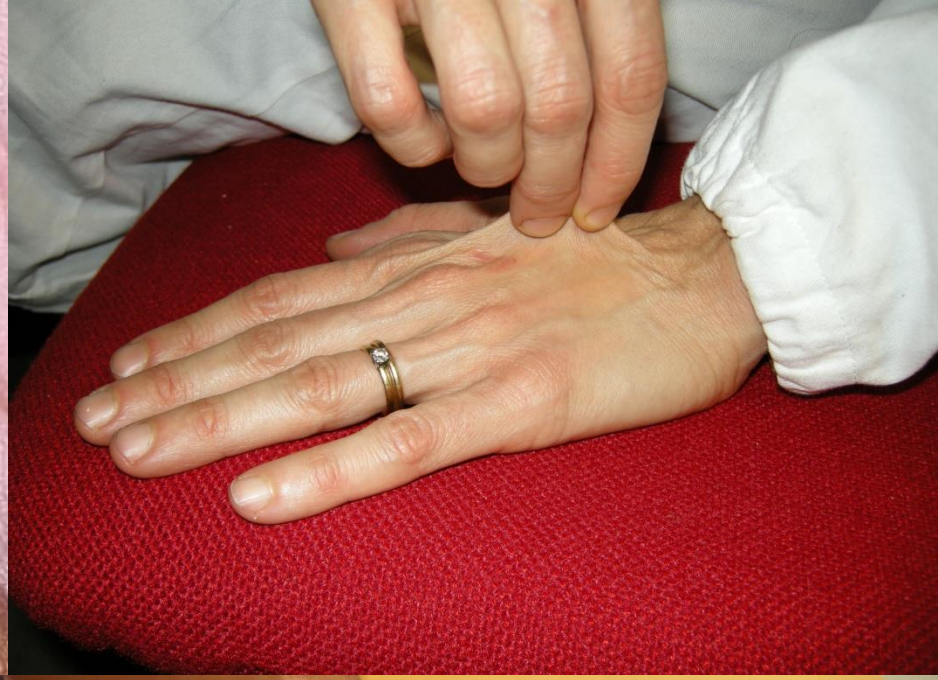


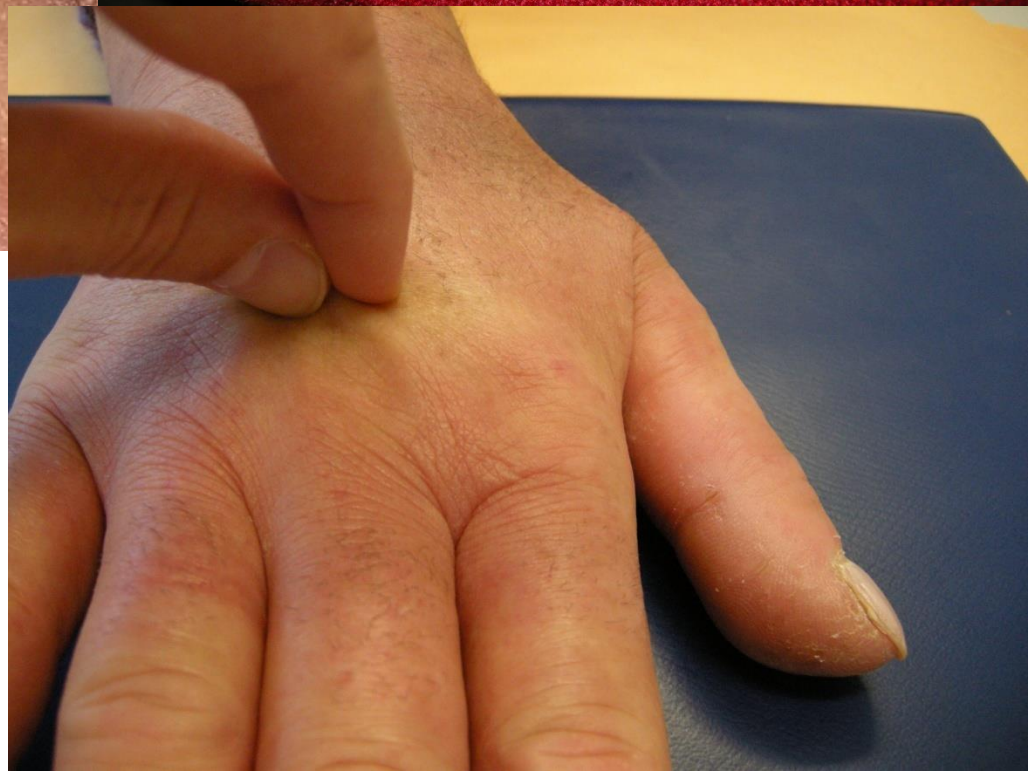


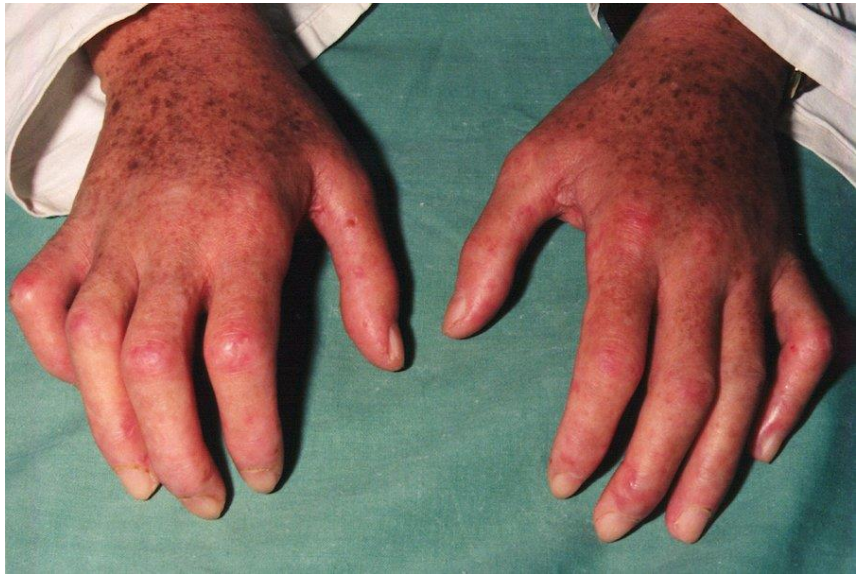
La Sclerodermia:
dal fenomeno di Raynaud alla sclerodattilia

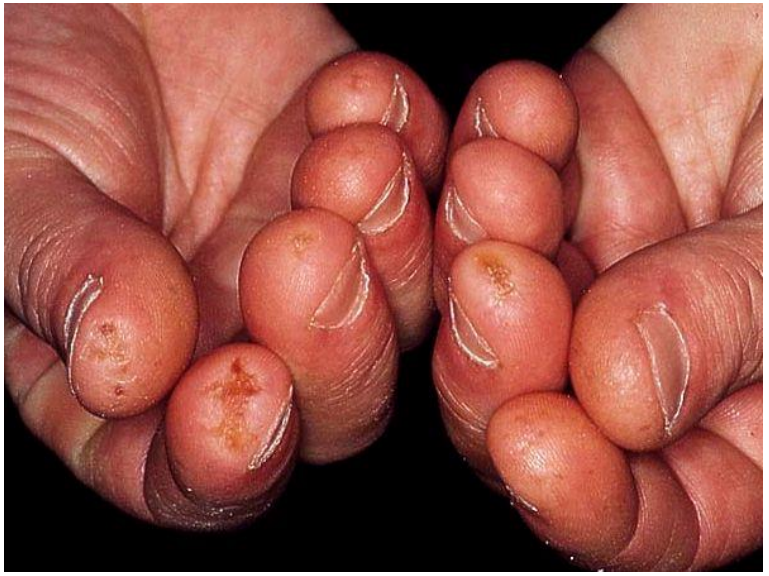


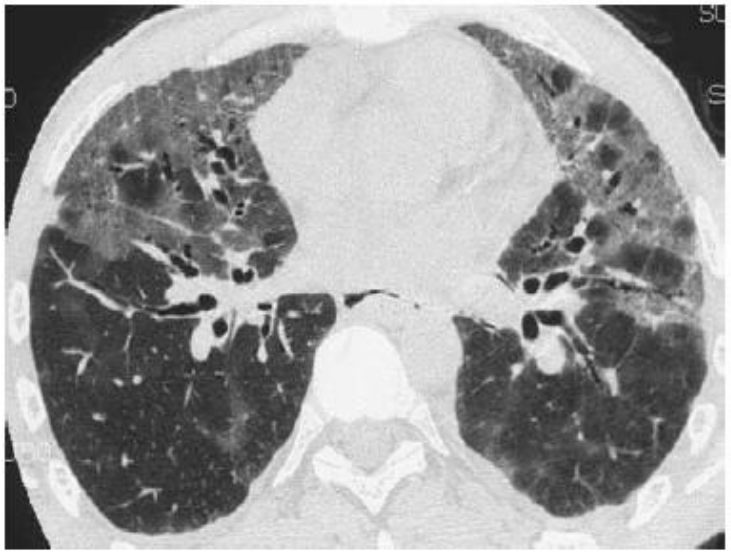


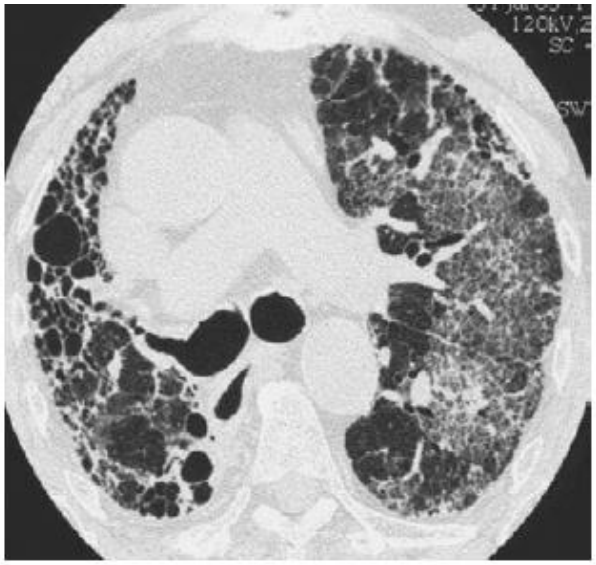








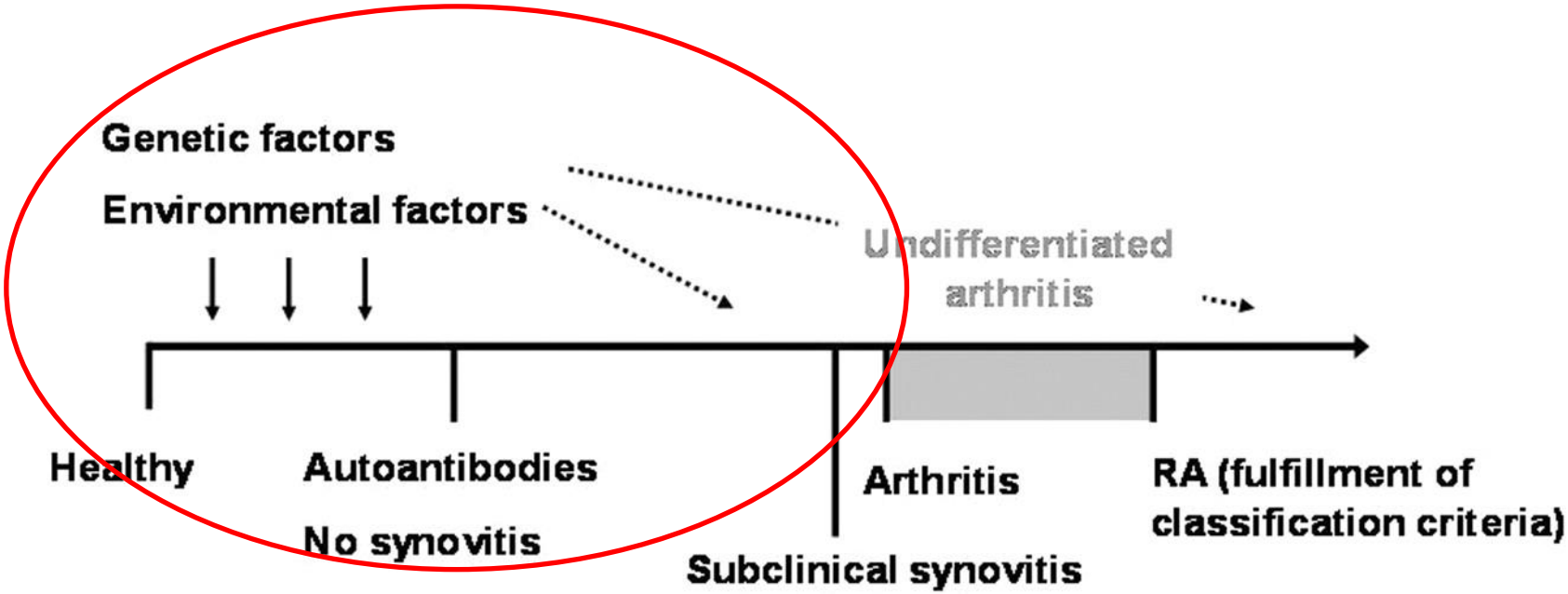




Early arthritis e «Window of opportunity»

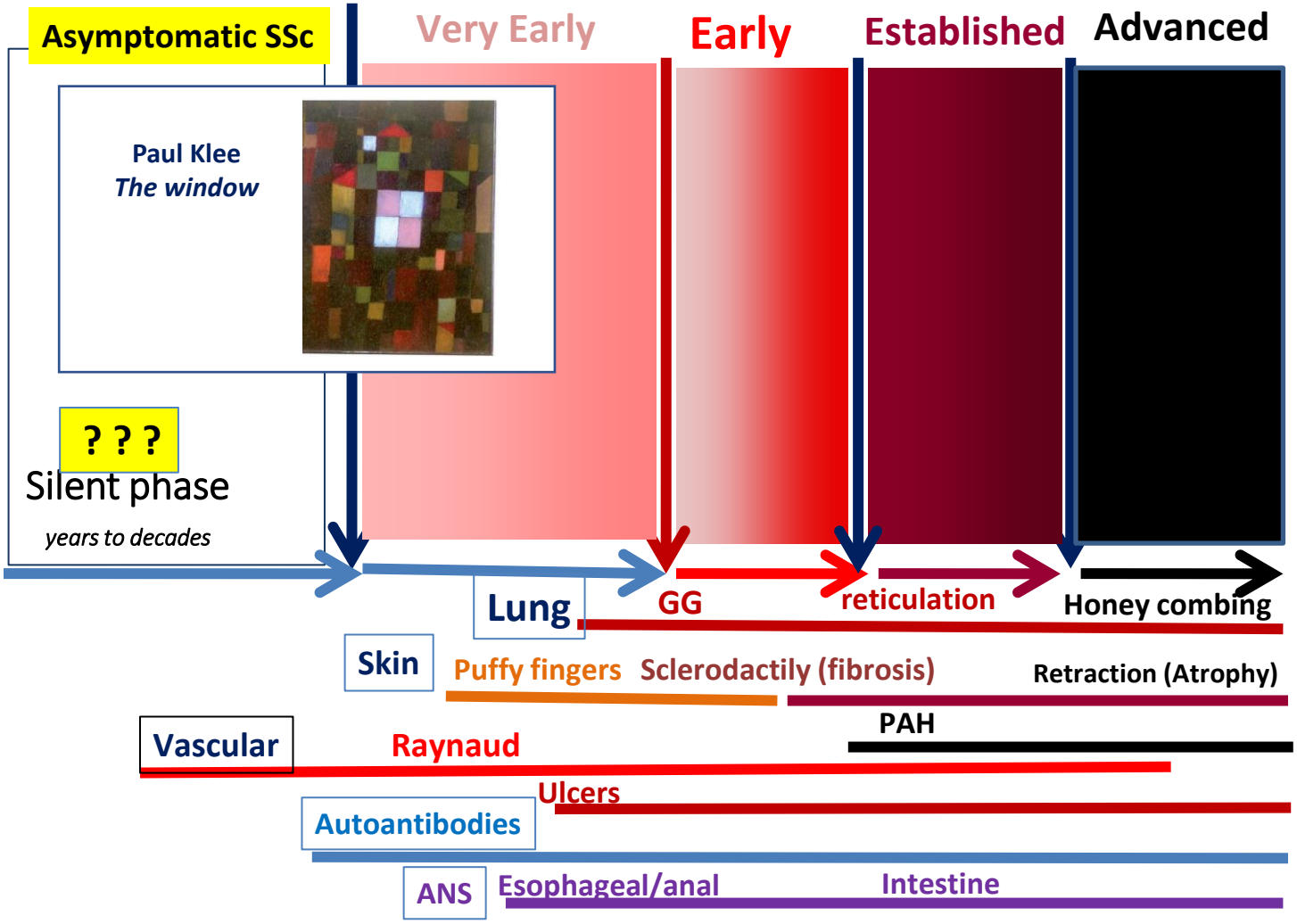
diagnosi precoce→ terapia precoce →blocco o rallentamento della malattia

«Diagnosi precoce»: razionale patogenetico



Sparks J et al. The Roles of Cigarette Smoking and the Lung in the Transitions between Phases of Preclinical Rheumatoid Arthritis
Curr Rheumatol Rep. 2016 March ; 18(3): 15

Diagnosi precoce»: razionale patogenetico



Matucci Cerinic M. Kahaleh B, Wigley F: «Scleroderma is a vascular disease», A&R 2013

ARTHRITIS & RHEUMATOLOGY
Vol. 67, No. 9, September 2015, pp 2427–2436
DOI 10.1002/art.39214

Prediction of Sjögren's Syndrome Years Before Diagnosis and Identification of Patients With Early Onset and Severe Disease Course by Autoantibody Profiling

Elke Theander,[1] Roland Jonsson,[2] Bitte Sjöström,[3] Karl Brokstad,[4] Peter Olsson,[1] and Gunnel Henriksson[3]

Results. **Considering all patients with primary SS who were autoantibody positive after diagnosis, at least one autoantibody specificity was detected in 81% up to 20 years (median 4.3–5.1 years) before diagnosis. Those found most often were ANAs, followed by RF, anti–Ro 60/SSA, anti–Ro 52/SSA, and anti-La/SSB. Anti-Ro/SSA and anti-La/SSB antibodies were strongly associated with the risk of developing primary SS, especially early-onset disease and a severe disease course. When Bayesian prior prevalence estimates for primary SS were included in the calculation, prediagnostic anti–Ro 60/SSA and anti–Ro 52/SSA had the highest positive predictive values (25% and 100%, respectively).**

The NEW ENGLAND JOURNAL of MEDICINE

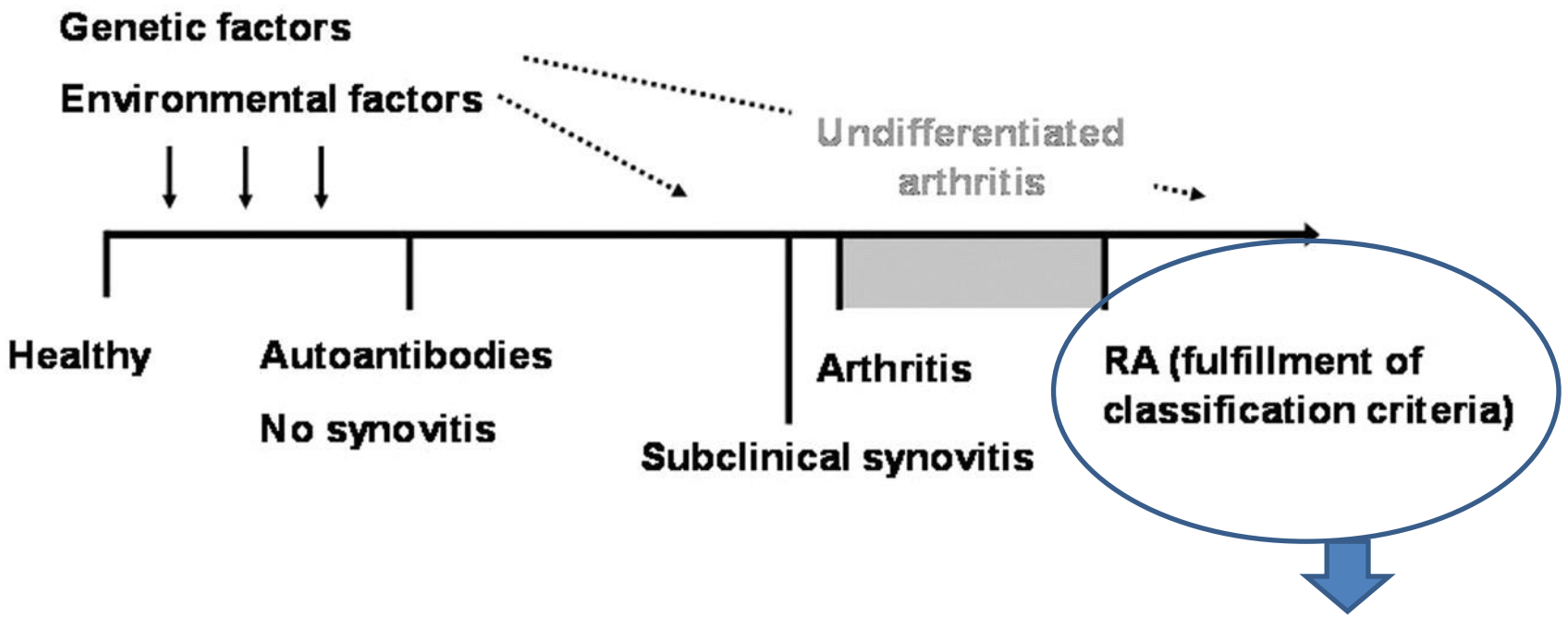
ORIGINAL ARTICLE

Development of Autoantibodies before the Clinical Onset of Systemic Lupus Erythematosus

Melissa R. Arbuckle, M.D., Ph.D., Micah T. McClain, Ph.D., Mark V. Rubertone, M.D., R. Hal Scofield, M.D., Gregory J. Dennis, M.D., Judith A. James, M.D., Ph.D., and John B. Harley, M.D., Ph.D.

N Engl J Med 2003;349:1526-33.

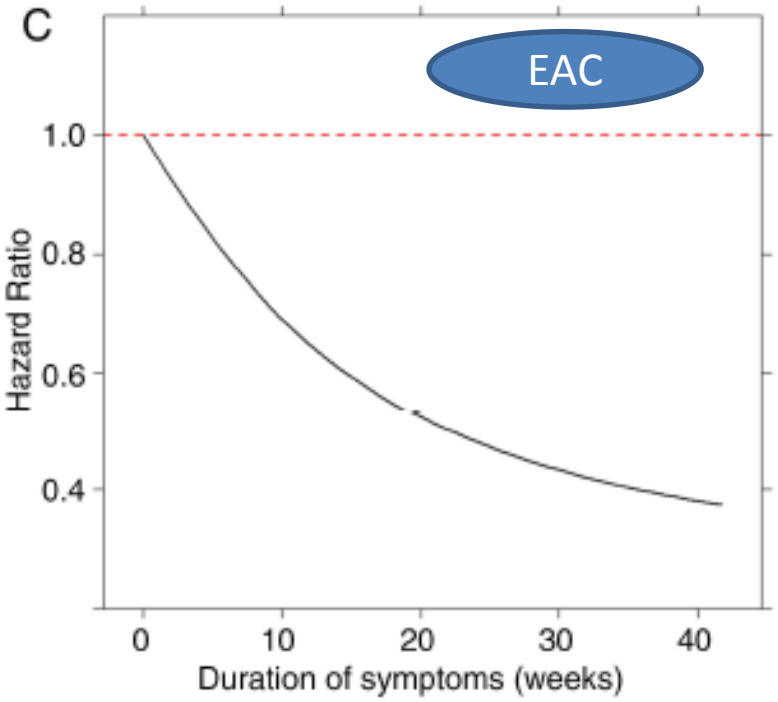
«Diagnosi precoce»: razionale clinico

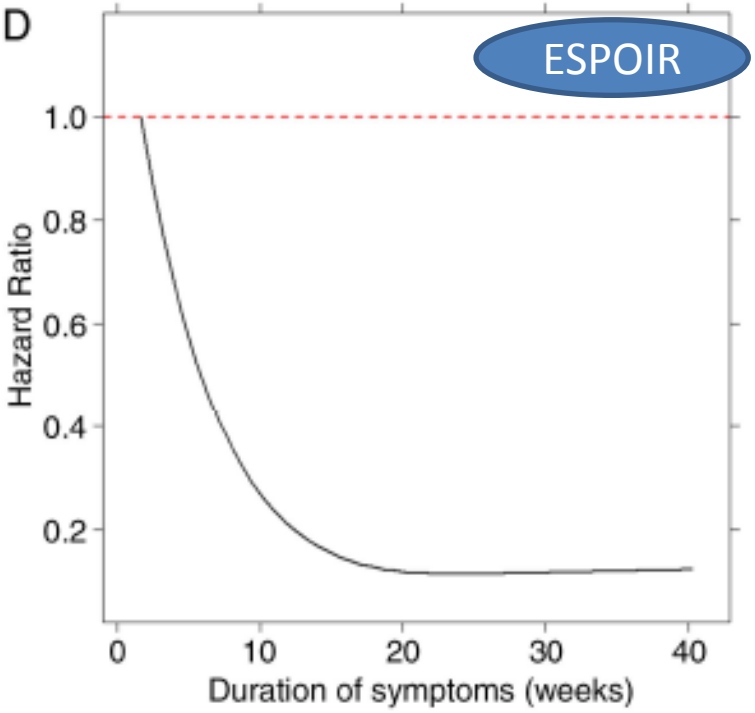


Maggiore è la durata dei sintomi → Minore è la reversibilità della malattia

Evaluating relationships between symptom duration and persistence of rheumatoid arthritis: does a window of opportunity exist? Results on the Leiden Early Arthritis Clinic and ESPOIR cohorts

J A B van Nies,[1] R Tsonaka,[2] C Gaujoux-Viala,[3] B Fautrel,[4] A H M van der Helm-van Mil[1]

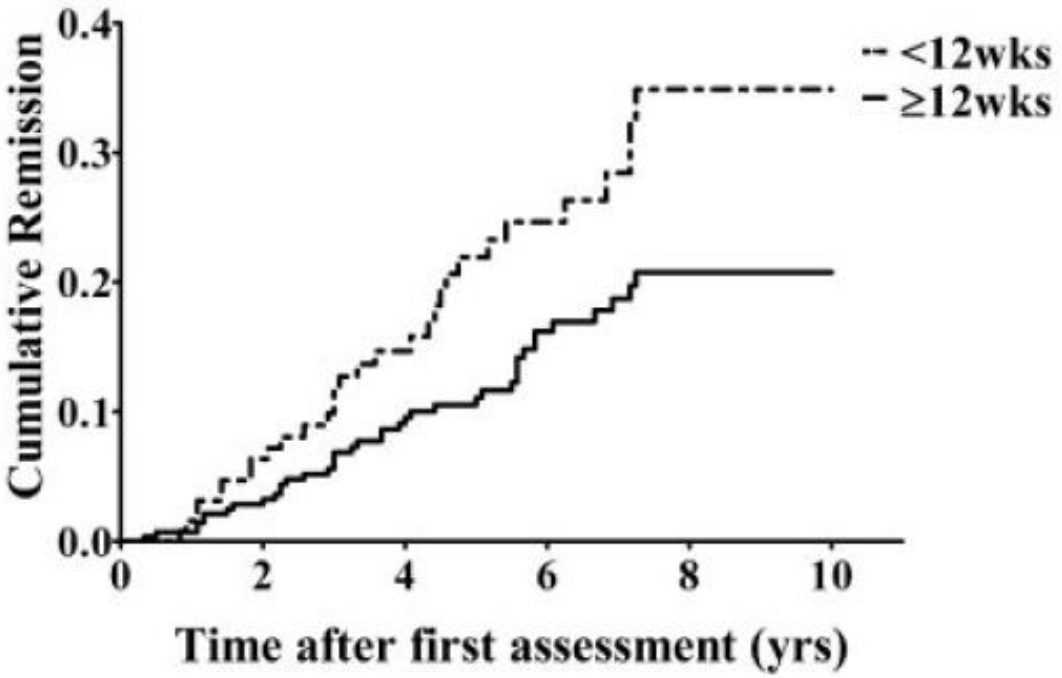




van Nies JAB, *et al. Ann Rheum Dis* 2015;**74**:806–812.

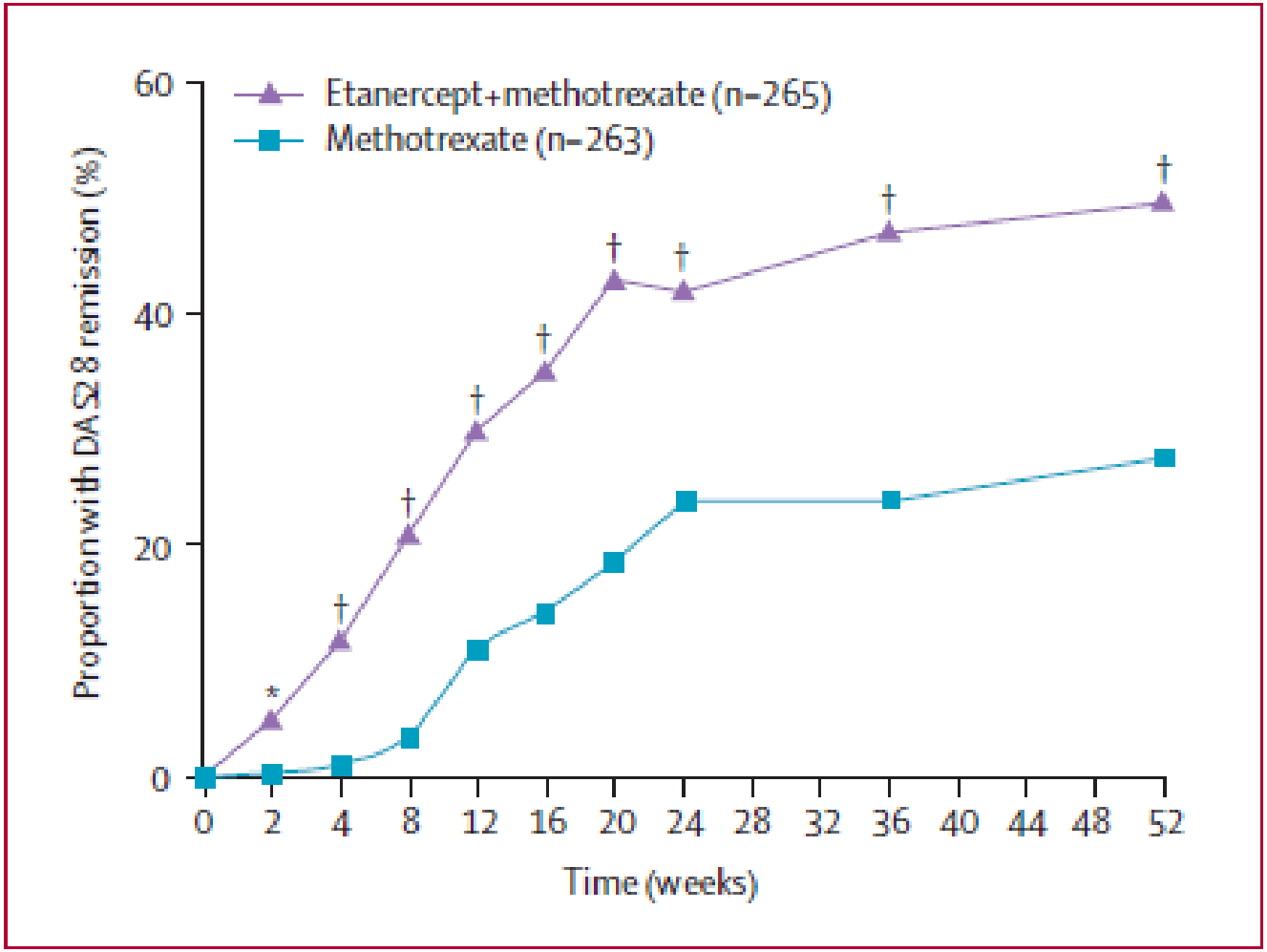
Long-Term Impact of Delay in Assessment of Patients With Early Arthritis

Michael P. M. van der Linden,[1] Saskia le Cessie,[1] Karim Raza,[2] Diane van der Woude,[1] Rachel Knevel,[1] Tom W. J. Huizinga,[1] and Annette H. M. van der Helm-van Mil[1]



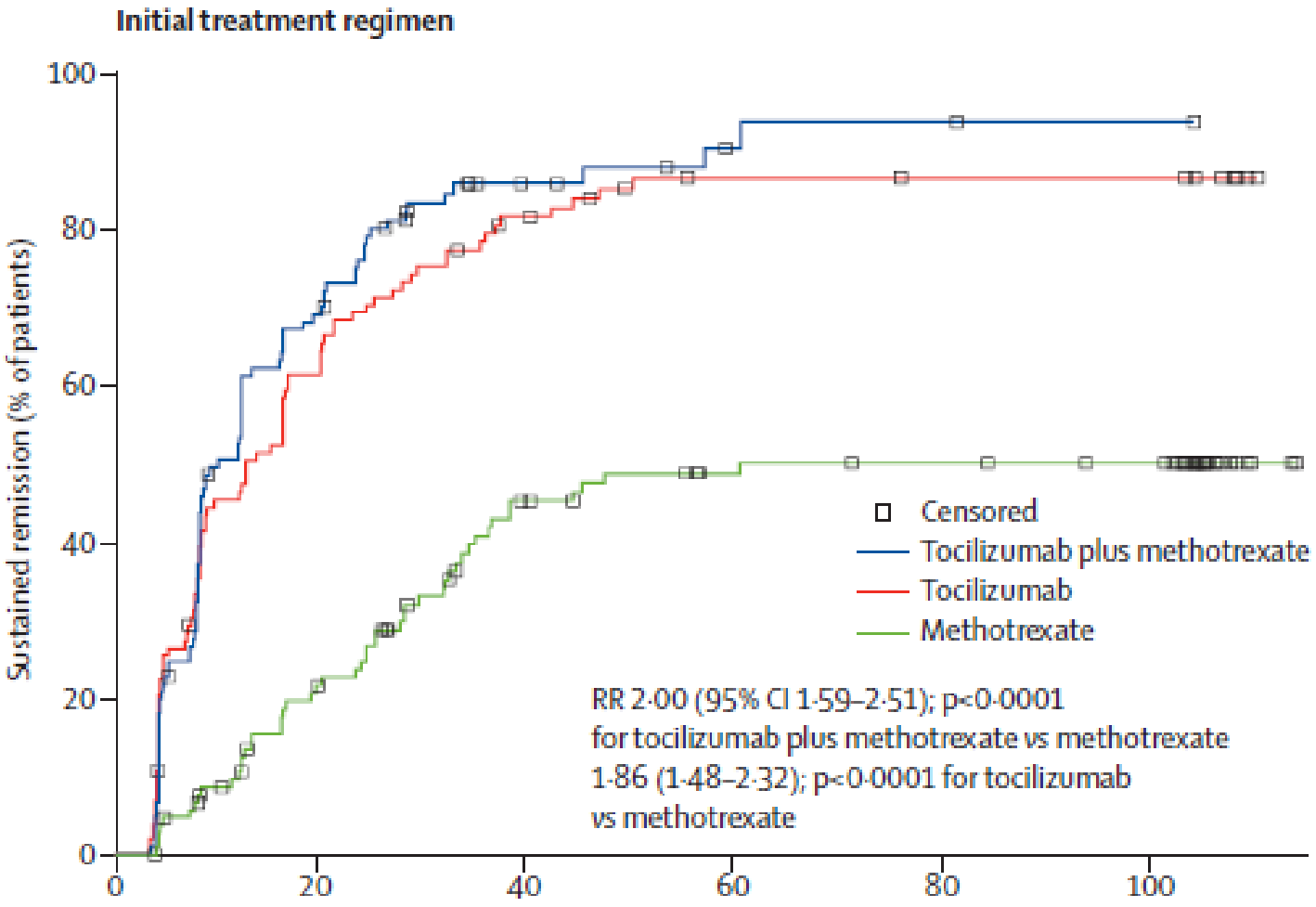
ARTHRITIS & RHEUMATISM
Vol. 62, No. 12, December 2010, pp 3537–3546

COMET trial



Emery P. et al Lancet 2009

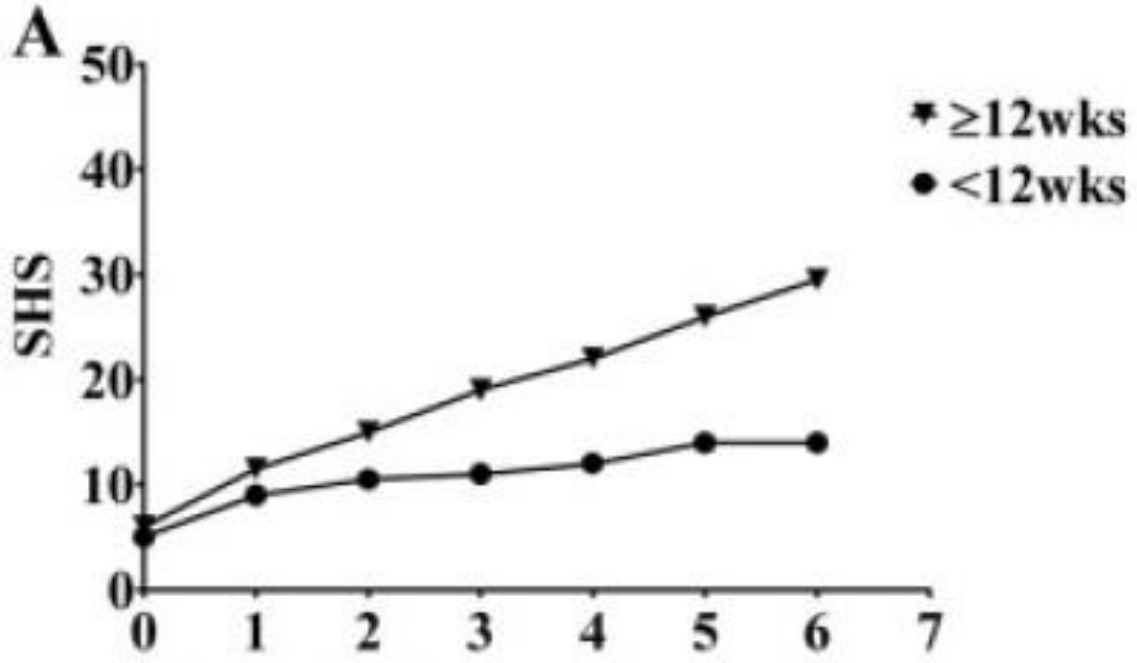
U ACT Early Strategy trial



Bijsma , Lancet 2016

Long-Term Impact of Delay in Assessment of Patients With Early Arthritis

Michael P. M. van der Linden,[1] Saskia le Cessie,[1] Karim Raza,[2] Diane van der Woude,[1] Rachel Knevel,[1] Tom W. J. Huizinga,[1] and Annette H. M. van der Helm-van Mil[1]



ARTHRITIS & RHEUMATISM
Vol. 62, No. 12, December 2010, pp 3537–3546

Evoluzione del danno articolare nella AR: polsi

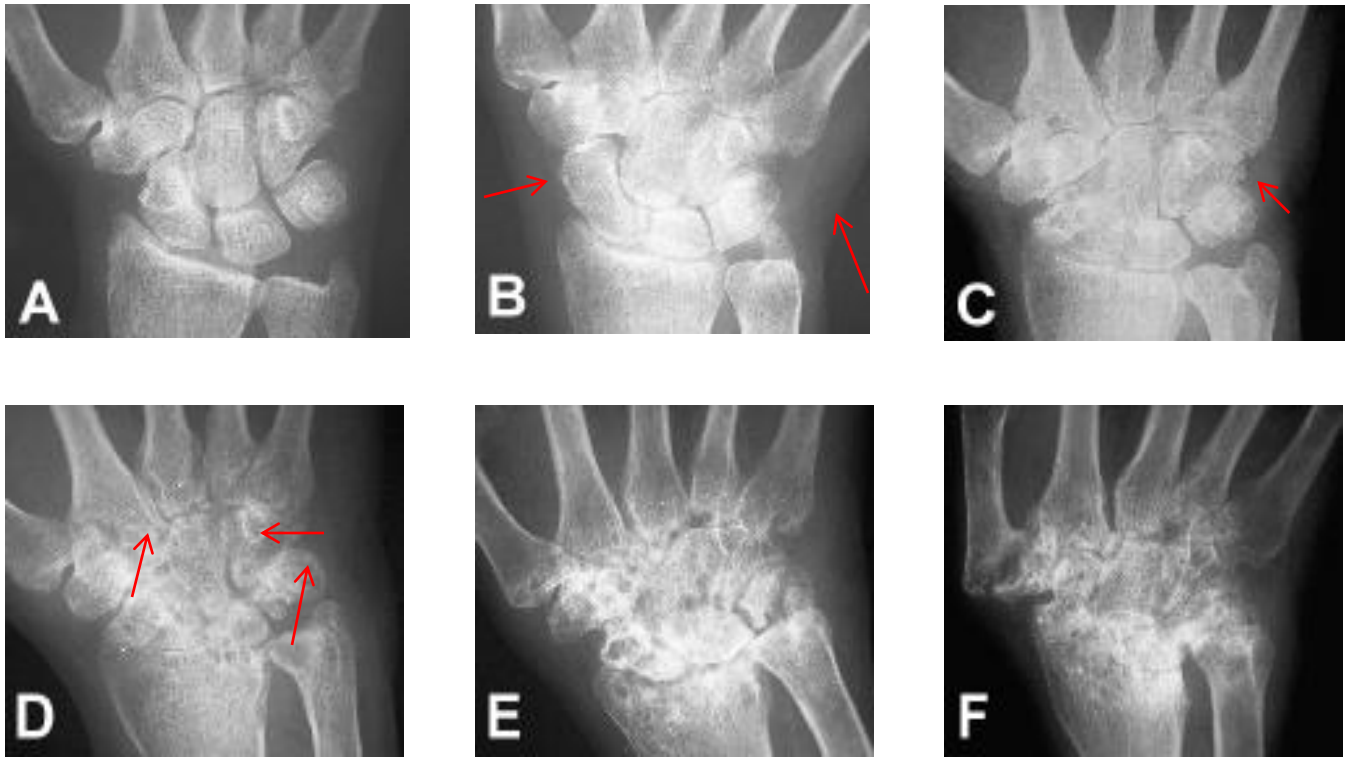


Fig. A: Articolazioni normali (3/1989);
Fig. B: Tumefazione dei tessuti molli e riduzione degli spazi articolari (11/1990);
Fig. C: Numerose piccole erosioni e chiaro restringimento degli spazi articolari (3/1992);
Fig. D: Erosioni multiple con marcata riduzione degli spazi articolari (11/1993);
Fig. E: Erosioni multiple con alterazioni distruttive. Rimangono piccole parti delle superfici articolari (1/1995);
Fig. F: Completa distruzione delle superfici articolari prossimali e distali (6/1996).

Evoluzione del danno articolare nella AR: articolazioni interfalangee prossimali

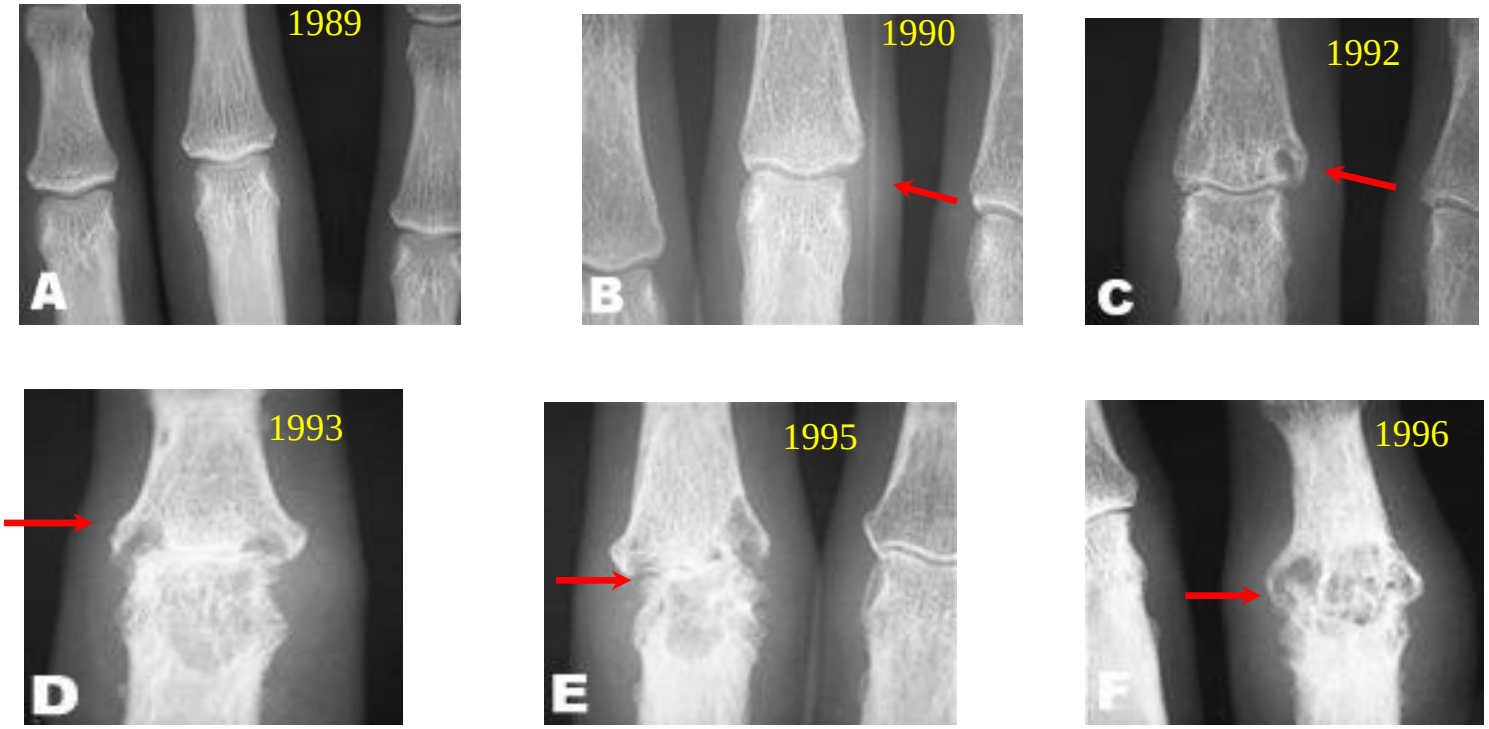


Fig. A: Articolazione normale (3/1989);
Fig. B: Tumefazione dei tessuti molli (11/1990);
Fig. C: piccola erosione e restringimento dello spazio articolare (3/1992);
Fig. D: erosioni più grosse con marcato restringimento dello spazio articolare (11/1993);
Fig. E: gravi erosioni (1/1995);
Fig. F: Erosioni mutilanti (6/1996).

ARTHRITIS & RHEUMATISM
Vol. 54, No. 1, January 2006, pp 68–75
DOI 10.1002/art.21548

Association of Early Radiographic Damage With Impaired Physical Function in Rheumatoid Arthritis

A Ten-Year, Longitudinal Observational Study in 238 Patients

Sigrid Ødegård,[1] Robert Landewé,[2] Désirée van der Heijde,[2] Tore K. Kvien,[1] Petter Mowinckel,[1] and Till Uhlig[1]

Artrite Reumatoide: Aspetti Invalidanti

Authors	Disability
Yelin et al. 1987	Social relations, religious activities, leisure pursuits, transportation
Katz 1995	Service, cultural, leisure, social partecipation areas
Cornelissen et al. 1988	Social relations, transportation
Reisine et al. 1987	Social relations
Ostenssen et al 1992	Household activities, bathing, dressing, lifting, carryng children

La work disability è solo un aspetto delle potenziali invalidità correlate all'artrite reumatoide che può influenzare tutti gli aspetti sociali e personali della vita di un paziente

ARTRITE REUMATOIDE: INABILITA' AL LAVORO

Anni di follow-up	Prevalenza (%)
1	15-30
3	30-40
10	40-50
20	80

Conclusioni: la inabilità lavorativa tra pazienti con AR è 4-5 volte maggiore rispetto alla popolazione generale (2.6%)

Markenson JA. Seminars in Arthritis and Rheumatism 1991

Qual Life Res (2017) 26:1767–1775
DOI 10.1007/s11136-017-1534-4

Differential impact of systemic lupus erythematosus and rheumatoid arthritis on health-related quality of life

Benjamin Chaigne[1] · Axel Finckh[2] · Deshire Alpizar-Rodriguez[2] · Delphine Courvoisier[2] · Camillo Ribi[3] · Carlo Chizzolini[1] · For The Swiss Clinical Quality Management Program For Rheumatoid ArthritisThe Swiss Systemic Lupus Erythematosus Cohort Study Group

Accepted: 21 February 2017 / Published online: 11 March 2017

Sindrome di Sjögren:
impatto sulla qualità di vita e sulla work disability

Arthritis Care & Research
Vol. 64, No. 11, November 2012, pp 1760–1764
DOI 10.1002/acr.21738

BRIEF REPORT

69 pts

Impaired Functional Status in Primary Sjögren's Syndrome

KATIE L. HACKETT,[1] JULIA L. NEWTON,[1] JAMES FRITH,[1] CHRIS ELLIOTT,[1] DENNIS LENDREM,[2] HEATHER FOGGO,[2] SUZANNE EDGAR,[2] SHERYL MITCHELL,[2] AND WAN-FAI NG[3]

Conclusion. Primary SS patients experience significant functional disability compared to age-matched healthy controls. Impaired function is associated with reduced quality of life and symptoms such as pain, fatigue, and depression, as well as disease activity, illustrating the importance of optimal management of all aspects of the disease.

Rheumatology 2009;48:1077–1082
Advance Access publication 24 June 2009
doi:10.1093/rheumatology/kep141

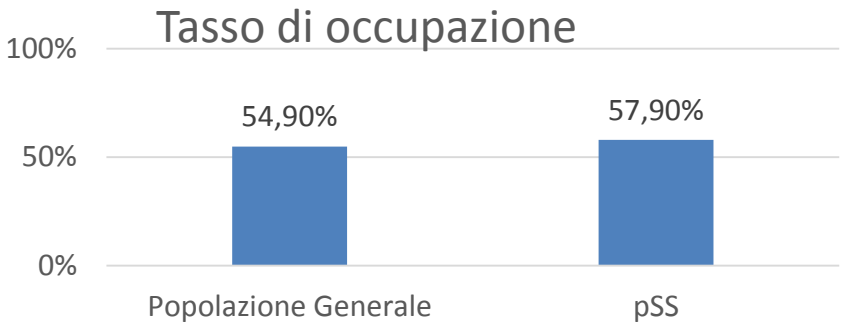
Health-related quality of life, employment and disability in patients with Sjögren's syndrome

235 pts

Jiska M. Meijer[1,*], Petra M. Meiners[1,*], James J. R. Huddleston Slater[1,2], Fred K. L. Spijkervet[1], Cees G. M. Kallenberg[3], Arjan Vissink[1] and Hendrika Bootsma[3]

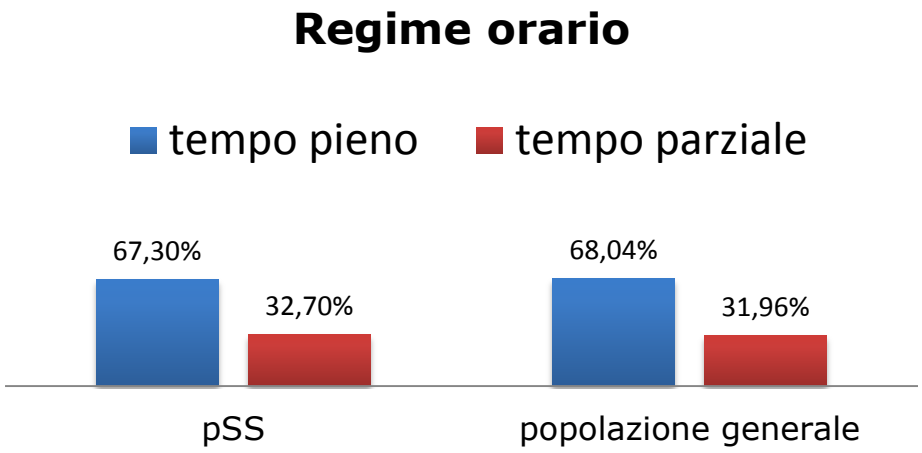
Conclusion. SS has a large impact on HR-QOL, employment and disability.

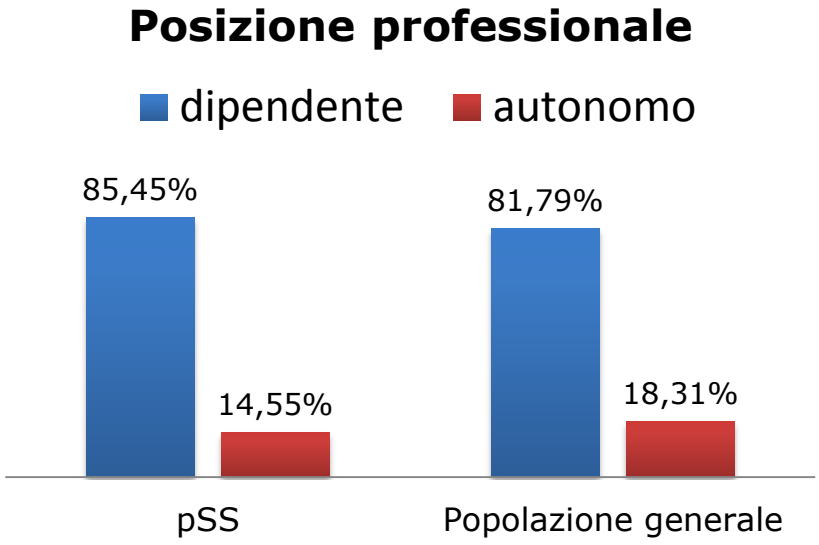
Sindrome di Sjögren: impatto sulla work disability



360 pts

Profilo occupazionale **sovrapponibile** a quello della popolazione generale.





Abstract EULAR 2016 del Gruppo SS-SIR

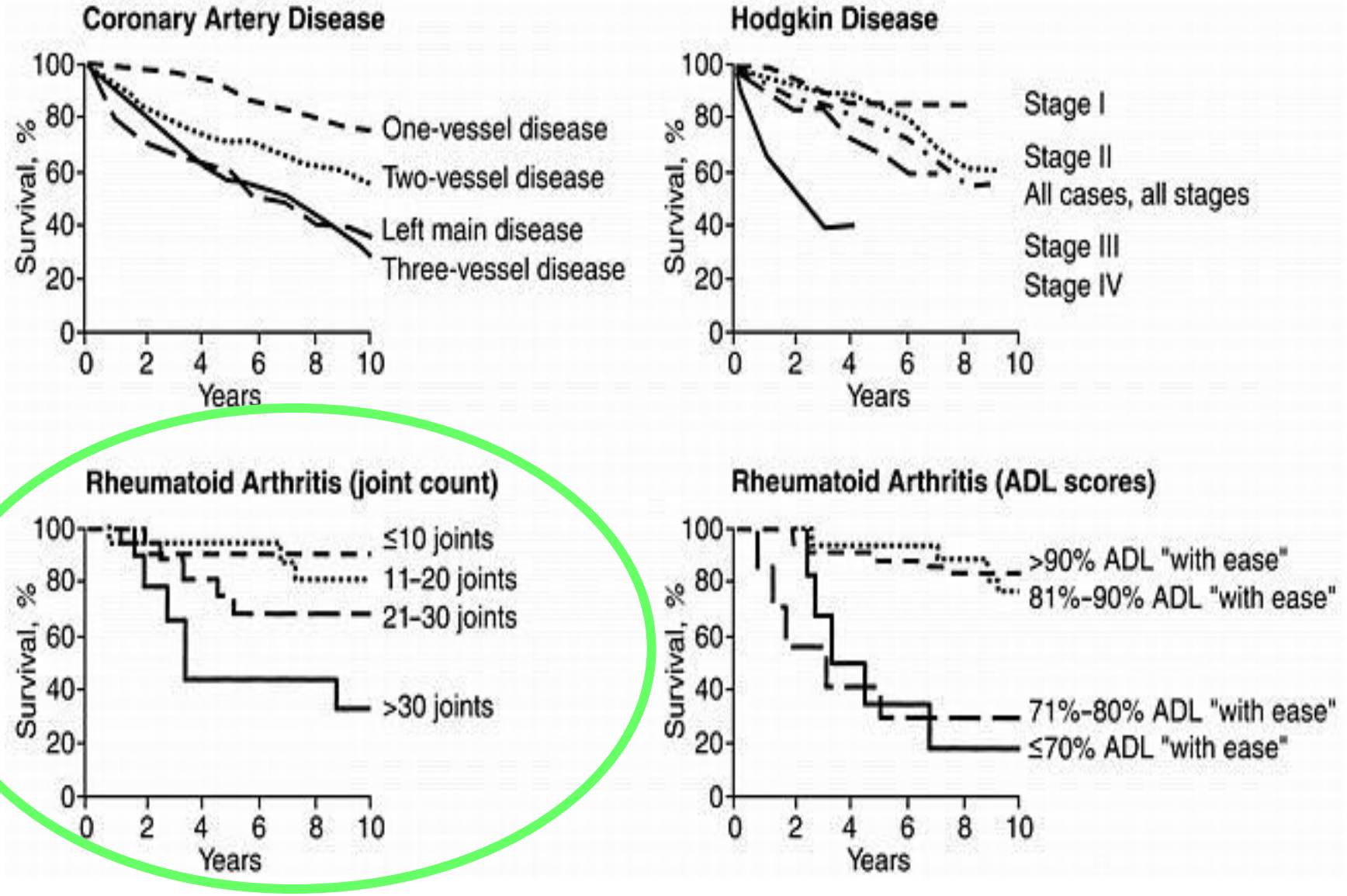
Sindrome di Sjögren: impatto sulla work disability

Disabilità Lavorativa	Media % (DS)
Assenteismo (%): media (DS)	6,7% (17)
Numero di ore perse per “salute” (DS)	2,4 (6,7)
Presenteismo (%): media (DS)	36,5 % (31)
OWI (%): media (DS)	39 % (33)
AI (%): media (DS)	51,5% (30)

Correlati a fatigue, dolore, FM

Abstract EULAR 2016 del Gruppo SS-SIR

ARTRITE REUMATOIDE: SOPRAVVIVENZA



Pincus T, Ann Intern Med, 1999

EXTENDED REPORT

Mapping and predicting mortality from systemic sclerosis

Muriel Elhai,[1] Christophe Meune,[2] Marouane Boubaya,[3] Jérôme Avouac,[1] Eric Hachulla,[4] Alexandra Balbir-Gurman,[5] Gabriela Riemekasten,[6] Paolo Airò,[7] Beatriz Joven,[8] Serena Vettori,[9] Franco Cozzi,[10] Susanne Ullman,[11] László Czirják,[12] Mohammed Tikly,[13] Ulf Müller-Ladner,[14] Paola Caramaschi,[15] Oliver Distler,[16] Florenzo Iannone,[17] Lidia P Ananieva,[18] Roger Hesselstrand,[19] Radim Becvar,[20] Armando Gabrielli,[21] Nemanja Damjanov,[22] Maria J Salvador,[23] Valeria Riccieri,[24] Carina Mihai,[25] Gabriella Szücs,[26] Ulrich A Walker,[27] Nicolas Hunzelmann,[28] Duska Martinovic,[29] Vanessa Smith,[30] Carolina de Souza Müller,[31] Carlo Maurizio Montecucco,[32] Daniela Opris,[33] Francesca Ingegnoli,[34] Panayiotis G Vlachoyiannopoulos,[35] Bojana Stamenkovic,[36] Edoardo Rosato,[37] Stefan Heitmann,[38] Jörg H W Distler,[39] Thierry Zenone,[40] Matthias Seidel,[41] Alessandra Vacca,[42] Ellen De Langhe,[43] Srdan Novak,[44] Maurizio Cutolo,[45] Luc Mouthon,[46] Jörg Henes,[47] Carlo Chizzolini,[48] Carlos Alberto von Mühlen,[49] Kamal Solanki,[50] Simona Rednic,[51] Lisa Stamp,[52] Branimir Anic,[53] Vera Ortiz Santamaria,[54] Maria De Santis,[55] Sule Yavuz,[56] Walter Alberto Sifuentes-Giraldo,[57] Emmanuel Chatelus,[58] Jiri Stork,[59] Jacob van Laar,[60] Esthela Loyo,[61] Paloma García de la Peña Lefebvre,[62] Kilian Eyerich,[63] Vanesa Cosentino,[64] Juan Jose Alegre-Sancho,[65] Otylia Kowal-Bielecka,[66] Grégoire Rey,[67] Marco Matucci-Cerinic,[68] Yannick Allanore,[1] on behalf of EUSTAR group

MALATTIE REUMATICHE IN ITALIA: COSTI

- **Osteoartrosi: 2170 euro/anno per paziente:**
  - 934 euro costi diretti (terapia medica, ausilii ospedalizzazione, procedure diagnostiche)
  - 1236 euro costi indiretti (36% per perdita di produttività lavorativa)

  (Leardini G et al. Clin Exp Rheumatol. 2004)

- **Artrite Reumatoide nelle diverse classi funzionali:**
  - da 1643.4 a 5696.8 euro **costi diretti** (visite mediche, trattamenti farmacologici e non, indagini strumentali, degenze in ospedale, degenze in unità di riabilitazione, interventi chirurgici)
  - da 2704.9 a 17249.2 euro **costi indiretti** (perdita di produttività lavorativa legata a malattia e pre-penzionamento)

  (Leardini G et al. Clin Exp Rheumatol. 2002)

Agenda

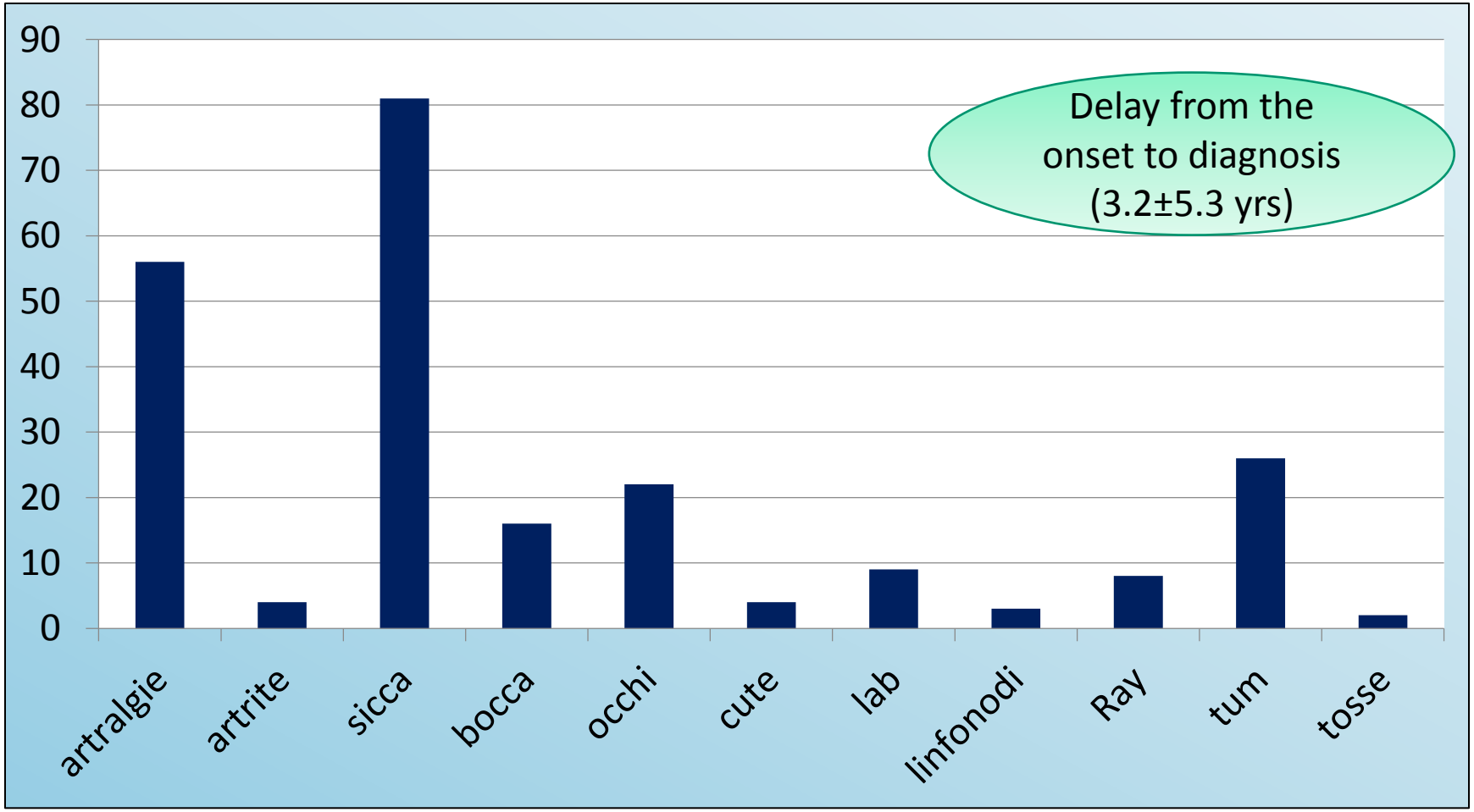
- Diagnosi precoce:
  - Razionale patogenetico
  - Razionale clinico
- L'esperienza delle Early Clinics e il ritardo diagnostico
- Prospettive future per la diagnosi precoce

L’esperienza delle Early Clinics: il ritardo diagnostico

- Rotterdam Early Arthritis CoHort:

Condizione	Ritardo diagnostico
Artrite Reumatoide	12 settimane
Artrite «acuta»	7 settimane
Artralgie infiammatorie	16 settimane

Sindrome di Sjögren: ritardo diagnostico



Ritardo diagnostico: possibili fattori

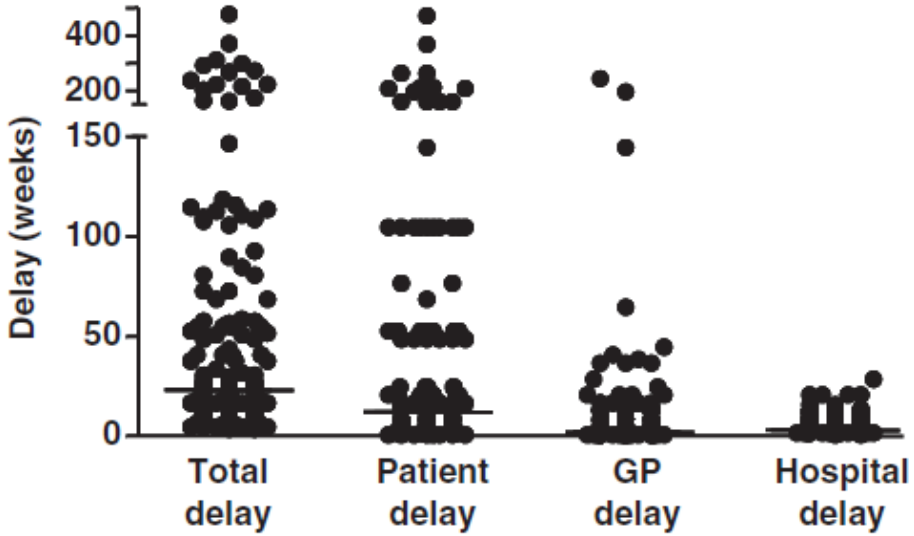
- Esordio «aspecifico»
- Esordio «atipico» e «eterogeneo»
- Criteri classificativi stringenti

Rheumatology 2007;46:1438–1440
Advance Access publication 18 June 2007
doi:10.1093/rheumatology/kem130

Concise Report

Delay in presentation to primary care physicians is the main reason why patients with rheumatoid arthritis are seen late by rheumatologists

K. Kumar[1,2], E. Daley[1], D. M. Carruthers[1], D. Situnayake[1], C. Gordon[1,2], K. Grindulis[1], C. D. Buckley[1,2], F. Khattak[1] and K. Raza[1,2]



Evoluzione delle UCTD

Durata di malattia> 1 year

91 UCTD
(M: 4 / F: 87)

1 UCTD persa al FU

26 (29%) EVOLUTE

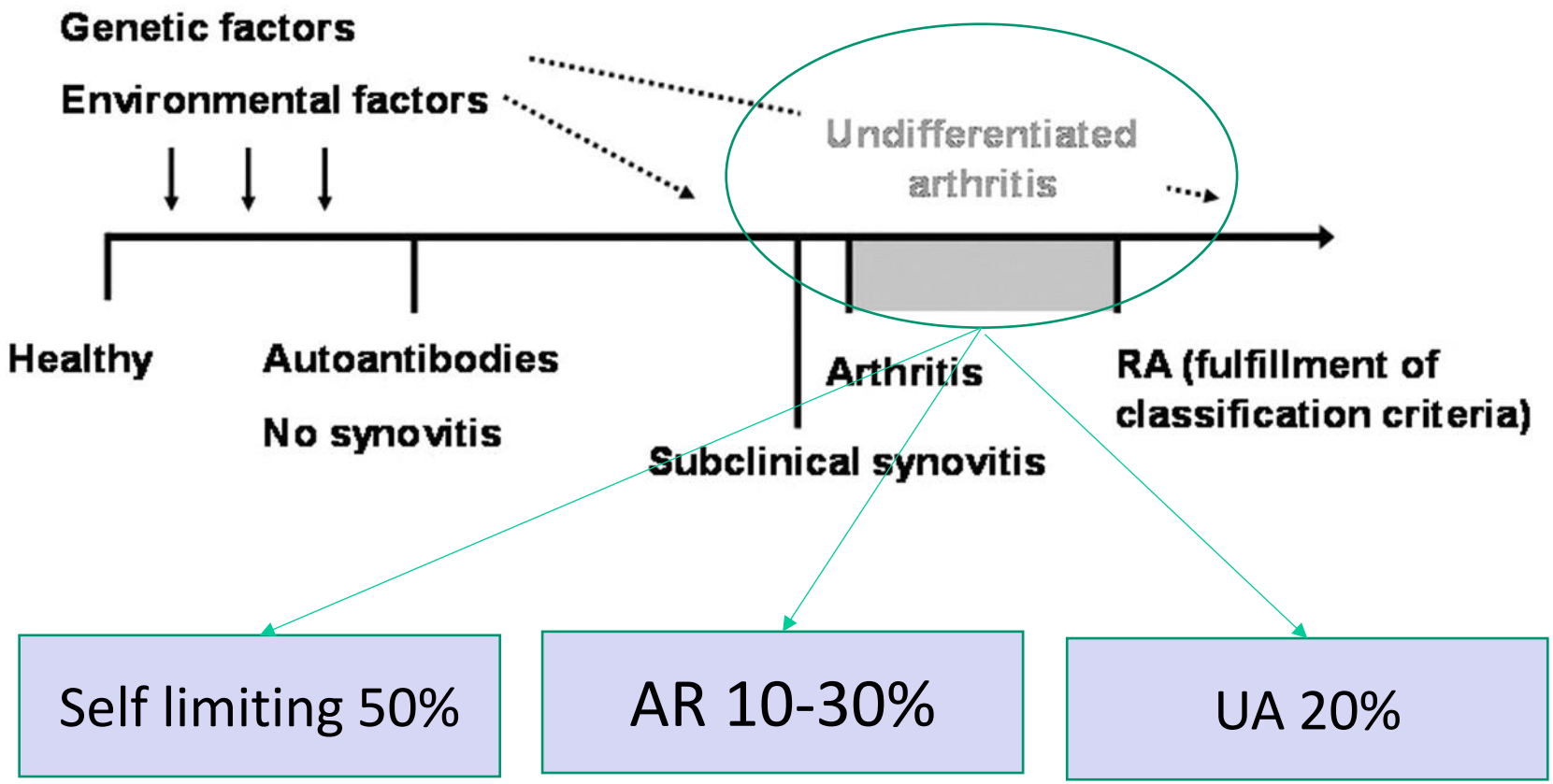
64 ‘STABILI’

22 LES
2 SS
1 RA
1 SSc

follow up medio 151.6 ± 77.4 mesi
follow up minimo: 3 anni

Mosca, Bombardieri. Lupus 1998, J Rheumatol 2002, unpublisehd data

Le artriti indifferenziate e il rischio di under e over-treatment



Ritardo diagnostico: possibili fattori

- Esordio «aspecifico»
- Esordio «atipico» ed «eterogeneo»
- Criteri classificativi stringenti

Esordio atipico o eterogeneo

EARLY DIAGNOSIS in SS

Early diagnosis of primary Sjögren's syndrome: EULAR-SS task force clinical recommendations

Pilar Brito-Zerón, Elke Theander, Chiara Baldini, Raphaèle Seror, Soledad Retamozo, Luca Quartuccio, Hendrika Bootsma, Simon J Bowman, Thomas Dörner, Jacques-Eric Gottenberg, Xavier Mariette, Stefano Bombardieri, Salvatore de Vita, Thomas Mandl, Wan-Fai Ng, Aike A. Kruize, Athanasios Tzioufas, Claudio Vitali, Jill Buyon, Peter Izmirly, Robert Fox, Manuel Ramos-Casals & on behalf of the EULAR Sjögren Syndrome Task Force

Journal Expert Review of Clinical Immunology
Volume 12, 2016 - Issue 2

Ritardo diagnostico: possibili fattori

- Esordio «aspecifico»
- Esordio «atipico» ed «eterogeneo»
- Criteri classificativi stringenti

2010 ACR/EULAR Rheumatoid Arthritis Classification Criteria

Arthritis Rheum 2010; 62 (9): 2569-2581

	Score
Popolazione obiettivo (chi deve essere testato?): pazienti che	
1. hanno almeno 1 articolazione con sinovite clinica sicura (tumefazione)*	
2. con sinovite non meglio spiegata da altra malattia†	
Criteri classificativi per AR (algoritmo a punteggio: sommare lo score delle categorie A-D); per classificare un paziente come AR definita è necessario un punteggio totale ≥6/*	
A. Coinvolgimento articolare‡	
1 grandi articolazioni§	0
2-10 grandi articolazioni	1
1-3 piccole articolazioni (con o senza coinvolgimento di grandi articolazioni)¶	2
4-10 piccole articolazioni (con o senza coinvolgimento di grandi articolazioni)	3
>10 articolazioni (almeno 1 piccola articolazione)**	5
B. Sierologia (è necessario almeno 1 test per la classificazione)††	
FR negativo e ACPA negativi	0
FR a basso titolo o ACPA a basso titolo	2
FR ad alto titolo o ACPA ad alto titolo	3
C. Reattanti di fase acuta (è necessario almeno 1 test per la classificazione)††	
PCR normale e VES normale	0
PCR elevata o VES elevata	1
D. Durata dei sintomi‡‡	
<6 settimane	0
≥6 settimane	1

"The need to better classify and diagnose Early and Very Early Rheumatoid Athritis"

Zeidler H. Journal of Rheum 2012; 39:212-217

How accurate is our standardized clinical assessment of synovitis?

Diagnosing early rheumatoid arthritis (RA). What are the problems and opportunities ?

H.R. Schumacher, F. Pessler, L.X. Chen

- There are concerns about the **reproducibility of the clinical assessment** of synovitis and even the **sensitivity of physical examination for the detection of mild synovitis**
- Recent ultrasound and MRI studies have demonstrated apparent synovitis not appreciated on physical examination

Clin Exp Rheumatol, 2003

L'esperienza delle Early Clinics: il ritardo diagnostico

ABSTRACT NUMBER: 2042

Referral Criteria to an Early Arthritis Clinic: Poor Agre between Referring Physicians and Rheumatologists

Filipa Farinha[1,2], Gisela Eugénio[2], Mary Marques[2], Francisco Freitas[3], José António P. da S
Cátia Duarte[2,4], [1]Rheumatology, Centro Hospitalar do Baixo Vouga, E.P.E., Aveiro, Portug
[2]Rheumatology, Centro Hospitalar e Universitário de Coimbra, Coimbra, Portugal, [3]Centr
Studies, Universidade de Coimbra, Coimbra, Portugal, [4]Faculty of Medicine, Universidade
Coimbra, Coimbra, Portugal

Meeting: 2017 ACR/ARHP Annual Meeting

Date of first publication: September 18, 2017

Keywords: Early Rheumatoid Arthritis, Referrals and inflammatory arthritis

Conclusion: Among the clinical criteria, there was poor agreement regarding the presence of arthritis and no significant agreement regarding the characterization of the arthralgia as inflammatory, the morning stiffness and the squeeze test. The weak performance of all sets of criteria in predicting inflammatory arthritis is probably due to deficient recognition of each criterium. These results suggest the need for improving education among the physicians referring patients to the EAC.

Diagnosing early rheumatoid arthritis (RA). What are the problems and opportunities ?

H.R. Schumacher, F. Pessler, L.X. Chen

How helpful are serologic and genetic tests?

1) Fattore Reumatoide
2) Anticorpi Anticitrullina

Clin Exp Rheumatol, 2003

Not all RF positive arthritides are RA!

- ***CH*** Chronic disease, esp hepatic and pulmonary
- ***R*** Rheumatoid arthritis
- ***O*** Other rheumatic diseases
  - SLE, Scl, MCTD,
  - Sjogrens (95%)
  - Polymyositis (10%)
  - Sarcoidosis
- ***N*** Neoplasms
- ***I*** Infections
  - AIDS, parasitic, SBE, TB, Viral
- ***C*** Cryoglobulinemia, esp Hepatitis C associated

CONCISE REPORT

Differences in the symptomatic phase preceding ACPA-positive and ACPA-negative RA: a longitudinal study in arthralgia during progression to clinical arthritis

Leonie E Burgers, Hanna W van Steenbergen, Robin M ten Brinck, Tom WJ Huizinga, Annette HM van der Helm-van Mil

DISCUSSION

This study identified phenotypic differences between ACPA-positive and ACPA-negative patients in the symptomatic phase preceding arthritis development. Initial symptoms in ACPA-negative patients were less often located in the lower extremities. At first presentation with arthralgia, ACPA-positive patients had less tender joints, less difficulty making a fist and longer symptom duration compared with ACPA-negative patients. However, ACPA-positive patients progressed to arthritis more rapidly. This study is the first showing that, in addition to the differences in underlying risk factors, there are also clinical differences in very early symptomatic disease phases. This suggests that ACPA-positive and ACPA-negative RA are intrinsically different.

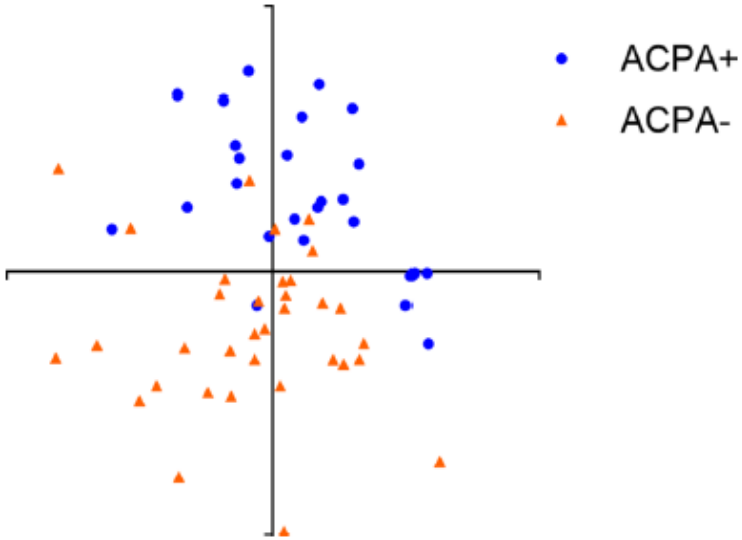


Figure 2 Clustering of anticitrullinated protein antibody (ACPA)-positive and ACPA-negative patients based on a partial least squares regression analysis that included only clinical information. Scores on

L'esperienza delle Early Clinics: il ritardo diagnostico

ABSTRACT NUMBER: 1819

Delay of Diagnosis and Treatment in Seronegative Rheumatoid Arthritis: Missing the Window of Opportunity

Caitrin Coffey[1], Cynthia S. Crowson[2], Elena Myasoedova[3], Eric L. Matteson[4] and John M. Davis III[5], [1]Internal Medicine, Mayo Clinic, Rochester, MN, [2]Health Sciences Research, Mayo Clinic College of Medicine and Science, Rochester, MN, [3]Rheumatology, Mayo Clinic, Rochester, MN, [4]Rheumatology, Mayo Clinic College of Medicine and Science, Rochester, MN, [5]Division of Rheumatology, Mayo Clinic, Rochester, MN

Meeting: 2017 ACR/ARHP Annual Meeting

Date of first publication: September 18, 2017

Keywords: diagnostic criteria and rheumatoid arthritis (RA), Rheumatoid Factor

Results:

156 patients were included; 113 were seropositive and 43 seronegative. Age, sex, smoking status, and obesity did not differ between groups. Median time from first documented joint swelling to fulfillment of the 1987 (100 vs. 3 days, p=0.003) and 2010 (58 vs. 0 days, p=0.011) criteria was significantly longer in seronegative than seropositive patients. The median time from first documented joint swelling to first DMARD was also significantly longer in seronegative patients (129.5 vs. 16 days, p=0.003). Methotrexate was the first DMARD for 97 patients (62%), with no significant differences between groups.

Agenda

- Diagnosi precoce:
  - Razionale patogenetico
  - Razionale clinico
- L'esperienza delle Early Clinics e il ritardo diagnostico
- Prospettive future per la diagnosi precoce
  - Red flags
  - Nuovi biomarkers

Curr Rheumatol Rep (2017) 19: 65
DOI 10.1007/s11926-017-0684-2

SCLERODERMA (J VARGA, SECTION EDITOR)

Very Early Systemic Sclerosis and Pre-systemic Sclerosis: Definition, Recognition, Clinical Relevance and Future Directions

Silvia Bellando-Randone[1,2] · Marco Matucci-Cerinic[1,2]

EXTENDED REPORT

Preliminary analysis of the Very Early Diagnosis of Systemic Sclerosis (VEDOSS) EUSTAR multicentre study: evidence for puffy fingers as a pivotal sign for suspicion of systemic sclerosis

Tünde Minier,[1] Serena Guiducci,[2] Silvia Bellando-Randone,[2] Cosimo Bruni,[2] Gemma Lepri,[2] László Czirják,[1] Oliver Distler,[3] Ulrich A Walker,[4] Jaap Fransen,[5] Yannick Allanore,[6] Christopher Denton,[7] Maurizio Cutolo,[8] Alan Tyndall,[4] Ulf Müller-Ladner,[9] Marco Matucci-Cerinic,[2] and the EUSTAR co-workers

Very early diagnosis of SSc-VEDOSS:

Criteria to trigger early referral

VEDOSS red flags

1. Raynaud's phenomenon

2. Puffy fingers

3. Positive antinuclear antibodies

Avouac J, *et al. Ann Rheum Dis* 2011; 70:476-81.

ARD

The challenge of early systemic sclerosis for the EULAR Scleroderma Trial and Research group (EUSTAR) community. It is time to cut the Gordian knot and develop a prevention or rescue strategy

M Matucci-Cerinic, Y Allanore, L Czirják, A Tyndall, U Müller-Ladner, C Denton, G Valentini, O Distler, K Fligelstone, A Tyrrel-Kennedy, D Farge, O Kowal-Bielecka, F van den Hoogen, M Cutolo, P D Sampaio-Barros, P Nash, K Takehara and D E Furst

Ann Rheum Dis 2009;68;1377-1380
doi:10.1136/ard.2008.106302

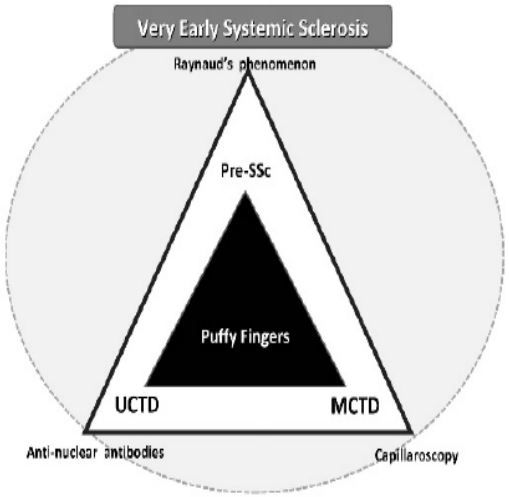


Figure 1 The three main diseases—undifferentiated connective tissue disease (UCTD), mixed connective tissue disease (MCTD) and prescleroderma—and the main early signs and symptoms—Raynaud phenomenon, antibodies positivity and capillaroscopic abnormalities—are presented in two overlapping "triangles" in a composite pyramid whose key to very early SSc still needs to be identified. Puffy fingers are presented in the centre of the black pyramid as a sign present in MCTD, UCTD and prescleroderma.

autoantibodies and SSc capillaroscopic pattern. From a clinical point of view, SSc can develop from "prescleroderma", MCTD,

Box 1 Preliminary criteria, still to be validated, for the very early diagnosis of systemic sclerosis (SSc)*

- **Major criteria**
  - Raynaud's phenomenon
  - antibodies (antinuclear, anticentromere, antitopoisomerase I)
  - diagnostic nailfold videocapillaroscopy
- **Additional criteria**
  - calcinosis
  - puffy fingers
  - digital ulcers
  - dysfunction of the oesophageal sphincter
  - telangiectasia
  - ground glass at chest high-resolution computed tomography

*Provisional criteria for the diagnosis of very early systemic sclerosis proposed by EULAR Scleroderma Trial and Research group (EUSTAR) (to be validated through a Delphi Technique) Diagnosis will be achieved when at least three major criteria are satisfied or two major plus one additional criteria are satisfied

Ann Rheum Dis. 2013 Nov;72(11):1747-55. doi: 10.1136/annrheumdis-2013-204424.

2013 classification criteria for systemic sclerosis: an American college of rheumatology/European league against rheumatism collaborative initiative.

Table 1 The American College of Rheumatology/European League Against Rheumatism criteria for the classification of systemic sclerosis*

Item	Sub-item(s)	Weight/ score†
Skin thickening of the fingers of both hands extending proximal to the metacarpophalangeal joints *(sufficient criterion)*	–	9
Skin thickening of the fingers *(only count the higher score)*	Puffy fingers	2
	Sclerodactyly of the fingers (distal to the metacarpophalangeal joints but proximal to the proximal interphalangeal joints)	4
Fingertip lesions *(only count the higher score)*	Digital tip ulcers	2
	Fingertip pitting scars	3
Telangiectasia	–	2
Abnormal nailfold capillaries	–	2
Pulmonary arterial hypertension and/or interstitial lung disease *(maximum score is 2)*	Pulmonary arterial hypertension	2
	Interstitial lung disease	2
Raynaud's phenomenon	–	3
SSc-related autoantibodies (anticentromere, anti–topoisomerase I [anti–Scl-70], anti–RNA polymerase III) *(maximum score is 3)*	Anticentromere	3
	Anti–topoisomerase I	
	Anti–RNA polymerase III	

*These criteria are applicable to any patient considered for inclusion in a systemic sclerosis study. The criteria are not applicable to patients with skin thickening sparing the fingers or to patients who have a scleroderma-like disorder that better explains their manifestations (eg, nephrogenic sclerosing fibrosis, generalised morphea, eosinophilic fasciitis, scleredema diabeticorum, scleromyxedema, erythromyalgia, porphyria, lichen sclerosis, graft-versus-host disease, diabetic cheiroarthropathy).
†The total score is determined by adding the maximum weight (score) in each category. Patients witha total score of ≥9 are classified as having definite systemic sclerosis.
SSc, systemic sclerosis.

Score ≥ 9 Sclerosi sistemica

Agenda

- Diagnosi precoce:
  - Razionale patogenetico
  - Razionale clinico
- L'esperienza delle Early Clinics e il ritardo diagnostico
- Prospettive future per la diagnosi precoce
  - Red flags
  - Nuovi biomarkers

La biopsia sinoviale può essere considerata un nuovo biomarcatore precoce di malattia?

- Le biopsie possono aiutare a identificare fattori prognostici o di risposta terapeutica.

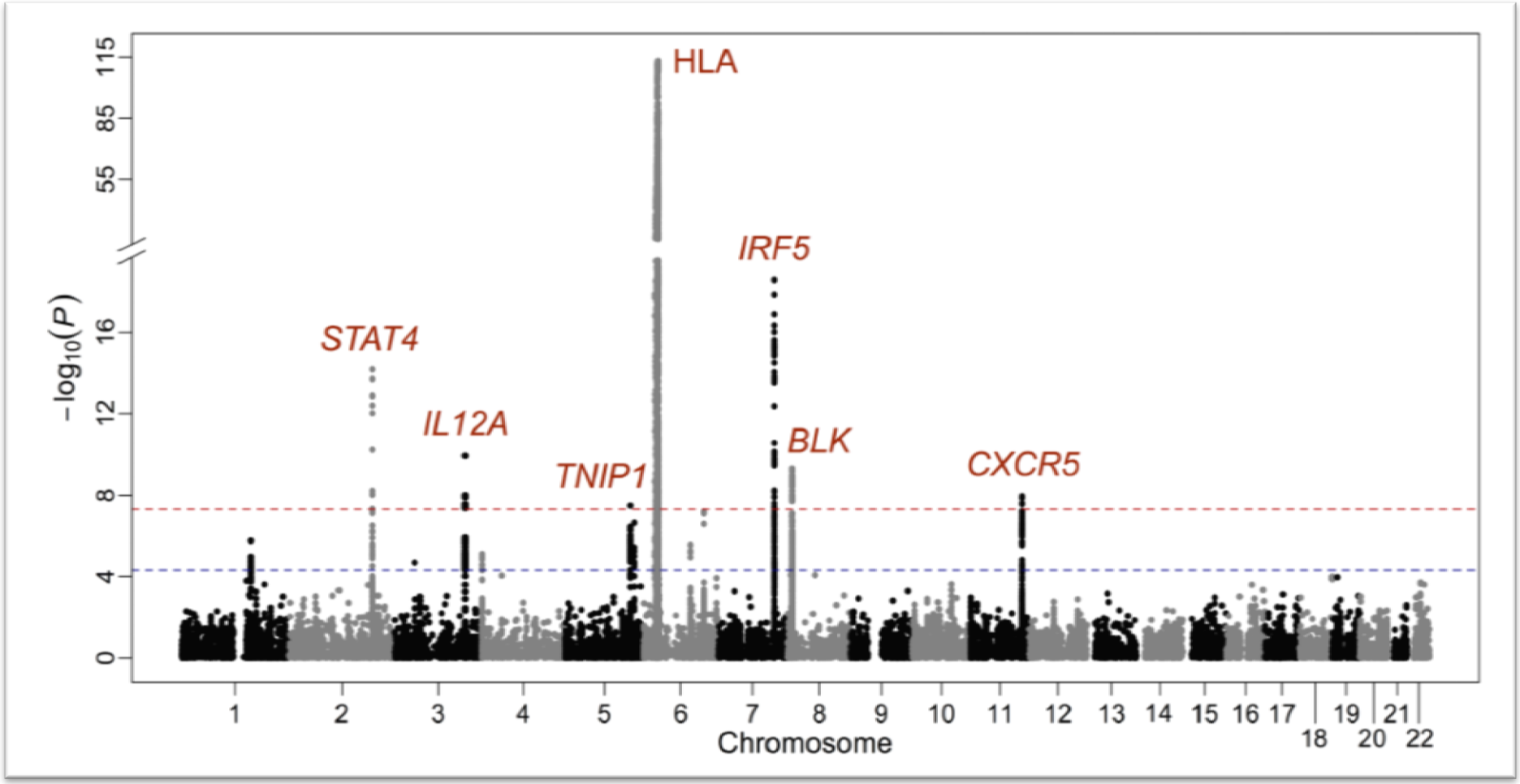
RESEARCH ARTICLE

Stromal cell markers are differentially expressed in the synovial tissue of patients with early arthritis

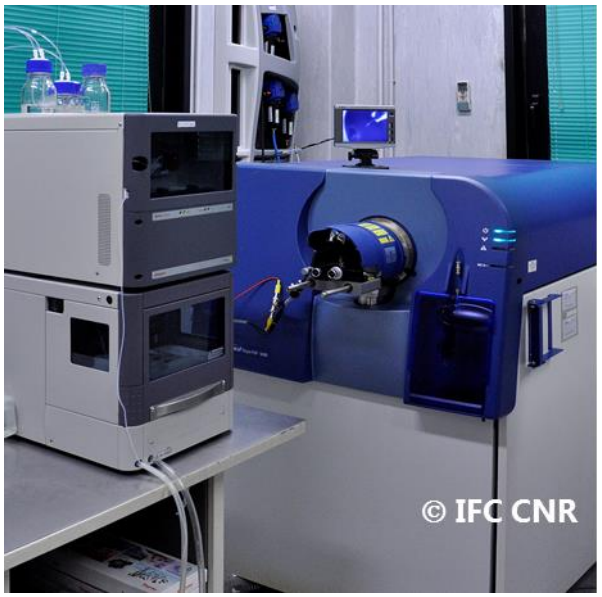
Ivy Y. Choi[1☯], Olga N. Karpus[2☯], Jason D. Turner[3], Debbie Hardie[3], Jennifer L. Marshall[3], Maria J. H. de Hair[1], Karen I. Maijer[1], Paul P. Tak[1¤a¤b], Karim Raza[3,4], Jörg Hamann[2], Christopher D. Buckley[3], Danielle M. Gerlag[1¤c‡*], Andrew Filer[3,5‡*]

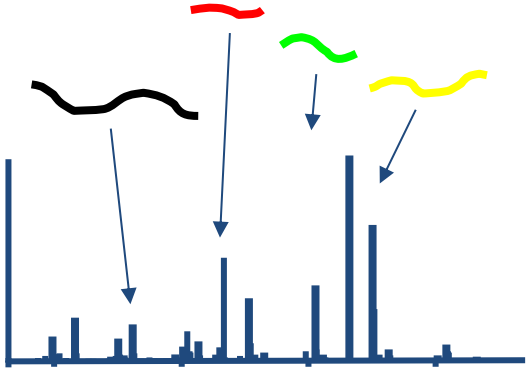
PLOS One , 2017

Nuovi biomarkers: Genomici



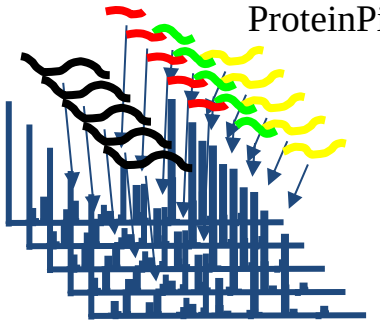
Nuovi biomarkers: Proteomica salivare





m/z vs intensity SPECTRA

ProteinPilot™

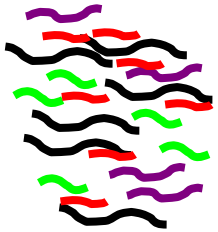


MS/MS

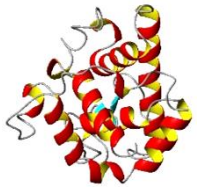
Depletion

Trypsin Digestion

nanoLC-MS Proteomic Analysis

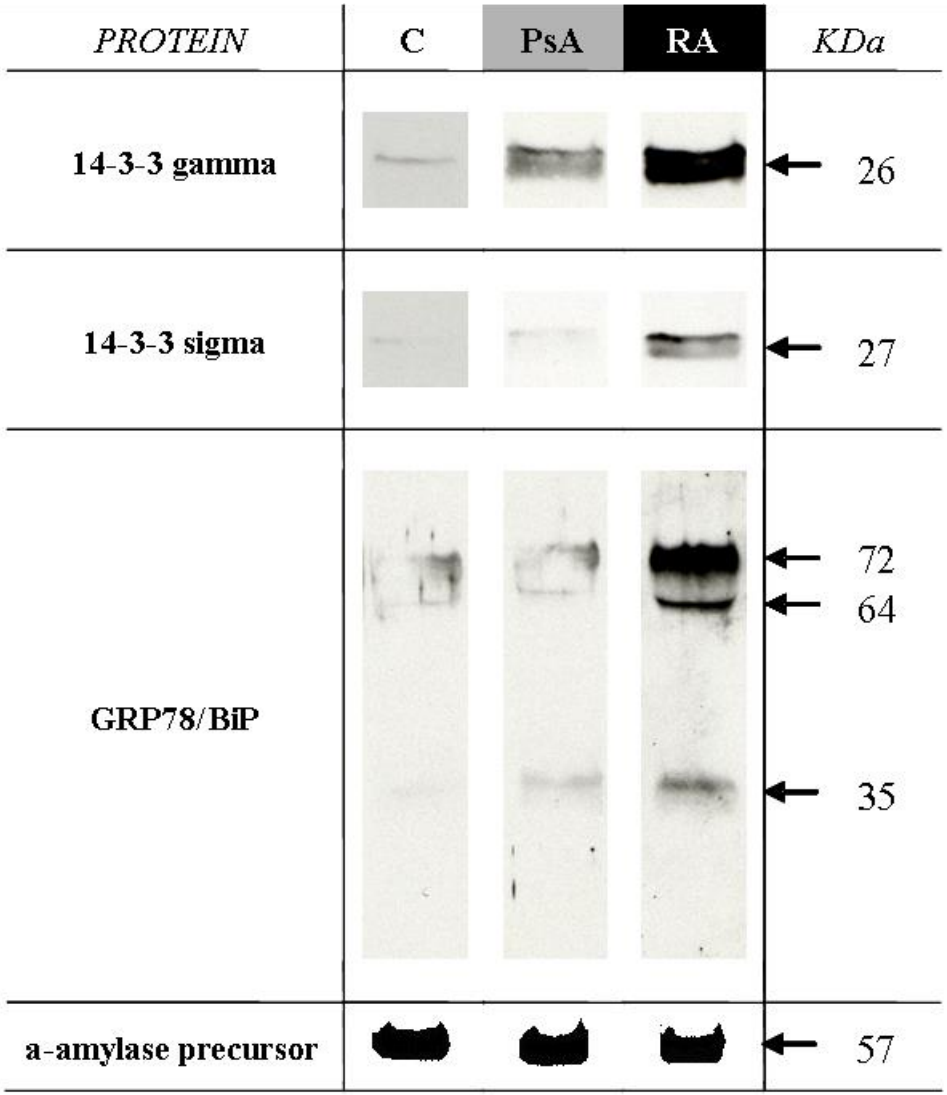


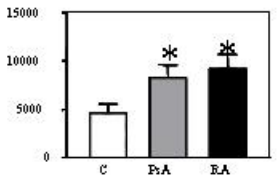
Peptide ions

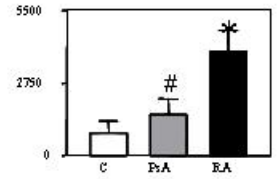


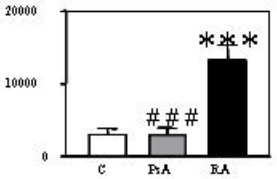
Protein identification

Rheumatoid Arthritis









	20
	15 F, 5 M
	57.6 ± 11
s)	9.5 ± 6
	RF+ 74% aCCP+ 70%

Baldini C. et al Journal Clin Prot 2008

Conclusioni