



**ΑΞΟΝΙΚΕΣ ΣΠΟΝΔΥΛΑΡΘΡΙΤΙΔΕΣ**

# **Συννοσηρότητα και θεραπευτικές επιλογές στην Αγκυλοποιητική Σπονδυλαρθρίτιδα**



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ΕΠΕΜΥ  
Καρπενήσι 27/11/2016**



## Disclosures - Conflict of interest

Για την παρουσίαση: Pfizer

Εκπαιδευτικές-ερευνητικές-συμβουλευτικές επιχορηγήσεις την  
τελευταία διετία:

Amgen, Roche, UCB, MSD, Pfizer, Menarini, Novartis, Angelini Pharma, Abbvie.  
Bristol





SPondyloArthritis Research & Treatment Network

Νεοδιαγνωσθέντες ασθενείς με ΑΣ χωρίς συννοσηρότητες πριν τη διάγνωση:

2 x ρυθμός ανάπτυξης νέας **κατάθλιψης** στην 3ετία

60% υψηλότερο ρυθμό ανάπτυξης νέας **καρδιαγγειακής νόσου**

15 x **ραγοειδίτιδα**

6 x **ΦΝΕ**

3 x **οστεοπόρωση**



SPondyloArthritis Research & Treatment Network

80 % υπνική άπνοια

50 % άσθμα

44 % υπέρταση

23 % κακοήθεια

20 % Διαβήτη

11 % Δυσλιπιδαιμία

Εισαγωγές σε Νοσοκομείο 12% vs 6%

Επίσκεψη στα επείγοντα 23% vs 15%

Επίσκεψη ιατρείου 2x

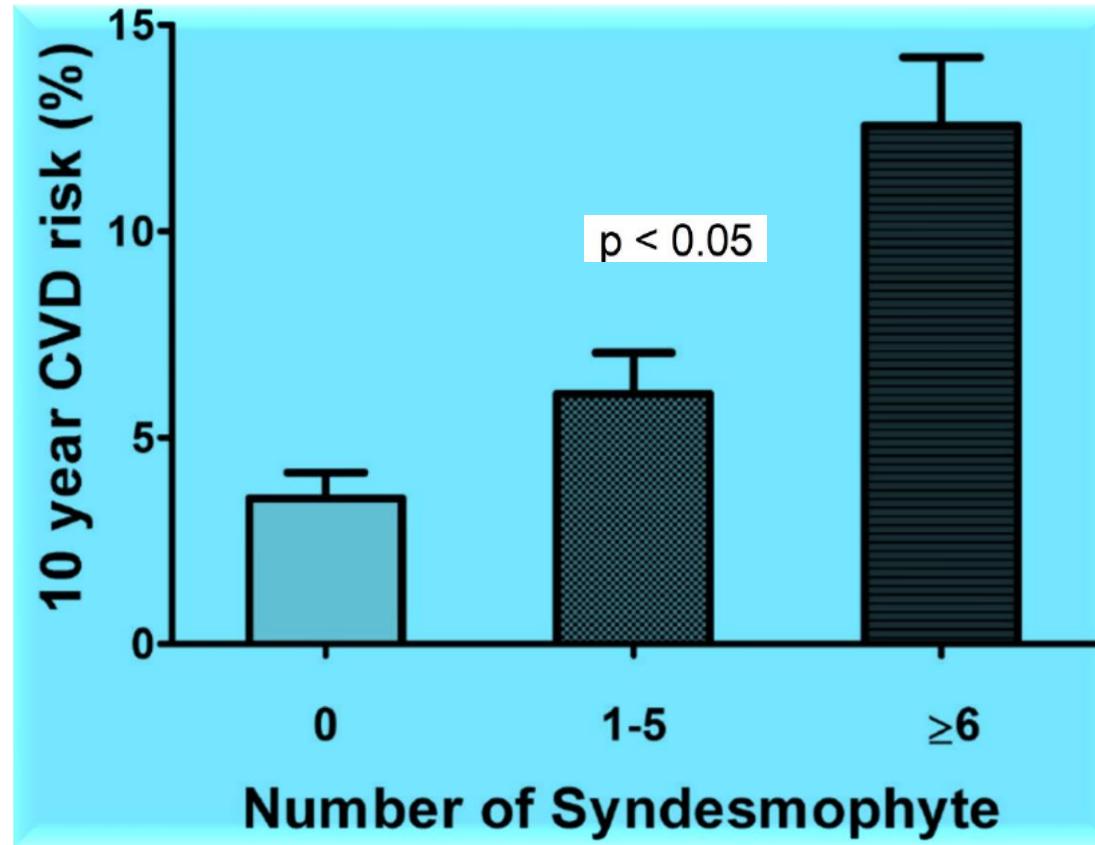
Συνταγογράφηση 2 x

# Radiographic progression is associated with increased cardiovascular risk in patients with axial spondyloarthritis

	Controls (n = 925)	AxSpA (n = 185)	P-value
Age (years)	38 ± 11	38 ± 11	0.994
20–29 (%)	215 (23)	43 (23)	
30–39 (%)	355 (38)	71 (38)	
40–49 (%)	210 (23)	42 (23)	
50+ (%)	145 (16)	29 (16)	
Male (%)	730 (79)	146 (79)	1.000
BMI	24.2 ± 3.5	23.8 ± 3.6	0.109
Total cholesterol (mg/dl)	186 ± 36	186 ± 37	0.980
HDL cholesterol (mg/dl)	50 ± 14	46 ± 16	0.004
LDL cholesterol (mg/dl)	125 ± 34	122 ± 35	0.276
Triglycerides (mg/dl)	141 ± 85	136 ± 75	0.389
Glucose (mg/dl)	94 ± 19	96 ± 11	0.135
Systolic blood pressure (mmHg)	116 ± 14	122 ± 14	<0.001
Diastolic blood pressure (mmHg)	78 ± 11	77 ± 10	0.687
Current smoker (%)	355 (38)	66 (36)	0.508
Framingham risk score (%)	5.0 ± 6.6	6.3 ± 8.7	0.046
Hypertension (%)	66 (7)	19 (10)	0.171
Lipid-lowering agents (%)	11 (1)	5 (3)	0.165
Patients on NSAIDs	-	154 (83)	
Patients on TNF inhibitors	-	55 (30)	

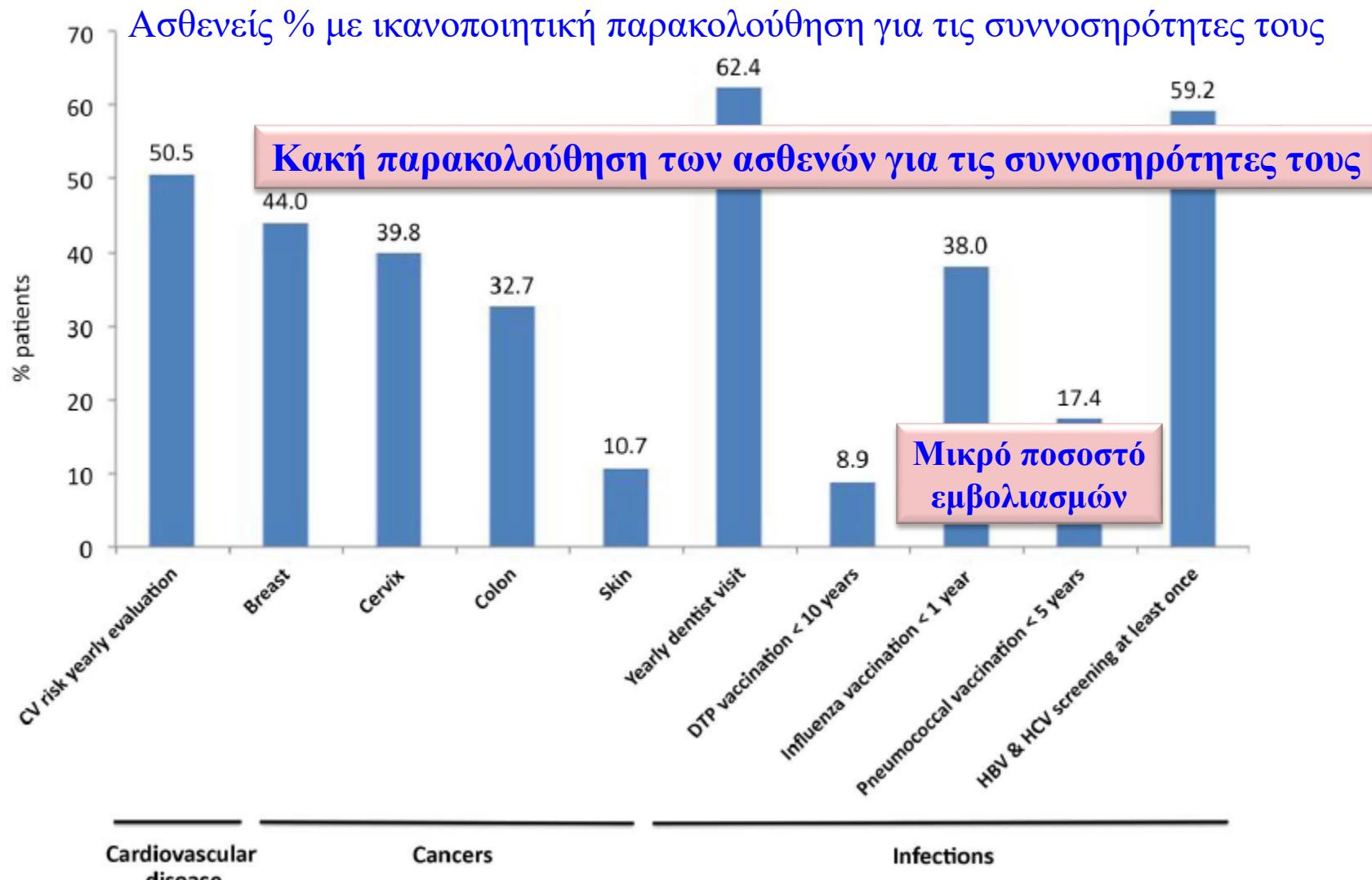
	All	10 year CVD risk			P-value
		<10% (n = 147)	10–20% (n = 26)	>20% (n = 12)	
Age (years)	38 ± 11	35 ± 8	50 ± 9	55 ± 9	<0.001
Male (%)	146 (79)	109 (74)	25 (96)	12 (100)	0.007
BMI	23.8 ± 3.6	23.5 ± 3.7	24.9 ± 2.4	24.6 ± 3.0	0.149
Duration of axSpA (years)	6 ± 7	6 ± 6	7 ± 9	4 ± 5	0.388
Years after Sx. onset (years)	12 ± 9	11 ± 8	18 ± 11	10 ± 11	0.001
HLA B27 positive* (%)	160 (91)	127 (92)	22 (88)	11 (92)	0.803
ESR (mm/hr)	21 ± 20	21 ± 21	20 ± 19	16 ± 13	0.648
CRP (mg/l)	6.5 ± 11.7	6.6 ± 11.9	7.3 ± 12.8	2.9 ± 4.9	0.535
BASDAI	3.2 ± 2.2	3.3 ± 2.2	2.9 ± 2.1	2.6 ± 2.1	0.570
BASFI	1.6 ± 2.1	2.1 ± 0.2	1.6 ± 1.6	1.4 ± 1.9	0.961
ASDAS-ESR	2.3 ± 1.1	2.4 ± 1.2	2.3 ± 0.9	2.1 ± 0.7	0.801
ASDAS-CRP	2.1 ± 1.2	2.1 ± 1.2	2.1 ± 1.0	1.7 ± 0.6	0.701
Grade of sacroiliitis on X-ray	2.9 ± 1.0	2.8 ± 1.0	3.5 ± 0.6	3.0 ± 1.2	0.009
mSASSS	14 ± 21	10 ± 18	28 ± 24	28 ± 22	<0.001
Number of syndesmophytes	5 ± 7	3 ± 7	9 ± 8	10 ± 8	<0.001
Current smoker (%)	66 (36)	46 (32)	12 (46)	8 (67)	0.025
Total cholesterol (mg/dl)	186 ± 37	184 ± 37	193 ± 40	186 ± 24	0.523
HDL cholesterol (mg/dl)	46 ± 16	49 ± 15	41 ± 12	26 ± 16	<0.001
LDL cholesterol (mg/dl)	122 ± 35	113 ± 29	122 ± 34	118 ± 18	0.235
Triglycerides (mg/dl)	136 ± 75	119 ± 71	161 ± 69	217 ± 84	<0.001
Systolic BP (mmHg)	122 ± 14	120 ± 14	126 ± 11	132 ± 16	0.003
Diastolic BP (mmHg)	77 ± 10	76 ± 9	82 ± 11	84 ± 11	0.001
Framingham risk score (%)	6 ± 9	3 ± 3	14 ± 3	34 ± 9	<0.001
Patients on NSAIDs	154 (83)	125 (85)	21 (81)	8 (67)	0.245
Patients on TNF inhibitors	55 (30)	41 (22)	11 (42)	3 (25)	0.311

# Radiographic progression is associated with increased cardiovascular risk in patients with axial spondyloarthritis

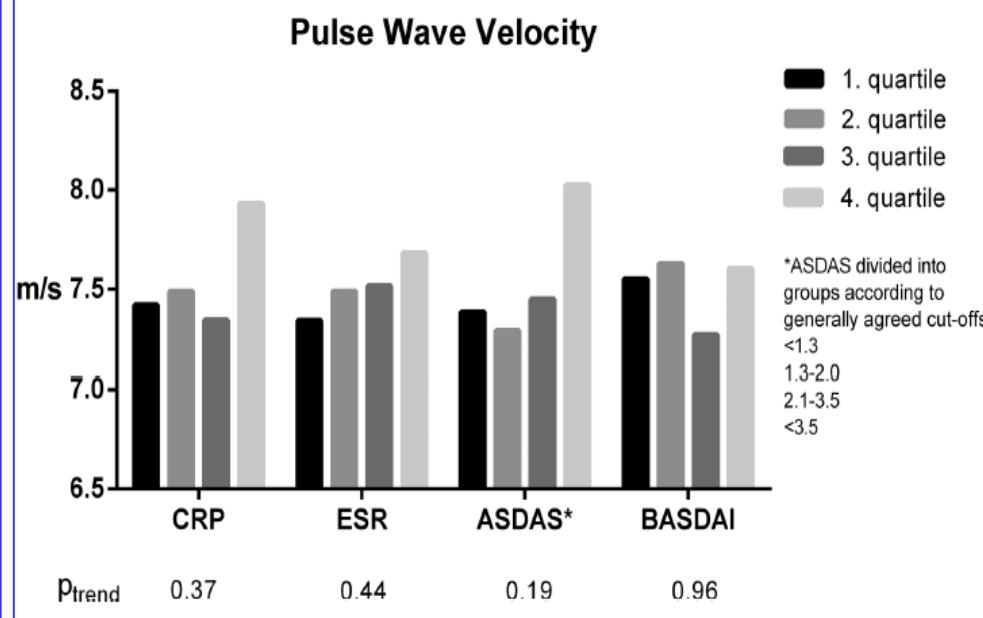
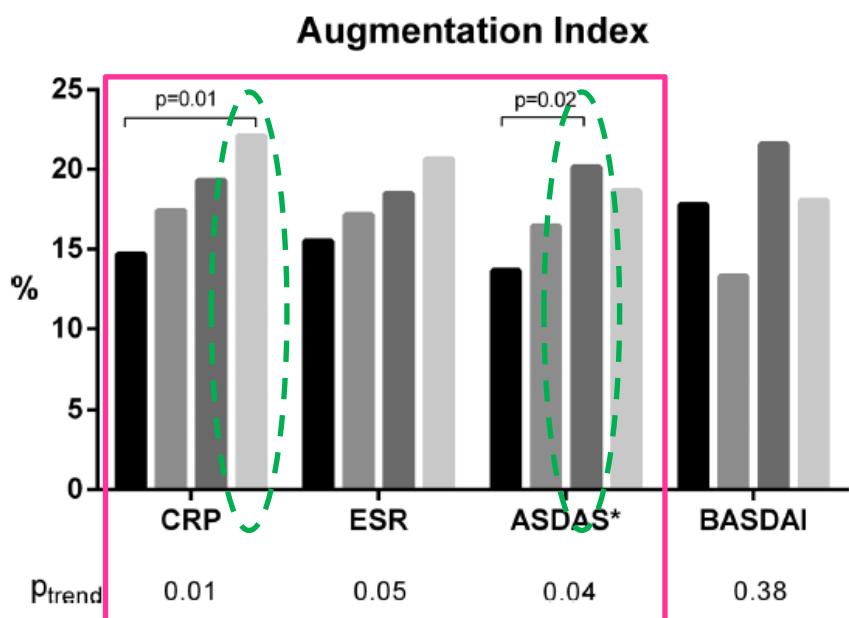


Περισσότερα συνδεσμόφυτα μεγαλύτερος καρδιαγγειακός κίνδυνος

# EXTENDED REPORT Prevalence of comorbidities and evaluation of their screening in spondyloarthritis: results of the international cross-sectional ASAS-COMOSPA study

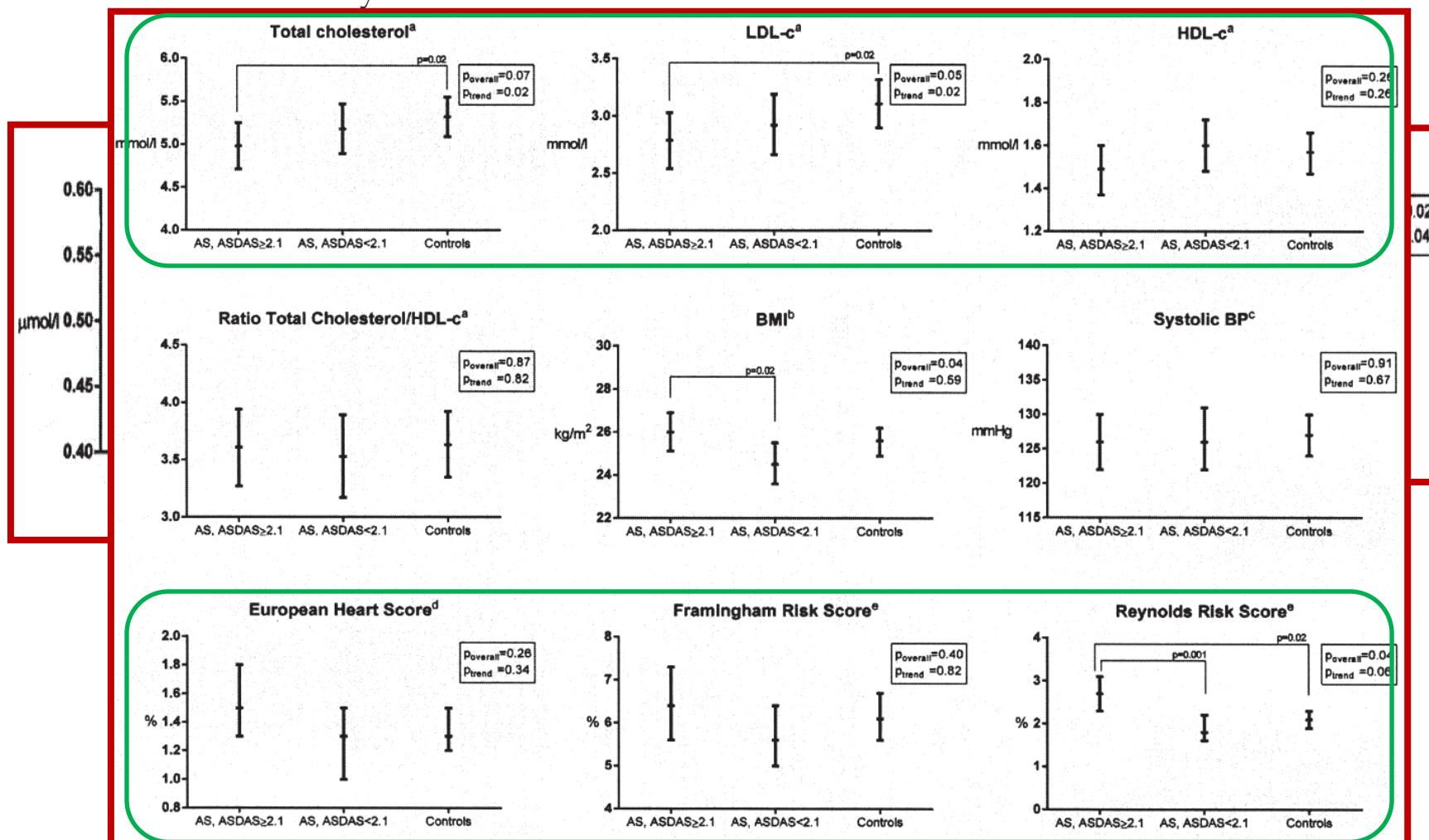


**CONCISE REPORT** CRP and ASDAS are associated with future elevated arterial stiffness, a risk marker of cardiovascular disease, in patients with ankylosing spondylitis: results after 5-year follow-up



Augmentation Index: Κεντρικός Αυξητικός Δείκτης

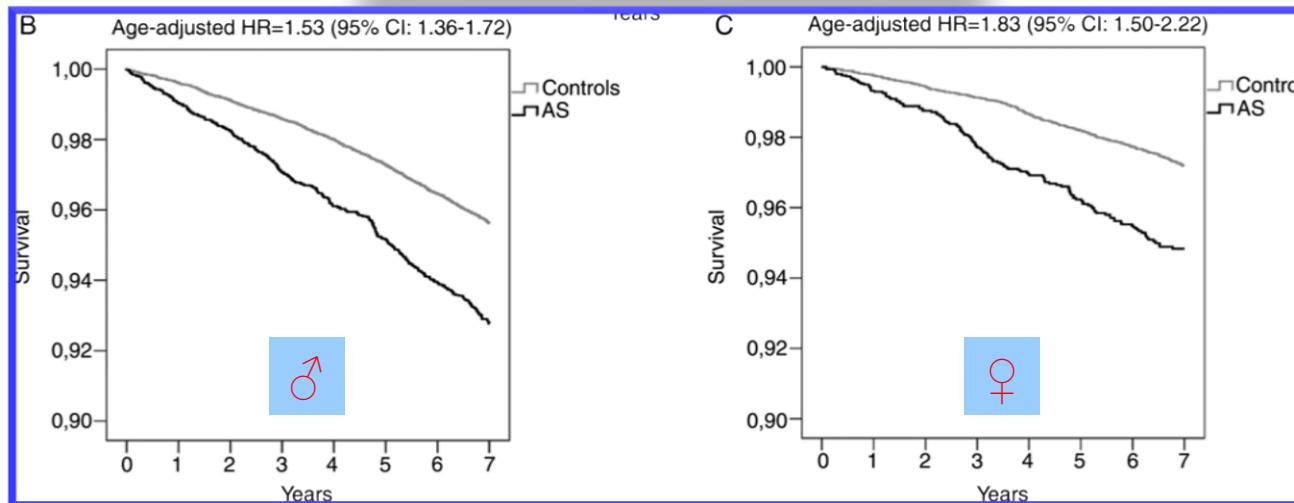
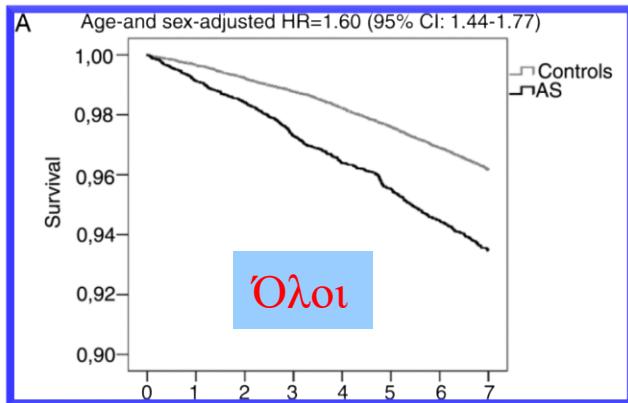
Disease Activity in Ankylosing Spondylitis and  
Associations to Markers of Vascular Pathology and  
Traditional Cardiovascular Disease Risk Factors:  
A Cross-sectional Study



# Mortality in ankylosing spondylitis: results from a nationwide population-based study

## Ενδείκτες θανάτου

- Χαμηλό επίπεδο εκπαίδευσης
- Συννοσηρότητα
  - ΣΔ
  - Λοιμώξεις
  - Καρδιαγγειακές παθήσεις
  - Πνευμονολογικές
  - Κακοήθειες
- Προηγηθείσα αρθροπλαστική ισχίου



# Osteoporosis and osteopenia in long-standing AS

N = 80, mean disease duration: **21.8 ± 10.3 years**

WHO classification of osteoporosis	Lumbar spine N (%)	Hip [total] N (%)	Hip [femoral neck] N (%)
Normal	44 (55.0%) <sup>a</sup>	53 (66.3%)	24 (30.0%)
Osteopenia	16 (20.0%) <sup>a</sup>	21 (26.2%)	38 (47.5%)
Osteoporosis	20 (25.0%) <sup>b</sup>	6 (7.5%)	18 (22.5%)

<sup>a</sup>  $P = 0.001$  lumbar spine: femoral neck (*t* test)

<sup>b</sup>  $P = 0.016$  lumbar spine: total hip (*t* test)

**BMD correlated negatively with inflammatory activity (CRP, ESR)**

# Risk of fractures in AS

*A primary care-based nested case-control study*

Fracture type	Ankylosing spondylitis	No of cases	No of controls	Crude OR (95% CI)	Adjusted OR* (95% CI)
Any	No	231436	231362	Reference	Reference
	Yes	416	342	1.22 (1.05 to 1.40)	1.02 (0.88 to 1.18)
Radius/ulna	No	44138	44119	Reference	Reference
	Yes	82	63	1.30 (0.94 to 0.81)	1.21 (0.87 to 1.69)
Hip	No	14362	14363	Reference	Reference
	Yes	25	26	0.96 (0.56 to 1.67)	0.77 (0.43 to 1.37)
Vertebral	No	8701	8678	Reference	Reference
	Yes	34	11	3.08 (1.56 to 6.08)	3.26 (1.51 to 7.02)

\*Adjusted for medications and illnesses associated with risk of fracture (as outlined in the Methods section), and smoking and body mass index when known.

CI, confidence interval; OR, odds ratio.

**Risk of fractures is increased:**

- in the presence of IBD.

**Risk of fractures is decreased:**

- with NSAIDs intake.



# High frequency of vertebral fractures in early spondyloarthritis

**Fracture = reduction of  $\geq 20\%$  of the vertebral height (Genant score grade 1)**

Types of SpA	Patients with VF
Ankylosing spondylitis (AS) ( $n=80$ )	9 (11%)
Axial psoriatic arthritis ( $n=10$ )	4 (40%)
AS and inflammatory bowel disease ( $n=5$ )	1 (20%)
Undifferentiated spondylarthropathy ( $n=13$ )	3 (23%)

Factors significantly associated with fractures:

- lower BMD in the lumbar spine,
- psoriasis.

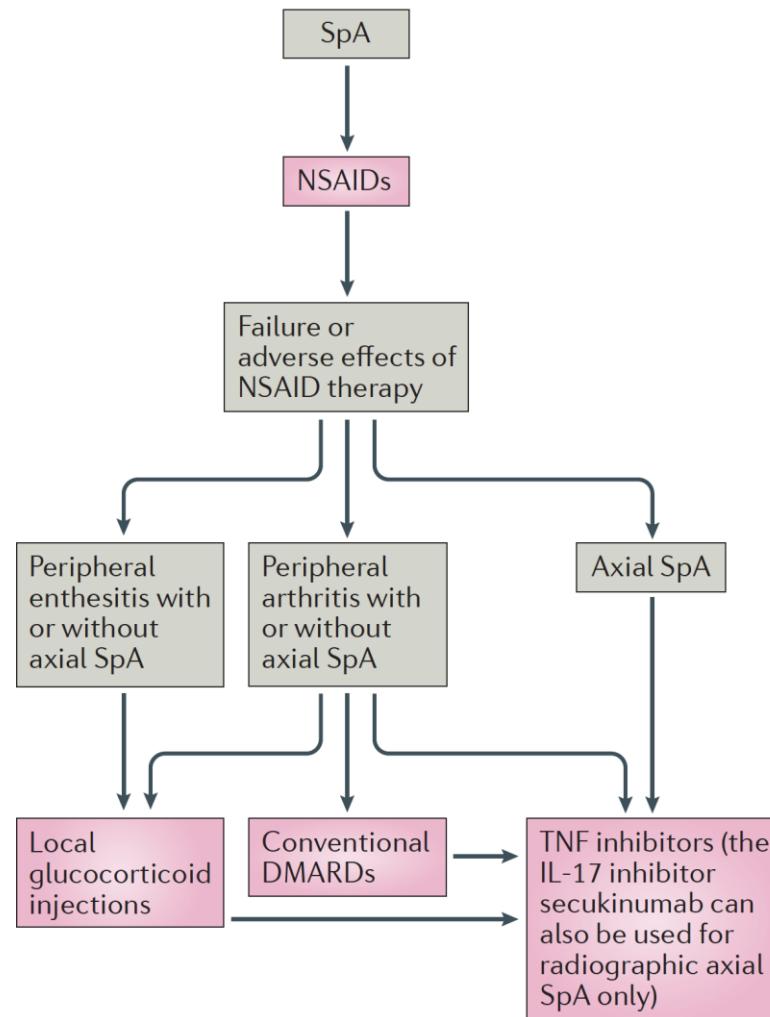
# Cardiovascular and selected comorbidities in early arthritis and early spondyloarthritis, a comparative study: results from the ESPOIR and DESIR cohorts

**Table 1** Characteristics and comorbidities of the ESPOIR and DESIR cohorts

	ESPOIR (Nr=689) Patients with ERA N (%) or mean±SD	DESIR (Nr=645) Patients with ESpA N (%) or mean±SD
Male gender	161 (23.4)	304 (47.1)
Age (years)	48.2±12.1	32.8±8.4
Symptoms duration (weeks)	14.2±14.5	79.0±45.7
Alcohol use	105 (15.2)	94 (14.6)
ESR*	30.4±24.8	14.2±16.3
CRP†	22.6±33.9	9.4±15.0‡
<b>At least one comorbidity</b>	<b>294 (42.7)</b>	<b>131 (20.3)</b>
<b>Arterial hypertension</b>	<b>125 (18.1)</b>	<b>33 (5.1)</b>
Receive treatment (%)	93.6	54.5
Hypercholesterolaemia	101 (14.7)	42 (6.5)
Receive treatment (%)	69.3	2.4
Hypertriglyceridaemia	21 (3.0)	18 (2.8)
<b>Dysthyroidism</b>	<b>82 (11.9)</b>	<b>24 (3.7)</b>
Previous tuberculosis	32 (4.6)	6 (0.9)
Diabetes mellitus	28 (4.1)	6 (0.9)
Previous solid malignancies	24 (3.5)	3 (0.5)
Previous lymphoma	4 (0.6)	2 (0.3)
Coronary heart disease	6 (0.9)	0
Stroke	4 (0.6)	0
Peptic ulcer	35 (5)	26 (4)
Previous gastrointestinal bleeding	8 (1.2)	12 (1.9)
Hepatitis B	4 (0.6)	3 (0.5)
Hepatitis C	6 (0.9)	1 (0.2)

# New evidence on the management of spondyloarthritis

Joachim Sieper and Denis Poddubnyy



Target	Therapeutic agent	Efficacy				
		Axial SpA*	PsA	Psoriasis	Crohn's disease	RA
TNF	Adalimumab (monoclonal antibody to TNF)	+	+	+	+	+
	Certolizumab pegol (monoclonal antibody to TNF)	+	+	+	+	+
	Etanercept (fusion protein against TNF)	+	+	+	-	+
	Golimumab (monoclonal antibody to TNF)	+	+	+	+	+
	Infliximab (monoclonal antibody to TNF)	+	+	+	+	+
IL-1	Anakinra (IL-1 receptor antagonist)	-?	+?	?	?	+
	Rituximab (monoclonal antibody to CD20)	+?	+?	?	-	+
T cells	Abatacept (inhibitor of T-cell co-stimulation)	-?	+	+?	-	+
IL-6	Tocilizumab (monoclonal antibody to IL-6 receptor)	-	?	?	?	+
	Sarilumab (monoclonal antibody to IL-6 receptor)	-	?	?	?	+
IL-17	Secukinumab (monoclonal antibody to IL-17)	+	+	+	-	-
	Ixekizumab (monoclonal antibody to IL-17)	?	?	+	?	+?
	Brodalumab (monoclonal antibody to IL-17 receptor)	?	+	+	?	-
IL-12 and IL-23	Ustekinumab (monoclonal antibody to IL-12 and IL-23)	+?	+	+	+	-
	Guselkumab (monoclonal antibody to IL-23)	?	?	+	?	-
	Tildrakizumab (monoclonal antibody to IL-23)	?	?	+	?	?
	BI 655066 (monoclonal antibody to IL-23)	?	?	+	?	?
PDE4	Apremilast (PDE4 inhibitor, small molecule)	-?	+	+	?	-
JAK	Tofacitinib (JAK1 and JAK3 inhibitor, small molecule)	+	?	+	-	+

# Κατασκευάζονται νεότερες κατευθύνσεις για τη θεραπεία της Αγκυλοποιητική Σπονδυλαρθρίτιδας ?

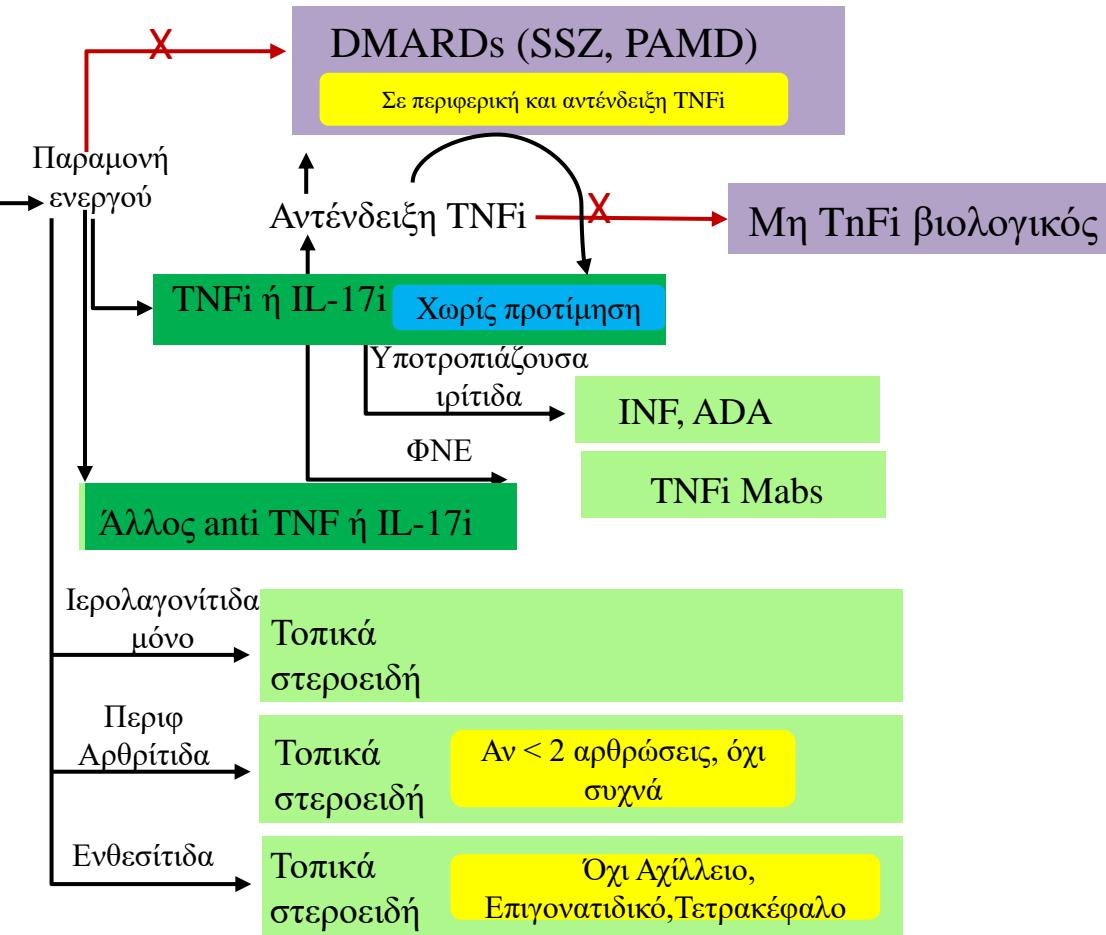
## ΕΝΕΡΓΟΣ ΑΣ

ΜΣΑΦ Συνεχής χορήγηση  
Χωρίς προτίμηση

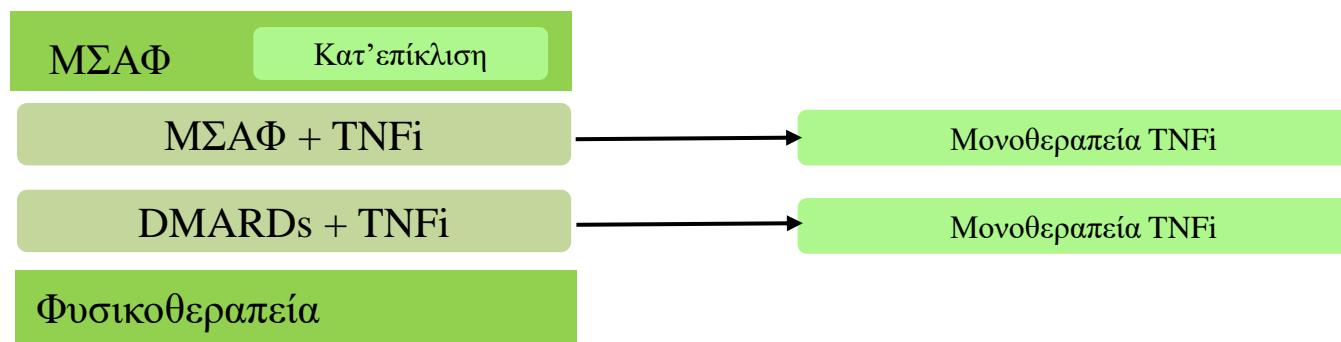
Φ/Θ Ενεργός όχι παθητική  
Γυμναστική παρά κολύμβηση

Κορτιζόνη Συστηματικά Περιφ. ή εντερική έξαρση, εγκυμοσύνη

- Ισχυρή σύσταση
- Υπό συνθήκες σύσταση
- Υπό συνθήκες αρνητική σύσταση
- Ισχυρά αρνητική σύσταση
- Qualifier



## ΣΤΑΘΕΡΗ ΑΣ



## ΑΣ ΚΑΙ:

Προχωρημένη αρθρίτιδα ισχίου

Αρθροπλαστική

Βαριά κύφωση

Επανορθωτική οστεοτομία

Επιλογή κέντρου

Οξεία ιρίτιδα

Θεραπεία από Οφθαλμίατρο

Υποτροπιάζουσα ιρίτιδα

Τοπικά κορτικοειδή  
INFIX, ADA

ΦΝΕ

Anti TNF μονοκλωνικά  
Δεν προτιμώνται ΜΣΑΦ

## **Μη ακτινολογικά εκδηλωμένη Αξονική Σπονδυλαρθρίτιδα**

Therefore, the panel relied on the AS literature as the basis for most recommendations, which are also provided in Supplement B.

**These recommendations  
were the same as for AS,**

with the exception of the PICO question on use of TNFi. This question also had the highest level of evidence among those for nonradiographic axial SpA

## EXTENDED REPORT

A tailored approach to reduce dose of anti-TNF drugs may be equally effective, but substantially less costly than standard dosing in patients with ankylosing spondylitis over 1 year: a propensity score-matched cohort study

**Table 3** Measures of activity/function, quality of life and costs of anti-TNF therapy over one year of observation

		Standard dosing group	Reduced dosing group	p Value
BASDAI at baseline	Mean (SD)	83	53	
<b>BASDAI at 12 M</b>	Mean (SD)	1.4 (1.0)	1.4 (1.1)	0.796
Change in BASDAI (per year)	Mean (95% CI)	1.9 (1.5)	1.7 (1.3)	0.453
Difference of mean change (per year)	Mean (95% CI)	0.47 (0.18 to 0.76)	0.36 (0.01 to 0.71)	0.615
CRP at baseline	Mean (SD)	Reference	-0.12 (-0.57 to 0.34)	
CRP at 12 M	Mean (SD)	4.4 (5.9)	4.3 (7.9)	0.713
Change in CRP (per year)	Mean (95% CI)	7.5 (15.6)	5.4 (7.9)	0.992
Difference of mean change (per year)	Mean (95% CI)	3.42 (-0.16 to 7.01)	2.19 (-2.09 to 6.47)	0.663
HAQ at baseline	Mean (SD)	Reference	-1.23 (-6.81 to 4.35)	
<b>HAQ at 12 M</b>	Mean (SD)	0.4 (0.4)	0.4 (0.4)	0.833
Change in HAQ (per year)	Mean (SD)	0.4 (0.4)	0.4 (0.5)	0.479
Difference of mean change (per year)	Mean (95% CI)	0.07 (0.00 to 0.14)	0.08 (-0.01 to 0.17)	0.942
<b>BASFI at baseline</b>	Mean (SD)	Reference	0.00 (-0.11 to 0.12)	
<b>BASFI at 12 M</b>	Mean (SD)	1.9 (1.7)	1.8 (1.7)	0.644
Change in BASFI (per year)	Mean (SD)	2.1 (1.8)	1.9 (1.7)	0.481
Difference of mean change (per year)	Mean (95% CI)	0.07 (-0.21 to 0.35)	0.09 (-0.24 to 0.43)	0.907
EQ-5D* utility at baseline	Mean (SD)	Reference	0.03 (-0.41 to 0.46)	
EQ-5D* utility at 12 months	Mean (SD)	0.80 (0.09)	0.79 (0.11)	0.667
QALY area under the curve*	Mean (SD)	0.78 (0.14)	0.78 (0.11)	0.901
Annual cost of anti-TNF therapy (€)	Mean (SD)	0.78 (0.12)	0.76 (0.14)	0.436
		12 000 (-)	7784 (2 254)	<0.001

Η μειωμένη δόση δεν είναι αποδεκτή για κανένα από τους anti-TNF. Για την αποδεκτή δόση και θεραπευτικά σχήματα να αναφέρεστε στο SmPC των προϊόντων