Preventing cardiovascular disease in New Zealand: making better use of statins but also tobacco control, changing the food supply and other strategies

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ABSTRACT

There is new evidence from a very large systematic review and meta-analysis (Navarese et al 2018), that using statins for reducing levels of low-density lipoprotein cholesterol reduces the risk of premature death. In this viewpoint article we consider the implications of this new evidence for New Zealand but also examine how the use of statins may be improved for primary prevention of cardiovascular disease (CVD) in this country. We suggest the need to explore such options as fixed-dose combination pills containing statins, three-drug polypills, behind-the-counter dispensing and six-month prescriptions. But in addition to pharmaceutical prevention of CVD, there is a need for improved population-wide changes to the environment. These include adopting policies to improve tobacco control, the nutrition environment (eg, particularly around sodium), alcohol control and making walking and cycling easier options.

Recent systematic review evidence on statins

A systematic review and meta-analysis has recently been published in the Journal of the American Medical Association (JAMA) by Navarese et al. The authors found that intensive therapy with lipid-lowering medicines such as statins reduced the overall risk of death from all causes and also from cardiovascular disease (CVD), relative to those on less intensive therapy. But surprisingly, this benefit of a lower death rate was only statistically detectable for people with levels of LDL-Cholesterol (LDL-C) above 100mg/dL (which is equivalent to 2.6mmol/L—the units used in New Zealand’s CVD management consensus statement). Conversely, heart attacks and strokes were statistically significantly lower for those receiving intensive treatment (compared to less intensive therapy) both at above or below the 100mg/dL level. For this reason we think there is probably no immediate need to adjust the current New Zealand consensus statement away from the emphasis on CVD risk to any focus on just treating LDL levels. Indeed, New Zealand is a world leader in using absolute CVD risk levels for guiding prevention and management (albeit with this approach not always dominating in clinical practice). Furthermore, the country now has newly developed New Zealand-specific risk equations which are used in the latest consensus statement. Even so there is a need for a pooled analysis of the individual participant data from studies considered by Navarese et al (rather than just the meta-analysis using aggregated data as they used). Specifically, the international health sector needs to see the interaction of baseline LDL and LDL reduction from this individual participant level data, so as to better understand possible management implications at relatively low levels of LDL.
The current New Zealand context

In New Zealand, ischaemic heart disease is the leading cause of death and cerebrovascular disease is the third ranked cause of death. Furthermore, CVD is currently the leading pharmacologically undertreated chronic condition. Recent data reaffirm CVD's contribution to health inequalities, with Māori, Pacific and Indian populations at higher risk. In addition to the disease burden, inequalities are also present in disease treatment. Māori populations are less likely than non-Māori populations to be prescribed CVD medicines, a situation that has not improved substantially over the past decade. The ethnicity-based gap in CVD medication treatment adherence has fortunately decreased in recent years, but a gap still remains.

The need for improved CVD preventive management is further reflected in recent cohort study data. This study used a sub-sample of the PREDICT cohort involving 55–74-year-old patients without prior CVD (ie, a population of 127,000 New Zealanders with a mean age of 62 years, of whom 43% are men and 7% are on a statin). The average LDL-C level in this population was 3.2mmol/L (SD=0.8), suggesting that for most of these New Zealanders, lifestyle change with or without statins to lower LDL-C levels, are appropriate. Furthermore, by absolute levels of CVD risk, there are also large gaps in the provision of treatment among New Zealanders (Figure 1). For example, all those in the highest risk group (>15% risk in this figure should ideally be on statins unless they have experienced notable adverse effects from them. Similarly, a reasonable proportion of those in the next highest risk group (10–15%) should be on statins if they can't reduce their risk via dietary change. New Zealand seems to be prescribing statins at a higher level than Australia for those in the highest risk category, but at lower levels than Australia for the lower risk categories (Figure 1). Other evidence based on a wider sub-sample of the PREDICT cohort (all 35–74-year-old patients) reports that even for people with a prior CVD hospitalisation and where this is known by their primary care clinician, there is suboptimal use of medications for lipid-lowering (ie, at 85% coverage, based on dispensing data).

Figure 1: Proportion of the population-dispensed statins by level of CVD risk in New Zealanders in a sub-sample of 55–74-year-old patients without prior CVD from the larger PREDICT cohort and a similar Australian population (with average ages of 62 and 64 years, respectively; data abstracted from Schilling et al).
How might statin use in New Zealand be improved?

Here we outline some areas for creating a more supportive environment for sustained use of statins, which may be worthy of immediate consideration by New Zealand policy-makers.

Two CVD medicines in one pill

There seems little doubt that fixed-dose combinations (FDCs) of medicines are effective in improving adherence to multiple medicines as per this recent systematic review. FDCs are already on the New Zealand market for combinations of anti-hypertensives but there is no statin and anti-hypertensive option such as the combination of atorvastatin and amlodipine in Australia. Pharmac could therefore consider encouraging the pharmaceutical industry to register such products in New Zealand. This would potentially benefit the large proportion of New Zealanders who are prescribed a statin and who are already prescribed anti-hypertensives. It would also potentially save them prescription charges (at least under current funding arrangements).

Three CVD medicines in one pill—a polypill

Where multiple CVD medicines have been prescribed, improving adherence is also an argument for further evaluating a CVD polypill for this country. Polypill use may potentially reduce Māori versus non-Māori gaps in treatment adherence. Similar to the two-medicine FDCs described above, this product would potentially save prescription charges for patients, dependent on current funding arrangements. Those polypills that combine a statin, anti-hypertensive and aspirin, are now marketed in some other OECD countries (eg, Trinomia). Recent reviews of such polypills are favourable and there is evidence from New Zealand and other countries that use of polypills does not lead to neglect of lifestyle risk factors (eg, dietary change). Overall we suspect that these advantages of such polypills for people with appropriate indications, are likely to outweigh the potential downsides of clinicians having to occasionally revert to monotherapies in order to determine if a specific polypill component is suspected of causing adverse effects etc.

Of note is a recent report that Pharmac's Cardiovascular Subcommittee has recommended that Trinomia be funded in New Zealand. This is a polypill that combines atorvastatin, ramipril (an anti-hypertensive) and aspirin. The use of such a polypill might be justified even further if CVD guidelines were broadened to consider the prevention on colorectal cancer via low-dose aspirin use (as argued previously for New Zealand).

Behind-the-counter (BTC) statins at pharmacies

Regulations could be changed to allow pharmacists to provide controlled access to statins and anti-hypertensives for people with a past doctor's prescription in the last year or two using a BTC arrangement. This would be analogous to how New Zealand pharmacists can now dispense oral contraceptives, ie, a doctor's prescription is not needed for every dispensing. Statins are BTC at pharmacies in the UK with some evidence of this approach being beneficial.

Six-month prescriptions for CVD pharmacotherapy

This approach is currently used for oral contraceptives in New Zealand, but could be reasonably explored for statins, anti-hypertensives, low-dose aspirin or FDC/polypill equivalents. Longer duration statin prescriptions have been associated with greater adherence and enhanced treatment effectiveness. This would probably reduce costs to patients in terms of doctor visit costs and prescription charges. Consideration could also be given to the Australian 'continued dispensing' model. This approach enables pharmacists to dispense a one-month supply of statins to a patient without a valid prescription, thereby ensuring a non-interrupted supply (eg, when the user runs out of supply when travelling away from home).

Improved health literacy and information for decision-making

More research into why New Zealanders who are recommended to take statins by their doctors and who are not taking them (their knowledge, attitudes and behaviours) could build on the findings of a systematic review. This is particularly so in terms of how such research might help reduce ethnic inequalities in the use of this preventive medication (eg, health literacy around statins among Māori, along
with clinician attitudes around offering preventive medication).

More specifically there is a likely need for patients to have answers to such questions as, “If I take this statin for the rest of my life, how many extra years of life might I expect from it?” Similarly, for policy-makers, “What is the likely cost-effectiveness and cost-savings to the health system with use of statins in different age/sex/ethnic-groups?” The Burden of Disease Epidemiology, Equity and Cost-Effectiveness Programme (BODE) at the University of Otago Wellington are exploring such issues using multi-state life-table modelling. When completed, this work may allow for more informative guidelines and facilitate more meaningful patient-clinician discussions around what is the best personalised path to preventing CVD.

Tackling other key drivers of the CVD epidemic in New Zealand: smoking, processed food, alcohol and physical inactivity

Although the more targeted strategy of increasing the use of medicines such as statins is important in those at the appropriate levels of elevated CVD risk, another priority is to improve population health strategies. In particular, smoking is a major contributor to CVD in New Zealand and so it seems necessary to progress the Government’s Smokefree 2025 goal more vigorously as per this proposed plan and various endgame strategies (eg, a sinking lid on supply, the ‘tobacco-free generation’ strategy, retail outlet restrictions and tobacco tax increases). Many New Zealand modelling studies show that tobacco control interventions are cost-saving to the health sector (including higher tobacco taxes, specific endgame interventions and more traditional quitting support interventions).

There is also a need to make improvements to New Zealand’s hazardous food environment since processed foods contribute to CVD by being high in salt (sodium) and saturated fat. To progress things further there is a need for additional action on 19 widely recommended good practice food environment policies to improve population nutrition. In particular, there is a need to consider taxes on unhealthy food and soft drinks. Indeed, Mexico has a ‘junk food’ tax which appears to be working and some European countries tax salty products. Favourable results have also come from a potential salt tax modelled for New Zealand, a modelled salt tax in the US, and a range of food taxes modelled for Australia (on saturated fat, salt, sugar and sugar-sweetened beverages).

The level of sodium in processed food could be reduced by regulation (especially now that there is clearer evidence that the relationship with the risk of death linearly increases from low to high sodium intakes). Indeed, there is now published New Zealand modelling work on dietary salt reduction, which suggests cost savings to the health system with these and other sodium reduction interventions detailed in an online interactive league table.

The largest study to date indicates that alcohol consumption monotonically increases overall risk of health loss at all levels of intake. Even though this study found a J-shaped curve for ischaemic heart disease risk (eg, with a minimum risk for men at 0.83 standard drinks daily), this benefit was eliminated by other health risks (eg, cancer risk). Furthermore, a high level of alcohol intake is a net contributor to increased CVD risk (ie, via stroke, arrhythmias, heart failure, fatal hypertensive disease and fatal aortic aneurysm, all outweighing any reduced risk of myocardial infarction). This evidence, combined with that of another recent large study and New Zealand-specific evidence for harm from alcohol, could be used to justify further advances in alcohol control in this country. These interventions could include such evidence-based ones as higher alcohol excise taxes and warning notices on health risks.

Finally, since physical inactivity contributes to CVD risk, New Zealand could benefit from improved infrastructure so that walking and cycling to work are more viable options. This could be done by building more cycleways, upgrading walkways and reducing urban sprawl. For example, in some American cities there has been good adoption of cycling infrastructure along with favourable evaluations eg, as per a study of investing in bicycle lanes in New York City. The latter study suggested a cost of only $1,300 per quality-adjusted life-year.
(QALY) gained, which is very good value-for-money. Similarly, in Portland Oregon, a study of bicycling infrastructure reported that: “The benefit-cost ratios for healthcare and fuel savings are between 3.8 and 1.2 to 1, and an order of magnitude larger when value of statistical lives is used”. Municipal investment in off-road trails has also been found to benefit bicycle commuting in the city of Minneapolis.

Conclusions

The new systematic review published in JAMA highlights again the value of statins for preventing death from all-causes and from CVD. Ideally more work will better clarify the size of the benefits for treating those with low LDL-C levels (<2.6 mmol/L). In the meantime, New Zealand probably needs to do more work to increase statin use among those at increased CVD risk. There seems to be a need to explore various options such as fixed-dose combination pills, polypills, BTC dispensing and six-month prescriptions. But there is also a strong case for the New Zealand Government to do more population-level CVD prevention via adopting policies to advance tobacco control, improve the nutrition environment (eg, particularly around sodium and saturated fat), improve alcohol control and making walking and cycling easier options.

Competing interests:
Nil.

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