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

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آقای ۵۵ساله با سابقه فشار خون و مصرف سیگار جهت چک آپ به پزشک مراجعه می کند نامبرده شکایت خاصی ندارد و لوزارتان ۲۵میلی گرم دوبار در روز و هیدروکلرو تیازید ۱۲,۵میلیگرم روزانه مصرف می کند در معاینه فشار خون ۱۶۰/۹۰میلی متر جیوه است در بررسی لیپید ها و سایر آزمایشات بصورت زیر است

TChoL=197 mg/dl, LDL=110 mg/dl, TG=260

GFR=85cc/min,HGB A1C=6%

علاوه بر اقدامات مربوط به فشار خون آیا نیاز به به داروی پایین آورنده لیپید دارد؟

در صورت نیاز چه دارویی با چه دوزی؟

در صورت عدم پاسخ کافی قدم بعدی چیست؟

Central Illustration Upper panel Treatment goals for low-density lipoprotein cholesterol (LDL-C) across categories of total cardiovascular disease risk

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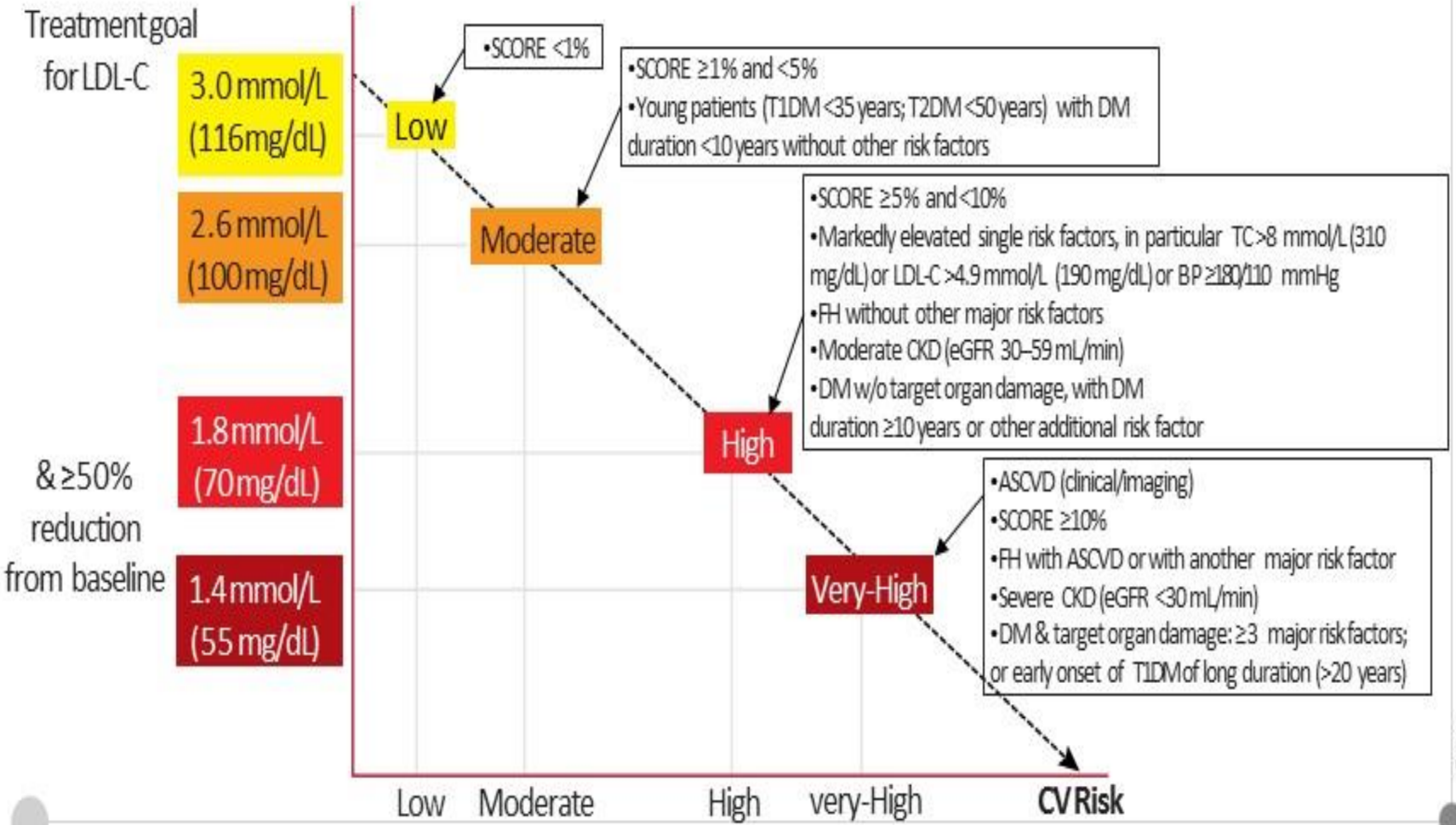

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2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk (European Heart Journal 2019 -doi: 10.1093/eurheartj/ehz455)

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

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	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	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
	Class[a]/Level[b]	I/C	I/C	IIa/A	IIa/A	IIa/A	IIa/A
	≥5 to <10, or high- risk	Lifestyle advice	Lifestyle advice	Lifestyle intervention, consider adding drug if uncontrolled	Lifestyle intervention and concomitant drug intervention	Lifestyle intervention and concomitant drug intervention	Lifestyle intervention and concomitant drug intervention
	Class[a]/Level[b]	IIa/A	IIa/A	IIa/A	I/A	I/A	I/A
	≥10, or at very-high risk due to a risk condition	Lifestyle advice	Lifestyle intervention, consider adding drug if uncontrolled	Lifestyle intervention and concomitant drug intervention	Lifestyle intervention and concomitant drug intervention	Lifestyle intervention and concomitant drug intervention	Lifestyle intervention and concomitant drug intervention
	Class[a]/Level[b]	IIa/B	IIa/A	I/A	I/A	I/A	I/A
Secondary Prevention	Very-high risk	Lifestyle intervention, consider adding drug if uncontrolled	Lifestyle intervention and concomitant drug intervention	Lifestyle intervention and concomitant drug intervention	Lifestyle intervention and concomitant drug intervention	Lifestyle intervention and concomitant drug intervention	Lifestyle intervention and concomitant drug intervention
	Class[a]/Level[b]	IIa/A	I/A	I/A	I/A	I/A	I/A

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SCORE Cardiovascular Risk Chart

10-year risk of fatal CVD

High-risk regions of Europe

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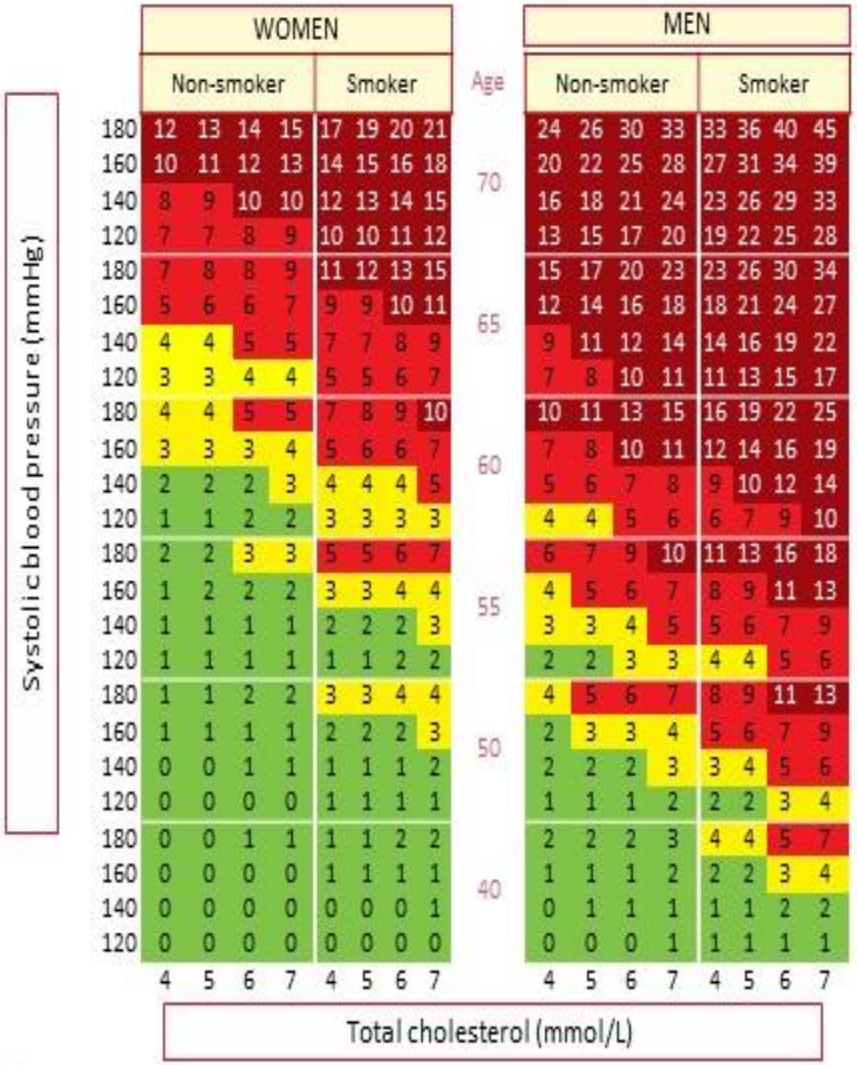

SCORE chart for European populations at high cardiovascular disease risk

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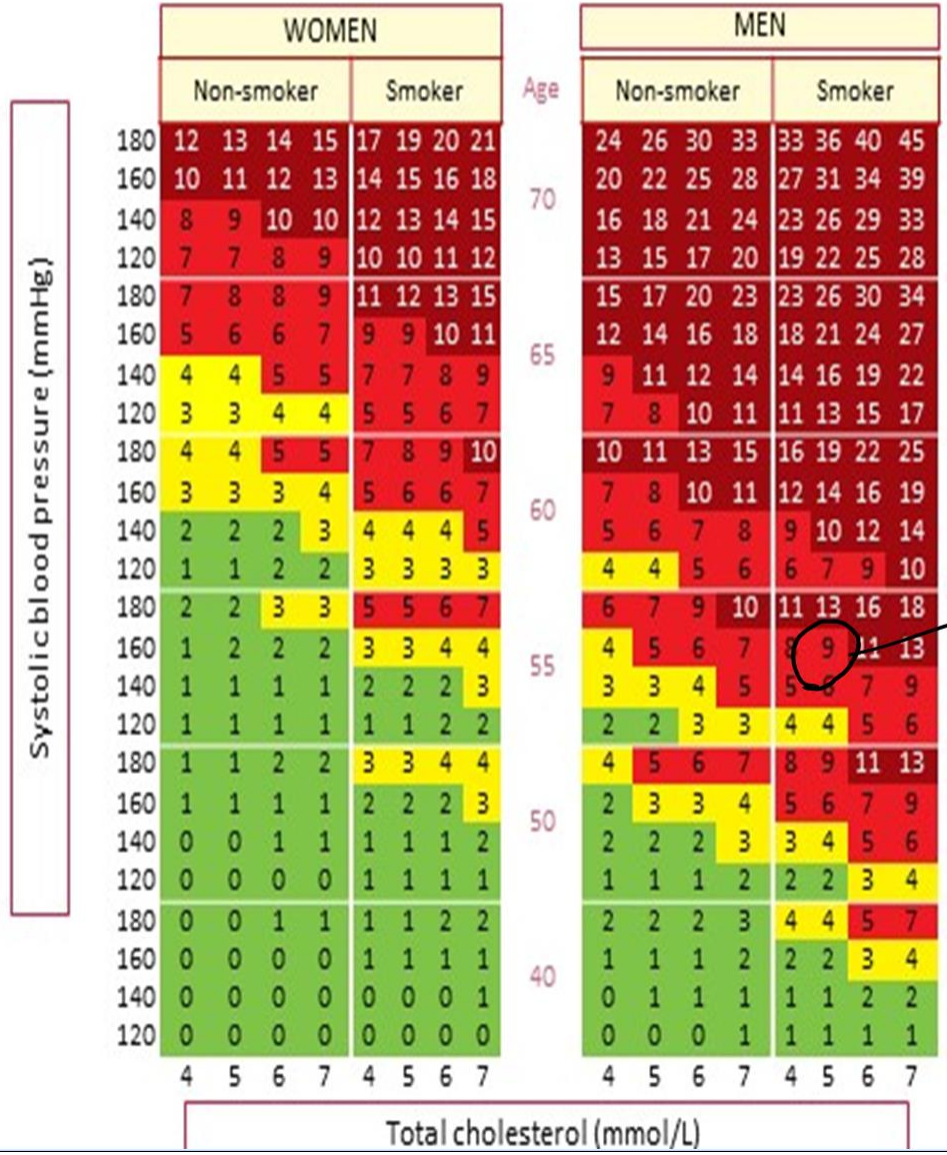
SCORE Cardiovascular Risk Chart
10-year risk of fatal CVD
High-risk regions of Europe



SCORE chart for European populations at high cardiovascular disease risk

9%

دقت شود با وجود مصرف داروی فشار خون ریسک

CVS بالا است و بدون دارو ریسک

حدود ۳۰٪ به بالا یعنی حدود 13٪ است

پس بیمار در قسمت very high risk

قرار دارد.

How to use the risk estimation charts

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To estimate a person's 10-year risk of cardiovascular disease (CVD) death, find the table for his/her gender, smoking status, and age. Within the table find the cell nearest to the person's blood pressure (BP) and total cholesterol (TC). Risk estimates will need to be adjusted upwards as the person approaches the next age category.

Risk is initially assessed on the level of TC and systolic BP before treatment, if known. The longer the treatment and the more effective it is, the greater the reduction in risk, but in general it will not be more than about one-third of the baseline risk. For example, for a person on antihypertensive drug treatment in whom the pre-treatment BP is not known, if the total cardiovascular (CV) SCORE risk is 6%, then the pre-treatment total CV risk may have been 9%.

Low-risk persons should be offered advice to maintain their low-risk status. While no threshold is universally applicable, the intensity of advice should increase with increasing risk.

The charts may be used to give some indication of the effects of reducing risk factors, given that there is apparently a time lag before the risk reduces. In general, people who stop smoking halve their cumulative risk over a relatively short period of time.

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cardiovascular risk (European Heart Journal 2019 -doi: 10.1093/eurheartj/ehz455)

کدام درمان رو پیشنهاد می کنید؟

۱- Atorvastatin 10mg OD

۲- Atorvastatin 20mg OD

۳- Atorvastatin 40mg OD

۴- resuvastatin 20mg OD

High-, Moderate-, and Low-Intensity Statin Therapy		
High-Intensity	**Moderate-Intensity**	**Low-Intensity**
Lowers LDL–C by ≥50%	Lowers LDL–C by 30-49%	Lowers LDL–C by <30%
Atorvastatin 40-80 mg Rosuvastatin 20-40 mg	Atorvastatin 10-20 mg Rosuvastatin 5-10 mg Simvastatin 20-40 mg Pravastatin 40-80 mg Lovastatin 40-80 mg Fluvastatin XL 80 mg Fluvastatin 40 mg bid Pitavastatin 1-4 mg	Simvastatin 10 mg Pravastatin 10-20 mg Lovastatin 20 mg Fluvastatin 20-40 mg

در صورتیکه به LDL هدف نرسیم قدم بعدی چیست؟

۱-اضافه کردن ezetimab

۲-اضافه کردن PCSK9 inhi

۳-اضافه کردن دوز استاتین

۴-اضافه کردن فیبرات

Central Illustration Lower panel: Treatment algorithm for pharmacological LDL-C lowering (2)

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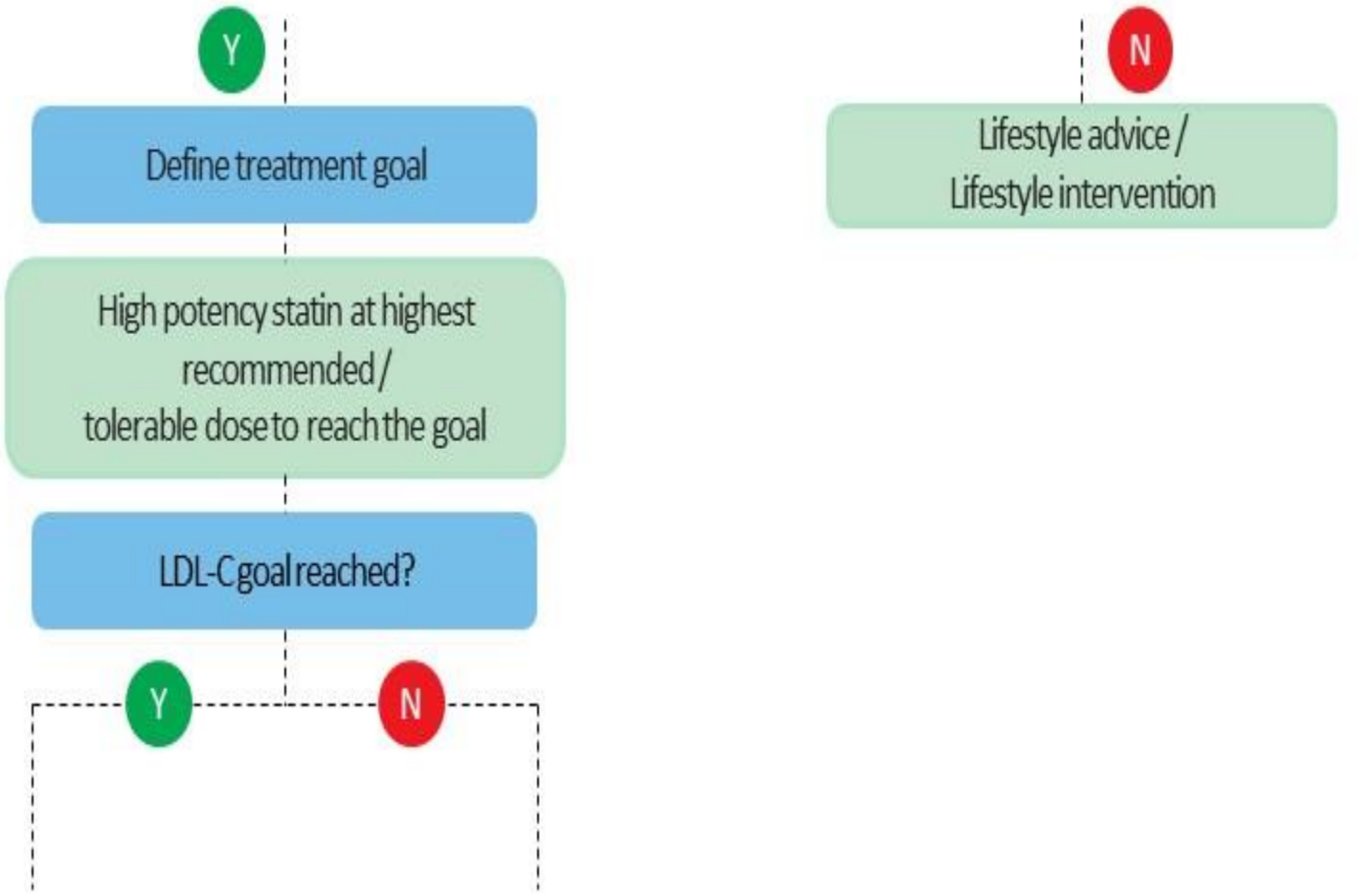

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در صورت نرسیدن به LDL هدف قدم بعدی چیست؟

از صدر نسخه به هدف قدم بعدی اضافه کرده است Ezetimib

10 mg OD

از صدر نسخه به هدف اضافه کرده PCSK9 inhibitor

Central Illustration Lower panel: Treatment algorithm for pharmacological LDL-C lowering (3)

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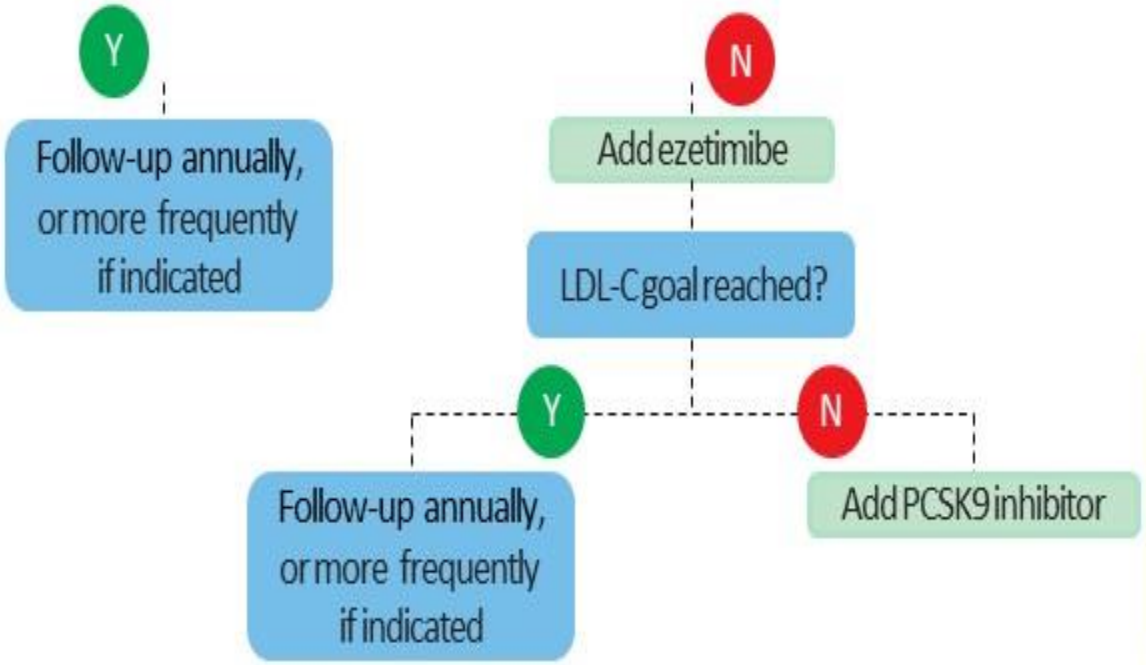


- Secondary prevention (very-high-risk)
- Primary prevention: patients with FH and another major risk factor (very-high-risk)

Consider adding PCSK9 inhibitor

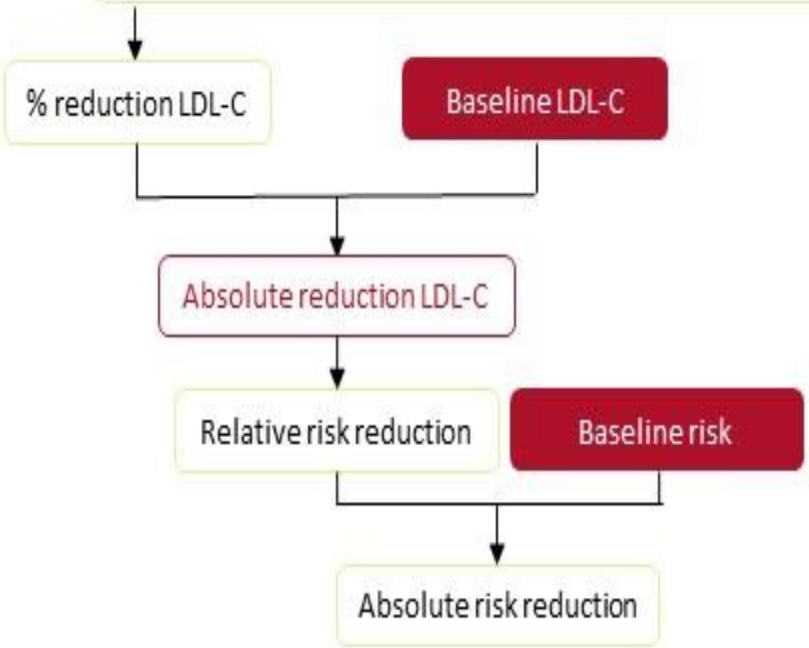
- Primary prevention: patients at very-high risk but without FH

2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk (European Heart Journal 2019 -doi: 10.1093/eurheartj/ehz455)

Expected clinical benefit of low-density lipoprotein cholesterol lowering therapies

Intensity of lipid lowering treatment

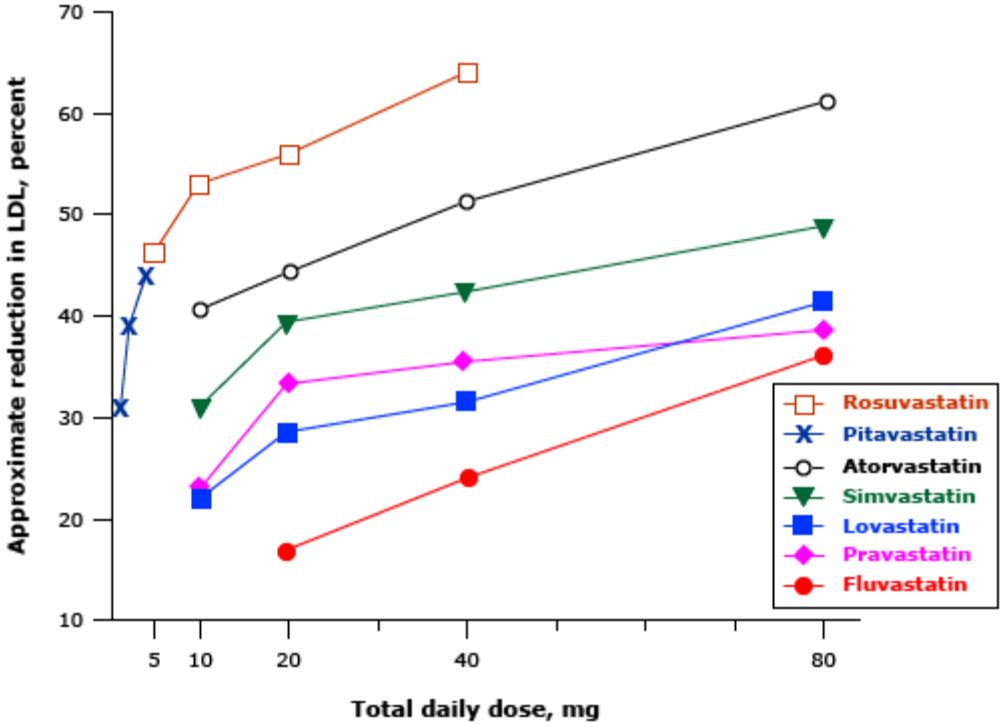
Treatment	Average LDL-C reduction
Moderate intensity statin	≈ 30%
High intensity statin	≈ 50%
High intensity statin plus ezetimibe	≈ 65%
PCSK9 inhibitor	≈ 60%
PCSK9 inhibitor plus high intensity statin	≈ 75%
PCSK9 inhibitor plus high intensity statin plus ezetimibe	≈ 85%



LDL-C = low-density lipoprotein cholesterol;
PCSK9 = proprotein convertase subtilisin/kexin type 9.

2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk (European Heart Journal 2019 -doi: 10.1093/eurheartj/ehz455)

Drug class	Serum LDL cholesterol (% change)	Serum HDL cholesterol (% change)	Serum triglycerides (% change)
Bile acid sequestrants	↓ 15 to 30	0 to slight increase	No change or increase
Cholesterol absorption inhibitors	↓ 17	↑ 1	↓ 7 to 8
Fenofibrate (micronized form)	↓ 6 to 20	↑ 5 to 20¶	↓ 41 to 53
Gemfibrozil◊	↓ 10 to 15	↑ 5 to 20¶	↓ 35 to 50
Neomycin	↓ 20 to 25	No change	No change
Nicotinic acid (niacin)	↓ 10 to 25	↑ 15 to 35	↓ 25 to 30
Omega 3 fatty acids Δ	↑ 4 to 49	↑ 5 to 9	↓ 23 to 45
PCSK9 inhibitors	↓ 38 to 72	↑ 4 to 9	↓ 2 to 23
Statins	↓ 20 to 60	↑ 5 to 10	↓ 10 to 33


Approximate reduction in LDL, percent
70
60
50
40
30
20
10
5
10
20
40
80
Total daily dose, mg
Rosuvastatin
Pitavastatin
Atorvastatin
Simvastatin
Lovastatin
Pravastatin
Fluvastatin

در بیمار فوق چه مدت بعد پروفایل لیپید را چک می کنیم؟
آیا چک ALT ضروری است؟
چک CPK چطور؟

Summary of recommendations for monitoring lipids and enzymes in patients before and on lipid-lowering therapy (1)

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Testing lipids

How often should lipids be tested?

- Before starting lipid-lowering drug treatment, at least two measurements should be made, with an interval of 1–12 weeks, with the exception of conditions where concomitant drug treatment is suggested, such as acute coronary syndromes (ACS) and very-high-risk patients.

How often should a patient's lipids be tested after starting lipid-lowering treatment?

- 8 (±4) weeks after starting treatment.
- 8 (±4) weeks after adjustment of treatment until the goal is achieved.

How often should lipids be tested once a patient has achieved the target or optimal lipid level?

- Annually (unless there are adherence problems or other specific reasons for more frequent reviews).

2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk (European Heart Journal 2019 -doi: 10.1093/eurheartj/ehz455)

Summary of recommendations for monitoring lipids and enzymes in patients before and on lipid-lowering therapy (2)

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Monitoring liver and muscle enzymes

How often should liver enzymes (alanine aminotransferase [ALT]) be routinely measured in patients on lipid-lowering drugs?

- Before treatment.
- Once 8–12 weeks after starting a drug treatment or after dose increase.
- Routine control of ALT thereafter is not recommended during statin treatment, unless symptoms suggesting liver disease evolve. During treatment with fibrates, control of ALT is still recommended.

2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk (European Heart Journal 2019 -doi: 10.1093/eurheartj/ehz455)

درصورتیکه ALT=85باشد اقدام بعدی چیست؟

۱-قطع استاتین و چک انزیم ۴تا۶هفته بعد

۲-کاهش استاتین و چک آنزیم ۴تا۶هفته بعد

۳-ادامه استاتین با دوز قبلی و تکرار آنزیم ۴تا۶هفته بعد

۴-تعویض استاتین با استاتین دیگر

Summary of recommendations for monitoring lipids and enzymes in patients before and on lipid-lowering therapy (3)

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Monitoring liver and muscle enzymes

What if liver enzymes become elevated in a person taking lipid-lowering drugs?

If ALT <3x upper limit of normal (ULN):

- Continue therapy.
- Recheck liver enzymes in 4–6 weeks.

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Summary of recommendations for monitoring lipids and enzymes in patients before and on lipid-lowering therapy (4)

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Monitoring liver and muscle enzymes

What if liver enzymes become elevated in a person taking lipid-lowering drugs?

If ALT ≥3x ULN:

- Stop lipid-lowering therapy or reduce dose and recheck liver enzymes within 4–6 weeks.
- Cautious reintroduction of therapy may be considered after ALT has returned to normal.
- If ALT remains elevated check for the other reasons.

2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk (European Heart Journal 2019 -doi: 10.1093/eurheartj/ehz455)

در صورتیکه پس از مصرف استاتین بیما دچار میالژی شود و CK=1000باشد اقدام بعدی چیست؟

۱-قطع استاتین و چک ck ۲هفته بعد

۲-کاهش استاتین و چک ck 2هفته بعد

۳-با توجه به اینکه افزایش ckکمتر از ۱۰برار نرمال است نیازی به قطع دارو نیست و مونیتورینگ ck هر ۲هفته کافیست

۴-بررسی علل دیگر افزایش ckتوصیه می گردد

Summary of recommendations for monitoring lipids and enzymes in patients before and on lipid-lowering therapy (5)

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Monitoring liver and muscle enzymes

How often should creatine kinase (CK) be measured in patients taking lipid- lowering drugs?

Pre-treatment:

- Before starting therapy.
- If baseline CK is >4x ULN, do not start drug therapy; recheck.

Monitoring:

- Routine monitoring of CK is not necessary.
- Check CK if patient develops myalgia.

Be alert regarding myopathy and CK elevation in patients at risk such as: elderly patients, concomitant interfering therapy, multiple medications, liver or renal disease, or athletes.

2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk (European Heart Journal 2019 -doi: 10.1093/eurheartj/ehz455)

Summary of recommendations for monitoring lipids and enzymes in patients before and on lipid-lowering therapy (6)

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Monitoring liver and muscle enzymes

What if CK becomes elevated in a person taking lipid-lowering drugs? Re-evaluate indication for statin treatment.

If ≥4x ULN:

- If CK >10x ULN: stop treatment, check renal function and monitor CK every 2 weeks.
- If CK <10x ULN: if no symptoms, continue lipid-lowering therapy while monitoring CK between 2 and 6 weeks.
- If CK <10x ULN: if symptoms present, stop statin and monitor normalization of CK, before re-challenge with a lower statin dose.
- Consider the possibility of transient CK elevation for other reasons such as exertion.
- Consider myopathy if CK remains elevated.
- Consider combination therapy or an alternative drug.

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lipids and enzymes in patients before and on lipid-lowering therapy (6)

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Monitoring liver and muscle enzymes

What if CK becomes elevated in a person taking lipid-lowering drugs? Re-evaluate indication for statin treatment.

If ≥4x ULN:

- If CK >10x ULN: stop treatment, check renal function and monitor CK every 2 weeks.
- If CK <10x ULN: if no symptoms, continue lipid-lowering therapy while monitoring CK between 2 and 6 weeks.
- If CK <10x ULN: if symptoms present, stop statin and monitor normalization of CK, before re-challenge with a lower statin dose.
- Consider the possibility of transient CK elevation for other reasons such as exertion.
- Consider myopathy if CK remains elevated.
- Consider combination therapy or an alternative drug.

Summary of recommendations for monitoring lipids and enzymes in patients before and on lipid-lowering therapy (7)

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Monitoring liver and muscle enzymes

What if CK becomes elevated in a person taking lipid-lowering drugs? Re-evaluate indication for statin treatment.

If <4x ULN:

- If no muscle symptoms, continue statin (patient should be alerted to report symptoms; check CK).
- If muscle symptoms, monitor symptoms and CK regularly.
- If symptoms persist, stop statin and re-evaluate symptoms after 6 weeks; re-evaluate indication for statin treatment.
- Consider re-challenge with the same or another statin.

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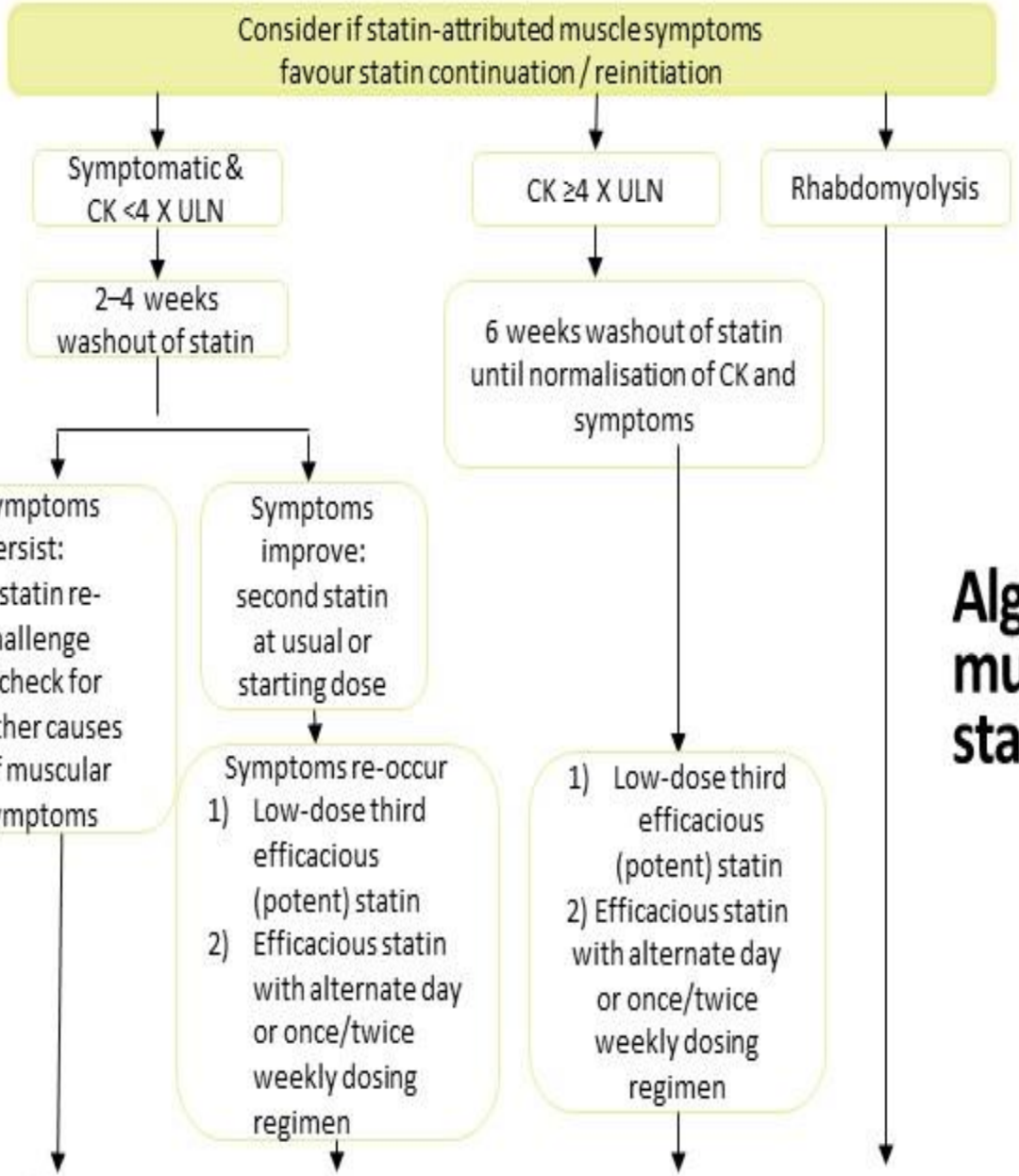

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Algorithm for treatment of muscular symptoms during statin treatment (1)

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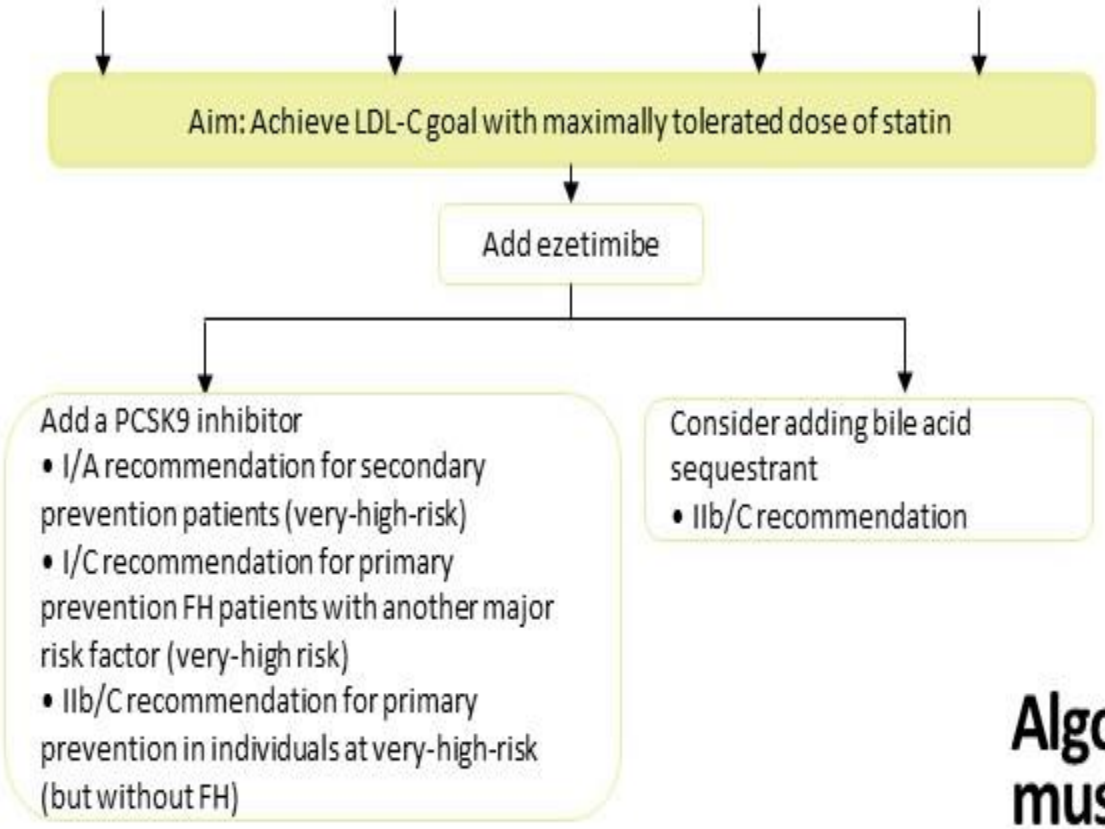

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Algorithm for treatment of muscular symptoms during statin treatment (2)

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در بیمار فوق در صورتیکه با مصرف استاتین پروفایل لیپید به صورت زیر باشد قدم بعدی چیست؟

Tchol= 155 LDL=55 HDL=45 TG=220

۱-ادامه استاتین با دوز قبلی

۲-بالا بردن دوز استاتین به حداکثر دوز قابل تحمل

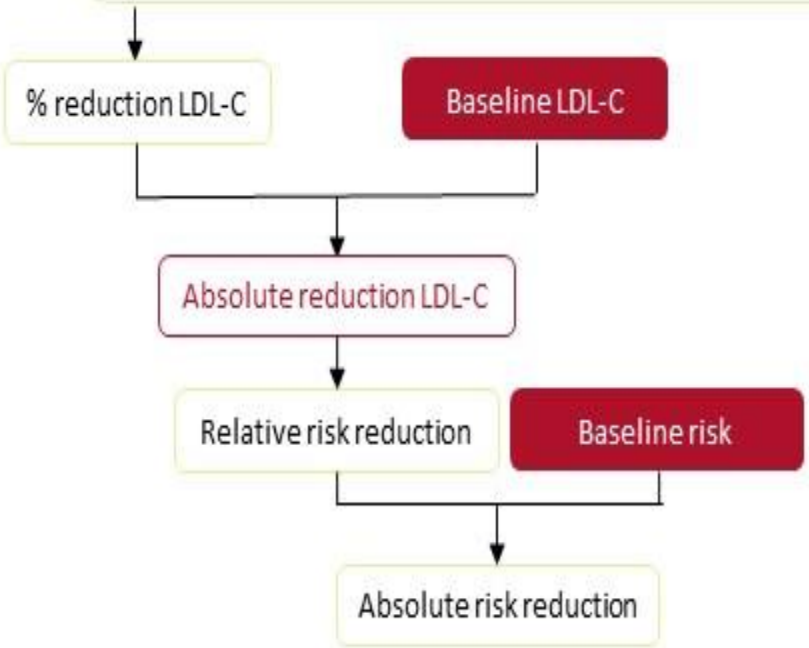
۳-اضافه کردن فیبرات

۴-اضافه کردن n-3 PUFAs

Expected clinical benefit of low-density lipoprotein cholesterol lowering therapies

Intensity of lipid lowering treatment

Treatment	Average LDL-C reduction
Moderate intensity statin	≈ 30%
High intensity statin	≈ 50%
High intensity statin plus ezetimibe	≈ 65%
PCSK9 inhibitor	≈ 60%
PCSK9 inhibitor plus high intensity statin	≈ 75%
PCSK9 inhibitor plus high intensity statin plus ezetimibe	≈ 85%



LDL-C = low-density lipoprotein cholesterol;
PCSK9 = proprotein convertase subtilisin/kexin type 9.

2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk (European Heart Journal 2019 -doi: 10.1093/eurheartj/ehz455)

Recommendations for drug treatments of patients with hypertriglyceridaemia (1)

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Recommendations	Class	Level
Statin treatment is recommended as the first drug of choice for reducing CVD risk in high-risk individuals with hypertriglyceridaemia (TG >2.3 mmol/L (>200 mg/dL)).	I	B
In high-risk (or above) patients with TG between 1.5 and 5.6 mmol/L (135–499 mg/dL) despite statin treatment, n-3 PUFAs (icosapent ethyl 2 x 2 g/day) should be considered in combination with statin.	IIa	B

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Recommendations for drug treatments of patients with hypertriglyceridaemia (2)

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Recommendations	Class	Level
In primary prevention patients who are at LDL-C goal with TG >2.3 mmol/L (>200 mg/dL), fenofibrate or bezafibrate may be considered in combination with statins.	IIb	B
In high-risk patients who are at LDL-C goal with TG >2.3 mmol/L (>200 mg/dL), fenofibrate or bezafibrate may be considered in combination with statins.	IIb	C

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Thank you