

La main sclérodermique

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Inserm

Institut national
de la santé et de la recherche médicale



Groupement d'hôpitaux Paris Centre

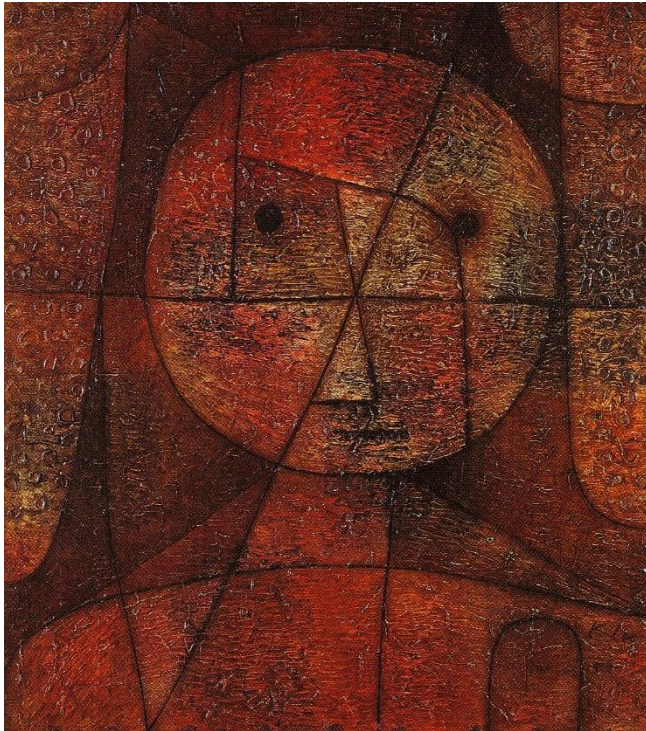


Conflicts of interest

- Consultant: **Actelion, CSL Behring, Cytheris, GSK, LFB Biotechnologies, Lilly, Pfizer**
 - Financial support to ARMIIC
- Investigator: **Actelion, CSL Behring, Pfizer**
- Financial support (grants): **Actelion, CSL Behring, GSK, LFB Biotechnologies, Pfizer**

Paul Klee : 1879-1940 (I)

Paul Klee
(1879-1940)



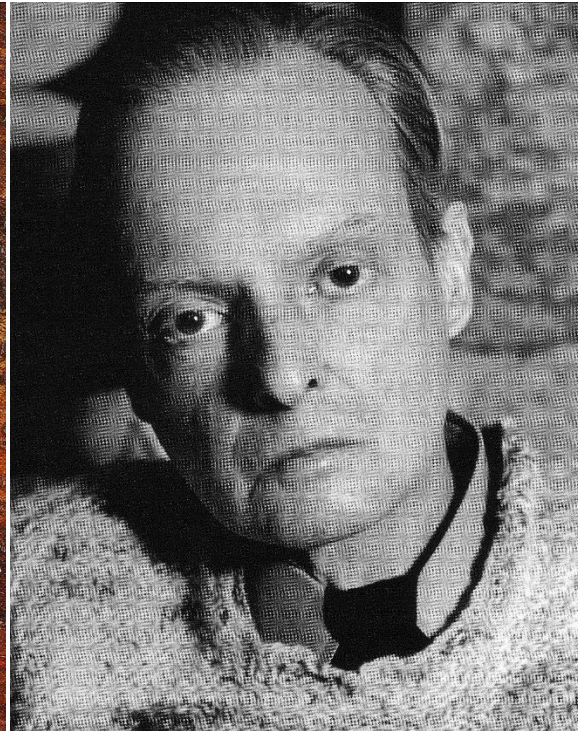
1933 Raynaud's
phenomenon

1934 Fatigue,
dyspnea,
thickened skin

1936 Extension of
skin fibrosis

1940 Hospitalisation
at Sant' Agnes,
Locarno
(worsening of
dyspnea)

Died in June 1940



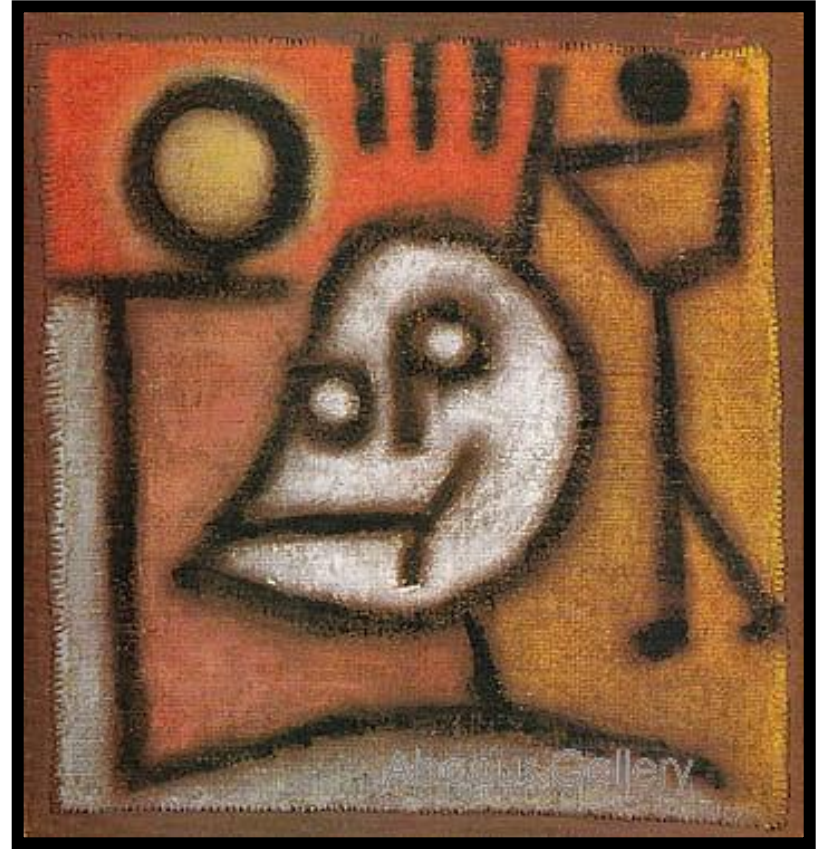
Gezeichnet 1935

„portant la marque de la mort“

Paul Klee: 1879-1940



Mask – 1921



Death and Fire – 1940

Paul Klee Polyphonies, Cité de la *musique*, Paris
18 October 2011 – 15 January 2012

Atteinte de la main dans la sclérodermie systémique

- Atteinte de la main fréquente, précoce et très utile pour poser le diagnostic de ScS
- Atteinte vasculaire
- Atteinte cutanée
- Atteinte articulaire
- La prise en charge doit être globale: pharmacologique et non pharmacologique.

2013 classification criteria for SSc: an ACR/EULAR collaborative initiative (I)

- Skin thickening of the fingers extending proximal to the metacarpophalangeal joints: SSc;
- If that is not present, 7 additive items apply:
 - skin thickening of the fingers,
 - fingertip lesions,
 - telangiectasia,
 - abnormal nailfold capillaries,
 - interstitial lung disease or pulmonary arterial hypertension,
 - Raynaud's phenomenon,
 - SSc-related autoantibodies.

Skin thickening of the fingers (I)



Score = 2

Puffy fingers

Only count higher score

Skin thickening of the fingers (II)



Sclerodactily

Score = 4

Only count higher score



fingertip lesions

Digital ulcers

Score = 2



Fingertip pitting scars

Score = 3



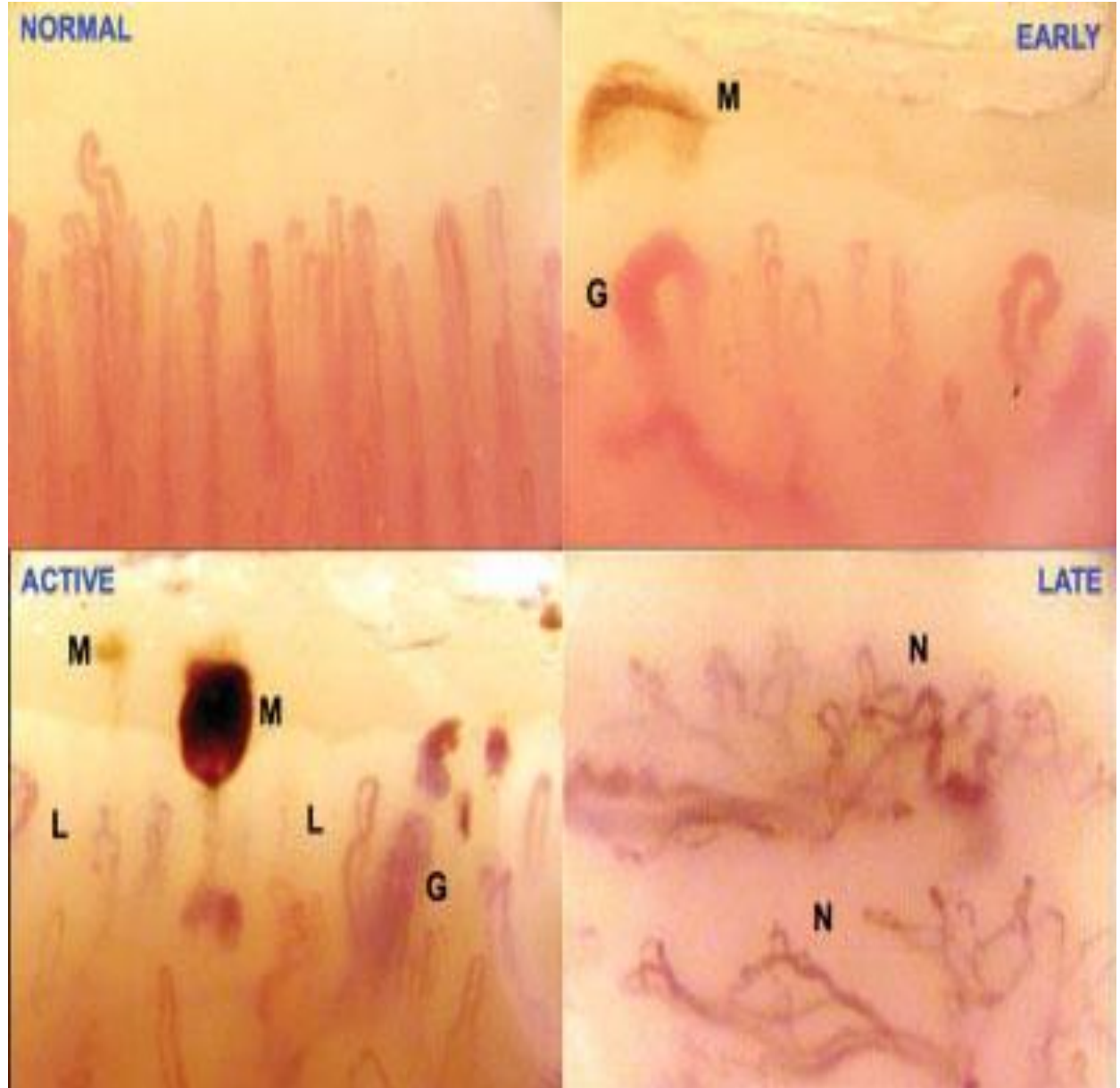
Only count higher score

telangiectasia



Score = 2

Abnormal nailfold capillaries



Score =

Raynaud's phenomenon



Score = 3

Hand involvement in systemic sclerosis

- Three consecutive phases
 - Oedematous phase, particularly in diffuse SSc.
 - Sclerotic phase: oedematous areas transform to plaques.
 - Atrophic phase: the skin gets atrophic and deformations increase.

Sclerotic phase



Atrophic phase



Juvenile systemic sclerosis: atrophic phase



Hand involvement in systemic sclerosis

- Skin involvement
- Sub-cutaneous tissues
- Joint and periarticular involvement
- Bone involvement
- Tendon involvement
- Muscle involvement
- Vascular involvement
- Peripheral nervous system

Skin and musculoskeletal complications: Diffuse versus limited disease

	dcSSc	lcSSc	dcSSc vs. lcSSc
RP	96%	96%	0.58
Digital ulcers	43%	33%	< 0.001
Synovitis	21%	14%	< 0.001
Contractures	47%	24%	< 0.001
Friction rubs	22%	7%	< 0.001
Muscle weakness	37%	23%	< 0.001
CK elevation	11%	4%	< 0.001

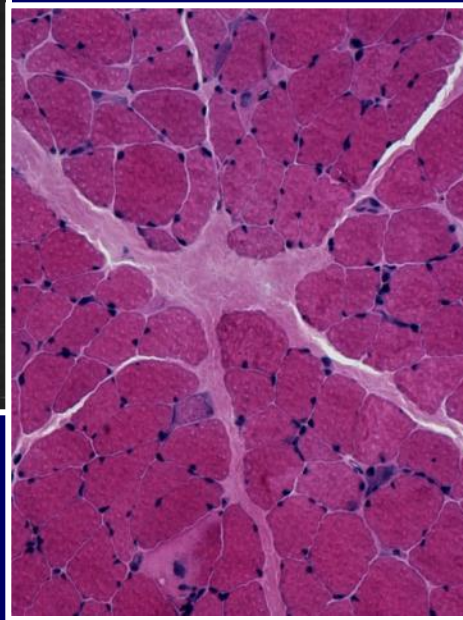
Hypertrophy of the nail cuticle



Systemic sclerosis: depigmentation



Musculoskeletal manifestations of SSc

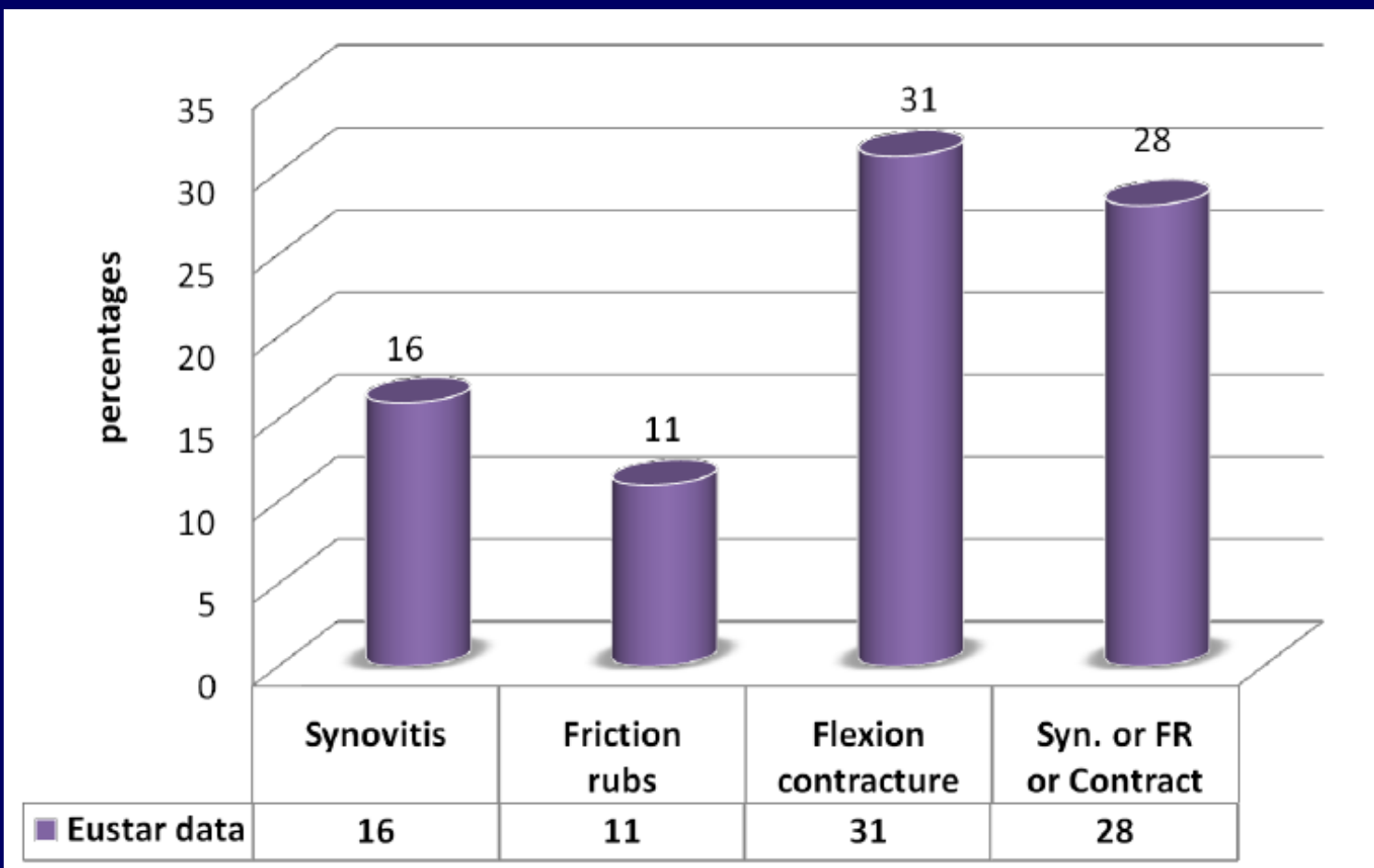


- A major cause of morbidity and disability in SSc
- Includes
 - Muscle involvement (inflammatory myopathy)
 - Arthralgias
 - Arthritis
 - Flexion contractures
 - Nerve entrapment

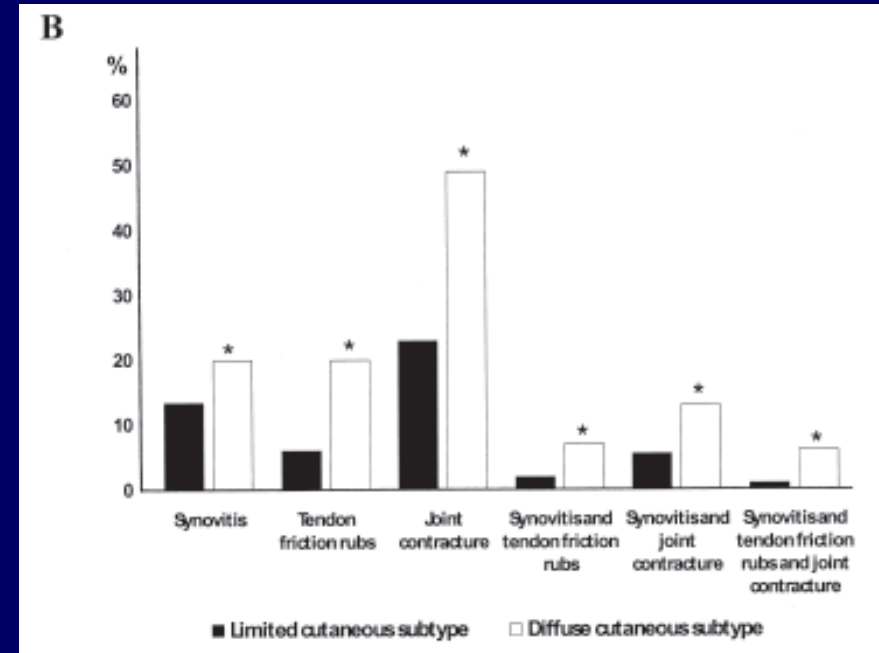
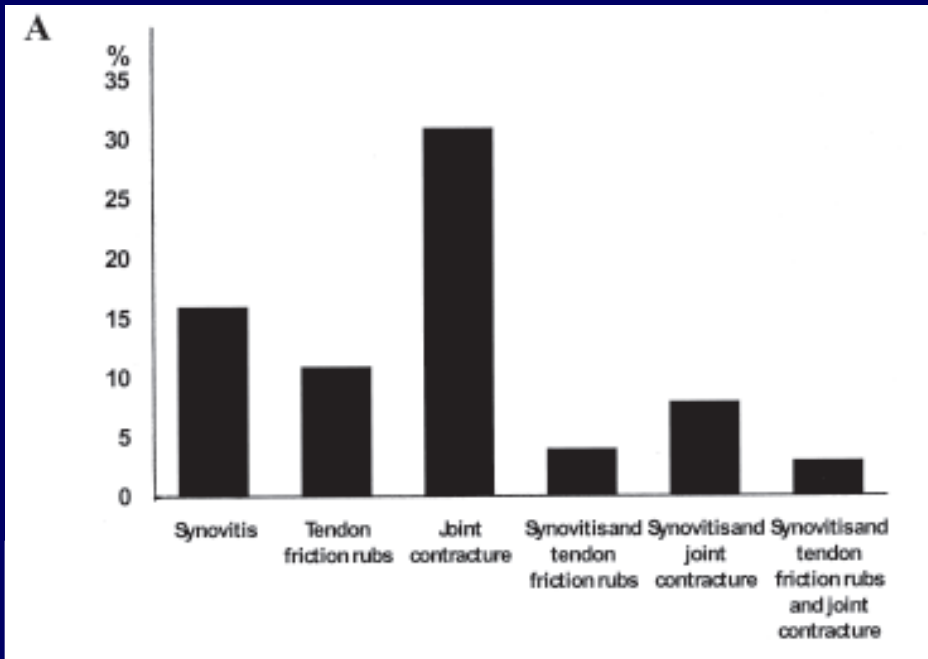
Joint and tendon involvement predict disease progression in systemic sclerosis: a EUSTAR prospective study.

Baseline characteristics	Univariate analysis		Multivariate analysis	
	<i>P-value</i>	Hazard ratio (95% CI)	<i>P-value</i>	Hazard ratio (95% CI)
Joint synovitis (n=234)	0.0001	1.43 (1.17-1.74)	0.04	1.26 (1.01-1.59)
Tendon friction rubs (n=166)	<0.0001	1.61 (1.29-2.01)	0.03	1.32 (1.03-1.70)
Diffuse cutaneous subset (n=500)	<0.0001	1.58 (1.33-1.88)	0.01	1.30 (1.05-1.61)
mRSS >14 (n=382)	<0.0001	1.54 (1.29-1.82)	_*	-
Positive scl70 antibodies (n=457)	<0.0001	1.48 (1.25-1.75)	0.03	1.25 (1.02-1.53)
Increased CK levels (n=147)	0.01	1.35 (1.06-1.72)	0.7	1.06 (0.79-1.41)
Muscle weakness (n=330)	0.006	1.30 (1.08-1.57)	0.6	1.07 (0.86-1.34)
FVC <75% predicted (n=305)	0.0001	1.46 (1.22-1.76)	0.07	1.22 (0.98-1.50)

Characteristics of joint involvement and relationships with systemic inflammation in systemic sclerosis: results from the EULAR Scleroderma Trial and Research Group (EUSTAR) database.



Prevalence of joint involvement in patients with SSc.



Radiological hand involvement in systemic sclerosis

- 120 consecutive SSc patients
- Radiological abnormalities in SSc:
 - Erosion (21%)
 - Joint space narrowing (28%)
 - Arthritis (erosion and joint space narrowing) (18%)
 - Demineralisation (23%)
 - Acro-osteolysis (22%)
 - Flexion contracture (27%)
 - Calcinosis (23%)

Calcinosis: major disability



Calcinosis: spontaneous elimination



Tendon friction rubs (TFR)

- Detected by physical examination
- Highly associated with dcSSc
 - 91% of patients with TFR classified as dcSSc
- **Associated with poor prognosis**
 - e.g. scleroderma renal crisis
- May aid early diagnosis of dcSSc and identification of patients at high risk for serious organ-based complications

Flexion contractures

- **Common, especially in hands**
 - **MCP, PIP, DIP joints and wrists**
- **Often related to skin, fascia and tendon involvement**
- **Responsible for functional disability**
- **May favour digital ulcerations**



Nerve entrapment

- **Carpal tunnel syndrome**
 - **Patients with early SSc are likely to develop median nerve entrapment secondary to oedema and inflammation**
 - **Often settles spontaneously**
- **Ulnar nerve entrapment**
- **Brachial plexopathy**

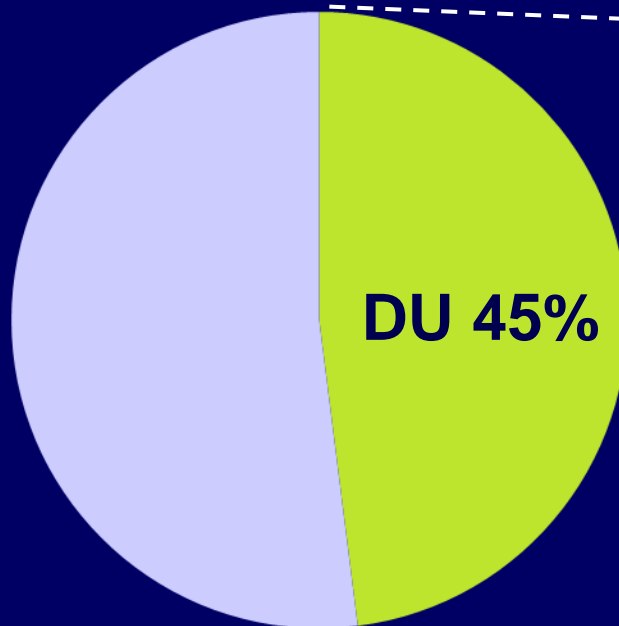
Pope JE, *Rheum Dis Clin North Am* 2003; 29:391-408.

Mouthon L, *et al. Rheumatology* 2000; 39:682-3.

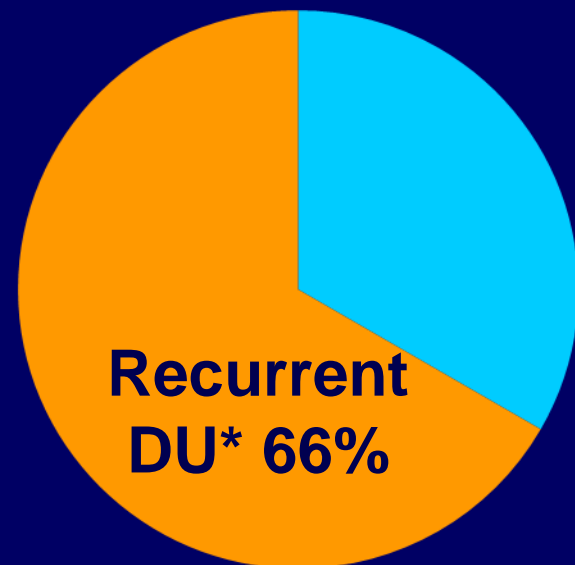
Mouthon L, *et al. Ann Med Intern* 2000; 151:303-5.

DU are a common and recurrent manifestation of SSc

All SSc patients
($n = 101$)

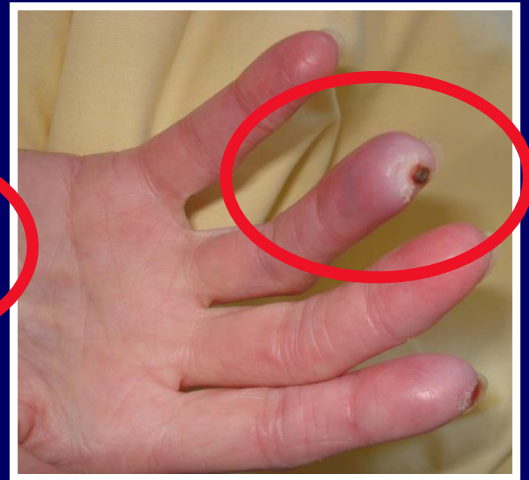


Patients with DU
($n = 44$)

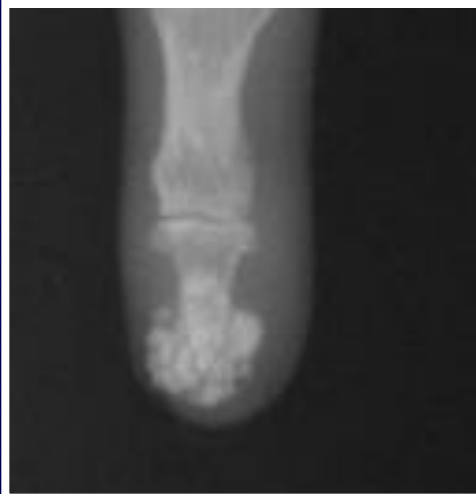
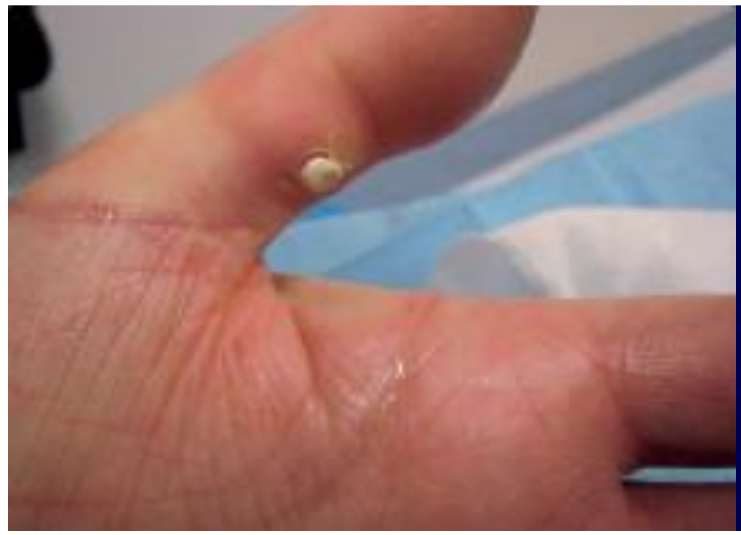


*Recurrent DU: Having more than one DU after the first DU

Digital ulcers: Vascular mechanisms



Calcinosis/mechanical



IMPACT OF DIGITAL ULCERS IN SYSTEMIC SCLEROSIS



**Infection
Gangrene
Amputation**



**Disability
Pain
Loss of function**

Digital ulcers: Infection

- ◆ 1/3 infections
- ◆ 10% osteomyelitis
- ◆ Delayed healing++++



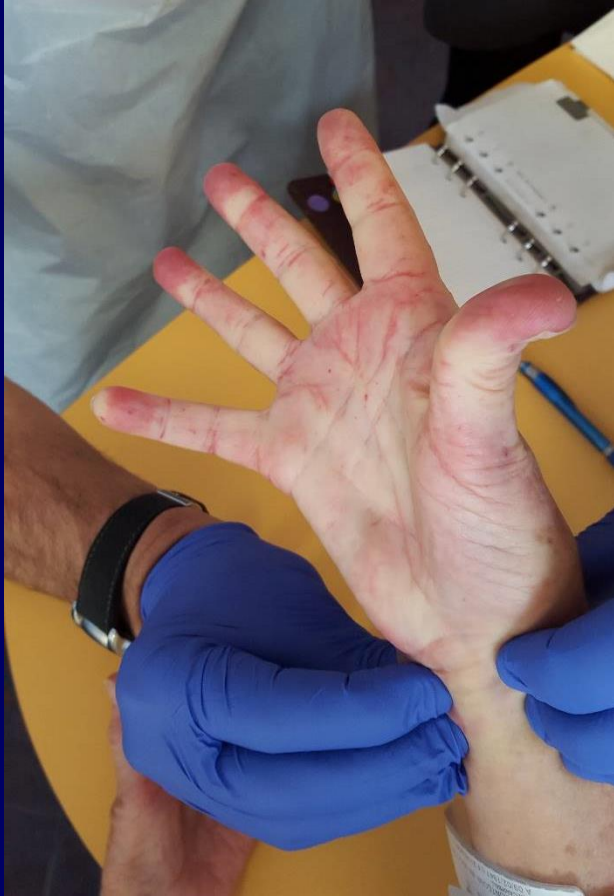
Hachulla E, et al. *J Rheum* 2007; 34:2423-30.
Nihtyanova SI, et al. *Ann Rheum Dis* 2008; 67:120-3.

Digital necrosis/gangrene



—————> Perform arterial doppler

Ulnar artery stenosis



Cochin hand function scale (CHFS)

Without the help of adapted instruments, in the past two weeks, did you:

- ◆ **Categories for assessment**



- ◆ **The scale is based on the following answer scores**

0 = Yes , without difficulty

1 = Yes, with a little difficulty

2 = Yes, with some difficulty

3 = Yes, with much difficulty

4 = Nearly impossible to do

5 = Impossible

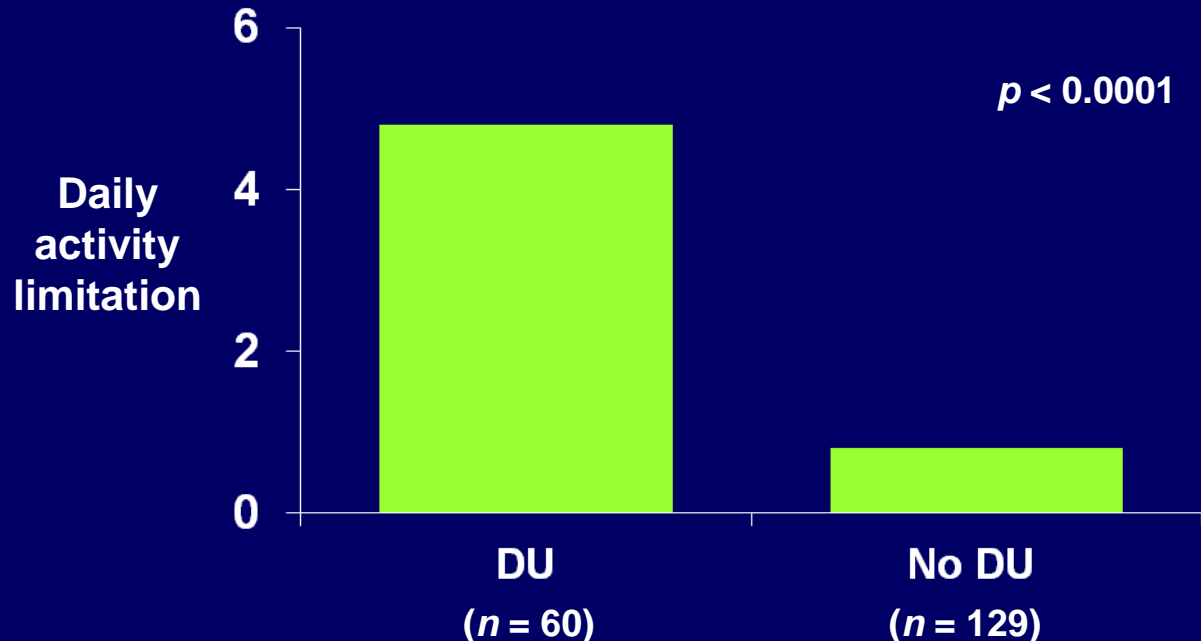
Hand disability contribute to 75 % of the variance of the HAQ in SSc

Duruöz MT, et al. *J Rheumatol* 1996

Rannou et al *Arthritis Rheum.* 2007.

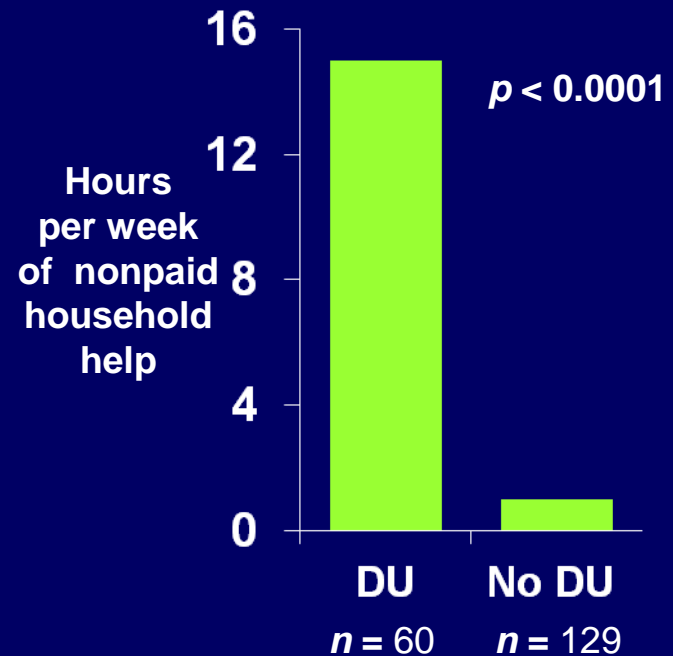
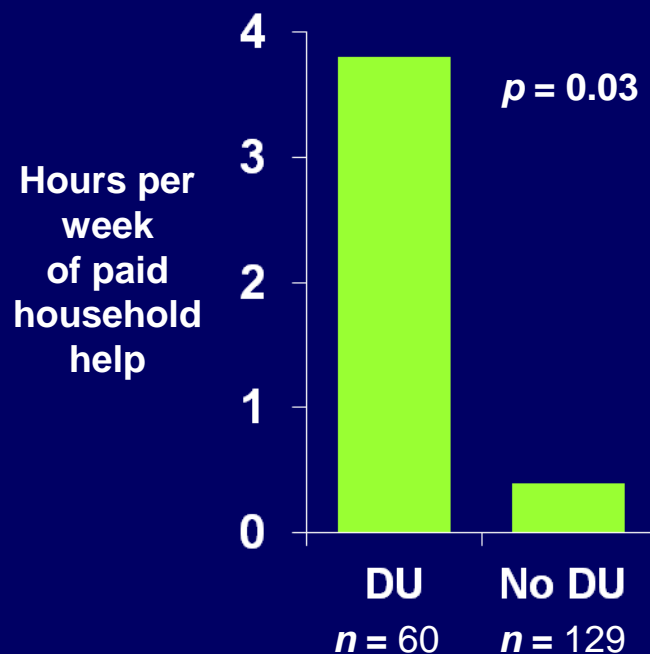
Digital ulcers influence daily living activities

- Daily activity is measured on a scale of 0-10, with 0 being no limitation and 10 being major limitations; $n = 189$



Digital ulcers influence ability to perform household tasks

- Due to the inability to perform household tasks, patients with DU seek help in the form of paid or unpaid labour



Management of DU: Multidisciplinary approach

Prevention of complications
Including patient education

Pharmacological treatment
Prevention of new DU
Healing pre-existing DU

Antibiotics

Pain relief

Non-pharmacological
treatment: rehabilitation



Local treatment
& wound care

→ Surgery
only when necessary

Prophylactic measures

A. Cold

- Reduce cold exposure by wearing long and warm clothes, mittens
- Reduce professional cold exposure

B. Drugs

C. Vasoconstrictive agents

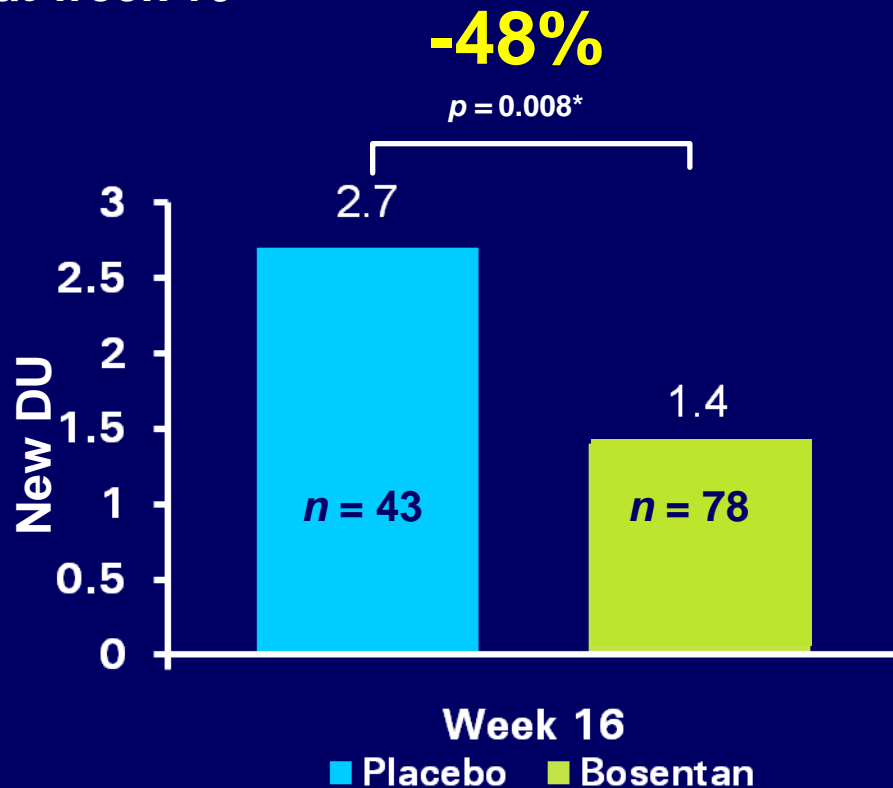
- Withdrawal of tobacco, cannabis, cocaine

D. Injuries

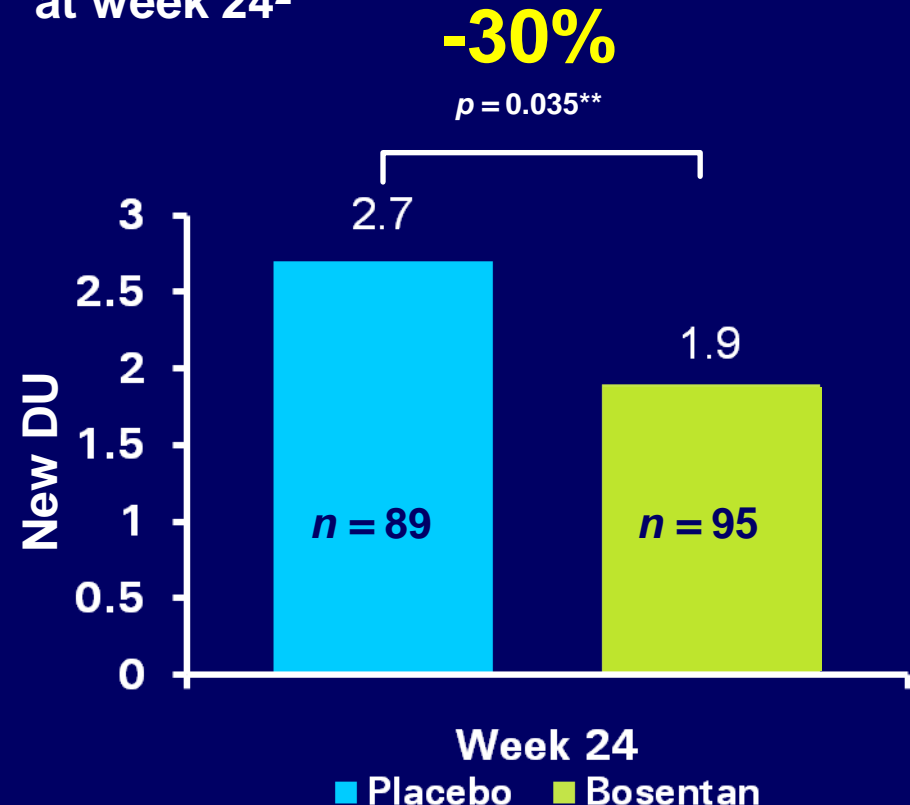
- Avoid hand injury, avoid repeated microtrauma
- Work-related trauma
- Occlusion

Effect of bosentan in reducing the number of new DU

RAPIDS-1: Occurrence of new DU at week 16¹



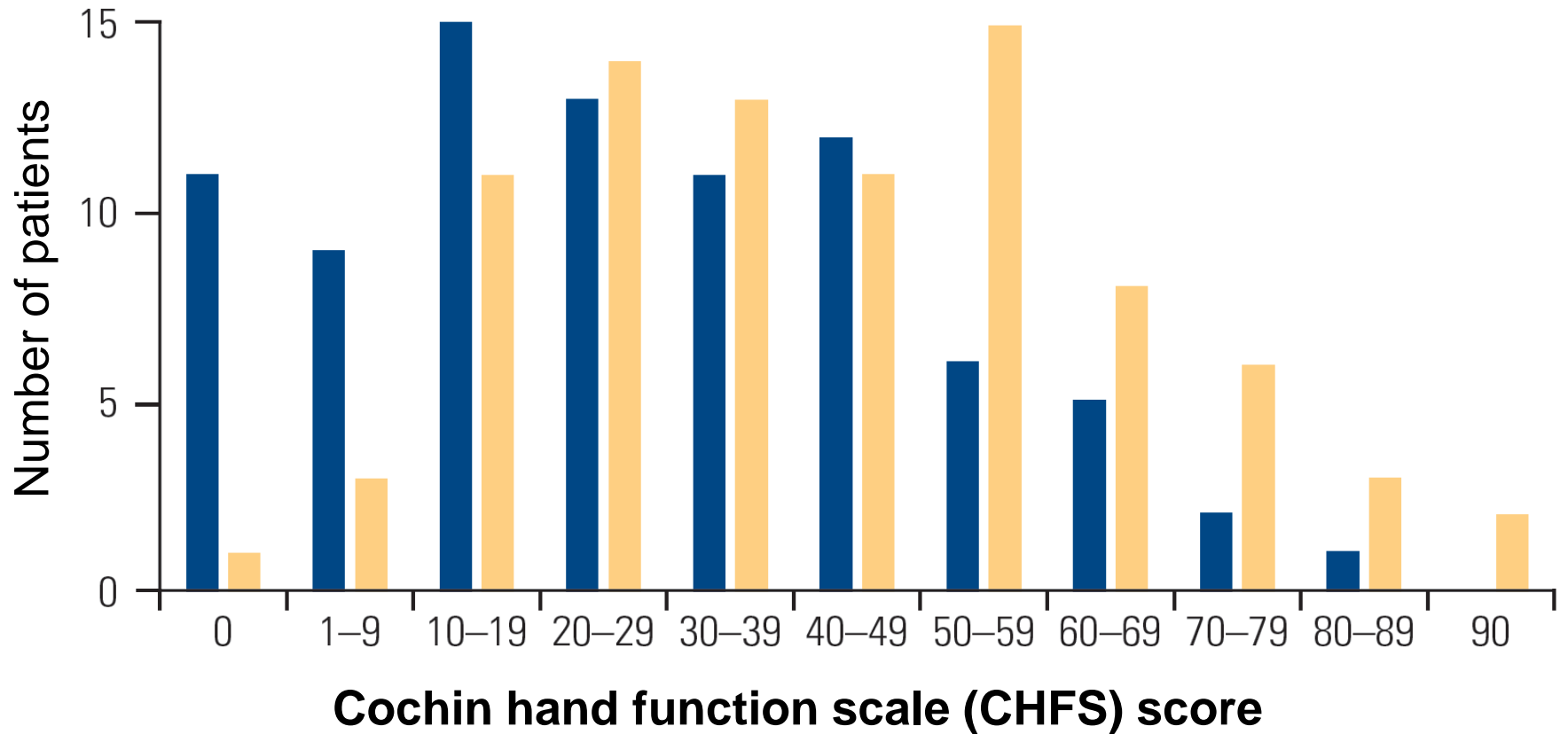
RAPIDS-2: Occurrence of new DU at week 24²



1. Korn JH, et al. *Arthritis Rheum* 2004; 50:3985-93.
2. Matucci Cerinic M, et al. *Ann Rheum Dis* 2011; 70:32-38.

Impact of DU on Cochin hand function scale (CHFS) score

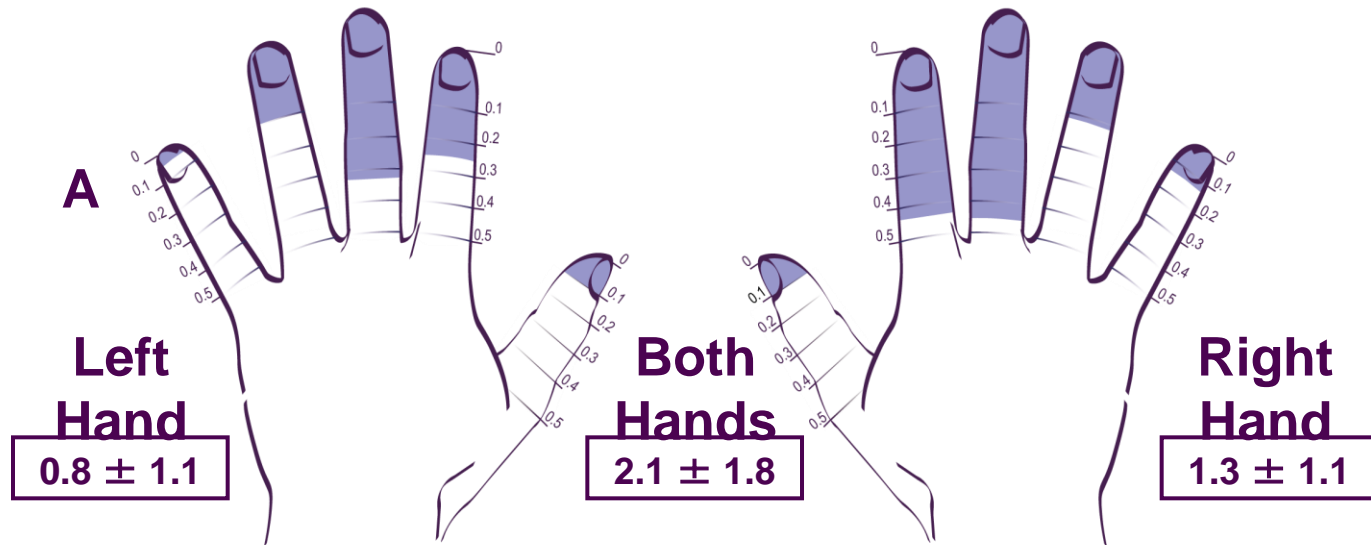
Eclipse study



Without active DU
 28 ± 22
Median 26

With active DU
 43 ± 23
Median 42

Distribution of digital ulcers (DU) at inclusion (A) and at one year (B).



■ Number of DU per patient

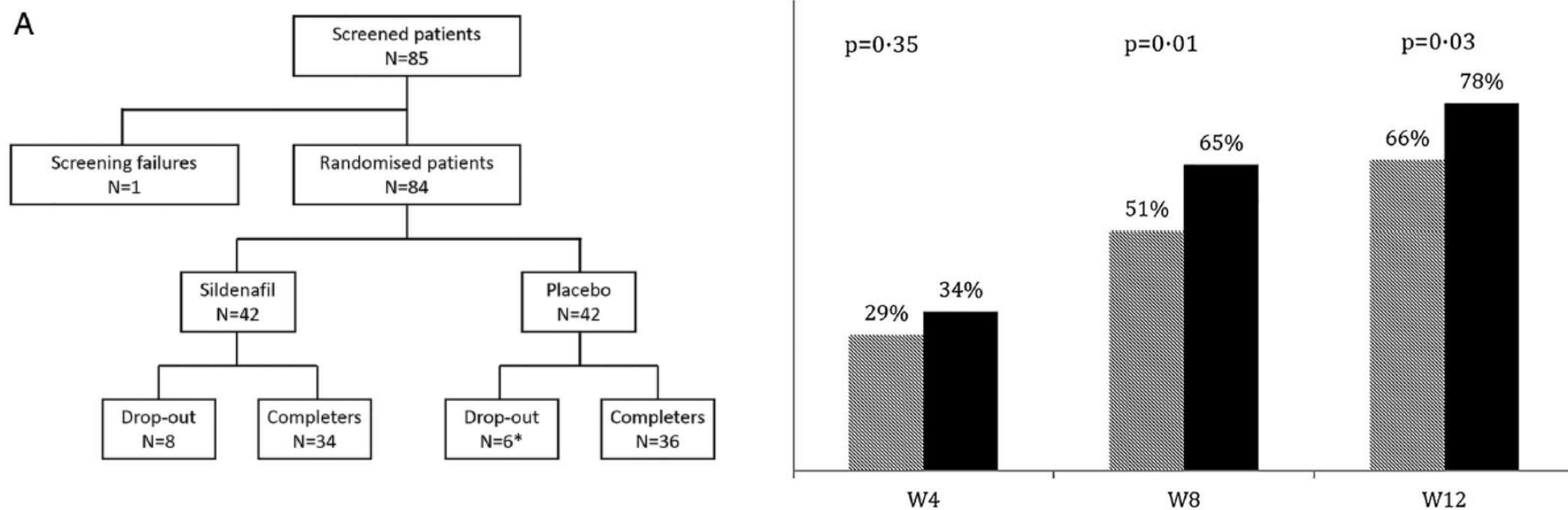
Data is presented for 79 patients with active DU at inclusion and/or at one year

Mouthon et al. In revision 2016

Ongoing / recent studies in DU-SSc

- Seduce: sildenafil vs placebo
- Dual: macitentan vs placebo
- Selexipag vs placebo

Efficacy of sildenafil on ischaemic digital ulcer healing in SSc: the placebo-controlled SEDUCE study



HR for DU healing was 1.33 (0.88 to 2.00) ($p=0.18$) and 1.27 (0.85 to 1.89) ($p=0.25$) when adjusted for the number of DUs at entry (favouring sildenafil). Primary end point: not reached (unexpectedly high healing rate in the placebo group).

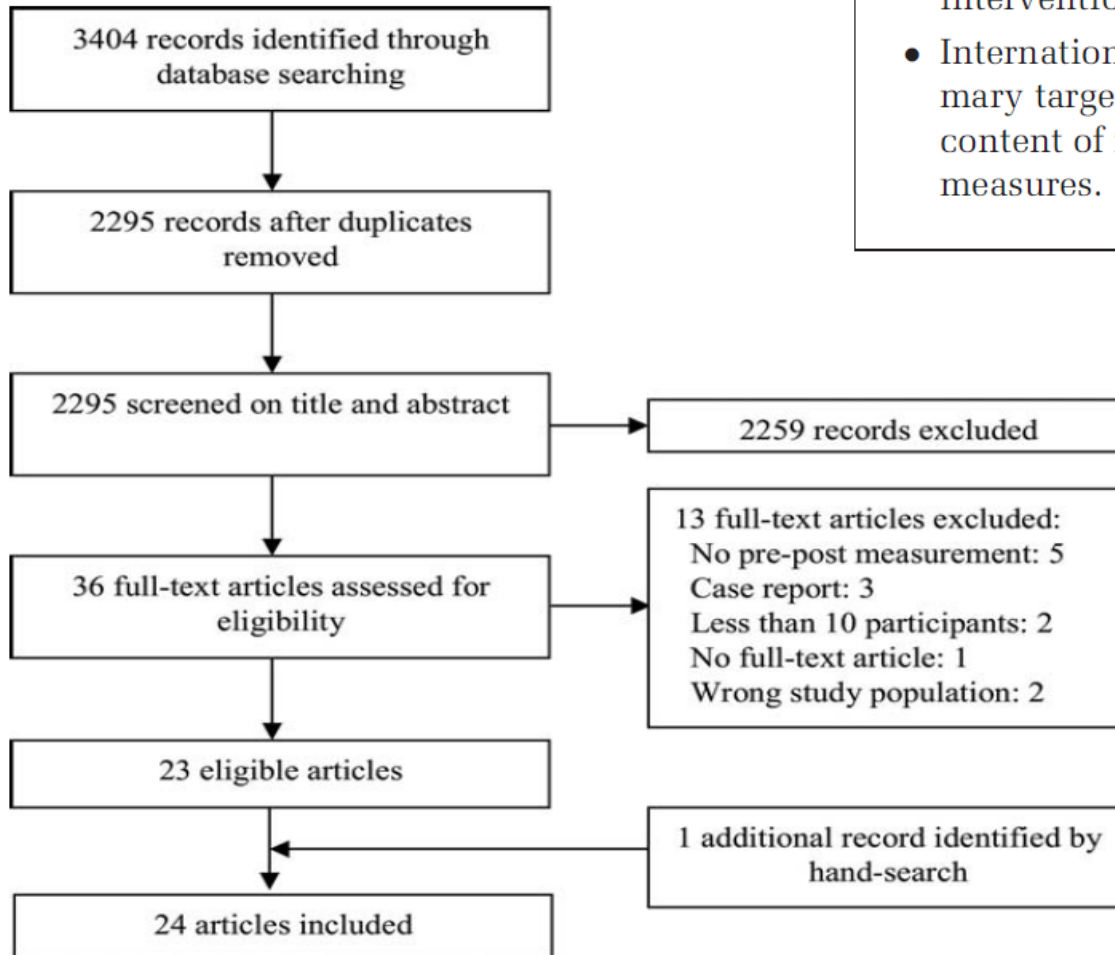
Significant decrease in the number of DUs in favour of sildenafil compared with placebo at W8 and W12

Joint involvement in systemic sclerosis: Treatment

- ✓ Colchicine
- ✓ Low dose prednisone
- ✓ Methotrexate
- ✓ Biologics (Rituximab, Tocilizumab, Abatacept)
- ✓ Surgical procedures
- ✓ Physiotherapy
- ✓ Occupational therapy

Effectiveness of Nonpharmacologic Interventions in Systemic Sclerosis: A Systematic Review

LINDA M. WILLEMS,¹ JOHANNA E. VRIEZKOLK,¹ ANNE A. SCHOUFFOER,² JANET L. POOLE,³
TANJA A. STAMM,⁴ CARINA BOSTRÖM,⁵ LINDA KWAKKENBOS,⁶
THEODORA P. M. VLIET VLIELAND,⁷ AND CORNELIA H. M. VAN DEN ENDE¹



Significance & Innovations

- The body of knowledge regarding nonpharmacologic care in systemic sclerosis (SSc) is limited and fragmented.
- In SSc research a wide variety exists in treatment targets, the content of nonpharmacologic interventions, and outcomes measures.
- International consensus is needed to prioritize primary targets for nonpharmacologic treatment, the content of interventions, and a core set of outcome measures.

Figure 1. Flow diagram of inclusion procedure.

Rehabilitation and systemic sclerosis

- Multicenter randomized controlled study
 - Randomization: Zelen method
 - 220 patients
 - Primary criteria : HAQ
 - 12 supervised rehabilitation sessions
 - Daily non supervised rehabilitation sessions
 - Analysis of qualitative and quantitative observance

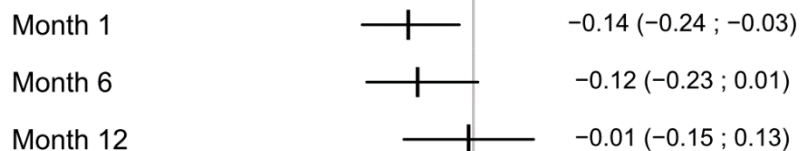


Table 2

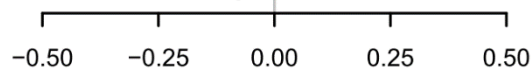
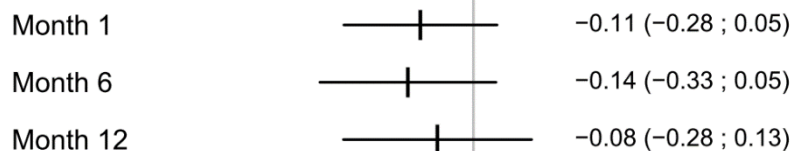
Outcome	Physical therapy	Usual care	Unadjusted difference (95% CI)*	Adjusted difference (95% CI)**	p***	
Kapandji index (0-100)						
Baseline	77.97 (16.82)	103	77.05 (19.27)	104		
M1	82.69 (16.12)	93	77.51 (18.08)	93	3.80 (2.07; 5.53)	<0.0001
M6	82.54 (16.90)	90	80.33 (17.18)	84	2.06 (0.01; 4.11)	0.0490
M12	81.76 (16.65)	88	80.00 (18.05)	83	0.16 (-2.60; 2.93)	0.91
CHFS (0-90)						
Baseline	20.05 (15.59)	102	22.18 (18.19)	100		
M1	14.82 (13.47)	92	21.20 (18.95)	91	-3.65 (-6.12; -1.17)	0.0039
M6	16.60 (15.59)	89	18.46 (17.20)	81	-0.77 (-3.57; 2.04)	0.59
M12	18.64 (16.78)	91	20.26 (18.69)	82	0.48 (-3.05; 4.01)	0.79

Main analysis (ITT)

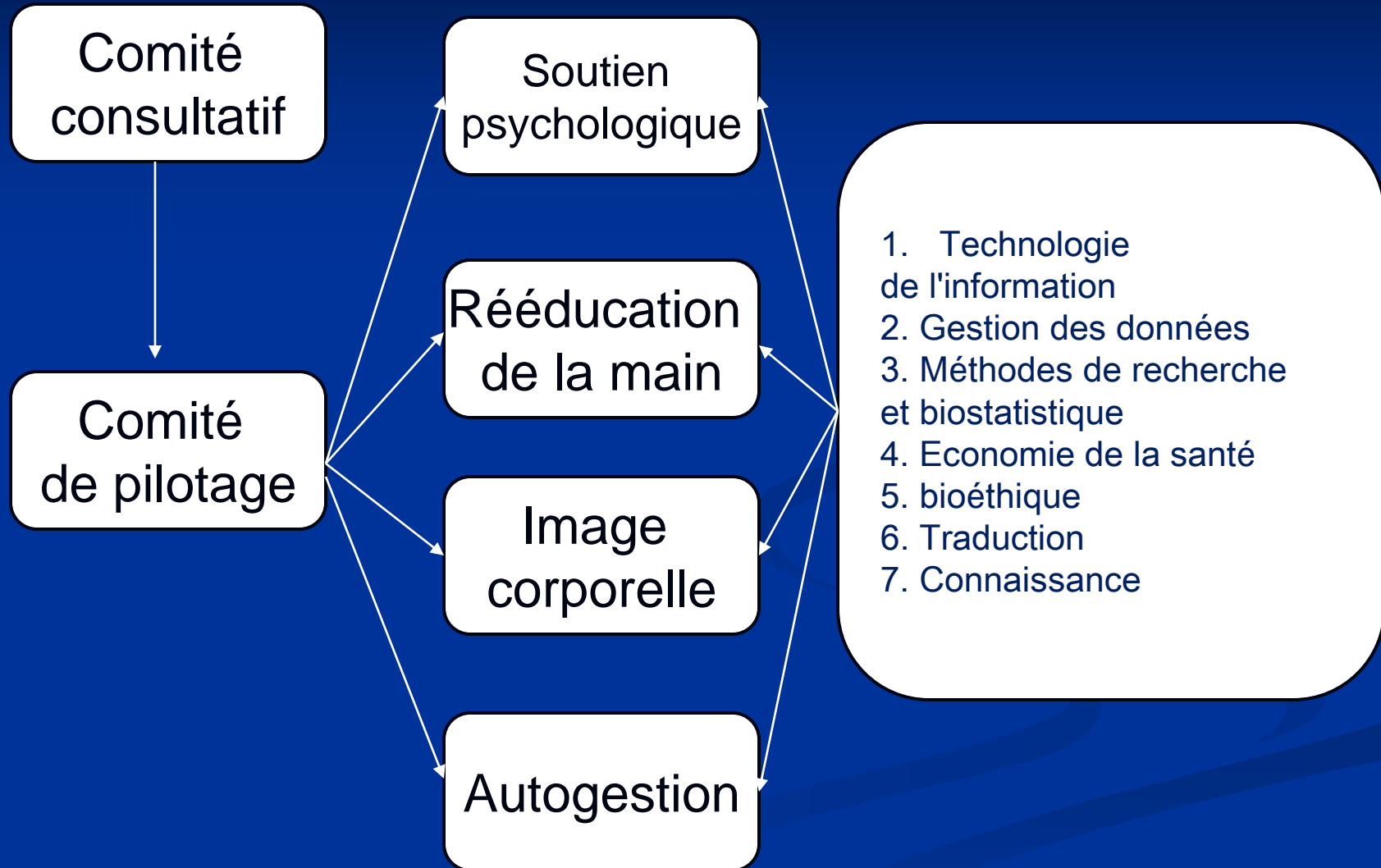
Estimate (95% CI)



Home program complier
 exploratory analysis (CACE)

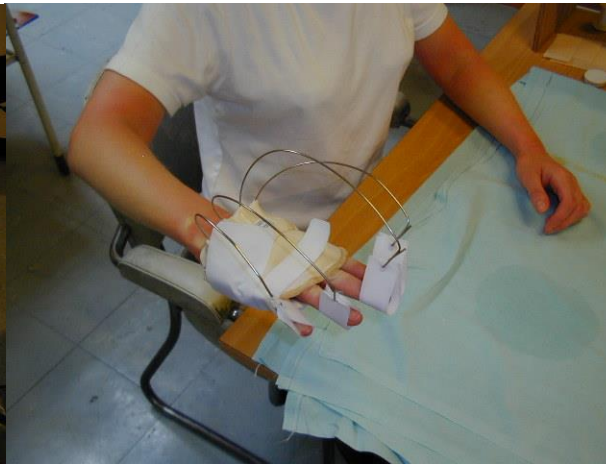


Réseau d'intervention centrée sur le patient sclérodermique (RIPS)



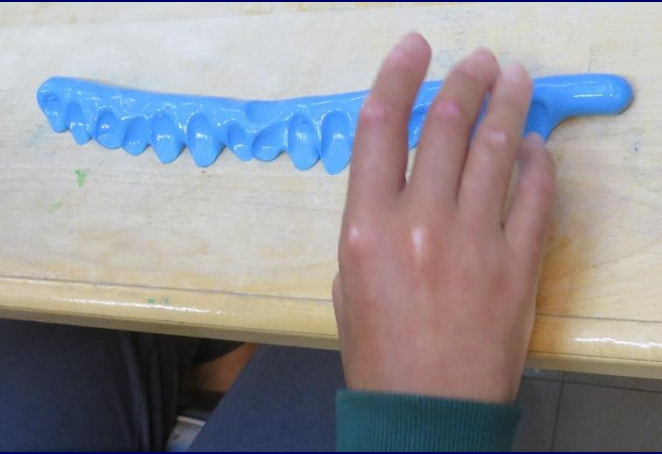
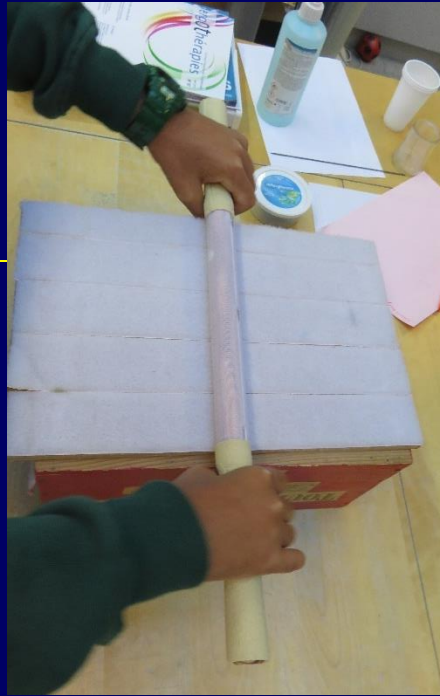
Appareillage

- Orthèses pour les mains et poignets
 - De repos
 - Dynamiques d'extension
 - D'enroulement



Ergothérapie: aides techniques





Atteinte de la main dans la sclérodermie systémique

- Atteinte de la main fréquente, précoce au cours de la ScS
- Atteinte vasculaire au premier plan
- Atteinte cutanée
- Atteinte articulaire
- La prise en charge doit être globale: pharmacologique et non pharmacologique
 - Education thérapeutique
 - Traitement des UD, des arthrites
 - Traitements non pharmatologiques (kinésithérapie, ergothérapie)

20eme réunion annuelle du GFRS

23 novembre 2016

Cochin



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