Risque cardiovasculaire des maladies inflammatoires et dysimmunitaires chroniques

Dr Camille Roubille

Médecine interne – CHU Lapeyronie Montpellier

Conflits d’intérêt

- Personal fees from Servier and Pfizer

Pourquoi prendre en charge le risque cardiovasculaire dans les maladies inflammatoires chroniques (MIC) ?

Parce que les CVD sont fréquentes dans les MIC


Augmentation du risque cardiovasculaire des maladies inflammatoires chroniques

Maladies cardiovasculaires dans les MIC: ex. de la PR, du lupus, du psoriasis, des vascularites à ANCA

PubMed.gov

("Cardiovascular Diseases"[Mesh]) AND "Arthritis, Rheumatoid"[Mesh] Search

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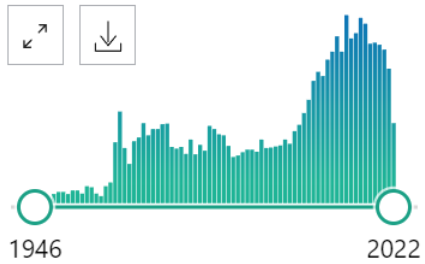
MY NCBI FILTERS 8,740 results



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ardiovascular Diseases"[Mesh]) AND "Lupus Erythematosus, Systemic"[Mesh] Search

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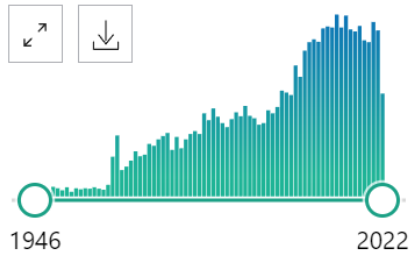
RESULTS BY YEAR



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ı]) AND "Anti-Neutrophi Cytoplasmic Antibody-Associated Vasculitis"[Mesh] Search

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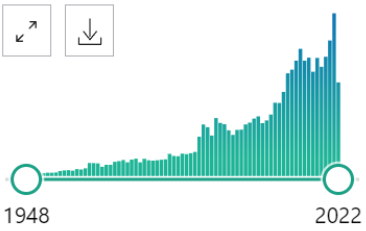
RESULTS BY YEAR



PubMed.gov

("Cardiovascular Diseases"[Mesh]) AND "Psoriasis"[Mesh] Search

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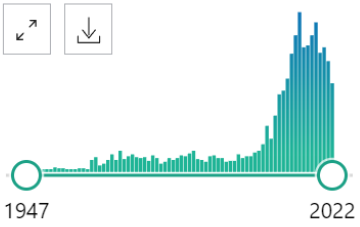
RESULTS BY YEAR



-**PR ont réduction de l'espérance de vie de 3 à 10 ans vs pop générale**

Myasoedova E. et al Curr Rheumatol Rep.2010 Oct;12(5):379-85.

Comorbidités qui augmentent la mortalité (n=882):

- **CVD + 60%**
- **Maladies respiratoires +43%**
- **Dépression +35%**

Van den Hoek J.et al Arthritis Care Res. 2016 Aug;68(8):1055-60.

-**Psoriasis:CVD expliquent 48,3% d'augmentation de la mortalité si Pso modéré, 33,4% si Pso sévère.**

Svedbom A. et al. Acta Derm Venereol 2015; 95: 809–815

-**Vascularite ANCA**

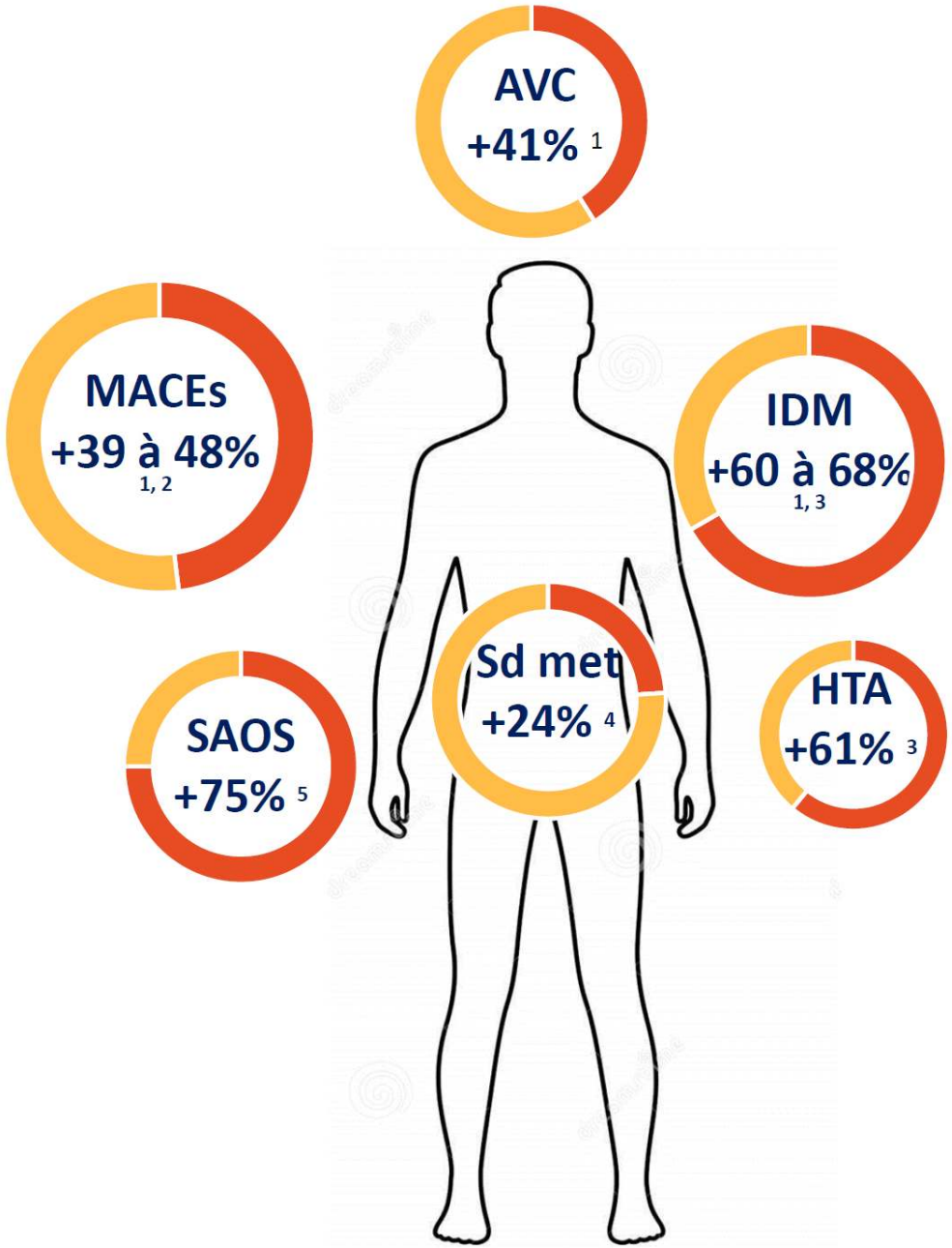
Mortalité la 1ère année: infections (48%)

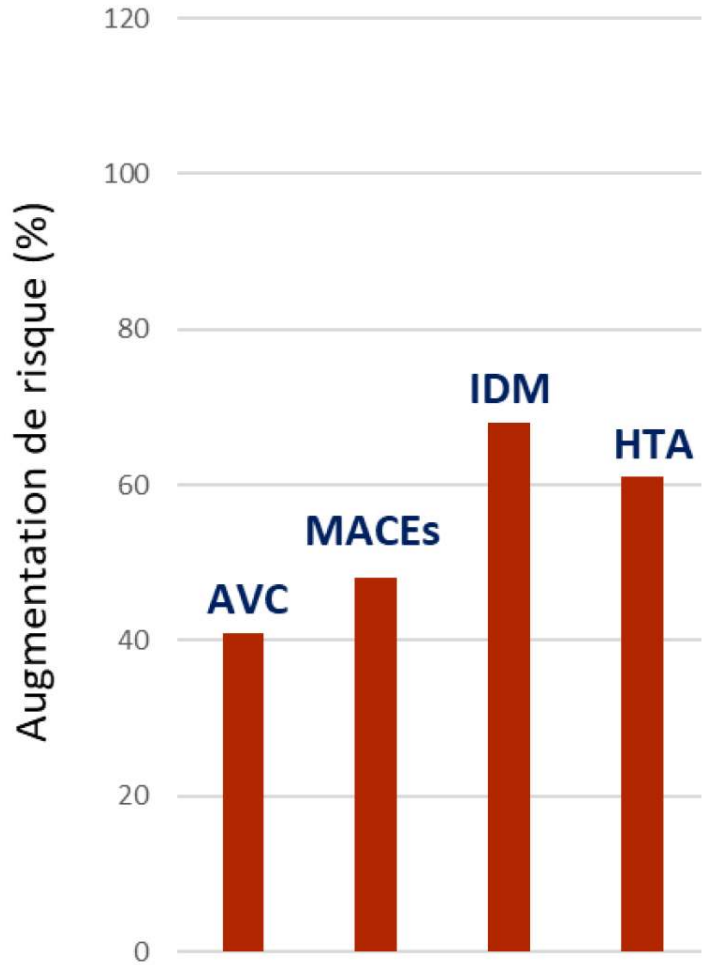
Mortalité après 1ère année: CVD (26%), néoplasie (22%) et infections (20%)

Flossmann O, et al. Ann Rheum Dis 2011; 70: 488–494.

Les patients atteints de maladies inflammatoires ont une mortalité prématurée

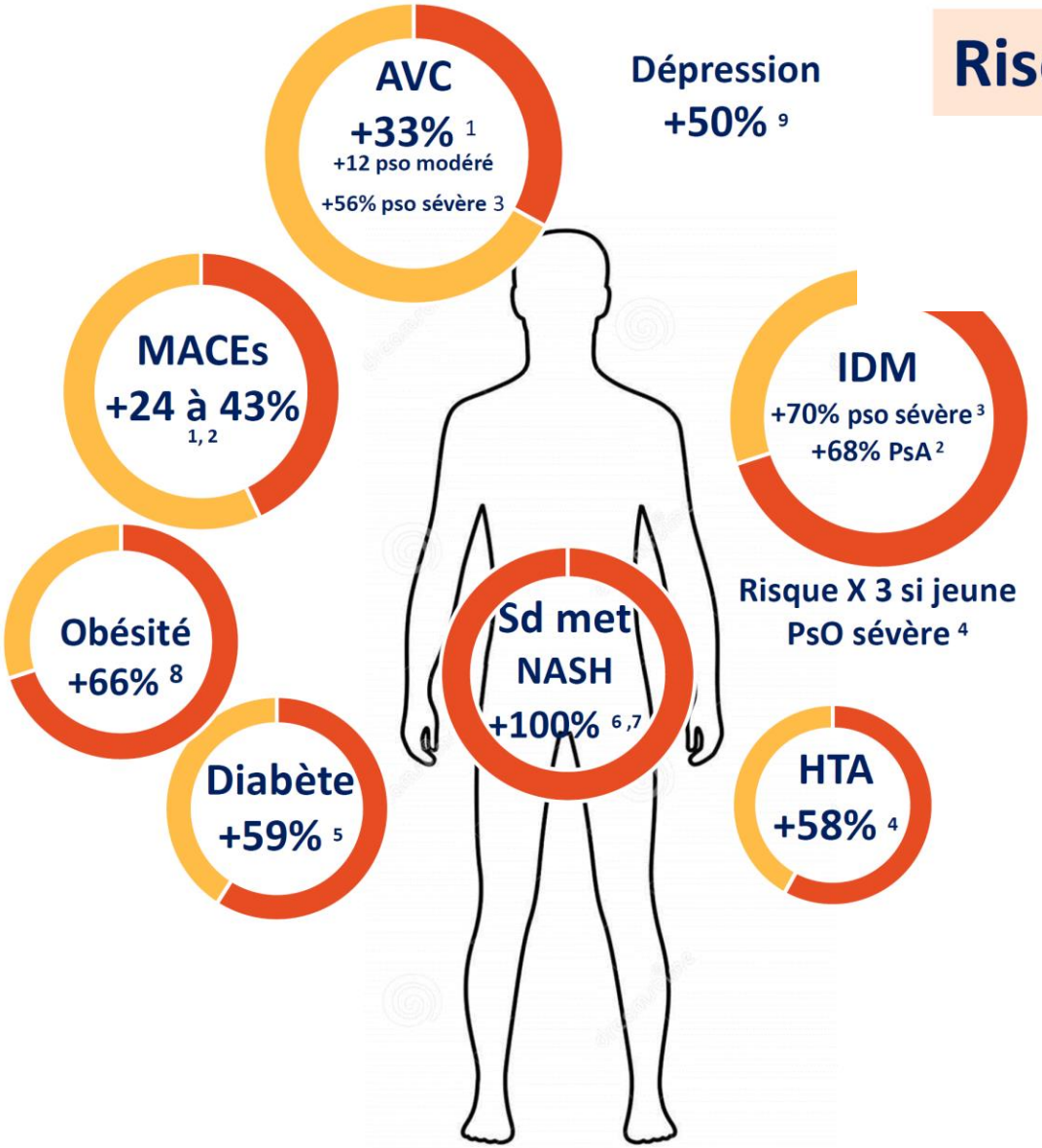
Risque cardiovasculaire dans la PR

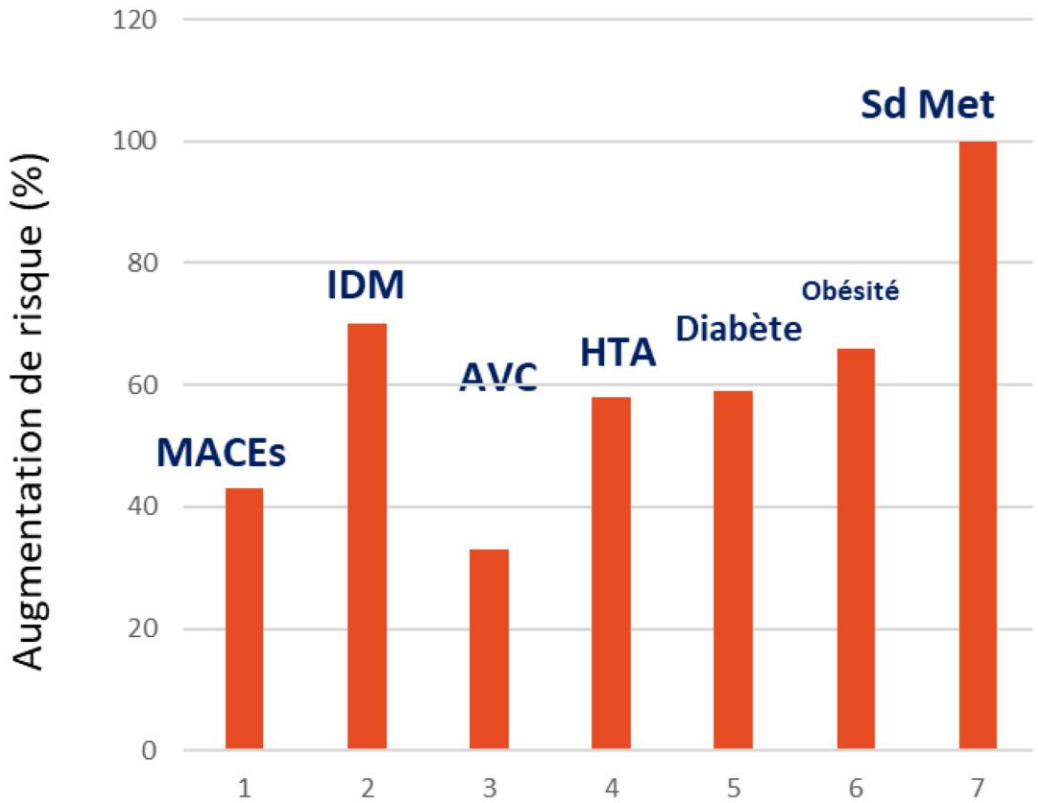




[1] Avina-Zubieta JA, et al. Annals of the rheumatic diseases. 2012; 71(9):1524–9. [2] Ogdie A. et al. Ann Rheum Dis. 2015; 74(2):326-32. [3]Norton S. et al. Rheumatology.2013;52-99-110 [4] Zhang et al. Plos One 2013.25;8(10):e78151. [5] Shen T-C, et al. BMJ Open. 2016 28;6(11):e013151.

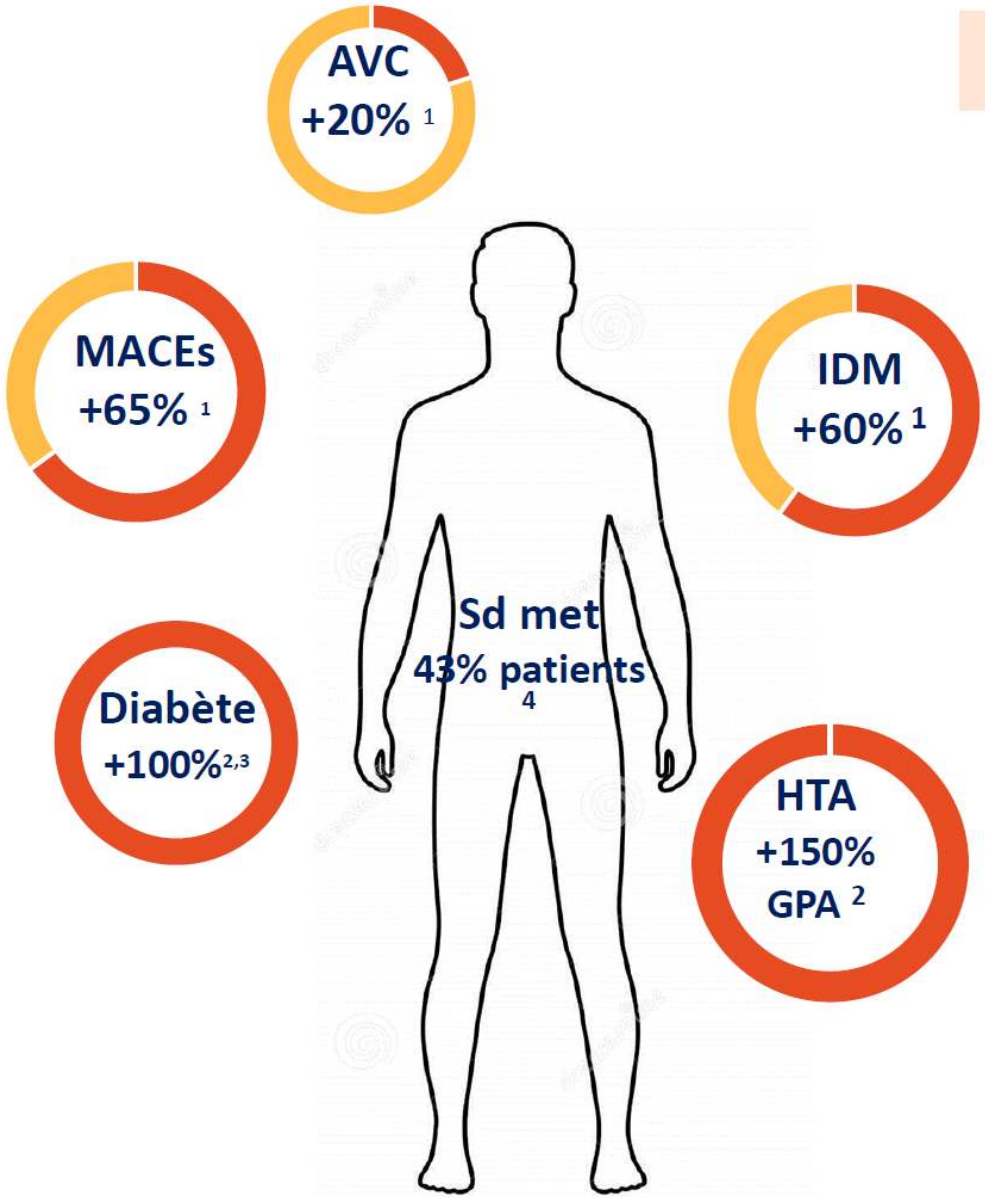
Risque cardiovasculaire dans le psoriasis

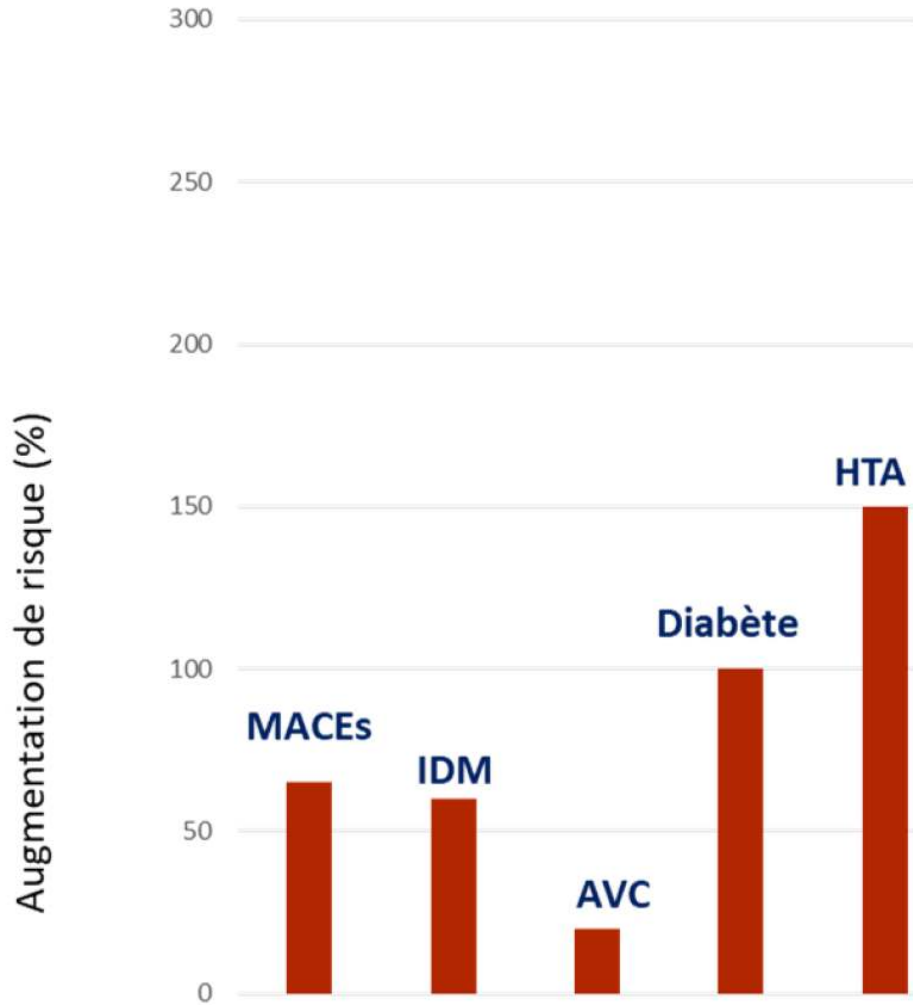




[1]Ogdie A. et al. Ann Rheum Dis. 2015; 74(2):326-32. [2] Polachek A. et al. Arthritis Care Res 2017;69: 67-74 . [3] Armstrong et al. Am Heart Assoc 2013;2:e000062 doi: 10.1161. [4] Gelfand JM. JAMA 2006 Oct 11;296(14):1735-41. [4] Armstrong et al. Journal of Hypertension 2013, 31:433–443. [5]Armstrong AW. et al. JAMA Dermatol 2013; 149(1):84–91. [6]Singh et al. Plos One. 2017 Jul 18;12(7). [7] Candia R. et al.J Eur Acad Dermatol Venereol. 2015 Apr;29(4):656-62. [8] Armstrong AW.et al. Nutr Diabetes 2012:2:e54.

Risque cardiovasculaire dans les vascularites ANCA





[1]Houben E. et al. Rheumatology (Oxford). 2018 Mar 1;57(3):555-562. [2] Li et al. Rheumatology (Oxford). 2018 Feb 1;57(2):291-299. [3]Englund M. et al. J Rheumatol. 2016 Aug;43(8):15538

Autoimmunity Reviews 20 (2021) 102708

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journal homepage: www.elsevier.com/locate/autrev

Review

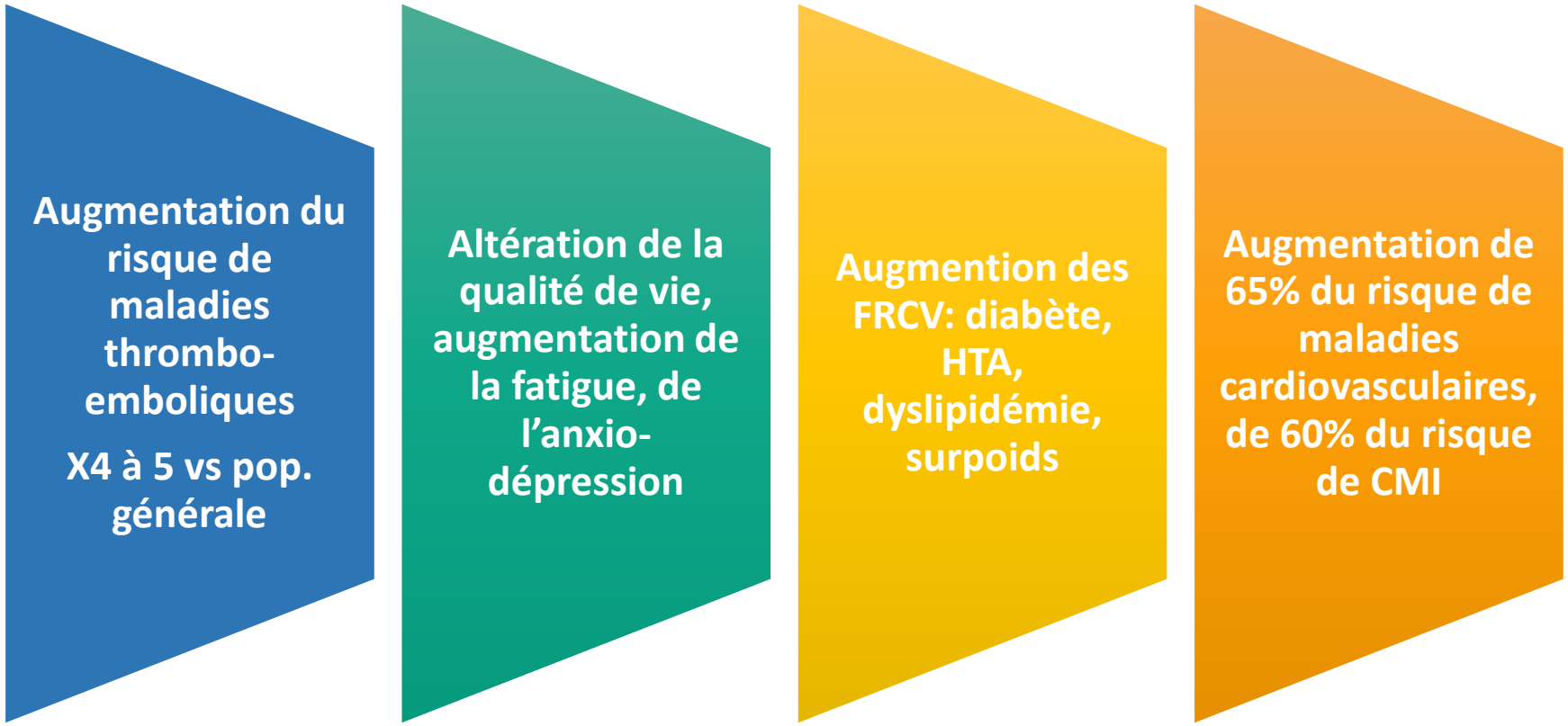
Comorbidities and health-related quality of life in Patients with Antineutrophil Cytoplasmic Antibody (ANCA) - associated vasculitis

Cédric Mercuzot [a], Simon Letertre [a], Claire I Daien [b], Laetitia Zerkowski [a], Philippe Guilpain [c,d], Benjamin Terrier [e,g], Pierre Fesler [a,f], Camille Roubille [a,f,*]

Revue systématique de la littérature sur les comorbidités dans les vascularites à ANCA, incluant les comorbidités cardiovasculaires

La survie globale à 1 an des patients atteints de VAA est estimée entre 77 et 95%, et celle à 5 ans, entre 62 et 97%.

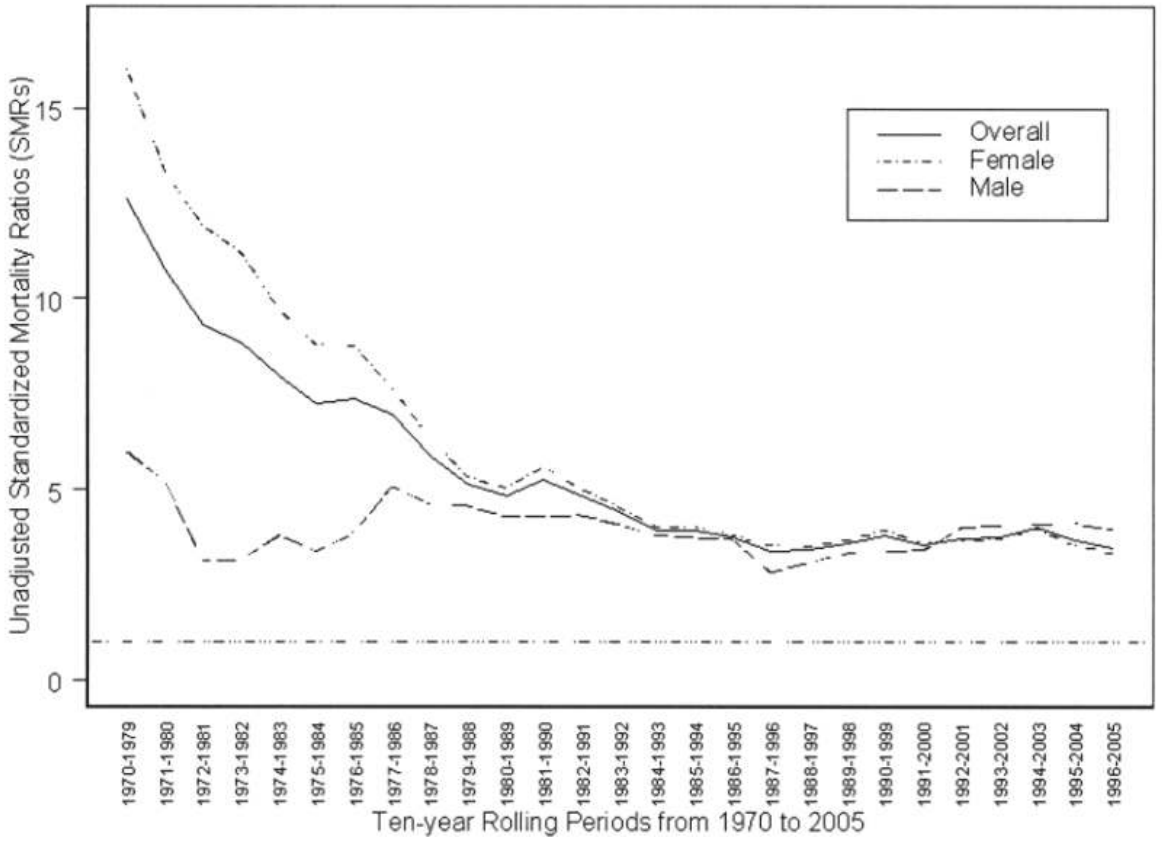
La mortalité demeure plus de 2.5 fois plus élevée que la population générale, avec un impact net des comorbidités, notamment des maladies cardiovasculaires.



LUPUS: Persistance d'une surmortalité cardiovasculaire

Etude MORTALUP (data CépiDc): **la principale cause de décès des patients lupiques est cardiovasculaire**.

Standardized Mortality Ratio (SMR, nombre de décès observés sur le nombre de décès attendus) = 1,58 [IC95 % : 1,42–1,76], avec un maximum de 5,16 [IC95 % : 3,60–7,18] pour les décès survenus avant l'âge de 40 ans.



The Journal of Rheumatology 2008; 35:11

LUPUS = facteur de risque cardiovasculaire indépendant

RR de CVD X 2 à 3

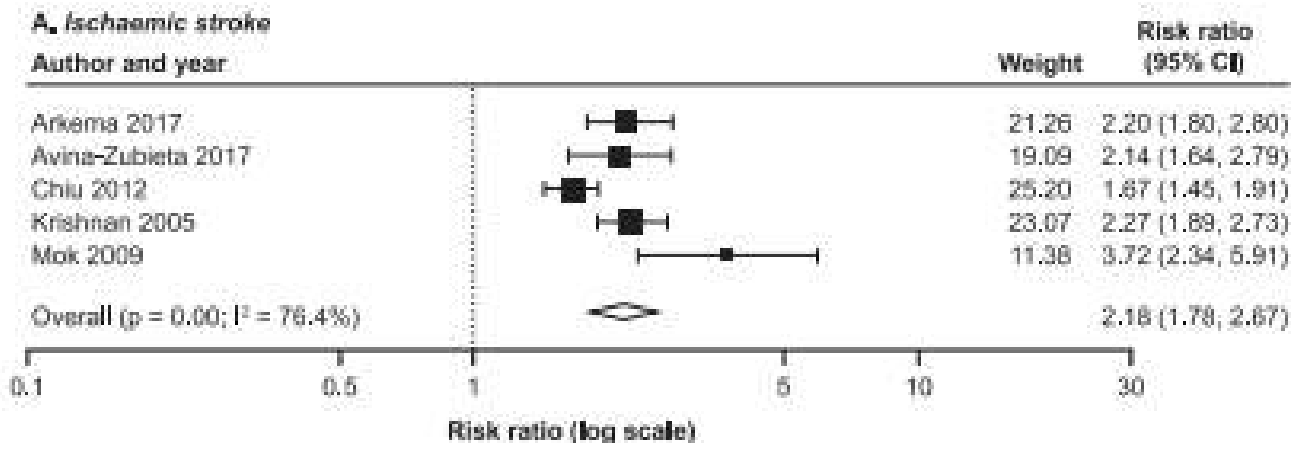
RMD Open
Rheumatic & Musculoskeletal Diseases

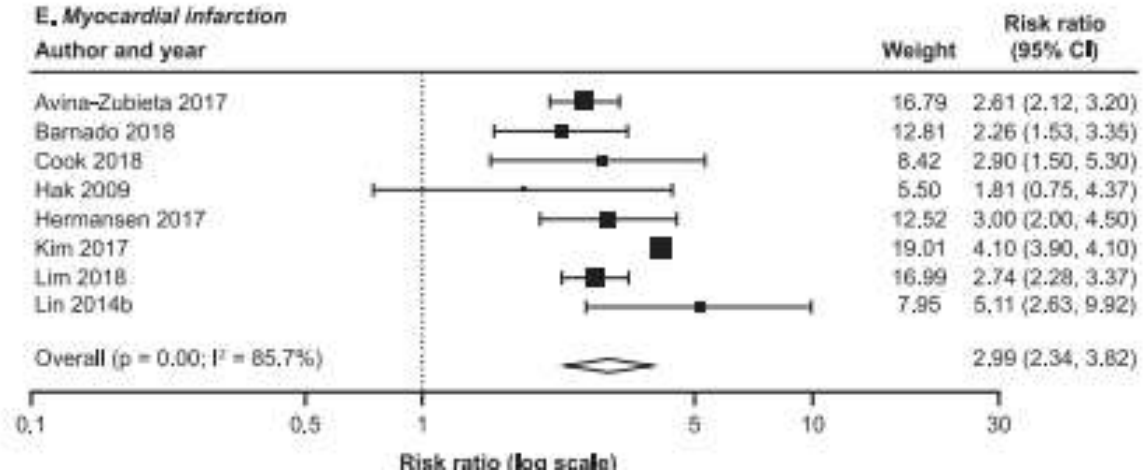
Original research

Systemic lupus erythematosus; stroke and myocardial infarction risk: a systematic review and meta-analysis

Jinoos Yazdany,[1] Nick Pooley,[2] Julia Langham,[3] Lindsay Nicholson,[2] Sue Langham,[4] Nina Embleton,[5] Xia Wang,[6] Barnabas Desta,[7] Volkan Barut,[8] Edward Hammond[9]

RMD Open. 2020 Sep;6(2):e001247.





Risque d'AVC ischémique X 2

Risque d'IDM X 3

Yazdany J, et al. RMD Open 2020;6:e001247. doi:10.1136/rmdopen-2020-001247

Journal of
Clinical Medicine

MDPI

Article

Cardiovascular Events, Sleep Apnoea, and Pulmonary Hypertension in Primary Sjögren's Syndrome: Data from the French Health Insurance Database

Radjiv Goulabchand [1,2,3,*], Camille Roubille [2,4,5], David Montani [6], Pierre Fesler [2,4,5], Arnaud Bourdin [2,5,7], Nicolas Malafaye [8], Jacques Morel [2,5,9], Erik Arnaud [1], Benoit Lattuca [2,10], Lucie Barateau [2,11,12,13], Philippe Guilpain [2,3,14,*,†] and Thibault Mura [2,15,*,†]

Table 2. Incidence of first hospitalisation for cardiovascular reasons in primary Sjögren's syndrome patients and controls.

	pSS Patients				Matched Controls									
	Incident Cases [#]	Py	Incidence [#]	CI	Incident Cases [#]	Py	Incidence [#]	CI	Crude HR	Crude CI	Crude *p* Value	aHR	Adjusted CI	Adjusted *p* Value
Cardiovascular events														
Ischemic heart disease	535	98611	5.43	(4.97–5.89)	3723	967246	3.85	(3.73–3.97)	1.39	(1.27–1.52)	0.000	1.20	(1.06–1.34)	**0.003**
Stroke	227	101241	2.24	(1.95–2.53)	2159	1000199	2.16	(2.07–2.25)	1.01	(0.88–1.16)	0.845	1.05	(0.88–1.25)	0.606
Heart failure	486	100321	4.84	(4.41–5.27)	3339	991590	3.37	(3.26–3.48)	1.42	(1.29–1.56)	0.000	1.05	(0.92–1.19)	0.497
Cardiovascular risk factors														
Hypertension	137	101508	1.35	(1.12–1.58)	807	1008796	0.8	(0.74–0.86)	1.71	(1.42–2.05)	0.000	1.39	(1.07–1.80)	**0.014**
Sleep apnoea syndrome	438	99839	4.39	(3.98–4.8)	1645	995874	1.65	(1.57–1.73)	2.66	(2.39–2.95)	0.000	1.97	(1.70–2.28)	**<0.001**
Venous thromboembolic events														
Pulmonary embolism	131	101747	1.29	(1.07–1.51)	887	1011218	0.88	(0.82–0.94)	1.45	(1.21–1.75)	0.000	1.10	(0.86–1.41)	0.460
All vein thromboses	214	101027	2.12	(1.84–2.4)	1400	1002691	1.4	(1.33–1.47)	1.50	(1.30–1.73)	0.000	1.04	(0.85–1.27)	0.701
Pulmonary hypertension	72	102319	0.70	(0.54–0.86)	126	1019457	0.12	(0.10–0.14)	5.72	(4.27–7.68)	0.000	3.32	(2.10–5.25)	**<0.001**

pSS, primary Sjögren's syndrome; CI, confidence interval; py, person-years; [#] number of incident cases per 1000 person-years; HR, hazard ratio; aHR, adjusted HR. Bold is significance of *p* value.

	PR	PSO	VAA	LES
 CMI	+68%	+70%	+60%	X 3
 AVC	+41%	+33%	+20%	X 2
 MACEs	+48%	+43%	+65%	X 2,7

Autoimmune diseases and cardiovascular risk: a population-based study on 19 autoimmune diseases and 12 cardiovascular diseases in 22 million individuals in the UK

Nathalie Conrad, Geert Verbeke, Geert Molenberghs, Laura Goetschalckx, Thomas Callender, Geraldine Cambridge, Justin C Mason, Kazem Rahimi, John J V McMurray, Jan Y Verbakel

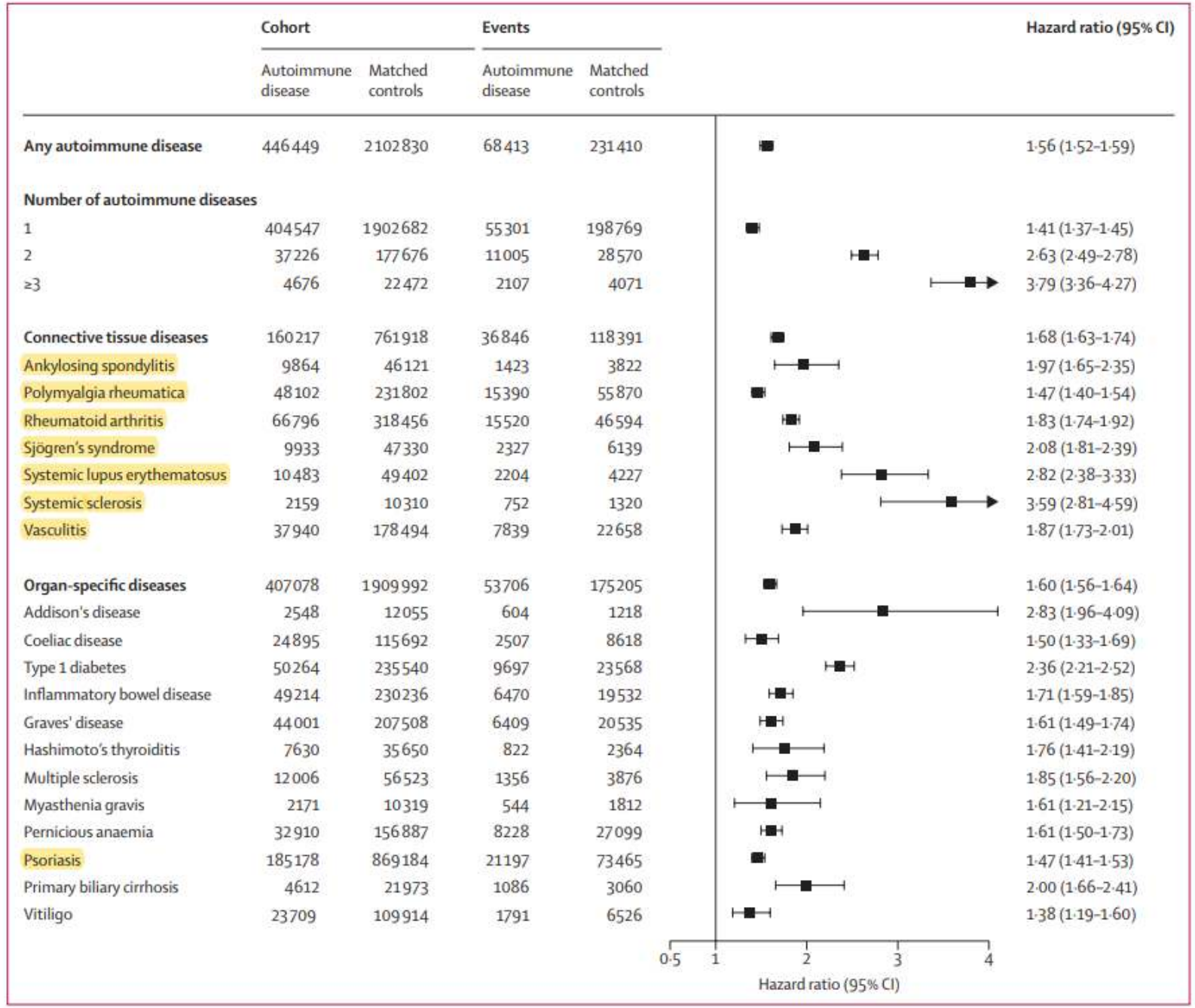
Patients atteints de maladies dysimmunitaires (n=446 449) vs personnes ne souffrant d'aucune pathologie auto-immune (n=2 102 830 personnes, appariés pour l'âge, le sexe, le statut socioéconomique et la région)

Risque X 1,4 à 3,6 de développer une maladie cardiovasculaire

Ordre de grandeur similaire au risque causé par le diabète de type 2

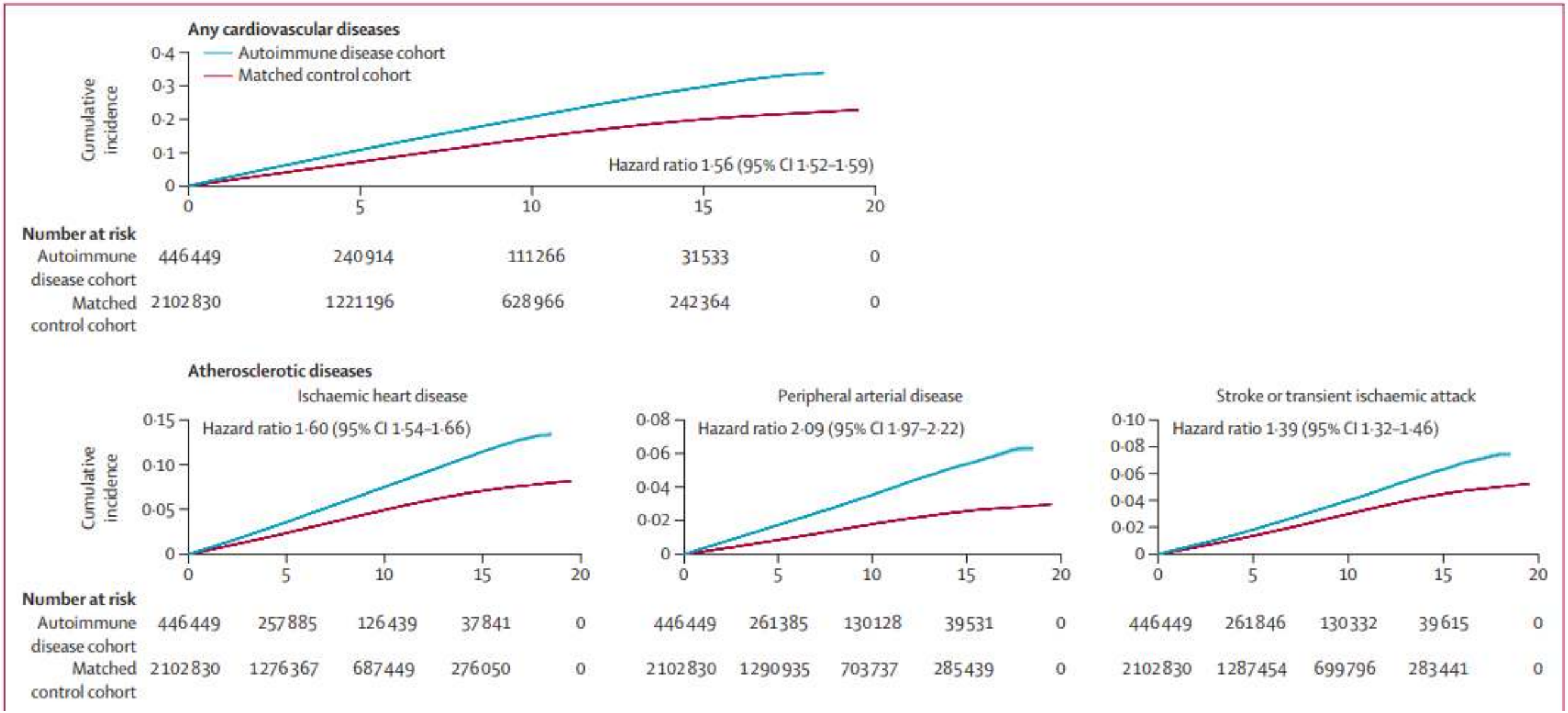
(surtout si <45 ans).

Lancet 2022; 400: 733-43



	Cohort		Events		Hazard ratio (95% CI)
	Autoimmune disease	Matched controls	Autoimmune disease	Matched controls	
Any autoimmune disease	446 449	2 102 830	68 413	231 410	1·56 (1·52–1·59)
Number of autoimmune diseases					
1	404 547	1 902 682	55 301	198 769	1·41 (1·37–1·45)
2	37 226	177 676	11 005	28 570	2·63 (2·49–2·78)
≥3	4676	22 472	2107	4071	3·79 (3·36–4·27)
Connective tissue diseases	160 217	761 918	36 846	118 391	1·68 (1·63–1·74)
Ankylosing spondylitis	9864	46 121	1423	3822	1·97 (1·65–2·35)
Polymyalgia rheumatica	48 102	231 802	15 390	55 870	1·47 (1·40–1·54)
Rheumatoid arthritis	66 796	318 456	15 520	46 594	1·83 (1·74–1·92)
Sjögren's syndrome	9933	47 330	2327	6139	2·08 (1·81–2·39)
Systemic lupus erythematosus	10 483	49 402	2204	4227	2·82 (2·38–3·33)
Systemic sclerosis	2159	10 310	752	1320	3·59 (2·81–4·59)
Vasculitis	37 940	178 494	7839	22 658	1·87 (1·73–2·01)
Organ-specific diseases	407 078	1 909 992	53 706	175 205	1·60 (1·56–1·64)
Addison's disease	2548	12 055	604	1218	2·83 (1·96–4·09)
Coeliac disease	24 895	115 692	2507	8618	1·50 (1·33–1·69)
Type 1 diabetes	50 264	235 540	9697	23 568	2·36 (2·21–2·52)
Inflammatory bowel disease	49 214	230 236	6470	19 532	1·71 (1·59–1·85)
Graves' disease	44 001	207 508	6409	20 535	1·61 (1·49–1·74)
Hashimoto's thyroiditis	7630	35 650	822	2364	1·76 (1·41–2·19)
Multiple sclerosis	12 006	56 523	1356	3876	1·85 (1·56–2·20)
Myasthenia gravis	2171	10 319	544	1812	1·61 (1·21–2·15)
Pernicious anaemia	32 910	156 887	8228	27 099	1·61 (1·50–1·73)
Psoriasis	185 178	869 184	21 197	73 465	1·47 (1·41–1·53)
Primary biliary cirrhosis	4612	21 973	1086	3060	2·00 (1·66–2·41)
Vitiligo	23 709	109 914	1791	6526	1·38 (1·19–1·60)

Hazard ratios for incident cardiovascular disease among patients with autoimmune diseases compared with matched controls, stratified by autoimmune disease Patients with autoimmune diseases were compared with up to five individuals matched on age, calendar year, sex, socioeconomic status, and region, free of autoimmune disease at any time. Hazard ratios and 95% CIs were calculated using Cox proportional hazards models, clustered by matching set



CMI **PAD** **AVC**

Lancet 2022; 400: 733–43

Pourquoi prendre en charge le risque cardiovasculaire dans les maladies inflammatoires chroniques (MIC) ?

Parce que les comorbidités cardiovasculaires existent dès le stade précoce.
Leur fréquence augmente avec l'âge, et avec l'évolution et l'activité de la maladie

Comorbidités fréquentes dès le stade précoce de PR

	Baseline (n =950)	New co-morbidity during 5 years of disease (n = 726)
	%	%
Co-morbidity overall[a]	53.2	41.0
Hypertension	27.3	15.1
Asthma/COPD	13.9 (11.2/4.1)	2.4 (0.6/1.8)
Any endocrine disease	19.2	10.5
Diabetes mellitus	8.0	3.3
Hypothyroidism	6.3	1.9
Thyroid disease[b]	10.4	2.4
Osteoporosis	1.4	3.7
Hyperparathyroidism	0.6	0.6
Malignancy	5.0	7.6
Myocardial infarction	4.5	4.3
Stroke/TIA	3.9	5.1

Values are percent for all. [a]Co-morbidity defined according to Charlson [40]. [b]Defined as hypothyroidism, hyperthyroid disease and goiter. *COPD* chronic obstructive lung disease, *TIA* transient ischemic attack

n=950. *Innala L. et al. Arthritis Res Ther. 2016 Jan 28;18:33.*

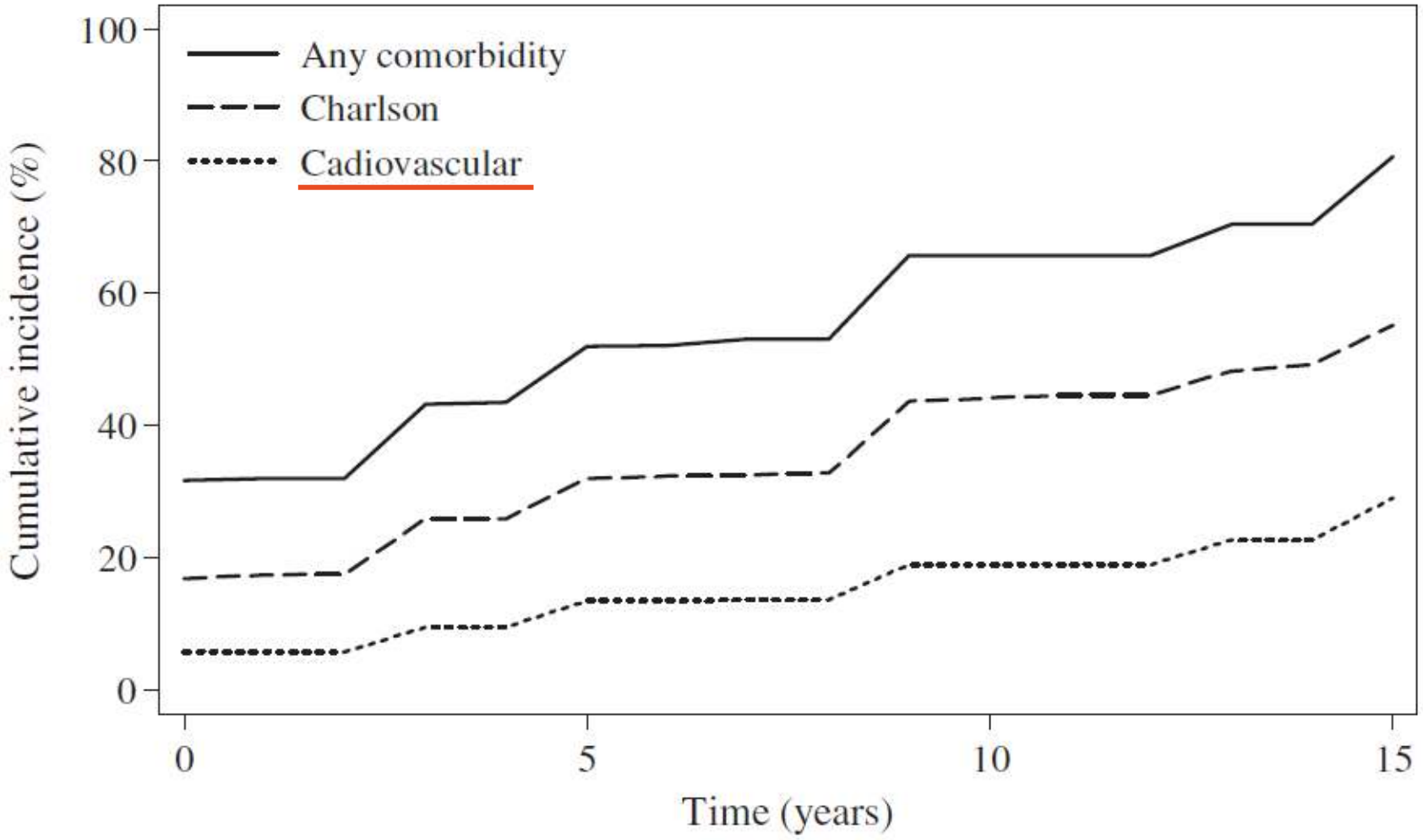
Male gender	161 (23.4)
Age (years)	48.2±12.1
Symptoms duration (weeks)	14.2±14.5
Alcohol use	105 (15.2)
ESR*	30.4±24.8
CRP†	22.6±33.9
At least one comorbidity	294 (42.7)
Arterial hypertension	125 (18.1)
Receive treatment (%)	93.6
Hypercholesterolaemia	101 (14.7)
Receive treatment (%)	69.3
Hypertriglyceridaemia	21 (3.0)
Dysthyroidism	82 (11.9)
Previous tuberculosis	32 (4.6)
Diabetes mellitus	28 (4.1)
Previous solid malignancies	24 (3.5)
Previous lymphoma	4 (0.6)
Coronary heart disease	6 (0.9)
Stroke	4 (0.6)
Peptic ulcer	35 (5)
Previous gastrointestinal bleeding	8 (1.2)
Hepatitis B	4 (0.6)
Hepatitis C	6 (0.9)

n=689. *Gherghe AM.et al. RMD Open. 2015 Sep 14;1(1).*

n= 1460 PR précoces: **augmentation de l'incidence cumulative des comorbidités sur 15 ans (81%):**

Baseline: 0,9 comorbidités vs 1,8 à 5 ans vs 2,3 à 10 ans

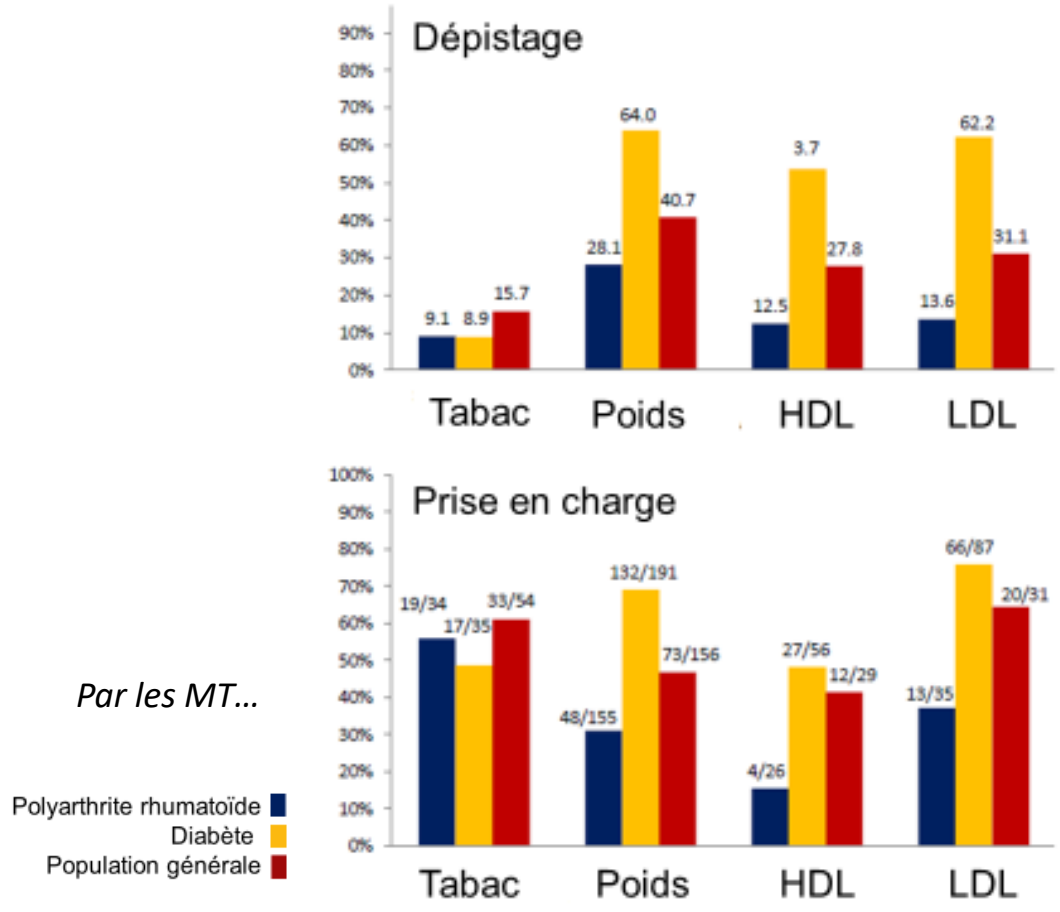
Norton S. et al. Rheumatology.2013;52-99-110



Parce que les comorbidités sont souvent sous-diagnostiquées et leur prise en charge insuffisante

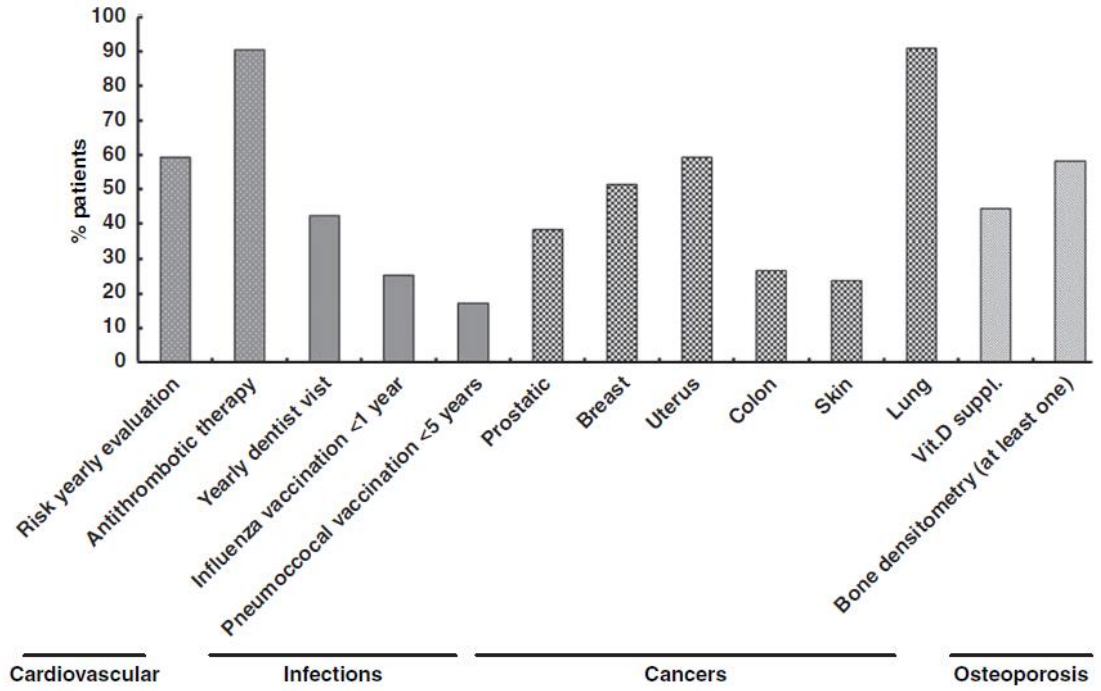
Facteurs de risque cardiovasculaire moins bien gérés dans la PR que dans le diabète de type 2

Par les MT…



Desai et al. Arthritis Res Ther 2012 Dec 13;14(6):R270.

PR

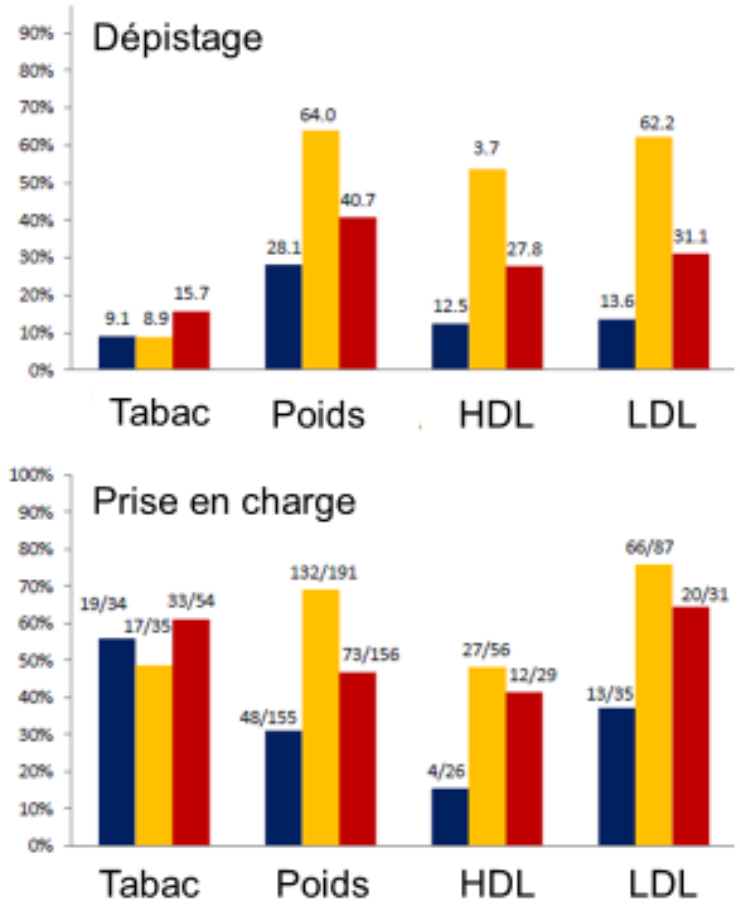


Percentage of patients optimally monitored with respect to some comorbidities. Vit.D suppl., vitamin D supplementation.

…Par les rhumatologues

Dougados M, *et al*. *Ann Rheum Dis* 2014;**73**:62–68. doi:10.1136/annrheumdis-2013-204223

Facteurs de risque cardiovasculaire moins bien gérés dans la PR que dans le diabète de type 2



Par les MT…

Polyarthrite rhumatoïde
Diabète
Population générale

Desai et al. Arthritis Res Ther 2012 Dec 13;14(6):R270.

PR

412 RA and 438 non-RA

Patients PR ont moins de bilan lipidique que non-PR…

Parmi ceux qui ont une indication d'hypolipémiant, **seuls 27% des PR en ont une prescription.**

Akkara Veetil BM, et al. J Rheumatol 2013;40:1082–8.

Les patients avec PR sont à risque de ne pas être diagnostiqués hypertendus: HR=0,71, 0,55-0,93.

Alors que les patients diabétiques ou dyslipidémiques étaient plus rapidement diagnostiqués hypertendus.

Bartels CM, et al. Arthritis Care Res 2014;66:1281–8.

…Par les rhumatologues

Facteurs de risque cardiovasculaire sous-dépistés dans le psoriasis également

- Etude 2005-2009: Seulement 41% des patients PSO ont un dépistage d'au moins un FRCV (TA, glycémie, cholestérolémie, IMC) vs 66% des patients sans PSO [1].
- Sondage en 2015 de 127 dermatologues (USA): moins de 50% dépistent l'HTA, la dyslipidémie, le diabète [2].
- Les patients PSO ont plus de risque d'avoir une HTA non contrôlée que les patients sans PSO (UK) [3].

[1] Alamdari HS, et al. J Drugs Dermatol. 2013; 12(1):e14–19. [2] Manalo IF, et al. J Am Acad Dermatol. 2015; 73(5):872–874. e874. [3]Friedewald VE, et al. Am J Cardiol. 2008; 102(12):1631–1643

Prévalence et prise en charge des FRCV des patients atteints de vascularite à ANCA

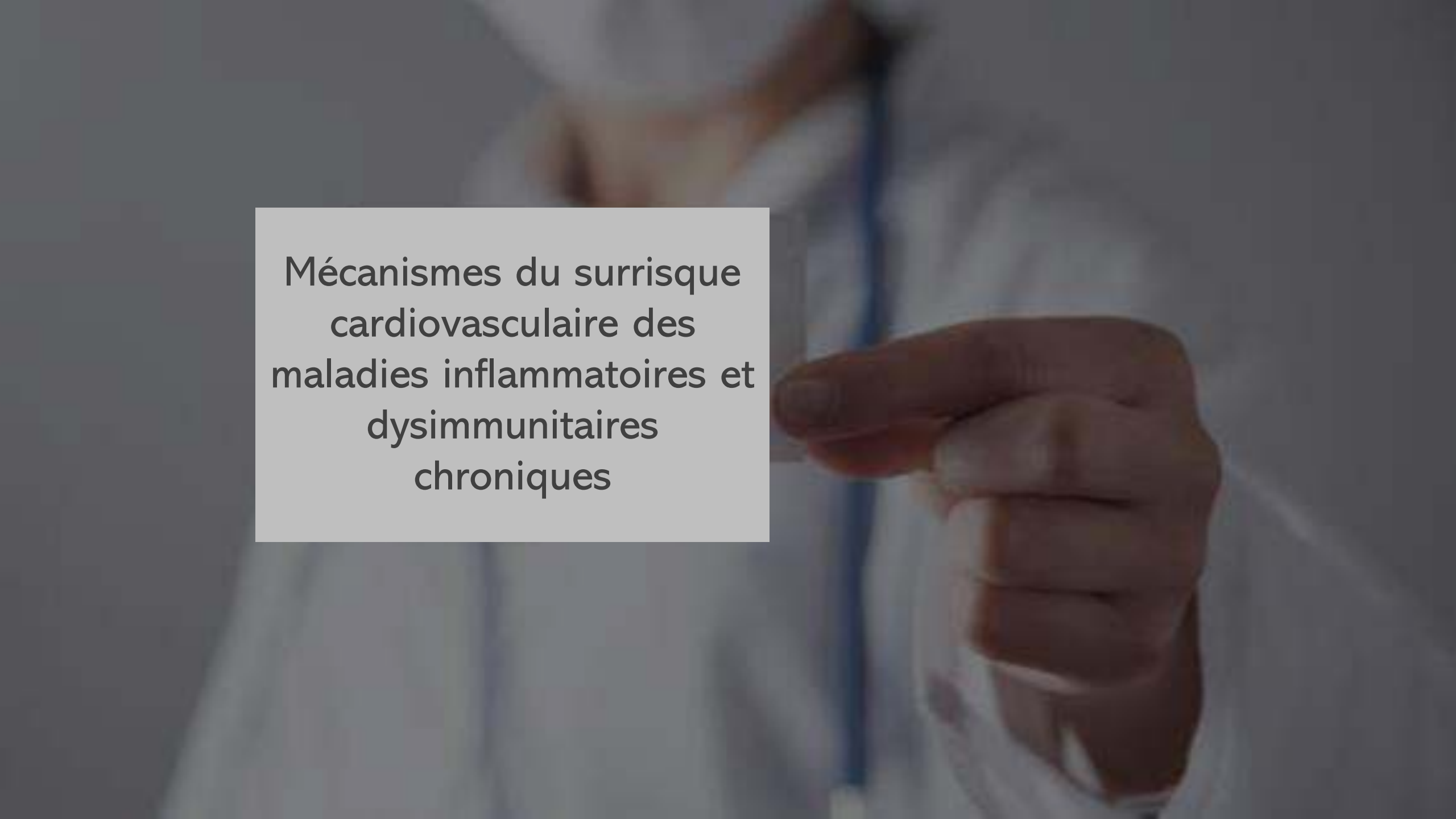
Sur 144 patients

36% des patients ne sont pas à l'objectif tensionnel

25% des patients qui devraient avoir une statine n'en ont pas

Houben E, et al. Rheumatology. 2019;58:2333–2335.

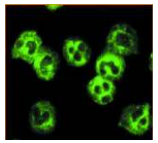
Pourquoi un sur-risque cardiovasculaire dans les MIC?



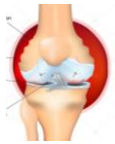
Mécanismes du surrisque cardiovasculaire des maladies inflammatoires et dysimmunitaires chroniques

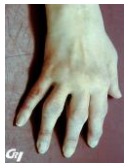
ATHEROSCLEROSE ACCELEREE

Maladie inflammatoire chronique



vascularite





polyarthrite rhumatoïde

INFLAMMATION SYSTEMIQUE

Traitement luttant contre l'inflammation systémique

Facteurs de risque cardiovasculaire traditionnels +

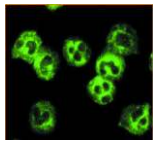
Risque cardiovasculaire induit par l'inflammation +

Risque cardiovasculaire par le traitement (ex. diabète cortico-induit)

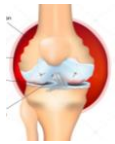
Radner, H. *et al. Nat. Rev. Rheumatol.* **10**, 252–256 (2014); published online 14 January 2014;

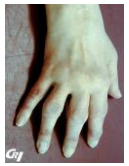
ATHEROSCLEROSE ACCELEREE

Maladie inflammatoire chronique



vascularite





polyarthrite rhumatoïde

INFLAMMATION SYSTEMIQUE

Traitement luttant contre l'inflammation systémique

Facteurs de risque cardiovasculaire traditionnels +

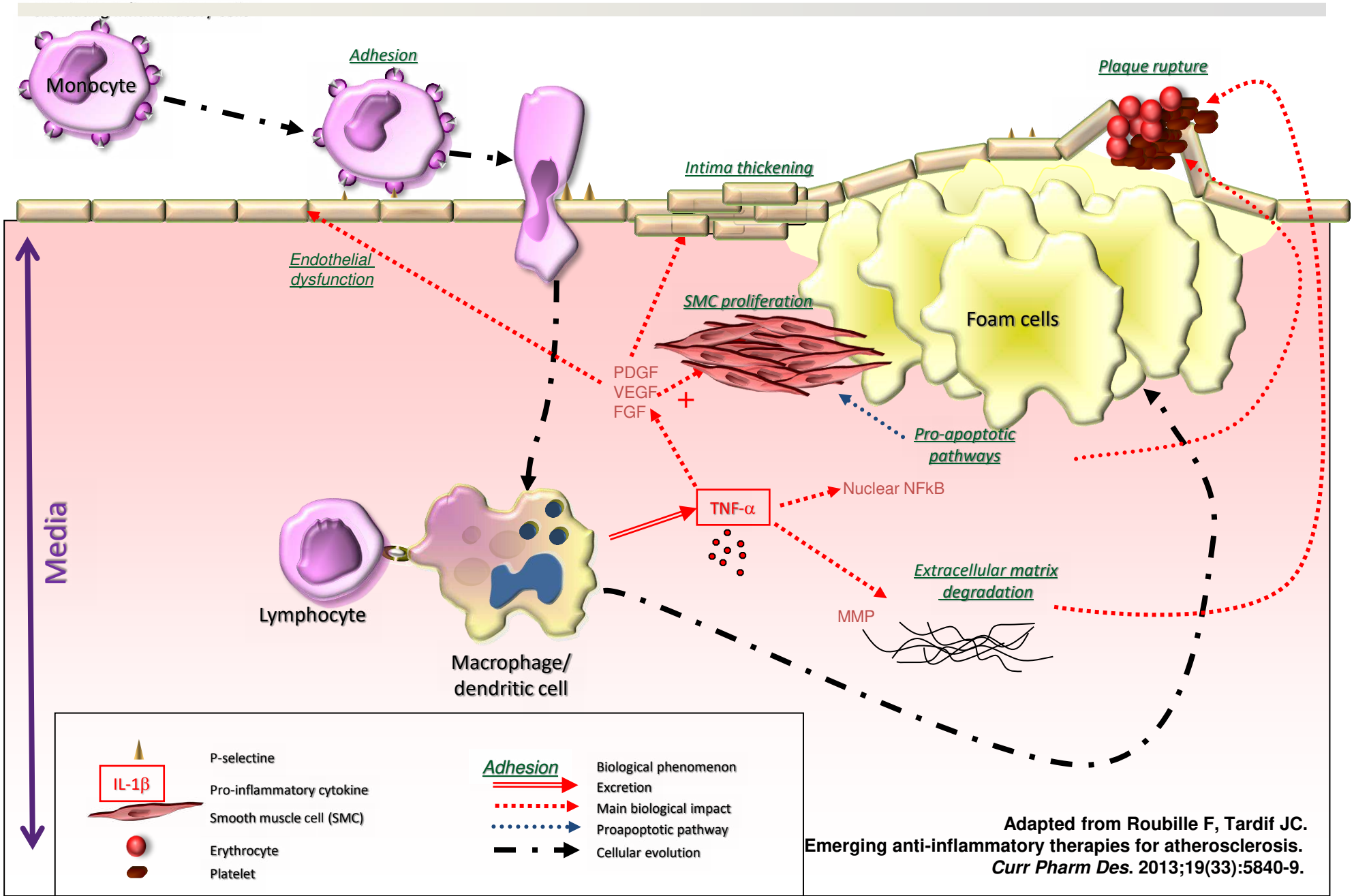
Risque cardiovasculaire induit par l'inflammation +

Risque cardiovasculaire par le traitement (ex. diabète cortico-induit)

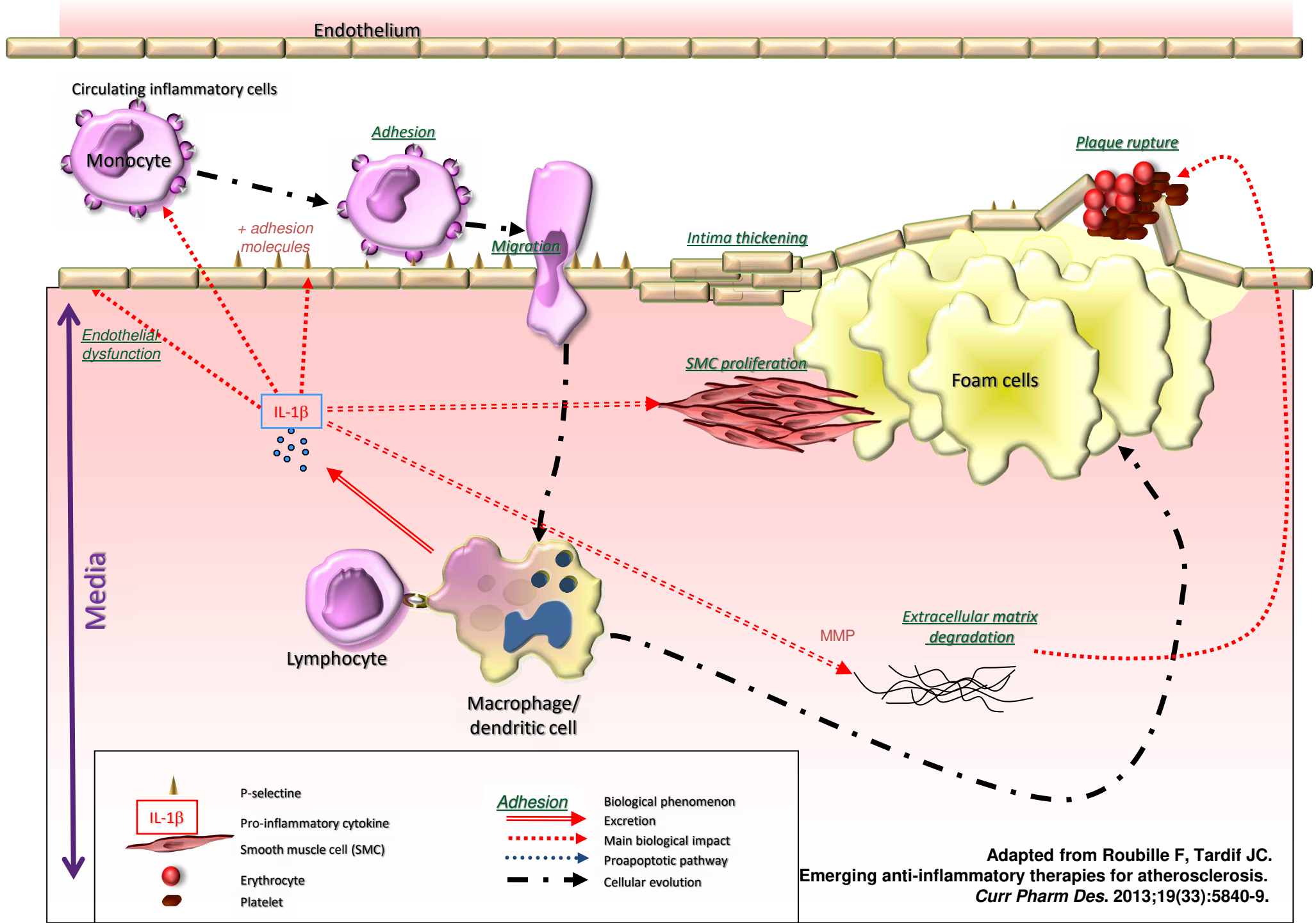
Principalement au cours de la première année de la maladie

Radner, H. *et al. Nat. Rev. Rheumatol.* **10**, 252–256 (2014); published online 14 January 2014;

L'athérosclérose est au moins en partie une maladie inflammatoire …



Adapted from Roubille F, Tardif JC. Emerging anti-inflammatory therapies for atherosclerosis. *Curr Pharm Des.* 2013;19(33):5840-9.



Adapted from Roubille F, Tardif JC. Emerging anti-inflammatory therapies for atherosclerosis. *Curr Pharm Des.* 2013;19(33):5840-9.

Contents lists available at ScienceDirect

Autoimmunity Reviews

journal homepage: www.elsevier.com/locate/autrev

Review

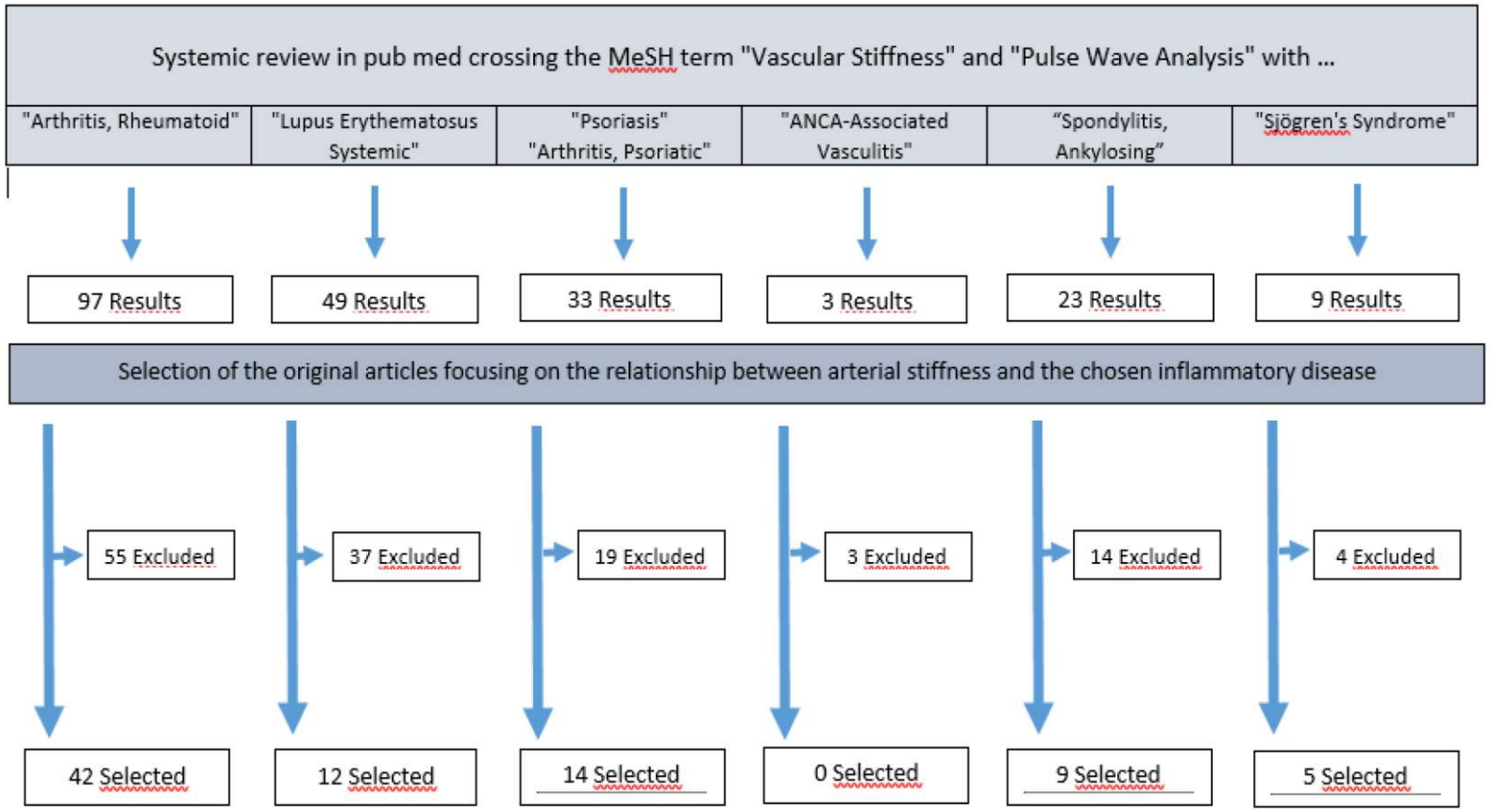
Arterial stiffness, the hidden face of cardiovascular risk in autoimmune and chronic inflammatory rheumatic diseases

Marie Berger [a], Pierre Fesler [a,b], Camille Roubille [a,b,*]

[a] Department of Internal Medicine, CHU Montpellier, Montpellier University, Montpellier, France
[b] PhyMedExp, University of Montpellier, INSERM U1046, CNRS UMR 9214, Montpellier Cedex 5, France

Augmentation de la rigidité artérielle

Autoimmun Rev. 2021 Sep;20(9):102891.



Augmentation de la rigidité artérielle, indicateur pré-clinique de risque cardiovasculaire, évalué de manière non invasive par la vitesse d'onde de pouls (VOP) et indirectement par l'indice d'augmentation (AIx).

Marqueur indirect d'athérosclérose infra-clinique

Facteurs de risque cardiovasculaire

Facteurs liés à la maladie

Facteurs de risque cardiovasculaires traditionnels:

Sédentarité

Genre

Age

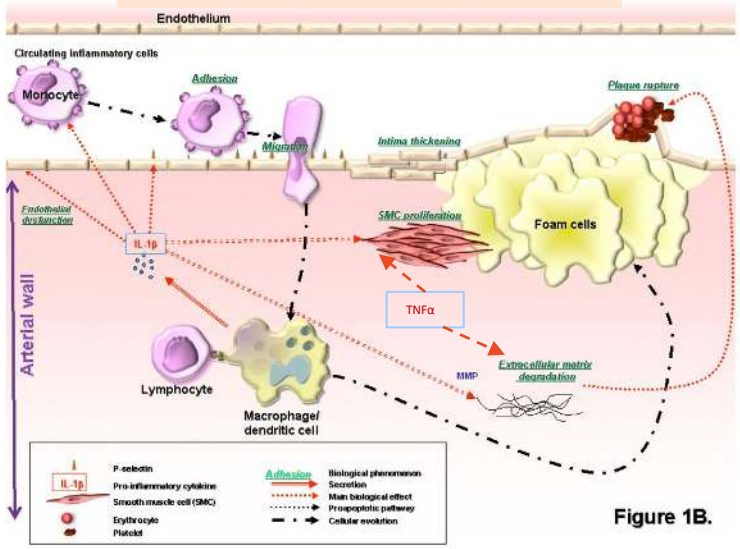
Facteurs génétiques

↗ Prévalence

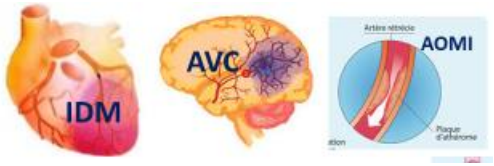
Facteurs de risque cardiovasculaire non traditionnels:
Dépression
SAOS

INFLAMMATION SYSTEMIQUE (dès le stade précoce)

ATHEROSCLEROSE

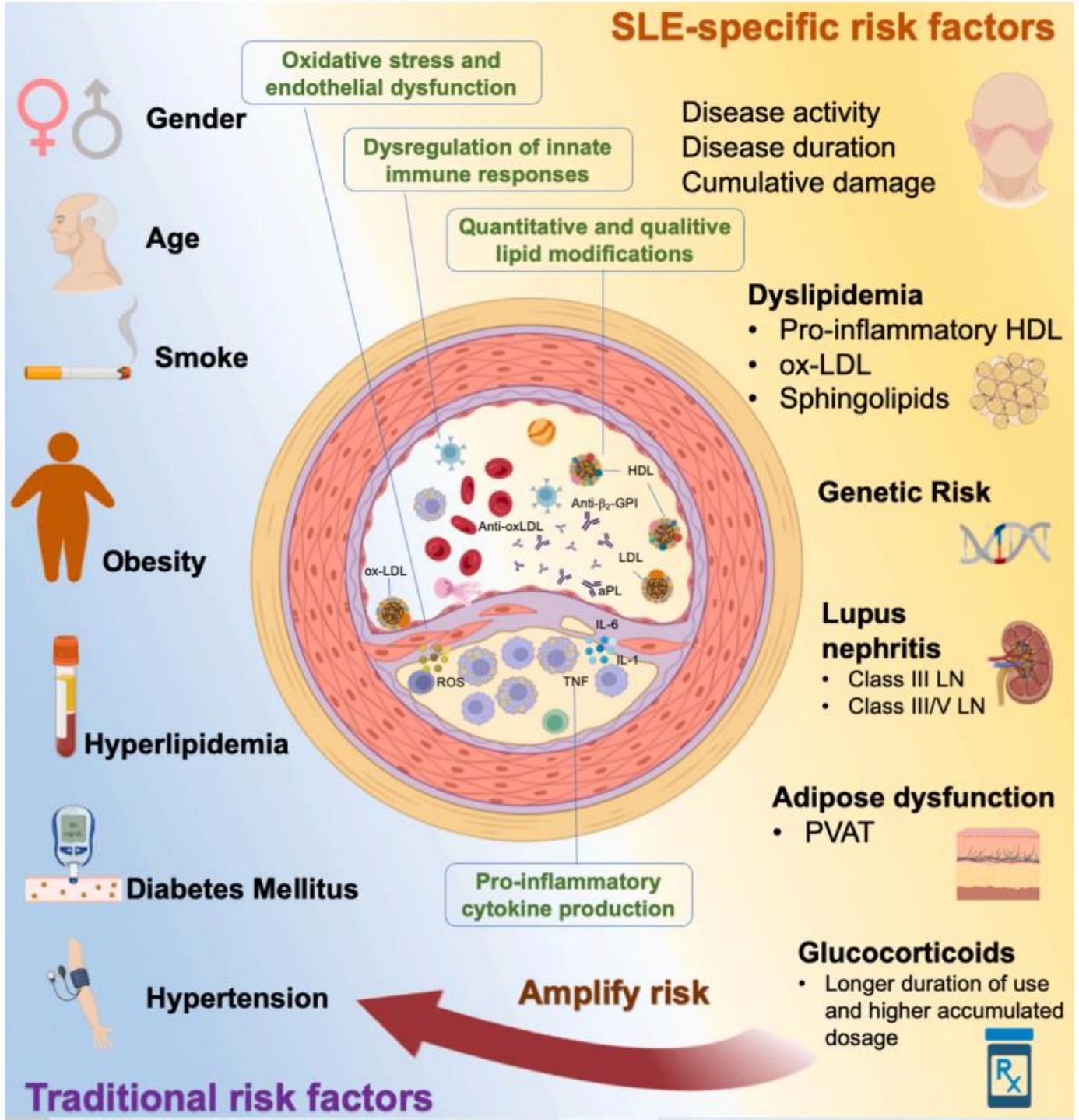


Roubille F.et al. Current Pharmaceutical Design, 2013



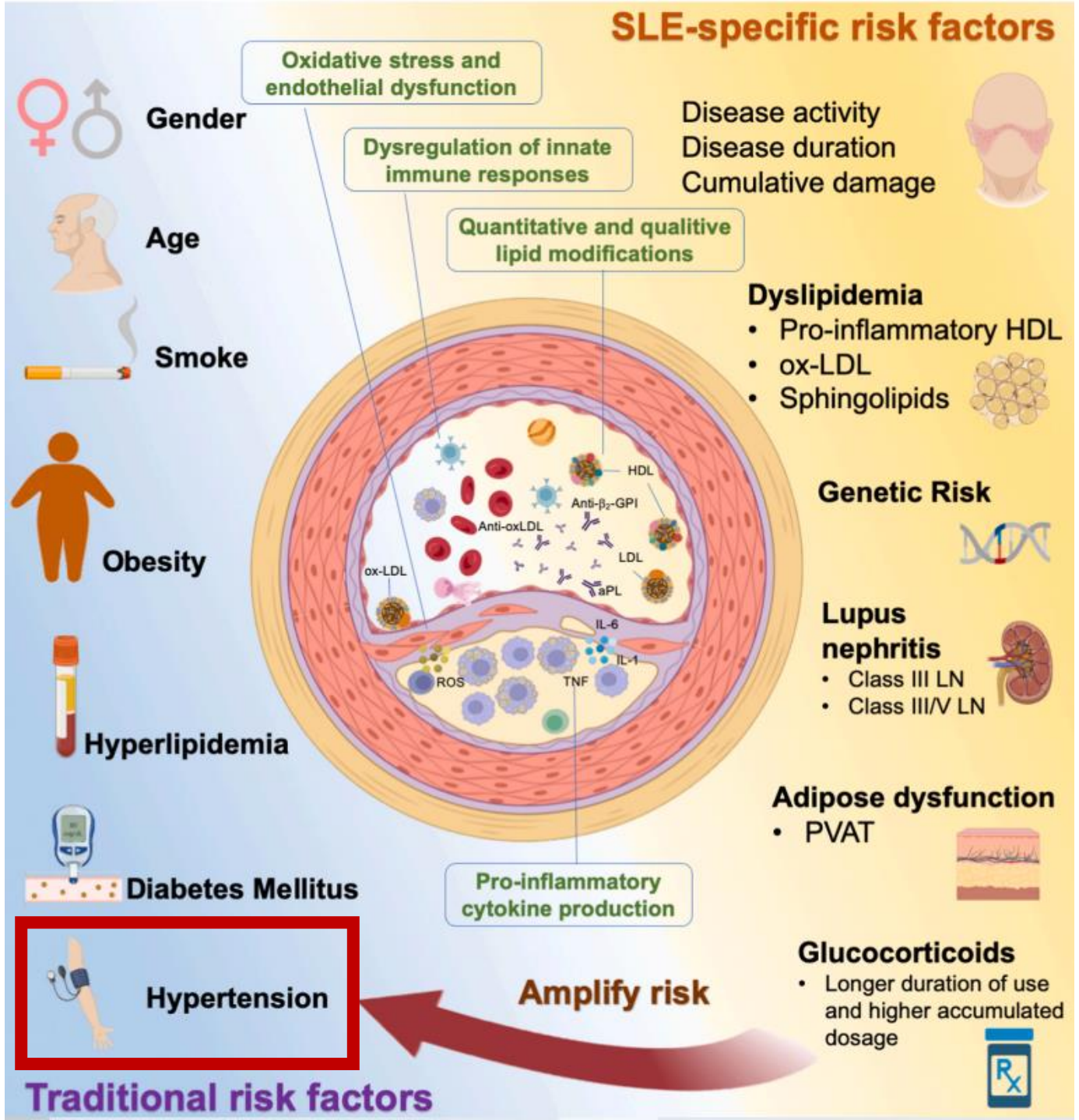
CVD

↗ Risque cardiovasculaire dans les maladies inflammatoires chroniques



+ APL

https://doi.org/10.1016/j.jaut.2022.102863



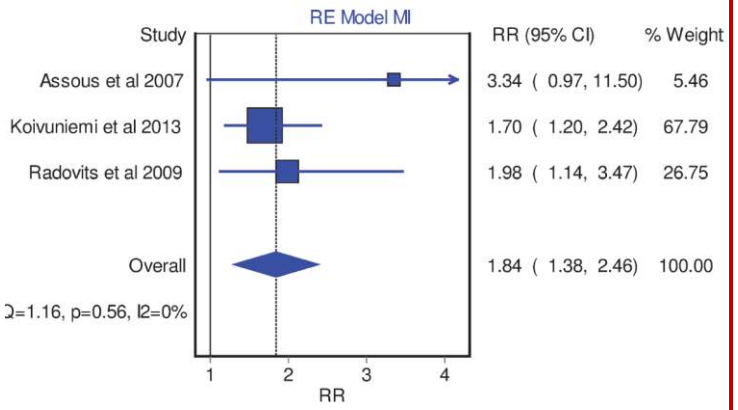
+ APL

https://doi.org/10.1016/j.jaut.2022.102863

Quel poids des FRCV dans le surrisque cardiovasculaire des maladies inflammatoires et dysimmunitaires chroniques?

PR

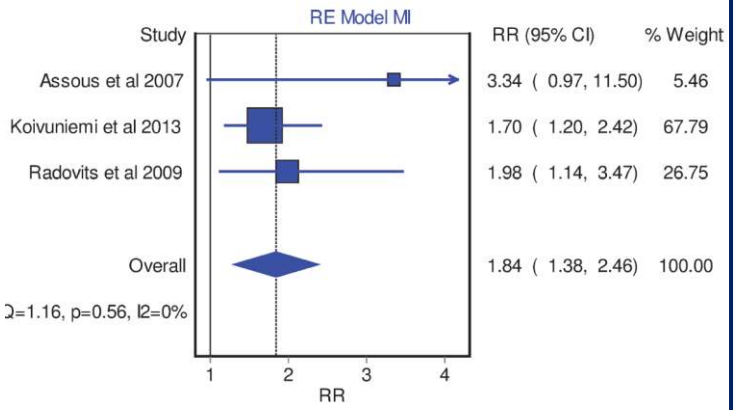
HR d'IDM=1,84 (1,39-2,46) si RA+HTA vs RA sans HTA



Baghdadi LR. Plos One. 2015 Feb 17;10(2):e0117952.

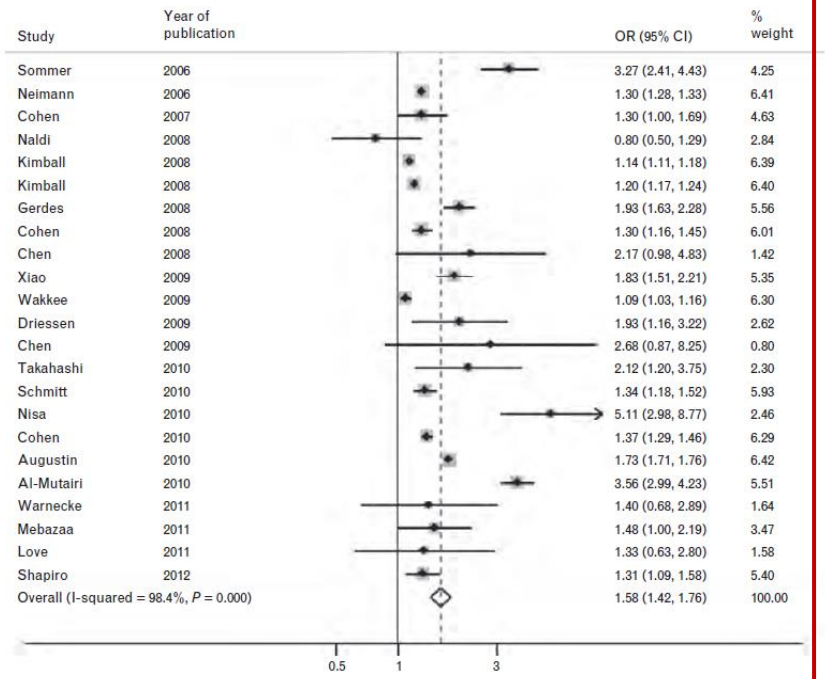
PR

HR d'IDM=1,84 (1,39-2,46) si RA+HTA vs RA sans HTA



Baghdadi LR. Plos One. 2015 Feb 17;10(2):e0117952.

Psoriasis



Armstrong et al. Journal of Hypertension 2013, 31:433–443

OR=1.56 (1.42-1.76)

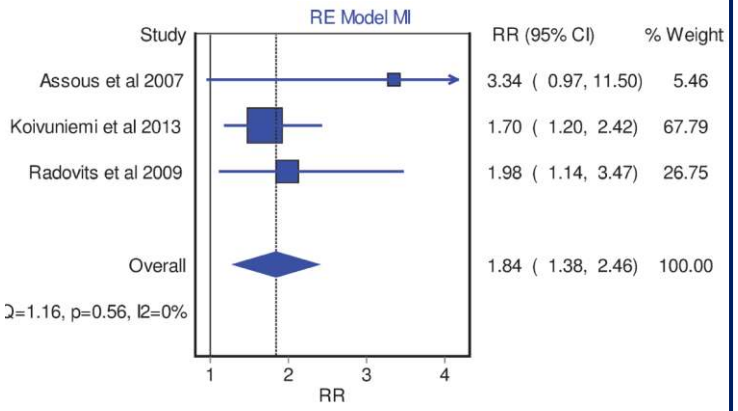
Impact inflammation systémique

Production d'angiotensine II dans la graisse viscérale

↗endothéline 1

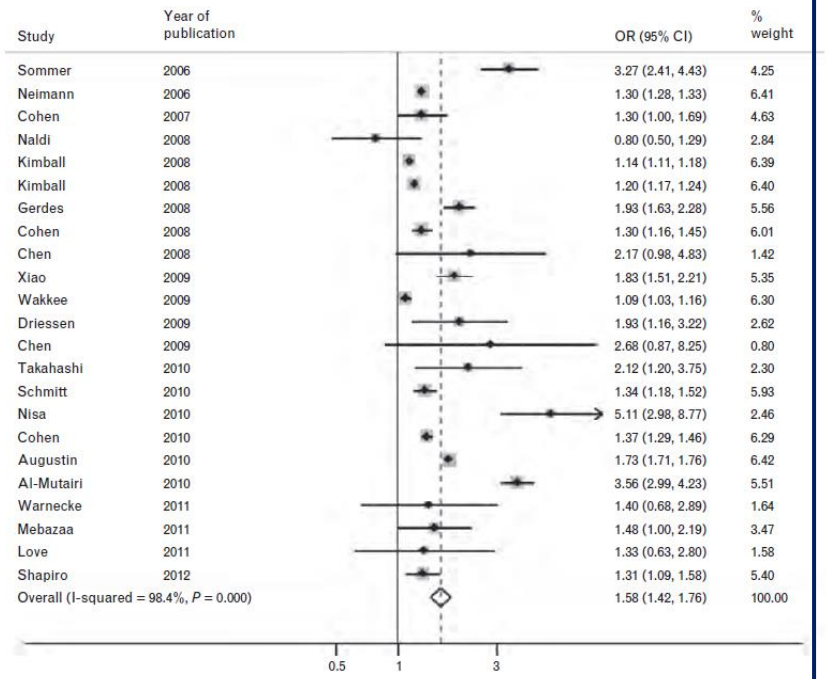
PR

HR d'IDM=1,84 (1,39-2,46) si RA+HTA vs RA sans HTA



Baghdadi LR. Plos One. 2015 Feb 17;10(2):e0117952.

Psoriasis



Armstrong et al. Journal of Hypertension 2013, 31:433–443

OR=1.56 (1.42-1.76)

Impact inflammation systémique

Production d'angiotensine II dans la graisse viscérale

↗endothéline 1

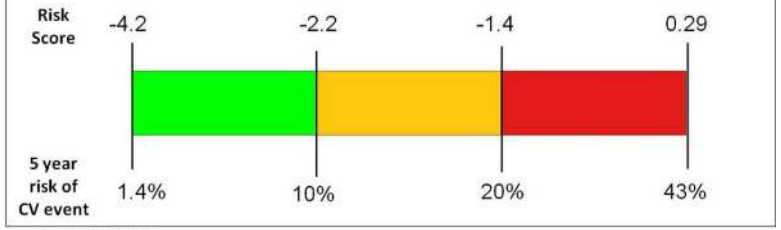
Vascularites ANCA

A MODEL TO PREDICT CARDIOVASCULAR EVENTS IN PATIENTS WITH NEWLY DIAGNOSED WEGENER'S GRANULOMATOSIS AND MICROSCOPIC POLYANGIITIS

Les facteurs prédictifs de MACEs: age [OR 1.45 (95%CI 1.11 – 1.90)]; **hypertension diastolique [OR 1.97 (95%CI 0.98 – 3.95)],** et positivité PR3 ANCA [OR 0.39 (95%CI 0.20 – 0.74)].

Risk score = -3.9 + (0.04*Age) – (0.95* PR3 ANCA) + (0.68*HTN)

Predicted risk of a cardiovascular event in 5 years = 1/ (1 + $e^{-risk\ score}$)



- **Age in years.**
- **HTN = Diastolic blood pressure > 95 mmHg at time of diagnosis. Score 1 if present, 0 if absent.**
- **PR3 ANCA = 1 if present, 0 if absent.**

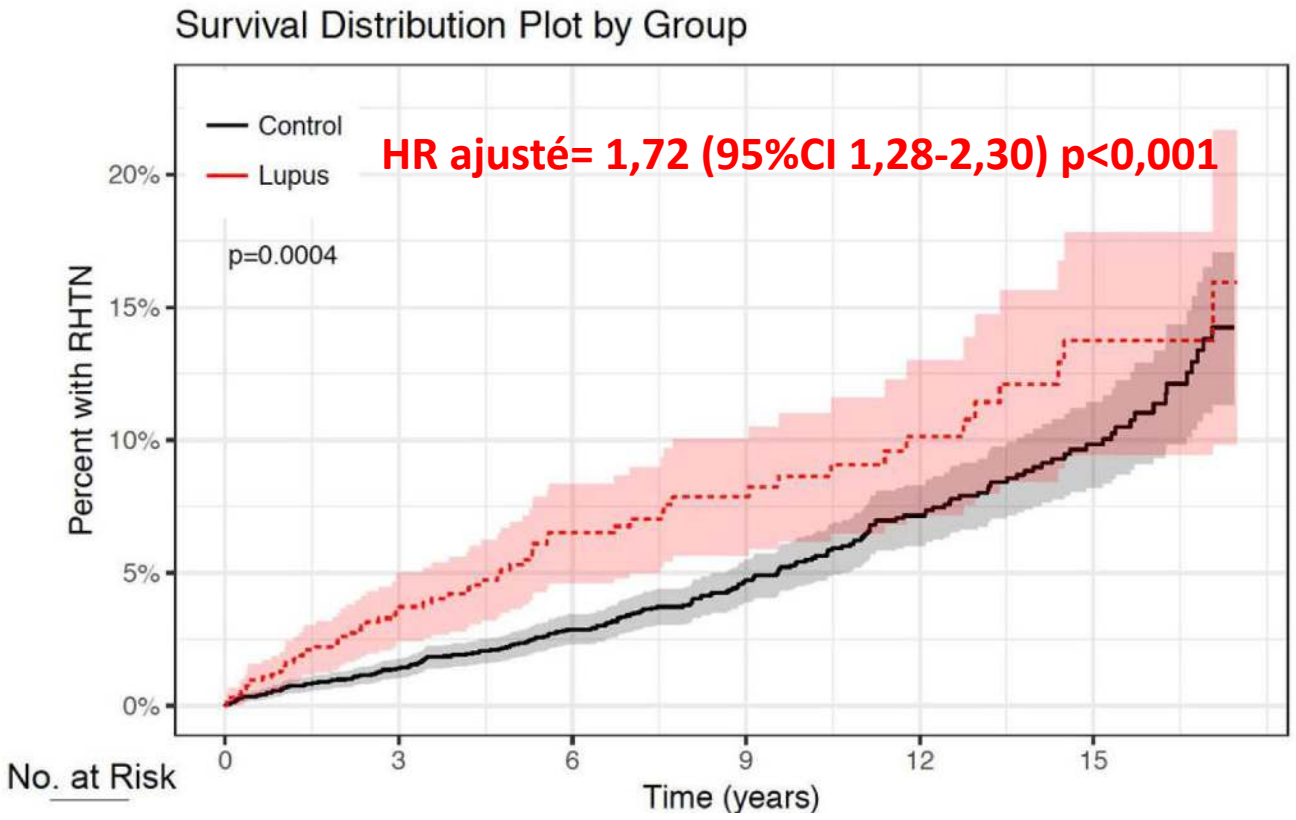
(EUVAS) trial, testé sur WGET

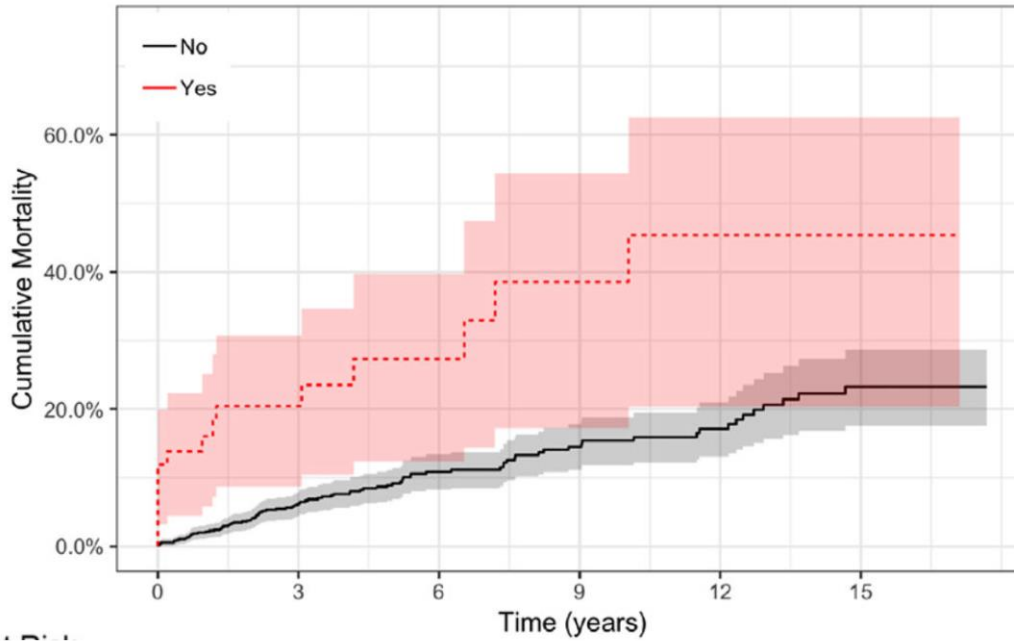
Suppiah R.et al. Arthritis Care Res (Hoboken). 2011 April ; 63(4): 588–596.

Increased Incidence of Resistant Hypertension in Patients with Systemic Lupus Erythematosus: A Retrospective Cohort Study

1044 SLE vs 5241 contrôles

HTA résistante quasiment 2 fois plus fréquente chez lupiques
Associée à un sur-risque de mortalité x 3 (HR 2,91)





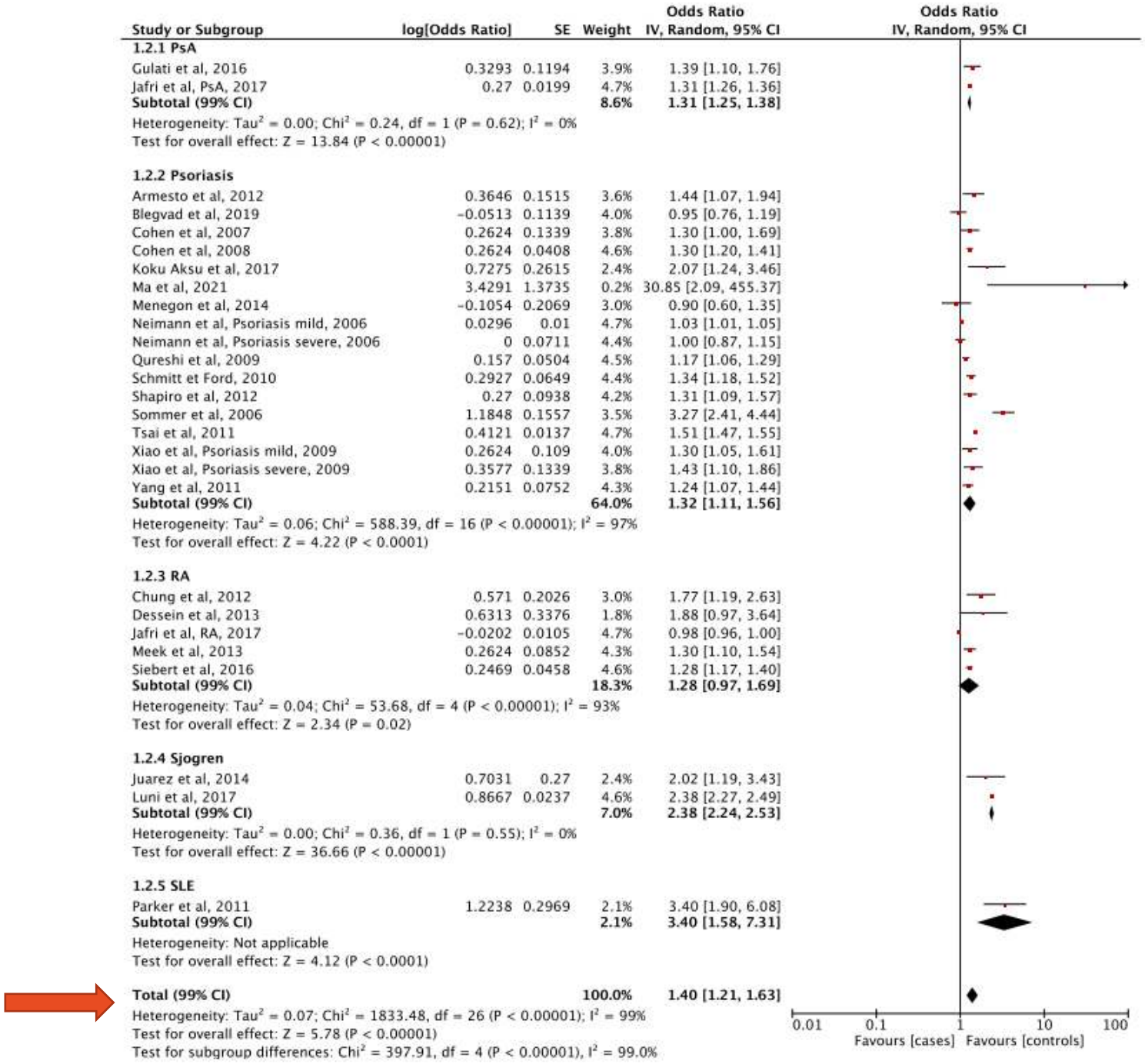
Mortality in SLE Patients with and without RHTN

Arthritis Care Res (Hoboken). Author manuscript; available in PMC 2020 September 15.

Méta-analyse sur la prévalence de l'HTA dans les maladies inflammatoires et dysimmunitaires

Prevalence of HTA among patients with an auto-immune disease vs healthy controls

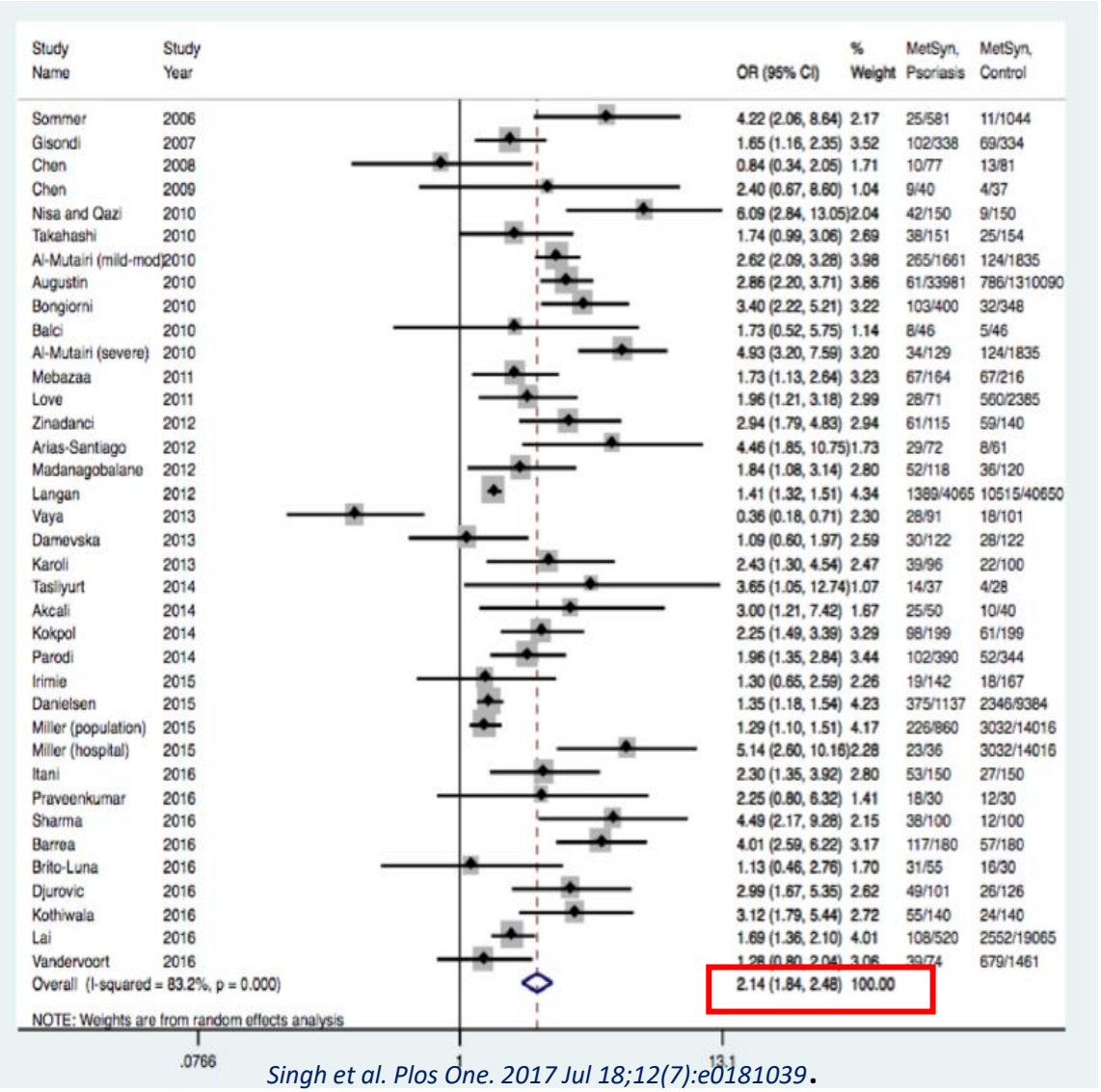
Subgroups	Crude OR (99% CI)	Nb of studies	Adjusted OR (99% CI)	Nb of studies
Psoriasis	**1.59 (1.40-1.80)**	41	**1.32 (1.11-1.56)**	17
PsA	**1.64 (1.31-2.05)**	14	**1.31 (1.25-1.38)**	2
RA	**1.44 (1.25-1.66)**	43	1.28 (0.97-1.69)	5
SLE	**2.62 (2.0-3.42)**	33	**3.40 (1.58-7.31)**	1
Sjogren	1.26 (0.62-2.56)	10	**2.38 (2.24-2.53)**	2
ANCA	**12.35 (1.37-111.47)**	1		
TOTAL	**1.64 (1.52-1.77**	**141**	**1.40 (1.21-1.63)**	**27**


Study or Subgroup
log[Odds Ratio]
SE
Weight
Odds Ratio
IV, Random, 95% CI
Odds Ratio
IV, Random, 95% CI
1.2.1 PsA
Gulati et al, 2016 0.3293 0.1194 3.9% 1.39 [1.10, 1.76]
Jafri et al, PsA, 2017 0.27 0.0199 4.7% 1.31 [1.26, 1.36]
Subtotal (99% CI) 8.6% 1.31 [1.25, 1.38]
Heterogeneity: Tau² = 0.00; Chi² = 0.24, df = 1 (P = 0.62); I² = 0%
Test for overall effect: Z = 13.84 (P < 0.00001)
1.2.2 Psoriasis
Armesto et al, 2012 0.3646 0.1515 3.6% 1.44 [1.07, 1.94]
Blegvad et al, 2019 -0.0513 0.1139 4.0% 0.95 [0.76, 1.19]
Cohen et al, 2007 0.2624 0.1339 3.8% 1.30 [1.00, 1.69]
Cohen et al, 2008 0.2624 0.0408 4.6% 1.30 [1.20, 1.41]
Koku Aksu et al, 2017 0.7275 0.2615 2.4% 2.07 [1.24, 3.46]
Ma et al, 2021 3.4291 1.3735 0.2% 30.85 [2.09, 455.37]
Menegon et al, 2014 -0.1054 0.2069 3.0% 0.90 [0.60, 1.35]
Neimann et al, Psoriasis mild, 2006 0.0296 0.01 4.7% 1.03 [1.01, 1.05]
Neimann et al, Psoriasis severe, 2006 0 0.0711 4.4% 1.00 [0.87, 1.15]
Qureshi et al, 2009 0.157 0.0504 4.5% 1.17 [1.06, 1.29]
Schmitt et Ford, 2010 0.2927 0.0649 4.4% 1.34 [1.18, 1.52]
Shapiro et al, 2012 0.27 0.0938 4.2% 1.31 [1.09, 1.57]
Sommer et al, 2006 1.1848 0.1557 3.5% 3.27 [2.41, 4.44]
Tsai et al, 2011 0.4121 0.0137 4.7% 1.51 [1.47, 1.55]
Xiao et al, Psoriasis mild, 2009 0.2624 0.109 4.0% 1.30 [1.05, 1.61]
Xiao et al, Psoriasis severe, 2009 0.3577 0.1339 3.8% 1.43 [1.10, 1.86]
Yang et al, 2011 0.2151 0.0752 4.3% 1.24 [1.07, 1.44]
Subtotal (99% CI) 64.0% 1.32 [1.11, 1.56]
Heterogeneity: Tau² = 0.06; Chi² = 588.39, df = 16 (P < 0.00001); I² = 97%
Test for overall effect: Z = 4.22 (P < 0.0001)
1.2.3 RA
Chung et al, 2012 0.571 0.2026 3.0% 1.77 [1.19, 2.63]
Dessein et al, 2013 0.6313 0.3376 1.8% 1.88 [0.97, 3.64]
Jafri et al, RA, 2017 -0.0202 0.0105 4.7% 0.98 [0.96, 1.00]
Meek et al, 2013 0.2624 0.0852 4.3% 1.30 [1.10, 1.54]
Siebert et al, 2016 0.2469 0.0458 4.6% 1.28 [1.17, 1.40]
Subtotal (99% CI) 18.3% 1.28 [0.97, 1.69]
Heterogeneity: Tau² = 0.04; Chi² = 53.68, df = 4 (P < 0.00001); I² = 93%
Test for overall effect: Z = 2.34 (P = 0.02)
1.2.4 Sjogren
Juarez et al, 2014 0.7031 0.27 2.4% 2.02 [1.19, 3.43]
Luni et al, 2017 0.8667 0.0237 4.6% 2.38 [2.27, 2.49]
Subtotal (99% CI) 7.0% 2.38 [2.24, 2.53]
Heterogeneity: Tau² = 0.00; Chi² = 0.36, df = 1 (P = 0.55); I² = 0%
Test for overall effect: Z = 36.66 (P < 0.00001)
1.2.5 SLE
Parker et al, 2011 1.2238 0.2969 2.1% 3.40 [1.90, 6.08]
Subtotal (99% CI) 2.1% 3.40 [1.58, 7.31]
Heterogeneity: Not applicable
Test for overall effect: Z = 4.12 (P < 0.0001)
Total (99% CI) 100.0% 1.40 [1.21, 1.63]
Heterogeneity: Tau² = 0.07; Chi² = 1833.48, df = 26 (P < 0.00001); I² = 99%
Test for overall effect: Z = 5.78 (P < 0.00001)
Test for subgroup differences: Chi² = 397.91, df = 4 (P < 0.00001), I² = 99.0%
0.01
0.1
1
10
100
Favours [cases]
Favours [controls]

Syndrome métabolique

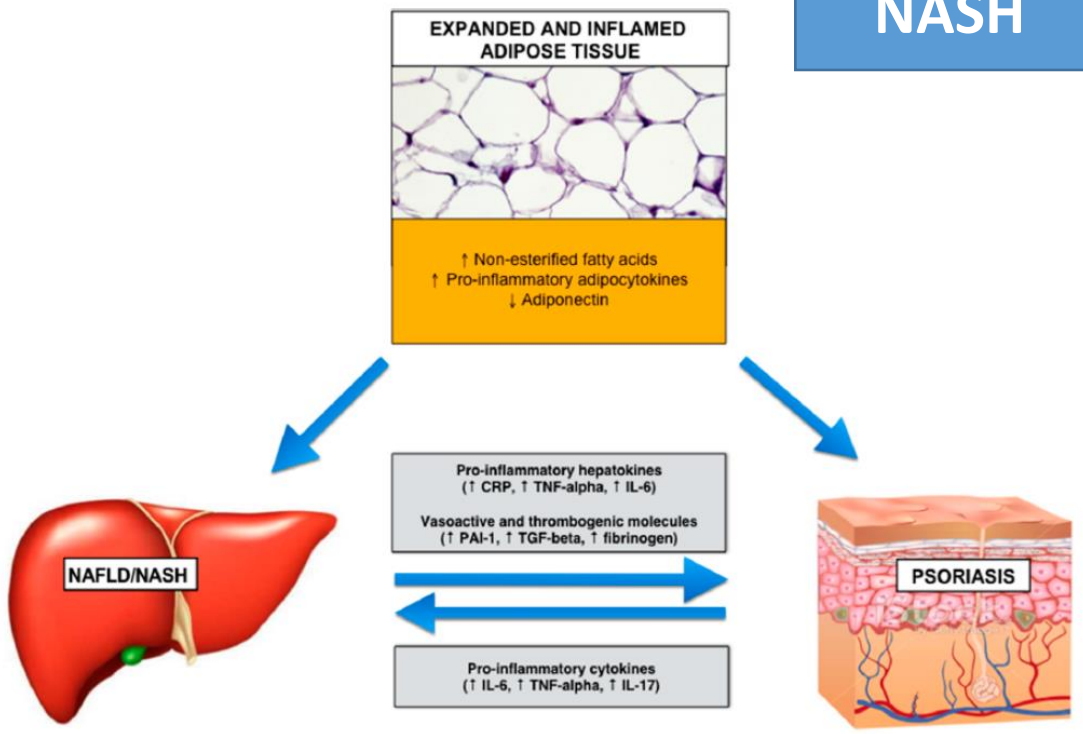
obésité abdominale, HTA, hypertriglycéridémie, HDL bas, diabète de type 2 / insulinorésistance,

PSORIASIS



Singh et al. Plos One. 2017 Jul 18;12(7):e0181039.

NASH



Int. J. Mol. Sci. 2016, 17, 217

Journal of
Clinical Medicine

MDPI

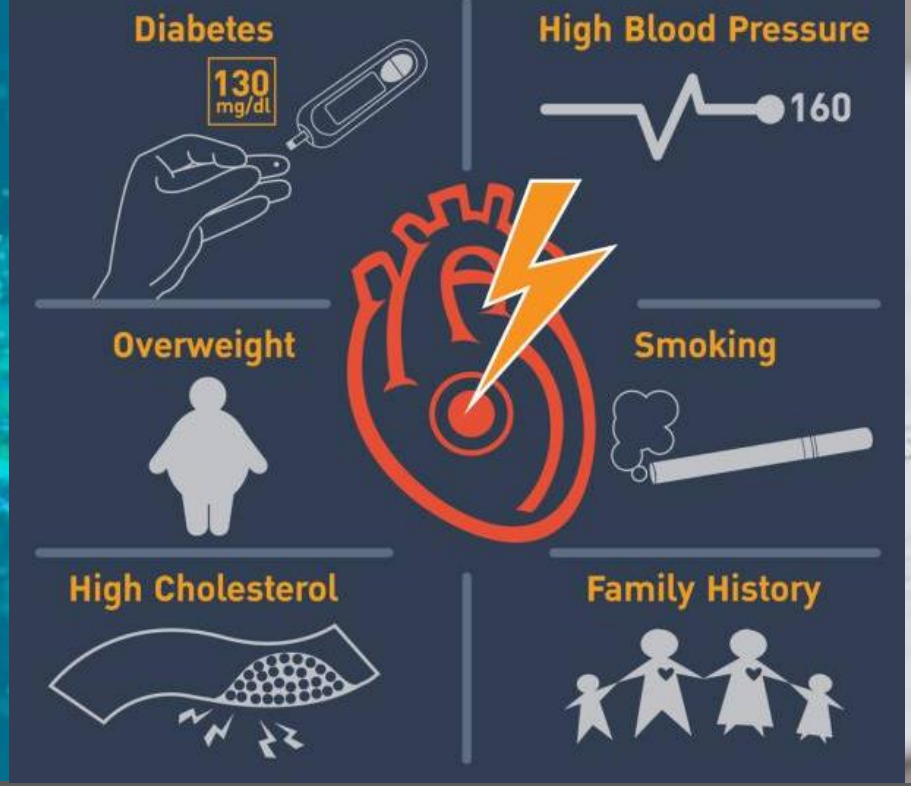
Article

Impact of Cardiovascular Risk Factors on the Occurrence of Cardiovascular Events in Antineutrophil Cytoplasmic Antibody (ANCA)-Associated Vasculitides

Camille Roubille [1,2,*], Soledad Henriquez [3,4], Cédric Mercuzot [1], Claire Duflos [5], Bertrand Dunogue [3,4], Karine Briot [4,6], Loic Guillevin [3,4], Benjamin Terrier [3,4] and Pierre Fesler [1,2]

1 Department of Internal Medicine, Lapeyronie Hospital, Montpellier University Hospital, 34000 Montpellier, France; c-mercuzot@chu-montpellier.fr (C.M.); p-fesler@chu-montpellier.fr (P.F.)
2 PhyMedExp, University of Montpellier, INSERM U1046, CNRS UMR 9214, 34000 Montpellier, France
3 Department of Internal Medicine, Assistance Publique Hôpitaux de Paris-Centre, Université de Paris, Hôpital Cochin, 75014 Paris, France; soledad.henriquez@aphp.fr (S.H.); bertrand.dunogue@aphp.fr (B.D.); loic.guillevin@aphp.fr (L.G.); benjamin.terrier@aphp.fr (B.T.)

Impact des FRCV sur le pronostic cardiovasculaire des patients atteints de vascularite à ANCA



Population: 103 patients atteints de VAA (cohorte OSTEOVAS de Cochin, collaboration Pr Terrier GFEV)

60% GPA, 11% MPA, 28% EGPA

FRCV: âge>50 ans hommes et >60 ans femmes, ATCD MCV, tabagisme, obésité, diabète, dyslipidémie, HTA, sédentarité

Survenue de MACEs à 3 ans de suivi

Association entre les FRCV et la survenue de MACEs

Table 1. Baseline demographic, clinical, biological, and functional characteristics of the study population from the OSTEO-VAS cohort.

	N	**Total Study Population (*n* = 103)**
Demographics and clinical parameters		
Age (years) (mean SD)	103	52.88 ± 17.40
Male, *n* (%)	103	46 (44.66)
Cardiovascular risk factors		
Older age (>50 years for men, >60 years for women), *n* (%)	103	46 (44.66)
BMI (kg/m^2) (mean SD)	103	25.34 ± 4.87
BMI > 30 kg/m^2, *n* (%)	103	17 (16.5)
Diabetes mellitus, *n* (%)	103	7 (6.8)
Hypertension, *n* (%)	103	54 (52.4)
Ever smokers, *n* (%)	103	43 (41.8)
History of CVD, *n* (%)	103	11 (10.7)
Dyslipidemia, *n* (%)	103	19 (18.5)
Sedentary lifestyle (yes), *n* (%)	103	20 (19.4)

C Roubille et al, J Clin Med. 25 mai 2021;10(11):2299

16 patients ont eu au moins 1 MACE (15,5%)

3 AVC / AIT

3 CMI

9 hospitalisations pour MCV

1 décès par MCV

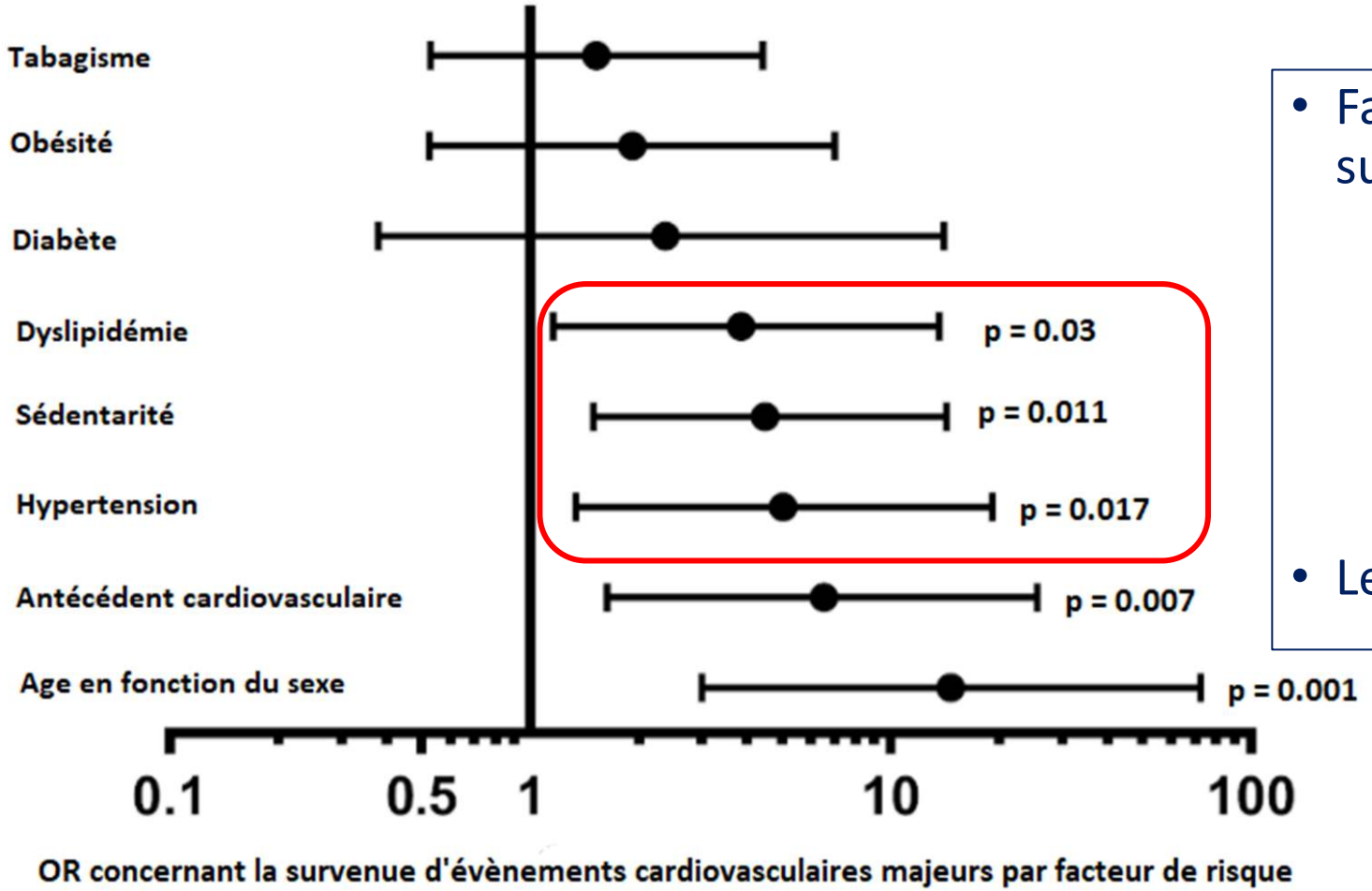
Table 2. Occurrence of MACEs according to the number of CVRFs present in patients from the OSTEOVAS cohort.

Number of CVRFs	Number of Patients without MACEs	Number of Patients in Whom ≥1 MACE Occurred, *n* (%)
0	20	1 (4.8%)
1	21	1 (4.5%)
2	28	2 (6.7%)
≥ 3	18	12 (40%)

CVRF, cardiovascular risk factor; MACE, major cardiovascular event. Cardiovascular risk factors included age >50 for men or >60 for women, medical history of cardiovascular disease, smoking status (current or former), obesity (body mass index ≥ 30 kg/m^2), diabetes mellitus, dyslipidemia, hypertension, or a sedentary lifestyle.

	OR (95% CI)	*p*
Number of cardiovascular risk factors	1.74 (1.28–2.37)	<0.001
Use of glucocorticoids	1.16 (0.50–2.72)	0.733
Use of cyclophosphamide	0.56 (0.17–1.85)	0.339

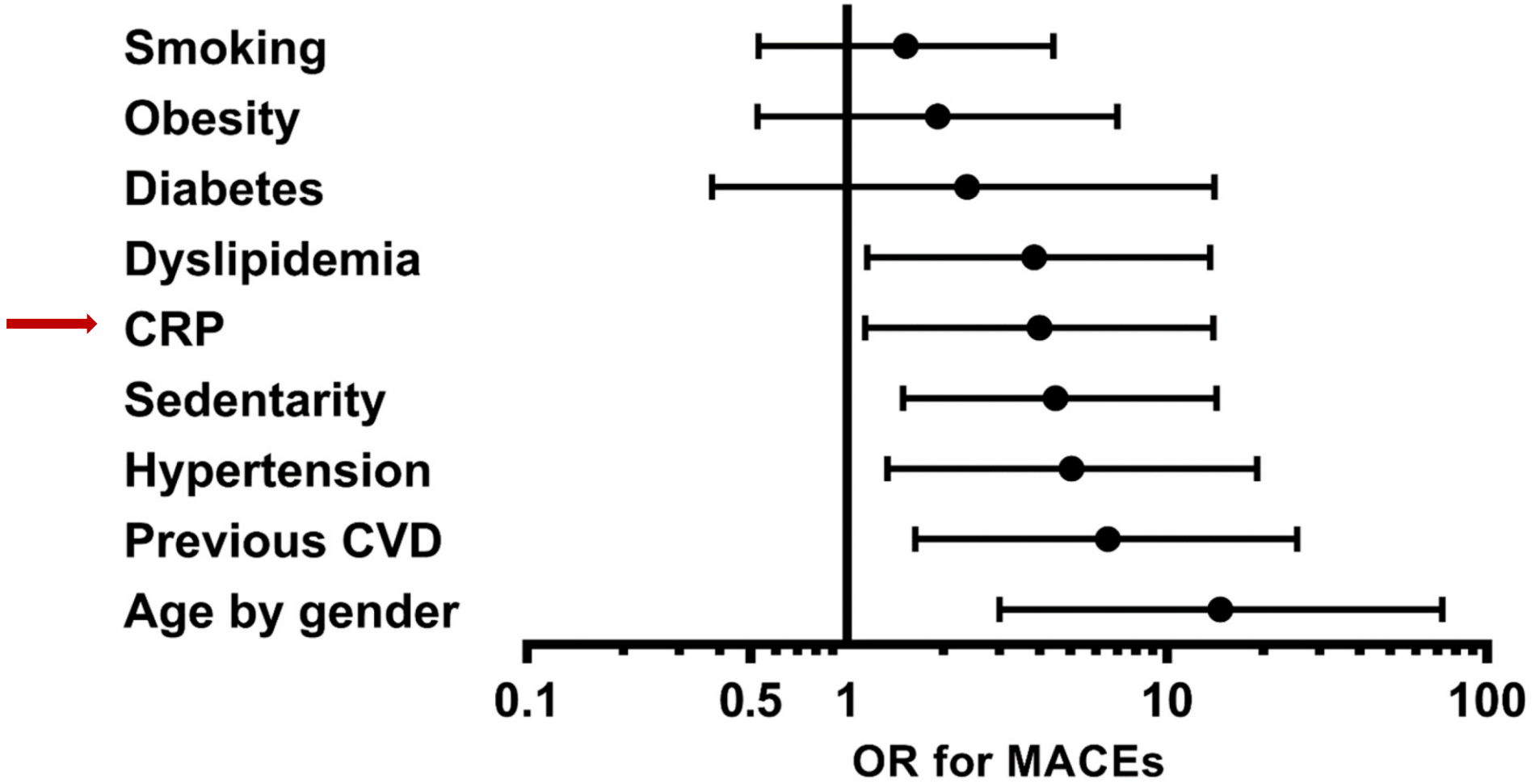
La survenue de MACEs est associée au nombre de FRCV



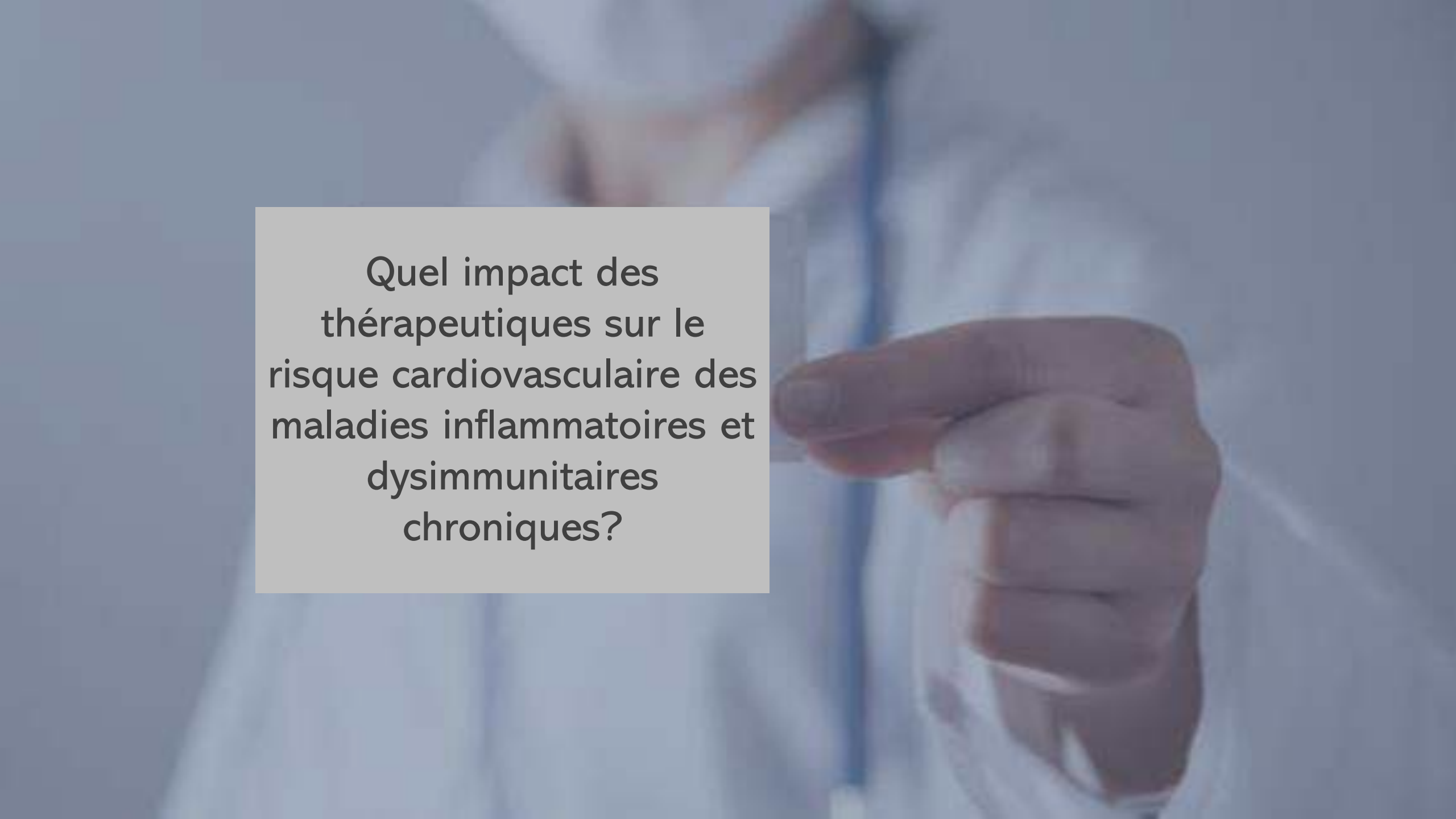
OR concernant la survenue d'évènements cardiovasculaires majeurs par facteur de risque

- Facteurs de risque associés à la survenue d'évènements majeurs:
  - Age en fonction du sexe (OR 14,7)
  - Antécédent cardiovasculaire (OR 6,5)
  - Hypertension artérielle (OR 5,0)
  - Sédentarité (OR 4,5)
  - Dyslipidémie (OR 3,9)
- Les trois derniers sont **modifiables**

La dyslipidémie, la sédentarité et l'HTA sont associées à la survenue de MACEs

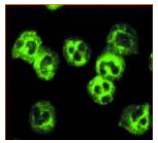


Association entre la survenue de MACEs et le niveau de CRP (p=0.028, OR=4.028, 95%CI=1.16-13.98)

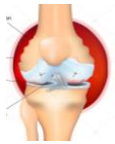

Quel impact des thérapeutiques sur le risque cardiovasculaire des maladies inflammatoires et dysimmunitaires chroniques?

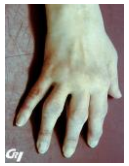
ATHEROSCLEROSE ACCELEREE

Maladie inflammatoire chronique



vascularite





polyarthrite rhumatoïde

INFLAMMATION SYSTEMIQUE

Traitement luttant contre l'inflammation systémique

Facteurs de risque cardiovasculaire traditionnels +

Risque cardiovasculaire induit par l'inflammation +

Risque cardiovasculaire par le traitement (ex. diabète cortico-induit)

Radner, H. *et al. Nat. Rev. Rheumatol.* **10**, 252–256 (2014); published online 14 January 2014;

Facteurs de risque cardiovasculaires traditionnels: n'expliquent pas à eux seuls le risque CV…

↗ Prévalence

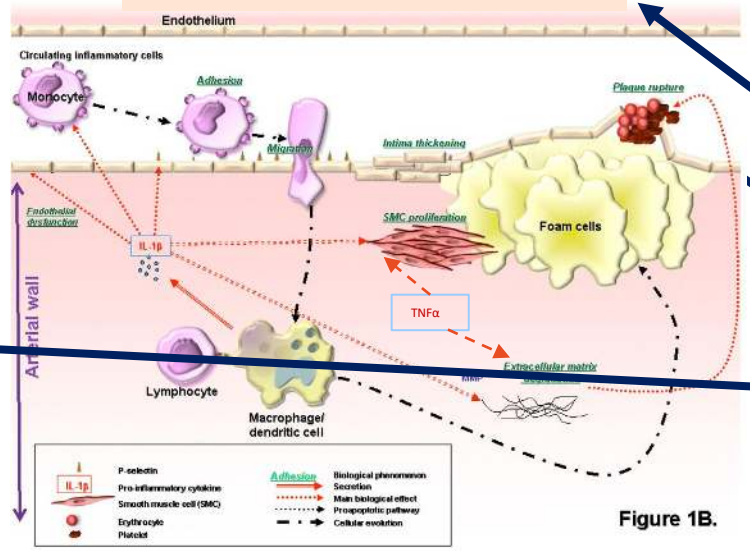
Sédentarité

Genre
Age
Facteurs génétiques

Facteurs de risque cardiovasculaire non traditionnels:
Dépression
SAOS

INFLAMMATION SYSTEMIQUE (dès le stade précoce)

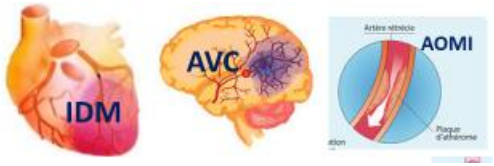
ATHEROSCLEROSE



Roubille F.et al. Current Pharmaceutical Design, 2013

Contrôle optimal de l'activité de la maladie « treat-to-target »

Thérapies visant l'inflammation systémique (DMARDS, GC, AINS)



CVD

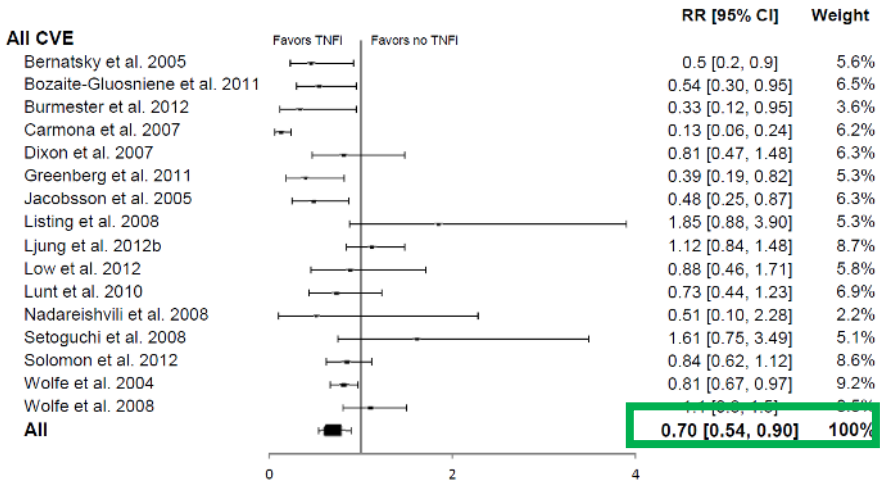
↗ Risque cardiovasculaire dans les maladies inflammatoires chroniques

The effects of tumour necrosis factor inhibitors, methotrexate, non-steroidal anti-inflammatory drugs and corticosteroids on cardiovascular events in rheumatoid arthritis, psoriasis and psoriatic arthritis: a systematic review and meta-analysis

Roubille C, *et al*. *Ann Rheum Dis* 2015;**74**:480–489. doi:10.1136/annrheumdis-2014-206624

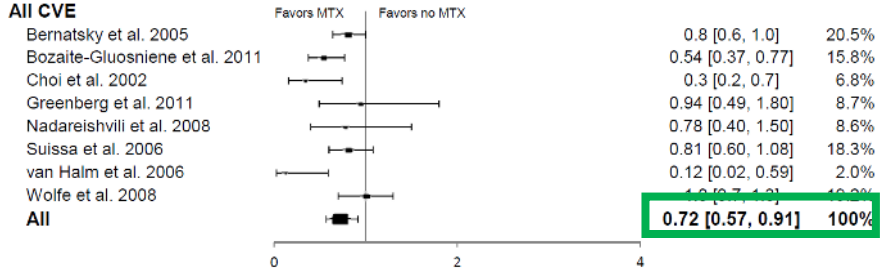
BMJ

Anti-TNF alpha



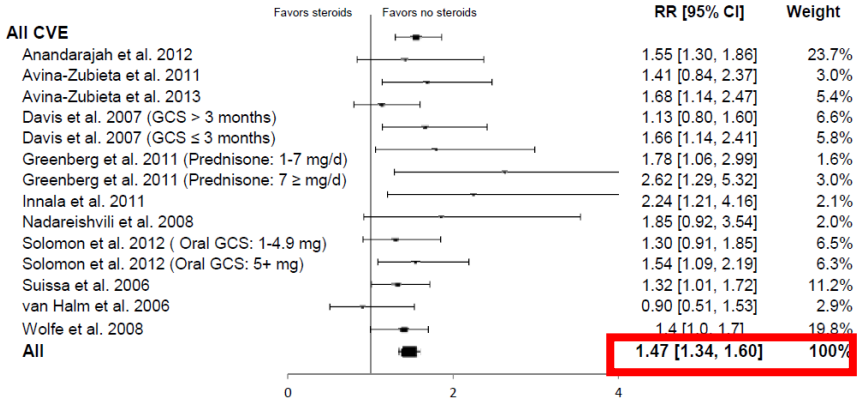
Heterogeneity: Tau² = 0.17; Chi² = 65.48, df = 15 (P < .00001); I² = 77%
Test for overall effect: Z = 2.81 (P = .005)

MTX



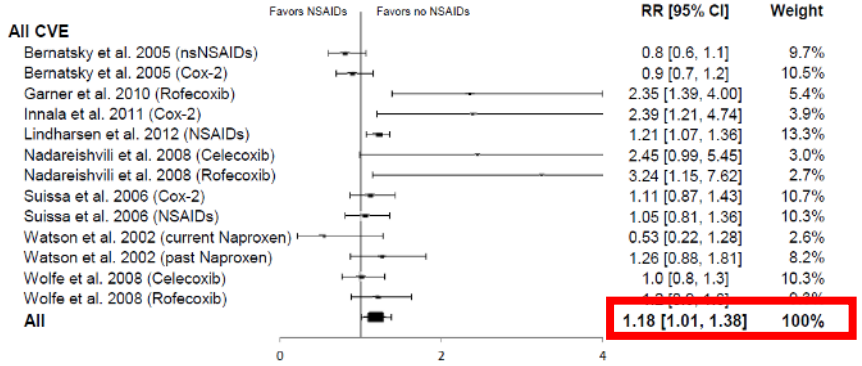
Heterogeneity: Tau² = 0.06; Chi² = 17.68, df = 7 (P = .01); I² = 60%
Test for overall effect: Z = 2.69 (P = .007)

Corticoïdes



Heterogeneity: Tau² = 0.00; Chi² = 13.44, df = 12 (p = .34); I² = 11%
Test for overall effect: Z = 7.60 (p < .00001)

AINS



Heterogeneity: Tau² = 0.04; Chi² = 35.64, df = 12 (p = .0004); I² = 66%
Test for overall effect: Z = 2.08 (p = .04)

Réduction des évènements cardio-vasculaires sous TNFi et MTX, augmentation sous corticoïdes et AINS dans la PR

RHEUMATOLOGY

Rheumatology 2020;0:1
doi:10.1093/rheumatology/keaa8

Original article

Ten-year analysis of the risk of severe outcomes related to low-dose glucocorticoids in early rheumatoid arthritis

Camille Roubille [1,2], Amandine Coffy[3], Nathalie Rincheval[3,4], Maxime Dougados[5], René-Marc Flipo[6], Jean-Pierre Daurès[3] and Bernard Combe [4]

Impact des thérapeutiques :
focus sur la corticothérapie dans la PR

Population: 608 patients atteints de PR précoce (cohorte ESPOIR)

Deux groupes: corticoides vs non corticoides au moins une fois au cours du suivi

Critère principal= critère composite: CVD (CMI, AVC, ins card), mortalité toute cause, infections sévères et fractures

Critères secondaires=chacune de ces composantes

Impact à 10 ans d'une faible corticothérapie

Utilisation d'un score de propension pour tenir compte du biais de prescription

397 patients ont reçu des corticoïdes (65%)

Dose faible de corticoïdes:

Dose moyenne 2,8 mg/j (2,8), médiane 1.9 mg/j [IQR 0.6-4.2]

Dose moyenne pendant la durée d'utilisation: 9 mg/j (9,6) (médiane 6,3 mg/j IQR 4,9-8,6)

Dose moyenne cumulative: 8,47 g ± 8,37 (médiane 5,65 g IQR 1940-13022)

Total de 95 évènements (15,6%)

10 décès

18 CVD

32 fractures

35 infections sévères

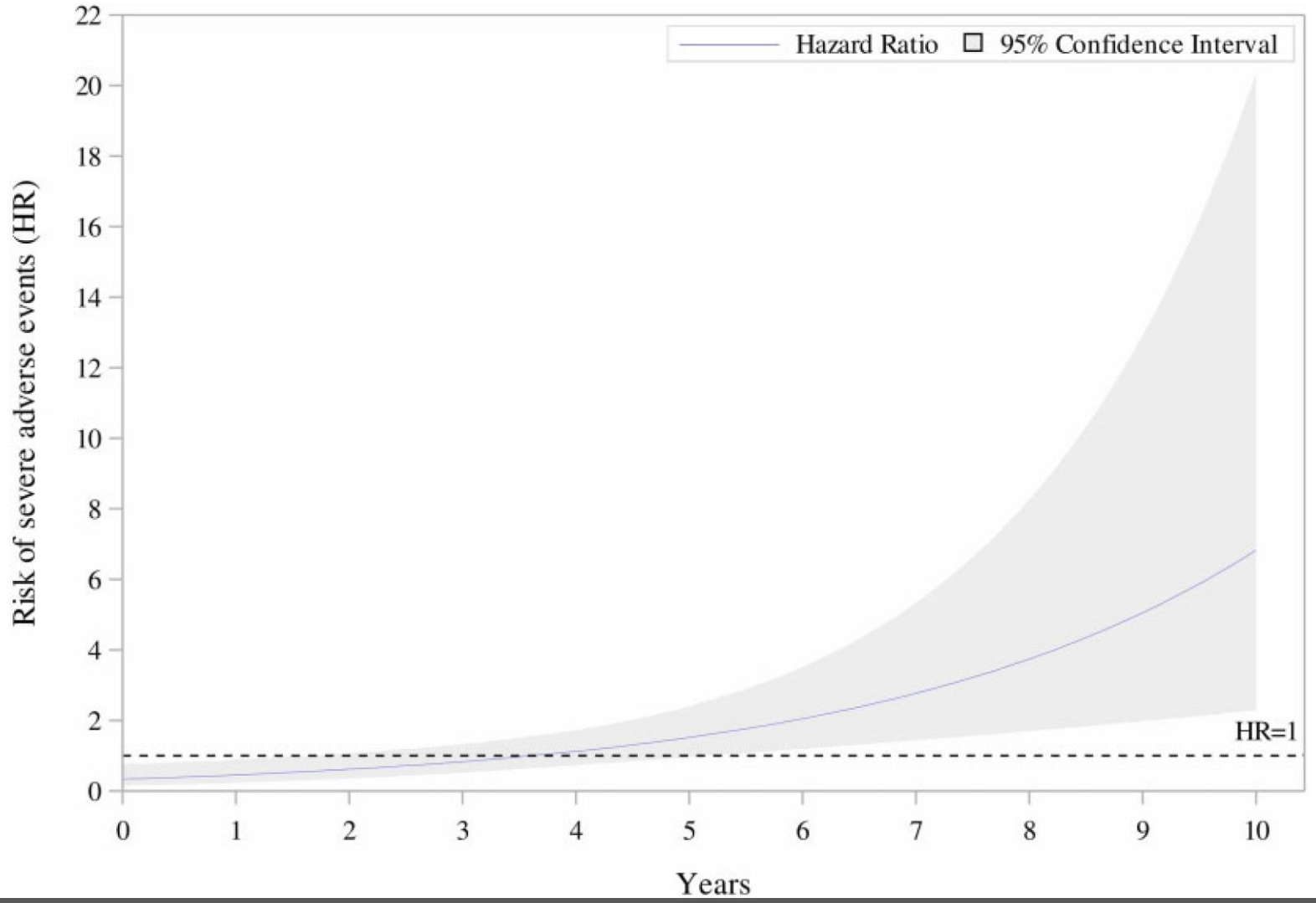
	Total study population (*n* = 608)	Without GC	With GC	*P*-value
Primary outcome, *n* (%)	95 (15.6%)	24 (11.4%)	71 (17.9%)	**0.035**
Death, *n* (%)	10 (1.6%)	1 (0.5%)	9 (2.3%)	0.103
Cardiovascular diseases, *n* (%)	18 (3%)	3 (1.4%)	15 (3.8%)	0.177
Severe infections, *n* (%)	35 (5.8%)	5 (2.4%)	30 (7.6%)	**0.009**
Fractures, *n* (%)	32 (5.3%)	15 (7.1%)	17 (4.3%)	0.137

Les patients ayant reçu des corticoïdes ont eu plus d'évènements (n=71) que ceux qui n'en ont pas reçu (n=24)

	Cumulative dose of GC treatment (mg): quartiles								*P*–value
	0		[0–1842]		[1842–8421.5]		>= 8421,5		
	n = 211	%	*n* = 93	%	*n* = 152	%	*n* = 152	%	
Primary outcome	24	11.4%	13	14.0%	21	13.8%	37	24.3%	**0.007**
Cardiovascular diseases	3	1.4%	2	2.2%	1	0.7%	12	7.9%	**0.001**
Death	1	0.5%	1	1.1%	4	2.6%	4	2.6%	0.248
Fractures	15	7.1%	5	5.4%	6	3.9%	6	3.9%	0.475
Severe infections	5	2.4%	5	5.4%	10	6.6%	15	9.9%	**0.024**

Avec un effet dose cumulée: parmi les patients ayant une dose cumulée: > 8,4 g de prednisone au cours du suivi, 24 % ont eu un évènement
(équivalent à la prise d'environ 5 mg/jour pendant 5 ans)

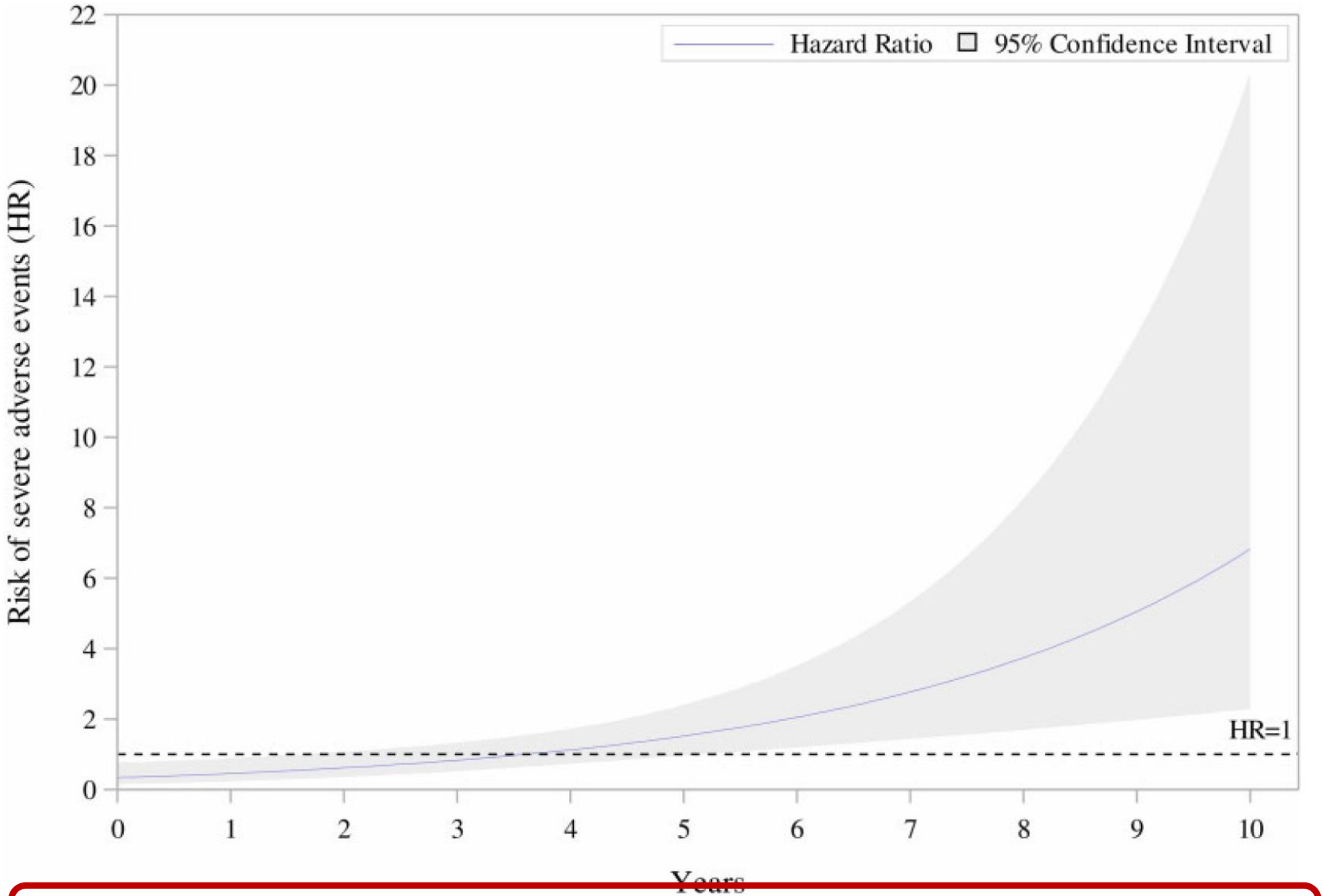
Weighted Cox time-dependent analysis, using the IPTW propensity score method



Le risque d'évènements augmente avec le temps et est associé aux corticoïdes (p <0.001), à l'âge, à l'HTA et à la VS.

Ce risque associé aux corticoïdes augmente entre la 1ere visite et 10 ans.

Weighted Cox time-dependent analysis, using the IPTW propensity score method

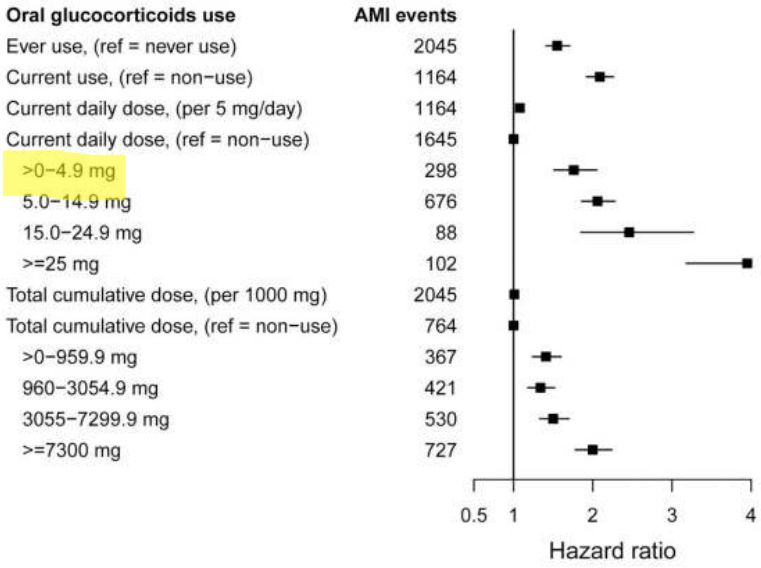


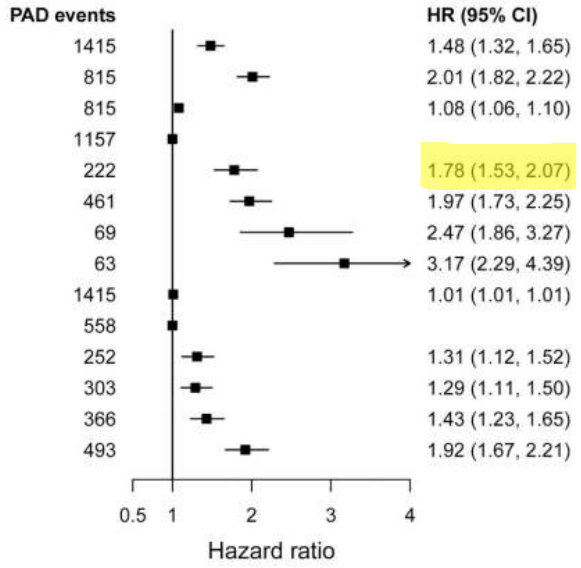
HR	**0.46**	**0.62**	**0.83**	**1.12**	**1.52**	**2.05**	**2.77**	**3.74**	**5.05**	**6.83**
95% CI	**(0.23-0.90)**	**(0.36-1.08)**	**(0.52-1.33)**	**(0.73-1.72)**	**(0.96-2.40)**	**(1.19-3.52)**	**(1.44-5.34)**	**(1.69-8.26)**	**(1.98-12.91)**	**(2.29-20.35)**

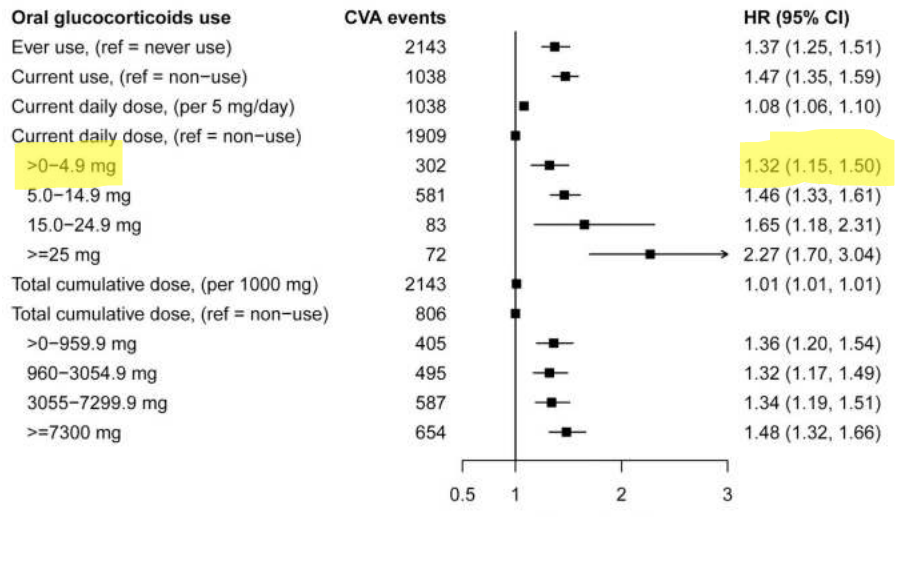
Dose-dependent oral glucocorticoid cardiovascular risks in people with immune-mediated inflammatory diseases: A population-based cohort study

Mar Pujades-Rodriguez[1☯*], **Ann W. Morgan**[2,3], **Richard M. Cubbon**[2], **Jianhua Wu**[4☯]

Citation: Pujades-Rodriguez M, Morgan AW, Cubbon RM, Wu J (2020) Dose-dependent oral glucocorticoid cardiovascular risks in people with immune-mediated inflammatory diseases: A population-based cohort study. PLoS Med 17(12): e1003432. https://doi.org/10.1371/journal.pmed.1003432







CMI **PAD** **AVC**

Dans l'ACG, le LES, et la PR, l'utilisation des corticoïdes, même à des doses quotidiennes <5 mg d'équivalent prednisone, est associée à un risque accru de MCV

Comment prendre en charge le surrisque cardiovasculaire des maladies inflammatoires et dysimmunitaires chroniques?

Contrôler l'inflammation systémique

Contrôler l'activité inflammatoire diminue les CVD.
Une diminution de 10 points du clinical disease activity index (CDAI) diminue de 21% les CVD.

Disease Activity Score-28 joint count DAS28 (≤3.2) est associé à moins de CVD vs DAS > 3.2

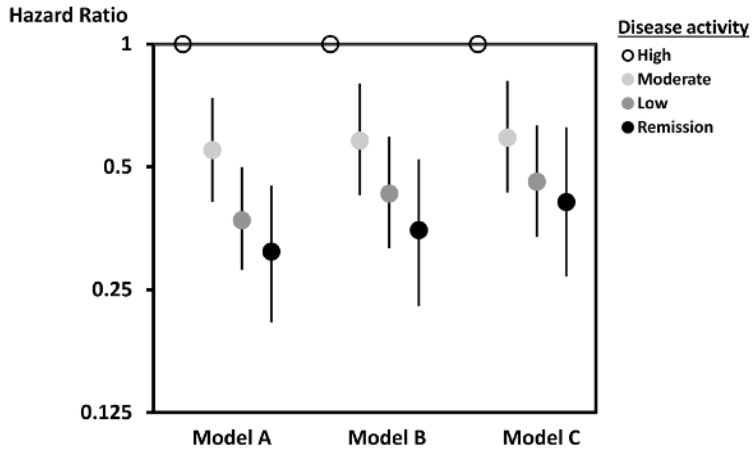
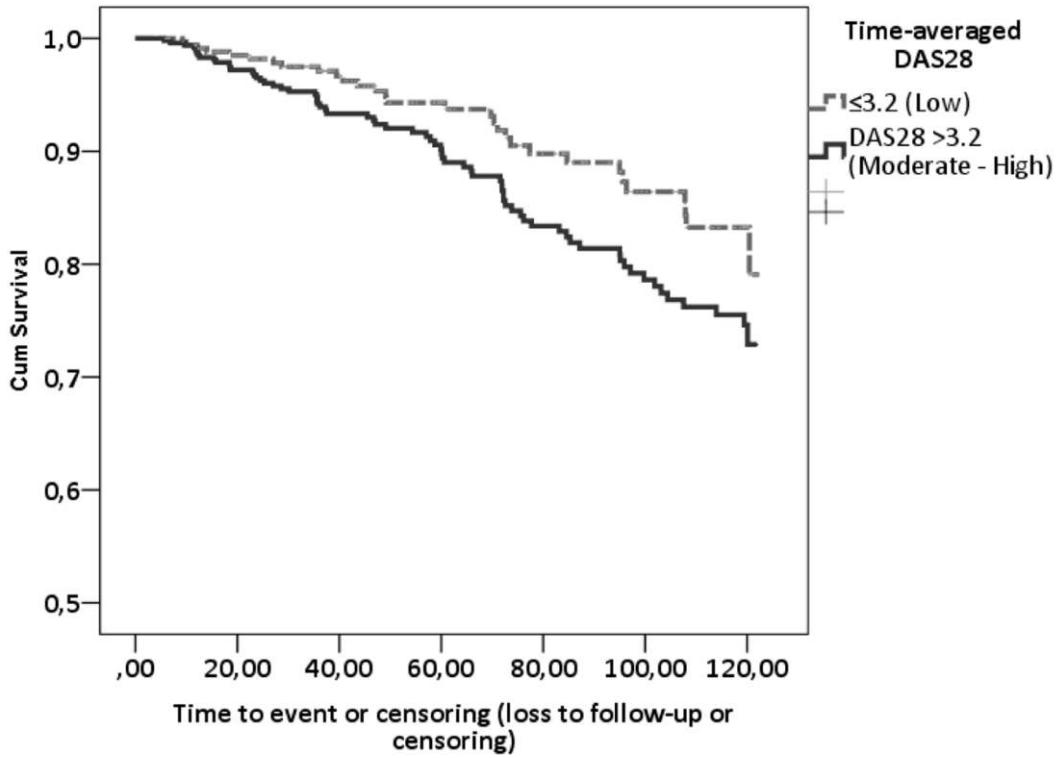


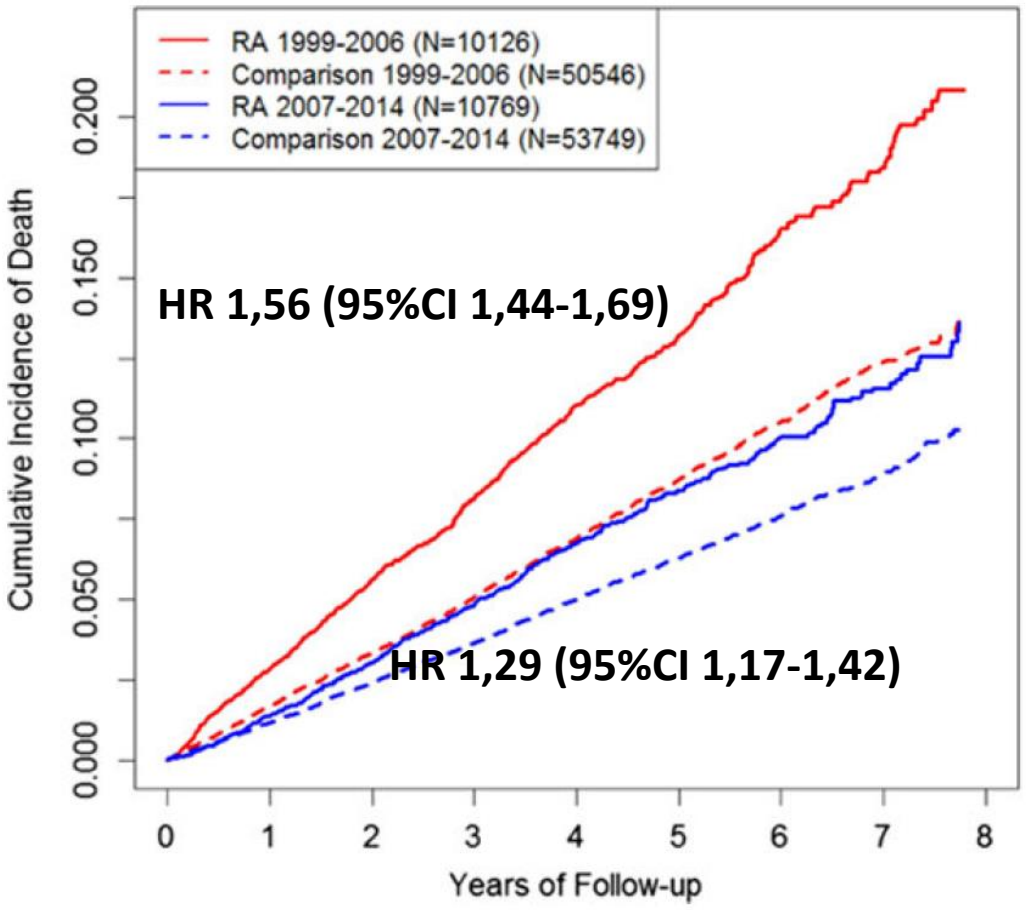
Figure 2.
This figure shows the hazard ratios for the primary analysis with the reference being high disease activity as measured by the Clinical Disease Activity Index. Model A is adjusted for age and gender only. Model B is adjusted for age, gender, age*gender interaction, and cardiovascular risk factors (prior MI, presence of CAD, diabetes, hypertension, hyperlipidemia, smoking, BMI (continuous), family history of MI, and aspirin use. Model C is adjusted for all variables in Model B + RA disease duration and baseline use of NSAIDs or selective COX-2 inhibitors, corticosteroids, disease modifying anti-rheumatic drugs, and biologic drugs.



Solomon DH, et al.Arthritis & rheumatology. 2015;67(6):1449–1455.

Evolution de la mortalité avec la prise en charge récente: « *down but not out* »

PR



Zhang et al. Ann Rheum Dis. 2017 February ; 76(2): 408–413.

Year	HR (95% CI)[a]	Adjusted HR (95% CI)[b]
1990	1.48 (1.15, 1.91)	1.30 (1.01, 1.67)
1991	1.57 (1.19, 2.07)	1.53 (1.15, 2.02)
1992	1.15 (0.86, 1.52)	1.21 (0.91, 1.61)
1993	1.49 (1.14, 1.94)	1.53 (1.17, 2.00)
1994	1.45 (1.11, 1.91)	1.51 (1.15,1.99)
1995	1.28 (0.95, 1.71)	1.23 (0.91,1.66)
1996	1.17 (0.89, 1.55)	1.19 (0.90,1.57)
1997	1.40 (1.11, 1.76)	1.45 (1.15, 1.82)
1998	1.40 (1.11, 1.78)	1.44 (1.13, 1.83)
1999	1.43 (1.16, 1.75)	1.31 (1.07, 1.62)
2000	1.65 (1.39, 1.95)	1.58 (1.32, 1.88)
2001	1.68 (1.42, 1.98)	1.69 (1.43, 1.99)
2002	1.51 (1.29, 1.77)	1.48 (1.26, 1.73)
2003	1.36 (1.16, 1.60)	1.25 (1.06, 1.48)
2004	1.54 (1.33,1.78)	1.42 (1.22, 1.65)
2005	1.35 (1.12, 1.62)	1.22 (1.01, 1.46)
2006	1.40 (1.18, 1.67)	1.27 (1.06, 1.51)
2007	1.31 (1.08, 1.58)	1.14 (0.94, 1.38)
2008	1.21 (1.01, 1.46)	1.11(0.92, 1.33)
2009	1.35 (1.10,1.66)	1.18 (0.96, 1.45)

[a]Age, sex and GP surgery matched. [b]Matched analysis adjusted for BMI (<20, 20–24.99, 25–29.99, 30–39.99, ⩾40 kg/m^2, missing), smoking status (current smoker, ex-smoker, non-smoker, missing data), alcohol intake (currently, previously, never, missing data) and Charlson comorbidity index (0, 1, ⩾2).

21 622 PR incidentes et 86 488 contrôles – suivi à 5 ans
Abhishek A.et al. Rheumatology 2018;57:977981

IDM

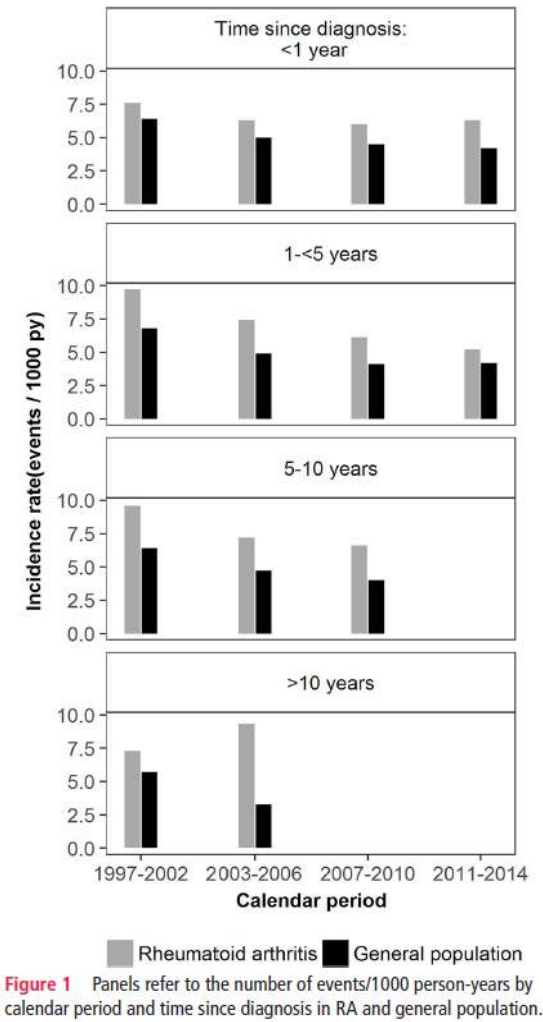


Figure 1 Panels refer to the number of events/1000 person-years by calendar period and time since diagnosis in RA and general population.

Holmqvist M, et al. Ann Rheum Dis 2017;76:1642–1647.

Persistance d'une sur-mortalité. Contrôle optimal de l'inflammation systémique n'est probablement pas suffisant pour réduire le risque CV et la mortalité: prendre en charge les FRCV!

…sans oublier de contrôler les FRCV!

Quelles recommandations pour prendre en charge le risque cardiovasculaire dans les MIC?

Evidence-based Recommendations for the Management of Comorbidities in Rheumatoid Arthritis, Psoriasis, and Psoriatic Arthritis: Expert Opinion of the Canadian Dermatology-Rheumatology Comorbidity Initiative

Topic	#	Recommendation Description	Level of Evidence	Grade of Recommendation	Level of Agreement, %
Risks of CVD	1.	Individuals with RA, PsA, and PsO have a greater risk of CVD than the general population. The diseases themselves and traditional risk factors contribute to this risk. The risk of MI in RA is comparable to that in DM. This should be recognized by healthcare providers and patients.	2b, 3b (RA), 2b, 5 (PsA), 2b (PsO)	C	87.7
	2.	Traditional modifiable risk factors should be screened for and managed appropriately to reduce the risk of CVD in RA, PsA, and PsO populations.	5	D	95.8
Effect of treatment on CVD	3.	CS use should be minimized in RA, especially in patients with CV risk factors.	2b, 5	C	93.3
	4.	In patients with RA or PsA, especially those with additional CV risk factors, the risk and benefits of NSAID use should be weighed.	3b, 5	C	91.9
	5.	Healthcare providers and patients should be aware that MTX and/or TNFi use may decrease the risk of CVE in RA. Their use may help to reduce CS and NSAID use, especially in patients with CV risk factors.	2b, 5	C	84.6
	6.	Healthcare providers and patients should be aware that MTX and/or TNFi use may decrease the risk of CVD in PsA/PsO.	2b, 5	C	83.3
Smoking	7.	Statement: Current smoking is associated with an increased prevalence and/or incidence and possibly a negative effect on disease severity in RA, PsA, and PsO.			
		Recommendation: Smoking status should be determined in all patients with RA, PsA, and PsO and smoking cessation should be encouraged.	2b, 5 5	C D	94.6
Weight	8.	Statement: PsO severity may be associated with increased BMI and obesity. Increased BMI may be associated with increased disease activity of RA and PsO.			
		Recommendation: Healthcare providers should be aware that higher BMI is associated with a reduced treatment response in RA, PsA, and PsO. TNFi may be associated with a mild increase in weight in RA, PsA, and PsO, but the clinical relevance is unknown.	4, 5 (RA), 3b, 4, 5 (PsA), 2b, 5 (PsO)	C	82.2
	9.	Statement: The effects of dietary manipulations on disease activity in RA, PsA, and PsO are still uncertain.			
		Recommendation: BMI should be determined in all patients with RA, PsA, and PsO.	5	D	80.9
	10.	Healthcare providers should encourage healthy BMI.	5	D	93.8

Evaluer le risque cardiovasculaire, limiter les AINS et les corticoïdes

Encourager sevrage tabagique et un IMC normal

Roubille C.et al. J Rheumatol 2015;42;1767-1780.

RECOMMANDATIONS EULAR 2015/2016 DE PRISE EN CHARGE du RISQUE CARDIOVASCULAIRE (PR, PsA)

Evaluer le risque cardiovasculaire/5 ans, avec le Heart score, X1,5, tous les 5 ans
Limiter les AINS et c les corticoïdes

	Level of evidence	Strength of recommendation
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
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
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
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
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
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
7. Lifestyle recommendations should emphasise the benefits of a healthy diet, regular exercise and smoking cessation for all patients	3	C
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. 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
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

Agca R.et al.Ann Rheum Dis. 2017 Jan;76(1):17-28.

EULAR recommendations for the management of psoriatic arthritis with pharmacological therapies: 2019 update

	Overarching principles	Level of agreement, mean (SD)
A	Psoriatic arthritis is a heterogeneous and potentially severe disease, which may require multidisciplinary treatment.	9.9 (0.4)
B	Treatment of psoriatic arthritis patients should aim at the best care and must be based on a shared decision between the patient and the rheumatologist, considering efficacy, safety and costs.	9.8 (0.5)
C	Rheumatologists are the specialists who should primarily care for the musculoskeletal manifestations of patients with psoriatic arthritis; in the presence of clinically significant skin involvement, a rheumatologist and a dermatologist should collaborate in diagnosis and management.	9.8 (0.7)
D	The primary goal of treating patients with psoriatic arthritis is to maximise health-related quality of life, through control of symptoms, prevention of structural damage, normalisation of function and social participation; abrogation of inflammation is an important component to achieve these goals.	9.9 (0.4)
E	In managing patients with psoriatic arthritis, consideration should be given to each musculoskeletal manifestation and treatment decisions made accordingly.	9.9 (0.3)
F	When managing patients with psoriatic arthritis, non-musculoskeletal manifestations (skin, eye and gastrointestinal tract) should be taken into account; comorbidities such as metabolic syndrome, cardiovascular disease or depression should also be considered.	9.8 (0.6)

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Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA): updated treatment recommendations for psoriatic arthritis 2021

Overarching principles	PRP agreement (%) ($n = 9$)	Clinician agreement (%) ($n = 161$)
Comorbidities and related conditions should be considered and their impact on the approach to the condition and its treatment addressed appropriately. Such conditions include obesity, metabolic syndrome, cardiovascular disease, depression and anxiety, liver disease (for example, non-alcoholic fatty liver disease), chronic infections, malignancy, bone health (for example, osteoporosis), central sensitization (for example, fibromyalgia) and reproductive health. Multidisciplinary and multispeciality assessment and management may be most beneficial for individual patients	87.5	93.8

Vascularites à ANCA

Statement	Level of evidence	Grade of recommendation
1. We recommend that patients with AAV are managed in close collaboration with, or at, centres of expertise.	3	C
2. A positive biopsy is strongly supportive of a diagnosis of vasculitis and we recommend biopsies to assist in establishing a new diagnosis and for further evaluation for patients suspected of having relapsing vasculitis.	3	C
3. For remission-induction of new-onset organ-threatening or life-threatening AAV we recommend treatment with a combination of glucocorticoids and either cyclophosphamide **OR** rituximab.	1 for GPA/MPA, 3 for EGPA	A for GPA/MPA, C for EGPA
4. For remission-induction of non-organ-threatening AAV we recommend treatment with a combination of glucocorticoids and either methotrexate or mycophenolate mofetil*.	1B	B for MTX, C for MMF
5. For a major relapse of organ-threatening or life-threatening disease in AAV we recommend treatment as per new disease with a combination of glucocorticoids and either cyclophosphamide OR rituximab.	1 for GPA/MPA, 3 for EGPA and CYC, 4 for EGPA and RTX	A for GPA/MPA, C for EGPA and CYC, C for EGPA and RTX
6. (i) Plasma exchange should be considered for patients with AAV and a serum creatine level of ≥500 μmol/L (5.7 mg/dL) due to rapidly progressive glomerulonephritis in the setting of new or relapsing disease.	1B	B
6. (ii) Plasma exchange can also be considered for the treatment of severe diffuse alveolar haemorrhage.	3	C
7. For remission-maintenance of AAV we recommend treatment with a combination of low-dose glucocorticoids and either azathioprine, rituximab, methotrexate or mycophenolate mofetil*.	1B for GPA/MPA 3 for EGPA and AZA	A for GPA/MPA, C for EGPA and AZA
8. We recommend that remission-maintenance therapy for AAV be continued for at least 24 months following induction of sustained remission.	4	D
9. For patients with AAV refractory to remission-induction therapy we recommend switching from cyclophosphamide to rituximab or from rituximab to cyclophosphamide. These patients should be managed in close conjunction with, or referred to, an expert centre for further evaluation and potential enrolment in clinical trials.	3	C
10. We recommend that structured clinical assessment rather than ANCA testing should inform decisions on changes in treatment for AAV.	4	D
11. We recommend the investigation of persistent unexplained haematuria in patients with prior exposure to cyclophosphamide.	2B	C
12. Hypoimmunoglobulinaemia has been noted after treatment with rituximab. We recommend testing of serum immunoglobulin levels prior to each course of rituximab and in patients with recurrent infection.	3	C
13. We recommend periodic assessment of cardiovascular risk for patients with AAV.	2B	B
14. We recommend that patients with AAV should be given a clear verbal explanation of the nature of their disease, the treatment options, the side effects of treatment, and the short-term and long-term prognoses.	3	C
15. We recommend that following the remission-induction phase of treatment, patients with AAV be assessed for the extent and ongoing impact of comorbidities associated with their diagnosis. Patients should then be advised where they might find the necessary therapies or support for these conditions.	4	D

Yates M, et al. Ann Rheum Dis 2016;75:1583–1594.

2019 update of the EULAR recommendations for the management of systemic lupus erythematosus

4 Comorbidities	
4.1 Antiphospholipid syndrome	
4.1.1 All patients with SLE should be screened at diagnosis for aPL (**1a/A**).	10.0 (0)
4.1.2 Patients with SLE with high-risk aPL profile (persistently positive medium/high titres or multiple positivity) may receive primary prophylaxis with antiplatelet agents (**2a/C**), especially if other atherosclerotic/thrombophilic factors are present, after balancing the bleeding hazard.	9.45 (0.80)
4.1.3 For secondary prevention (thrombosis, pregnancy complication/loss), the therapeutic approach should be the same as for primary antiphospholipid syndrome (**1b/B**).	10.0 (0)
4.2 Infectious diseases	
4.2.1 Patients with SLE should be assessed for *general and disease-related risk factors* for infections, such as advanced age/frailty (**–/D**), diabetes mellitus (**–/D**), renal involvement (**2b/B**), immunosuppressive/biological therapy (**1b-2b/B-C**) and use of GC (**1a/A**).	9.85 (0.65)
4.2.2 General preventative measures (including immunisations) and early recognition and treatment of infection/sepsis are recommended (**–/D**).	9.90 (0.44)
4.3 Cardiovascular disease	
4.3.1 Patients with SLE should undergo regular assessment for *traditional* (**1b/B-C**) and *disease-related risk factors* for cardiovascular disease, including persistently active disease (**1b/B**), increased disease duration (**1b/A**), medium/high titres of aPL (**1b/A**), renal involvement (**1b/B**) (especially, persistent proteinuria and/or GFR <60 mL/min) and chronic use of GC (**1b/B**).	9.85 (0.65)
4.3.2 Based on their individual cardiovascular risk profile, patients with SLE may be candidates for preventative strategies as in the general population, including *low-dose aspirin* (**2b/D**) and/or *lipid-lowering agents* (**2b/D**).	9.85 (0.48)

aPL, antiphospholipid antibodies; GC, glucocorticoids; GFR, glomerular filtration rate; HCQ, hydroxychloroquine; SLE, systemic lupus erythematosus.

*Fanouriakis A, et al. Ann Rheum Dis 2019;**78**:736–745.*

2019 Update of the Joint European League Against Rheumatism and European Renal Association–European Dialysis and Transplant Association (EULAR/ERA–EDTA) recommendations for the management of lupus nephritis

5. Adjunct treatment		
5.1 Angiotensin-converting enzyme inhibitors or angiotensin receptor blockers are recommended for all patients with UPCR >500 mg/g or arterial hypertension.	**5/D**	**9.84** (**0.37**)
5.2 Statins are recommended on the basis of lipid levels and estimated 10-year cardiovascular disease risk using the Systematic Coronary Risk Evaluation or other validated tools.	**5/D**	**9.52** (**0.75**)

Fanouriakis A, *et al*. *Ann Rheum Dis* 2020;**79**:713–723.

Recommendation

EULAR recommendations for cardiovascular risk management in rheumatic and musculoskeletal diseases, including systemic lupus erythematosus and antiphospholipid syndrome

Drosos GC, et al. Ann Rheum Dis 2022;81:768–779. doi:10.1136/annrheumdis-2021-221733

Overarching principles	LoA* (SD)
A. Clinicians should be aware of increased CVR in patients with RMDs including gout, vasculitis, SSc, myositis, MCTD, SS, SLE and APS. For all RMDs, reduction of disease activity is likely to lessen CVR.	9.92 (0.39)
B. Rheumatologists are responsible for CVR assessment and management in collaboration with primary care providers, internists or cardiologists and other healthcare providers.	9.55 (1.12)
C. CVR factor screening should be performed regularly in all individuals with RMDs. Risk management should include screening for and strict control of CVR factors (smoking cessation, management of blood pressure, lipids and diabetes). CVR assessment is recommended within 6 months of diagnosis and repeated based on individual patient characteristics and risk levels.	9.55 (0.84)
D. Patient education and counselling on CVR, treatment adherence and lifestyle modifications, such as healthy diet and regular physical activity, are important in the management of CVR in these patients.	9.88 (0.42)
Recommendations for gout, vasculitis, SSc, myositis, MCTD and SS	
1. In patients with gout, vasculitis, SSc, myositis, MCTD and SS, we recommend thorough assessment of traditional CVR factors. The use of cardiovascular prediction tools for the general population is recommended. (LoE: 5, GoR‡: D)	9.48 (0.84)
2. For ANCA-associated vasculitis the Framingham score may underestimate the CVR. Information from the EUVAS model may supplement modifiable Framingham risk factors and is recommended to take into account. (LoE: 2b, GoR: D)	8.59 (1.50)
3. In patients with gout, vasculitis, SSc, myositis, MCTD and SS, blood pressure management should follow recommendations used in the general population. (LoE: 5, GoR: D)	9.66 (0.62)
4. In patients with gout, diuretics should be avoided. (LoE: 5, GoR: D)	8.88 (2.06)
5. In patients with SSc beta blockers should be avoided. (LoE: 5, GoR: D)	8.92 (2.11)
6. In patients with gout, vasculitis, SSc, myositis, MCTD and SS, lipid management should follow recommendations used in the general population. (LoE: 5, GoR: D)	9.48 (1.08)
7. In patients with gout, vasculitis, SSc, myositis, MCTD and SS, standard use of platelet inhibitors for primary prevention is not recommended. Treatment with platelet inhibitors should follow recommendations used in the general population. (LoE: 2b/5, GoR: D)	9.37 (1.14)
8. In patients with gout, we recommend a serum uric acid level below 0.36 mmol/L (6 mg/dL) to potentially lower the risk on cardiovascular events and cardiovascular mortality. (LoE: 2b, GoR: C)	9.03 (1.34)
9. In patients with gout there is no preference for a particular urate-lowering therapy from the cardiovascular point of view. (LoE: 1b, GoR: B)	9.14 (1.35)
10. In patients with ANCA-associated vasculitis, remission induction and remission maintenance will also reduce CVR. (LoE: 2b, GoR: D)	9.07 (1.35)
11. In patients with giant-cell arteritis an optimal glucocorticoid regimen that balances the risk of relapse and glucocorticoid use side effects may also reduce CVR. (LoE: 2b, GoR: D)	9.14 (1.06)

Recommendations for SLE and the APS	
1. In patients with SLE and/or APS, a thorough assessment of traditional CVR factors and disease-related risk factors is recommended to guide risk factor modification. (LoE: 2b, GoR: D)	9.88 (0.32)
2A. In patients with SLE, lower levels of blood pressures are associated with lower rates of cardiovascular events and a blood pressure target of <130/80 mm Hg should be considered. (LoE: 2b, GoR: C)	9.70 (0.54)
2B. In patients with lupus nephritis, ACE inhibitors or angiotensin receptor blockers are recommended for all patients with urine protein-to-creatinine ratio >500 mg/g or arterial hypertension. (LoE: 5, GoR: D)	9.51 (0.64)
2C. In patients with APS, blood pressure management should follow recommendations used in the general population. (LoE: 5, GoR: D)	9.81 (0.39)
3. In patients with SLE and/or APS, lipid treatment should follow recommendations used in the general population. (LoE: 5, GoR: D)	9.70 (0.54)
4A. Patients with SLE may be candidates for preventative strategies as in the general population, including low-dose aspirin, based on their individual CVR profile. (LoE: 2b, GoR: D)	9.29 (1.37)
4B. In asymptomatic aPL carriers (not fulfilling any vascular or obstetric APS classification criteria) with a high-risk aPL profile with or without traditional risk factors, prophylactic treatment with low-dose aspirin (75–100 mg daily) is recommended. (LoE: 2a, GoR: B) In patients with SLE and no history of thrombosis or pregnancy complications: (1) with high-risk aPL profile, prophylactic treatment with low-dose aspirin is recommended (LoE: 2a, GoR: B); (2) with low-risk aPL profile, prophylactic treatment with low-dose aspirin may be considered. (LoE: 2b, GoR: C)	9.44 (0.97)
5. In patients with SLE, low disease activity should be maintained to also reduce CVR. (LoE: 2b, GoR: B)	9.59 (1.11)
6. In patients with SLE, treatment with the lowest possible corticosteroid dose is recommended to minimise any potential cardiovascular harm. (LoE: 2b, GoR: C)	9.59 (0.79)
7. In patients with SLE, no specific immunosuppressive medication can be recommended for the purpose of lowering the risk of cardiovascular events. (LoE: 2b, GoR: C)	9.44 (0.89)
8. In patients with SLE, treatment with hydroxychloroquine (which is recommended for all patients unless contraindicated) should be considered to also reduce the risk of cardiovascular events. (LoE: 2b, GoR: B)	9.66 (0.73)

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