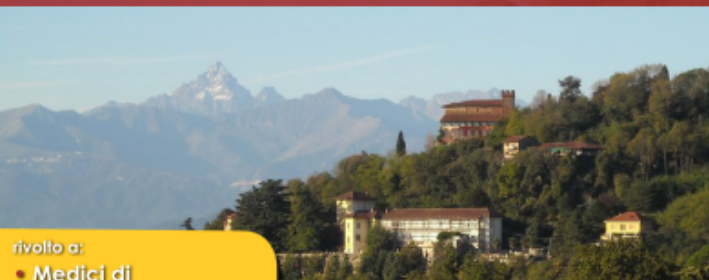


*Dal caso clinico  
alle nuove strategie  
terapeutiche:*

*confronto tra Cardiologi Ospedalieri  
e Medici di Medicina Generale*

Responsabili del Convegno:

Dott. Ferdinando Varbella, Dott. Riccardo Riccardi,  
Dott.ssa Maria Milano



rivolto a:

- Medici di Medicina Generale
- Cardiologi



**Sabato 23 Settembre 2017**

**IL MULINO DI PIOSSASCO**

**Sala Teatro**

Via Riva Po 9 - Piovascò (TO)

**6,4  
crediti  
ECM**

**DAL CASO CLINICO ALLE NUOVE  
STRATEGIE TERAPEUTICHE:  
L'IPERCOLESTEROLEMIA DELLA SIGNORA  
ANTONIA**

**GINO BARRAL - ROSARIO TRIPODI**

**PIOSSASCO 23 SETTEMBRE 2017**

A.G. di anni 43, sesso femminile

Ipercolesterolemia (familiare?)

Colesterolo totale 340 mg/dl

HDL 46 mg/dl

TG 128 mg/dl

LDL 269 mg/dl

Non altri fattori di rischio

# Cosa fareste ?

Televoto I

- 1) Solo dieta ipocolesterolemica
- 2) Statina di I classe es. simvastatina
- 3) Statina di II classe atorva o rosuvastatina
- 4) Associazione statina con ezetimibe

# Risk categories

<b>Very high-risk</b>	<p>Subjects with any of the following:</p> <ul style="list-style-type: none"><li>• Documented CVD, clinical or unequivocal on imaging. Documented clinical CVD includes previous AMI, ACS, coronary revascularization and other arterial revascularization procedures, stroke and TIA, aortic aneurysm and PAD. Unequivocally documented CVD on imaging includes significant plaque on coronary angiography or carotid ultrasound. It does NOT include some increase in continuous imaging parameters such as intima-media thickness of the carotid artery.</li><li>• DM with target organ damage such as proteinuria or with a major risk factor such as smoking or marked hypercholesterolaemia or marked hypertension.</li><li>• Severe CKD (GFR &lt;30 mL/min/1.73 m<sup>2</sup>).</li><li>• A calculated SCORE =/&gt;10%.</li></ul>
<b>High-risk</b>	<p>Subjects with:</p> <ul style="list-style-type: none"><li>• Markedly elevated single risk factors, in particular cholesterol &gt;8 mmol/L (&gt;310 mg/dL) (e.g. in familial hypercholesterolaemia) or BP ≥180/110 mmHg.</li><li>• Most other people with DM (with the exception of young people with type 1 DM and without major risk factors that may be at low or moderate risk).</li><li>• Moderate CKD (GFR 30–59 mL/min/1.73 m<sup>2</sup>).</li><li>• A calculated SCORE ≥5% and &lt;10%.</li></ul>
<b>Moderate-risk</b>	SCORE is ≥1% and <5% at 10 years. Many middleaged subjects belong to this category.
<b>Low-risk</b>	SCORE <1%.

# Treatment goals for LDL-cholesterol

Recommendations	Class	Level
In patients at <b>VERY HIGH CV risk</b> , an LDL-C goal of <b>&lt;1.8 mmol/L (70 mg/dL)</b> or a reduction of at least 50% if the baseline LDL-C is between 1.8 and 3.5 mmol/L (70 and 135 mg/dL) is recommended.	I	B
In patients at <b>HIGH CV risk</b> , an <b>LDL-C goal of &lt;2.6 mmol/L (100 mg/dL)</b> , or a reduction of at least 50% if the baseline LDL-C is between 2.6 and 5.2 mmol/L (100 and 200 mg/dL) is recommended.	I	B
In subjects at <b>LOW or MODERATE risk</b> an LDL-C goal of <b>&lt;3.0 mmol/L (&lt;115 mg/dL)</b> should be considered.	IIa	C

Il Curante prescrive simvastatina da 20 mg die  
(siamo in prevenzione primaria!)  
dopo circa 1 mese profilo lipidico:

### PROFILO LIPIDICO

Col totale 260 mg/dl  
HDL 41 mg/dl  
TG 140 mg/dl  
LDL 191 mg /dl

Giugno 2015: IMA STEMI Infero-laterale e PCI con stent su CFx occlusa (lesione colpevole), ma malattia coronarica plurivasale con lesione lunga e complessa su IVA prox e media e CDx critica. FE 45%. Dimessa in DAPT Ticagrelor ed ASA : sta bene a parte un po' di menometrorragia

Dopo circa 2 mesi stop ticagrelor ed intervento CCH di BPAC con AMIS su IVA e AMID su Destra. Decorso regolare.

# Alle dimissioni dopo la PCI cosa avreste prescritto per il suo colesterolo?

Televoto II

1. Rosuvastatina ad alto dosaggio
2. Rosuvastatina ed ezetimibe
3. PCSK9 inibitori
4. Continua sinvastatina



# Risk categories

<b>Very high-risk</b>	<p>Subjects with any of the following:</p> <ul style="list-style-type: none"><li>• Documented CVD, clinical or unequivocal on imaging. Documented clinical CVD includes previous AMI, ACS, coronary revascularization and other arterial revascularization procedures, stroke and TIA, aortic aneurysm and PAD. Unequivocally documented CVD on imaging includes significant plaque on coronary angiography or carotid ultrasound. It does NOT include some increase in continuous imaging parameters such as intima-media thickness of the carotid artery.</li><li>• DM with target organ damage such as proteinuria or with a major risk factor such as smoking or marked hypercholesterolaemia or marked hypertension.</li><li>• Severe CKD (GFR &lt;30 mL/min/1.73 m<sup>2</sup>).</li><li>• A calculated SCORE =/&gt;10%.</li></ul>
<b>High-risk</b>	<p>Subjects with:</p> <ul style="list-style-type: none"><li>• Markedly elevated single risk factors, in particular cholesterol &gt;8 mmol/L (&gt;310 mg/dL) (e.g. in familial hypercholesterolaemia) or BP ≥180/110 mmHg.</li><li>• Most other people with DM (with the exception of young people with type 1 DM and without major risk factors that may be at low or moderate risk).</li><li>• Moderate CKD (GFR 30–59 mL/min/1.73 m<sup>2</sup>).</li><li>• A calculated SCORE ≥5% and &lt;10%.</li></ul>
<b>Moderate-risk</b>	SCORE is ≥1% and <5% at 10 years. Many middleaged subjects belong to this category.
<b>Low-risk</b>	SCORE <1%.

# Treatment goals for LDL-cholesterol

Recommendations	Class	Level
In patients at <u>VERY HIGH CV risk</u> , an LDL-C goal of $<1.8$ mmol/L (70 mg/dL) or a reduction of at least 50% if the baseline LDL-C is between 1.8 and 3.5 mmol/L (70 and 135 mg/dL) is recommended.	I	B
In patients at HIGH CV risk, an LDL-C goal of $<2.6$ mmol/L (100 mg/dL), or a reduction of at least 50% if the baseline LDL-C is between 2.6 and 5.2 mmol/L (100 and 200 mg/dL) is recommended.	I	B
In subjects at LOW or MODERATE risk an LDL-C goal of $<3.0$ mmol/L ( $<115$ mg/dL) should be considered.	IIa	C

# Recommendations for the pharmacological treatment of elevated LDL-cholesterol

---

- **Prescribe statin up to the highest recommended dose or highest tolerable dose to reach the goal.**
- **In the case of statin intolerance, ezetimibe or bile acid sequestrants, or these combined, should be considered.**
- **If goal is not reached, statin combination with a cholesterol absorption inhibitor should be considered.**
- **If goal is not reached, statin combination with a bile acid sequestrant may be considered.**
- **In patients at very high risk, with persistent high LDL-C despite treatment with maximal tolerated statin dose, in combination with ezetimibe or in patients with statin intolerance, a PCSK9 inhibitor may be considered.**



Cosa abbiamo fatto noi

rosuvastatina 20 mg die associata ad ezetimibe 10 mg die

dopo circa 1 mese profilo lipidico

Col Totale 216 mg/dl

HDL 45 mg/dl

TG 158 mg/dl

**LDL 140 mg /dl**

dopo 10-15 gg mialgia e CPK 320 mg/dl

# Va bene così o potremmo fare altro?

## Televoto III

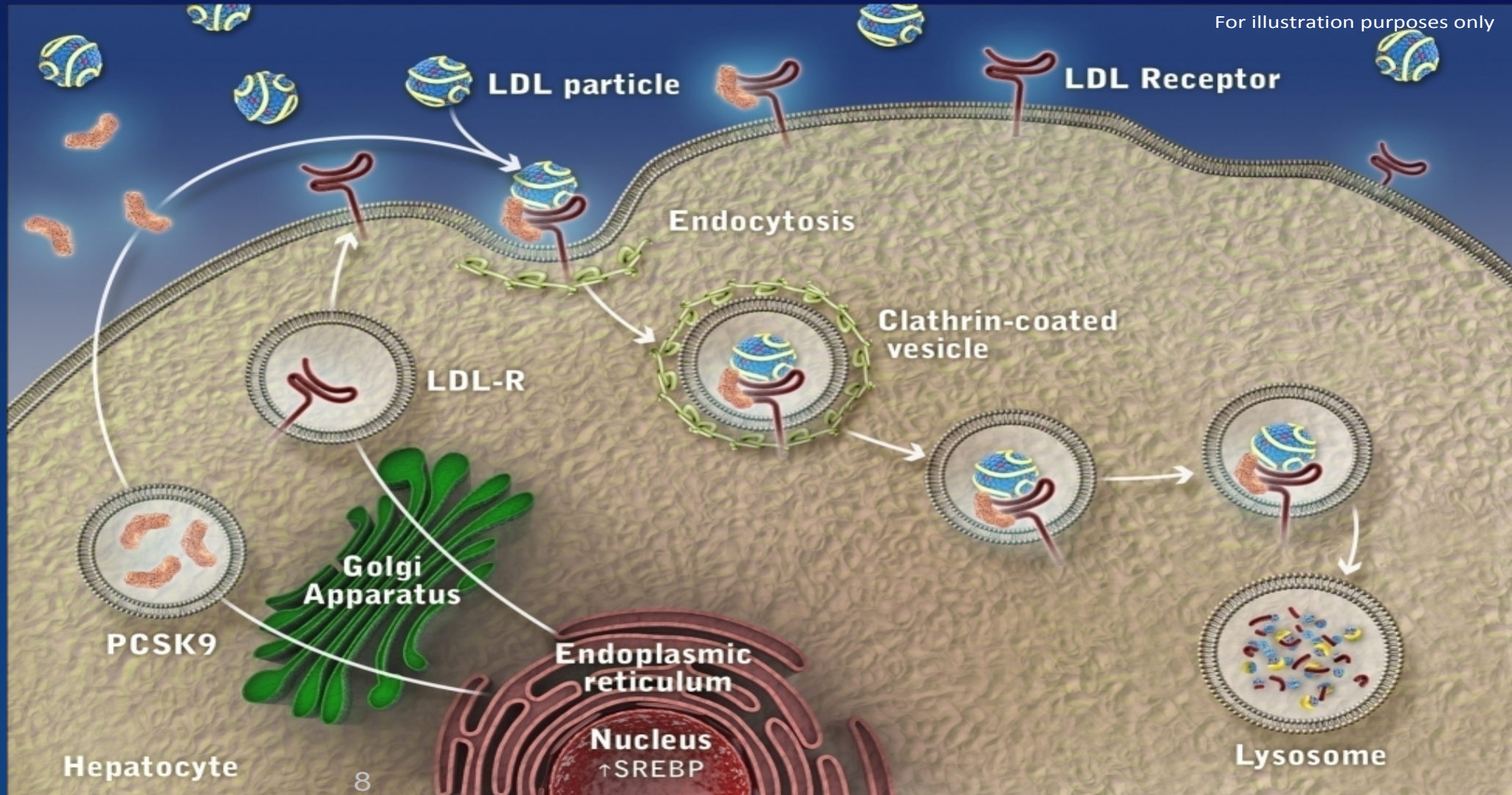
1. Ci accontentiamo dei valori di LDL e chiediamo alla paziente di tollerare la mialgia
2. Riduciamo la statina
3. Cambiamo la statina
4. Proviamo gli inibitori del PCSK9

# Recommendations for the pharmacological treatment of elevated LDL-cholesterol

---

- **Prescribe statin up to the highest recommended dose or highest tolerable dose to reach the goal.**
- **In the case of statin intolerance, ezetimibe or bile acid sequestrants, or these combined, should be considered.**
- **If goal is not reached, statin combination with a cholesterol absorption inhibitor should be considered.**
- **If goal is not reached, statin combination with a bile acid sequestrant may be considered.**
- **In patients at very high risk, with persistent high LDL-C despite treatment with maximal tolerated statin dose, in combination with ezetimibe or in patients with statin intolerance, a PCSK9 inhibitor may be considered.**

# The Role of PCSK9 in the Regulation of LDL Receptor Expression



Iniziamo **Evolocumab** 140 mg sc due volte al mese in associazione a rosuvastatina ed ezetimibe

dopo 1 mese:

Col totale 110 mg/dl

HDL 40 mg/dl

TG 120 mg/dl

**LDL 50 mg /dl**

riduciamo a solo 5 mg die la rosuvastatina e stop ezetimibe → non più mialgie, ha ricominciato a fare Pilates!

Dopo 1 mese profilo lipidico:

Col totale 140 mg /dl

HDL 45 mg/dl

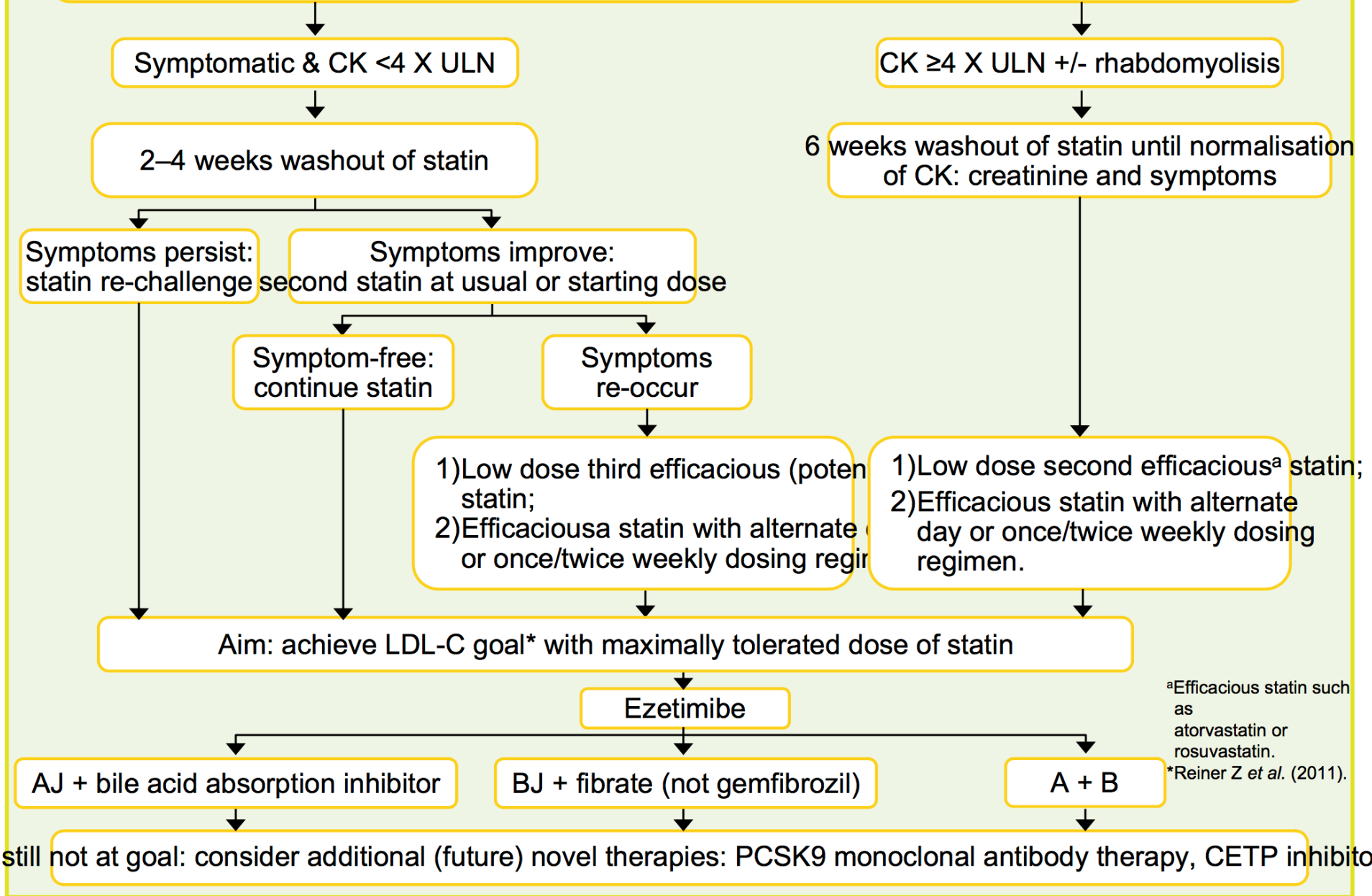
TG 130 mg/dl

**LDL 69 mg /dl**



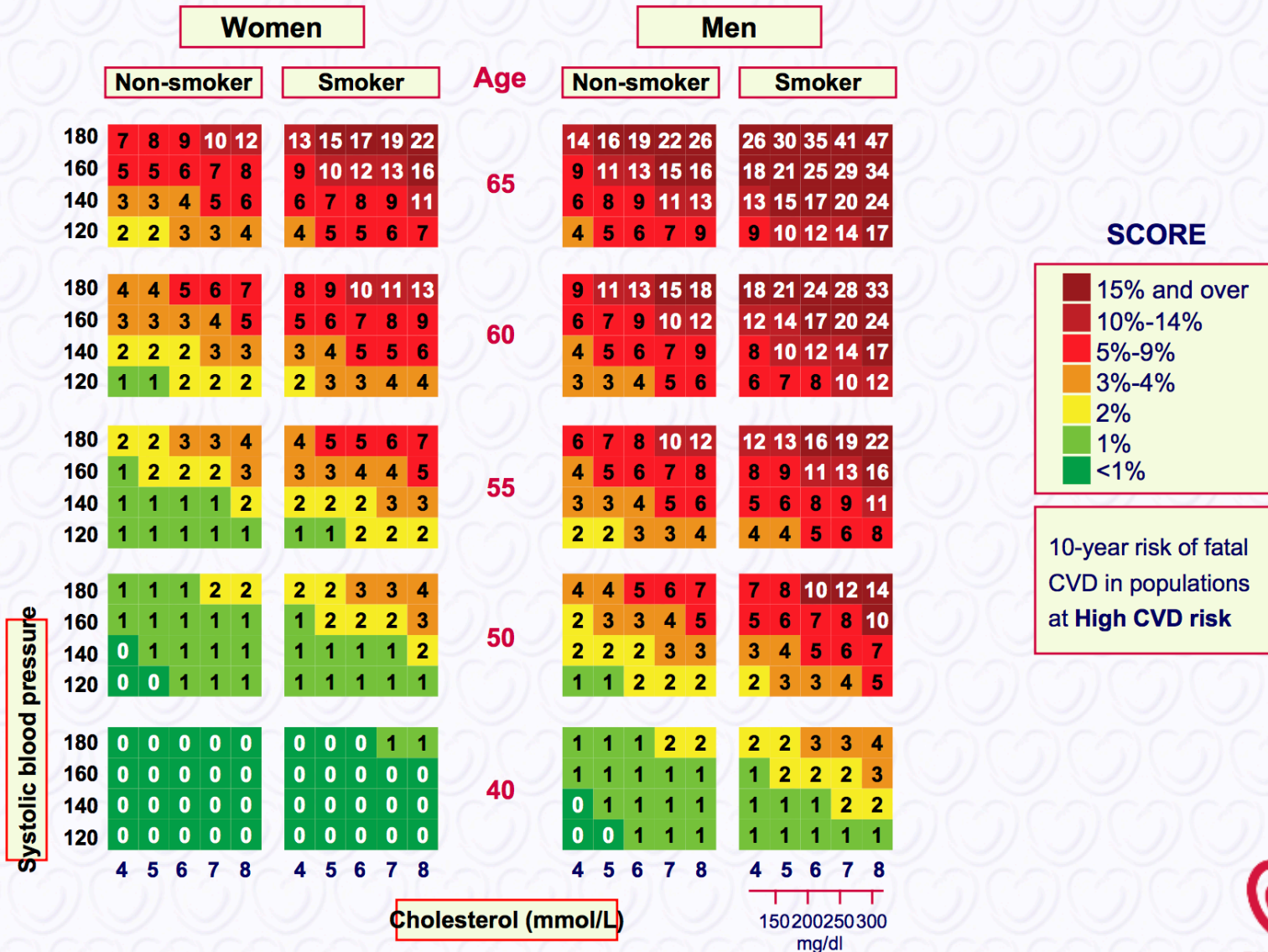
# Algorithm for treatment of muscular symptoms during statin

Consider if statin-attributed muscle symptoms favour statin continuation / reinitiation



If still not at goal: consider additional (future) novel therapies: PCSK9 monoclonal antibody therapy, CETP inhibitor

# SCORE chart: 10-year risk fatal cardiovascular disease (CVD) in population at high CVD risk



# Intervention strategies

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

<sup>a</sup>In patients with myocardial infarction, statin therapy should be considered irrespective of total cholesterol levels.