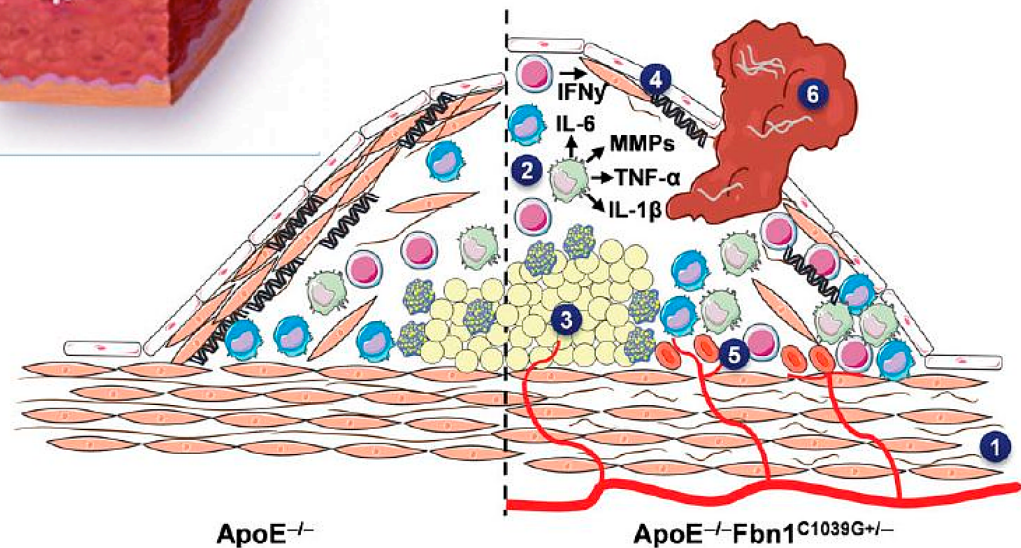
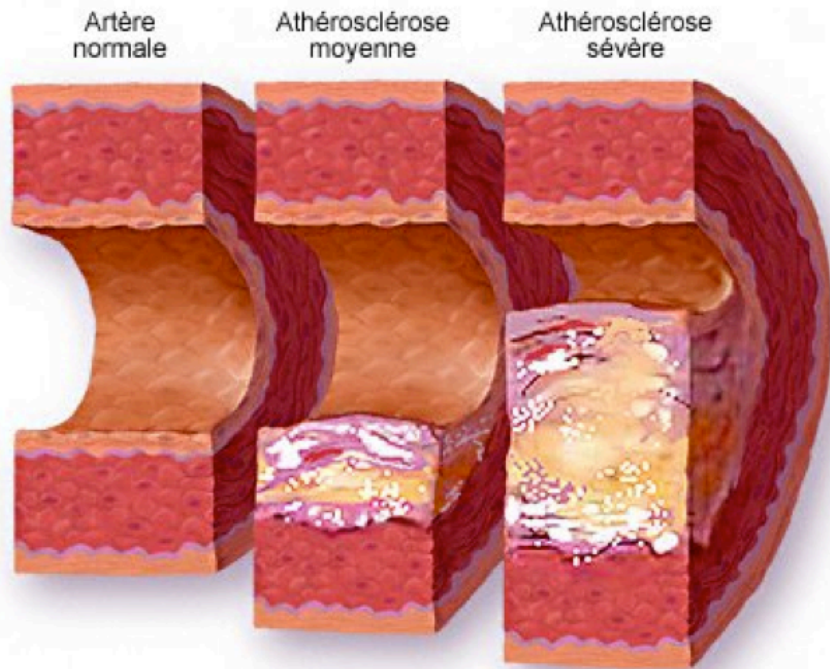


Colchicine dans le traitement du coronarien

Aucun conflit d'intérêt en la matière

La maladie coronaire est aussi une maladie inflammatoire des artères coronaires



**Les arguments pour la théorie
inflammatoire
de l'athéro-thrombose coronaire**

Arguments pour théorie inflammatoire de l'athéro-thrombose

1) Augmentation de l'incidence des infarctus du myocarde après certaines épidémies virales

ORIGINAL ARTICLE

Acute Myocardial Infarction after Laboratory-Confirmed Influenza Infection

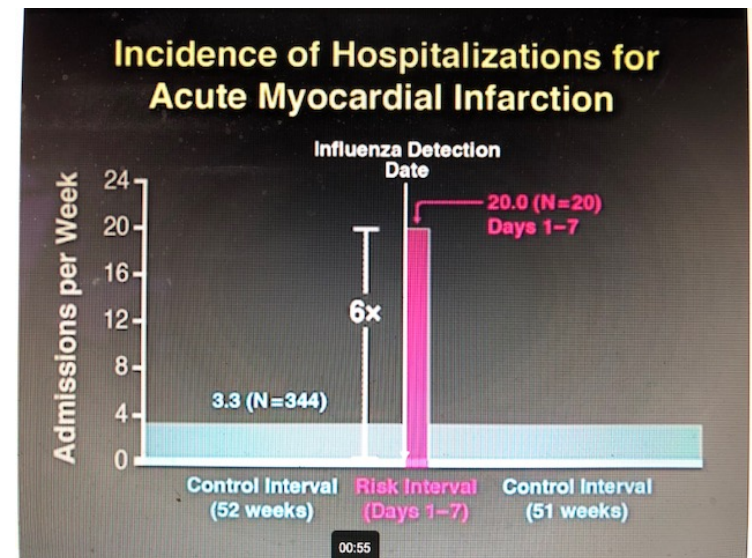
Jeffrey C. Kwong, M.D., Kevin L. Schwartz, M.D., Michael A. Campitelli, M.P.H.,
Hannah Chung, M.P.H., Natasha S. Crowcroft, M.D., Timothy Karnauchow, Ph.D.,
Kevin Katz, M.D., Dennis T. Ko, M.D., Allison J. McGeer, M.D.,
Dayre McNally, M.D., Ph.D., David C. Richardson, M.D.,
Laura C. Rosella, Ph.D., M.H.Sc., Andrew Simor, M.D.,
Marek Smieja, M.D., Ph.D., George Zahariadis, M.D.,
and Jonathan B. Gubbay, M.B., B.S., M.Med.Sc. Ontario/Canada

Acute Myocardial Infarction after Laboratory-Confirmed Influenza Infection

Jeffrey C. Kwong, M.D., Kevin L. Schwartz, M.D., Michael A. Campitelli, M.P.H., Hannah Chung, M.P.H., Natasha S. Crowcroft, M.D., Timothy Karnauchow, Ph.D., Kevin Katz, M.D., Dennis T. Ko, M.D., Allison J. McGeer, M.D., Dayre McNally, M.D., Ph.D., David C. Richardson, M.D., Laura C. Rosella, Ph.D., M.H.Sc., Andrew Simor, M.D., Marek Smieja, M.D., Ph.D., George Zahariadis, M.D., and Jonathan B. Gubbay, M.B., B.S., M.Med.Sc.

Table 2. Incidence Ratios for Acute Myocardial Infarction after Laboratory-Confirmed Influenza Infection.*

Variable	Incidence Ratio (95% CI)
Primary analysis: risk interval, days 1–7	6.05 (3.86–9.50)
Days 1–3	6.30 (3.25–12.22)
Days 4–7	5.78 (3.17–10.53)
Days 8–14	0.60 (0.15–2.41)
Days 15–28	0.75 (0.31–1.81)



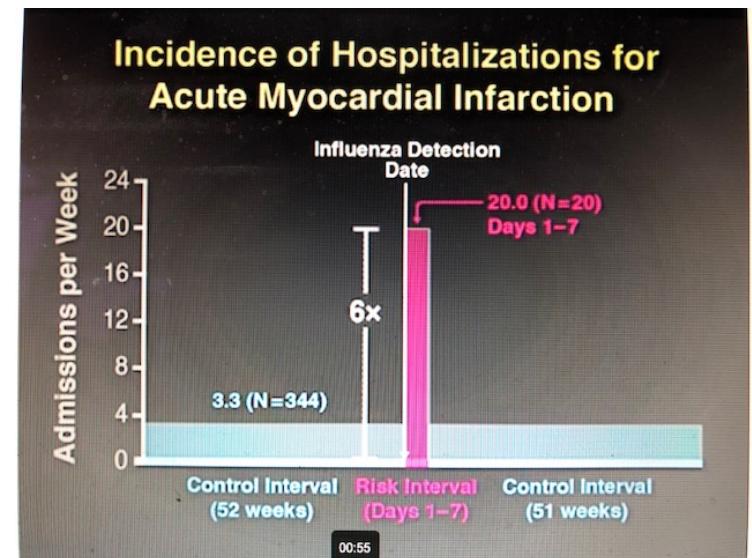
Acute MI after Influenza. NEJM 2018

Acute Myocardial Infarction after Laboratory-Confirmed Influenza Infection

Jeffrey C. Kwong, M.D., Kevin L. Schwartz, M.D., Michael A. Campitelli, M.P.H., Hannah Chung, M.P.H., Natasha S. Crowcroft, M.D., Timothy Karnauchow, Ph.D., Kevin Katz, M.D., Dennis T. Ko, M.D., Allison J. McGeer, M.D., Dayre McNally, M.D., Ph.D., David C. Richardson, M.D., Laura C. Rosella, Ph.D., M.H.Sc., Andrew Simor, M.D., Marek Smieja, M.D., Ph.D., George Zahariadis, M.D., and Jonathan B. Gubbay, M.B., B.S., M.Med.Sc.

Table 2. Incidence Ratios for Acute Myocardial Infarction after Laboratory-Confirmed Influenza Infection.*

Variable	Incidence Ratio (95% CI)
Primary analysis: risk interval, days 1–7	6.05 (3.86–9.50)
Days 1–3	6.30 (3.25–12.22)
Days 4–7	5.78 (3.17–10.53)
Days 8–14	0.60 (0.15–2.41)
Days 15–28	0.75 (0.31–1.81)



6 x plus de risque de presenter un IDM après une grippe

2013 ESC guidelines on the management of stable coronary artery disease

**The Task Force on the management of stable coronary artery disease
of the European Society of Cardiology**

7.1.2.11 Influenza vaccination

An annual influenza vaccination is recommended for patients with CAD, especially the elderly.^{279,280}

La 1^{ere} étude randomisée sur l'effet de la vaccination grippale chez des coronariens

10.1161/CIRCULATIONAHA.121.057042

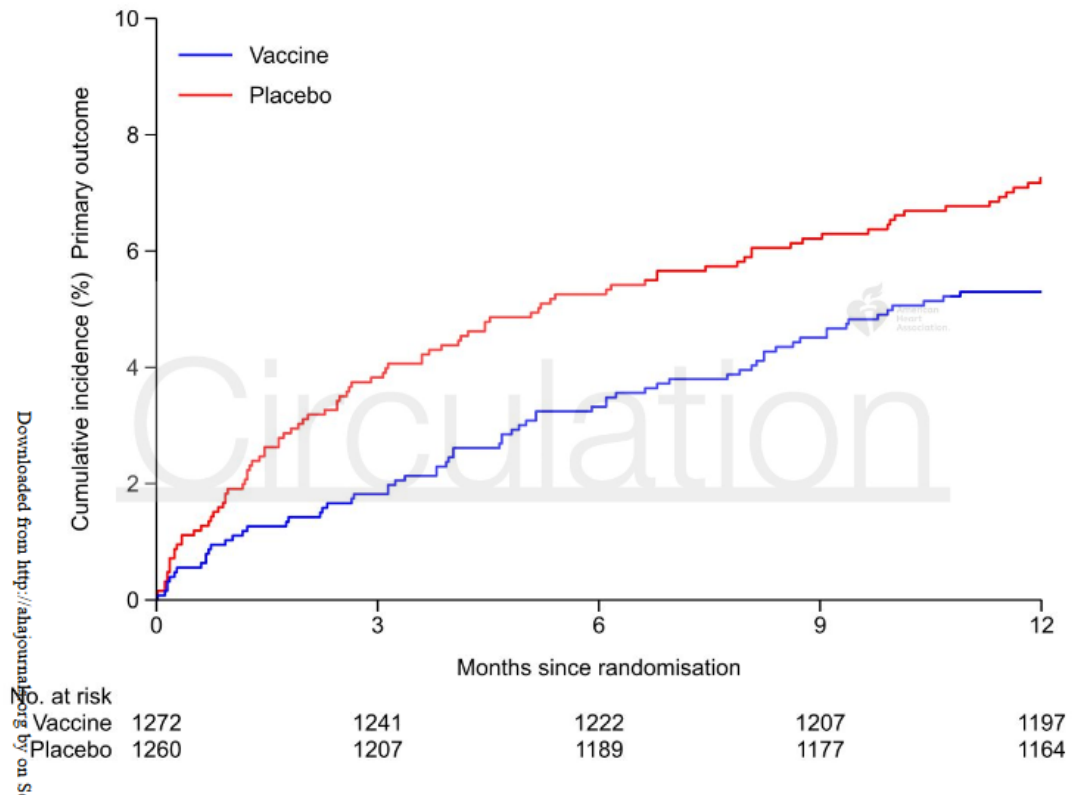
Influenza Vaccination after Myocardial Infarction:

A Randomized, Double-Blind, Placebo-Controlled, Multicenter Trial

Sweeden

Running Title: *Fröbert, et al.; Influenza Vaccination after Myocardial Infarction*

Ole Fröbert, MD¹; Matthias Götberg, MD²; David Erlinge, MD



Vaccin grippal et MACE post SCA

	Vaccine (N=1272)	Placebo (N=1260)	Hazard Ratio (95% CI)	P-value
Primary Endpoint, no (%)				
All-cause death, myocardial infarction, stent thrombosis	67 (5.)	91 (7.2)	0.72 (0.52-0.99)	0.040
Key Secondary Endpoints, (no. (%))				
All-cause death	37 (2.9)	61 (4.9)	0.59 (0.39-0.89)	0.010
CV death	34 (2.7)	56 (4.5)	0.59 (0.39-0.90)	0.014
Myocardial infarction	25 (2.0)	29 (2.4)	0.86 (0.50-1.46)	0.57
Stent Thrombosis	6 (0.5)	3 (0.2)	1.94 (0.48-7.76)	0.34

Vaccin grippal et MACE post SCA

	Vaccine (N=1272)	Placebo (N=1260)	Hazard Ratio (95% CI)	P-value
Primary Endpoint, no (%)				
All-cause death, myocardial infarction, stent thrombosis	67 (5.)	91 (7.2)	0.72 (0.52-0.99)	0.040
Key Secondary Endpoints, (no.%)				
All-cause death	37 (2.9)	61 (4.9)	0.59 (0.39-0.89)	0.010
CV death	34 (2.7)	56 (4.5)	0.59 (0.39-0.90)	0.014
Myocardial infarction	25 (2.0)	29 (2.4)	0.86 (0.50-1.46)	0.57
Stent Thrombosis	6 (0.5)	3 (0.2)	1.94 (0.48-7.76)	0.34

2020 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation

The Task Force for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation of the European Society of Cardiology (ESC)

Authors/Task Force Members: Jean-Philippe Collet * (Chairperson) (France), Holger Thiele * (Chairperson) (Germany), Emanuele Barbato (Italy), Olivier Barthélémy (France), Johann Bauersachs (Germany), Deepak L. Bhatt (United States of America), Paul Dendale (Belgium), Maria Dorobantu (Romania), Thor Edvardsen (Norway), Thierry Folliguet (France), Chris P. Gale (United Kingdom), Martine Gilard (France), Alexander Jobs (Germany), Peter Jüni (Canada), Ekaterini Lambrinou (Cyprus), Basil S. Lewis (Israel), Julinda Mehilli (Germany), Emanuele Meliga (Italy), Béla Merkely (Hungary), Christian Mueller (Switzerland), Marco Roffi (Switzerland), Frans H. Rutten (Netherlands), Dirk Sibbing (Germany), George C.M. Siontis (Switzerland)

Recommendations for lifestyle managements after non-ST-segment elevation acute coronary syndrome

Improvement of lifestyle factors in addition to appropriate pharmacological management is recommended in order to reduce all-cause and cardiovascular mortality and morbidity and improve health-related quality of life. ^{487–497}	I	A
Cognitive behavioural interventions are recommended to help individuals achieve a healthy lifestyle. ^{498–500}	I	A
Multidisciplinary exercise-based cardiac rehabilitation is recommended as an effective means for patients with CAD to achieve a healthy lifestyle and manage risk factors in order to reduce all-cause and cardiovascular mortality and morbidity, and improve health-related quality of life. ^{487,497,501}	I	A
Involvement of multidisciplinary healthcare professionals (cardiologists, general practitioners, nurses, dieticians, physiotherapists, psychologists, pharmacists) is recommended in order to reduce all-cause and cardiovascular mortality and morbidity, and improve health-related quality of life. ^{492,499,502,503}	I	A
Psychological interventions are recommended to improve symptoms of depression in patients with CAD in order to improve health-related quality of life. ^{504,505}	I	B
Annual influenza vaccination is recommended for patients with CAD, especially in the older person, in order to improve morbidity. ^{505–511}	I	B

Vaccination grippale chez le coronarien: IB

Plus généralement: toute infection aigue augmente le risque d'évènement cardiovasculaire ..parfois pendant longtemps

Acute Infection and Myocardial Infarction

N Engl J Med 2019;380:171-6.

Daniel M. Musher, M.D., Michael S. Abers, M.D.,
and Vicente F. Corrales-Medina, M.D.

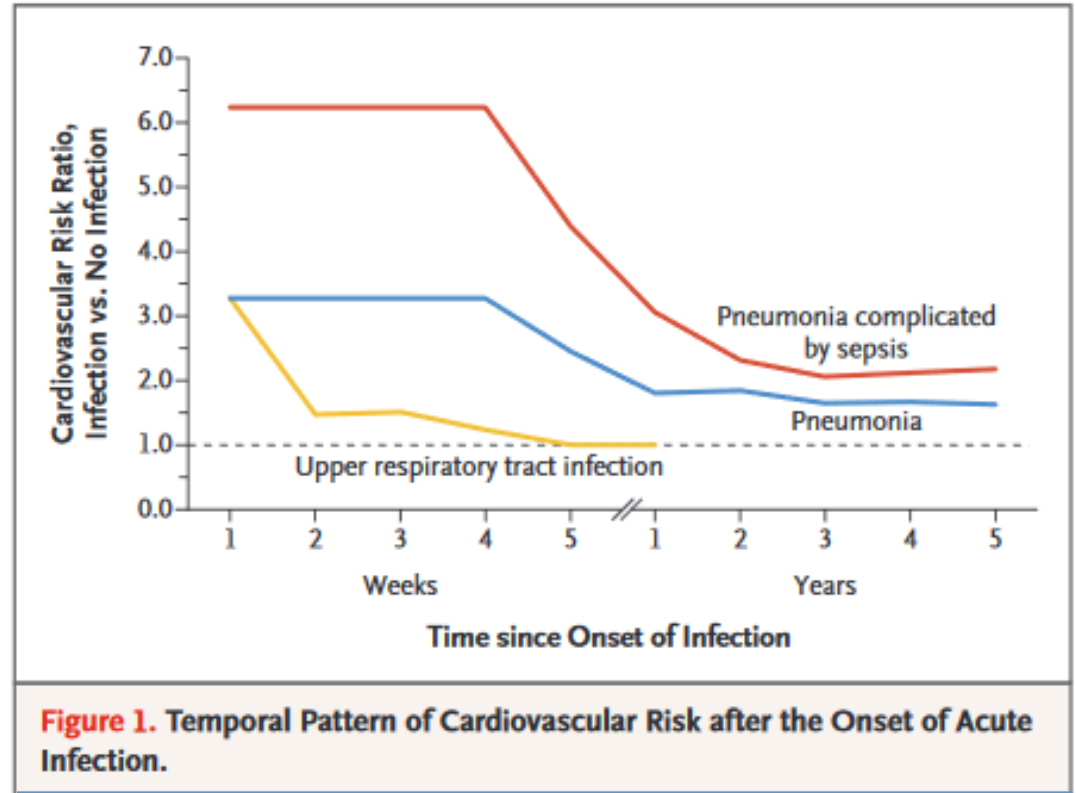
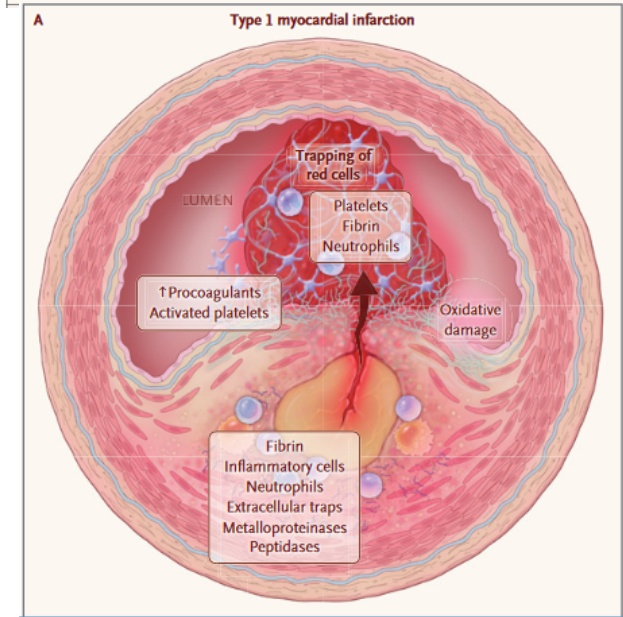
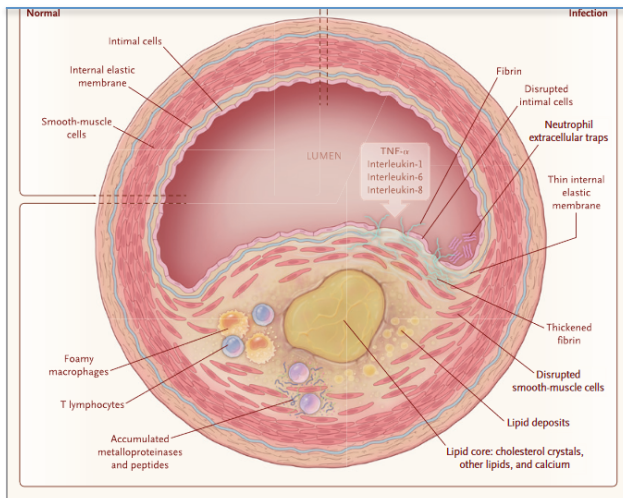


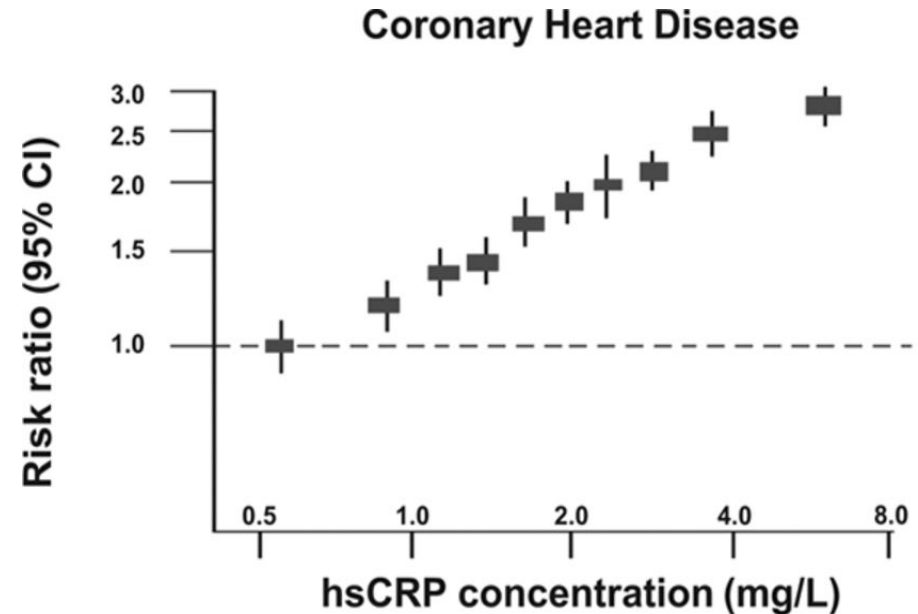
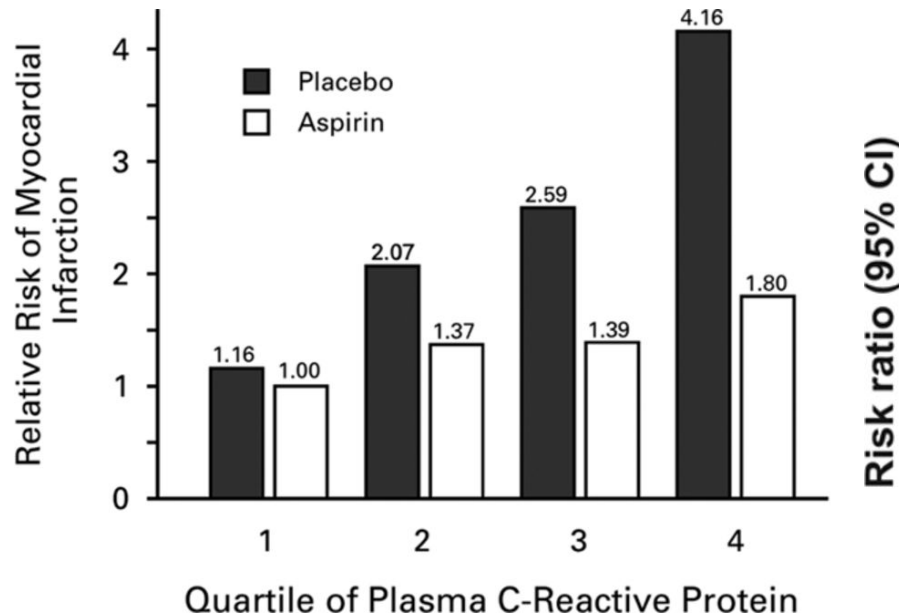
Figure 1. Temporal Pattern of Cardiovascular Risk after the Onset of Acute Infection.

Arguments pour théorie inflammatoire de l'athéro-thrombose

Corrélation

CRP us / IL 1 et IL 6 et évènements coronariens

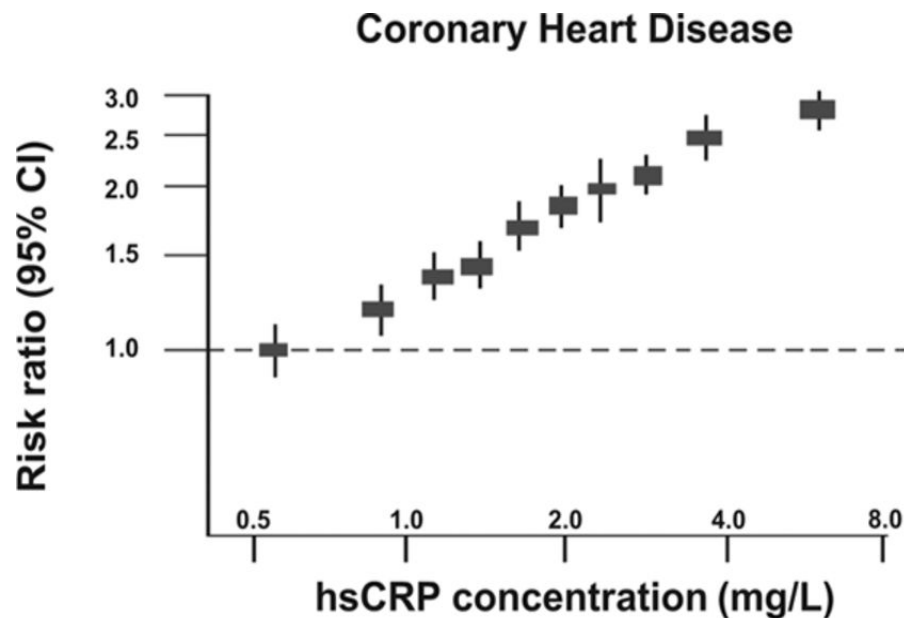
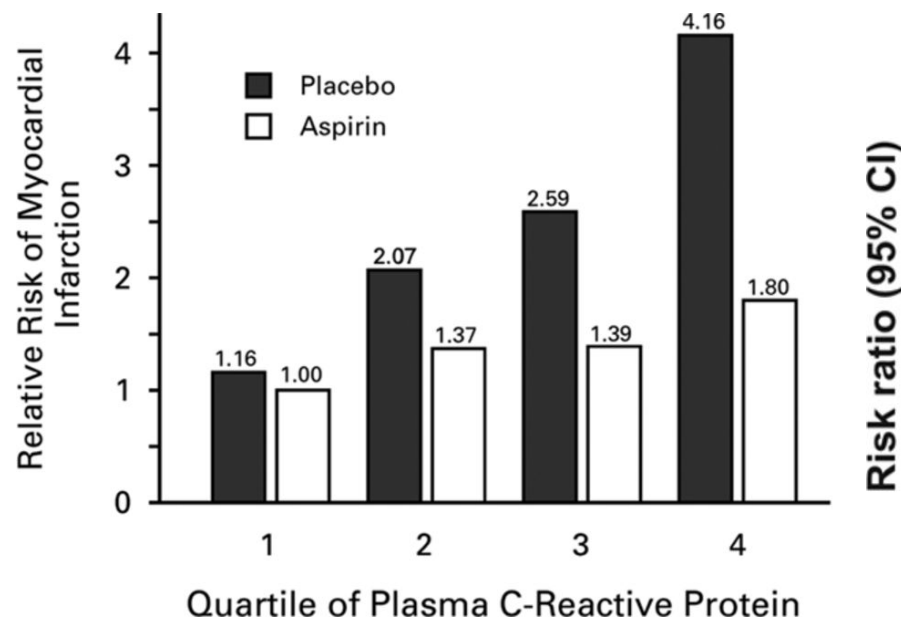
Left, Relationship of baseline plasma levels of high-sensitivity C-reactive protein (hsCRP) to risks of future myocardial infarction, stroke, and cardiovascular death in the prospective Physicians' Health Study among those randomly allocated to aspirin or placebo.



Physicians' Health Study en Prévention primaire

Paul M Ridker Circ Res. 2016;118:145-156

Left, Relationship of baseline plasma levels of high-sensitivity C-reactive protein (hsCRP) to risks of future myocardial infarction, stroke, and cardiovascular death in the prospective Physicians' Health Study among those randomly allocated to aspirin or placebo.

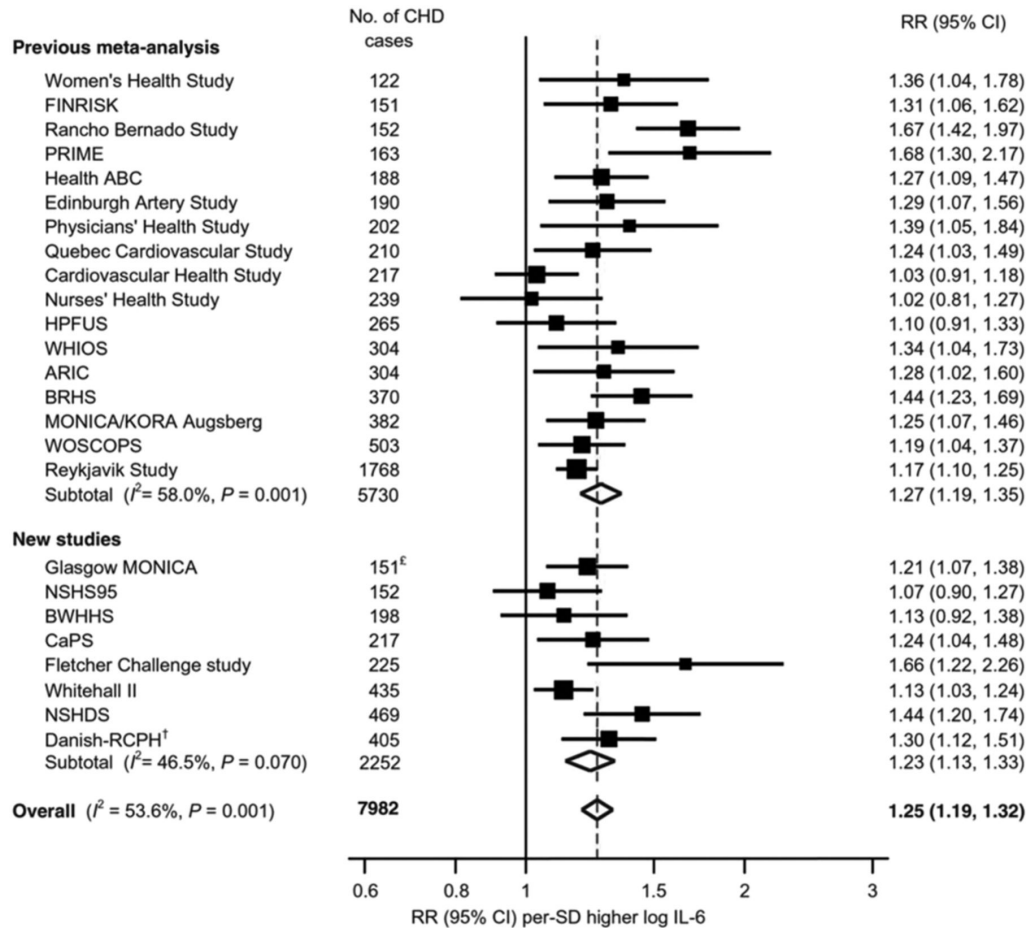


Plus la CRPus est élevée plus le risqué d'IDM augmente

Paul M Ridker Circ Res. 2016;118:145-156

Relationship of plasma levels of interleukin-6 (IL-6) to future risks of cardiovascular disease in 25 prospective epidemiologic cohorts.

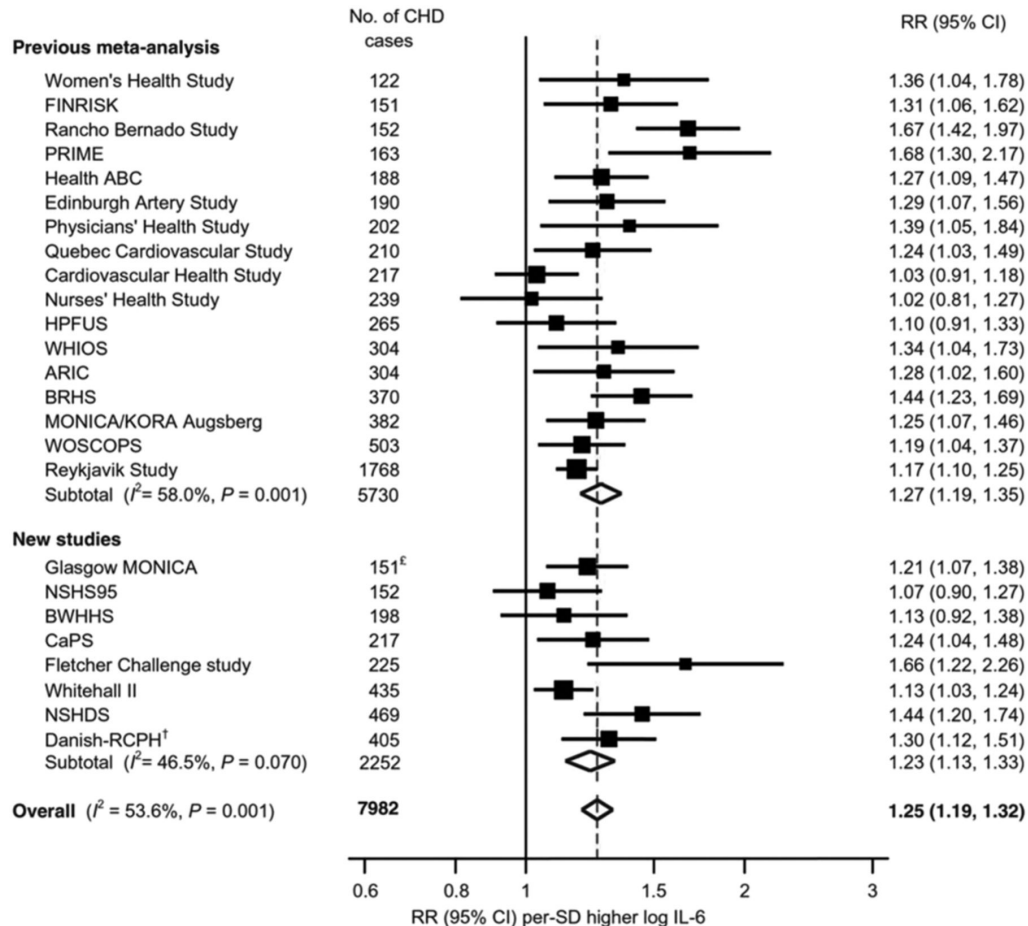
Paul M Ridker Circ Res. 2016;118:145-156



Relationship of plasma levels of interleukin-6 (IL-6) to future risks of cardiovascular disease in 25 prospective epidemiologic cohorts.



Paul M Ridker Circ Res. 2016;118:145-156

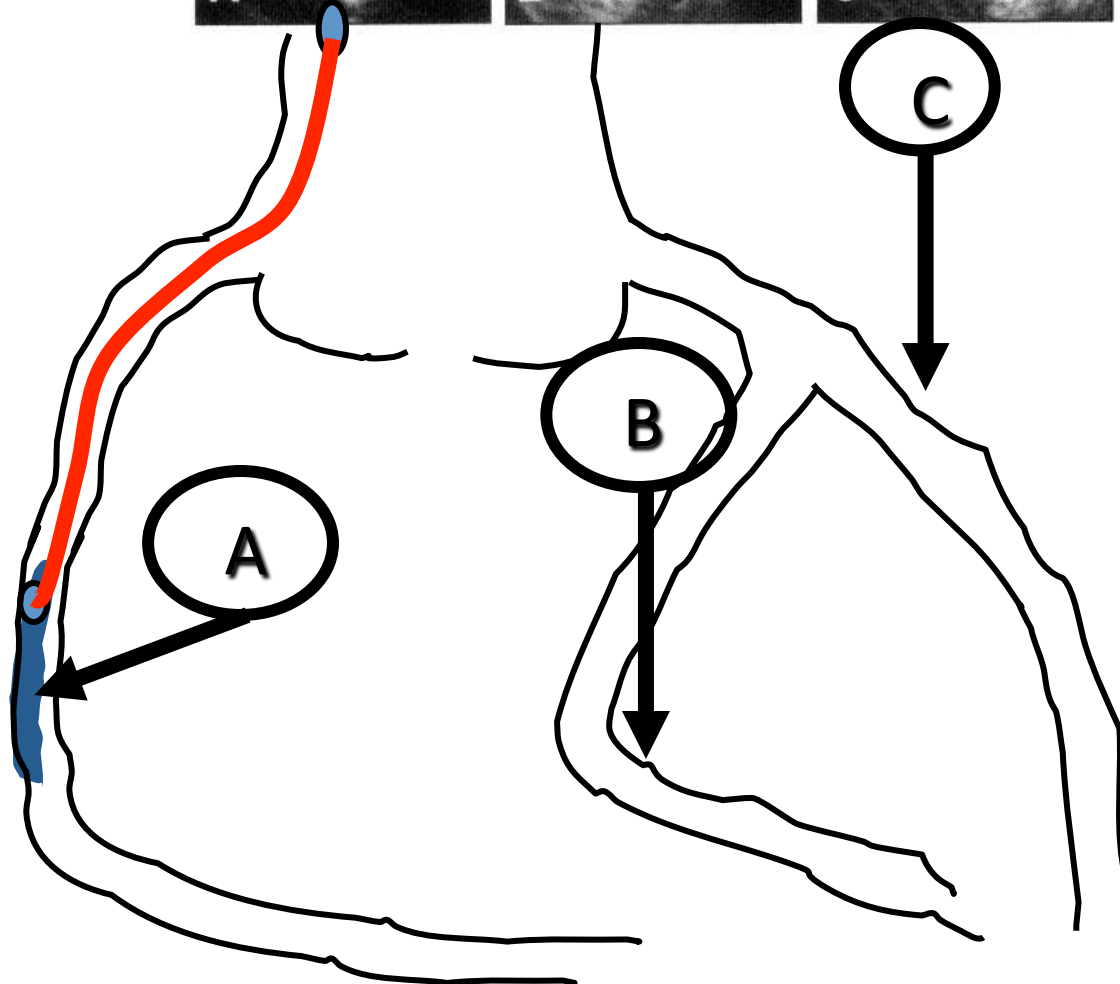
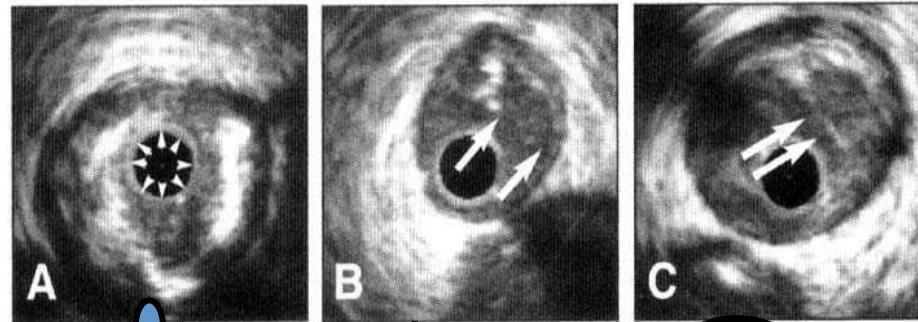


Plus l'IL6 est élevée plus le risqué d'IDM augmente

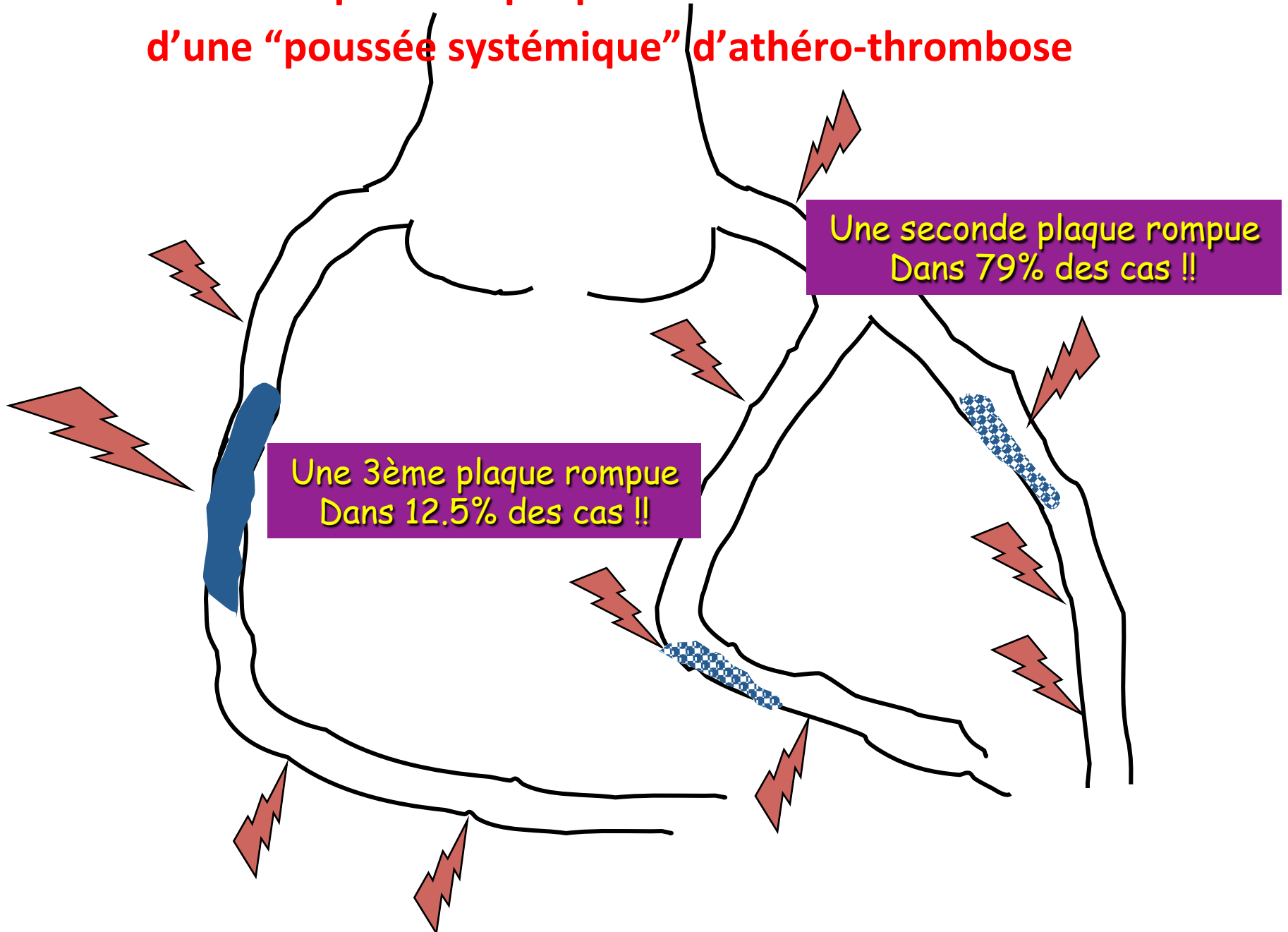
Arguments pour théorie inflammatoire de l'athéro-thrombose

**La rupture de plaque est souvent le fait
d'une "poussée systémique" d'athéro-thrombose**

Multiple atherosclerotic plaque rupture in acute coronary syndrome.
A three vessel intravascular ultrasound study.
Rioufol G et al. Circulation 2002;106:804-8.



**La rupture de plaque est souvent le fait
d'une "poussée systémique" d'athéro-thrombose**



Arguments pour théorie inflammatoire de l'athéro-thrombose

Les statines n'agissent pas seulement par l'effet hypolipémiant ($\neq$ fibrates)

Arguments pour théorie inflammatoire de l'athéro-thrombose

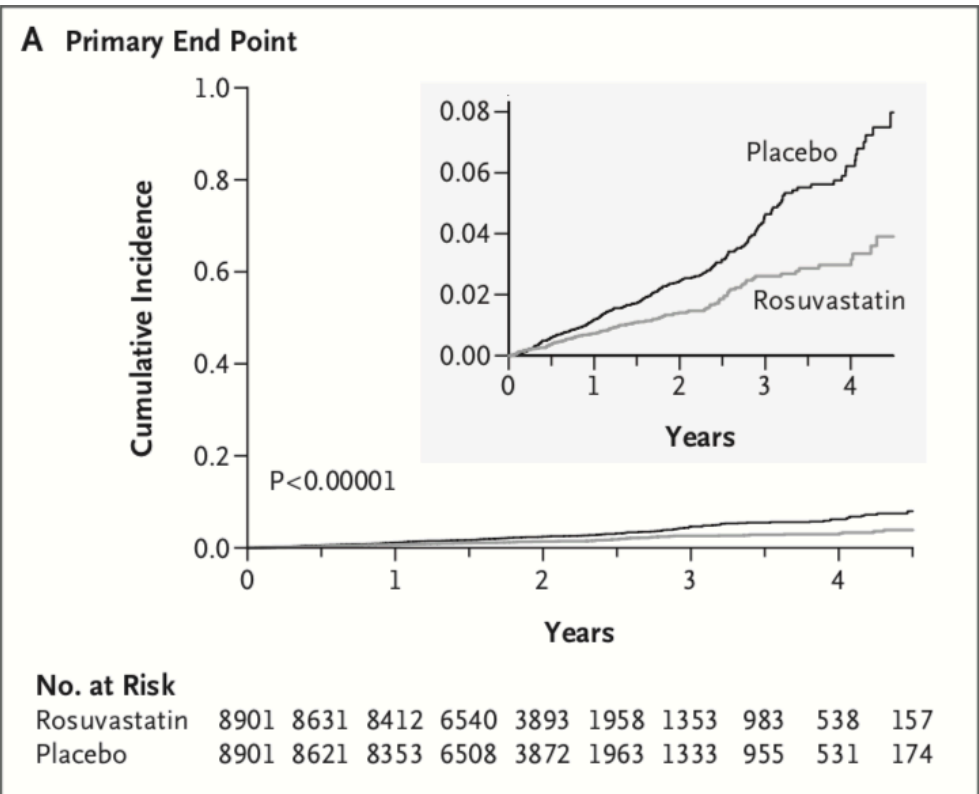
Essai JUPITER

Les patients avec taux de LDL bas mais CRP élevée bénéficiaient plus de la statine

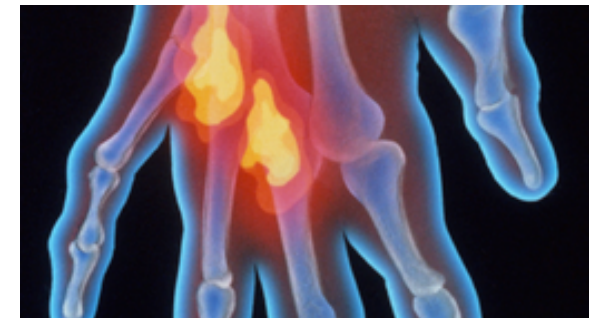
ORIGINAL ARTICLE

Rosuvastatin to Prevent Vascular Events in Men and Women with Elevated C-Reactive Protein

Paul M Ridker, M.D., Eleanor Danielson, M.I.A., Francisco A.H. Fonseca, M.D., Jacques Genest, M.D., Antonio M. Gotto, Jr., M.D., John J.P. Kastelein, M.D., Wolfgang Koenig, M.D., Peter Libby, M.D., Alberto J. Lorenzatti, M.D., Jean G. MacFadyen, B.A., Børge G. Nordestgaard, M.D., James Shepherd, M.D., *et al.*, for the JUPITER Study Group*



**Les maladies inflammatoires “chroniques”
présentent un sur-risque de coronaropathie**



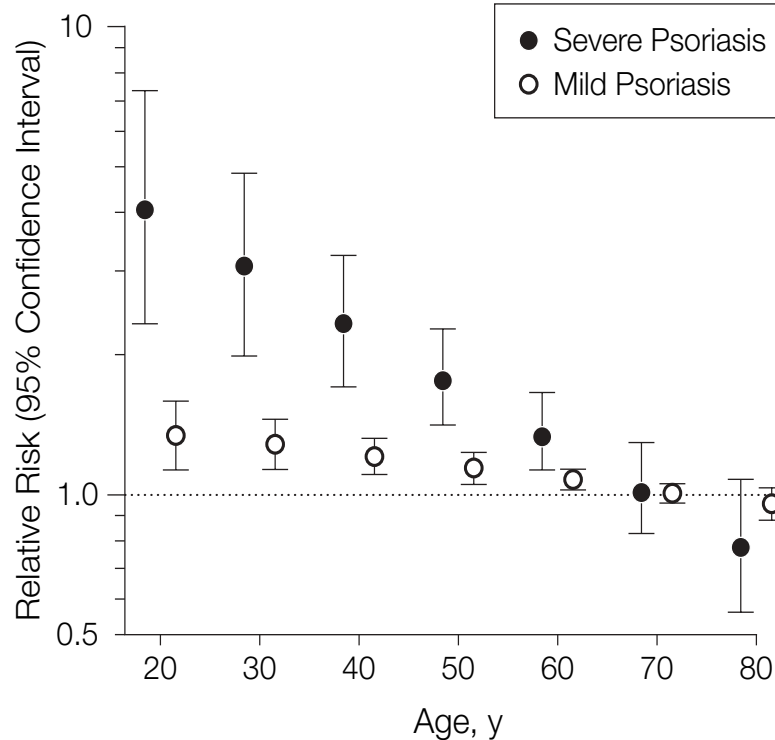
Le risque cardiovasculaire est augmenté au cours des rhumatismes inflammatoires (PR -SPA)

La PR est un facteur de risque CV aussi important que le diabète

Recommendations	Class	Level
The use of a 1.5 factor risk multiplier for CV risk in rheumatoid arthritis should be considered, particularly if disease activity is high.	IIa	B
The use of a 1.5 risk multiplier for CV risk in immune inflammatory diseases other than rheumatoid arthritis may be considered on a patient-by-patient basis, depending on disease activity/severity.	IIb	C

Risque coronarien du psoriasis sévère

Figure. Adjusted Relative Risk of Myocardial Infarction in Patients With Psoriasis Based on Patient Age



Adjusted relative risk is shown on a log scale.

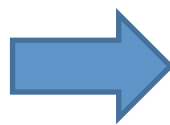
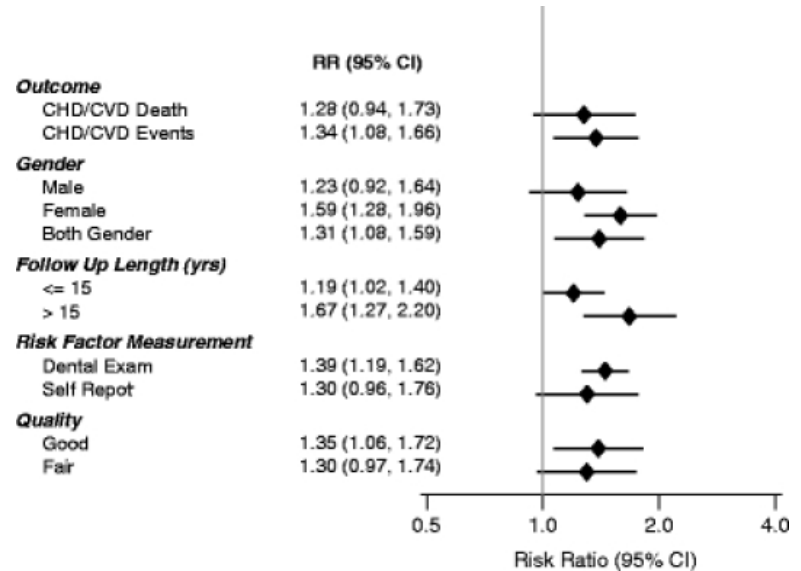
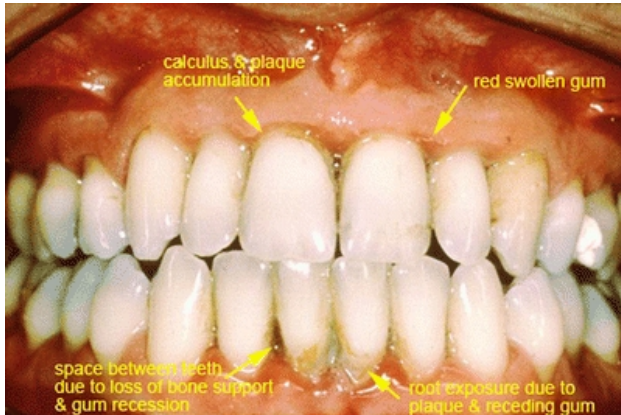


Recommendations	Class	Level
The use of a 1.5 factor risk multiplier for CV risk in rheumatoid arthritis should be considered, particularly if disease activity is high.	IIa	B
The use of a 1.5 risk multiplier for CV risk in immune inflammatory diseases other than rheumatoid arthritis may be considered on a patient-by-patient basis, depending on disease activity/severity.	IIb	C

Concept Inflammatoire de la coronaropathie

Periodontal Disease and Coronary Heart Disease Risk

Philippe P. Hujoel, PhD; Mark Drangsholt, DDS, MPH; Charles Spiekerman, PhD; [et al](#)



Foyer dentaire à éradiquer

Si vous voulez démontrer un concept

Facteur (l'inflammation) associé à un surrisque
cardiaque....



Il faut démontrer que la suppression de ce
facteur à un impact positif sur le suri-risque
cardiaque

L'effet présumé de certains traitements anti-inflammatoires

Cantos: la demonstration du concept



Antiinflammatory Therapy with Canakinumab for Atherosclerotic Disease

P.M. Ridker, B.M. Everett, T. Thuren, J.G. MacFadyen, W.H. Chang, C. Ballantyne, F. Fonseca, J. Nicolau, W. Koenig, S.D. Anker, J.J.P. Kastelein, J.H. Cornel, P. Pais, D. Pella, J. Genest, R. Cifkova, A. Lorenzatti, T. Forster, Z. Kobalava, L. Vida-Simiti, M. Flather, H. Shimokawa, H. Ogawa, M. Dellborg, P.R.F. Rossi, R.P.T. Troquay, P. Libby, and R.J. Glynn, for the CANTOS Trial Group*

Anti-Inflammatory Therapy with Canakinumab for Atherosclerotic Disease



Paul M Ridker, MD, MPH
Eugene Braunwald Professor of Medicine
Brigham and Women's Hospital,
Harvard Medical School, Boston MA, USA



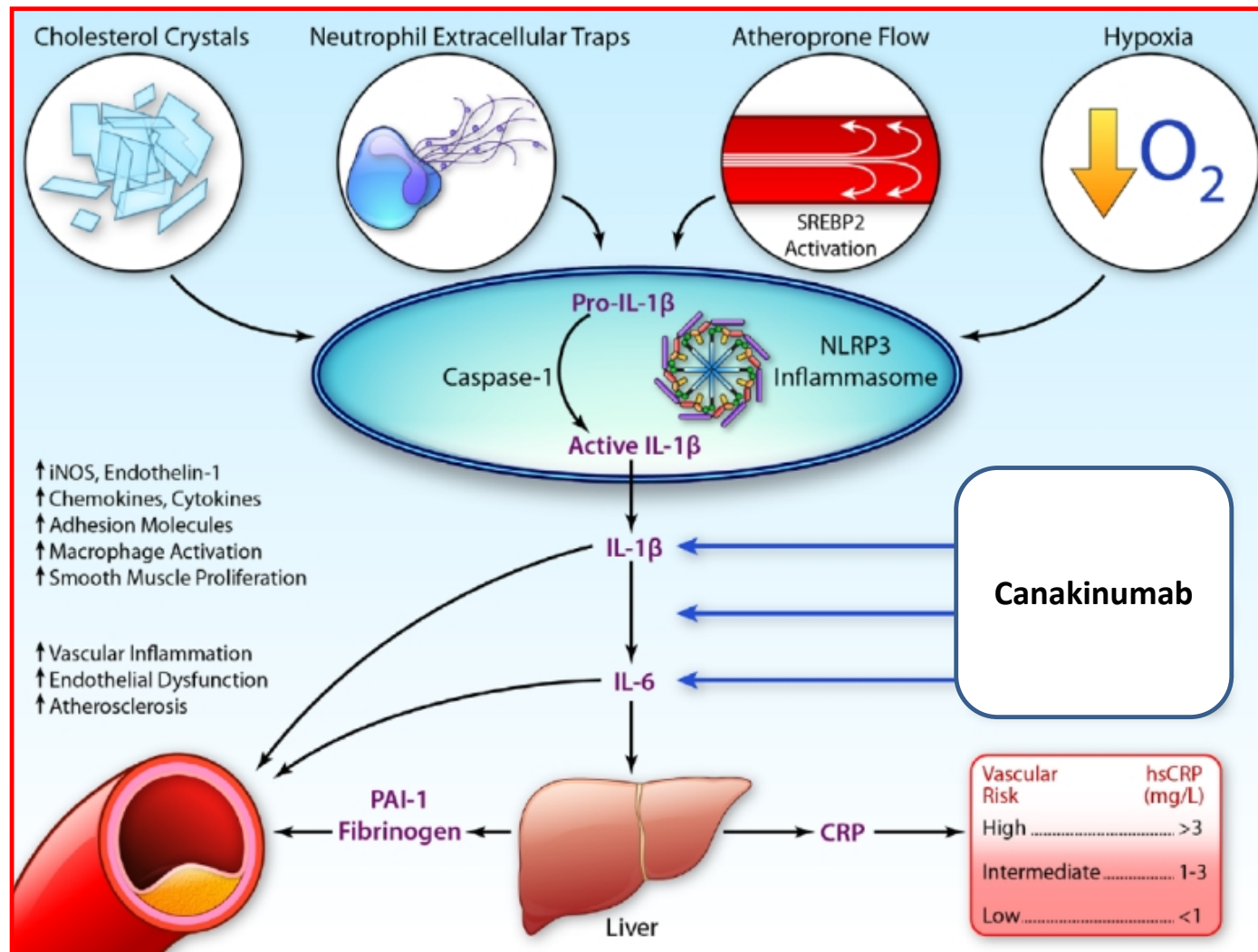
on behalf of the worldwide investigators and participants in the
Canakinumab Anti-Inflammatory Thrombosis Outcomes Study (CANTOS)

Ridker ACC 2017

*La plus belle étude en cardiologie
depuis Framingham*

Eugène Braunwald

From CRP to IL-6 to IL-1: Moving Upstream to Identify Novel Targets for Atheroprotection



Ridker PM. Circ Res 2016;118:145-156.

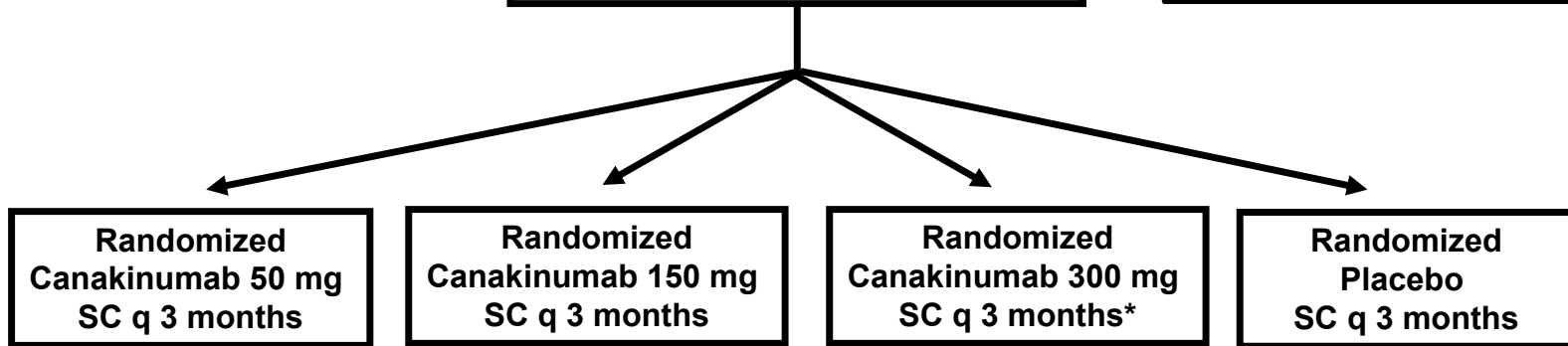
Ridker ESC 2017

Canakinumab Anti-Inflammatory Thrombosis Outcomes Study (CANTOS)



**Stable CAD (post MI)
On Statin, ACE/ARB, BB, ASA
Persistent Elevation
of hsCRP (≥ 2 mg/L)**

**N = 10,061
39 Countries
April 2011 - June 2017
1490 Primary Events**

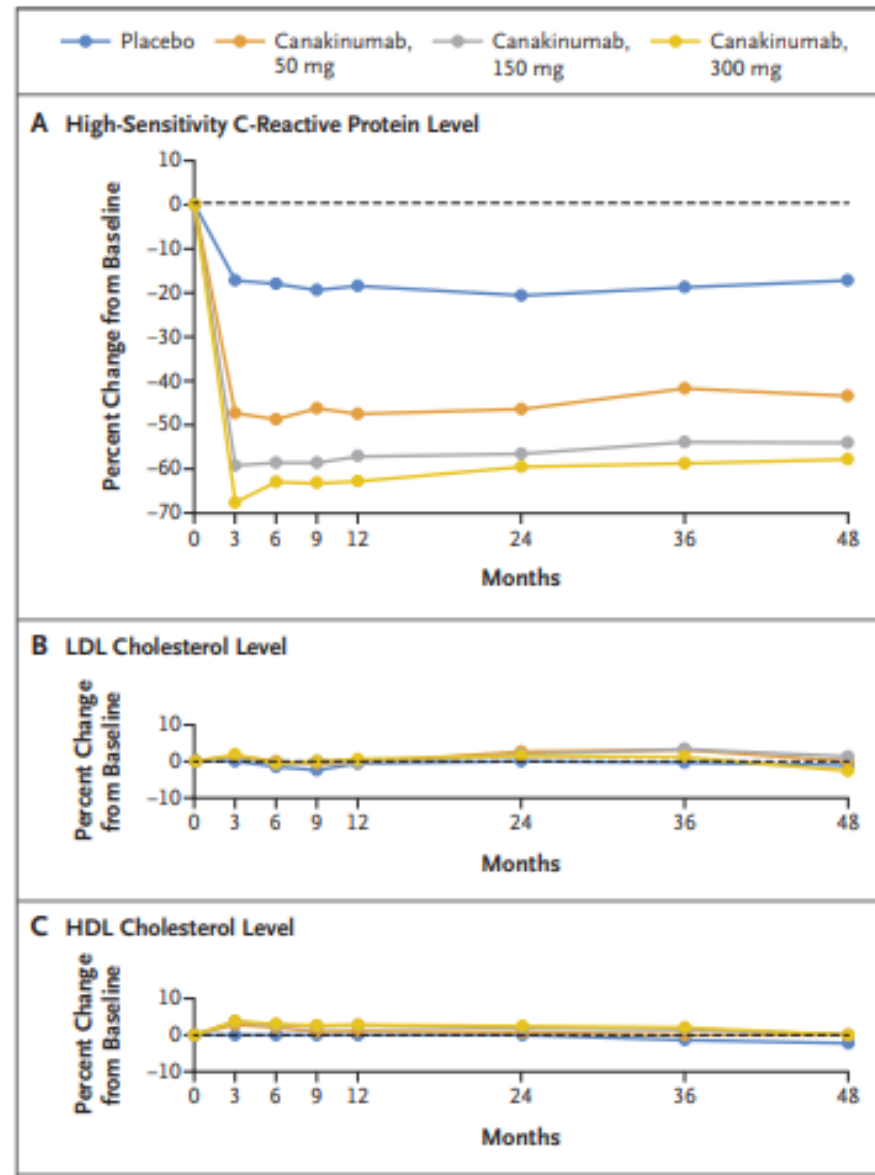


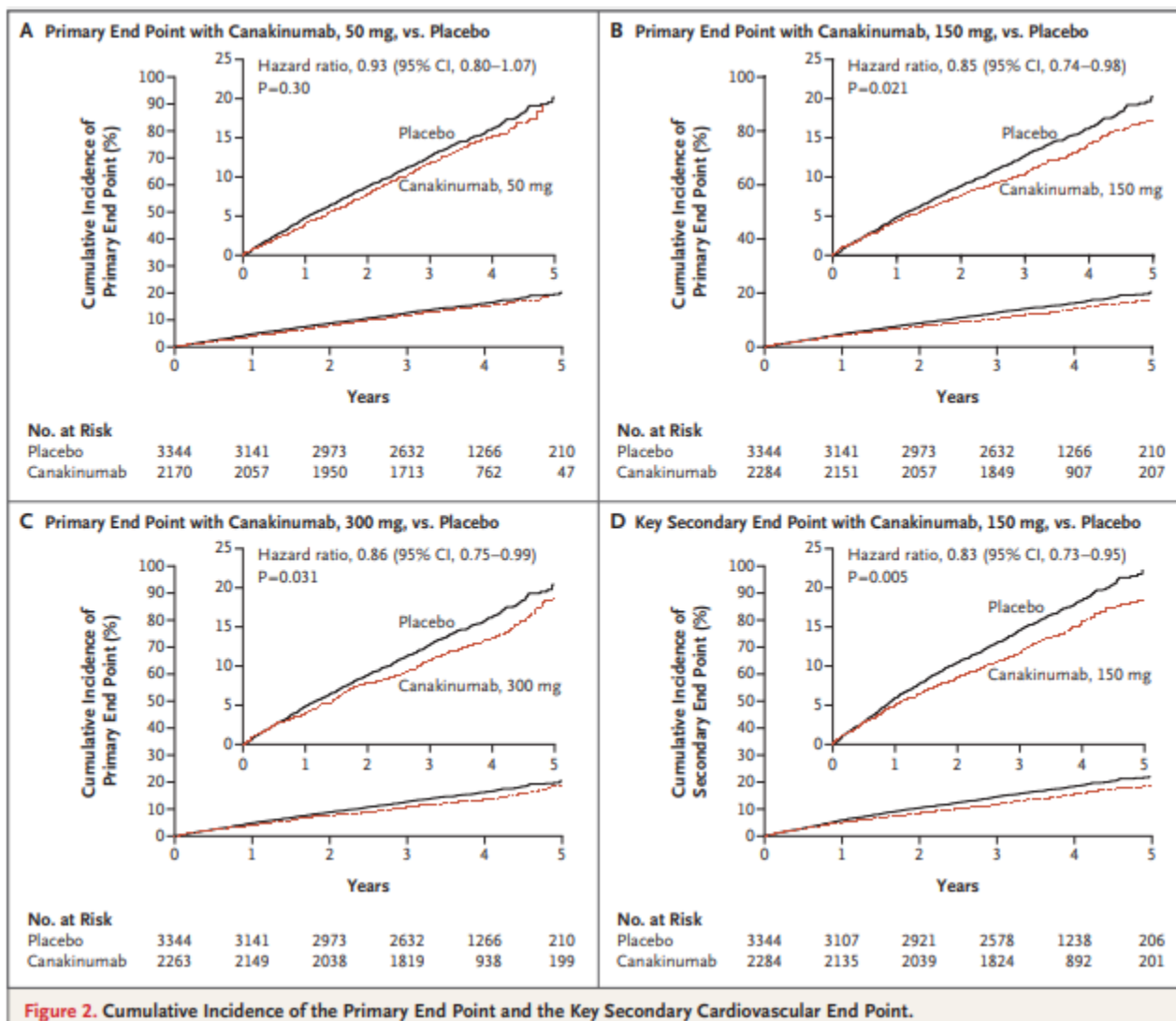
Primary CV Endpoint: Nonfatal MI, Nonfatal Stroke, Cardiovascular Death (MACE)

Key Secondary CV Endpoint: MACE + Unstable Angina Requiring Unplanned Revascularization (MACE+)

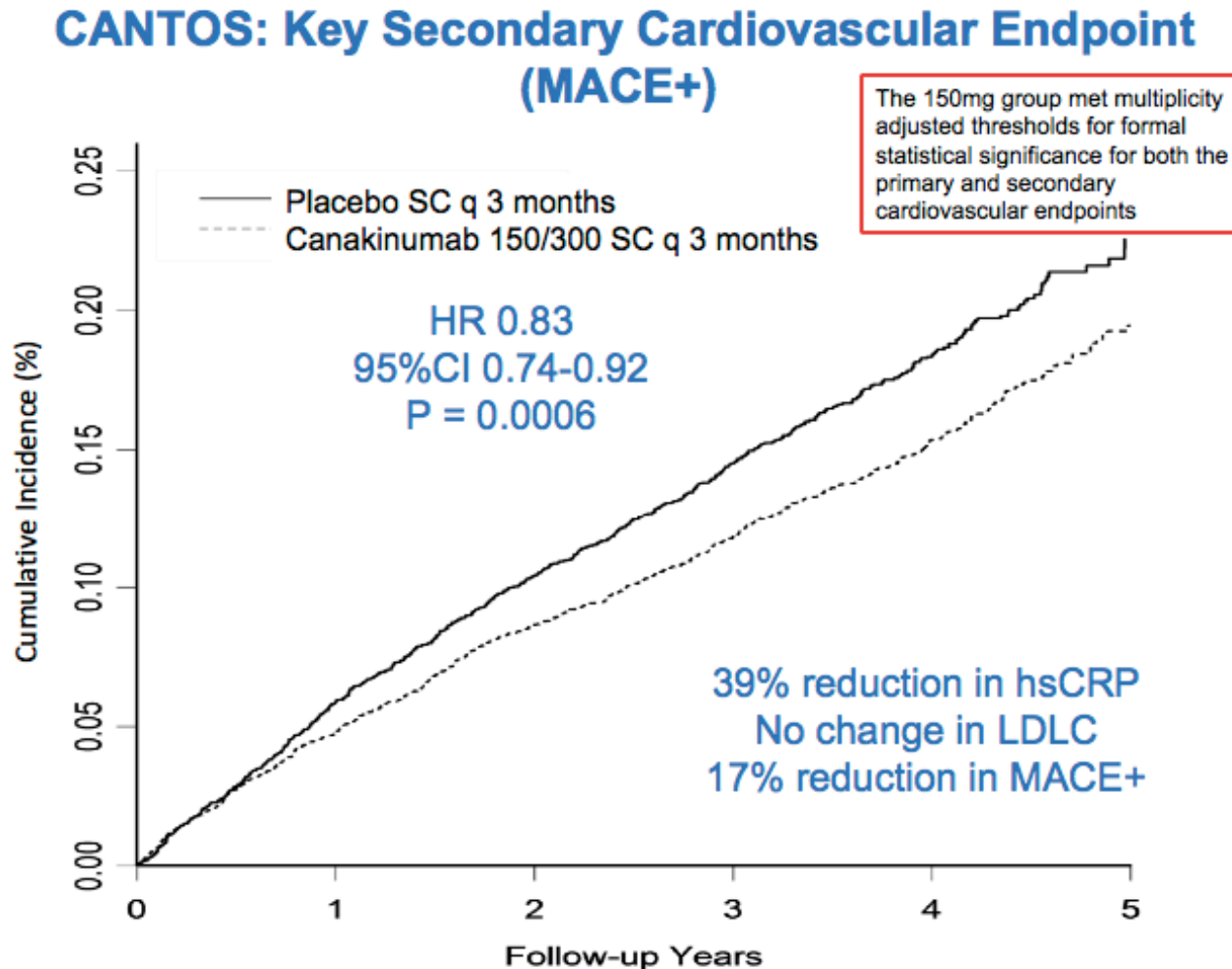
Critical Non-Cardiovascular Safety Endpoints: Cancer and Cancer Mortality, Infection and Infection Mortality

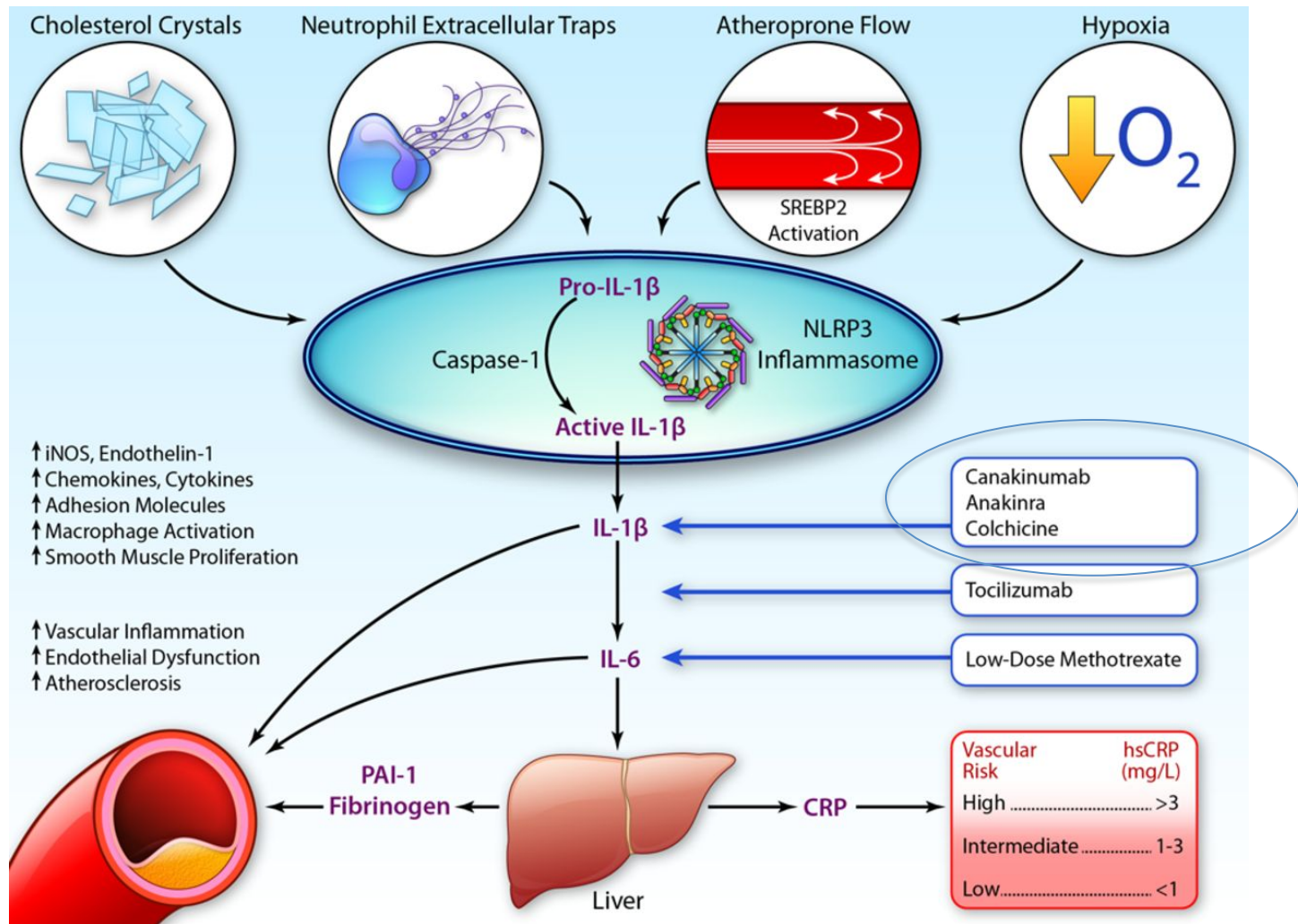
Cantos: la demonstration du concept



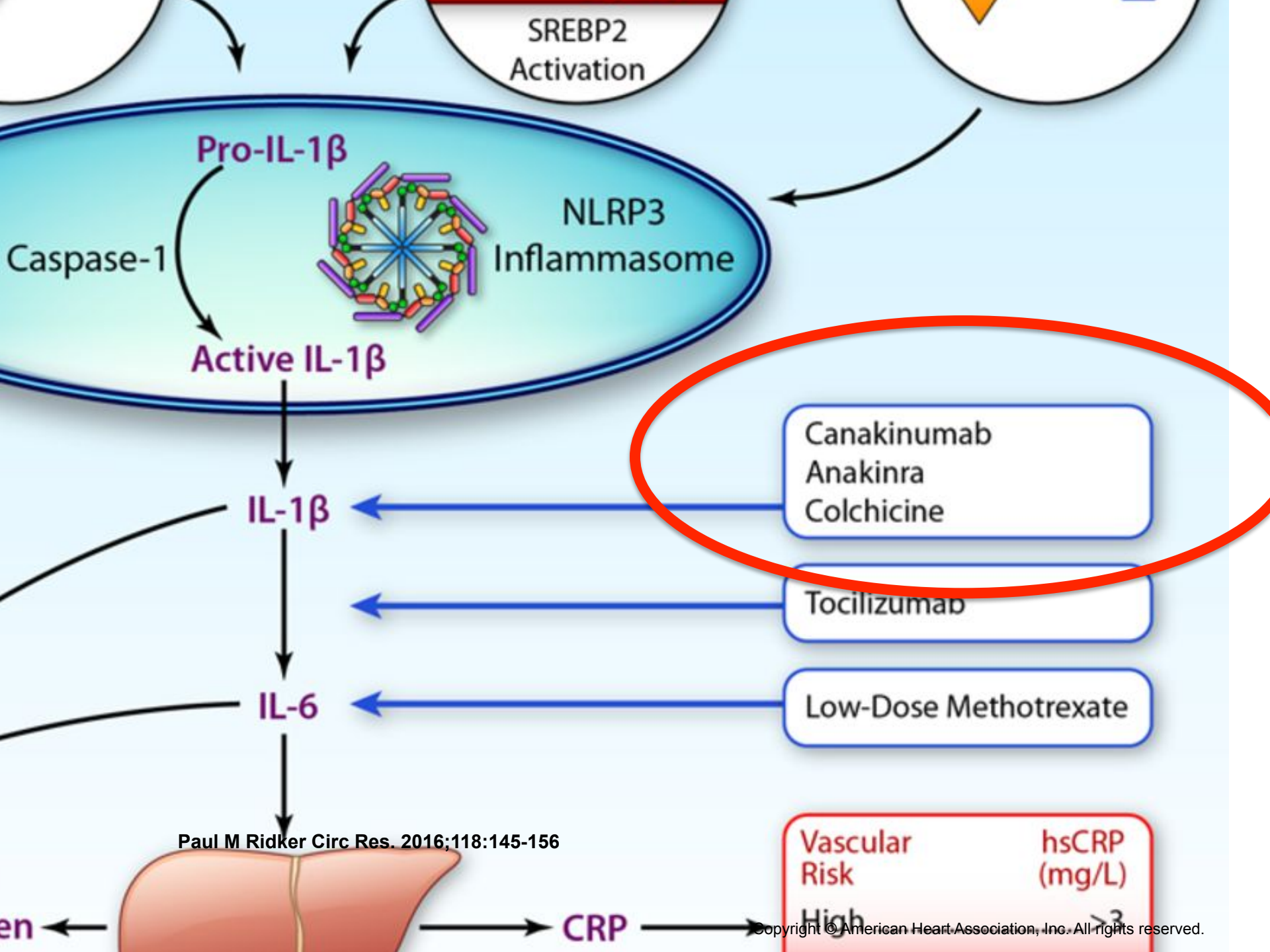


CANTOS: Canakinumab et MACE





Paul M Ridker Circ Res. 2016;118:145-156



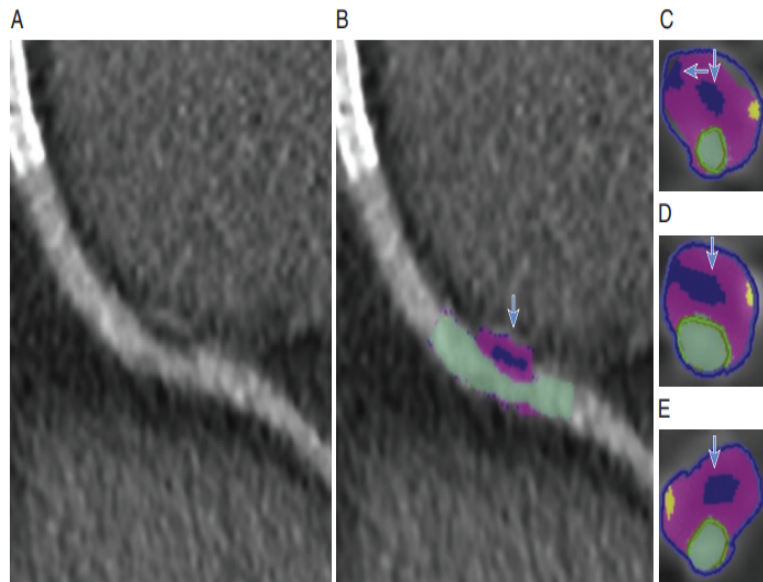
Colchicine Therapy and Plaque Stabilization in Patients With Acute Coronary Syndrome

A CT Coronary Angiography Study

Kaivan Vaidya, MBBS, MMSc(CUN Epi),^a Clare Arnott, MBBS,^{a,b} Gonzalo J. Martinez, MD,^{c,d} Bernard Ng, MBBS,^e Samuel McCormack, MBChB,^e David R. Sullivan, MD,^{b,f,g} David S. Celermajer, MBBS, PhD, DSc,^{a,h,i} Sanjay Patel, MBBS, PhD^{a,h,i,f}

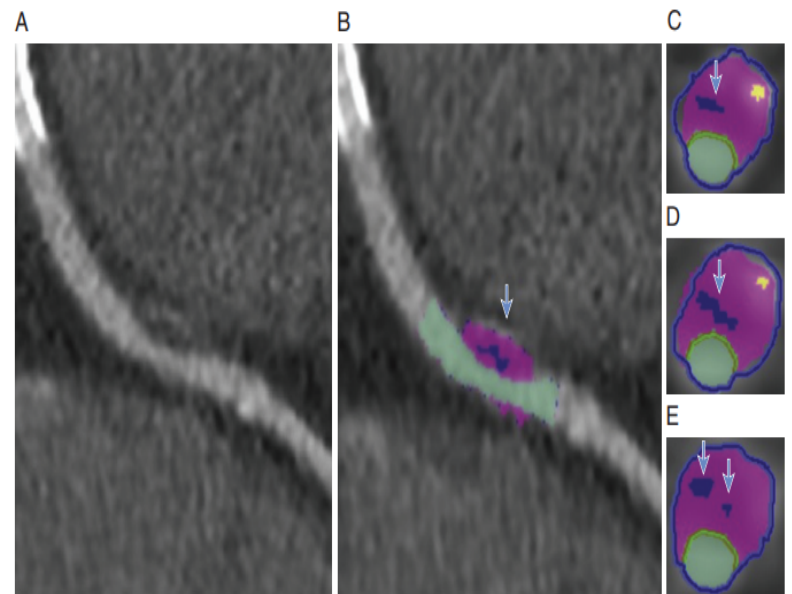
Morphologie de la plaque avant et 12 mois de colchicine

FIGURE 2 Distal Right Coronary Artery Plaque Identified at Baseline



(A) Curved planar reformat; (B) curved planar reformat with color overlay coded image map to identify plaque components; (C to E) representative cross-sectional views with color overlay. Light blue arrows indicate low attenuation plaque (dark blue); noncalcified plaque, purple; dense calcified plaque, yellow; lumen green. LAP volume = 4.2 mm³, NCP volume = 46.5 mm³, DCP volume = 2.2 mm³, lumen volume = 41.4 mm³. DCP = dense calcified plaque; LAP = low attenuation plaque; NCP = noncalcified plaque.

FIGURE 3 Distal Right Coronary Artery Plaque Reimaged After 12 Months of Oral Colchicine (0.5 mg/day)



(A) Curved planar reformat; (B) curved planar reformat with color overlay coded image map to identify plaque components; (C to E) representative cross-sectional views with color overlay. See Figure 1 legend for color descriptions. LAPV = 3.2 mm³ (-23.8%), NCPV = 65.8 mm³ (+41.5%), DCPV = 0.3 mm³ (-86.4%), lumen volume = 47.2 mm³ (+14.0%). DCPV = dense calcified plaque volume; LAPV = low attenuation plaque volume; NCPV = noncalcified plaque volume.

Nette diminution du « noyau actif »

Colchicine /coronaires > 12 000 pts randomisés

Table 1 Key features of included trials

Trial acronym	Author	Year	Trial size	Key inclusion criteria	Key exclusion criteria	Active treatment	Comparator	Multi-centre	Open-label run-in	Follow-up (median, months)
IoDoCO		2020	5522	Chronic coronary disease, clinically stable >6 months	Heart failure (NYHA class III/IV); renal failure (eGFR <50 mL/min/1.73 m ²); severe valvular heart disease	Colchicine 0.5 mg once daily	Placebo	Yes	Yes	29
COPS	Tong ²⁵	2020	795	Acute coronary syndrome with presence of coronary disease	Requiring bypass surgery; severe liver impairment; severe renal impairment (eGFR <30 mL/min/1.73 m ²)	Colchicine 0.5 mg twice daily for 1 month, followed by 0.5 mg once daily	Placebo	Yes	No	12
Colcot		2019	4745	Post-myocardial infarction	Heart failure (LVEF <35%); renal impairment (creatinine level >2× upper limit of normal); bypass surgery <3 years or planned	Colchicine 0.5 mg once daily	Placebo	Yes	No	23
NA	Deftereos ²³	2013	222	Diabetes and undergoing percutaneous coronary revascularization	Acute myocardial infarction; renal impairment (eGFR <20 mL/min/1.73 m ²); liver failure	Colchicine 0.5 mg twice daily	Placebo	No	No	6
LoDoCo	Nidorf ²⁴	2013	532	Chronic coronary disease, clinically stable >6 months	Bypass surgery <10 years, major competing comorbidities	Colchicine 0.5 mg once daily	No colchicine	No	No	36

eGFR, estimated glomerular filtration rate; LVEF, left ventricular ejection fraction; NA, not available; NYHA, New York Heart Association.

Colchicine /coronaires > 12 000 pts randomisés

	n	Situation clinique
COLCOT	4745	SCA
LODOCO2	5522	Coronaropathie stable



European Society
of Cardiology

European Heart Journal (2021) 42, 2800–2801
doi:10.1093/eurheartj/ehab020

DISCUSSION FORUM

Lessons from COLCOT and LoDoCo2: colchicine for secondary prevention in coronary artery disease

Nadia Bouabdallaoui , **Lucie Blondeau** , and **Jean-Claude Tardif** *

Montreal Heart Institute and the Montreal Health Innovations Coordinating Center (MHICC), 5000 Belanger Street, Montreal, QC H1T 1C8, Canada

Received 28 December 2020; editorial decision 2 January 2021; accepted 6 January 2021; online publish-ahead-of-print 26 January 2021

Efficacy and safety of low-dose colchicine in patients with coronary disease: a systematic review and meta-analysis of randomized trials

Aernoud T.L. Fiolet^{1,2†}, **Tjerk S.J. Opstal**^{3,4†}, **Arend Mosterd**^{2,5,6}, **John W. Eikelboom**⁷, **Sanjit S. Jolly**⁸, **Anthony C. Keech**⁹, **Peter Kelly**¹⁰, **David C. Tong**^{11,12}, **Jamie Layland**^{11,12,13}, **Stefan M. Nidorf**^{14,15}, **Peter L. Thompson**^{14,16,17}, **Charley Budgeon**¹⁷, **Jan G.P. Tijssen**^{18,19‡}, and **Jan H. Cornel**^{2,3,4*‡}; on behalf of the Colchicine Cardiovascular Trialists Collaboration

Colchicine in Coronary Disease

A meta-analysis of 5 studies

MACE

Myocardial infarction,
stroke, or
cardiovascular death



Colchicine 0.5 mg

4.2%

250/5806



Placebo
or no colchicine

5.7%

328/5788

Pooled relative risk reduction 25%

(RR 0.75. 95% CI 0.61 to 0.92)

Myocardial infarction

Significant relative risk reduction

↓ 22%



RR 0.78 (95% CI 0.64 to 0.94)

Stroke

Significant relative risk reduction

↓ 46%



RR 0.54 (95% CI 0.34 to 0.86)

Coronary revascularisation

Significant relative risk reduction

↓ 23%



RR 0.77 (95% CI 0.66 to 0.90)

Cardiovascular death

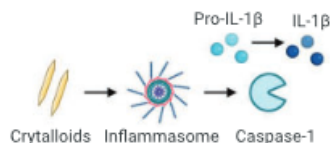
No significant relative risk reduction



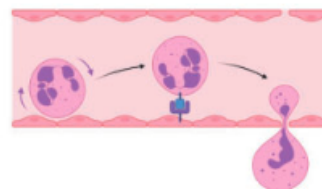
RR 0.82 (95% CI 0.55 to 1.23)

Potential mechanisms

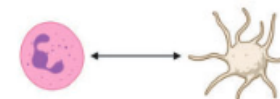
① Inhibiting inflammasome activation



② Inhibiting neutrophil chemotaxis, adhesion and activation



③ Inhibiting neutrophil-platelet interaction



Colchicine in coronary disease

Keywords

Colchicine • Atherosclerosis • Coronary disease • Major adverse cardiovascular events • Myocardial infarction • Stroke

Colchicine in Coronary Disease

A meta-analysis of 5 studies

MACE

Myocardial infarction,
stroke, or
cardiovascular death



Colchicine 0.5 mg

4.2%

250/5806



Placebo
or no colchicine

5.7%

328/5788

Pooled relative risk reduction 25%

(RR 0.75, 95% CI 0.61 to 0.92)

Myocardial infarction

Significant relative risk reduction

↓ 22%



RR 0.78 (95% CI 0.64 to 0.94)

Stroke

Significant relative risk reduction

↓ 46%



RR 0.54 (95% CI 0.34 to 0.86)

Coronary revascularisation

Significant relative risk reduction

↓ 23%



RR 0.77 (95% CI 0.66 to 0.90)

Cardiovascular death

No significant relative risk reduction



RR 0.82 (95% CI 0.55 to 1.23)

Potential mechanisms

① Inhibiting inflammasome activation

② Inhibiting neutrophil chemotaxis, adhesion and activation

③ Inhibiting neutrophil-platelet interaction



22% reduction risk for MI
p=0.005

Keywords

Colchicine • Atherosclerosis • Coronary disease • Major adverse cardiovascular events • Myocardial infarction • Stroke

Colchicine in Coronary Disease

A meta-analysis of 5 studies

MACE

Myocardial infarction,
stroke, or
cardiovascular death



Colchicine 0.5 mg

4.2%

250/5806



Placebo
or no colchicine

5.7%

328/5788

Pooled relative risk reduction 25%

(RR 0.75, 95% CI 0.61 to 0.92)

Myocardial infarction

Significant relative risk reduction

↓ 22%



RR 0.78 (95% CI 0.64 to 0.94)

Stroke

Significant relative risk reduction

↓ 46%



RR 0.54 (95% CI 0.34 to 0.86)

Coronary revascularisation

Significant relative risk reduction

↓ 23%



RR 0.77 (95% CI 0.66 to 0.90)

Cardiovascular death

No significant relative risk reduction



RR 0.82 (95% CI 0.55 to 1.23)

Potential mechanisms

(1) Inhibiting inflammasome

(2) Inhibiting neutrophil chemotaxis,

(3) Inhibiting neutrophil-platelet

**46% reduction risk for
stroke p=0.009**

Keywords

Colchicine • Atherosclerosis • Coronary disease • Major adverse cardiovascular events • Myocardial infarction • Stroke

Colchicine in Coronary Disease

A meta-analysis of 5 studies

MACE

Myocardial infarction,
stroke, or
cardiovascular death



Colchicine 0.5 mg

4.2%

250/5806



Placebo
or no colchicine

5.7%

328/5788

Pooled relative risk reduction 25%

(RR 0.75. 95% CI 0.61 to 0.92)

Myocardial infarction

Significant relative risk reduction

↓ 22%



RR 0.78 (95% CI 0.64 to 0.94)

Stroke

Significant relative risk reduction

↓ 46%



RR 0.54 (95% CI 0.34 to 0.86)

Coronary revascularisation

Significant relative risk reduction

↓ 23%



RR 0.77 (95% CI 0.66 to 0.90)

Cardiovascular death

No significant relative risk reduction



RR 0.82 (95% CI 0.55 to 1.23)

Potential mechanism

(1) Inhibiting inflammasome

(2) Inhibiting neutrophil chemotaxis

(3) Inhibiting neutrophil-platelet

23% reduction risk for coronary revascularisation p<0.001

Colchicine in

Keywords

Colchicine • Atherosclerosis • Coronary disease • Major adverse cardiovascular events • Myocardial infarction • Stroke

Colchicine in Coronary Disease

A meta-analysis of 5 studies

MACE

Myocardial infarction,
stroke, or
cardiovascular death



Colchicine 0.5 mg

4.2%

250/5806



Placebo
or no colchicine

5.7%

328/5788

Pooled relative risk reduction 25%

(RR 0.75, 95% CI 0.61 to 0.92)

Myocardial infarction

Significant relative risk reduction

↓ 22%



RR 0.78 (95% CI 0.64 to 0.94)

Stroke

Significant relative risk reduction

↓ 46%



RR 0.54 (95% CI 0.34 to 0.86)

Coronary revascularisation

Significant relative risk reduction

↓ 23%



RR 0.77 (95% CI 0.66 to 0.90)

Cardiovascular death

No significant relative risk reduction



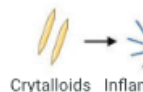
RR 0.82 (95% CI 0.55 to 1.23)

Potential mechanisms

① Inhibiting inflammasome activation

② Inhibiting neutrophil chemotaxis, adhesion and activation

③ Inhibiting neutrophil-platelet interaction



Crystalloids → Inflammation

18% reduction risk for CV death p=0.34

Colchicine in coronary disease

Keywords

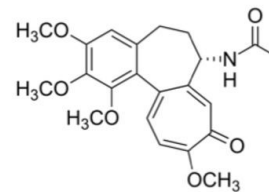
Colchicine • Atherosclerosis • Coronary disease • Major adverse cardiovascular events • Myocardial infarction • Stroke



Ancient kingdom of Colchis



Colchicum autumnale

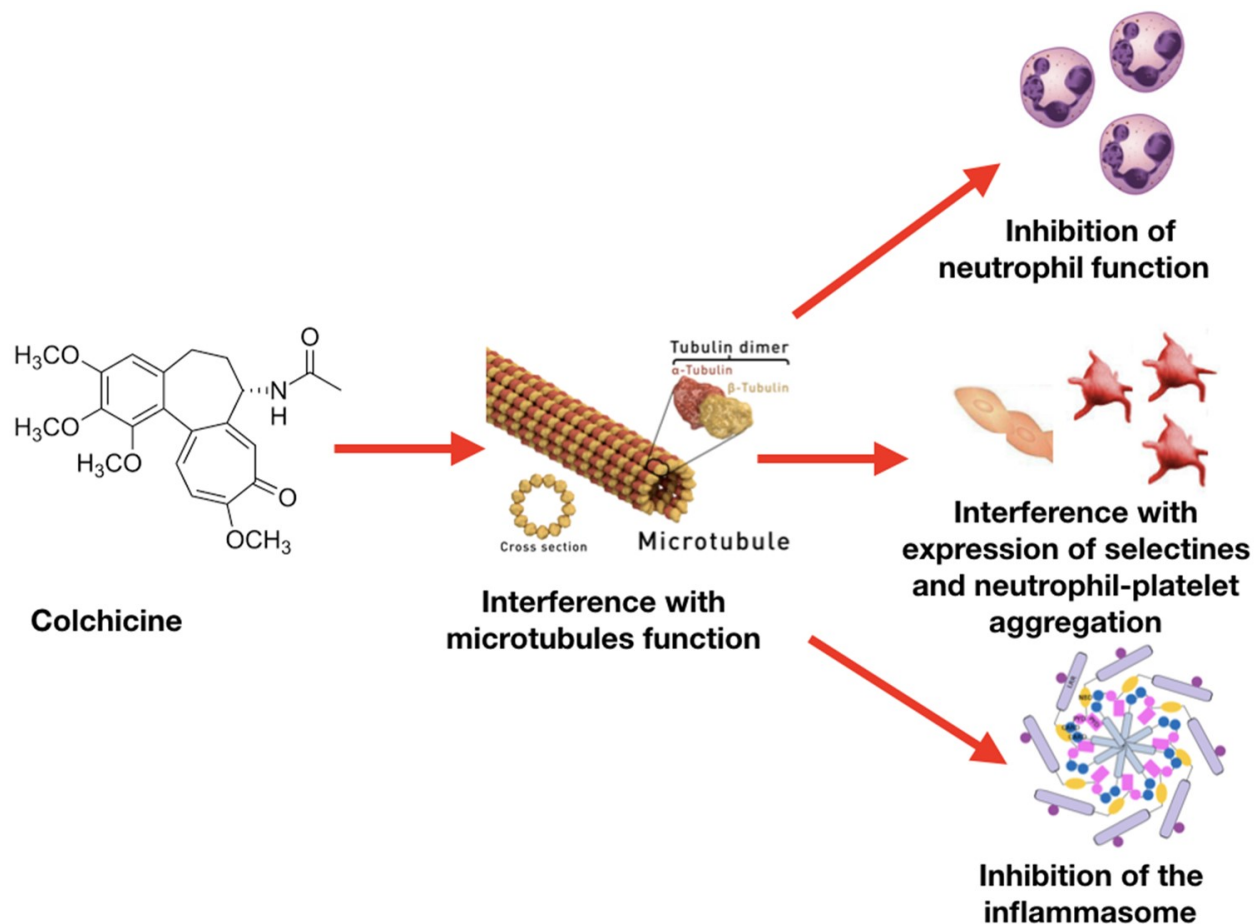


Colchicine



**20 cp: 2.8 Euro
0.07 Euro par jour**

Figure 2 Colchicine anti-inflammatory actions start with the interference with microtubule assembly and function and ...



Associations contre-indiquées

Macrolides

Télithromycine

Azithromycine

Clarithromycine

Erythromycine

Josamycine

Roxithromycine

Midécamycine

Risque d'augmentation des effets indésirables

Risque de **surdosage** potentiellement fatal

Pristinamycine

Risque d'augmentation des effets indésirables de la colchicine

Risque de **surdosage** potentiellement fatal

Associations déconseillées

Ciclosporine

Risque d'addition des effets indésirables des 2 médicaments (myopathie, rhabdomyolyse)

Vérapamil

Risque de majoration des effets indésirables de la colchicine

Inhibiteurs de la protéase boostés par le ritonavir

Lopinavir

Atazanavir

Darunavir

Risque de majoration des effets indésirables de la colchicine

Inhibiteurs puissants du cytochrome P450 3A4

Kétoconazole

Itraconazole,

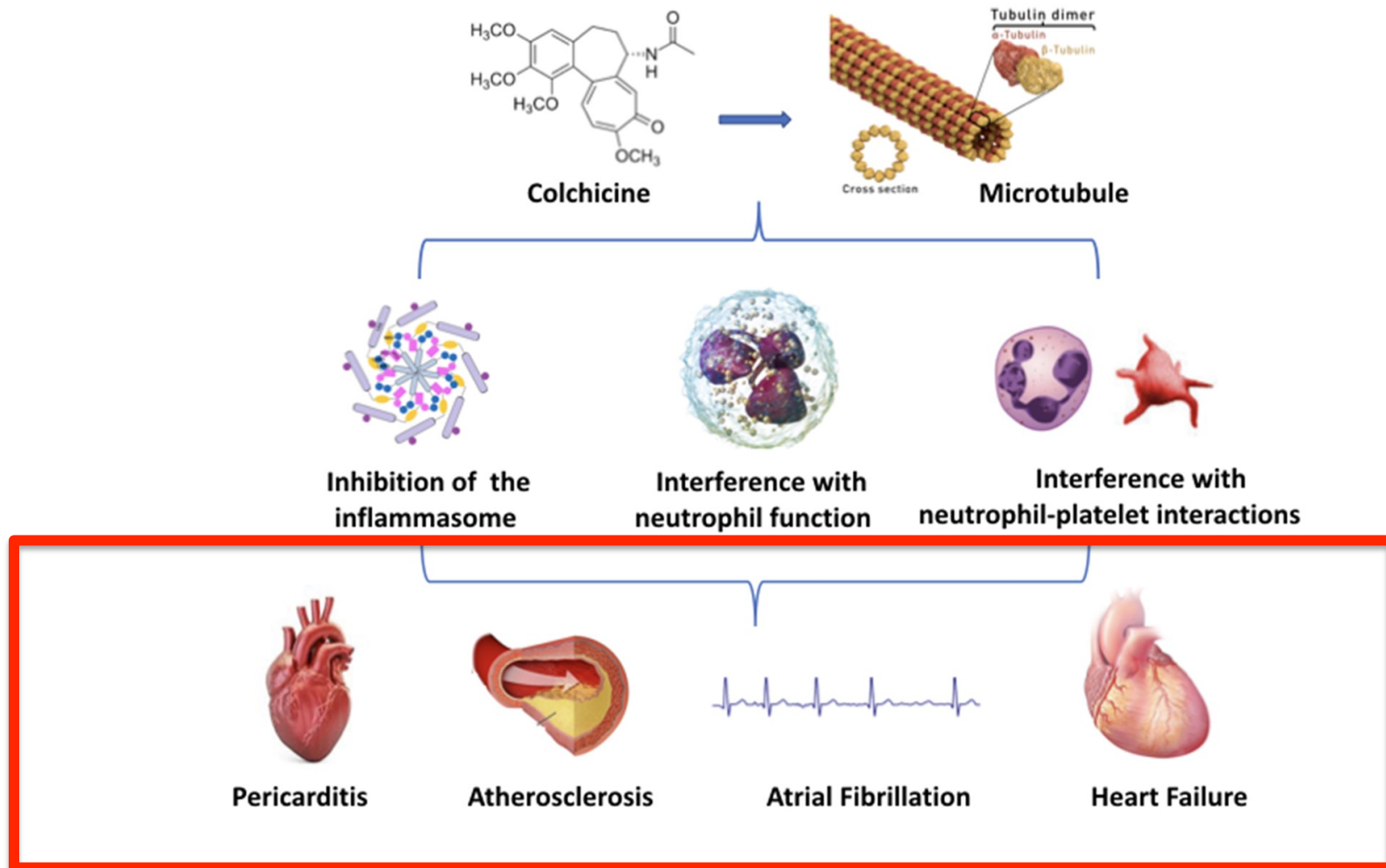
Voriconazole

Posaconazole

Fluconazole

Risque de majoration des effets indésirables de la colchicine

The central mechanism of the anti-inflammatory action of colchicine is the inhibition of microtubule function ...



Pourquoi en avez-vous peu (ou pas) entendu parler ?

Pourquoi en avez-vous peu (ou pas) entendu parler ?



**20 cp: 2.8 Euro
0.07 Euro par jour**

Les reco

4.10. Anti-inflammatory therapy

Recommendation for anti-inflammatory therapy

Recommendation	Class ^a	Level ^b
Low-dose colchicine (0.5 mg <i>o.d.</i>) may be considered in secondary prevention of CVD, particularly if other risk factors are insufficiently controlled or if recurrent CVD events occur under optimal therapy. ^{85,86}	IIb	A

© ESC 2021

CVD = cardiovascular; *o.d.* = *omni die* (once a day).

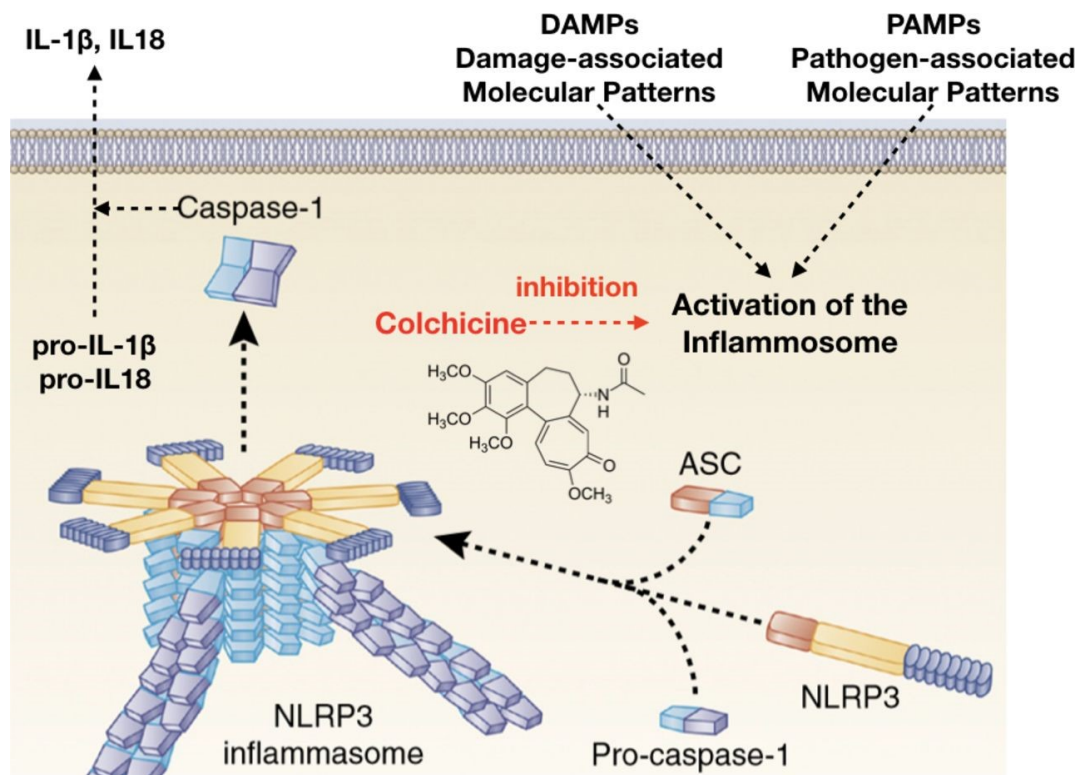
^aClass of recommendation.

^bLevel of evidence.

Priorisation des effets thérapeutiques chez le coronarien stable à l'ère moderne

- AAP
 - Statine
 - BB
 - IEC/ARA 2
 - Fibrates
 - Omega 3
 - PCSK9
 - Ca(-)
 - AOD
 -
- AOD (Riva 2.5 dans Compass)
 - Colchicine
 - Statine
 - AAP

coronary artery disease
 oCo trial, showing
 (0.5 mg/day) and
 up in stable CAD
 confirmed by the
 starting a 31% lower
 s treated with col-
 coronary syndromes,



In this scenario, Bouabdallaoui *et al.*⁵ performed a meta-analysis defining three time frames for time-to-event analysis: namely 0–3 days, 4–7 days, and 8–30 days following MI. To evaluate the optimal timing for colchicine treatment, the study provides precious evidence showing that the administration of low-dose colchicine within 3 days following MI resulted in a significant reduction of cardiovascular outcomes compared to placebo (HR 0.52, 95% CI 0.32–0.84; $P = 0.001$). The incidence of MI, strokes, and urgent hospitalizations for revascularization. Conversely, later colchicine treatment was not associated with a significant reduction in

Role of colchicine in stroke prevention: an updated meta-analysis

L.M. Lobo¹, G. Masson², G. Molinero³, G. Masson³, A. Lavalle Cobo³, P. Losada¹, F. Benincasa¹, F. Suarez¹, M. Huerin³

¹Campo de Mayo Military Hospital, Buenos Aires, Argentina; ²Italian Hospital, Caba, Argentina; ³Council of Epidemiology and Cardiovascular Prevention, Argentine Society of Cardiology, Caba, Argentina

Funding Acknowledgement: Type of funding source: None

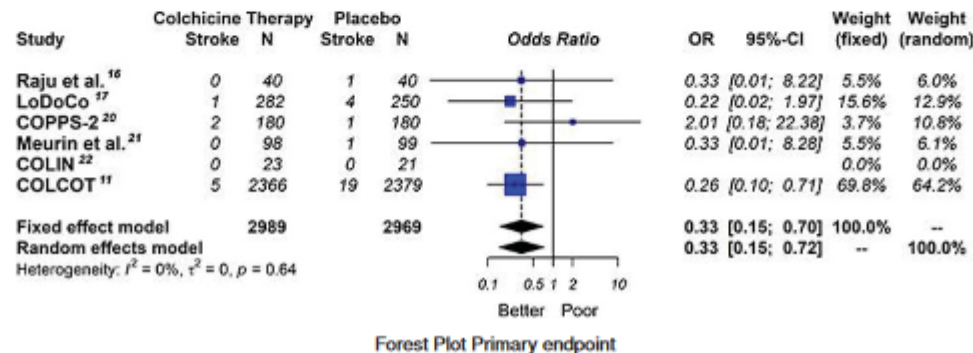
Background: Colchicine is a microtubule inhibitor with anti-inflammatory properties. As the body and quality of evidence regarding the efficacy of colchicine for cardiovascular prevention is controversial, the aims of this study was to evaluate the effect of colchicine therapy on vascular events.

Methods: A meta-analysis was performed of randomized controlled clinical trials of colchicine on high cardiovascular risk populations, reporting data from stroke, myocardial infarction, cardiovascular mortality and all-cause mortality, after searching the PubMed/MEDLINE, Embase and Cochrane Controlled Trials databases. A random-effects meta-analysis model was then applied.

Results: Nine eligible trials of colchicine therapy, involving a total of 6630

patients, were considered eligible for analysis (3359 subjects were allocated to receive colchicine while 3271 subjects were allocated to the respective control arms). The stroke incidence was lower in the colchicine group compared with placebo arm (OR, 0.33; 95% CI, 0.15–0.70; six studies evaluated). We did not find a significant reduction in the incidence of myocardial infarction, cardiovascular mortality or all-cause mortality.

Conclusion: Our data suggest that in a population with high cardiovascular risk, the use of colchicine results in significantly reduction on stroke risk. Colchicine is an accessible drug that could be successfully utilized for the prevention of atherosclerotic cerebrovascular disease. The tolerability and benefits should be confirmed in ongoing clinical trials.



Efficacy and safety of low-dose colchicine in patients with coronary disease: a systematic review and meta-analysis of randomized trials

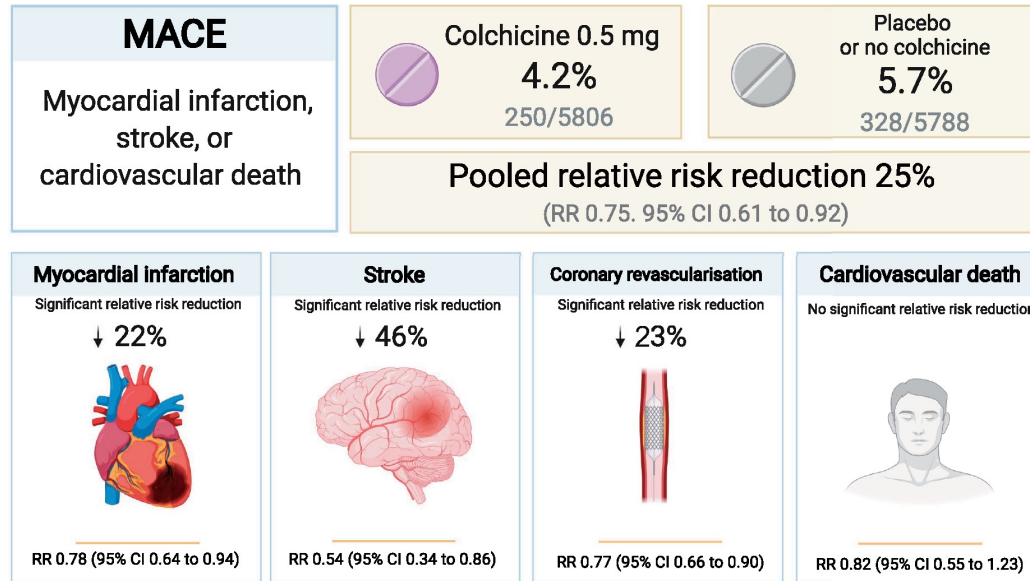
Aernoud T.L. Fiolet^{1,2†}, Tjerk S.J. Opstal^{3,4†}, Arend Mosterd^{2,5,6}, John W. Eikelboom⁷, Sanjit S. Jolly⁸, Anthony C. Keech⁹, Peter Kelly¹⁰, David C. Tong^{11,12}, Jamie Layland^{11,12,13}, Stefan M. Nidorf^{14,15}, Peter L. Thompson^{14,16,17}, Charley Budgeon¹⁷, Jan G.P. Tijssen^{18,19‡}, and Jan H. Cornel^{2,3,4*‡}; on behalf of the Colchicine Cardiovascular Trialists Collaboration

Methods and results

We searched the literature for randomized clinical trials of long-term colchicine in patients with atherosclerosis published up to 1 September 2020. The primary efficacy endpoint was MACE, the composite of myocardial infarction, stroke, or cardiovascular death. We combined the results of five trials that included 11 816 patients. The primary endpoint occurred in 578 patients. Colchicine reduced the risk for the primary endpoint by 25% [relative risk (RR) 0.75, 95% confidence interval (CI) 0.61–0.92; $P = 0.005$], myocardial infarction by 22% (RR 0.78, 95% CI 0.64–0.94; $P = 0.010$), stroke by 46% (RR 0.54, 95% CI 0.34–0.86; $P = 0.009$), and coronary revascularization by 23% (RR 0.77, 95% CI 0.66–0.90; $P < 0.001$). We observed no difference in all-cause death (RR 1.08, 95% CI 0.71–1.62; $P = 0.73$), with a lower incidence of cardiovascular death (RR 0.82, 95% CI 0.55–1.23; $P = 0.34$) counterbalanced by a higher incidence of non-cardiovascular death (RR 1.38, 95% CI 0.99–1.92; $P = 0.060$).

Colchicine in Coronary Disease

A meta-analysis of 5 studies



Potential mechanisms

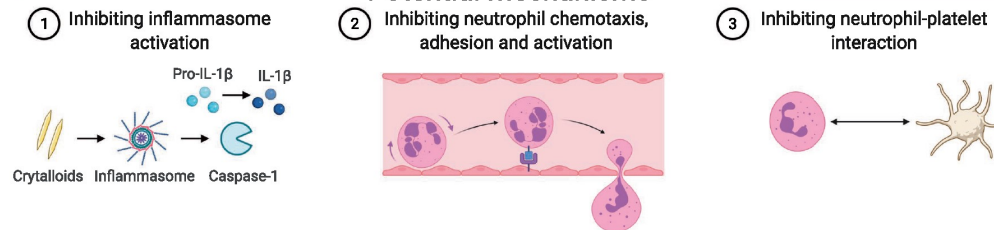


Figure 5 Risk of pericarditis in patients treated with or without colchicine in different settings (acute, recurrent ...

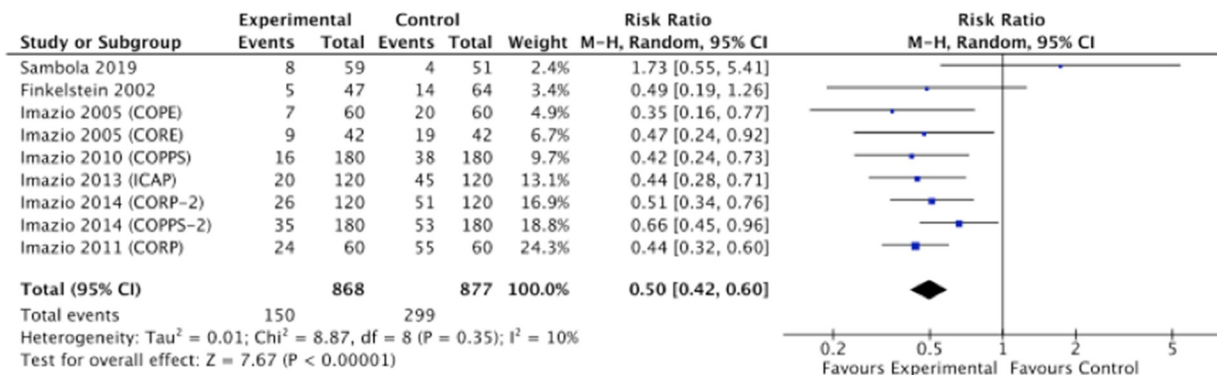
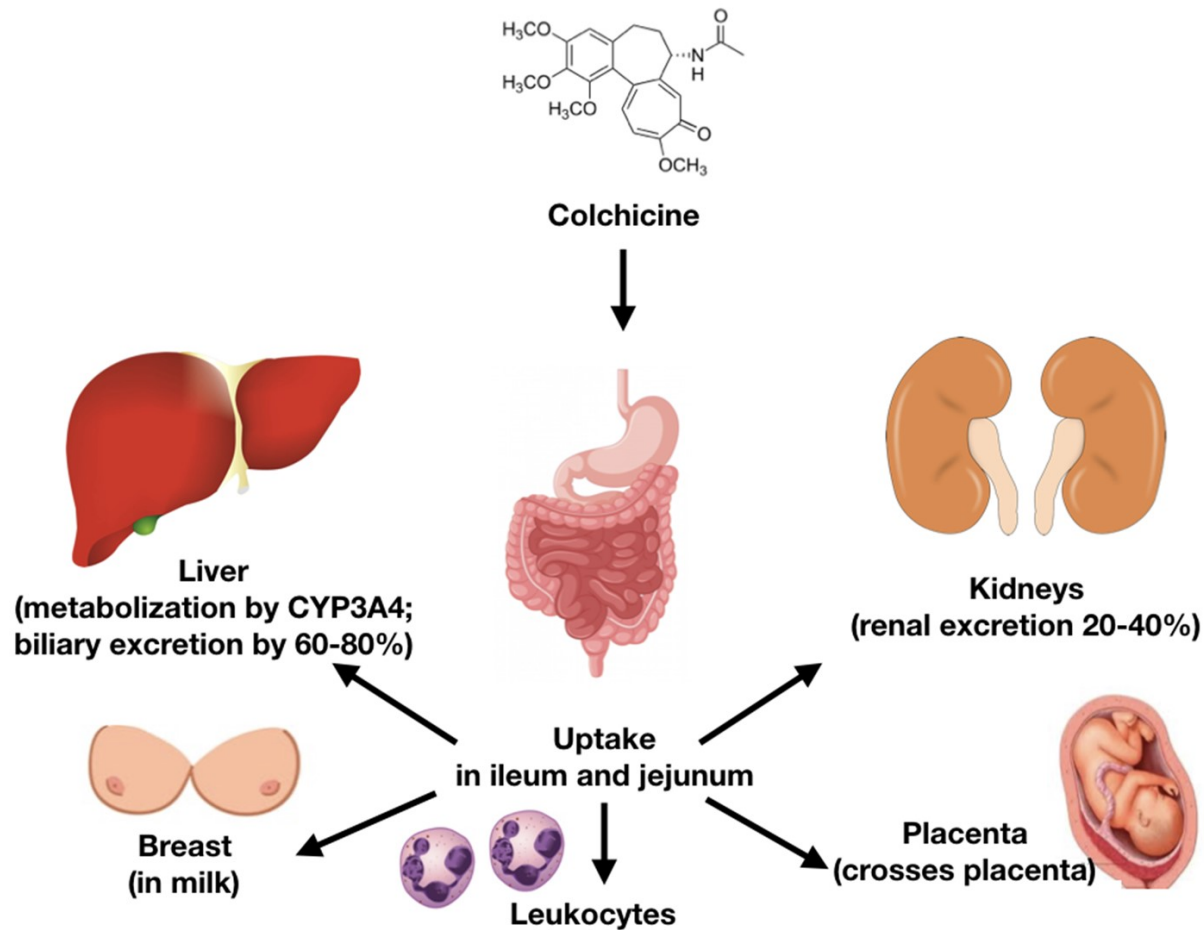


Figure 3 Colchicine uptake occurs in the ileum and jejunum. The drug is metabolized by the liver through cytochrome ...



Role of colchicine in stroke prevention: an updated meta-analysis

L.M. Lobo¹, G. Masson², G. Molinero³, G. Masson³, A. Lavalle Cobo³, P. Losada¹, F. Benincasa¹, F. Suarez¹, M. Huerin³

¹ Campo de Mayo Military Hospital, Buenos Aires, Argentina; ² Italian Hospital, Caba, Argentina; ³ Council of Epidemiology and Cardiovascular Prevention, Argentine Society of Cardiology, Caba, Argentina

Funding Acknowledgement: Type of funding source: None

Background: Colchicine is a microtubule inhibitor with anti-inflammatory properties. As the body and quality of evidence regarding the efficacy of colchicine for cardiovascular prevention is controversial, the aims of this study was to evaluate the effect of colchicine therapy on vascular events.

Methods: A meta-analysis was performed of randomized controlled clinical trials of colchicine on high cardiovascular risk populations, reporting data from stroke, myocardial infarction, cardiovascular mortality and all-cause mortality, after searching the PubMed/MEDLINE, Embase and Cochrane Controlled Trials databases. A random-effects meta-analysis model was then applied.

Results: Nine eligible trials of colchicine therapy, involving a total of 6630

patients, were considered eligible for analysis (3359 subjects were allocated to receive colchicine while 3271 subjects were allocated to the respective control arms). The stroke incidence was lower in the colchicine group compared with placebo arm (OR, 0.33; 95% CI, 0.15–0.70; six studies evaluated). We did not find a significant reduction in the incidence of myocardial infarction, cardiovascular mortality or all-cause mortality.

Conclusion: Our data suggest that in a population with high cardiovascular risk, the use of colchicine results in significantly reduction on stroke risk. Colchicine is an accessible drug that could be successfully utilized for the prevention of atherosclerotic cerebrovascular disease. The tolerability and benefits should be confirmed in ongoing clinical trials.

