Cholestérol et prévention primaire:

Qui traiter?
Le score calcique peut-il m'aider?

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FMH Cardiologie

Cholestérol et prévention primaire:

Qui traiter?
Le score calcique peut-il m’aider?

Conflit d’intérêt: aucun

Prévention primaire de la maladie cardio-vasculaire

- Maladies cardio-vasculaires:
  - Causes majeures de morbidité et mortalité dans notre société
  - Dues en grande partie à des FRCVs modifiables
    - Tabac
    - HTA
    - Diabète
    - Inactivité
    - Hypercholestérolémie

Prévention primaire de la maladie cardio-vasculaire

Premières actions à entreprendre par le corps médical:

- Arrêt du tabac!!!!
- Alimentation saine
- Activité physique

-> Mesures les plus efficaces en prévention primaire, et surtout très «cost-effective»

DM1

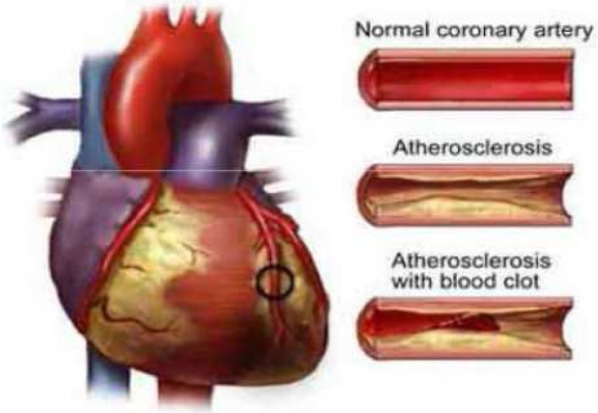
Prévention primaire de la maladie cardio-vasculaire

Prévention primaire:

- Avant toute manifestation clinique de la maladie

Prévention secondaire:

- Maladie athéromateuse clinique manifeste (infarctus, AVC, IAMI)
- -> risque cardiovasculaire considéré élevé d'office
- -> autre recommandations thérapeutiques



Diapositive 5

DM1 Dr Mossaz; 19.09.2020

Le cholestérol, un facteur de risque cardio-vasculaire?

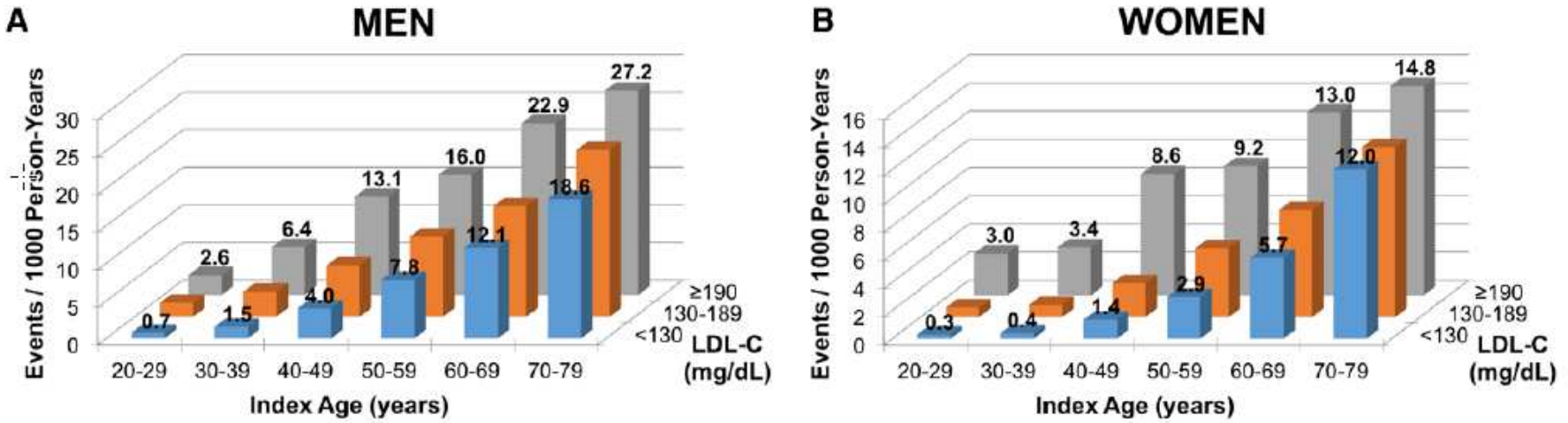
Le cholestérol, un facteur de risque cardio-vasculaire?

- Données de multiples études:
    - de cohorte (Framingham etc…)
    - Études de génétique mendelienne
    - Observationnelles
    - Etudes randomisées contrôlées

-> Plus le cholestérol est élevé, plus le risque CV augmente

->Marqueur le plus important: le LDL

Le cholestérol, un facteur de risque cardio-vasculaire?



Perak et al, Circulation 2016

Le cholestérol, un facteur de risque cardio-vasculaire?

Table 1 **Criteria for causality: low-density lipoprotein (LDL) and atherosclerotic cardiovascular disease (ASCVD)**

Criterion (modified from reference[5])	Evidence grade	Summary of the evidence (references)
1. Plausibility	1	LDL and other apolipoprotein (apo) B-containing lipoproteins (very low-density lipoprotein their remnants, intermediate-density lipoprotein and lipoprotein(a)) are directly implicated in the initiation and progression of ASCVD; experimentally induced elevations in plasma LDL and other apoB-containing lipoproteins lead to atherosclerosis in all mammalian species studied.[2,5–12]
2. Strength	1	Monogenic and polygenic-mediated lifelong elevations in LDL lead to markedly higher lifetime risk.[13–20,27–31,40,43]
3. Biological gradient	1	Monogenic lipid disorders, prospective cohort studies, Mendelian randomization studies, and randomized intervention trials uniformly demonstrate a dose-dependent, log-linear association between the absolute magnitude of exposure to LDL and risk of ASCVD[13–22,27–36,38–40,42–47]
4. Temporal sequence	1	Monogenic lipid disorders and Mendelian randomization studies demonstrate that exposure to elevated LDL precedes the onset of ASCVD[13–20,27–31,40,43]
5. Specificity	1	Mendelian randomization studies and randomized intervention trials both provide unconfounded randomized evidence that LDL is associated with ASCVD independent of other risk factors[28,31–33,40,43]
6. Consistency	1	Over 200 studies involving more than 2 million participants with over 20 million person-years of follow-up and more than 150 000 cardiovascular events consistently demonstrate a dose-dependent, log-linear association between the absolute magnitude of exposure to LDL and risk of ASCVD[13–22,27–36,38–40,42–47]
7. Coherence	1	Monogenic lipid disorders, prospective cohort studies, Mendelian randomization studies, and randomized intervention trials all show a dose-dependent, log-linear association between the absolute magnitude of exposure to LDL and risk of ASCVD[15–18,21,22,28,30–32,35,36,43,44,47]
8. Reduction in risk with intervention	1	More than 30 randomized trials involving over 200 000 participants and 30 000 ASCVD events evaluating therapies specifically designed to lower LDL (including statins, ezetimibe, and PCSK9 inhibitors) consistently demonstrate that reducing LDL cholesterol (LDL-C) reduces the risk of ASCVD events proportional to the absolute reduction in LDL-C[32–34,38,39,42,45–47]

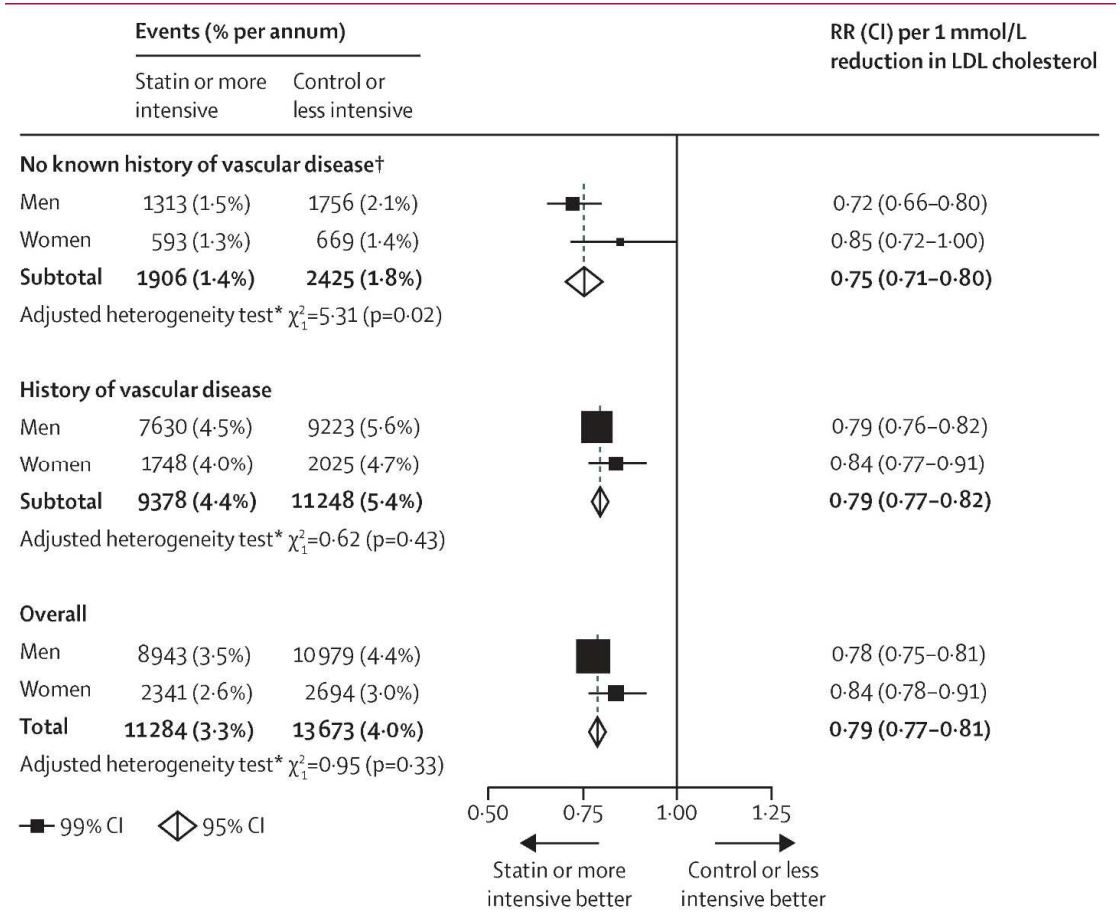
Eur Heart J 2017;38:2459

Diminuer le cholestérol, est-ce utile?

Diminuer le cholestérol, est-ce utile?

- Oui!!
  - Données d'étude randomisées et de méta-analyses
  - Prévention primaire et secondaire

Diminuer le cholestérol, est-ce utile?



Meta-analyse
27 études randomisées
statine vs placebo
174 000 patients

CTT:
Cholesterol treatment trialists' collabortion

CTT et al. Lancet. 2015 Apr 11;385(9976):1397-405.

Diminuer le cholestérol, est-ce utile?

Bénéfices:

- Pour chaque mmol/L de LDL abaissé

  - > diminution sur 5 ans en risque relatif:

    - 22% d'évènements coronariens
    - 20 % mort coronarienne
    - 17% AVC
    - 10% mortalité globale

CTT et al. Lancet. 2015 Apr 11;385(9976):1397-405.

Qui traiter???

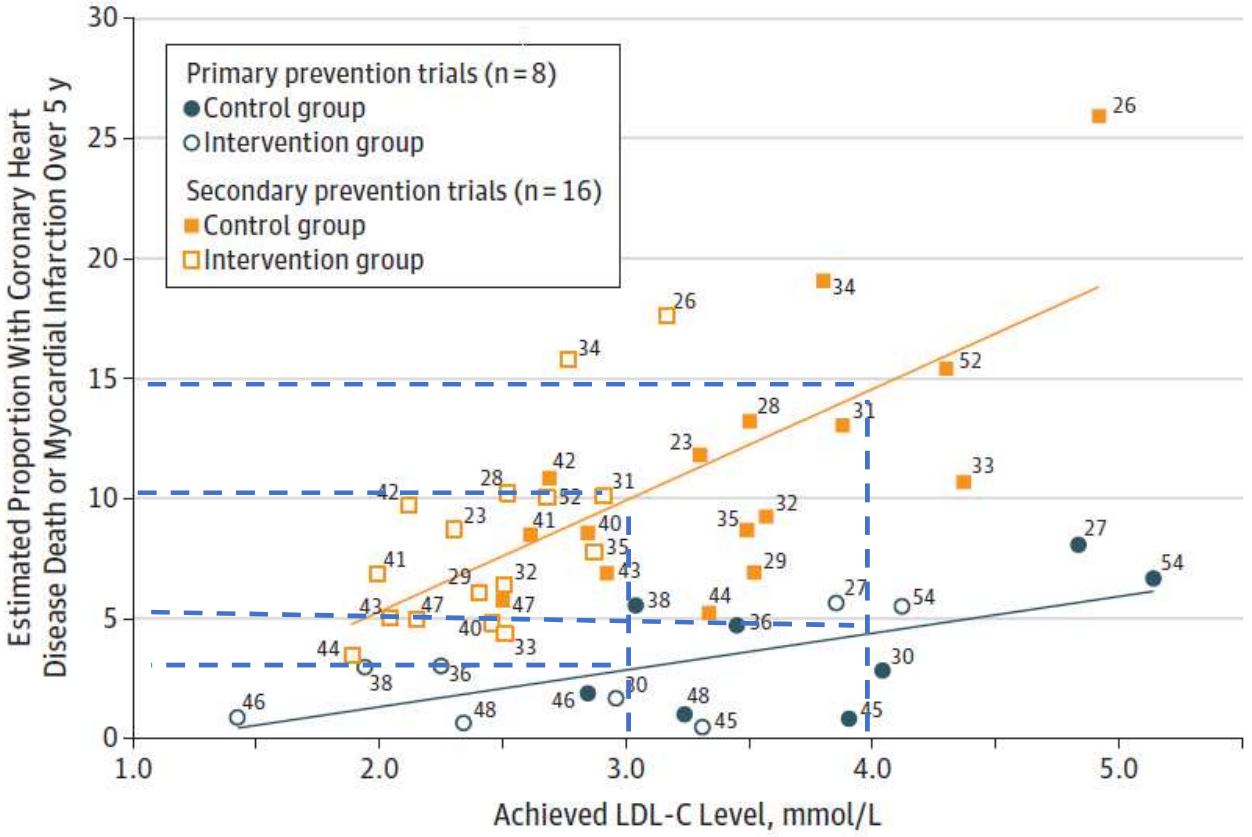
Bénéfices cardiovasculaires à 5 ans de baisser le LDL-cholestérol

Réduction du risque

absolu relatif

5% 30%

2% 30%

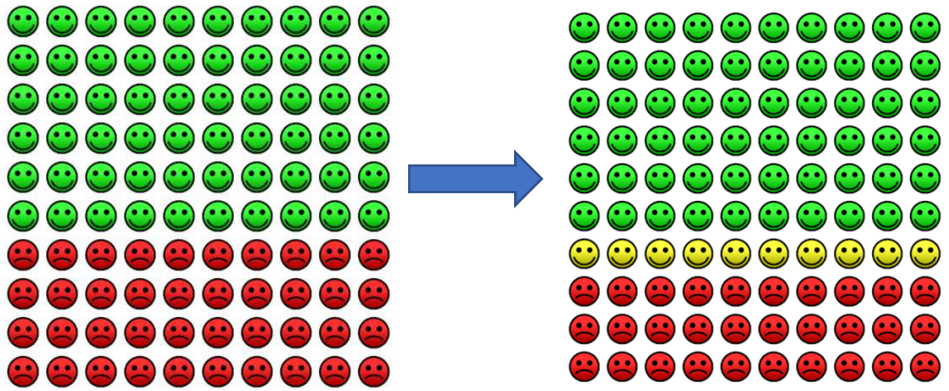


Silverman et al. JAMA 2016

Le bénéfice du traitement dépend du risque cardiovasculaire absolu

Intervention réduisant le risque cardiovasculaire de 25% = risque relatif

Risque absolu à 5 ans 40%

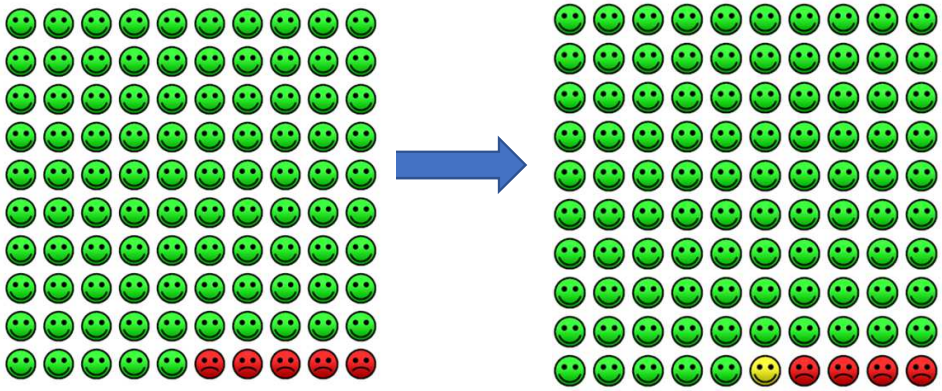


Risque absolu 30%

Différence de risque absolu = 10% = 0.1

Number needed to treat (NNT)
= 1/différence de risque absolu = **10 pendant 5 ans**

Risque absolu à 5 ans 5%



Risque absolu 4%

Différence de risque absolu = 1% = 0.01

Number needed to treat (NNT)
= 1/différence de risque absolu = **100 pendant 5 ans**

Slide: Dr . Nanchen, PMU, CHUV

Réduction risque relatif/risque absolu

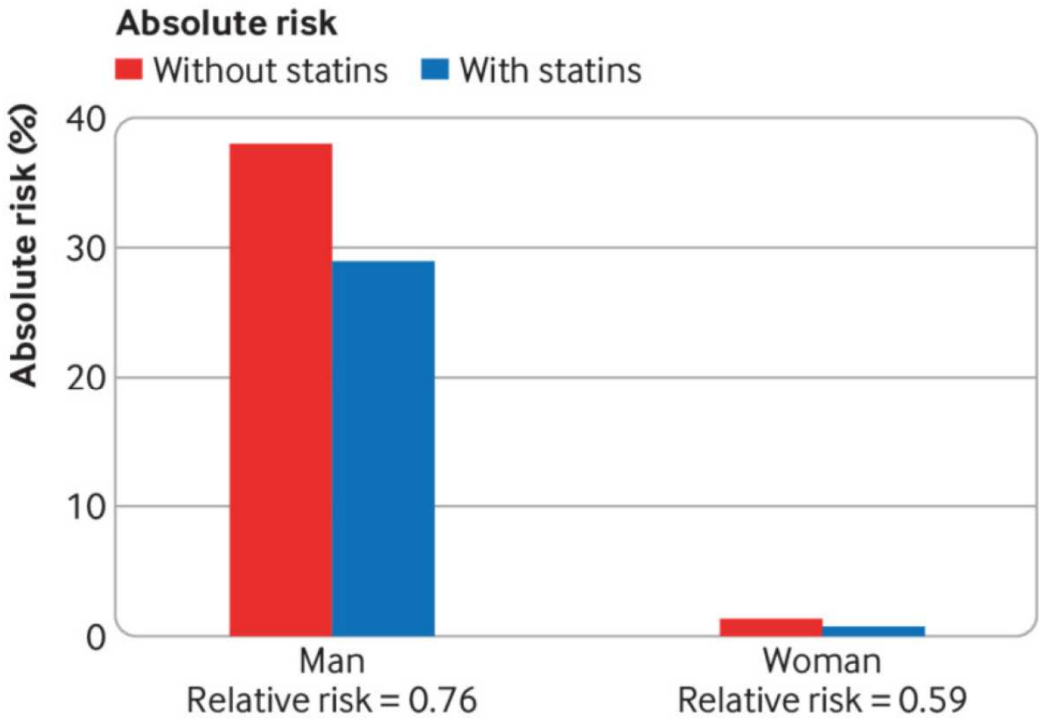


Fig 1 Reduction in absolute risk of major coronary event in next 10 years from taking statins for a hypothetical high risk man and low risk woman

Byrne and al. BMJ 2019

Qui traiter???

- **Nécessité d'évaluer le risque cardiovasculaire global**

  - Risque considéré comme élevé d'office chez certaines catégories de la population (par exemple prévention secondaire)

  - Prévention primaire:
    - Risque estimé dans une population générale
    - Comment est-il évalué??

    -> Dérivé d'étude de cohorte (Framingham, Procam etc…)

Qui traiter???

Comment évaluer le risque CV des patients sans maladie CV (ou équivalent) connue?

-> Calculateurs de risque cardiovasculaire:

- Européen: SCORE
- American College of Cardiology
- Framingham
- Suisse: AGLA/GSLA

Qui traiter???

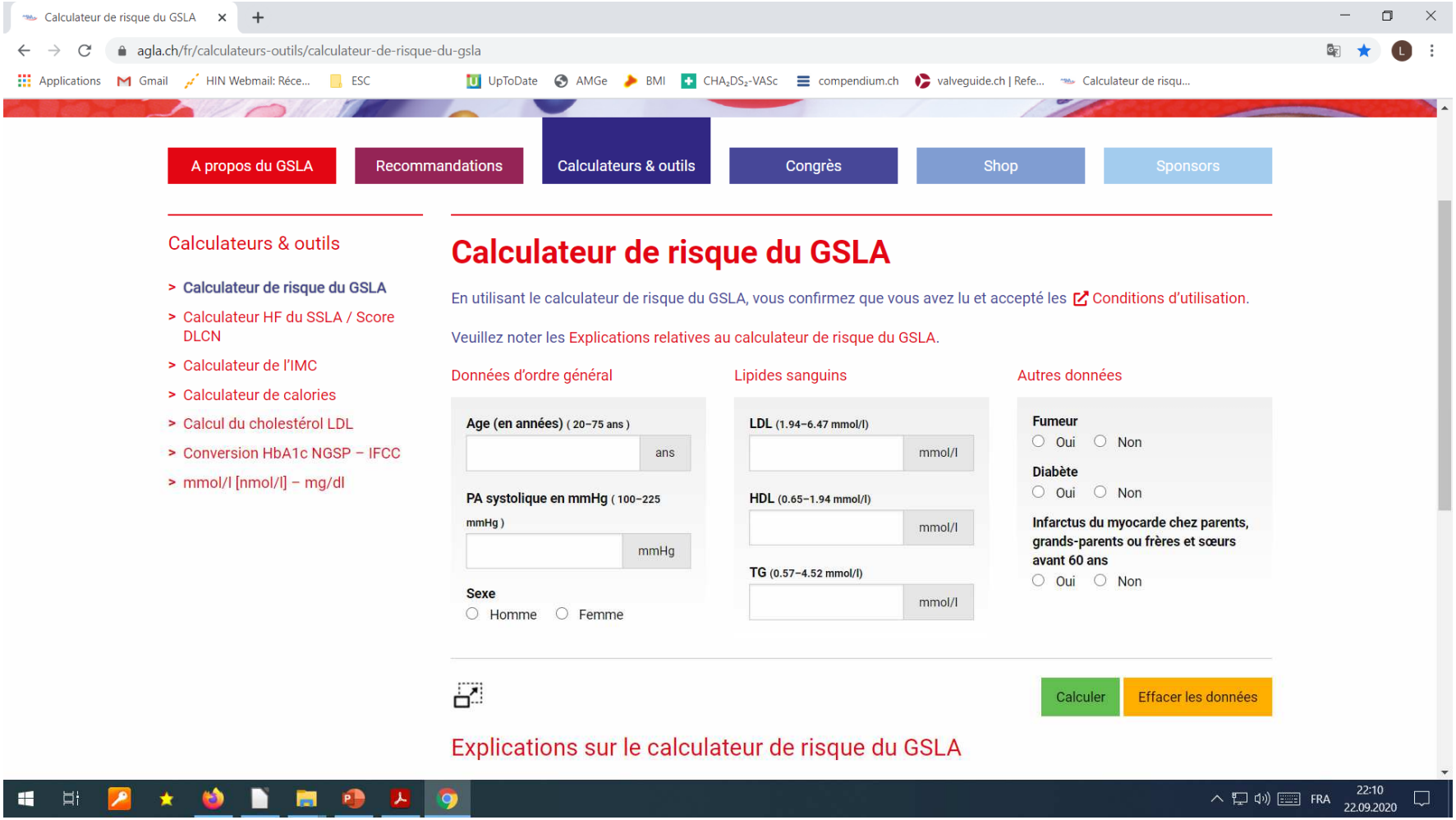
Suisse ->

Score proposé par le GSLA:

- Dérivé de l'étude PROCAM (population allemande)
- Adaptation discrète en fonction des données de la population cible

PROCAM Study Assman. G; American Heart J, 1988

Site: gsla.ch


Calculateur de risque du GSLA
agla.ch/fr/calculateurs-outils/calculateur-de-risque-du-gsla
A propos du GSLA
Recommandations
Calculateurs & outils
Congrès
Shop
Sponsors
Calculateurs & outils
> Calculateur de risque du GSLA
> Calculateur HF du SSLA / Score DLCN
> Calculateur de l'IMC
> Calculateur de calories
> Calcul du cholestérol LDL
> Conversion HbA1c NGSP – IFCC
> mmol/l [nmol/l] – mg/dl
Calculateur de risque du GSLA
En utilisant le calculateur de risque du GSLA, vous confirmez que vous avez lu et accepté les Conditions d'utilisation.
Veuillez noter les Explications relatives au calculateur de risque du GSLA.
Données d'ordre général
Age (en années) (20–75 ans)
ans
PA systolique en mmHg (100–225 mmHg)
mmHg
Sexe
Homme
Femme
Lipides sanguins
LDL (1.94–6.47 mmol/l)
mmol/l
HDL (0.65–1.94 mmol/l)
mmol/l
TG (0.57–4.52 mmol/l)
mmol/l
Autres données
Fumeur
Oui
Non
Diabète
Oui
Non
Infarctus du myocarde chez parents, grands-parents ou frères et sœurs avant 60 ans
Oui
Non
Calculer
Effacer les données
Explications sur le calculateur de risque du GSLA

Calculateur risque CV selon le GSLA

Profil de risque personnel

du 20.09.2020 pour _____

Données d'ordre général	
Âge	69 ans
Sexe	Femme
Lipides sanguins	
LDL	3.9 mmol/l
HDL	0.9 mmol/l
TG	1.2 mmol/l
Autres données	
Pression artérielle maximale	140 mmHg
Fumeur	Non
Diabète	Non
Infarctus du myocarde chez parents, grands-parents ou frères et sœurs avant 60 ans	Non

Bewertung

10.4 %

Risque intermédiaire

Risque Cardiovasculaire Global

Risque en % de subir un événement coronarien (p. ex. infarctus) mortel ou une crise cardiaque non mortelle en l'espace de 10 ans.

Catégories de risque cardio-vasculaire

Risque faible :

- Score/algorithme de risque du GSLA : risque à 10 ans[4] <10%

Risque modéré :

- Score/algorithme de risque du GSLA : risque à 10 ans[4] 10–20%

Risque élevé :

- Score/algorithme de risque du GSLA : risque à 10 ans[4] >20%

2020 Prévention de l'athérosclérose

Accent mis sur les dyslipidémies

Aperçu des recommandations du Groupe de travail Lipides et Athérosclérose (GSLA) de la Société Suisse de Cardiologie (SSC) ainsi que des European Society of Cardiology (ESC) et European Atherosclerosis Society (EAS)

www.gsla.ch

Qui traiter en prévention primaire???

2019 ESC/EAS Guidelines for the management of dyslipidaemias: *lipid modification to reduce cardiovascular risk*

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

Table 1 **Classes of recommendations**

Classes of recommendations	Definition	Wording to use
Class I	Evidence and/or general agreement that a given treatment or procedure is beneficial, useful, effective.	Is recommended or is indicated
Class II	Conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of the given treatment or procedure.	
Class IIa	Weight of evidence/opinion is in favour of usefulness/efficacy.	Should be considered
Class IIb	Usefulness/efficacy is less well established by evidence/opinion.	May be considered
Class III	Evidence or general agreement that the given treatment or procedure is not useful/effective, and in some cases may be harmful.	Is not recommended

CLINICAL PRACTICE GUIDELINE

2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the Management of Blood Cholesterol

A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines

Table 2 **Levels of evidence**

Level of evidence A	Data derived from multiple randomized clinical trials or meta-analyses.
Level of evidence B	Data derived from a single randomized clinical trial or large non-randomized studies.
Level of evidence C	Consensus of opinion of the experts and/or small studies, retrospective studies, registries.

Qui traiter en prévention primaire???

Recommandations européennes ESC 2019

Recommendations	Class[a]	Level[b]
In secondary prevention for patients at very-high risk,[c] an LDL-C reduction of ≥50% from baseline[d] and an LDL-C goal of <1.4 mmol/L (<55 mg/dL) are recommended.[33–35,119,120]	I	A
In primary prevention for individuals at very-high risk but without FH,[c] an LDL-C reduction of ≥50% from baseline[d] and an LDL-C goal of <1.4 mmol/L (<55 mg/dL) are recommended.[34–36]	I	C
In primary prevention for individuals with FH at very-high risk, an LDL-C reduction of ≥50% from baseline and an LDL-C goal of <1.4 mmol/L (<55 mg/dL) should be considered.	IIa	C
For patients with ASCVD who experience a second vascular event within 2 years (not necessarily of the same type as the first event) while taking maximally tolerated statin-based therapy, an LDL-C goal of <1.0 mmol/L (<40 mg/dL) may be considered.[119,120]	IIb	B
In patients at high risk,[c] an LDL-C reduction of ≥50% from baseline[d] and an LDL-C goal of <1.8 mmol/L (<70 mg/dL) are recommended.[34,35]	I	A
In individuals at moderate risk,[c] an LDL-C goal of <2.6 mmol/L (<100 mg/dL) should be considered.[34]	IIa	A
In individuals at low risk,[c] an LDL-C goal <3.0 mmol/L (<116 mg/dL) may be considered.[36]	IIb	A

Qui traiter en prévention primaire???

Recommandations européennes 2019

Recommendations	Class[a]	Level[b]
In patients at high risk,[c] an LDL-C reduction of ≥50% from baseline[d] and an LDL-C goal of <1.8 mmol/L (<70 mg/dL) are recommended.[34,35]	I	A
In individuals at moderate risk,[c] an LDL-C goal of <2.6 mmol/L (<100 mg/dL) should be considered.[34]	IIa	A
In individuals at low risk,[c] an LDL-C goal <3.0 mmol/L (<116 mg/dL) may be considered.[36]	IIb	A

Qui traiter en prévention primaire???

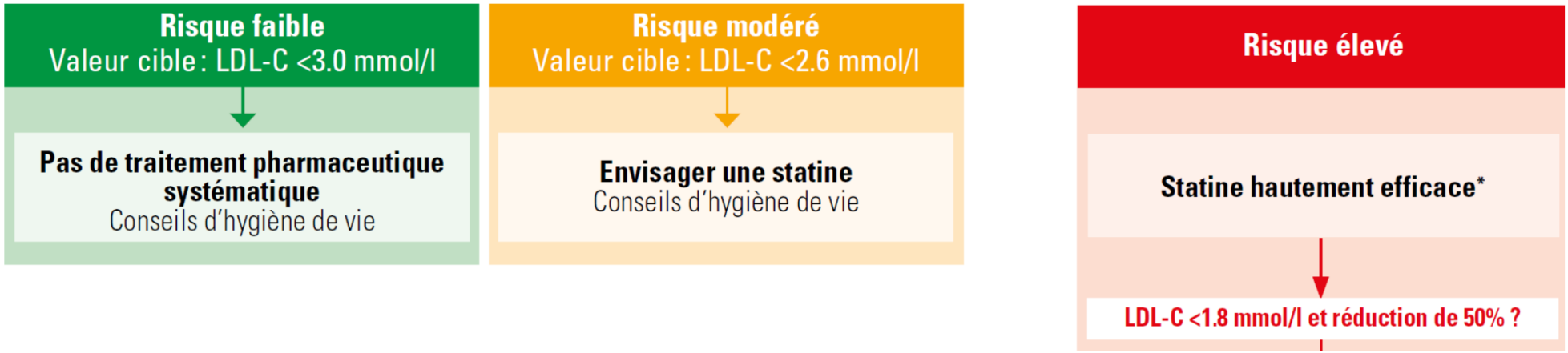
Recommandations européennes:

Table 5 Intervention strategies as a function of total cardiovascular risk and untreated low-density lipoprotein cholesterol levels

	Total CV risk (SCORE) %	Untreated LDL-C levels					
		<1.4 mmol/L (55 mg/dL)	1.4 to <1.8 mmol/L (55 to <70 mg/dL)	1.8 to <2.6 mmol/L (70 to <100 mg/dL)	2.6 to <3.0 mmol/L (100 to <116 mg/dL)	3.0 to <4.9 mmol/L (116 to <190 mg/dL)	≥4.9 mmol/L (≥190 mg/dL)
Primary prevention	<1, low-risk	Lifestyle advice	Lifestyle advice	Lifestyle advice	Lifestyle advice	Lifestyle intervention, consider adding drug if uncontrolled	Lifestyle intervention and concomitant drug intervention
	Class[a]/Level[b]	I/C	I/C	I/C	I/C	IIa/A	IIa/A
	≥1 to <5, or moderate risk (see *Table 4*)	Lifestyle advice	Lifestyle advice	Lifestyle advice	Lifestyle intervention, consider adding drug if uncontrolled	Lifestyle intervention, consider adding drug if uncontrolled	Lifestyle intervention and concomitant drug intervention

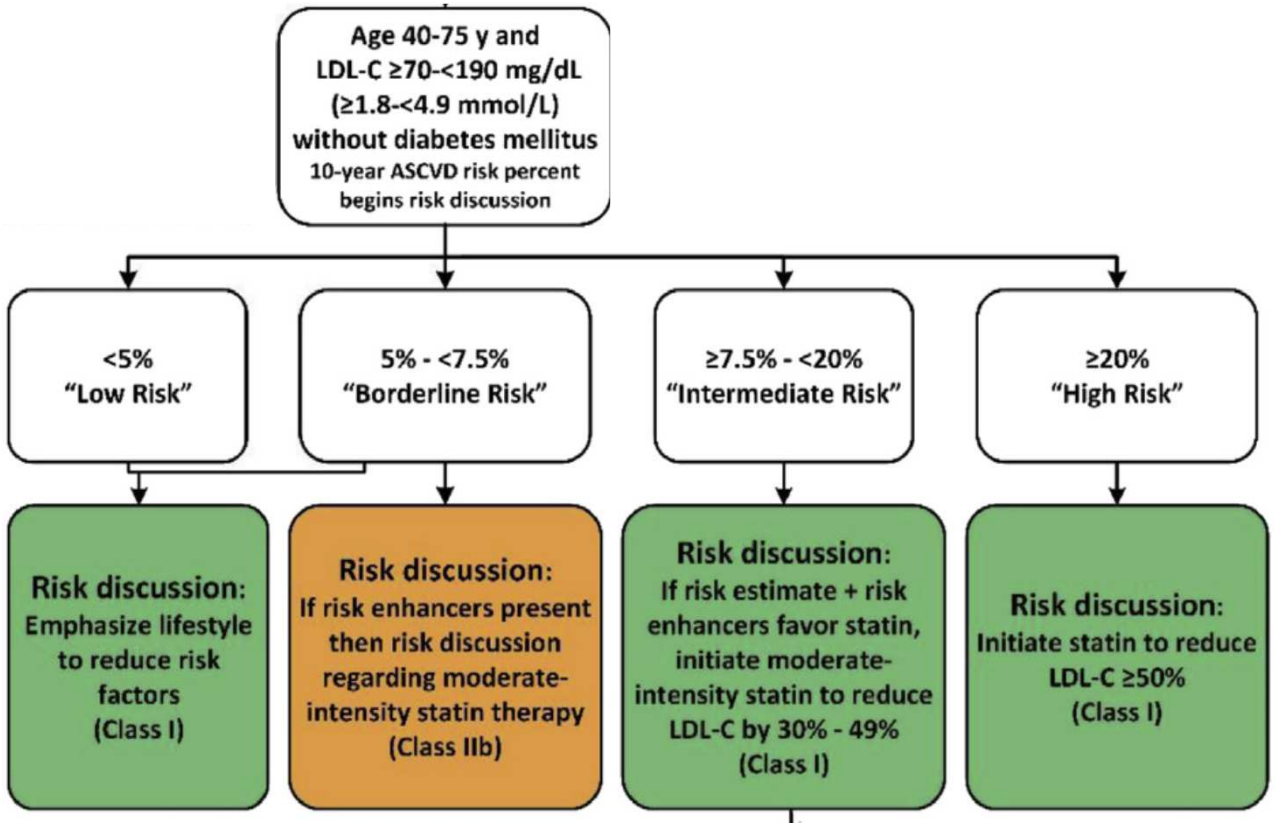
Qui traiter en prévention primaire???

Recommandation du GSLA:



Qui traiter en prévention primaire???

Recommandations américaines ACC 2018



- En résumé selon les Guidelines:

  - Risque calculé faible: pas de statine
  - Risque calculé intermédiaire: une statine doit/devrait être envisagée
  - Risque calculé élevé: statine nécessaire

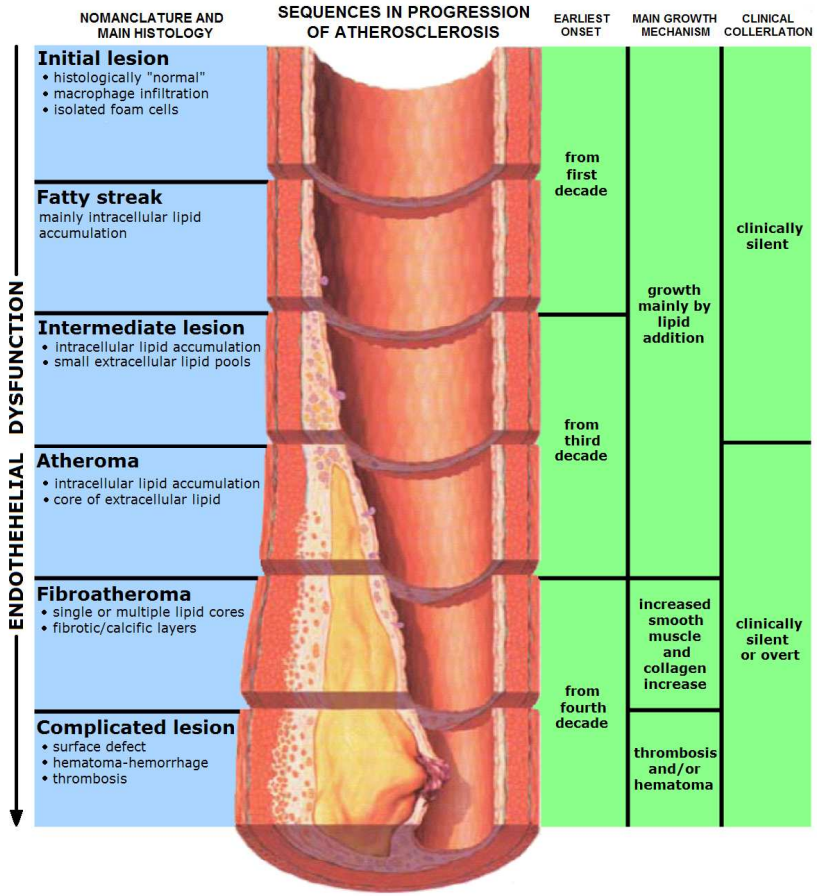
Comment affiner le risque estimé des patients classés «intermédiaires»

- En résumé selon les Guidelines:
  - Risque calculé faible: pas de statine
  - Risque calculé intermédiaire: une statine doit/devrait être envisagée
  - Risque calculé élevé: statine nécessaire

Le score calcique

Quantification de la masse globale de calcium présente autour des artères coronaires

Corrélation avec la «charge globale» de plaque d'athérosclérose



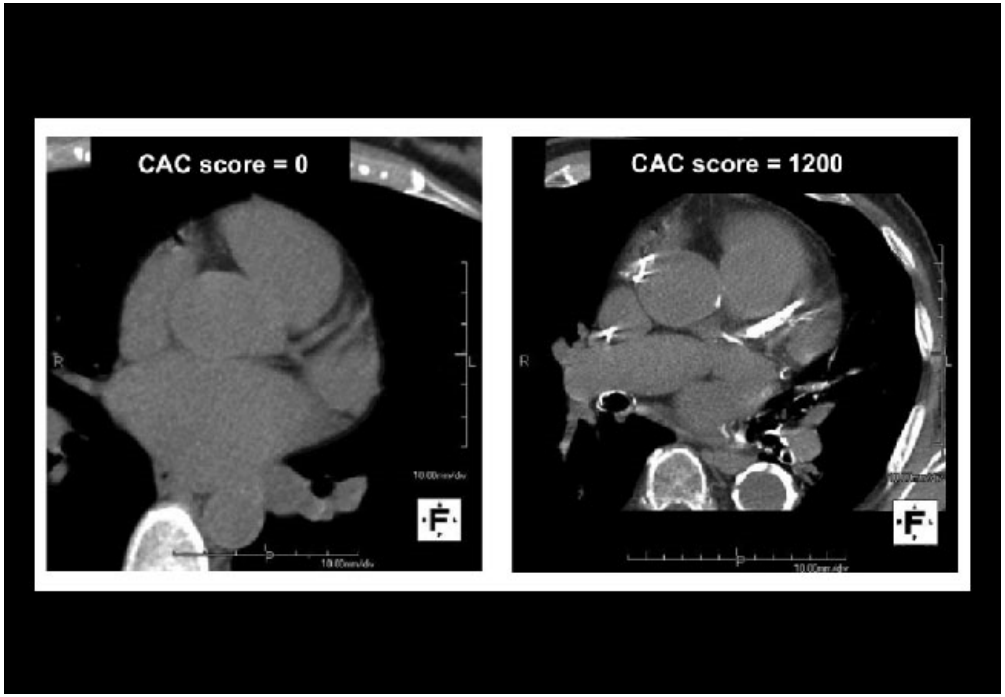
Le score calcique

Unité: Agatston

Réalisation:

- CT natif centré sur le médiastin
- Pas de contraste
- Irradiation: environ équivalent à une mammographie (0.8 mSivert)

- Mesure uniquement des calcifications péri-artérielles. Pas de visualisation de la lumière de l'artère -> pas d'évaluation d'une potentielle sténose



Le score calcique

Utilisation:

- Patient/e asymptomatique!!!
- Prévention primaire uniquement
- Pas d'utilité pour la recherche d'une maladie coronarienne sténosante (contrairement à l'angio-CT coronaire)

Score calcique

ORIGINAL ARTICLE

Coronary Calcium as a Predictor of Coronary Events in Four Racial or Ethnic Groups

Detrano and al; NEJM 2008

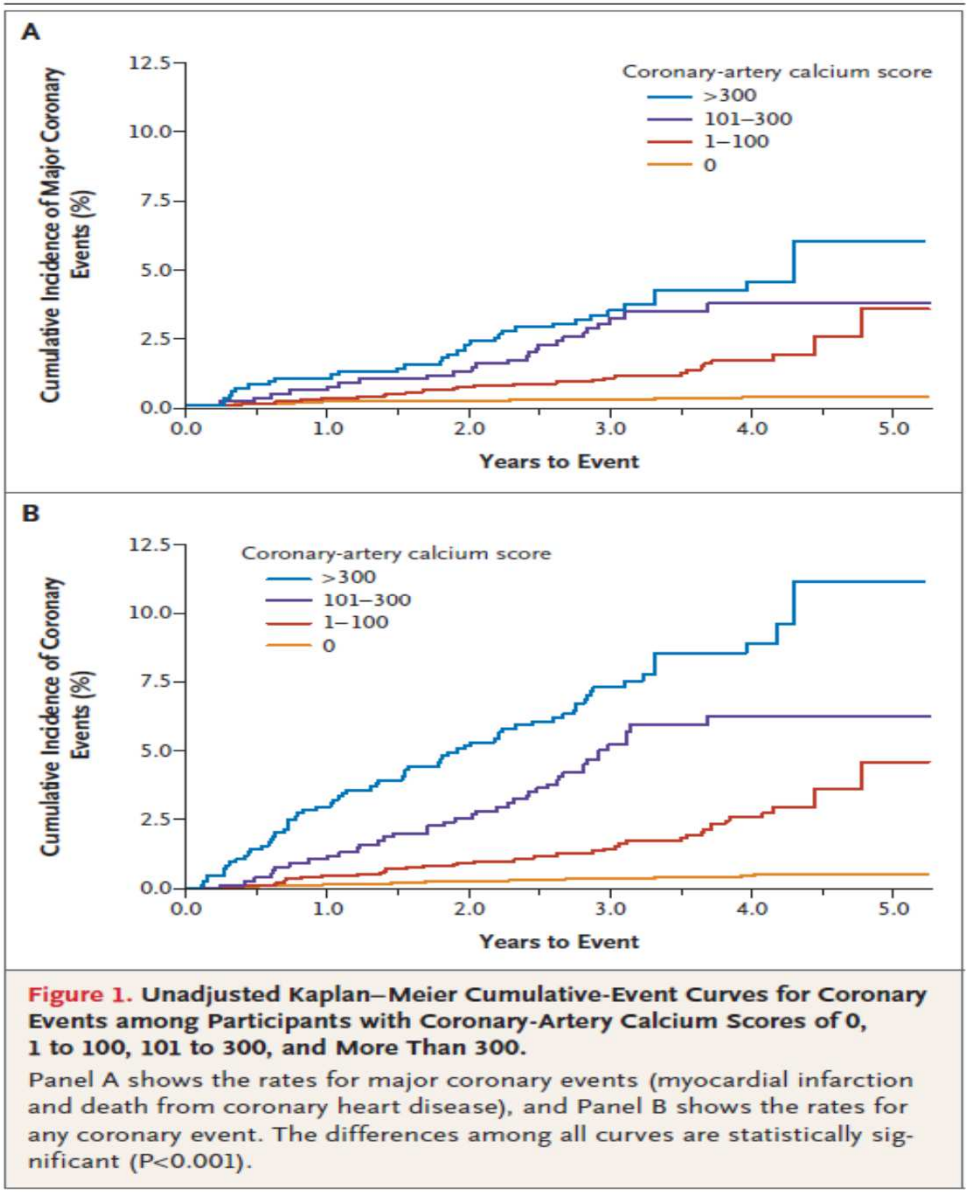


Figure 1. Unadjusted Kaplan–Meier Cumulative-Event Curves for Coronary Events among Participants with Coronary-Artery Calcium Scores of 0, 1 to 100, 101 to 300, and More Than 300.

Panel A shows the rates for major coronary events (myocardial infarction and death from coronary heart disease), and Panel B shows the rates for any coronary event. The differences among all curves are statistically significant ($P<0.001$).

6700 patients
Prévention primaire
Suivi sur 5 ans

Ten-year association of coronary artery calcium with atherosclerotic cardiovascular disease (ASCVD) events: the multi-ethnic study of atherosclerosis (MESA)

Budoff and al; European Heart Journal 2018

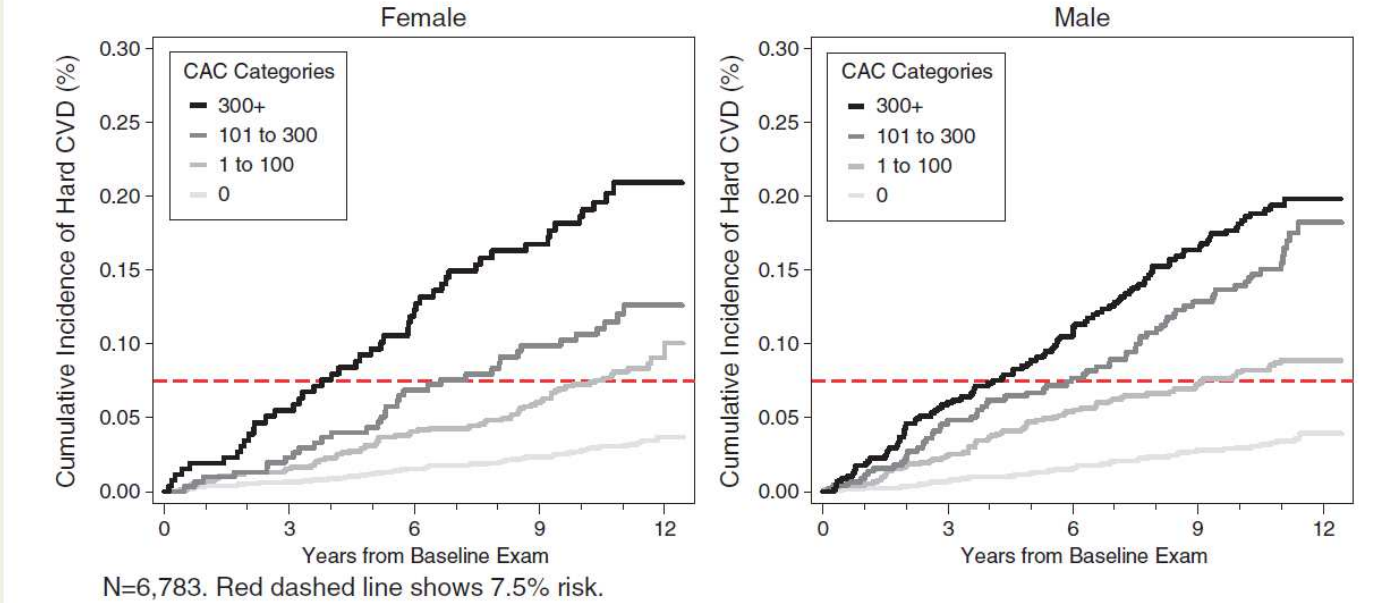


Figure 3 Unadjusted Kaplan–Meier cumulative incidence curves for hard atherosclerotic cardiovascular disease events by categories of coronary artery calcium and sex. *n* = 6783. Red dashed line shows 7.5% risk.

Le score calcique

Recommandations ESC/ACC:

- Précision du risque CV dans la population à risque intermédiaire
- Aide à la décision par rapport à un traitement

ESC:

CAC score assessment with CT may be considered as a risk modifier in the CV risk assessment of asymptomatic individuals at low or moderate risk.[14–16,24,26]	IIb	B

CAC = coronary artery calcium; CT = computed tomography; CV = cardiovascular.

ACC:

IIa	B-NR

6. In intermediate-risk or selected borderline-risk adults, if the decision about statin use remains uncertain, it is reasonable to use a CAC score in the decision to withhold, postpone or initiate statin therapy (S4.4.2-15, S4.4.2-17, S4.4.2-23).

Le score calcique

CENTRAL ILLUSTRATION: Proposed Decision-Making Approach to Selective Use of Coronary Artery Calcium Measurement for Risk Prediction

Using 10-year ASCVD risk estimate plus coronary artery calcium (CAC) score to guide statin therapy				
Patient's 10-year atherosclerotic cardiovascular disease (ASCVD) risk estimate:	<5%	5-7.5%	>7.5-20%	>20%
Consulting ASCVD risk estimate alone	Statin not recommended	Consider for statin	Recommend statin	Recommend statin
Consulting ASCVD risk estimate + CAC				
If CAC score =0	Statin not recommended	Statin not recommended	Statin not recommended	Recommend statin
If CAC score >0	Statin not recommended	Consider for statin	Recommend statin	Recommend statin
Does CAC score modify treatment plan?	✗ CAC not effective for this population	✓ CAC can reclassify risk up or down	✓ CAC can reclassify risk up or down	✗ CAC not effective for this population

Greenland, P. et al. J Am Coll Cardiol. 2018;72(4):434-47.

Le score calcique

TABLE 8 **Selected Examples of Candidates for CAC Measurement Who Might Benefit From Knowing Their CAC Score Is Zero**

CAC Measurement Candidates Who Might Benefit from Knowing Their CAC Score Is Zero
■ Patients reluctant to initiate statin therapy who wish to understand their risk and potential for benefit more precisely
■ Patients concerned about need to reinstitute statin therapy after discontinuation for statin-associated symptoms
■ Older patients (men, 55-80 y of age; women, 60-80 y of age) with low burden of risk factors (S4.4.2-60) who question whether they would benefit from statin therapy
■ Middle-aged adults (40-55 y of age) with PCE-calculated 10-year risk of ASCVD 5% to <7.5% with factors that increase their ASCVD risk, although they are in a borderline risk group

En pratique…

Qu’est ce que je fais dans mon cabinet?

En pratique…

- Traitement de l'hypercholestérolémie utile en prévention primaire sur **une population sélectionnée**

-> Calcul du risque cardiovasculaire

En pratique…

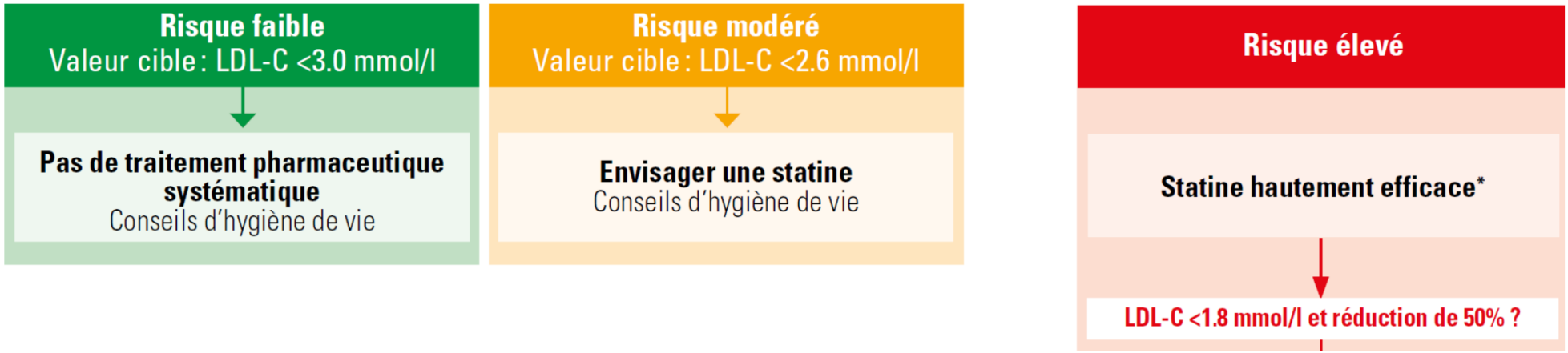
- Quand:
  - Prévention dès l'âge de 20 ans (tabac, sport, alimentation)
  - Estimation du risque CV: à environ 40 ans

En pratique…

- Pour le calcul du risque vers l'âge de 40 ans:
  - Utilisation d'un calculateur (**par ex. glsa.ch**)
  - Age, tabac, anamnèse familiale, tension artérielle
  - Laboratoire:
    - Dépistage du diabète
    - Bilan lipidique complet (Cholestérol total, HDL, LDL, triglycérides)

En pratique…

Recommandation du GSLA:



En pratique…

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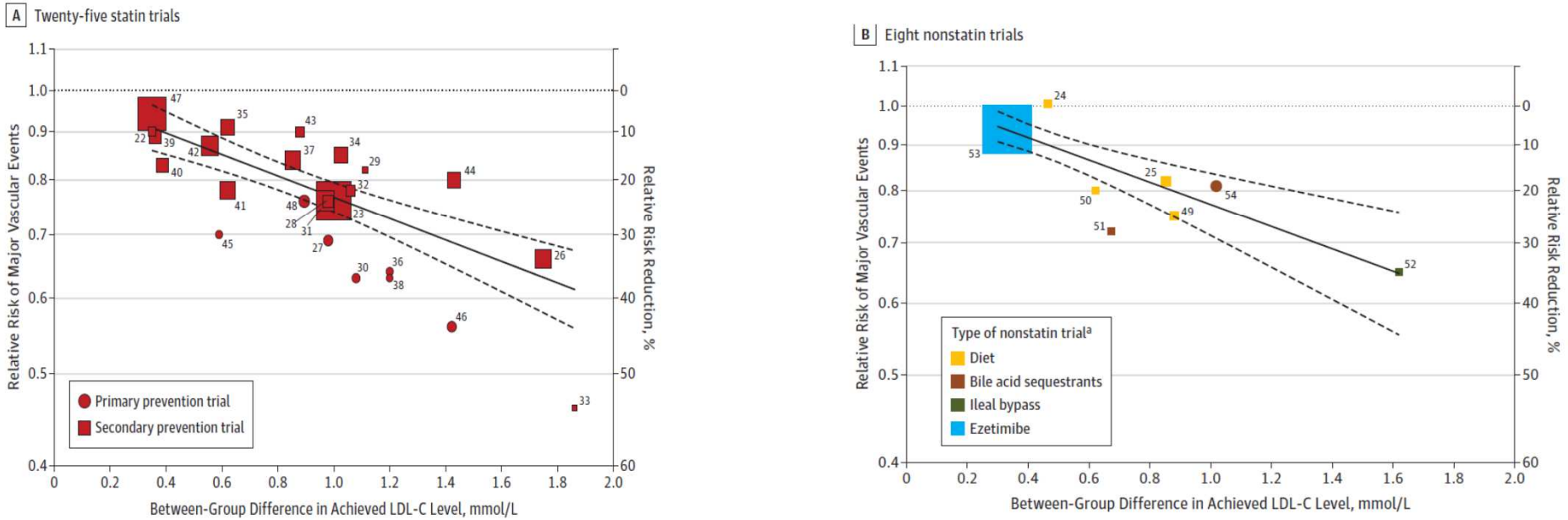
Greenland, P. et al. J Am Coll Cardiol. 2018;72(4):434–47.

Le traitement…

Le traitement

Figure 2. Association of Between-Group Difference in Achieved Low-Density Lipoprotein Cholesterol (LDL-C) Levels and Risk of Major Vascular Events



Silverman et al. JAMA 2016

Le traitement

2019 ESC/EAS Guidelines for the management of dyslipidaemias: *lipid modification to reduce cardiovascular risk*

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

Recommendations for pharmacological low-density lipoprotein cholesterol lowering

Recommendations	Class[a]	Level[b]
It is recommended that a high-intensity statin is prescribed up to the highest tolerated dose to reach the goals set for the specific level of risk.[32,34,38]	I	A
If the goals[c] are not achieved with the maximum tolerated dose of a statin, combination with ezetimibe is recommended.[33]	I	B
For primary prevention patients at very-high risk, but without FH, if the LDL-C goal is not achieved on a maximum tolerated dose of a statin and ezetimibe, a combination with a PCSK9 inhibitor may be considered.	IIb	C
For secondary prevention, patients at very-high risk not achieving their goal[c] on a maximum tolerated dose of a statin and ezetimibe, a combination with a PCSK9 inhibitor is recommended.[119,120]	I	A
For very-high-risk FH patients (that is, with ASCVD or with another major risk factor) who do not achieve their goal[c] on a maximum tolerated dose of a statin and ezetimibe, a combination with a PCSK9 inhibitor is recommended.	I	C
If a statin-based regimen is not tolerated at any dosage (even after rechallenge), ezetimibe should be considered.[197,265,353]	IIa	C
If a statin-based regimen is not tolerated at any dosage (even after rechallenge), a PCSK9 inhibitor added to ezetimibe may also be considered.[197,265,353]	IIb	C
If the goal[c] is not achieved, statin combination with a bile acid sequestrant may be considered.	IIb	C

Le traitement

Recommendations for pharmacological low-density lipoprotein cholesterol lowering

Recommendations	Class[a]	Level[b]
It is recommended that a high-intensity statin is prescribed up to the highest tolerated dose to reach the goals set for the specific level of risk.[32,34,38]	I	A

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Cible du traitement: LDL

In patients at high risk,[c] an LDL-C reduction of ≥50% from baseline[d] and an LDL-C goal of <1.8 mmol/L (<70 mg/dL) are recommended.[34,35]	I	A
In individuals at moderate risk,[c] an LDL-C goal of <2.6 mmol/L (<100 mg/dL) should be considered.[34]	IIa	A
In individuals at low risk,[c] an LDL-C goal <3.0 mmol/L (<116 mg/dL) may be considered.[36]	IIb	A

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Bénéfices des statines en fonction du sexe

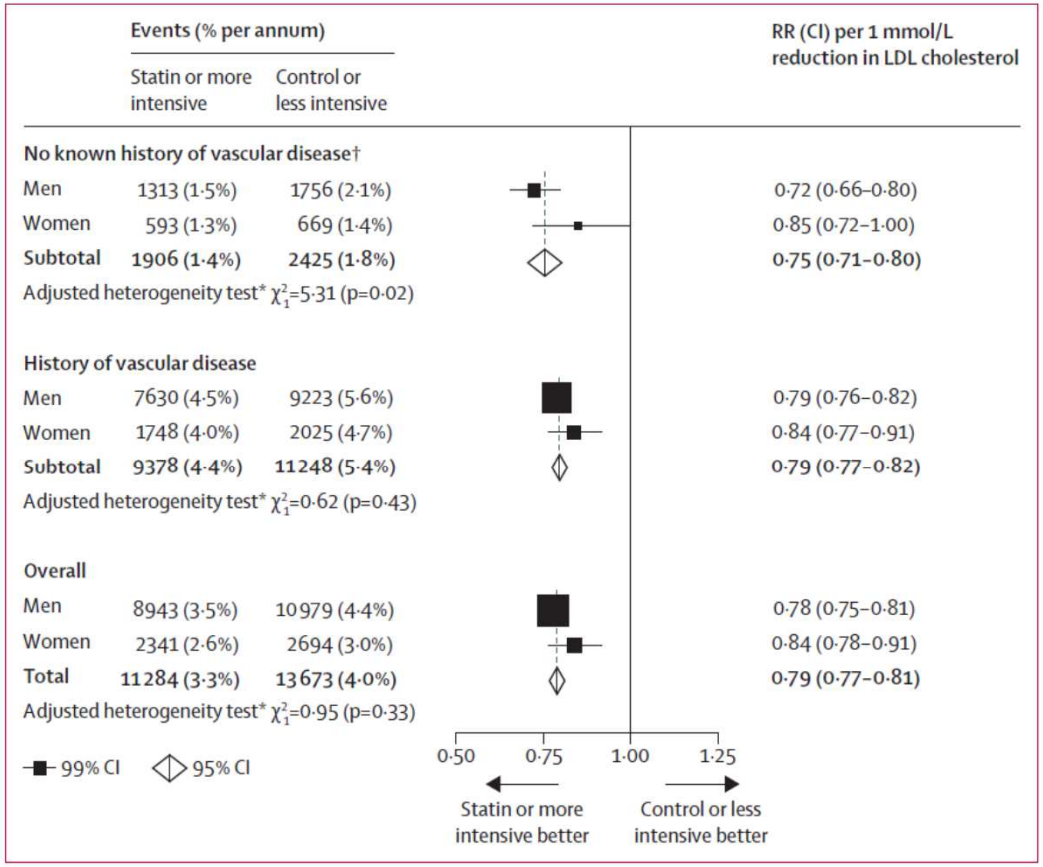

Figure 1: Effects on major vascular events per 1·0 mmol/L reduction in LDL cholesterol, subdivided by history of vascular disease and sex

CTT et al. Lancet. 2015 Apr 11;385(9976):1397-405.

Bénéfices des statines en fonction du sexe

Box 6 Management of dyslipidaemia in women

Statin treatment is recommended for primary prevention of ASCVD in high-risk women.[34,35]
Statins are recommended for secondary prevention in women with the same indications and goals as in men.[34,35]
Lipid-lowering drugs should not be given when pregnancy is planned, during pregnancy, or during the breastfeeding period. However, for severe FH patients, bile acid sequestrants (which are not absorbed) and/or LDL apheresis may be considered.

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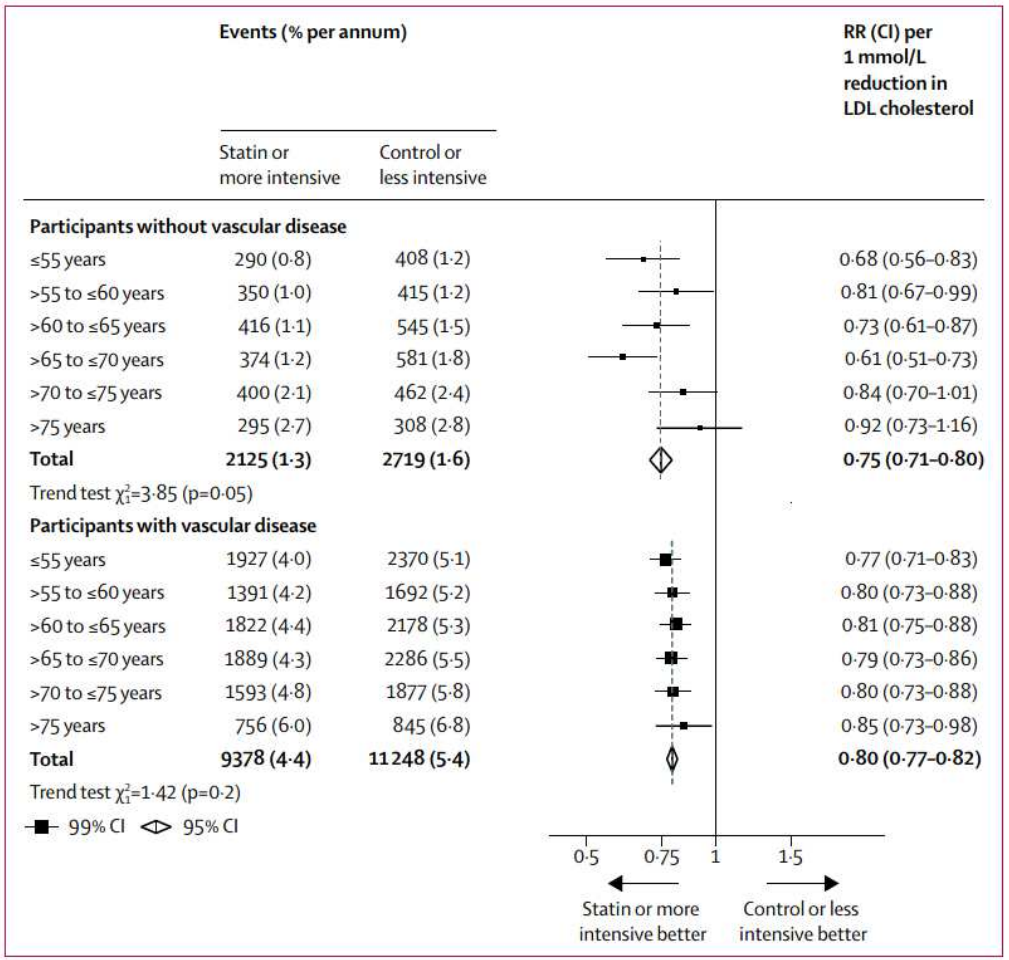
Bénéfices des statines en fonction de l'âge



CTT et al. Lancet. 2019

Bénéfices des statines en fonction de l'âge

Recommendations for the treatment of dyslipidaemias in older people (aged >65 years)

Recommendations	Class[a]	Level[b]
Treatment with statins is recommended for older people with ASCVD in the same way as for younger patients.[217]	I	A
Treatment with statins is recommended for primary prevention, according to the level of risk, in older people aged ≤75 years.[217]	I	A
Initiation of statin treatment for primary prevention in older people aged >75 years may be considered, if at high-risk or above.[217]	IIb	B
It is recommended that the statin is started at a low dose if there is significant renal impairment and/or the potential for drug interactions, and then titrated upwards to achieve LDL-C treatment goals.	I	C

2019 ESC/EAS Guidelines for the management of dyslipidaemias: *lipid modification to reduce cardiovascular risk*

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Quelle statine??

TABLE 3 High-, Moderate-, and Low-Intensity Statin Therapy*

	High Intensity	Moderate Intensity	Low Intensity
LDL-C lowering†	≥50%	30%–49%	<30%
Statins	**Atorvastatin (40 mg‡) 80 mg** **Rosuvastatin 20 mg (40 mg)**	**Atorvastatin 10 mg** (20 mg) **Rosuvastatin** (5 mg) **10 mg** **Simvastatin 20–40 mg§**	Simvastatin 10 mg
	…	**Pravastatin 40 mg** (80 mg) **Lovastatin 40 mg** (80 mg) Fluvastatin XL 80 mg **Fluvastatin 40 mg BID** Pitavastatin 1–4 mg	**Pravastatin 10–20 mg** **Lovastatin 20 mg** Fluvastatin 20–40 mg

CLINICAL PRACTICE GUIDELINE

2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the Management of Blood Cholesterol

A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines

Le traitement: ezetimibe?

Recommendations for pharmacological low-density lipoprotein cholesterol lowering

Recommendations	Class[a]	Level[b]
It is recommended that a high-intensity statin is prescribed up to the highest tolerated dose to reach the goals set for the specific level of risk.[32,34,38]	I	A
If the goals[c] are not achieved with the maximum tolerated dose of a statin, combination with ezetimibe is recommended.[33]	I	B
If a statin-based regimen is not tolerated at any dosage (even after rechallenge), ezetimibe should be considered.[197,265,353]	IIa	C

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Prix des traitements

Année	Nom	Baisse du LDL-cholestérol	Bénéfices cardiovasculaires	Prix /année
1987	**Statines** **Rosuvastatine** **Atorvastatine**	50%	Prévention primaire et secondaire	280.- CHF
2001	**Ezetimibe**	20%	Prévention primaire et secondaire	310.- CHF
2016	**Inhibiteurs du PCSK9** **Evolocumab** **Alirocumab**	60%	Prévention primaire si hypercholestérolémie familiale Prévention secondaire	6'700.- CHF Limitations OFSP

Slide: Dr . Nanchen, PMU, CHUV

Remerciements

- Dr Georg Ehret, Cardiologie HUG
- Dr David Nanchen, PMU CHUV

Remerciements

- Dre Lena Berchtold, Néphrologie HUG

- Ma femme…

Merci pour votre attention!

Recommandations alimentaires ESC 2019

Table 8 **Impact of specific lifestyle changes on lipid levels**

	Magnitude of the effect	Level	Reference
Lifestyle interventions to reduce TC and LDL-C levels			
Avoid dietary trans fats	++	A	129,138
Reduce dietary saturated fats	++	A	129,139
Increase dietary fibre	++	A	140,141
Use functional foods enriched with phytosterols	++	A	142,143
Use red yeast rice nutraceuticals	++	A	144–146
Reduce excessive body weight	++	A	147,148
Reduce dietary cholesterol	+	B	149,150
Increase habitual physical activity	+	B	151
Lifestyle interventions to reduce TG-rich lipoprotein levels			
Reduce excessive body weight	+	A	147,148
Reduce alcohol intake	+++	A	152,153
Increase habitual physical activity	++	A	151,154
Reduce total amount of dietary carbohydrates	++	A	147,155
Use supplements of n-3 polyunsaturated fats	++	A	156,157
Reduce intake of mono- and disaccharides	++	B	158,159
Replace saturated fats with mono- or polyunsaturated fats	+	B	129,137
Lifestyle interventions to increase HDL-C levels			
Avoid dietary trans fats	++	A	129,160
Increase habitual physical activity	+++	A	151,161
Reduce excessive body weight	++	A	147,148
Reduce dietary carbohydrates and replace them with unsaturated fats	++	A	147,162
Modest consumption in those who take alcohol may be continued	++	B	153
Quit smoking	+	B	163

Effets secondaires des statines

TABLE 11 Statin-Associated Side Effects (SASE)

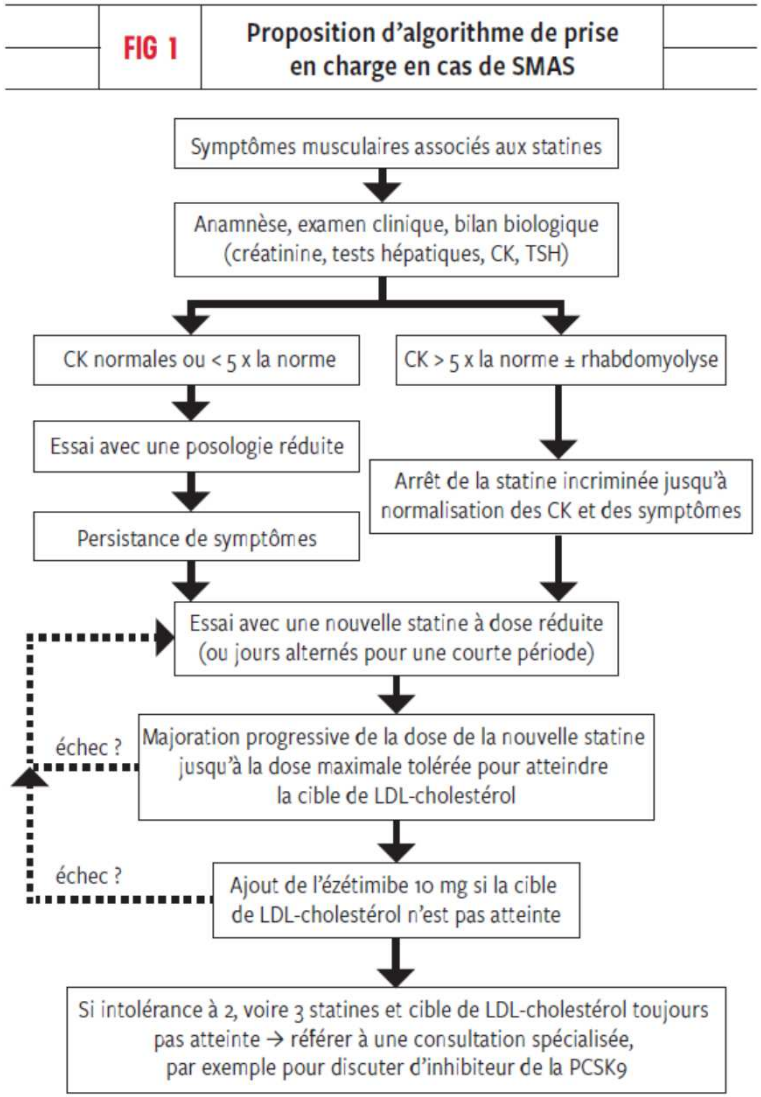
Statin-Associated Side Effects	Frequency	Predisposing Factors	Quality of Evidence
Statin-associated muscle symptoms (SAMS)			
Myalgias (CK Normal)	Infrequent (1% to 5%) in RCTs; frequent (5% to 10%) in observational studies and clinical setting	Age, female sex, low body mass index, high-risk medications (CYP3A4 inhibitors, OATP1B1 inhibitors), comorbidities (HIV, renal, liver, thyroid, preexisting myopathy), Asian ancestry, excess alcohol, high levels of physical activity, and trauma	RCTs cohorts/observational
Myositis/myopathy (CK > ULN) with concerning symptoms or objective weakness	Rare		RCTs cohorts/observational
Rhabdomyolysis (CK >10× ULN + renal injury)	Rare		RCTs cohorts/observational
Statin-associated autoimmune myopathy (HMGCR antibodies, incomplete resolution)	Rare		Case reports
New-onset diabetes mellitus	Depends on population; more frequent if diabetes mellitus risk factors are present, such as body mass index ≥30, fasting blood glucose ≥100 mg/dL; metabolic syndrome, or A1c ≥6% (8).	Diabetes mellitus risk factors/ metabolic syndrome High-intensity statin therapy	RCTs/meta-analyses

Effets secondaires des statines

Liver		
Transaminase elevation 3× ULN	Infrequent	RCTs/cohorts/observational Case reports
Hepatic failure	Rare	
Central nervous system		
Memory/cognition	Rare	Case reports; no increase in memory/cognition problems in 3 large-scale RCTs
Cancer	No definite association	RCTs/meta-analyses
Other		
Renal function	Unfounded	
Cataracts	Unfounded	
Tendon rupture	Unfounded	
Hemorrhagic stroke	Unfounded	
Interstitial lung disease	Unfounded	
Low testosterone	Unfounded	

CK indicates creatine kinase; HIV, human immunodeficiency virus; HMGCR, 3-hydroxy-3-methyl-glutaryl-coenzyme A reductase; SAMS, statin-associated muscle symptoms; SAAM, statin-associated autoimmune myopathy; SASE, statin associated side effects; and ULN, upper limit of normal.

Prise en charge des SMAS



Biais des études sponsorisées

- Etudes randomisées contrôlées: majoritairement sponsorisées par l'industrie

- Données d'études non sponsorisées:

  - Registres de patients, par ex registres nationaux

    Swedish Register of Cardiac Intensive Care (RIKS-HIA). Early statin treatment following acute myocardial infarction and 1-year survival. JAMA 2001 (285)

Biais des études sponsorisées

Industry sponsorship bias in research findings: a network meta-analysis of LDL cholesterol reduction in randomised trials of statins


OPEN ACCESS

Comparaison études sponsorisées vs non sponsorisée

End point: réduction du LDL (pas de end point clinique)

-> réduction dans les deux bras comparé
-> réduction moins importante du LDL dans les études non sponsorisées

Huseyin and al. BMJ 2014

Score calcique très élevé

- Si score > 400 Agatston
  - -> Environ 35% de patients/es avec maladie coronarienne significative (coronarographie ou test fonctionnel)
  - -> test fonctionnel à envisager

Quel traitement pour quel patient?

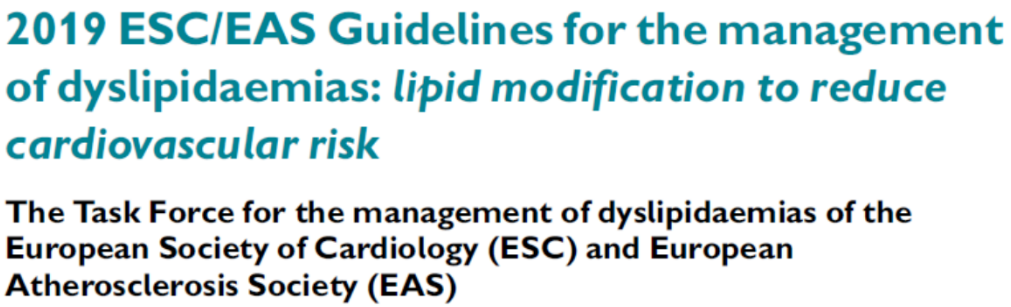
- Arvinostatine
- Roséstatine
- Syrahstatine

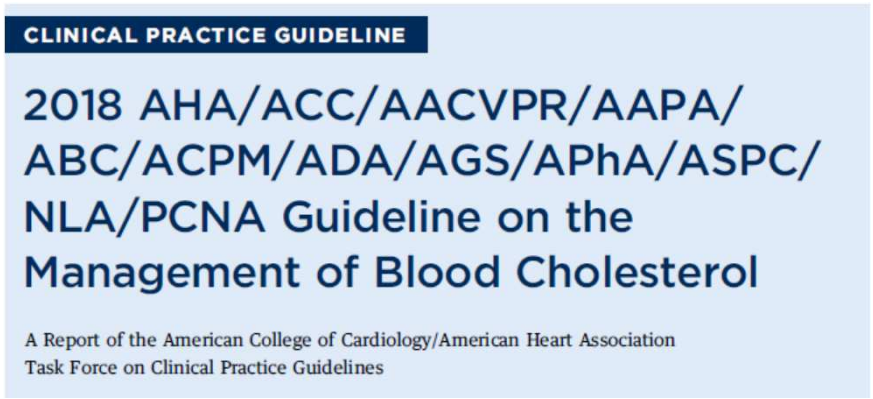
- -> choix du patient important!!!

- Décision partagée…

Catégories de risque cardiovasculaire

- Sources:
  - Guidelines ESC (Société Européenne de Cardiologie)
  - Guidelines ACC (American college of Cardiology)
  - Repris par le groupe de travail suisse sur les lipides et l'athérosclérose (GSLA-AGLA)





2020 Prévention de l'athérosclérose
Accent mis sur les dyslipidémies
Aperçu des recommandations du Groupe de travail Lipides et Athérosclérose (GSLA) de la Société Suisse de Cardiologie (SSC) ainsi que des European Society of Cardiology (ESC) et European Atherosclerosis Society (EAS)
www.gsla.ch

Evaluation du risque cardiovasculaire

Risque selon le GSLA:

Risque d'évènement CV sur 10 ans

- 0-10%: faible
- 10-20% modéré
- > 20%: élevé

Risque selon l'ESC «SCORE»:

Risque de mortalité sur 10 ans

- 0-1%: faible
- 1-5%: modéré
- 5-10%: élevé
- > 10%: très élevé

Qui traiter en prévention primaire???

Recommandations européennes:

Table 5 Intervention strategies as a function of total cardiovascular risk and untreated low-density lipoprotein cholesterol levels

	Total CV risk (SCORE) %	Untreated LDL-C levels					
		<1.4 mmol/L (55 mg/dL)	1.4 to <1.8 mmol/L (55 to <70 mg/dL)	1.8 to <2.6 mmol/L (70 to <100 mg/dL)	2.6 to <3.0 mmol/L (100 to <116 mg/dL)	3.0 to <4.9 mmol/L (116 to <190 mg/dL)	≥4.9 mmol/L (≥190 mg/dL)
Primary prevention	<1, low-risk	Lifestyle advice	Lifestyle advice	Lifestyle advice	Lifestyle advice	Lifestyle intervention, consider adding drug if uncontrolled	Lifestyle intervention and concomitant drug intervention
	Class[a]/Level[b]	I/C	I/C	I/C	I/C	IIa/A	IIa/A
	≥1 to <5, or moderate risk (see *Table 4*)	Lifestyle advice	Lifestyle advice	Lifestyle advice	Lifestyle intervention, consider adding drug if uncontrolled	Lifestyle intervention, consider adding drug if uncontrolled	Lifestyle intervention and concomitant drug intervention

Catégories de risque cardiovasculaire

Risque cardiovasculaire considéré comme élevé ou très élevé:

- -> traitement hypolipémiant indiqué d'office

Risque très élevé:

- Score ESC: risque calculé sur 10 ans[1] ≥10%
- Maladie cardiovasculaire athérosclérotique (ASCVD) cliniquement manifeste[2]
- ASCVD asymptomatique ou à haut risque, démontrée par imagerie[2]
- Hypercholestérolémie familiale avec un facteur de risque majeur
- Insuffisance rénale sévère (DFGe <30 ml/min/1.73 m^2)
- Diabète sucré avec atteinte des organes cibles ou ≥3 facteurs de risque majeurs[3]; ou diabète de type 1 de début précoce remontant à >20 ans

Risque élevé:

- Score/algorithme de risque du GSLA: risque à 10 ans[4] >20%
- Score ESC: risque calculé sur 10 ans[1] ≥5% et <10%
- Risque modéré et ASCVD asymptomatique, démontrée par imagerie[2]
- Facteur de risque individuel considérablement accru, spécifiquement CT >8 mmol/l; LDL-C >4.9 mmol/l; PA >180/110 mmHg
- Hypercholestérolémie familiale sans autres facteurs de risque
- Insuffisance rénale modérée (DFGe 30–59 ml/min/1.73 m2)
- Diabète sucré sans atteinte des organes cibles, mais durée de 10-20 ans ou présence d'un facteur de risque supplémentaire

Source: agla.ch

Qui traiter en prévention primaire???

Recommandations américaines ACC 2019:

IIa	B-R

5. In intermediate-risk adults, risk-enhancing factors favor initiation or intensification of statin therapy (S4.4.2-6, S4.4.2-15–S4.4.2-22).