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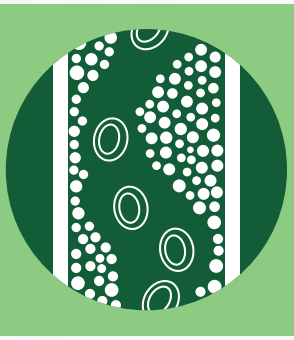
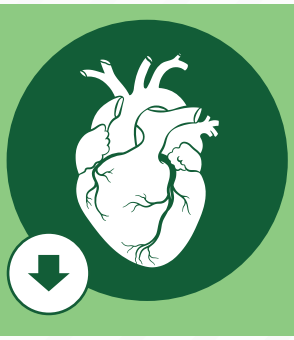
Managing the Side-Effects of Statin Therapy

Towards improving patient adherence



Statin therapy can reduce the levels of atherogenic proteins...[1]



...and significantly lower the risk of atherosclerotic cardiovascular disease (ASCVD)[1]

Existing statin therapies[2]

<30%*	30%–49%*	≥50%*
Low-intensity	Moderate-intensity	High-intensity
• Simvastatin 10 mg • Pravastatin 10–20 mg • Lovastatin 20 mg • Fluvastatin 20–40 mg	• Atorvastatin 10–20 mg • Rosuvastatin 5–10 mg • Simvastatin 20–40 mg • Pravastatin 40–80 mg • Lovastatin 40–80 mg • Fluvastatin 80 mg • Pitavastatin 1–4 mg	• Atorvastatin 40–80 mg • Rosuvastatin 20–40 mg

*Percentage reduction in low-density lipoprotein cholesterol (LDL-C) observed with the corresponding dose of statins

However, some patients experience adverse side-effects and statin intolerance, resulting in discontinuation of therapy[1]

Factors that lead to treatment discontinuation[1,2]

- Non-adherence to treatment[1]
- Lack of persistence[1]
- Adverse side-effects of statins[2,3]
  - Skeletal muscle-related symptoms (SAMS) or myalgias
  - Elevated levels of creatinine kinase (CK)
  - Abnormalities in liver function tests
  - Myopathy
- Statin intolerance

Associated with

Statin dose

Not associated with

LDL-C reduction

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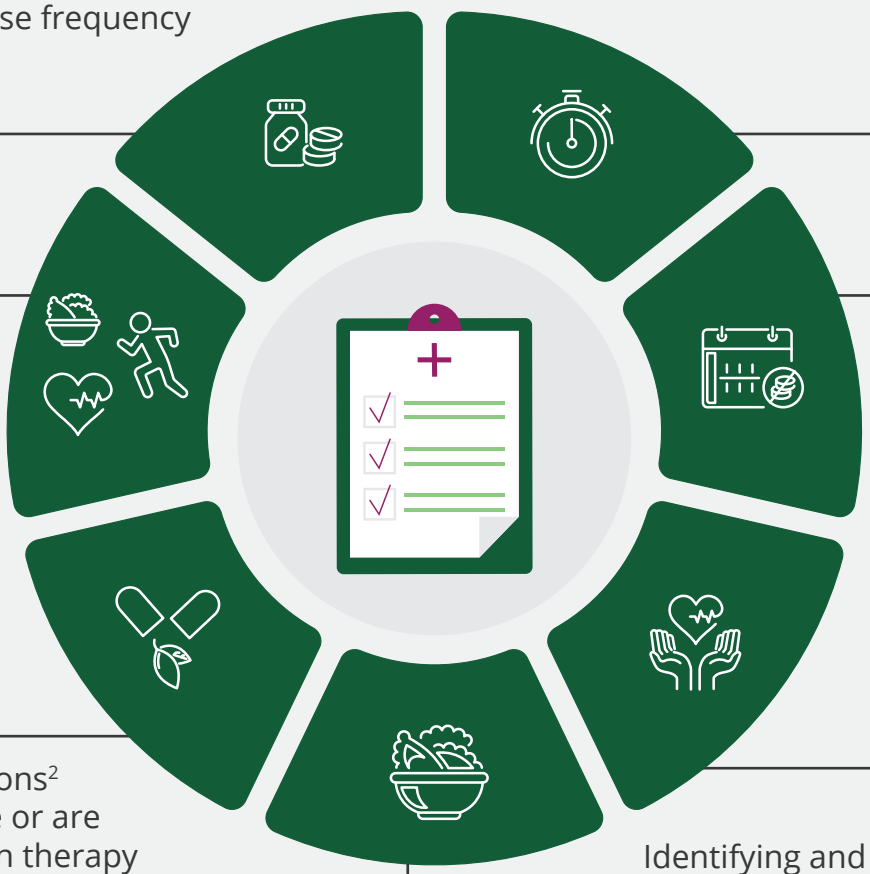
Strategies to overcome the limitations of statins

Switching to a tolerable statin regimen[1,3]
- Dose reduction
- Switching to a better suited statin agent
- Changing the dose frequency

Intermittent non-daily dosing
- 70% patients tolerate intermittent statin doses without the recurrence of treatment-limiting SAMS[4]



Optimizing lifestyle interventions[1,2]
- Diet modification
- Weight control
- Physical activity

Reassessing tolerance for the same statin after a washout period[3]

Non-statin medications[2] which either replace or are combined with statin therapy
- Ezetimibe
- Bile acid sequestrants
- Proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors

Identifying and modulating the risk factors associated with statin intolerance[1]
- Hypothyroidism
- Co-medications and potential drug interactions
- Alcohol use
- Strenuous exercise
- Vitamin D deficiency
- Obesity
- Diabetes
- Chronic kidney disease

Other lipid-lowering agents[2]
- Bempedoic acid (an ATP citrate lyase inhibitor)
- Fibrates
- Icosapent ethyl
- Nicotinic acid

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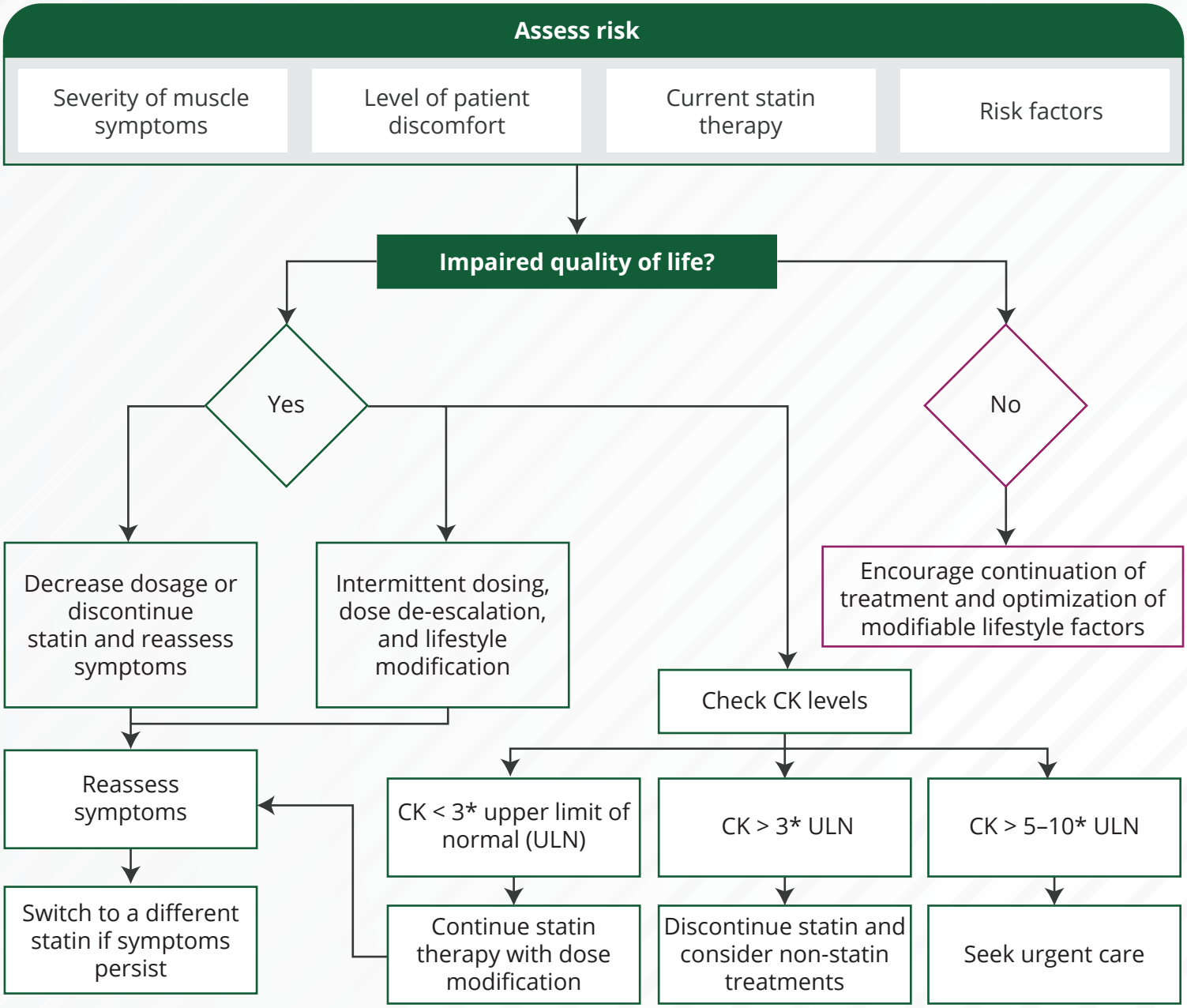
Management of SAMS[3]



Management of statin intolerance[1,3]

Identify a tolerable statin regimen

Modify dose or statin therapy based on clinical trial data that favor reduced cardiovascular event risk

Consider non-statin therapy in high-risk patients with a history of statin intolerance

Strategies for better patient adherence and outcomes[3]

- Inquire about treatment compliance and acknowledge the honest disclosure of adherence by the patient
- If patients report SAMS, assess adverse effects, specific muscle symptoms, and how these affect the patients' lives
- Address patient and family concerns regarding treatment options, medications, potential side-effects, and outcomes
- Encourage patients to adopt healthy lifestyles
- Involve the patient in the decision-making process regarding the choice of statin and dosing schedule
- Provide support in case of muscle symptoms and encourage patients to continue statin treatment if symptoms are not persistent
- Re-evaluate statin tolerability if symptoms persist and switch to a different treatment if necessary
- Encourage patients to maintain clinical follow-up

- **Patient non-adherence can negatively impact the outcomes of statin therapy and increase the risk of ASCVD and associated mortality**
- **Shared decision-making and communication between the clinician and patient may help improve treatment compliance**
- **Switching to a different statin or dose modification may benefit patients experiencing adverse effects like SAMS. Non-statin medications may be considered in high-risk patients with persistent symptoms**
- **Pharmacological and lifestyle modifications can help patients with treatment continuation**

References:

1. Cheeley, M.K., Saseen, J.J., Agarwala, A., Ravilla, S., Ciffone, N., Jacobson, T.A., ... & Maki, K.C. (2022). NLA scientific statement on statin intolerance: A new definition and key considerations for ASCVD risk reduction in the statin intolerant patient. *Journal of Clinical Lipidology, 16*(4), 361–375.
2. Grundy, S.M., Stone, N.J., Bailey, A.L., Beam, C., Birtcher, K.K., Blumenthal, R.S., ... & Yeboah, J. (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. *Circulation, 135*(25), e1082–e1143.
3. Warden, B.A., Guyton, J.R., Kovacs, A.C., Durham, J.A,, Jones, L.K., Dixon, D.L., ... & Duell, P.B. (2023). Assessment and management of statin-associated muscle symptoms (SAMS): A clinical perspective from the National Lipid Association. *Journal of Clinical Lipidology, 17*(1), 19–39.
4. Keating, A.J., Campbell, K.B., & Guyton, J.R. (2013). Intermittent nondaily dosing strategies in patients with previous statin-induced myopathy. *Annals of Pharmacotherapy, 47*(3), 398–404.

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