Hospital Universitari Sant Joan
REUS

MALALTIES AUTOIMMUNES I RISC CARDIOVASCULAR

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SOCIETAT CATALANOBALEAR MEDICINA INTERNA

L'Acadèmia
FUNDACIÓ ACADÈMIA DE CIÈNCIES MÈDIQUES I DE LA SALUT DE CATALUNYA I DE BALEARS

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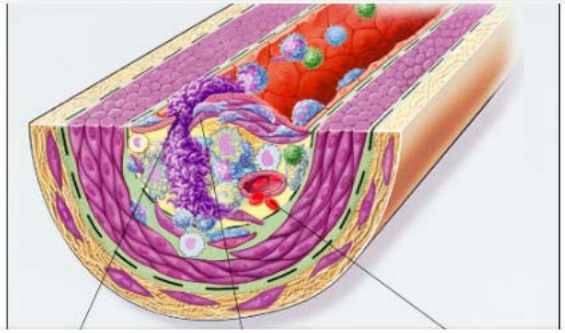
- Aterosclerosi: Inflamació-sistema immune
- Mortalitat cardiovascular
- Marcadors aterosclerosi subclínica. Dislipèmia aterògena
- Maneig terapèutic RCV en malalties autoimmunes

REVIEW ARTICLE MECHANISMS OF DISEASE FREE PREVIEW

Atherosclerosis — An Inflammatory Disease

Russell Ross, Ph.D.



NEJM

Atherosclerosis — An Inflammatory Disease | NEJM

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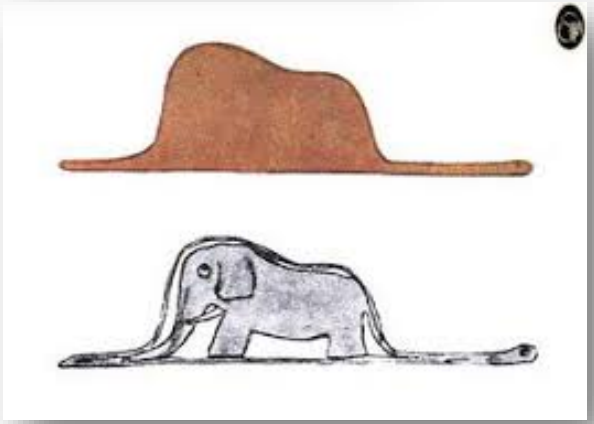
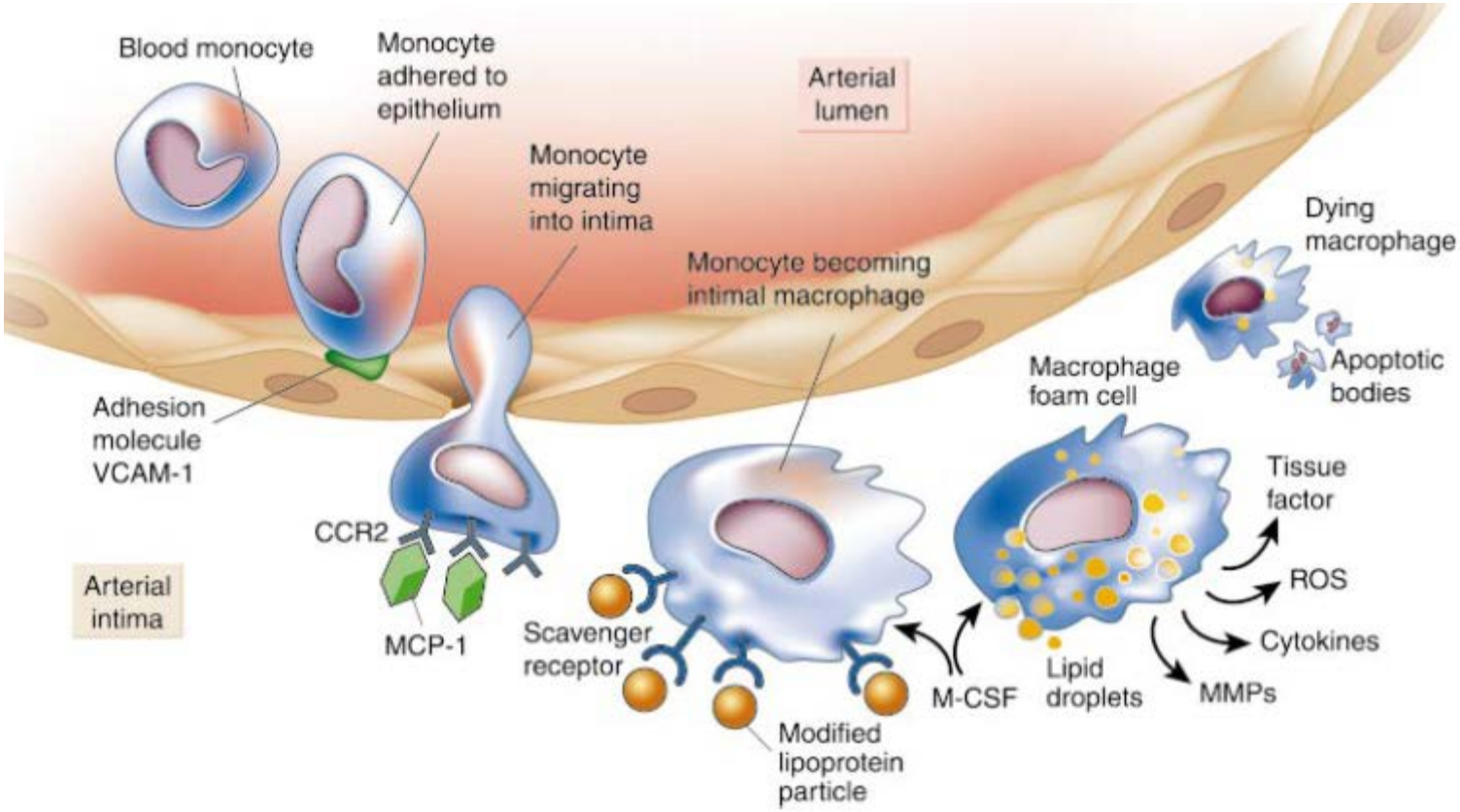
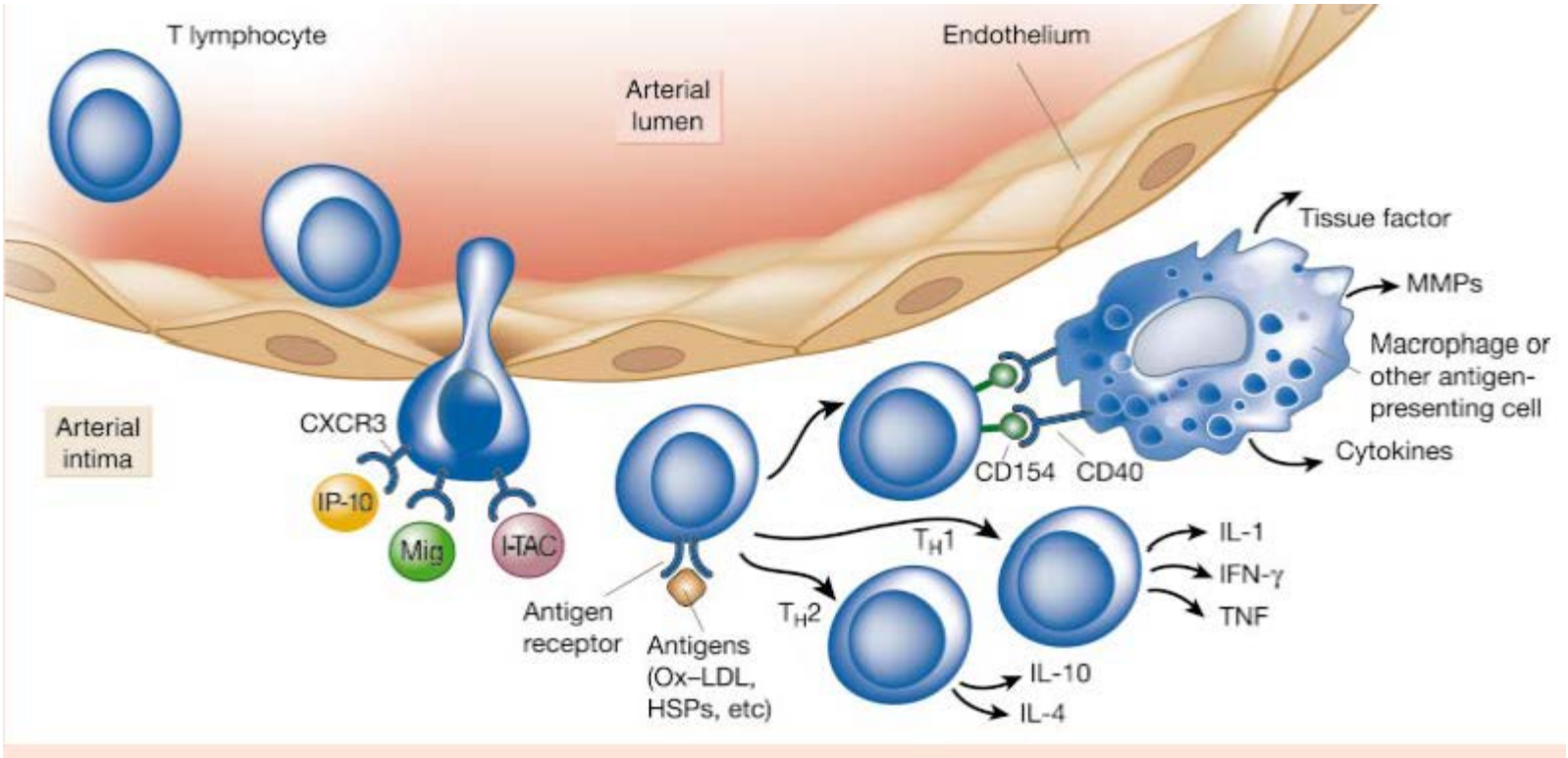
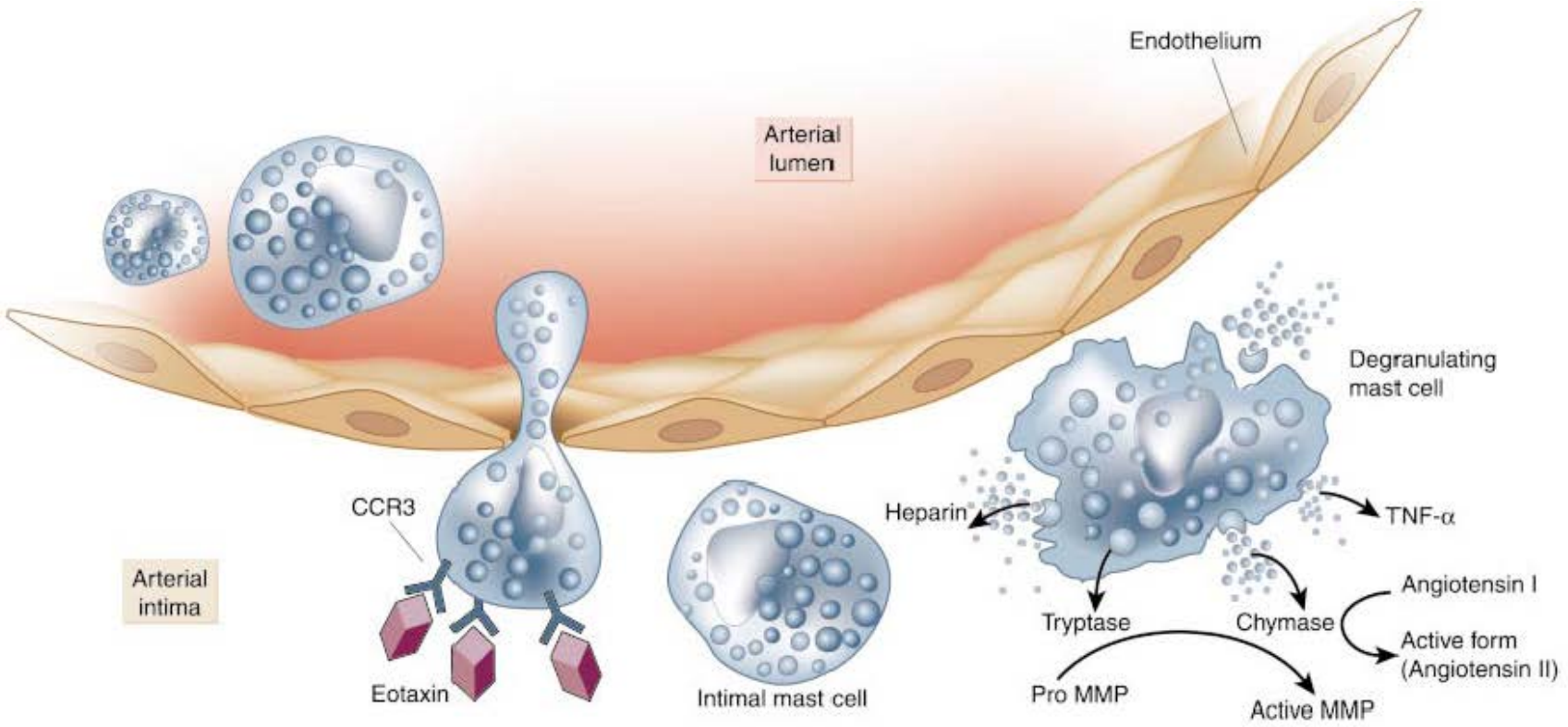


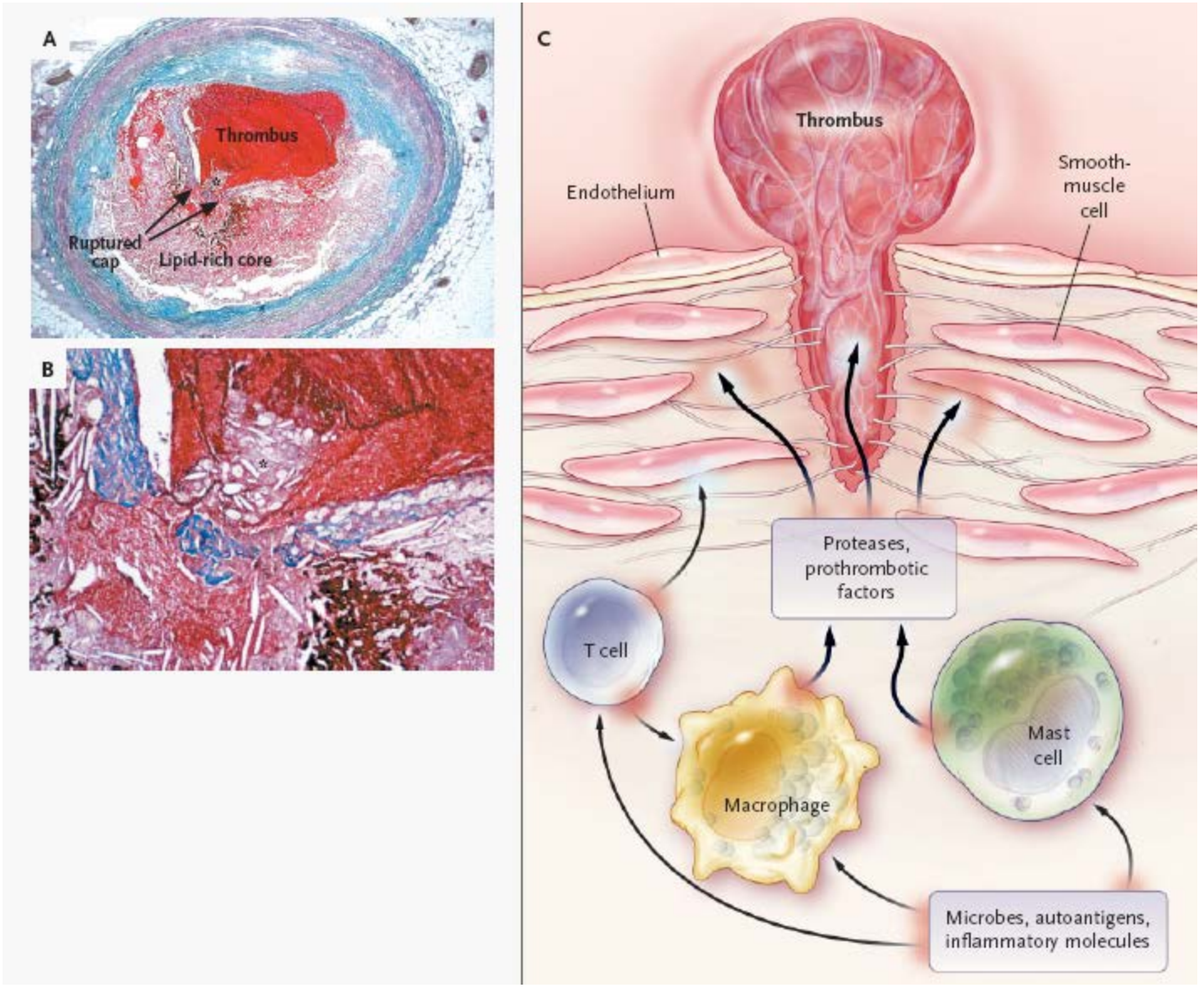
ATEROSCLEROSIS-MALALTIA INFLAMATORIA



NATURE | VOL 420 | 19/26 DECEMBER 2002


T lymphocyte
Endothelium
Arterial lumen
Arterial intima
CXCR3
IP-10
Mig
I-TAC
Antigen receptor
Antigens (Ox–LDL, HSPs, etc)
Tissue factor
MMPs
Macrophage or other antigen-presenting cell
Cytokines
CD154
CD40
T_H1
T_H2
IL-1
IFN-γ
TNF
IL-10
IL-4


Endothelium
Arterial lumen
Degranulating mast cell
Heparin
TNF-α
Angiotensin I
Tryptase
Chymase
Active form (Angiotensin II)
Pro MMP
Active MMP
CCR3
Arterial intima
Eotaxin
Intimal mast cell


A
Thrombus
Ruptured cap
Lipid-rich core
B
C
Thrombus
Endothelium
Smooth-muscle cell
Proteases, prothrombotic factors
T cell
Macrophage
Mast cell
Microbes, autoantigens, inflammatory molecules

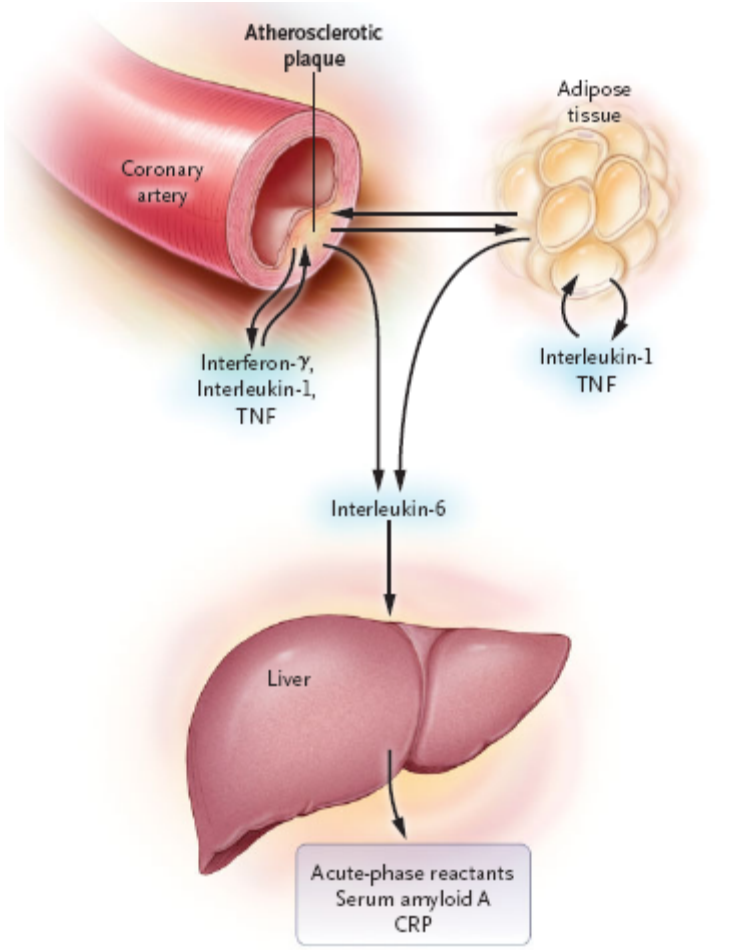
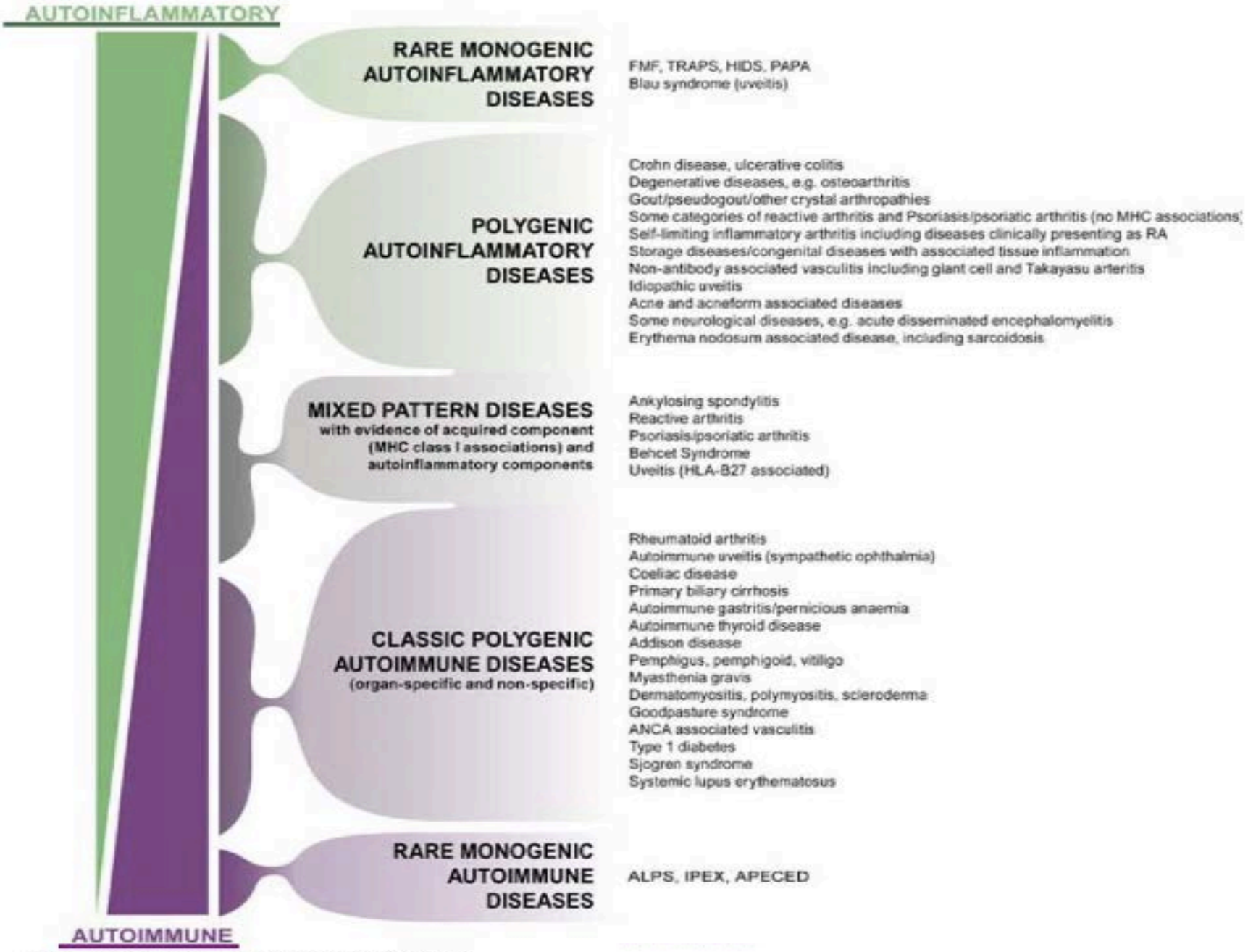


Figure 5. The Cytokine Cascade.

Activated immune cells in the plaque produce inflammatory cytokines (interferon-γ, interleukin-1, and tumor necrosis factor [TNF]), which induce the production of substantial amounts of interleukin-6. These cytokines are also produced in various tissues in response to infection and in the adipose tissue of patients with the metabolic syndrome. Interleukin-6, in turn, stimulates the production of large amounts of acute-phase reactants, including C-reactive protein (CRP), serum amyloid A, and fibrinogen, especially in the liver. Although cytokines at all steps have important biologic effects, their amplification at each step of the cascade makes the measurement of downstream mediators such as CRP particularly useful for clinical diagnosis.



DOI: 10.1371/journal.pmed.0030297.g001

McGonagle D et al. PLoS Med 2006; e297

ATEROSCLEROSIS
MALALTIA DE DEPÒSIT
AMB COMPONENT AUTOINFLAMATORI

Table 1: Clinical classification of autoinflammatory diseases.

Disease	Gene (protein)	Possible mechanism
Hereditary periodic fever syndromes		
Familial Mediterranean fever (FMF)	*MEFV* (pyrin)	increased inflammasome activity
TNF receptor-associated periodic syndrome (TRAPS)	*TNFRSF1A* (TNFR1)	misfolding of proteins
Hyperimmunoglobulinemia syndrome (HIDS)	*MVK* (mevalonate kinase)	increased inflammasome activity
Familial cold urticaria (FCAS)	*NLRP3* (cryopyrin)	intrinsic inflammasomopathy
Muckle-Wells syndrome (MWS)	*NLRP3* (cryopyrin)	intrinsic inflammasomopathy
Neonatal inflammatory multiorgan syndrome (NOMID)	*NLRP3* (cryopyrin)	intrinsic inflammasomopathy
Idiopathic fever syndromes		
Systemic juvenile idiopathic arthritis/ Still disease (SoJIA)	complex	unknown
Adult Still disease	complex	unknown
Schnitzler syndrome	*NLRP3* + Sporadic?	increased inflammasome activity
		pyrin
		-1α/β
Metabolic diseases		
Gout	complex	crystal-induced inflammasome activation
Pseudogout	complex	crystal-induced inflammasome activation
Type II diabetes mellitus	complex	hyperglycemia-induced inflammasome activation
Complement disorders		
Atypical hemolytic uremic syndrome (aHUS)	Complement factors H (CFH), B (CFB), I (CFI), MCP (CD46)	abnormal regulation of C3b
Senile macular degeneration	complex, complement factor B	disturbed inactivation of C3b
Vasculitis		
Behçet disease	complex	unknown
Macrophage activation syndromes		
Familial hemophagocytic lymphohistiocytosis (HLH)	*UNC13D* (munc13-4), *PRF1* (perforin 1) *STX11* (syntaxin 11)	disturbed function of cytotoxic T lymphocytes with compensatory activation of macrophages
Secondary HLH	complex	unknown
Disorder of deposition		
Morbus Gaucher	β-Glucocerebrosidase	unknown
Arteriosclerosis	complex	unknown
Sclerotic diseases		
Asbestosis/ silicosis	complex	foreign body-induced inflammasome activation

Adapted according to Kastner et al. [1].

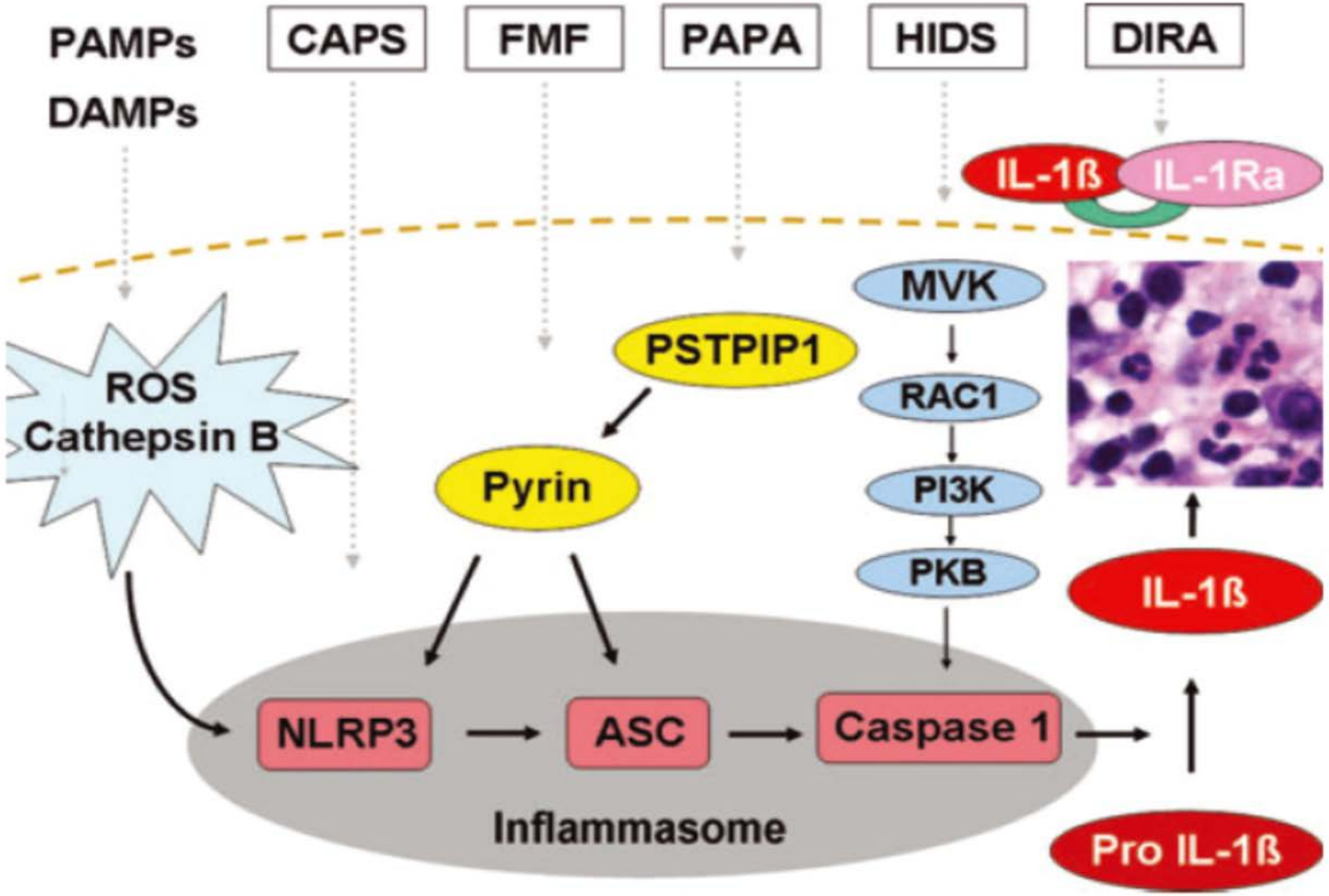


Figure 4: Targeted molecules influencing the activity of the NLRP3 inflammasome in autoinflammatory diseases.

September 21, 2017
N Engl J Med 2017; 377:1119-1131
DOI: 10.1056/NEJMoa1707914

Antiinflammatory Therapy with Canakinumab for Atherosclerotic Disease

Paul M Ridker, M.D., Brendan M. Everett, M.D., Tom Thuren, M.D., Jean G. MacFadyen, B.A., William H. Chang, Ph.D., Christie Ballantyne, M.D., Francisco Fonseca, M.D., Jose Nicolau, M.D., Wolfgang Koenig, M.D., Stefan D. Anker, M.D., John J.P. Kastelein, M.D., Jan H. Cornel, M.D., et al., for the CANTOS Trial Group*

Table 2. Incidence Rates and Hazard Ratios for Major Clinical Outcomes and All-Cause Mortality.*

Clinical Outcome	Placebo Group (N=3344)	Canakinumab				P Value for Trend across Doses vs. Placebo
		50-mg Group (N=2170)	150-mg Group (N=2284)	300-mg Group (N=2263)	All Doses (N=6717)	
Primary end point†						
Incidence rate per 100 person-yr (no. of patients)	4.50 (535)	4.11 (313)	3.86 (320)	3.90 (322)	3.95 (955)	0.02
Hazard ratio (95% CI)	1.00	0.93 (0.80–1.07)	0.85 (0.74–0.98)	0.86 (0.75–0.99)	0.88 (0.79–0.97)	
P value	—	0.30‡	0.021§	0.031‡	0.02	
Key secondary cardiovascular end point¶						
Incidence rate per 100 person-yr (no. of patients)	5.13 (601)	4.56 (344)	4.29 (352)	4.25 (348)	4.36 (1044)	0.003
Hazard ratio (95% CI)	1.00	0.90 (0.78–1.03)	0.83 (0.73–0.95)	0.83 (0.72–0.94)	0.85 (0.77–0.94)	
P value	—	0.12‖	0.005§	0.004‖	0.001	
Myocardial infarction, stroke, or death from any cause						
Incidence rate per 100 person-yr (no. of patients)	5.56 (661)	5.17 (394)	4.77 (395)	4.88 (403)	4.93 (1192)	0.02
Hazard ratio (95% CI)	1.00	0.94 (0.83–1.07)	0.85 (0.75–0.96)	0.87 (0.77–0.99)	0.89 (0.81–0.97)	
P value	—	0.35	0.01	0.03	0.01	
Myocardial infarction						
Incidence rate per 100 person-yr (no. of patients)	2.43 (292)	2.20 (169)	1.90 (159)	2.09 (174)	2.06 (502)	0.03
Hazard ratio (95% CI)	1.00	0.94 (0.78–1.15)	0.76 (0.62–0.92)	0.84 (0.70–1.02)	0.84 (0.73–0.97)	
P value	—	0.56	0.005	0.07	0.02	
Hospitalization for unstable angina that led to urgent revascularization						
Incidence rate per 100 person-yr (no. of patients)	0.69 (85)	0.48 (38)	0.44 (38)	0.40 (34)	0.44 (110)	0.005
Hazard ratio (95% CI)	1.00	0.70 (0.47–1.03)	0.64 (0.44–0.94)	0.58 (0.39–0.86)	0.64 (0.48–0.85)	
P value	—	0.07	0.02	0.006	0.002	
Any coronary revascularization						
Incidence rate per 100 person-yr (no. of patients)	3.61 (421)	2.53 (191)	2.49 (205)	2.56 (209)	2.53 (605)	<0.001
Hazard ratio (95% CI)	1.00	0.72 (0.60–0.86)	0.68 (0.58–0.81)	0.70 (0.59–0.83)	0.70 (0.62–0.79)	
P value	—	<0.001	<0.001	<0.001	<0.001	

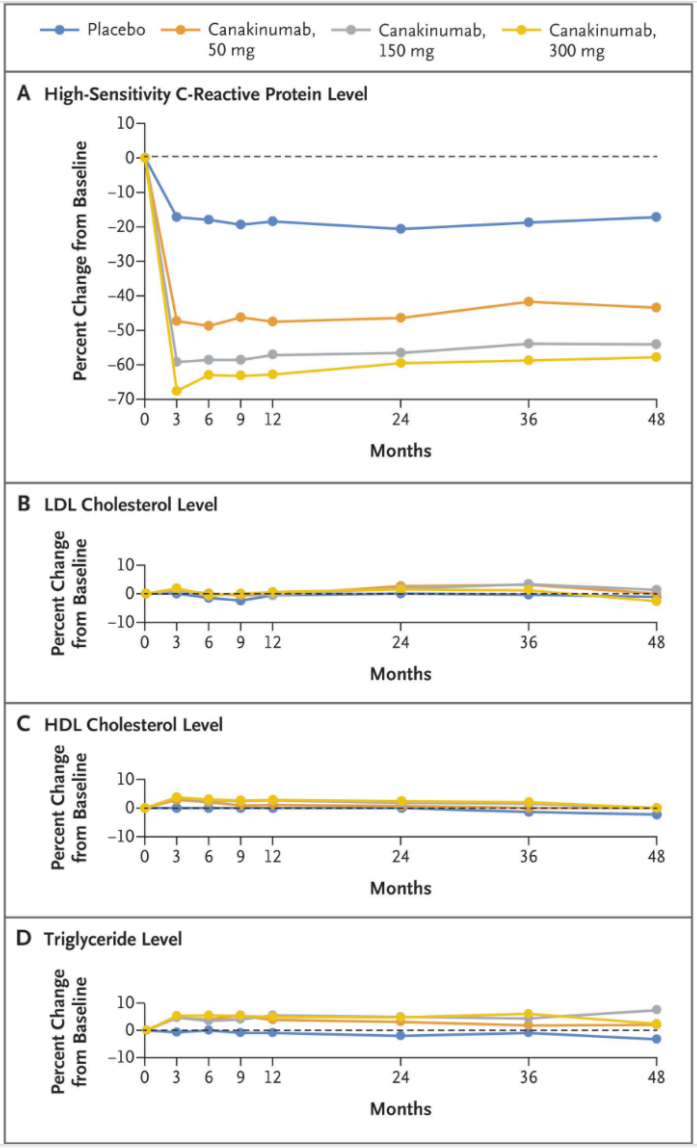


Figure 1. Effects of Canakinumab, as Compared with Placebo, on Plasma Levels of High-Sensitivity C-Reactive Protein, Low-Density Lipoprotein (LDL) Cholesterol, High-Density Lipoprotein (HDL) Cholesterol, and Triglycerides.

Table 3. Incidence Rates and Numbers of Serious Adverse Events and Selected Safety Laboratory Data During Treatment, Stratified According to Trial Group.*

Adverse Event or Laboratory Variable	Placebo Group (N=3344)	Canakinumab				P Value	
		50-mg Group (N=2170)	150-mg Group (N=2284)	300-mg Group (N=2263)	All Doses (N=6717)	For Trend across Doses vs. Placebo	For Combined Dose Groups vs. Placebo
Event — incidence rate per 100 person-yr (no. of patients with event)							
Any serious adverse event	11.96 (1202)	11.41 (741)	11.71 (812)	12.33 (836)	11.82 (2389)	0.43	0.79
Any serious adverse event of infection	2.86 (342)	3.03 (230)	3.13 (258)	3.25 (265)	3.14 (753)	0.12	0.14
Cellulitis	0.24 (30)	0.24 (19)	0.37 (32)	0.41 (35)	0.34 (86)	0.02	0.09
Pneumonia	0.90 (112)	0.94 (74)	0.94 (80)	0.99 (84)	0.95 (238)	0.56	0.62
Urinary tract infection	0.22 (27)	0.18 (14)	0.24 (21)	0.20 (17)	0.21 (52)	0.84	0.87
Opportunistic infection†	0.18 (23)	0.16 (13)	0.15 (13)	0.20 (17)	0.17 (43)	0.97	0.78
Pseudomembranous colitis	0.03 (4)	0.13 (10)	0.05 (4)	0.12 (10)	0.10 (24)	0.13	0.03
Fatal infection or sepsis	0.18 (23)	0.31 (25)	0.28 (24)	0.34 (29)	0.31 (78)	0.09	0.02
Any cancer‡	1.88 (231)	1.85 (144)	1.69 (143)	1.72 (144)	1.75 (431)	0.31	0.38
Fatal cancer‡	0.64 (81)	0.55 (44)	0.50 (44)	0.31 (27)	0.45 (115)	<0.001	0.02
Other adverse event							
Injection-site reaction†	0.23 (29)	0.27 (21)	0.28 (24)	0.30 (26)	0.28 (71)	0.49	0.36
Arthritis	3.32 (385)	2.15 (164)	2.17 (180)	2.47 (201)	2.26 (545)	0.002	<0.001
Osteoarthritis	1.67 (202)	1.21 (94)	1.12 (95)	1.30 (109)	1.21 (298)	0.04	<0.001
Gout	0.80 (99)	0.43 (34)	0.35 (30)	0.37 (32)	0.38 (96)	<0.001	<0.001
Drug-induced liver injury†	0.18 (23)	0.15 (12)	0.13 (11)	0.05 (4)	0.11 (27)	0.004	0.05
Leukopenia	0.24 (30)	0.30 (24)	0.37 (32)	0.52 (44)	0.40 (100)	0.002	0.01
Neutropenia	0.06 (7)	0.05 (4)	0.07 (6)	0.18 (15)	0.10 (25)	0.01	0.17
Any hemorrhage	4.01 (462)	3.33 (249)	4.15 (327)	3.82 (301)	3.78 (877)	0.94	0.31
Thrombocytopenia	0.43 (53)	0.56 (44)	0.54 (46)	0.71 (60)	0.60 (150)	0.02	0.03
Hepatic variable — percent of patients with condition (no.)							
Alanine aminotransferase >3× normal value	1.4 (46)	1.9 (42)	1.9 (44)	2.0 (45)	2.0 (131)	0.19	0.06
Aspartate aminotransferase >3× normal value	1.1 (36)	1.5 (32)	1.5 (35)	1.5 (34)	1.5 (101)	0.30	0.11
Alkaline phosphatase >3× normal value	0.4 (15)	0.5 (11)	0.4 (10)	0.5 (12)	0.5 (33)	0.67	0.82
Bilirubin >2× normal value	0.8 (26)	1.0 (21)	0.7 (15)	0.7 (15)	0.8 (51)	0.34	0.83

* Data are shown as incidence rates per 100 person-years (with numbers of patients with event) for adverse events and as percentages of patients with the condition (with numbers of patients) for hepatic variables to facilitate the comparison of rates between groups. All adverse-event categories are based on standardized queries or classification levels in the *Medical Dictionary for Regulatory Activities*, version 20.0, except those otherwise indicated.

† These adverse events, including drug-induced liver injury as a serious adverse event, were considered by the sponsor to be adverse events of special interest.

‡ Included here are cancers that were adjudicated by the cancer end-point adjudication committee.

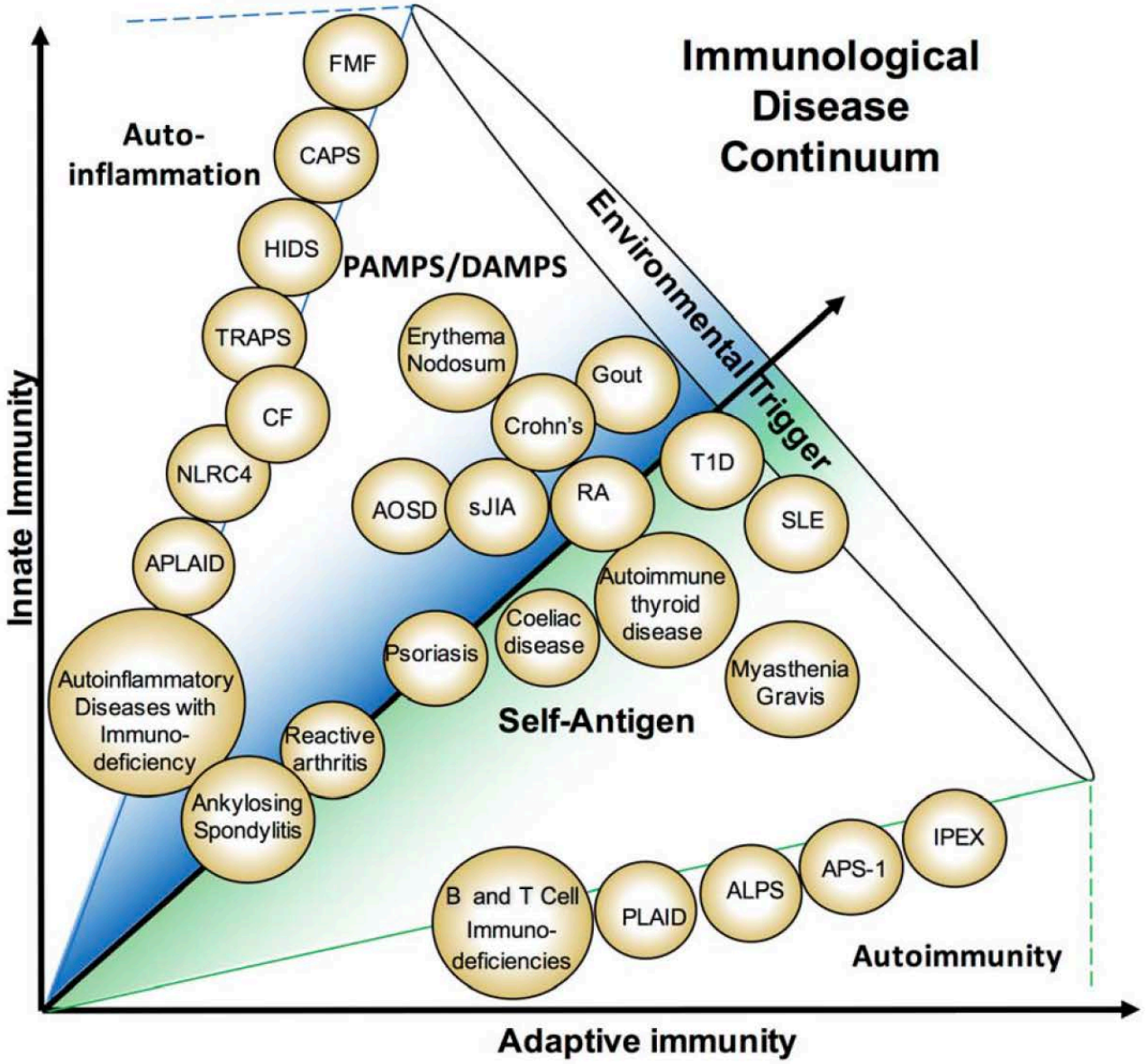


Figure 1: Diseases classified according myeloid (autoinflammation) or lymphoid lineage (autoimmune).

Pathak S, *et al*. *J Clin Pathol* 2017;**70**:1–8. doi:10.1136/jclinpath-2016-203810

MORTALITAT CARDIOVASCULAR I ARTRITIS REUMATOIDE

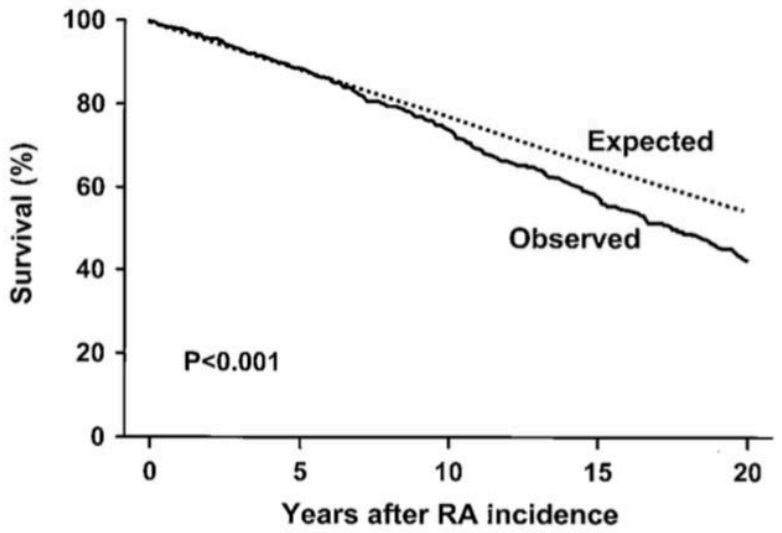


Figure 1. Survival among Rochester, Minnesota residents first diagnosed with rheumatoid arthritis (RA) between January 1, 1955 and December 31, 1994 (n = 609), compared with expected survival.

Table 3. Predictors of mortality in 609 incidence cases of rheumatoid arthritis

	Hazards ratio*	95% confidence interval
Extraarticular manifestations	4.4	3.2–6.3
Comorbidity		
Cardiovascular disease	1.6	1.2–2.1
Renal disease	2.2	1.4–3.4
Liver disease	3.3	1.7–6.7
Dementia	3.7	2.7–5.0
Cancer, no chemotherapy	1.9	1.4–2.6
Cancer, with chemotherapy	6.9	3.6–12.9
History of alcohol use	2.7	1.8–4.1
Steroid use	1.5	1.2–2.0

* From the Cox proportional hazards model adjusted for age, sex, body mass index, history of smoking, and rheumatoid factor positivity.

ARTHRITIS & RHEUMATISM
Vol. 48, No. 1, January 2003, pp 54–58

Risk of Cardiovascular Mortality in Patients With Rheumatoid Arthritis: A Meta-Analysis of Observational Studies

J. ANTONIO AVIÑA-ZUBIETA,[1] HYON K. CHOI,[1] MOHSEN SADATSAFAVI,[2] MAHYAR ETMINAN,[2] JOHN M. ESDAILE,[1] AND DIANE LACAILLE[1]

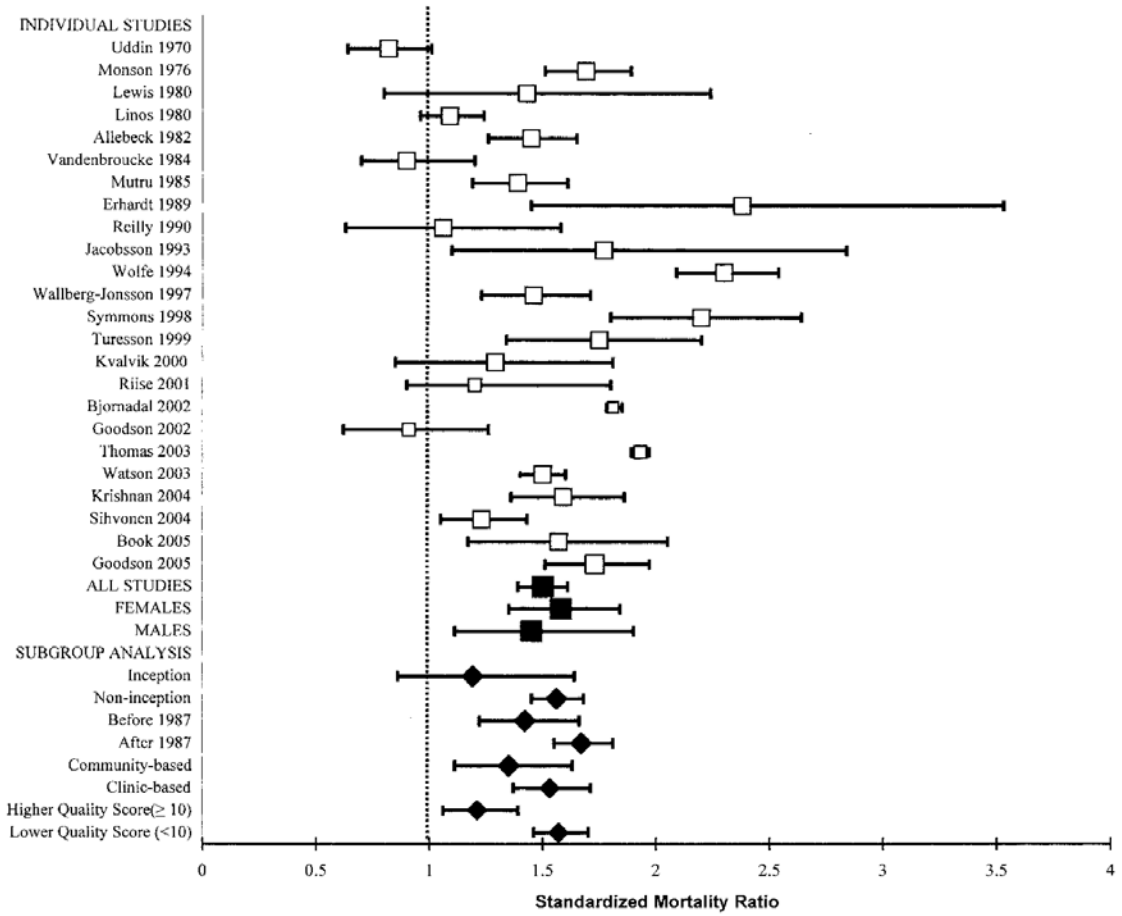


Figure 1. Meta-analysis of 24 studies on cardiovascular disease mortality in patients with rheumatoid arthritis.

Cardiovascular morbidity and associated risk factors in Spanish patients with chronic inflammatory rheumatic diseases attending rheumatology clinics: Baseline data of the CARMA Project

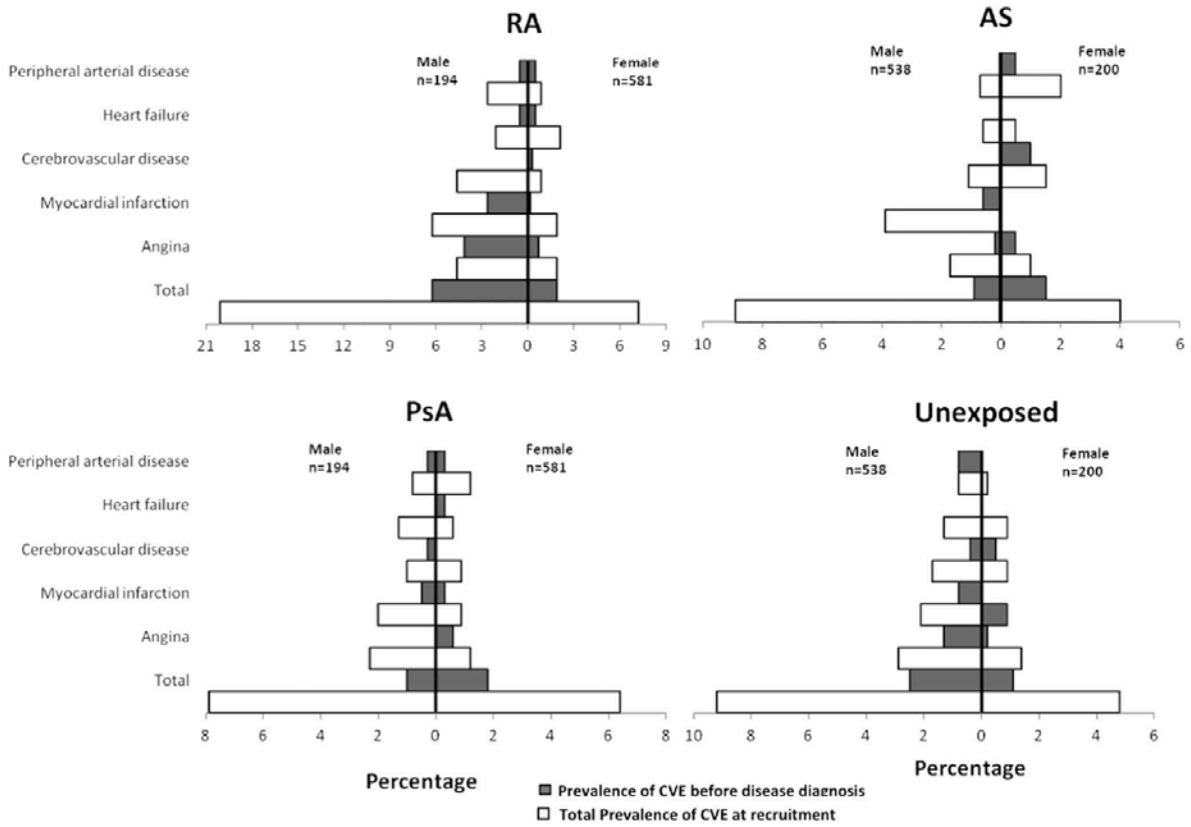


Fig. 1. Prevalence of cardiovascular events in both exposed (RA, AS, and PsA) and unexposed cohorts. Gray boxes represent prevalence of cardiovascular events before disease diagnosis (for each disease). Empty boxes represent total prevalence at the time of recruitment.

S. Castañeda et al. / Seminars in Arthritis and Rheumatism 44 (2015) 618–626

Variables	Rheumatoid arthritis ($n = 775$)	Ankylosing spondylitis ($n = 738$)	Psoriatic arthritis ($n = 721$)	Unexposed matched cohort ($n = 677$)	p
Sociodemographic features					
Age at inclusion, years, mean (SD)	57.1 (12.3)	48.1 (11.7)	51.8 (12.0)	54.0 (12.4)	< 0.001
Age at the beginning of disease, years, mean (SD)	45.8 (13.4)	29.7 (11.8)	39.5 (13.3)	48.5 (12.4)	< 0.001
Sex, female, *n* (%)	581 (75.0)	200 (27.1)	327 (45.4)	437 (64.5)	< 0.001
Educational level, *n* (%)					
Elementary	467 (60.9)	318 (43.3)	331 (46.3)	229 (34.1)	
Secondary/university	300 (39.1)	416 (56.7)	383 (53.7)	443 (65.9)	< 0.001
Traditional CV risk factors					
BMI, kg/m^2, mean (SD)	26.9 (4.8)	27.4 (4.4)	28.2 (4.7)	26.7 (4.4)	< 0.001
Abdominal perimeter, mean (SD)	93.7 (7.0)	96.3 (12.9)	97.6 (13.0)	93.5 (12.9)	< 0.001
Hypertension, *n* (%)	236 (30.5)	190 (25.7)	213 (29.5)	158 (23.3)	0.008
Hypercholesterolemia, *n* (%)	238 (30.7)	199 (27)	257 (35.6)	224 (33.1)	0.003
Diabetes, *n* (%)	60 (7.8)	56 (7.6)	66 (9.2)	34 (5.0)	0.030
Obesity (BMI $\geq$ 30), *n* (%)	180 (23.2)	186 (25.2)	209 (29.1)	147 (21.8)	0.010
Smoking status, *n* (%)					
Current smokers	189 (24.4)	254 (34.4)	157 (21.8)	143 (21.2)	
Past smokers	202 (26.1)	240 (32.5)	227 (31.5)	176 (26.0)	< 0.001
Never smokers	384 (49.5)	244 (33.1)	337 (46.7)	357 (52.8)	
Clinical characteristics					
Disease duration, years	8.0 (3.0–14.0)	15.0 (8.0–26.0)	9.0 (4.0–16.0)	2.0 (0.0–6.0)	< 0.001
DAS28-ESR	3.1 (2.3–4.0)	–	2.9 (2.0–3.8)	–	0.002
BASDAI (0–10)	–	3.5 (1.7–5.3)	–	–	–
HAQ (1–3)	0.5 (0.1–1.1)	–	0.4 (0.0–0.9)	–	< 0.001
BASFI (0–10)	–	3.1 (1.3–5.2)	–	–	–
ESR, mm/first hour	17.0 (9.0–29.0)	10.0 (6.0–21.0)	12.0 (6.0–21.0)	10.0 (5.0–18)	< 0.001
CRP, mg/L	3.1 (1.2–8.0)	3.6 (1.6–8.9)	2.9 (1.4–6.1)	1.9 (1.3–3.3)	< 0.001
RF positive, *n* (%)	528 (68.1)	–	–	–	–
ACPA positive, *n* (%)	482 (62.2)	–	–	–	–
HLA-B27, *n* (%)	–	561 (76)	–	–	–
Erosions (RA), *n* (%)	352 (45.4)				–
Biologic DMARD, *n* (%)	313 (40.4)	349 (47.4)	300 (41.7)	–	< 0.001
Synthetic DMARD, *n* (%)	674 (87.0)	239 (32.4)	536 (74.5)	–	< 0.001
NSAID, *n* (%)	309 (39.9)	431 (58.5)	329 (45.9)	142 (21.0)	< 0.001
GC, *n* (% ever treated)	357 (46.1)	59 (8.0)	129 (17.9)	–	< 0.001

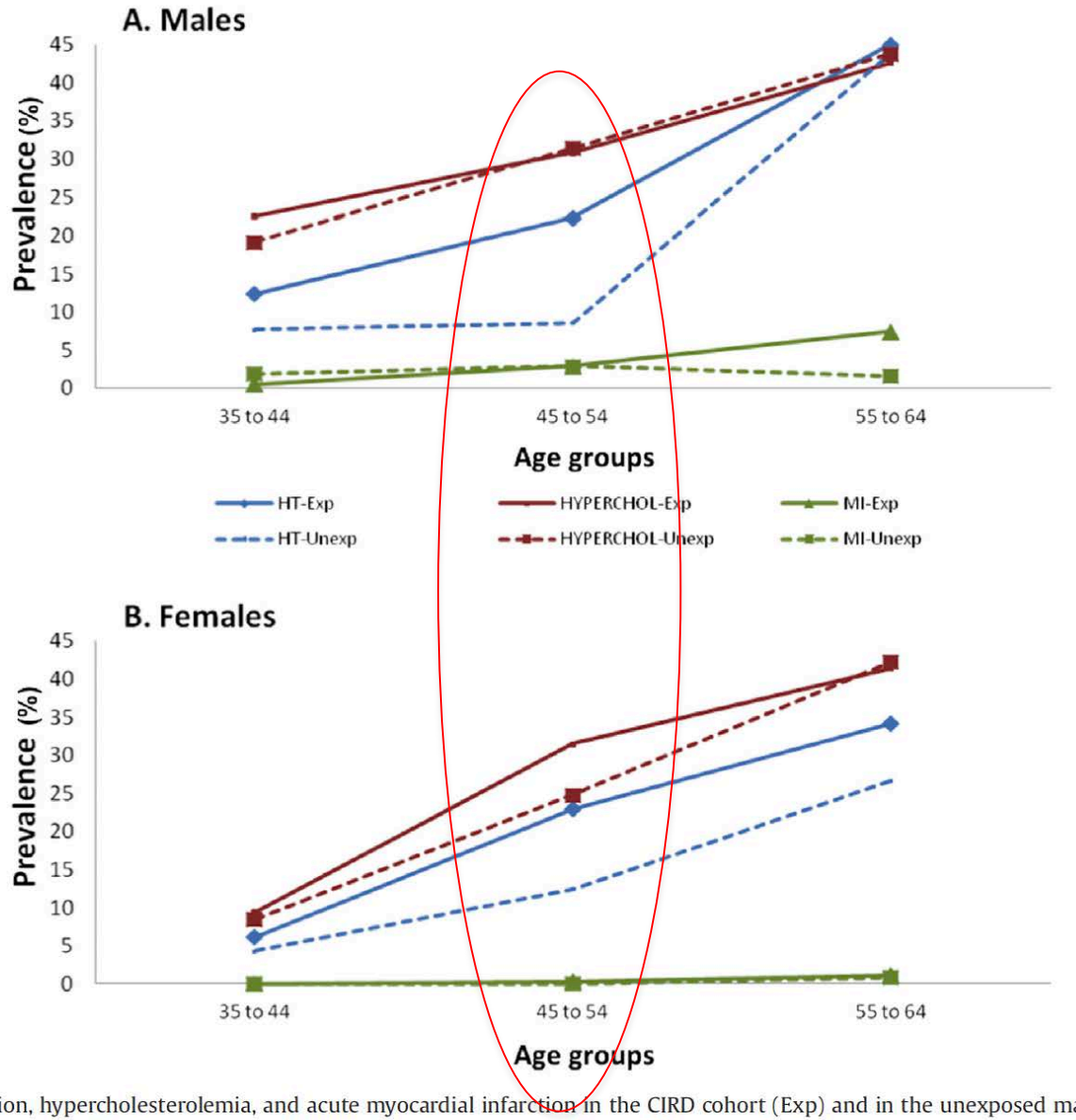


Fig. 2. Prevalence of hypertension, hypercholesterolemia, and acute myocardial infarction in the CIRD cohort (Exp) and in the unexposed matched cohort (Unexp). (Upper panel) males and (Lower panel) females. HT: hypertension; HYPERCHOL: hypercholesterolemia; MI: myocardial infarction.

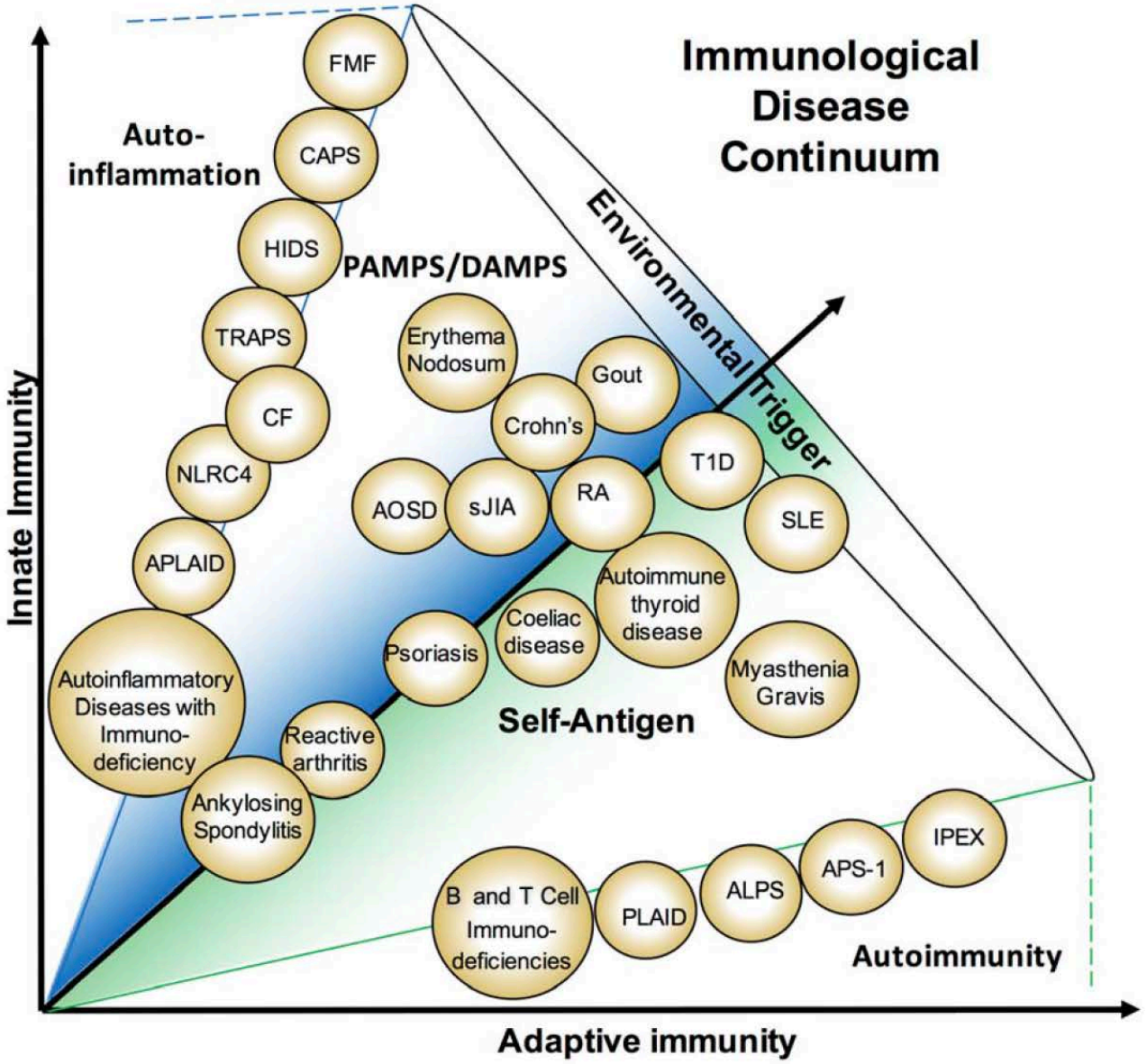


Figure 1: Diseases classified according myeloid (autoinflammation) or lymphoid lineage (autoimmune).

MORTALITAT CARDIOVASCULAR I LES

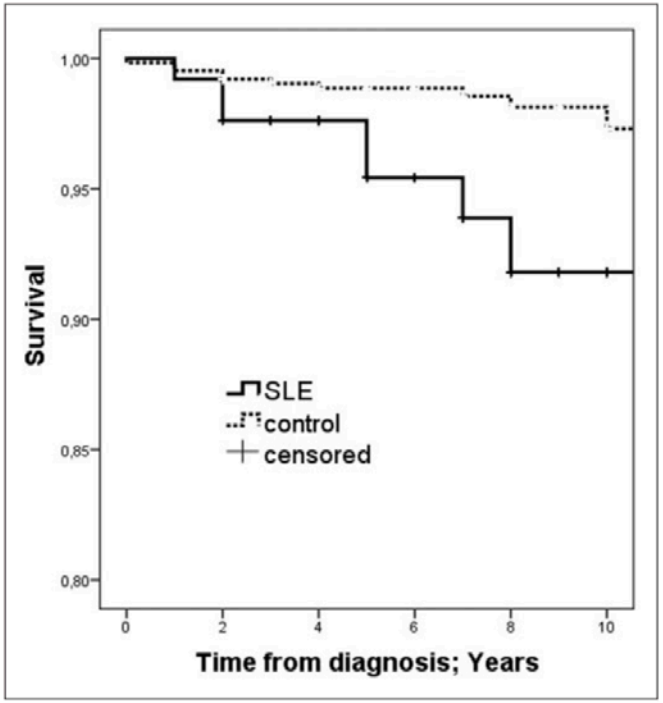


Figure 1 Kaplan-Meier estimated survival function for incident cases 1999–2010 captured within one year after diagnosis ($n = 127$).

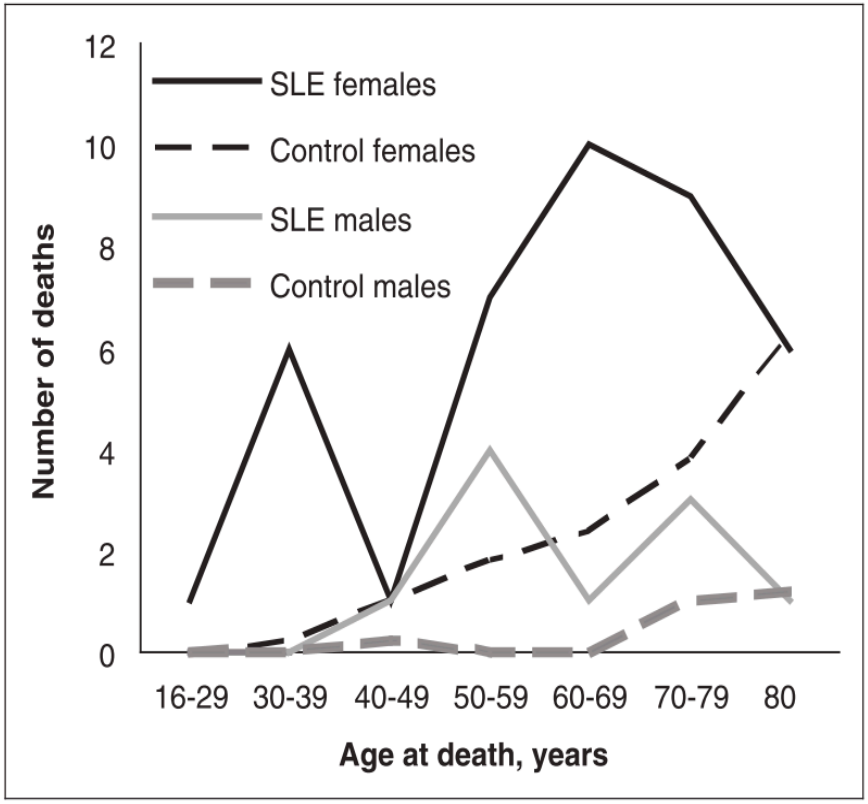
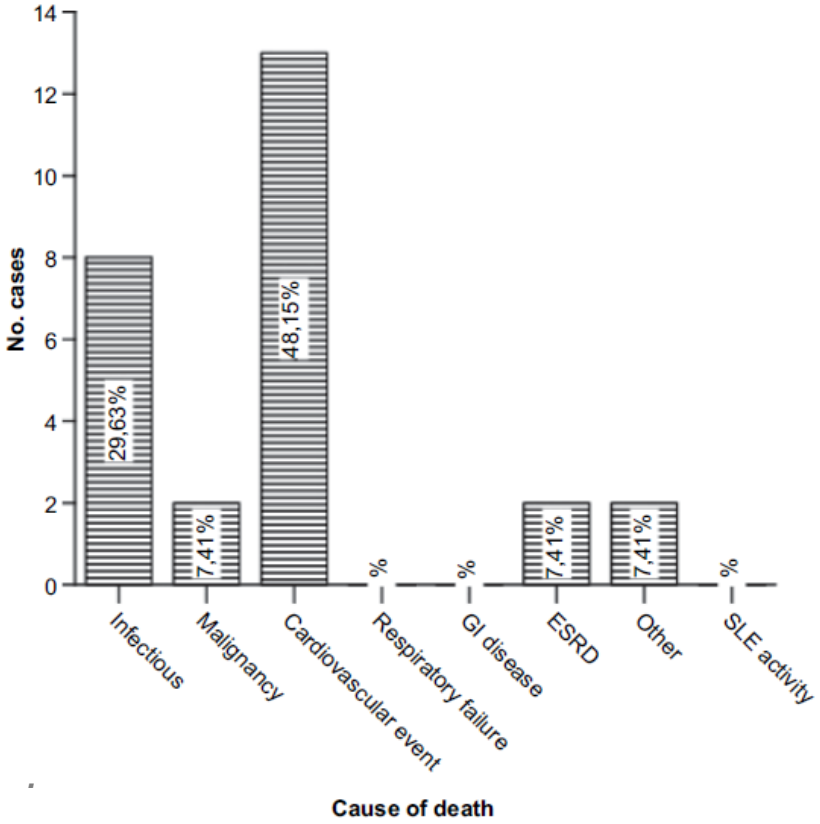


Figure 2 Distribution of age at death for male and female systemic lupus erythematosus (SLE) patients who died during 1999–2010 and their matched controls.

K. Lerang et al.2014. Lupus



J Nossent et al. **LUPUS**, *2007*

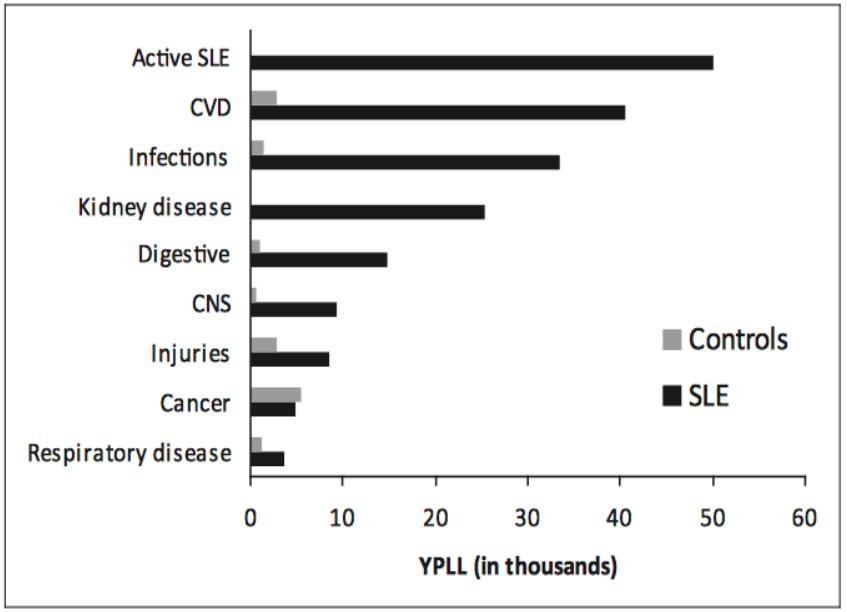


Figure 3 Years of potential life loss before 60 years of age (YPLL60) related to specific causes of death per 1000 person-years for systemic lupus erythematosus (SLE) patients and their control individuals (matched for sex, age and ethnicity). Diseases are all causes reported on the death certificate (underlying and associated), meaning that one SLE patient may be represented in more than one cause. Active SLE disease is registered from the medical record.
CVD: cardiovascular disease; CNS: central nervous system.

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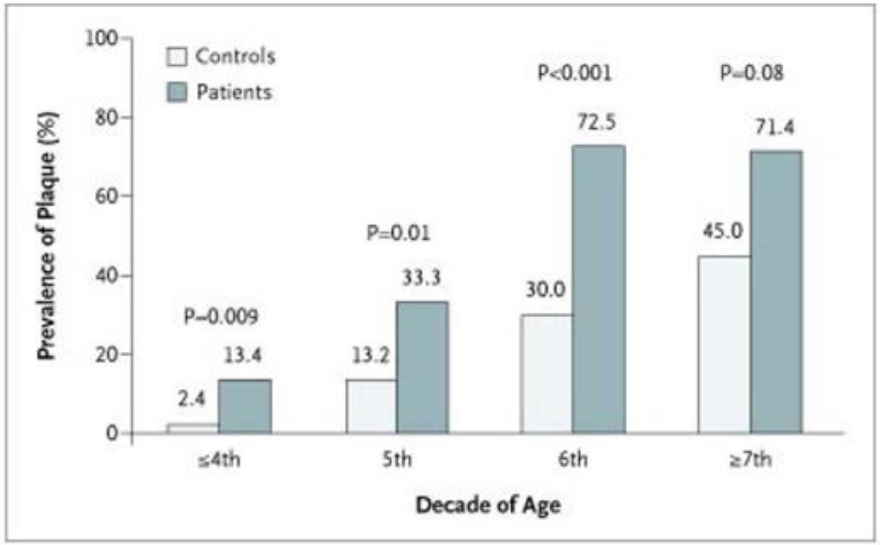
Table 1. Summary of risk factors for atherosclerotic coronary events in the Toronto, Baltimore, and Pittsburgh cohorts

Risk factor	Toronto [1]	Baltimore [5]	Pittsburgh [6]
Older age at SLE diagnosis	Yes	Yes	Yes
Longer disease duration	–	Yes	Yes
Hypercholesterolemia	Yes	Yes	Yes
Hypertension	Yes	Yes	–
Hypertriglyceridemia	Yes	–	–
Longer duration of steroid use	–	Yes	Yes
Other factors	Diabetes mellitus, pericarditis, myocarditis, congestive heart failure	Obesity, older age at clinic entry	Postmenopausal

SLE—systemic lupus erythematosus.

Prevalencia de placa de ateroma entre controles y pacientes en función de la década de la vida



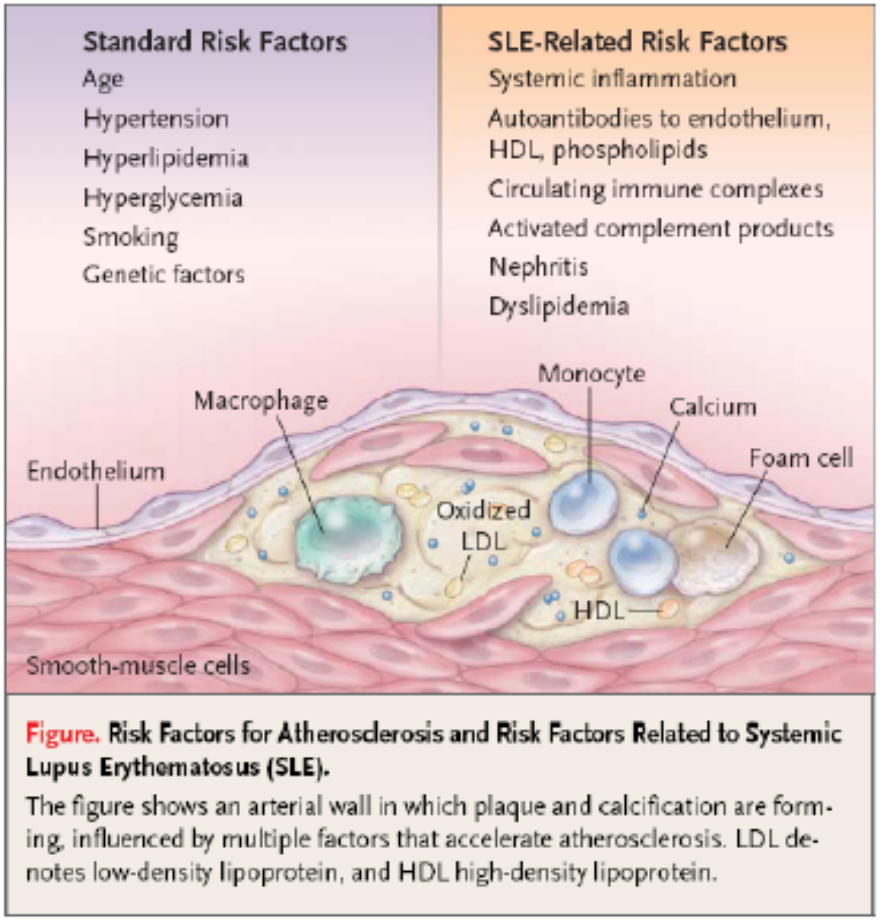
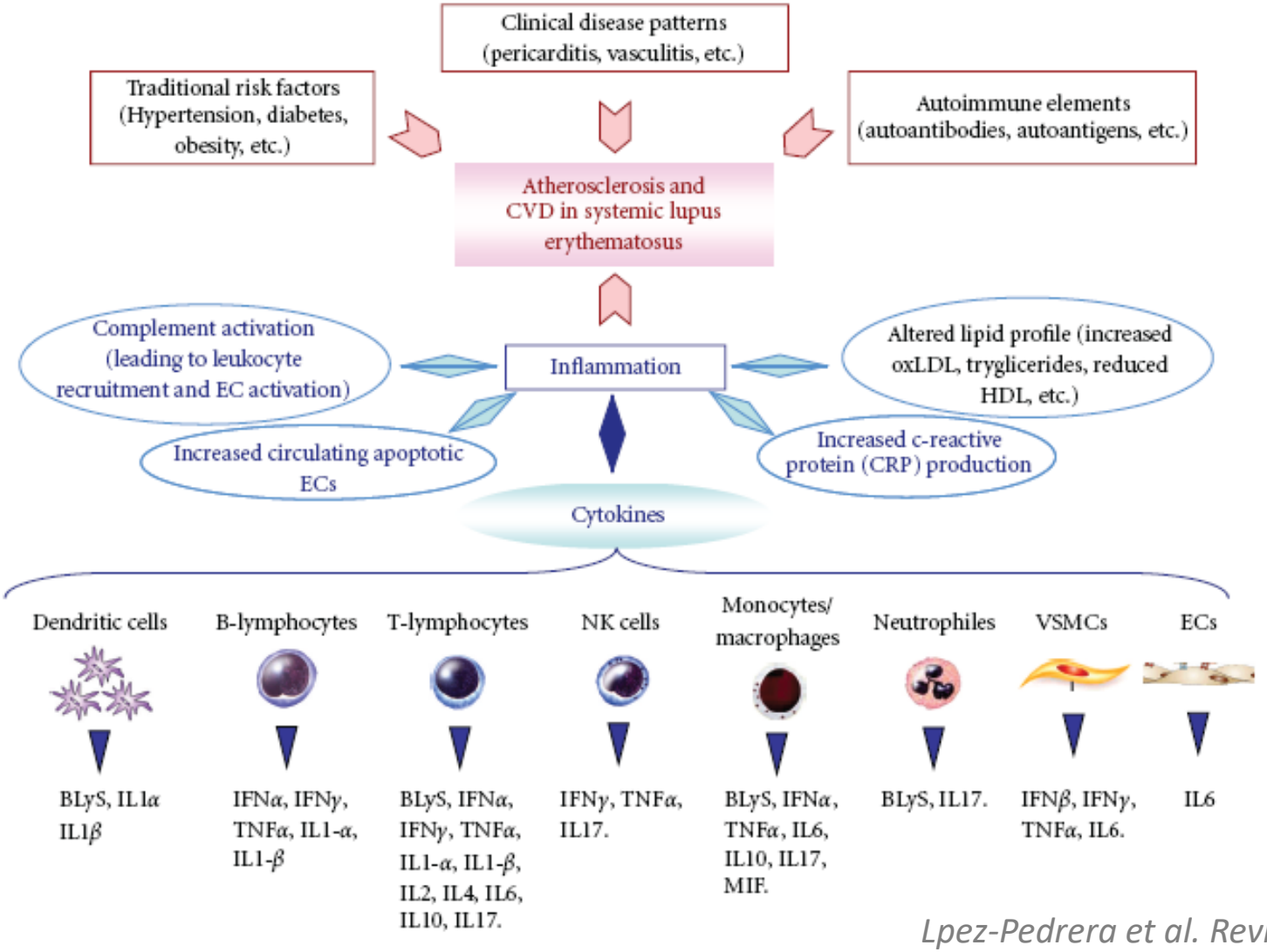


Figure. Risk Factors for Atherosclerosis and Risk Factors Related to Systemic Lupus Erythematosus (SLE).

The figure shows an arterial wall in which plaque and calcification are forming, influenced by multiple factors that accelerate atherosclerosis. LDL denotes low-density lipoprotein, and HDL high-density lipoprotein.



Lpez-Pedrera et al. Review. 2010

FIGURE 1: Mechanisms leading to atherogenesis and Cardiovascular disease in SLE patients. ECs: endothelial cells; VSMCs: vascular smooth muscle cells; TNF: tumour necrosis factor; ILs: interleukins; IFN: interferon; BLyS: B lymphocyte stimulator.

Table 2
Immune responses and pro-inflammatory molecules that promote atherosclerosis in autoimmunity and in persons without autoimmune diseases

A. Immune cells and molecules	
i	Autoantibodies (to Hsp65, OxLDL, cardiolipin, Beta2 glycoprotein 1, DNA, HDL, Apolipoprotein A1, lipoprotein lipase)
ii	Autoreactive T cells (recognizing Hsp, beta2 glycoprotein 1), including CD4+CD28− Th1-type cells in the arteries of patients with RA
B. Markers of Predisposition to Atherosclerosis	
i	Pro-inflammatory HDL (piHDL)
ii	OxLDL
iii	ESR
iv	CRP
v	Homocysteine
vi	OxDNA
vii	Chemokines (MCP-1)
viii	Cytokines (IL-1β, TNFα, IFNγ and others)

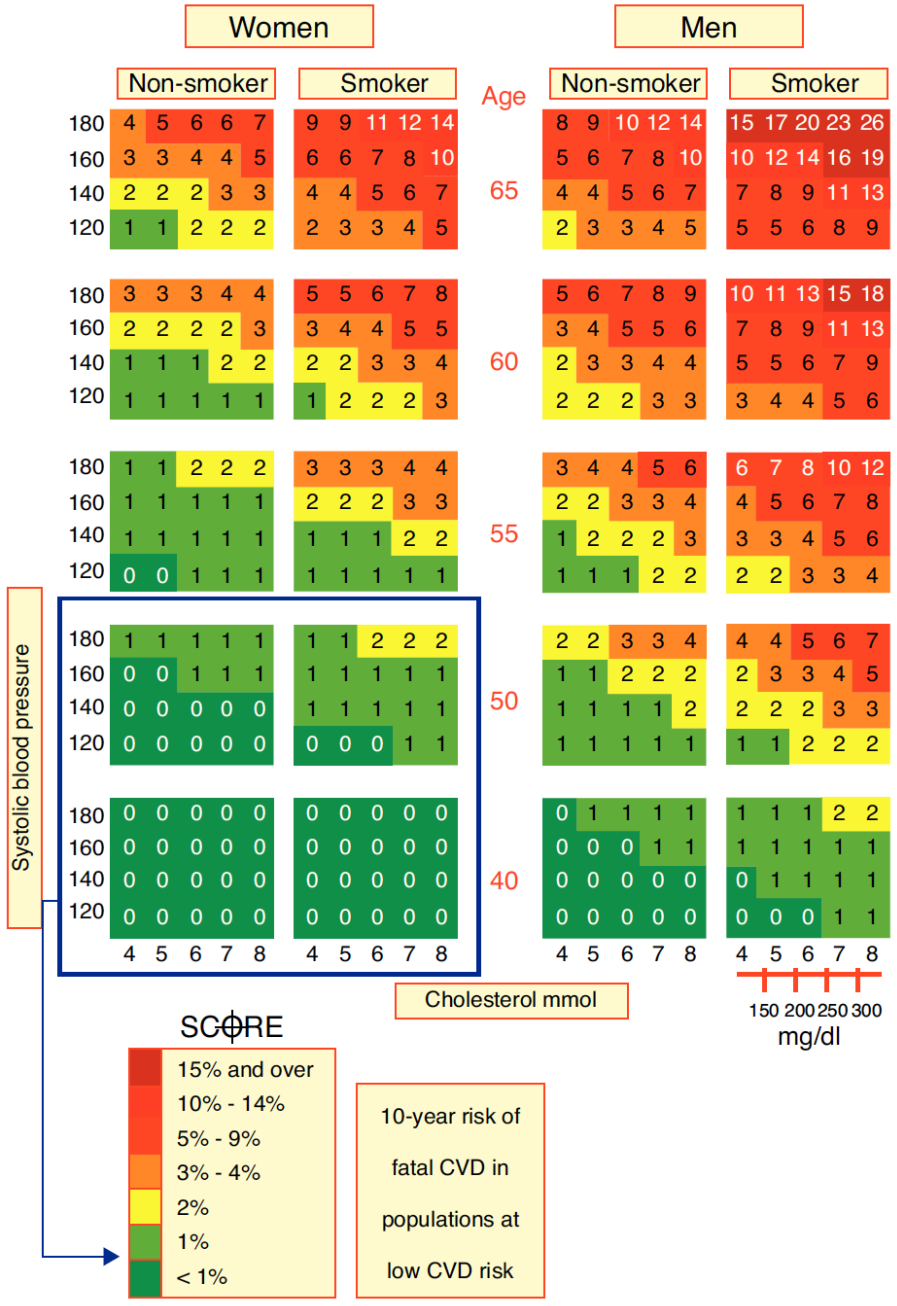


Figura 1. Tabla SCORE Europeo (bajo riesgo). En el recuadro azul se ejemplifica l infraestimación del riesgo cardiovascular en el grueso de las pacientes lúpicas.

Table 8 Recommendations for treatment targets for LDL-C

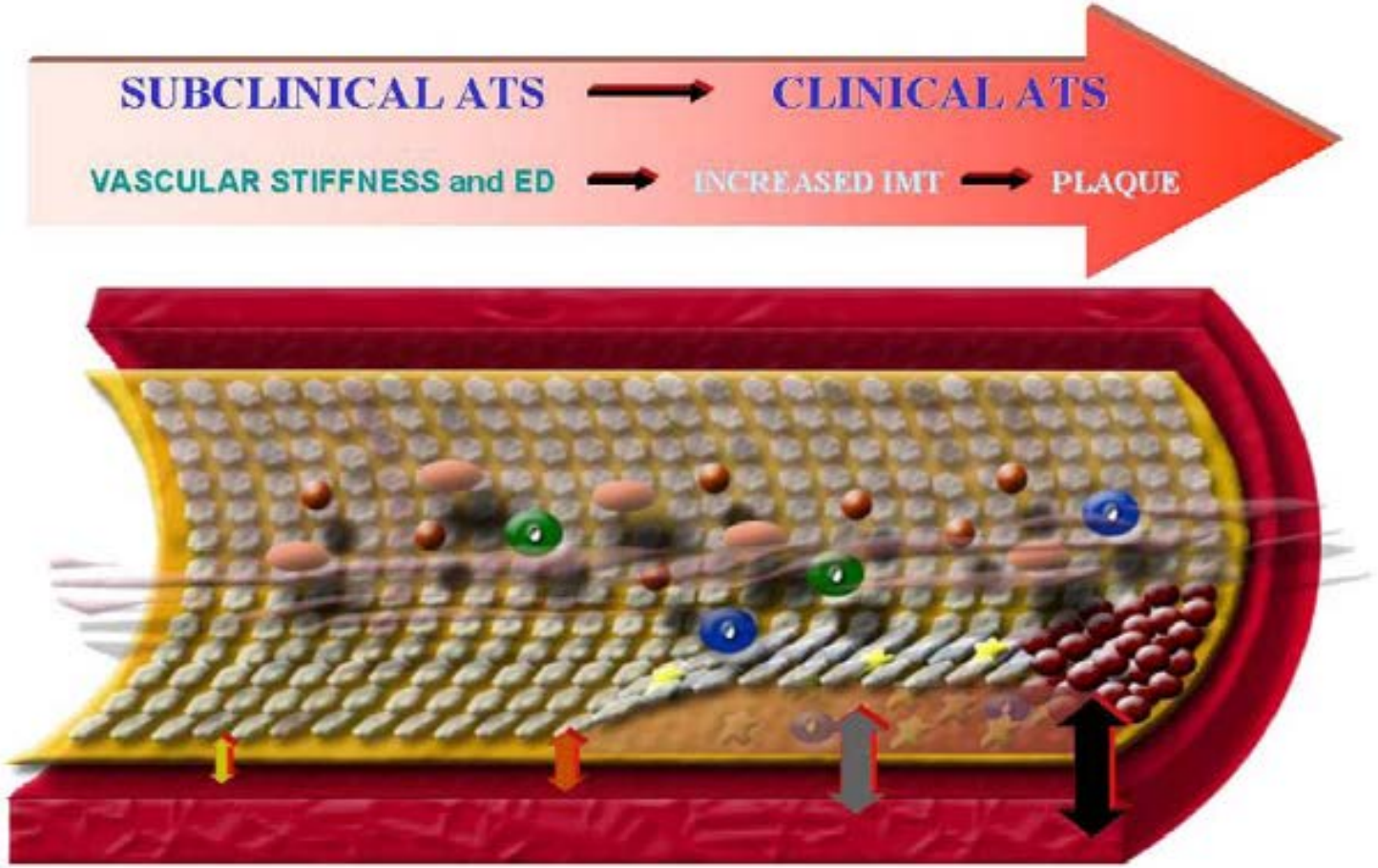
Recommendations	Class[a]	Level[b]	Ref[c]
In patients at VERY HIGH CV risk (established CVD, type 2 diabetes, type 1 diabetes with target organ damage, moderate to severe CKD or a SCORE level ≥10%) the LDL-C goal is <1.8 mmol/L (less than ~70 mg/dL) and/or ≥50% LDL-C reduction when target level cannot be reached.	I	A	15, 32, 33
In patients at HIGH CV risk (markedly elevated single risk factors, a SCORE level ≥5 to <10%) an LDL-C goal <2.5 mmol/L (less than ~100 mg/dL) should be considered.	IIa	A	15, 16, 17
In subjects at MODERATE risk (SCORE level >1 to ≤5%) an LDL-C goal <3.0 mmol/L (less than ~115 mg/dL) should be considered.	IIa	C	-

[a]Class of recommendation.
[b]Level of evidence.
[c]References.
CKD = chronic kidney disease; CV = cardiovascular; CVD = cardiovascular disease; LDL-C = low-density lipoprotein-cholesterol.

Table 27 Recommendations for treatment of dyslipidaemia in autoimmune diseases

Recommendations	Class[a]	Level[b]
As yet there is no indication for the preventive use of lipid-lowering drugs only on the basis of the presence of autoimmune diseases.	III	C

[a]Class of recommendation.
[b]Level of evidence.



ED: endothelial dysfunction; **ATS:** atherosclerosis; **IMT:** intima-media thickness

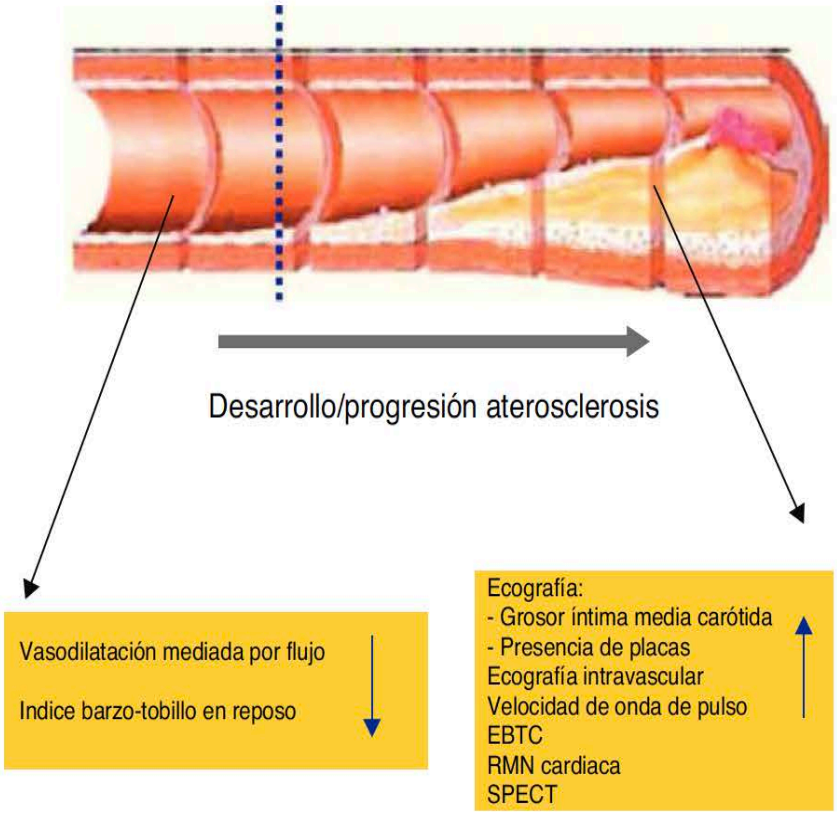


Figura 2. Técnicas de imagen para la valoración de la enfermedad aterosclerótica en el lupus eritematoso sistémico.

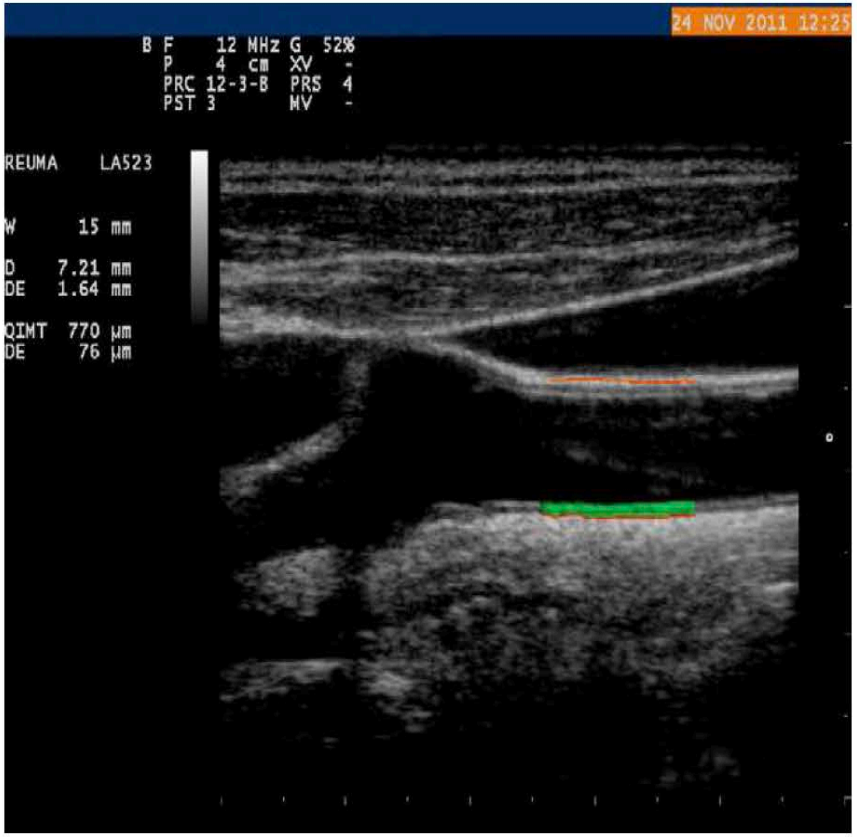
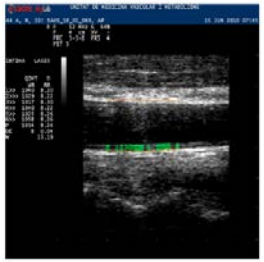
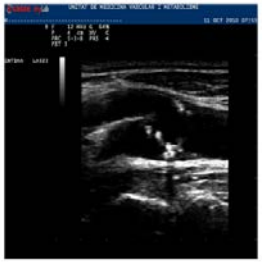


Figura 3. Ecografía carotídea de alta frecuencia y software específico para la medición del grosor íntima-media 1 cm por debajo de la bifurcación carotídea.

MARCADORS D'ARTERIOSCLEROSI SUBCLÍNICA





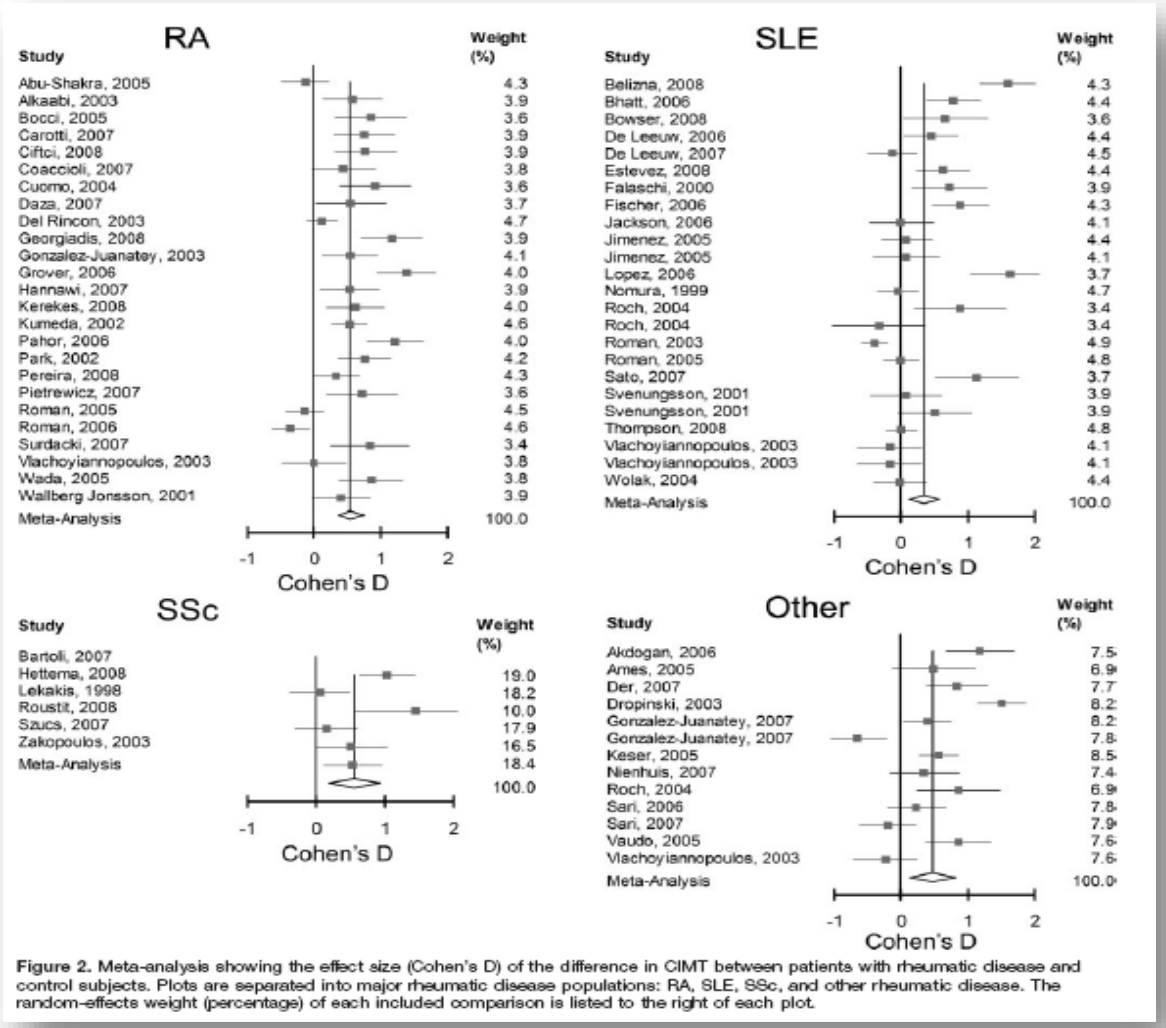


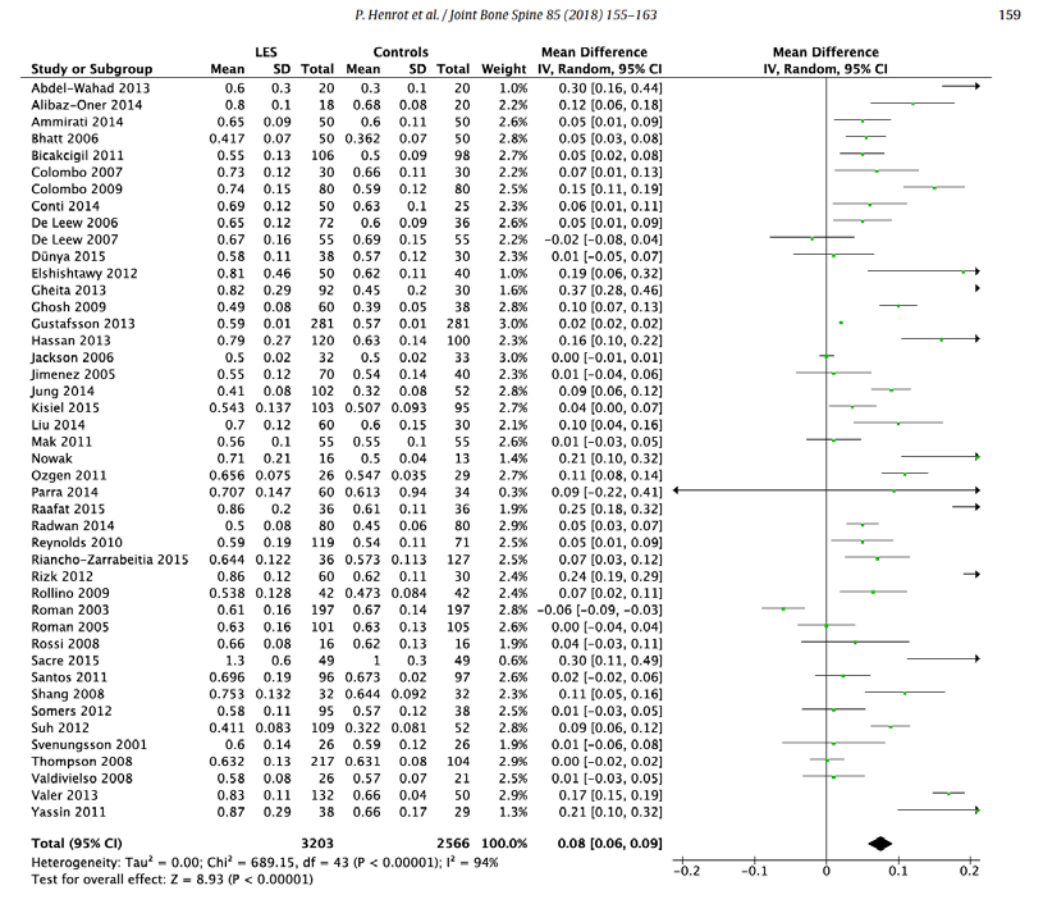
Figure 2. Meta-analysis showing the effect size (Cohen's D) of the difference in CIMT between patients with rheumatic disease and control subjects. Plots are separated into major rheumatic disease populations: RA, SLE, SSc, and other rheumatic disease. The random-effects weight (percentage) of each included comparison is listed to the right of each plot.

ATVB. 2010.

Recommendations and metaanalyses

Assessment of subclinical atherosclerosis in systemic lupus erythematosus: A systematic review and meta-analysis

Pauline Henrot[a,1], Jennifer Foret[b,1], Thomas Barnetche[a], Estibaliz Lazaro[c], Pierre Duffau[d], Julien Seneschal[e], Thierry Schaeverbeke[a], Marie-Elise Truchetet[a,1], Christophe Richez[a,1,*]



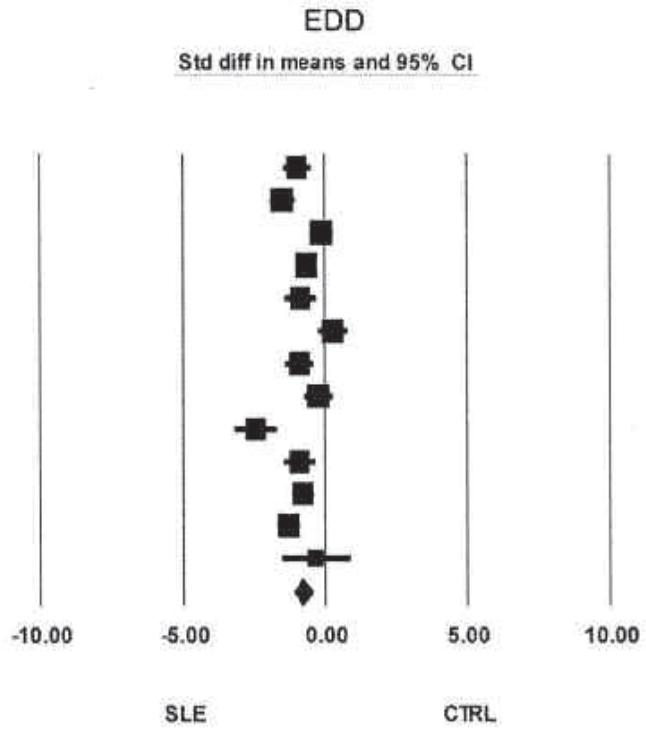
MARCADORS D'ARTERIOSCLEROSI SUBCLÍNICA: DISFUNCIÓ ENDOTELIAL

Mak A. Et al. 2011

Study name	Std diff in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value	Sample size SLE	Sample size Control	Relatieve weight
Ahmadi, 2009	-0.990	0.269	0.072	-1.517	-0.463	-3.682	0.000	84	18	7.95
Ghosh, 2009	-1.531	0.234	0.055	-1.991	-1.072	-6.533	0.000	60	38	8.34
Cypiene, 2009	-0.111	0.220	0.049	-0.543	0.321	-0.505	0.614	30	66	8.49
Zhang, 2009	-0.658	0.188	0.035	-1.027	-0.289	-3.493	0.000	111	40	8.81
Valdivielso, 2008	-0.885	0.307	0.094	-1.487	-0.283	-2.880	0.004	26	21	7.52
Svenungssor, 2008	0.282	0.279	0.078	-0.265	0.828	1.010	0.312	26	26	7.84
Piper, 2007	-0.918	0.284	0.080	-1.474	-0.362	-3.235	0.001	36	22	7.79
Kiss, 2006	-0.223	0.263	0.069	-0.738	0.293	-0.847	0.397	33	26	8.02
Karadag, 2007	-2.473	0.388	0.151	-3.233	-1.712	-6.374	0.000	25	22	6.59
Wright, 2006	-0.924	0.304	0.092	-1.520	-0.329	-3.043	0.002	32	19	7.56
Rajagopalan, 2004	-0.800	0.224	0.050	-1.239	-0.361	-3.569	0.000	43	43	8.45
Lima, 2002	-1.307	0.226	0.051	-1.751	-0.864	-5.773	0.000	69	35	8.42
Johnson, 2004	-0.337	0.637	0.406	-1.585	0.912	-0.529	0.597	5	5	4.23
Pooled SMD	-0.832	0.174	0.030	-1.172	-0.492	-4.797	0.000			

Random effects model: pooled SMD=-0.832

Test for heterogeneity: Q=65.004, df=12, p<0.001, I^2=81.54



The Journal of Rheumatology 2011

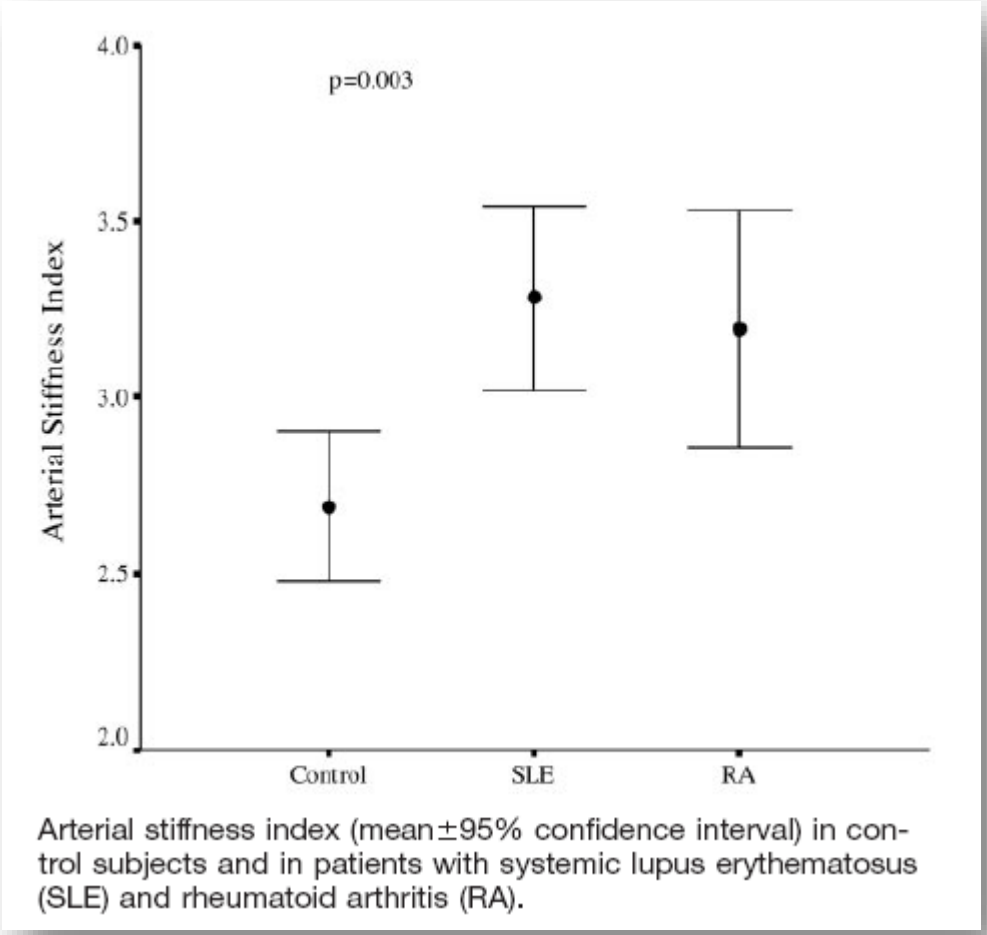
MARCADORS D'ARTERIOSCLEROSI SUBCLÍNICA: DISFUNCIÓ ENDOTELIAL

Table 2. Metaregression analysis of potential moderators of difference of endothelium-dependent flow-mediated dilation.

Factor	Regression Coefficient (SE)	Z Score	Tau^2	DF	p
Age, yrs	0.04716 (0.02261)	2.08579	0.21018	12	0.037
Female, %	–0.13693 (3.34813)	–0.04090	0.32448	12	0.967
Diabetes mellitus, %	1.26221 (1.09262)	0.11552	0.37872	10	0.908
Hypertension, %	0.24785 (1.17795)	0.21041	0.36537	11	0.834
Smoking, %	1.29497 (1.52302)	0.85026	0.36985	9	0.395
Menopause, %	1.21313 (0.86167)	1.40788	0.31034	8	0.159
Body mass index, kg/m^2	0.09065 (0.12067)	0.75123	0.40031	9	0.452
Systolic blood pressure, mm Hg	0.02016 (0.03157)	0.63849	0.39058	8	0.523
Diastolic blood pressure, mm Hg	–0.01463 (0.05198)	–0.28146	0.45404	7	0.778
Total cholesterol, mg/dl	0.01847 (0.01107)	1.66834	0.31260	9	0.095
HDL, mg/dl	0.02358 (0.01893)	1.24576	0.33741	9	0.213
LDL, mg/dl	0.01432 (0.01220)	1.17414	0.36586	9	0.240
TG, mg/dl	0.00114 (0.00792)	0.14364	0.53103	7	0.886
CRP, U/l	0.03293 (0.09250)	0.35594	0.47379	7	0.722
Prednisolone use, %	0.27961 (1.06867)	0.26164	0.43398	8	0.794
Mean prednisolone dose, mg/day	–0.01615 (0.03806)	–0.42429	0.33187	7	0.671
Hydroxychloroquine use, %	–2.40527 (0.76028)	–3.16360	0.17219	8	0.002
Baseline brachial artery diameter, mm	0.24629 (0.91395)	0.26948	0.29085	5	0.788
Disease durations, mo	0.00775 (0.00342)	2.26409	0.25260	9	0.024

HDL: high density lipoprotein; LDL: low density lipoprotein; TG: total triglyceride; CRP: C-reactive protein.

MARCADORS D'ARTERIOSCLEROSI SUBCLÍNICA: RIGIDESA ARTERIAL

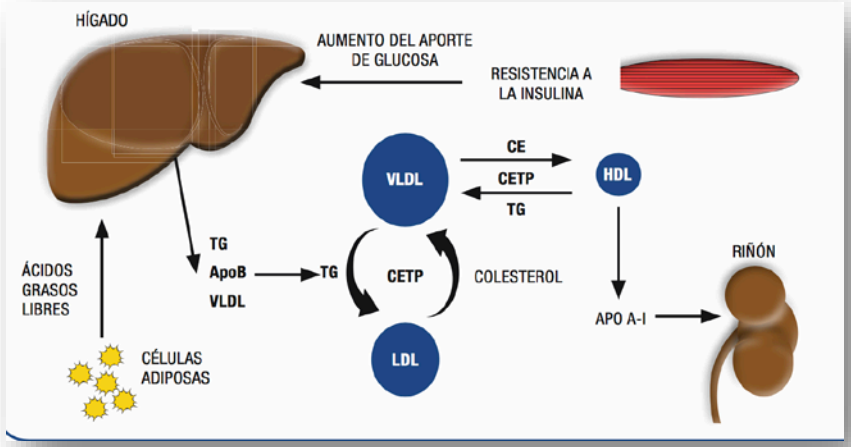


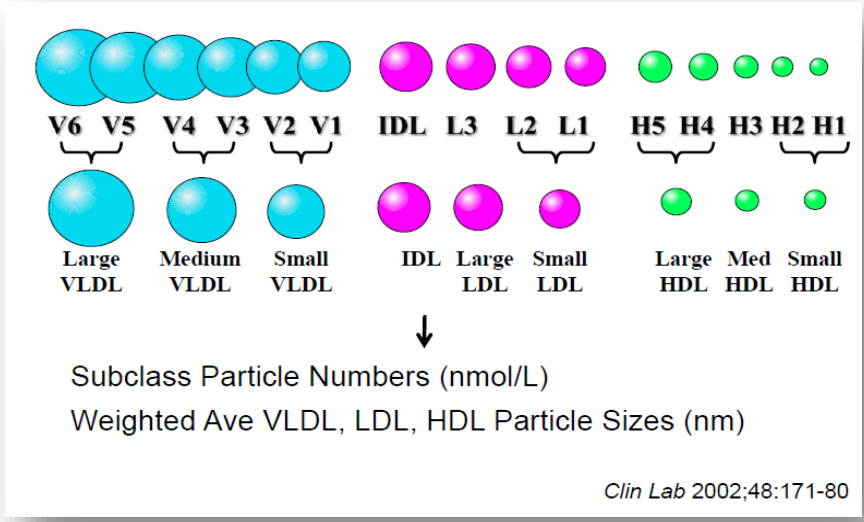
Arterial stiffness index (mean±95% confidence interval) in control subjects and in patients with systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA).

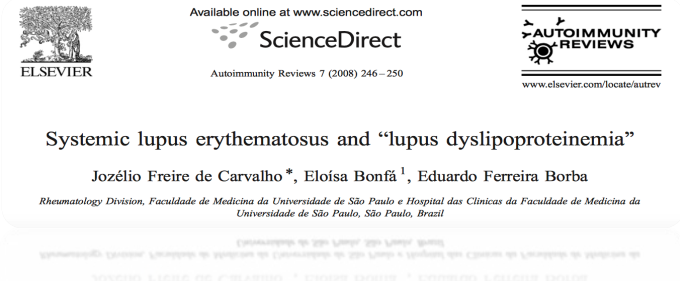
Roman et al Chronic Inflammation and Arterial Stiffness

DISLIPEMIA ATERÒGENA I MALALTIES AUTOIMMUNES

Síndrome metabòlica





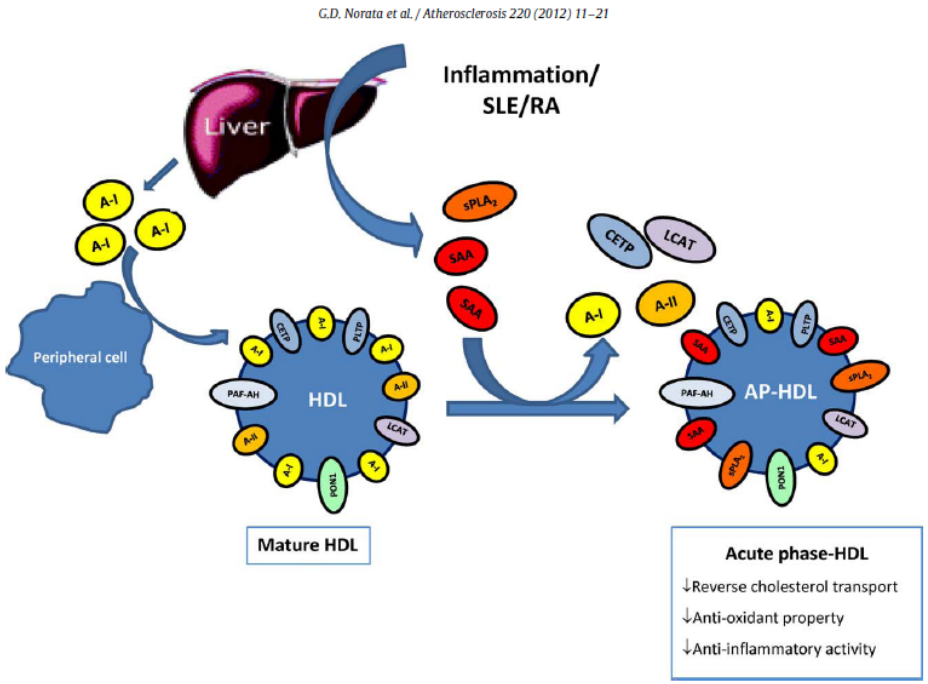


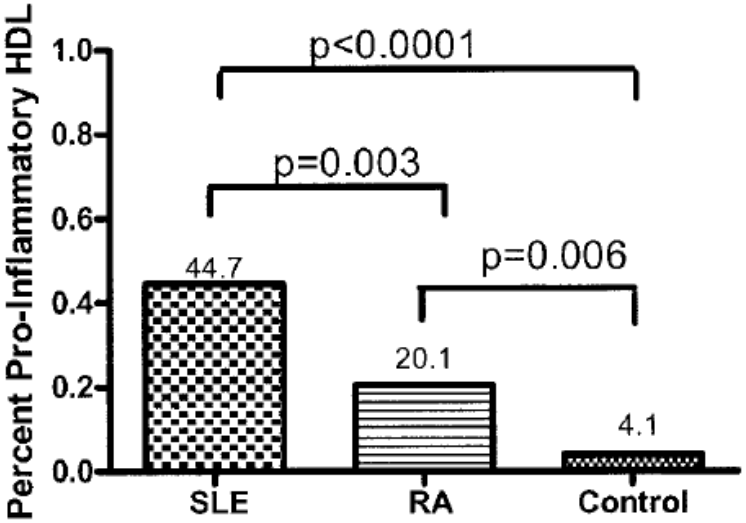
NMR lipo-profile	1st Tertil c-IMT	2st Tertil c-IMT	3st Tertil c-IMT	*P*
Remnants, mg/dL	5.07(2.97)	4.21(2.23)	6.26(3.6)	0.01*
VLDL & Chylomicron Particles				
(total), nmol/L	38.05(31.68)	46.56(47.88)	62.59(38.52)	0.127
Large VLDL & Chylomicrons				
Particles, nmol/L	0.50(0.62)	1.33(2.46)	1.22(1.63)	0.233
Medium VLDL Particles, nmol/L	10.83(12.17)	19.87(27.59)	22.42(8.70)	0.154
Small VLDL Particles, nmol/L	26.73(23.47)	25.34(20.66)	38.93(24.59)	0.096
VLDL Size, nm	54.01(13.07)	52.43(11.27)	46.18(8.09)	0.051
IDL Particles, nmol/L	24.95(37.49)	26.78(26.52)	84.72(81.18)	<0.001*
LDL Particles (total), nmol/L	1021.22(397.53)	1130.52(382.56)	1206.59(403.18)	0.299
Large LDL Particles, nmol/L	525.31(244.04)	594.0(269.90)	531.68(235.77)	0.597
Small LDL Particles (total), nmol/L	470.77(313.93)	509.91(475.74)	590.36(480.14)	0.645
Medium small LDL Particles, nmol/L	99.31(67.43)	110.82(102.79)	120.95(94.48)	0.727
Very Small LDL Particles, nmol/L	371.50(248.27)	399.04(378.9)	469.36(386.48)	0.625
LDL Size, nm	21.60(0.65)	21.66(0.95)	21.44(0.98)	0.672
HDL Particles (total), umol/L	28.84(5.09)	33.82(6.17)	32.73(4.05)	0.005*
Large HDL Particles, umol/L	9.07(3.27)	10.2(4.04)	8.98(3.25)	0.443
Medium HDL Particles, umol/L	2.35(2.02)	2.68(2.76)	2.50(2.41)	0.914
Small HDL Particles, umol/L	17.41(4.76)	20.93(5.30)	21.24(4.86)	0.023*
HDL Size. Nm	9.40(0.48)	9.42(0.54)	9.21(0.50)	0.327

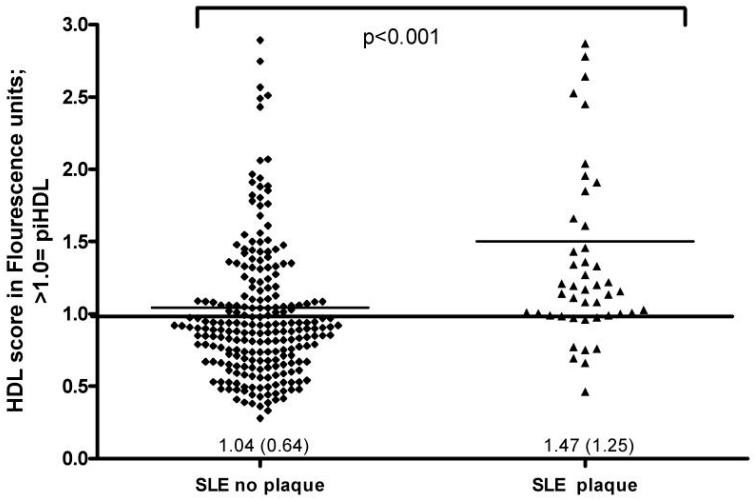
HDL I MALALTIES AUTOINMUNES

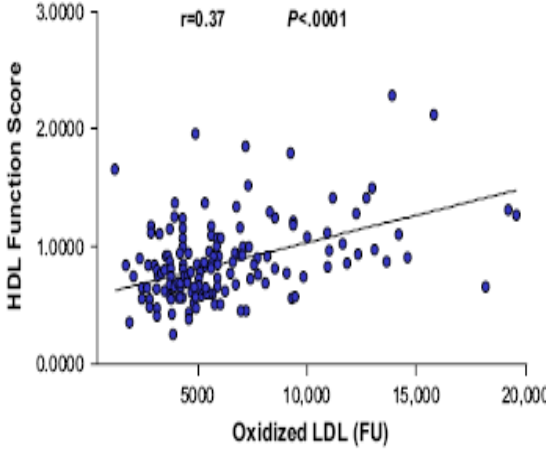
Disease	HDL plasma levels
Systemic lupus erythematosus	↓
Rheumatoid arthritis	↓/=
Sjogren's syndrome	=
Ankylosing sponditis	↓
Psoriatic arthritis	↓
Crohn's disease	↓
Ulcerative colitis	↓
Multiple sclerosis	↑

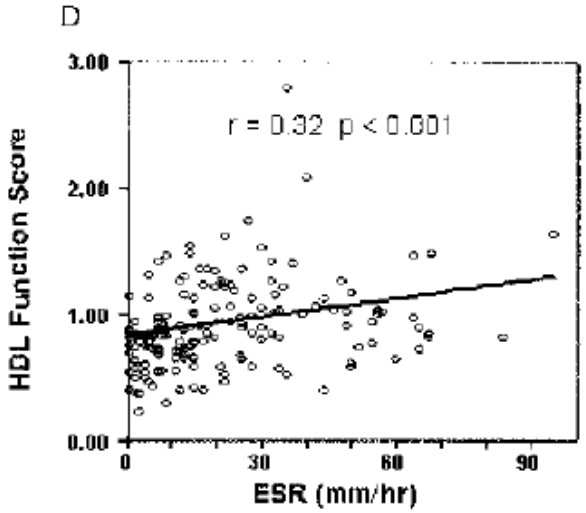
G.D. Norata et al. Atherosclerosis 2012



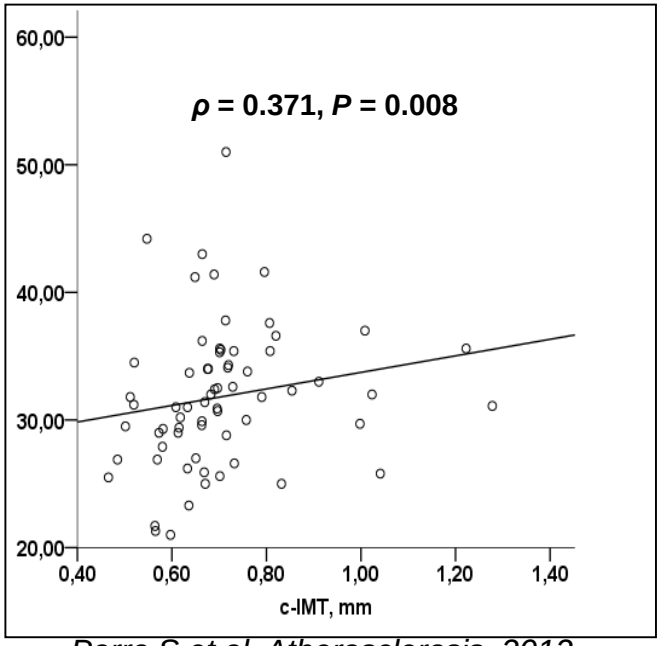








M. McMahon et al. Arthritis Rheum. 2009.



Parra S et al. Atherosclerosis. 2012.

Treatment targets and goals for cardiovascular disease prevention

Smoking	No exposure to tobacco in any form.
Diet	Healthy diet low in saturated fat with a focus on whole grain products, vegetables, fruit and fish.
Physical activity	2.5–5 h moderately vigorous physical activity per week or 30–60 min most days.
Body weight	BMI 20–25 kg/m^2, waist circumference <94 cm (men) and <80 cm (women).
Blodd pressure	<140/90 mmHg.
Lipid LDL-C is the primary target	**Very high-risk: LDL-C <1.8 mmol/L (70 mg/dL)** or a reduction of at least 50% if the baseline is between 1.8 and 3.5 mmol/L (70 and 135 mg/dL).
	High-risk: LDL-C <2.6 mmol/L (100 mg/dL) or a reduction of at least 50% if the baseline is between 2.6 and 5.2 mmol/L (100 and 200 mg/dL).
	Low to moderate risk: LDL-C <3 mmol/L (115 mg/dL).
	Non-HDL-C secondary targets are <2.6, 3.4 and 3.8 mmol/L (100, 130 and 145 mg/dL) for very high-, high- and moderate-risk subjects, respectively.
	HDL-C: no target, but >1.0 mmol/L (40 mg/dL) in men and >1.2 mmol/L (48 mg/dL) in women indicates lower risk.
	TG: no target but <1.7 mmol/L (150 mg/dL) indicates lower risk and higher levels indicate a need to look for other risk factors.
Diabetes	HbA1c: <7% (<8.6 mmol/L).

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Intervention stratégies

Total CV risk (SCORE) %	LDL-C levels				
	<70 mg/dL <1.8 mmol/L	70 to <100 mg/dL 1.8 to <2.6 mmol/L	100 to <155 mg/dL 2.6 to <4.0 mmol/L	155 to <190 mg/dL 4.0 to <4.9 mmol/L	≥190 mg/dL ≥4.9 mmol/L
<1	Lifestyle advice	Lifestyle advice	Lifestyle advice	Lifestyle advice	Lifestyle advice, consider drug if uncontrolled
Class/Level	I/C	I/C	I/C	I/C	IIa/A
≥1 to <5	Lifestyle advice	Lifestyle advice	Lifestyle advice, consider drug if uncontrolled	Lifestyle advice, consider drug if uncontrolled	Lifestyle advice, consider drug if uncontrolled
Class/Level	I/C	I/C	IIa/A	IIa/A	I/A
≥5 to <10, or high-risk	Lifestyle advice	Lifestyle advice, consider drug if uncontrolled	Lifestyle advice and drug treatment for most	Lifestyle advice and drug treatment	Lifestyle advice and drug treatment
Class/Level	IIa/A	IIa/A	IIa/A	I/A	I/A
≥10 or very high-risk	Lifestyle advice, consider drug[a]	Lifestyle advice and concomitant drug treatment	Lifestyle advice and concomitant drug treatment	Lifestyle advice and concomitant drug treatment	Lifestyle advice and concomitant drug treatment
Class/Level	IIa/A	IIa/A	I/A	I/A	I/A

[a]In patients with myocardial infarction, statin therapy should be considered irrespective of total cholesterol levels.

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ESC/EAS Guidelines for the management of dyslipidaemias

The Task Force for the management of dyslipidaemias of the European Society of Cardiology (ESC) and the European Atherosclerosis Society (EAS)

Developed with the special contribution of: European Association for Cardiovascular Prevention & Rehabilitation

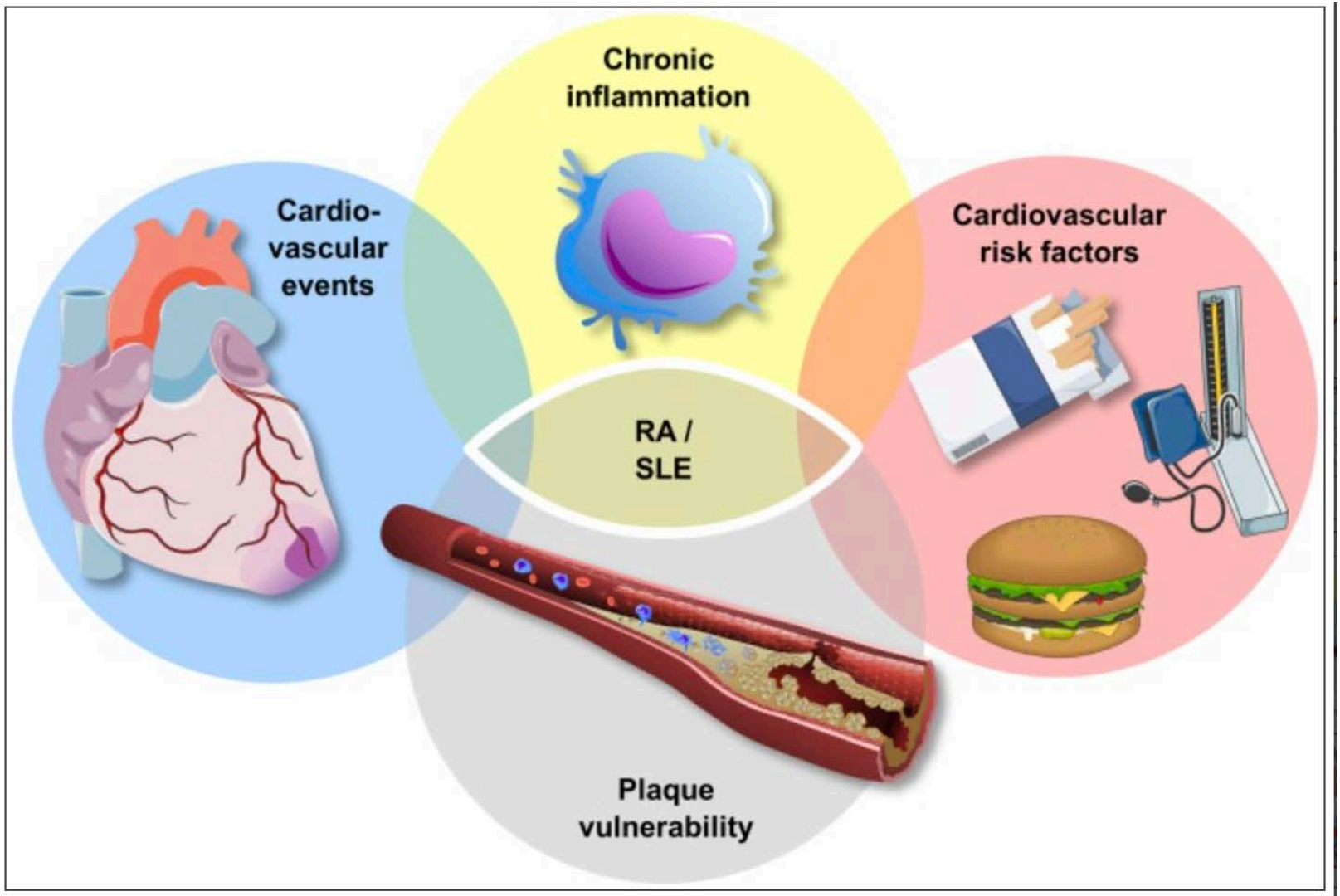
Table 1 Overarching principles and recommendations

	Level of evidence	Strength of recommendation	Level of agreement (SD)
Overarching principles A. Clinicians should be aware of the higher risk for CVD in patients with RA compared with the general population. This may also apply to AS and PsA. B. The rheumatologist is responsible for CVD risk management in patients with RA and other IJD. C. The use of NSAIDs and corticosteroids should be in accordance with treatment-specific recommendations from EULAR and ASAS			
Recommendations			
1. Disease activity should be controlled optimally in order to lower CVD risk in all patients with RA, AS or PsA	2b-3	B	9.1 (1.3)
2. CVD risk assessment is recommended for all patients with RA, AS or PsA at least once every 5 years and should be reconsidered following major changes in antirheumatic therapy	3–4	C	8.8 (1.1)
3. CVD risk estimation for patients with RA, AS or PsA should be performed according to national guidelines and the SCORE CVD risk prediction model should be used if no national guideline is available	3–4	C–D	8.7 (2.1)
4. TC and HDLc should be used in CVD risk assessment in RA, AS and PsA and lipids should ideally be measured when disease activity is stable or in remission. Non-fasting lipids measurements are also perfectly acceptable	3	C	8.8 (1.2)
5. CVD risk prediction models should be adapted for patients with RA by a 1.5 multiplication factor, if this is not already included in the model	3–4	C	7.5 (2.2)
6. Screening for asymptomatic atherosclerotic plaques by use of carotid ultrasound may be considered as part of the CVD risk evaluation in patients with RA	3–4	C–D	5.7 (3.9)
7. Lifestyle recommendations should emphasise the benefits of a healthy diet, regular exercise and smoking cessation for all patients	3	C	9.8 (0.3)
8. CVD risk management should be carried out according to national guidelines in RA, AS or PsA, antihypertensives and statins may be used as in the general population	3–4	C–D	9.2 (1.3)
9. Prescription of NSAIDs in RA and PsA should be with caution, especially for patients with documented CVD or in the presence of CVD risk factors	2a-3	C	8.9 (2.1)
10. Corticosteroids: for prolonged treatment, the glucocorticoid dosage should be kept to a minimum and a glucocorticoid taper should be attempted in case of remission or low disease activity; the reasons to continue glucocorticoid therapy should be regularly checked	3–4	C	9.5 (0.7)

AS, ankylosing spondylitis; ASAS, Assessment of Spondyloarthritis International Society; CVD, cardiovascular disease; EULAR, European League against Rheumatism; HDLc, high-density lipoprotein cholesterol; IJD, inflammatory joint disorder; NSAID, non-steroidal anti-inflammatory drug; PsA, psoriatic arthritis; RA, rheumatoid arthritis; SCORE, Systematic Coronary Risk Evaluation; TC, total cholesterol.

EULAR recommendations for cardiovascular disease risk management in patients with rheumatoid arthritis and other forms of inflammatory joint disorders: 2015/2016 update

TRACTAMENT RCV

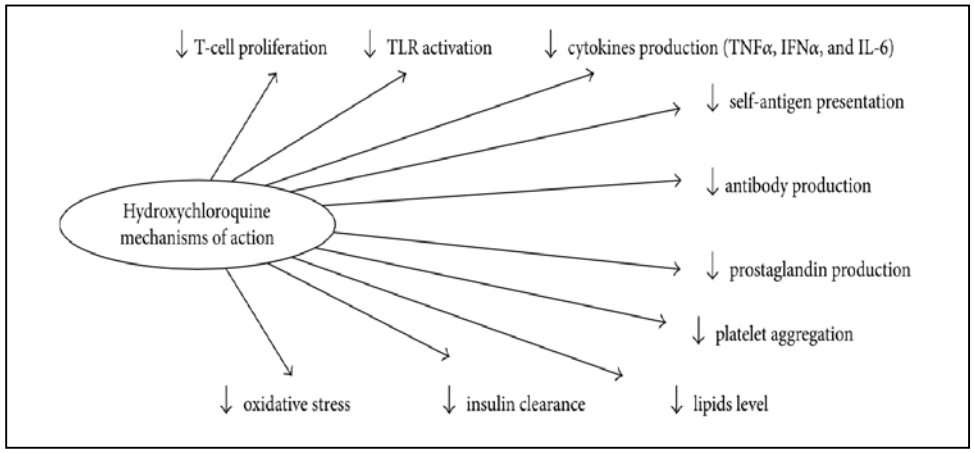



NOVARTIS
Sandimmun
Neoral
CICLOSPORINA
Cápsulas
100 mg


Antiinflamatorios
no esteroideos (aines)


Prednisona
50 mg
MK
100 Tabletas

Protective Effects of Hydroxychloroquine against Accelerated Atherosclerosis in Systemic Lupus Erythematosus



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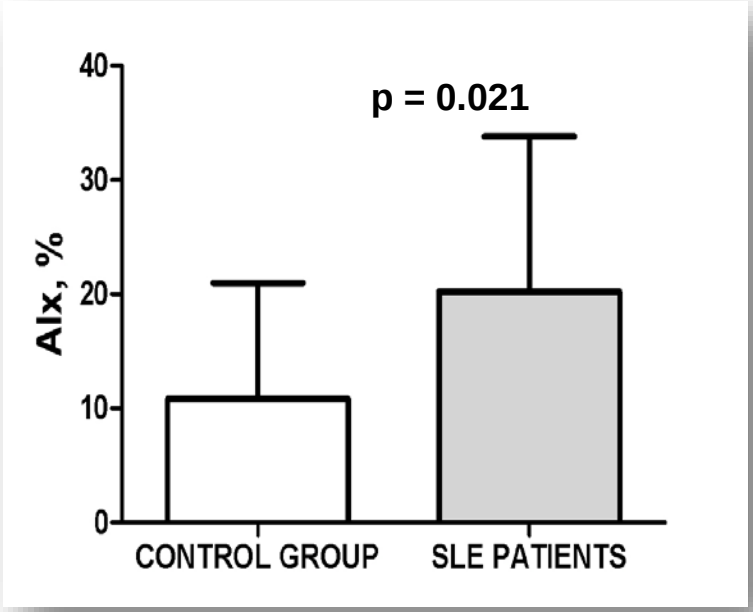

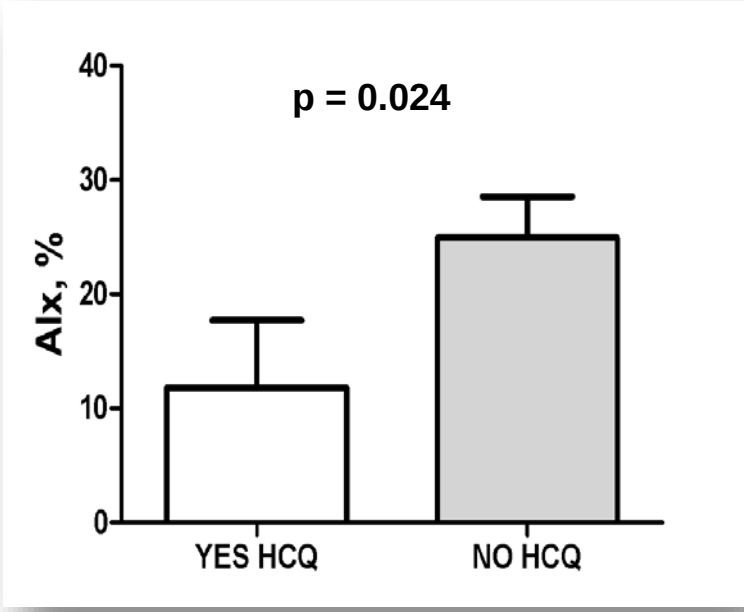

Lupus (2014) 0, 1–9
http://lup.sagepub.com

PAPER

Association between low 25-hydroxyvitamin D, insulin resistance and arterial stiffness in nondiabetic women with systemic lupus erythematosus

JM Sabio[1], JA Vargas-Hitos[1], J Martinez-Bordonado[1], N Navarrete-Navarrete[1], A Díaz-Chamorro[1], C Olvera-Porcel[2], M Zamora[1] and J Jiménez-Alonso[1]
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Table 4 Variables independently associated with pulse wave velocity in systemic lupus erythematosus using a multiple linear regression analysis

Variable	*ß coefficient*	*95% CI*	p
25-hydroxyvitamin D	−0.016	−0.034 to 0.001	0.065
Age	0.052	0.037 to 0.067	<0.001
Systolic blood pressure	0.026	0.013 to 0.039	<0.001

Adjusted R^2 for this model = 0.41. CI: confidence interval.

CONCLUSIONS

- Els pacients amb malalties autoimmunes sistèmiques presenten un increment de la morbimortalitat relacionada amb events cardiovasculars respecte la població general
- La presència de factors de risc cardiovascular clàssics com HTA, dislipemia i sindrome metabòlica tenen més incidència en aquesta població
- Compte amb els fàrmacs que afavoreixen FRCV. Evitar AINES, corticoides, ciclosporina, leflunomida ...
- Important monitoritzar els nivells de tensió arterial, pes, tabaquisme, glucosa, perfil lipídic i hàbits d'estil de vida cardiosaludable en aquests pacients.
- El control de l'activitat de la malaltia amb immunodepressors MTX i Anti-TNF en AR i (HCQ i CFs) en LES disminueix el risc de patir events cardiovasculars.


START
HERE