

Best Practice Message

May 2024

Statins for secondary prevention of cardiovascular events

Practice changing moments

- Māori are disproportionately affected by cardiovascular disease (CVD). Significantly more Māori die from cardiovascular disease and at a younger age.
- Lack of statin therapy is the primary driver for patients not receiving triple therapy for secondary prevention.
- Most of the perceived statin intolerance of muscle pain is unrelated to the statin therapy.
- Consider reviewing the intensity of statin therapy to ensure patients are receiving maximal benefit.

Introduction

Triple therapy (statin, antihypertensive and antiplatelet/anticoagulant) can reduce the risk of recurrent cardiovascular events by at least 50% over five years and is recommended by current New Zealand guidelines.^{1,2} While there will be a small group of patients for whom triple therapy is not appropriate, there is still a considerable rate of patients with previous cardiovascular events who are not receiving triple therapy. The main driver for this is low rates of prescribing of statins.

Rates of triple therapy in Māori and Non-Māori are similar, however Māori are disproportionately affected by cardiovascular events with a higher burden of disease and younger ages at presentation than Non-Māori.³



Figure 1: Proportion of patients with established CVD, enrolled in a Health Hawke's Bay practice, who have been prescribed a combination of Statin, Antihypertensive, and Antiplatelet/Anticoagulant in the last 5 months for Māori (green) and non-Māori (grey) as reported in Thalamus as of 31st March 2024.



Statin Aversion

About half of patients initiated on statins discontinuing therapy within a year⁴. Reasons for poor medication adherence is multifactorial.

A primary driver for patients to avoid statin therapy is the widespread belief around statin associated muscle pain⁴. However, the risk of true rate of statin related muscle pain or weakness is low at 11 per 1000 person-years in the first year of treatment, with this falling to effectively zero in subsequent years. It has also been shown that only 1 in 15 reports of muscle symptoms during the first year of treatment are directly attributable to statin therapy. ⁵ Furthermore, serious side effects are rare. For every 10,000 patients treated for 5 years there are 5 cases of myopathy¹. Where statin associated muscle pain has occurred consider whether statin-attributed muscle symptoms (SAMS) favour statin continuation or re-initiation by following the Management of SAMS flow chart (see appendix 1).

Since the FDA published a safety announcement in 2012 about a link between statin therapy and memory loss, there has been public concern around potentially developing dementia from statin use, with this being the second most commonly reported adverse effect with statin therapy.⁶ However, large scale studies investigating a link between statin therapy and dementia or reduced cognitive test scores have not found any association. ⁷ More recently there has been evidence that in some patient groups with a high risk of Alzheimer's disease that statin therapy is protective.⁸

Patients may also disregard the importance of statins particularly due to perceptions of their risk of a future cardiovascular event as well as the asymptomatic nature of dyslipidaemia in most patients. ^{9,10} He Ako Hiringa have great resources for <u>communicating CVD risk</u> and for strategies to <u>address the complexities of non-adherence</u> in CVD.

LDL Targets

While New Zealand guidelines written in 2018 suggest a target of 1.6 - 1.8 mmol/L LDL-C is suitable for patients with established CVD 1 , more up to date International guidelines have recently moved to an aggressive target of <1.4 mmol/L when treating patients. 11 It is expected that updates to New Zealand guidelines will follow this, with the NZSSD guidelines for managing patients with diabetes already using a target of <1.4 mmol/L. 12

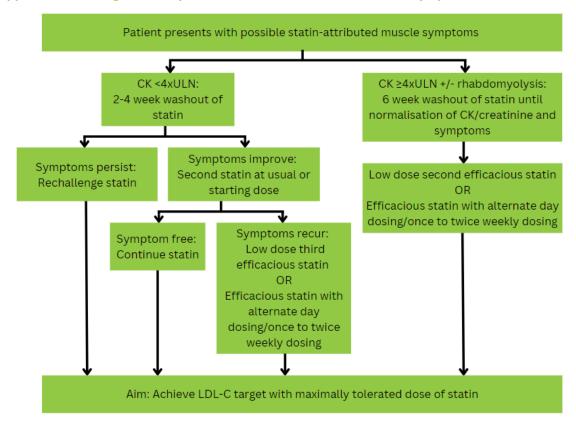
It is also important to remind patients that any LDL-C reduction is beneficial, with each 1mmol/L reduction in LDL-C reducing the relative risk of major adverse cardiovascular event (MACE) by 22%. Consider switching patients to a higher intensity statin at the highest tolerated dose to gain maximum benefit. Table 1 highlights the expected drop of LDL-C from current available statin therapy. Ezetimibe has a modest effect on lowering LDL-C, adding an approximate 13-15% reduction in LDL-C levels when combined with simvastatin, atorvastatin or rosuvastatin. Consider addition of ezetimibe therapy if LDL-C goal is not met with maximum tolerated intensity and dose of statin therapy.

Treatment Intensity	Pravastatin	Rosuvastatin	Atorvastatin	Simvastatin	Expected % drop in LDL-C
Low	20 mg			10 mg	30%
Medium	40 mg		10 mg	20 mg	38%
	80 mg	5 mg	20 mg	40mg	41%
High		10 mg	40mg	80 mg	47%
		20 mg	80 mg		55%
Very High		40 mg			63%

Table 1. Approximate equivalence of statins¹



Appendix 1: Management of patients with statin attributed muscle symptoms.



Adapted from Wiley Statin-Associated Muscle Symptoms May 2022



Resources:

Thalamus PPP Outcome measures dashboards

He Ako Hiringa EPiC Cardiovascular disease dashboard

He Ako Hiringa Understanding and communicating CVD risk and management recommendations

He Ako Hiringa Pondering the complexities of preventing cardiovascular disease

Heart foundation patient information: Statins

Healthify patient information: Statins

New Zealand formulary: Statins

New Zealand formulary: Interaction checker

CARM suspected adverse event reporting

<u>Health Pathways: Cardiovascular Risk Assessment</u> Heat Beat: Cardiac rehabilitation sessions for patients

References:

- 1. Ministry of Health. Cardiovascular disease risk assessment and management for primary care. Wellington: Ministry of Health; 2018.
- 2. Wells S, Poppe KK, Selak V, Kerr A, Pylypchuk R, Wu B, et al. Is general practice identification of prior cardiovascular disease at the time of CVD risk assessment accurate and does it matter? 2018;131(1475).
- 3. Selak V, Poppe K, Grey C, Mehta S, Winter-Smith J, Jackson R, et al. Ethnic differences in cardiovascular risk profiles among 475,241 adults in primary care in Aotearoa, New Zealand. Atrial fibrillation. 2020;133(1521).
- 4. Iatan I, Mancini GBJ, Yeoh E, Hegele RA. Statin associated muscle symptoms (SAMS): strategies for prevention, assessment and management. Expert Review of Cardiovascular Therapy. 2023 Jun 3;21(6):423–35.
- 5. Cholesterol Treatment Trialists' Collaboration. Effect of statin therapy on muscle symptoms: an individual participant data meta-analysis of large-scale, randomised, double-blind trials. Lancet. 2022 Sep 10;400(10355):832–45.
- 6. Golomb BA, McGraw JJ, Evans MA, Dimsdale JE. Physician response to patient reports of adverse drug effects: implications for patient-targeted adverse effect surveillance. Drug Saf. 2007;30(8):669–75.
- 7. Olmastroni E, Molari G, De Beni N, Colpani O, Galimberti F, Gazzotti M, et al. Statin use and risk of dementia or Alzheimer's disease: a systematic review and meta-analysis of observational studies. European Journal of Preventive Cardiology. 2022 Mar 1;29(5):804–14.
- 8. Rajan KB, Mcaninch EA, Wilson RS, Dhana A, Evans-Lacko S, Evans DA. Statin Initiation and Risk of Incident Alzheimer Disease and Cognitive Decline in Genetically Susceptible Older Adults. Neurology. 2024 Apr 9;102(7):e209168.
- 9. Butalia S, Lee-Krueger RCW, McBrien KA, Leung AAC, Anderson TJ, Quan H, et al. Barriers and Facilitators to Using Statins: A Qualitative Study With Patients and Family Physicians. CJC Open. 2020 Jul 4;2(6):530–8.
- 10. Fung V, Graetz I, Reed M, Jaffe MG. Patient-reported adherence to statin therapy, barriers to adherence, and perceptions of cardiovascular risk. PLoS One. 2018 Feb 8;13(2):e0191817.



- 11. Visseren FLJ, Mach F, Smulders YM, Carballo D, Koskinas KC, Bäck M, et al. 2021 ESC Guidelines on cardiovascular disease prevention in clinical practice: Developed by the Task Force for cardiovascular disease prevention in clinical practice with representatives of the European Society of Cardiology and 12 medical societies With the special contribution of the European Association of Preventive Cardiology (EAPC). European Heart Journal. 2021 Sep 7;42(34):3227–337.
- 12. New Zealand Society for the Study of Diabetes. Management of dyslipidaemia [Internet]. NZSSD; [cited 2024 Apr 11]. Available from: https://t2dm.nzssd.org.nz/Section-104-Management-of-dyslipidaemia
- 13. Foody JM, Toth PP, Tomassini JE, Sajjan S, Ramey DR, Neff D, et al. Changes in LDL-C levels and goal attainment associated with addition of ezetimibe to simvastatin, atorvastatin, or rosuvastatin compared with titrating statin monotherapy. Vasc Health Risk Manag. 2013;9:719–27.

Authored by: Ben Firestone Reviewed by: Riani Albertyn

Acknowledgements: Thanks to Brendan Duck and the Hawke's Bay Clinical Pharmacist Facilitator team for content contribution and guidance.

Disclaimer: The information and advice contained in this document is based upon evidence from available resources at our disposal at the time of publication and reflects best practice. However, this information is not a substitute for clinical judgment and individualised medical advice. Health Hawke's Bay accepts no responsibility or liability for consequences arising from use of this information.