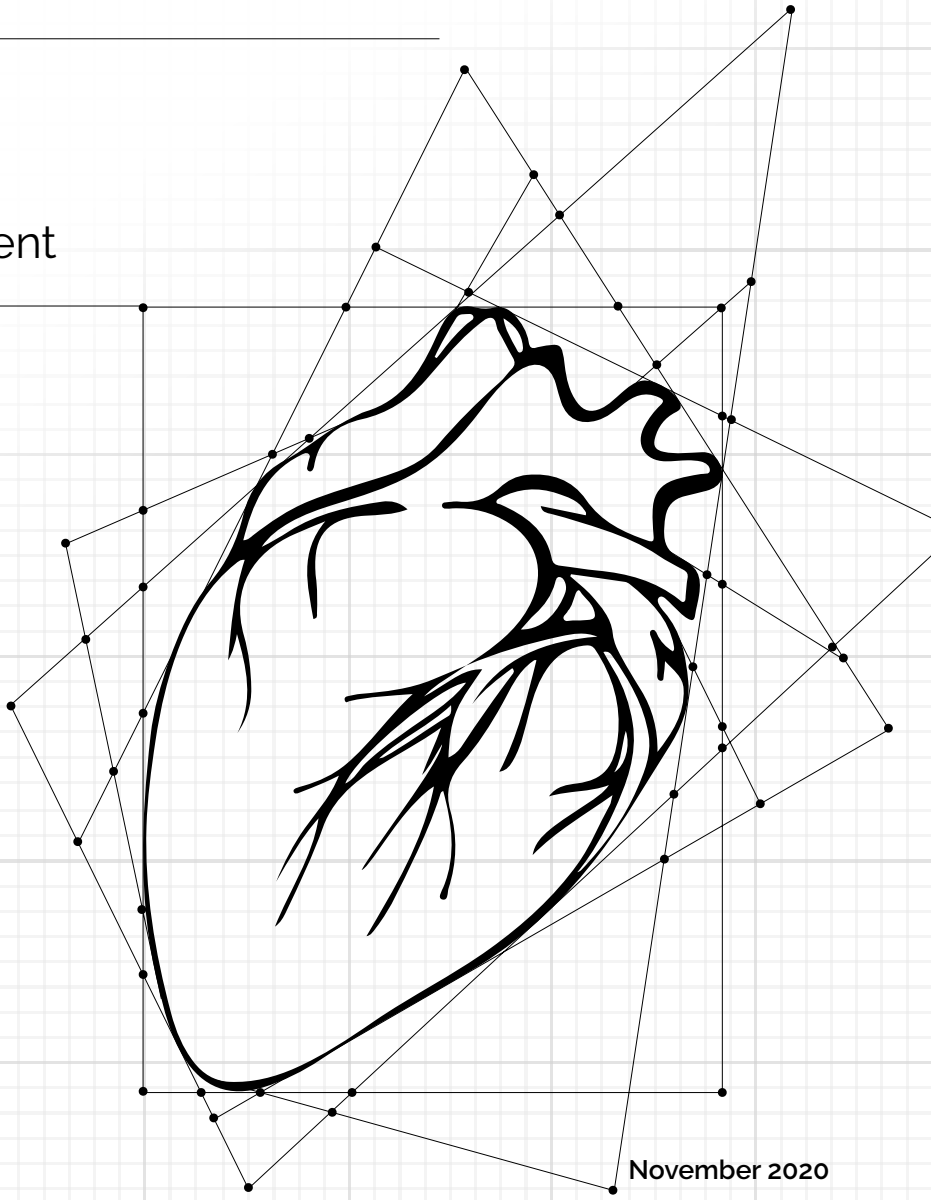
evohealth

Australia's cholesterol heartache

A simple roadmap
for urgent action on
cholesterol management



November 2020

About Evohealth

The delivery of healthcare is complex.
Our focus is not.

Evohealth was established in 2019 to challenge healthcare delivery through innovation and creativity.

Executive summary

Australia has become cholesterol complacent.

This complacency is putting Australians living with cardiovascular disease (CVD) - our nation's biggest killer - at risk of another cardiac event or death. Too many Australians continue to lose their lives unnecessarily (1).

In recent years, there has been significant focus and investment on primary prevention of CVD (prevention of a cardiovascular event such as a heart attack or stroke before it happens). This has been welcomed by Australia's cardiovascular community. However, few policy interventions or investment have been directed at preventing a subsequent cardiovascular event in high-risk patients (secondary prevention) leaving a significant number of Australians at risk of a further event.

For 10 years, we lacked the data to demonstrate how many of these Australians are at risk. In 2020, data published by the Baker Heart and Diabetes Institute revealed the true impact of under-treated cholesterol in high-risk Australians. The CODE RED: Overturning Australia's Cholesterol Complacency report (CODE RED) indicated that almost 500,000 Australians have 'bad cholesterol' or low-density-lipoprotein cholesterol (LDL-C) higher than the recommended target (2).

These Australians share an unaddressed, but inherently treatable disease burden. It is time we focused on how to reduce this burden and in doing so save lives.

To save the lives of these high-risk patients, we need to focus on modifiable risk factors - cholesterol levels, blood pressure and smoking status (3). We know, in particular, that high LDL-C or 'bad' cholesterol contributes to the risk of a subsequent CVD event (4). Fortunately, treating 'bad cholesterol' is straightforward and an effective way to reduce risk and the burden of disease for these Australians.

Yet, this does not appear to be the case. The CODE RED report revealed that 40 per cent of high-risk patients on lipid-lowering therapy have LDL-C levels above the accepted target of 1.8 mmol/L. Treatment is not being optimised, despite the fact that the solution is simple and straightforward.

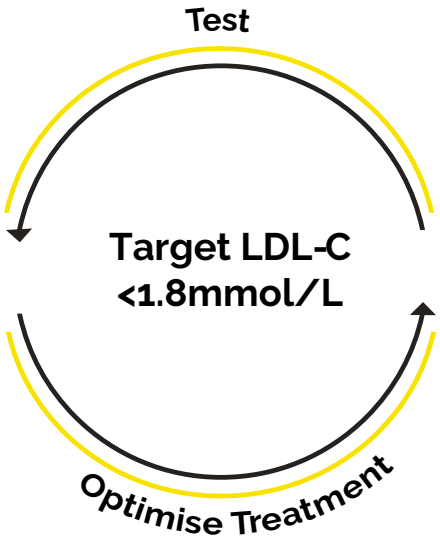
It's time to take urgent action on cholesterol

The road map to better managing cholesterol amongst high-risk Australians is clear, we need to utilise and leverage existing health infrastructure and policies. In doing so, we can save Australians from suffering a further event or worse. Developed together with Australia's clinical and patient CVD community, this report lays out an actionable policy plan to address the burden of poor LDL-C management.

Test and treat

At the centre of our road map is an ongoing cycle of test and treat. To be more specific, we need to ensure that each Australian at risk of a secondary CVD event has their LDL-C tested **every year** and their treatment adjusted relative to the **target of <1.8 mmol/L LDL-C.**

This cycle of 'test and treat' frames the policy solutions included in this report.



To ensure the 'test and treat' methodology is embedded in clinical practice, We propose a range of policy reforms that build on Australia's current health infrastructure to better address the burden of poor LDL-C management and improve clinical outcomes for high-risk CVD Australians.

The five solutions proposed are:

1. Ensure all high-risk Australians know their LDL-C level
2. Embed annual LDL-C tests for all high-risk Australians
3. Standardise lipid profile reporting across Australia
4. Update the guidelines to reflect best practice for secondary prevention of CVD
5. Enhance the role of quality cardiac rehabilitation across Australia

Our solutions will significantly reduce the burden of CVD in Australia. Our economic analysis reveals that these solutions will result in 20,704 fewer Australians dying from CVD, and 64,411 less non-fatal CVD events for a cost to Government of $226 million over 5 years.

In fact, the costs of ensuring that a majority of patients have a lipid profile test undertaken every twelve months, including establishing the baseline measurements (solution one and two), is $226 million or $197 per patient over a five year period (plus the costs of an awareness campaign). The policy solutions outlined in this report present an achievable road map for Government.

Solving Australia's cholesterol heartache

The CODE RED report demonstrated that, as a nation, Australia is failing the clinical care and management of many high-risk Australians with CVD. We know what we need to do to deliver better health outcomes. These solutions are simple, affordable and able to be delivered immediately using existing infrastructure and policies.

Together with the CVD community, we call on the Federal Government to commit to these policy reforms and act now to reduce the impact of CVD on all Australians.

This annual 'test and treat' cycle results in **20,704 fewer CVD deaths** and **64,411 non-fatal CVD events avoided** over a lifetime for a relatively low cost to Government.

TEST & TREAT

is the best way to address LDL-C burden

Solutions 1 & 2 of this report will result in

3,221 lives saved +

7,591 non-fatal CVD events avoided

at a cost to the Government of $197 per patient over 5 years

The LDL-C target in Australia for high-risk patients is **<1.8mmol/L** (7).

(7) Therapeutic Guidelines. Australian Therapeutic Guidelines. 2020.

10-15%

Lifestyle modifications have only been shown to result in a **10-15 per cent reduction** in LDL-C (6).

(6) Gylling H, Strandberg TE, Kovanen PT, Simonen P. Lowering Low-Density Lipoprotein Cholesterol Concentration with Plant Stanol Esters to Reduce the Risk of Atherosclerotic Cardiovascular Disease Events at a Population Level: A Critical Discussion. Nutrients. 2020;12(8):2346.

There are an estimated **1.15 million Australian** patients at high-risk of CVD (12).

(12) ABS. National Health Survey: First Results, 2017-18. . In: Statistics. ABo, editor. Canberra2019.

70% This plan will result in a **70% improvement** in those high-risk patients currently not on ANY treatment for LDL-C

In Australia there are approximately **169 acute coronary events** every day (5).

169

(5) AIHW. Australia's Health 2020. Canberra, Australia2020.

When it comes to lipid lowering therapy, the Australian Therapeutic Guidelines note that

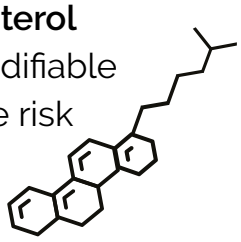
> ...the extent of the benefit [of therapy] depends on the extent of the LDL-C reduction achieved (7).

(7) Therapeutic Guidelines. Australian Therapeutic Guidelines. 2020.

40% Recent data shows **40% of high-risk patients** had an LDL-C result that did not meet the recommended LDL-C target of **<1.8 mmol/L**' (2)

(2) Carrington M, Cao T, Haregu T, Gao L, Moodie M, Yiallourou S, et al. CODE RED: Overturning Australia's cholesterol complacency. Melbourne, Australia: Baker Heart and Diabetes Institute,; 2020

Cholesterol is a modifiable disease risk factor



Cardiac rehab results in...

65% 65 per cent improvement in medication adherence comparatively (8).

26% 26 per cent reduction in mortality (8).

18% 18 per cent reduction in hospital readmission (8).

(8) Australian Cardiac Rehabilitation Association. Why cardiac rehabilitation really matters. 2016.

Cardiac Rehab participation is poor with just

1 in 3 patients referred at discharge (8).

Contents

Disclaimer

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November 2020

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- Professor Alun Jackson, Australian Centre for Heart Health
- Professor Tom Marwick, Baker Heart and Diabetes Institute
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- Mr Shoukat Khan, Heart Support Australia
- Mr Bill Stavreski, Heart Foundation of Australia

Why action is needed on CVD

CVD is a significant burden on the Australian health system and community

Cardiovascular Disease (CVD) is a major health concern in Australia. Coronary Heart Disease (CHD), a subset of CVD, is caused by the narrowing of arteries with cholesterol plaques (atherosclerosis). This condition is the leading single cause of death of Australians (5, 9). The Australian Institute of Health and Welfare (AIHW) estimates that in 2017, approximately 61,800 people aged 25 and over had an acute coronary event, a heart attack or unstable angina, which equates to 169 events every day (5). Consequently, CVD costs the Australian community more than any other condition accounting for approximately 8.9 per cent of healthcare expenditure or $10.4 billion (AUD) in 2015-16 (10).

Patients with CVD have elevated risk of stroke and heart attack with major implications for patient morbidity and mortality. The main risk factors contributing to CVD are high blood pressure, high cholesterol, diabetes, lifestyle factors (such as smoking and alcohol intake) and family history.

Recent focus on primary prevention

There has been significant focus and investment from Government on preventing CVD and subsequent events. Prevention is often considered in terms of two main groups of people: (11)

Primary prevention: people with risk factors who have not yet developed cardiovascular disease.

Secondary prevention: people with CHD, cerebrovascular disease or peripheral vascular disease.

Recently, in Australia, there has been a strong focus and significant Government investment in primary prevention, that is, prevention of a cardiovascular event before it happens. Primary prevention is often focused on lifestyle modification, such as diet and exercise, and therapeutic interventions such as cholesterol lowering medication, where appropriate. Examples include the development of the Absolute Cardiovascular Risk Guidelines and the introduction of the Medicare Benefit Schedule (MBS) funded Heart Health Check.

While this work is critical, there is a significant population of Australians at risk of an event or death (secondary prevention patients) who are, as a result, absent from policy debate. Recently published data estimates 1.15 million Australian patients fall into this high-risk category (12).

To ensure that this report adequately addresses the risk for patients who are most at risk of a secondary CVD event or death, two cohorts have been defined.

High-risk CVD patients

There are various definitions of high-risk patients with respect to secondary prevention of CVD. For the purpose of this report we have developed an evidenced based definition of high-risk (Appendix A). At a macro level, high-risk patients include those with:

- documented atherosclerotic CVD;
- Diabetes Mellitus with target organ damage;
- mild to moderate chronic kidney disease;
- markedly elevated low-density lipoprotein cholesterol (LDL-C) (prior to treatment >4.9mmol/L); or
- familial hypercholesterolemia (FH).

At-risk CVD patients

We have also included a second cohort of patients. These are patients who do not currently meet the high-risk definition based on lipid levels, but their LDL-C is still above target, and are therefore at risk of a subsequent event.

Specifically, these patients have a level of LDL-C (between 1.8mmol/L and 4.9mmol/L). The at-risk group has been identified to reflect the importance of optimising lipid therapy to achieve the accepted target level of <1.8mmol/L. An example of a patient in this group is one who may have met the high-risk definition prior to commencing on lipid therapy and has yet to reach target following intervention.

What is cholesterol?

Cholesterol is a fatty substance, present in the blood, that is necessary in the synthesis of some hormones and vitamin D as well as food metabolism (13). Cholesterol is transported through the bloodstream on two types of lipoproteins, these are (14):

- low-density lipoprotein (LDL-C), also referred to as 'bad' cholesterol, makes up the majority of the body's cholesterol.
- high-density lipoprotein (HDL-C), also referred to as 'good' cholesterol, absorbs cholesterol and returns it to the liver.

Cholesterol makes up a component of the body's lipid profile, otherwise known as serum lipids. The other key component is triglycerides. A full lipid profile requested by a medical practitioner will return measurements on total cholesterol (TC), HDL-C, LDL-C, non-HDL-C (TC minus HDL-C) and triglycerides (15). See Table 1 below.

Lipid	Abbreviation	Description
High density lipoprotein cholesterol	**HDL-C**	HDL-C is composed of cholesterol, triglycerides, and various apolipoprotein. The primary function of HDL is the transport of cholesterol from the peripheral tissues to the liver.
Low density lipoprotein cholesterol	**LDL-C**	LDL-C particles are enriched in cholesterol and are responsible for transporting the majority of the cholesterol that is in the circulation. LDL-C presents CVD risk as it can build up in arteries causing atherosclerotic plaques.
Triglycerides	**TG**	Triglycerides are fatty acid esters of glycerol and represent the main lipid component of dietary fat and fat deposits.
Total cholesterol	**TC**	TC is a measure of serum cholesterol and includes HDL-C, LDL-C and very low-density lipoproteins.
Non high-density lipoprotein cholesterol	**Non HDL-C**	Non–HDL-C level is defined as the difference between total cholesterol (TC) and HDL-C levels.

Table 1: Full lipid profile – abbreviations and descriptions (16-19)

Reducing risk of secondary CVD

CVD is an umbrella term for many disease states and events, and consequently is a complex condition to manage. This complexity is further compounded in patients considered at high-risk of CVD as they often present with several comorbidities and additional risk factors. While all risk factors and comorbidities must be considered holistically in the approach to managing these patients, personalised management to reduce the risk of future CVD events is required. This includes a focus on reducing risk from modifiable risk factors, namely, cholesterol, blood pressure and smoking status. If these risk factors are adequately addressed, there can be a substantial effect on lowering CVD events (3).

Clinical trial data identifies high cholesterol or elevated LDL-C as one of the main causative risk factors for CVD within the set of modifiable risk factors (4). Further, the results of epidemiological studies, as well as trials with clinical endpoints, confirm that a reduction in LDL-C reduces further CVD events (20).

Within this context, this report outlines actions the Government can undertake to improve the management of cholesterol, specifically LDL-C, among the high-risk and at-risk population.

We need to focus on LDL-C

Despite the evidence on the importance of reducing LDL-C for the prevention of CVD, there is a gap in how we are measuring and managing it in Australia. Consequently, the burden of poorly managed disease, specifically LDL-C levels, has not been adequately addressed.

The CODE RED report examined records of 107,664 high-risk patients with prior CVD over the period 2010 to mid-2019 and found that too many did not meet the recommended LDL-C target levels (2).

Further, CODE RED noted 21 per cent of the study population did not have a recorded prescription for recommended lipid lowering therapy.

> “ of the study population receiving recommended lipid-lowering treatment, **40% of patients** had an LDL-C result that did not meet the recommended LDL-C target of <1.8 mmol/L (2)

Improving the management of elevated LDL-C in high-risk patients presents a **simple**, **achievable** and **cost-effective** means of addressing the disease burden of CVD events, particularly in the high-risk patient cohort

1 population represents a sub-population of the high-risk cohort described in this report. Refer Appendix A.

Lifestyle interventions such as improved diet and exercise are considered first line approach to reducing cholesterol, including LDL-C. However, lifestyle modifications have been shown to result only in a 10-15 per cent reduction in LDL-C (7). Further, in patients with a genetic disease, such as FH, diet and lifestyle modifications alone will not be sufficient (21). For further detail on FH, refer to 'FH is more than family history' within this report.

Data from clinical trials consistently demonstrate the efficacy of pharmacologic interventions, in reducing the risk of cardiovascular events and total mortality (22). Treatment with statins, a lipid lowering therapy, is considered to be one of the most effective treatment options in terms of reducing serum lipids, particularly LDL-C, and is therefore a first-line therapy (23). The argument for pharmacologic intervention is proportionate to the level of patient risk, with the benefit being greatest for those patients with the highest CVD risk (7) (23).

Importantly, the benefits of therapies used in standard practice are noted as being greatest with LDL-C reduction. In fact, the Australian Therapeutic Guidelines note that most of the benefits accrue from reduction in LDL-C (7). The efficacy of pharmacologic therapies has also been consistently proven with respect to the treatment of FH.

> "…the extent of the benefit [of therapy] depends on the extent of the LDL-C reduction achieved." (7)

There are currently three types of subsidised medications available in Australia for the purposes of lipid management:

- 'Statins', which include drugs such as simvastatin and atorvastatin. These reduce cholesterol biosynthesis and regulate lipid metabolism and are the mostly widely prescribed medicines for lipid management.
- Ezetimibe, with a different mode of action, works to inhibit intestinal and biliary cholesterol absorption by targeting cholesterol transport protein.
- Proprotein convertase subtilisin/kexin type 9, or PCSK9 inhibitors. These inhibitors prevent the degradation of the LDL receptors in the liver and thereby control the level of LDL in plasma.

How these medicines are recommended for use in lipid management is explained in the chapter 'Best practice lipid management'.

FH is more than family history

A sub-set of patients at high-risk of CVD are those with Familial Hypercholesterolemia (FH). FH, is an autosomal dominant genetic disorder related to LDL-C metabolism, which often results in life-long elevated LDL-C levels (24). FH is present at birth and is responsible for accelerated forms of atherosclerotic CVD, especially CHD (9). The prevalence of FH in Australia is estimated as one in 350 or 1.25 million Australians (25).

Policy interventions targeted at FH are urgently required. Only 10 per cent of cases of FH have been diagnosed in most western countries, with only 5 per cent being treated appropriately (9).

Diagnosis of FH is alarmingly low. However, the diagnostic pathway including early detection and family screening, is well documented (25). For example, the Dutch Lipid Clinic Network Score (DLCNS) provides a validated set of criteria that supports clinicians in the identification of FH (26). The DLCNS considers patients' CVD history, family history, and clinical presentation and is the preferred FH screening tool in Australia (9) (26) (21).

In recognition of the unaddressed burden of FH, the Australian Government recently included a specific item number on the MBS (item 73352) for patients and family members with heritable mutations associated with FH.

Reducing the burden of FH

So low is the detection of this genetic disease, that a targeted policy program must be focused not only on patients, but the clinicians at the front line of patient care.

There is an opportunity to specifically enhance both clinician and consumer awareness of FH, in particular screening, diagnosis and appropriate treatment. Raising consumer awareness will also increase the likelihood that family members will participate in cascade screening where appropriate, which is also supported by the newly introduced MBS item code.

The tools available to GPs, such as the Absolute Risk Calculator, are not effective for diagnosing patients with FH (27). Many of these patients present with low risk overall, despite high lipid levels and/or family history of premature CVD. Further the Framingham model, established from the Framingham Heart Health Study data, notes age as the biggest predictor of risk for CVD and therefore does not appropriately identify the risk for younger FH patients (27) . Experts in the field of FH consistently agree that raised lipid levels in the absence of other risk factors requires further investigation.

Advances have recently been made in genetic diagnosis of patients with FH. It is anticipated, that given the MBS funding of item 73352 from July 2020, diagnosis of FH will increase. Whilst this is an advance for specialists, developing a targeted campaign at raising awareness amongst GPs needs to be a national priority. Policy interventions at the primary care level will result in increased diagnosis and treatment of FH, ultimately leading to fewer CVD events and lower mortality.

The solution is simple

FH, once diagnosed, is a relatively easy condition to treat. The treatment algorithm is the same as for non-FH hypercholesterolaemia and therapies are funded on the PBS. Therefore, any policy intervention that improves diagnosis and optimising therapy is likely to be cost-effective.

Best practice lipid management

There is a wealth of literature to support the need to achieve the desired LDL-C levels in terms of reducing the risk of CVD outlined in an established treatment escalation pathway. This pathway includes the use of maximum tolerated dose statins in combination with ezetimibe, and if this is not successful, the use of a PCSK9 inhibitor.

Globally, clinical guidance is increasingly focused on combination therapy (see Figure 1 below), particularly in high to very high-risk patients, to reduce the risk of a subsequent event. Australian data also demonstrates the benefit of the combination therapy approach. The CODE RED report found that results differed for patients according to the treatment prescribed:

> "…a higher proportion of patients who achieved the LDL-C treatment target [of 1.8mmol/L] were prescribed with statin plus ezetimibe therapy (72%) or PCSK9 inhibitor (75%) compared with 60% for statin monotherapy and 45% for ezetimibe alone." (2)

A recent shift in lipid management

In 2019, the European Society of Cardiology (ESC) issued revised guidelines for the management of dyslipidaemia, 'Lipid Modification to Reduce Cardiovascular Risk' (the ESC Guidelines). These updated guidelines reflect the latest evidence in lipid management. The consensus of the updated guidelines is that the lower the level, the lower the risk (28).

The ESC Guidelines also focus on early intervention with the aim of patients requiring less intensive treatment in the longer term (28, 29).

These guidelines advocate a more active approach for high-risk patients by adopting a 'higher risk the patient, the lower the LDL-C target' method to LDL-C management. This is one of the most significant changes in terms of clinical lipid management. LDL-C reduction targets for the very high-risk and very high-risk patient cohorts are described below (28):

> the lower the LDL-C level, **the lower the absolute risk of a CVD event.**

- high-risk: 50 per cent reduction of LDL-C from baseline and a target LDL-C of <1.8mmol/L
- very high-risk: 50 per cent reduction of LDL-C from baseline and a target LDL-C of <1.4mmol/L

One of the other shifts in the evidence since the previous version of the ESC Guidelines (published in 2016) was from major clinical trial results demonstrating the efficacy of PCSK9 inhibitors in reducing LDL-C below levels obtained on intensive statin treatment (30). These results also demonstrate a significant reduction in events in patients with established atherosclerotic cardiovascular disease (ASCVD) and acute coronary syndrome (ACS) when a PCSK9 is used in treatment (30-32).

Also apparent since the last ESC Guidelines update (2016), is increasing evidence to support the use of ezetimibe in combination with statin therapy, particularly for very high-risk individuals (33). In recognition of the growing evidence, the Guidelines urge combination therapy in high to very high-risk patients not responding to statin therapy alone. Furthermore, they encourage the use of maximum tolerated dose statins with ezetimibe and, if this is not successful, they then recommend the use of a PCSK9 inhibitor (28, 30).

Managing lipids in Australia

The Australian Therapeutic Guidelines reflect a treatment escalation that is similar to recent ESC Guidelines. In Australia, statins and ezetimibe can be prescribed in the primary care setting by a GP, however, PCSK9 inhibitors must be prescribed by a specialist physician. This pathway is reflected in Figure 1 below.

Figure 1 lipid management treatment escalation pathway

Source: Evohealth

Currently, the Australian Therapeutic Guidelines, and other guidance (34) approximate the same LDL-C target as the ESC Guidelines in terms of secondary prevention (<1.8mmol/L for all secondary prevention, regardless of risk category).

However, the Australian guidance is yet to reflect the 'the lower the better' approach adopted in Europe. In that, they do not yet recognise the evidence to support an LDL-C reduction target of <1.4mmol/L for patients at very high-risk of an event. Given the latest evidence, it is considered likely that a guideline revision will eventually result in similar targets to the ESC Guidelines.

Opportunities to optimise lipid management

Whilst guidance in Australia is broadly consistent with global best practice, it is important to note that patients will only benefit if this guidance is being followed by both clinician and patients. This includes adherence to the appropriate diagnostic pathways, prescribing, and patient persistence and compliance with treatment (35).

Recently published data through the CODE RED report suggests that this is not always the case and that, in fact, there are significant gaps in the way elevated LDL-C in high-risk patients is being managed in Australia (2). This presents an opportunity to improve the way we optimise management of LDL-C in high-risk patients and consequently save Australian lives and these opportunities are outlined below.

Increase frequency of lipid testing

The Royal College of General Practitioners (RACGP) Guidelines for Preventive Activities in General Practice (36) recommend annual testing of lipids for high-risk patients. Analysis undertaken in the CODE RED report (2) demonstrated wide variation in the number and frequency of lipid profile tests ordered amongst the cohort studied.

This data points to a significant opportunity to embed an annual cycle to review treatments and standardise the frequency of lipid testing in Australia.

Ensure clinical decision making is supported by full lipid profiles

The Australian Therapeutic Guidelines explicitly state the importance of reduced LDL-C for clinical benefit (7). Current policy and guidelines specifically reference TC and HDL-C in CVD risk calculation and management. Noting this, there is a risk that key clinical parameters such as LDL-C are not obtained by doctors to inform appropriate and effective clinical decision making.

An opportunity exists to ensure that clinicians obtain a full lipid profile which includes TC, triglycerides, HDL-C, LDL-C and non-HDL-C, at each pathology request to support effective clinical decision making.

Expand quality improvement programs in General Practice to include secondary CVD prevention.

Currently, the data capture requirements under the Practice Incentive Payment Quality Indicator (PIPQI) program are focused on absolute risk assessment for individual patients and therefore primary prevention. In its current format, many high-risk patients will be omitted from data collection and subsequent quality improvement in general practice. Therefore, an easily achievable opportunity exists to expand the PIPQI to include high-risk secondary prevention patients, therefore reducing preventable CVD events and saving lives.

Advocate for Government policy to include secondary CVD prevention

Australia, in recent years, has strongly focused on primary prevention of CVD - prevention of a cardiovascular event before it happens. This focus has been supported by various Government investments, including the National Strategic Framework for Chronic Conditions (37). Given the risk of a subsequent event is considerably higher in patients with prior events, there is an opportunity to complement the current focus on primary prevention with a commitment to secondary prevention in order to further reduce the CVD burden in Australia.

Enhance clinician support, including guidelines, to facilitate ongoing optimisation of lipid management

Given the evidence supporting the benefits of appropriate pharmacological intervention in the high-risk cohort, there is an opportunity to ensure that Australian lipid management is consistent with emerging global evidence. The opportunity for this guidance importantly includes both annual testing of a full lipid profile, and management of therapy if LDL-C target levels have not been reached. This will reduce the risk to Australian patients.

Empower patients with information regarding target lipid levels

As with any health condition, raising consumer awareness of the risk associated with a high LDL-C and the need for optimised treatment will empower patients and further support best practice management of lipids.

Programs, like Cardiac Rehabilitation (CR) have been shown to empower patients through provision of support and critical information. Outcomes from successful CR programs includes improvement in medication adherence by as much as 65 per cent (8). Unfortunately, Australian data demonstrates that participation in CR is poor in Australia with only 1 in 3 attending (8). Therefore a key opportunity is to improve CR access and service to support empowerment of patients.

The solutions at a glance

To better address the burden of LDL-C among the high-risk patient population, we have developed five simple, achievable, and cost-effective solutions. These solutions work to support improved management of, and outcomes for, secondary CVD patients. The solutions are provided at a macro level below and detailed in the next chapter.

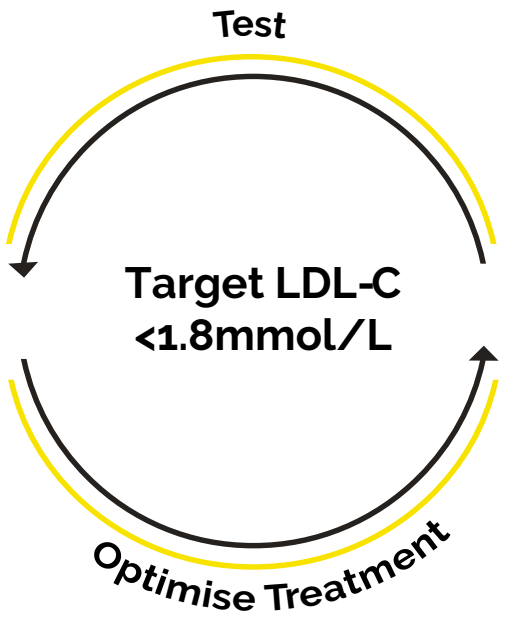
These solutions have been designed for rapid implementation within the current health system and form a comprehensive approach to improving the management of lipids in Australia. They provide a simple, actionable and affordable solution that build on the current health system structure. There are two key elements to these solutions, **test and treat.**

Test

To optimise patient lipid levels, Australia's clinicians need access to accurate and timely pathology results, in particular LDL-C relative to the target of <1.8 mmol/L. It is fortunate then, that lipid profile testing is relatively inexpensive and widely available across Australia.

Treat

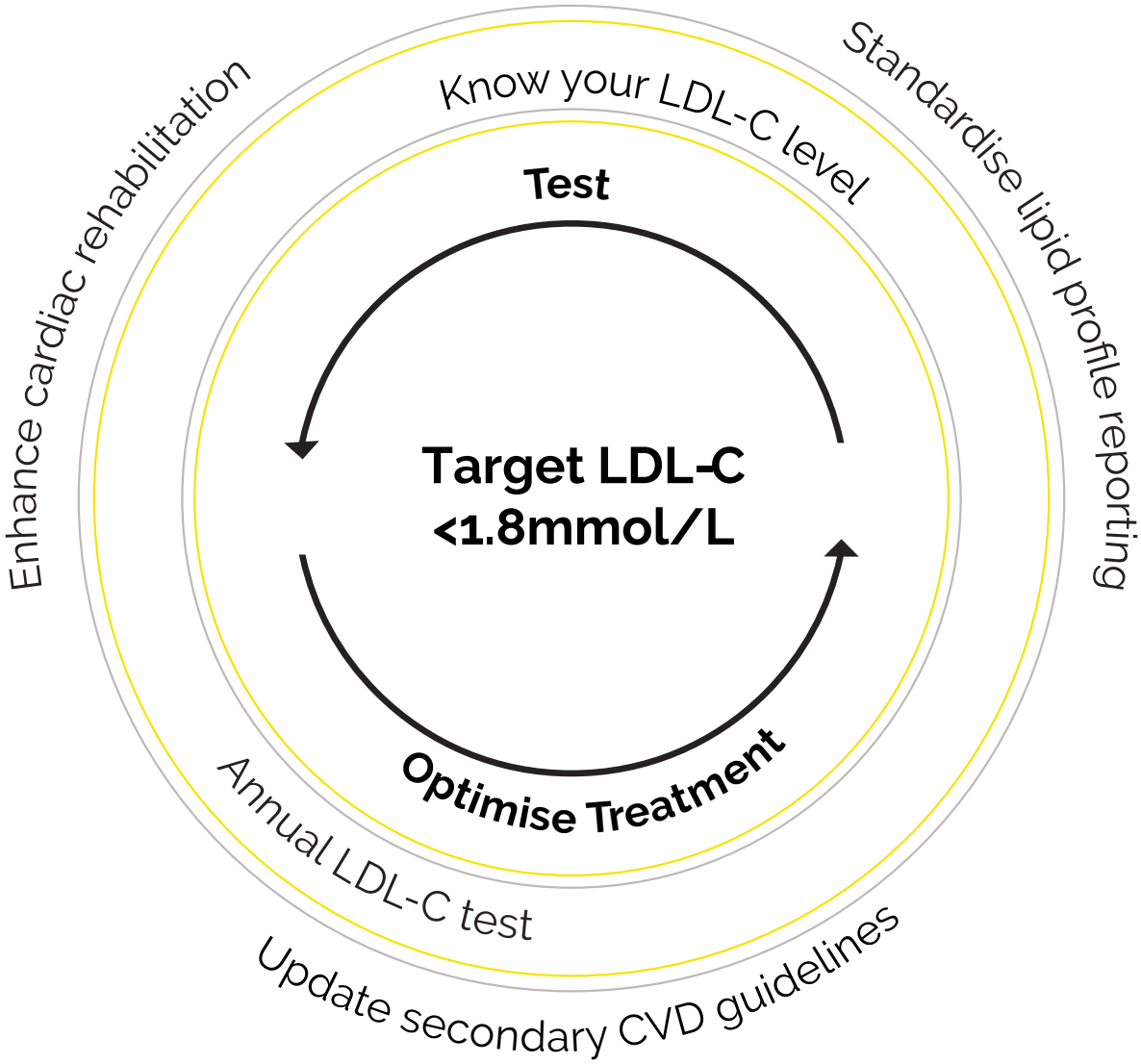
Testing, however, is only one part of the clinical decision framework. Once the result is received, treatment may need to be optimised to achieve the recommended targets set out in the clinical guidelines.



Test and treat cycle

This cycle of 'test and treat' relative to the target of <1.8 mmol/L of LDL-C frames the solutions of this report.

These solutions include specific initiatives to ensure that lipid profile testing is conducted at least annually, and clinicians are supported in how to optimise lipid management.



1 | Ensure all high-risk Australians know their LDL-C level

2 | Annual LDL-C test for all high-risk Australians

3 | Standardise lipid profile reporting across Australia

4 | Update the guidelines to reflect best practice for secondary prevention of CVD

5 | Enhance the role of cardiac rehabilitation across Australia

Summary of solutions

Solution	Summary	Benefit/impact	Cost
1	**Ensure all Australians know their LDL-C level** Establish the baseline LDL-C for both the at-risk and high-risk Australian population to successfully embed an annual 'test and treat' cycle into clinical practice.	• 18,403 CVD deaths avoided over a lifetime; • 60,731 non-fatal CVD events avoided over a lifetime; or In the five years of the program ◦ 2,760 CVD deaths avoided; and ◦ 7,361 non-fatal CVD events	• $181 per patient over five years; or • $208 million.
2	**Embed annual LDL-C tests for all high-risk Australians** Support general practitioners (GP) to conduct annual lipid profile testing of high-risk and at-risk CVD patients supported by a consumer awareness campaign to embed the annual 'test and treat' cycle into ongoing standard clinical practice.	• An additional 2,301 deaths avoided over a lifetime[2]; • An additional 3,680 non-fatal CVD events avoided over a lifetime; or In the five years of the program ◦ An additional 461 CVD deaths avoided; and ◦ An additional 230 non-fatal CVD events avoided.	• An additional $16 per patient over five years; or • $18 million.
Implementation of ONE and TWO together.		• 20,704 deaths avoided over a lifetime; • 64,411 non-fatal CVD events avoided over a lifetime; or In the five years of the program ◦ 3,221 CVD deaths avoided; and ◦ 7,591 non-fatal CVD events avoided.	• $197 per patient over five years; • or $226 million over five years plus the cost of a campaign.

[2] If solution 1 & 2 are implemented together

Solution	Summary	Benefit/impact	Cost
3	**Standardise lipid profile reporting** Facilitate the rollout of standardised lipid profile reporting across Australia to ensure that all clinicians in Australia have access to effective clinical decision support	• enables the optimisation of management and ensures that more Australians are able to reach the target of <1.8mmol/L LDL-C; • improved clinical decision support around FH; and • increased referral to specialist care for lipid management where appropriate.	• No cost to Government. Can be actioned within current resourcing.
4	**Update guidelines to reflect best practice** Update the clinical guidelines for the secondary prevention of CVD to reflect the latest evidence and support clinical decision making in treating to target.	• increased focus on secondary prevention of CVD; and • importance of LDL-C management in secondary prevention of CVD	• No cost to Government. Can be actioned within current resourcing.
5	**Enhance the role of quality comprehensive cardiac rehabilitation** Support to enhance the role of comprehensive cardiac rehabilitation including funding for guidelines to standardise approach and a focus on quality indicators.	• 65 per cent improvement in medication adherence comparatively; • 26 per cent reduction in mortality; and • 18 per cent reduction in hospital readmission.	• No cost to Government. Can be actioned within current resourcing.

Living with high cholesterol

Maja Sorenson | **27**

Maja Sorenson, 27, from Sydney is not someone you would guess is living with high cholesterol - she is young, active and vibrant. But in early 2019, a routine blood test showed that her cholesterol was elevated, with LDL-C levels of 2.3mmol/L. But due to her age she was advised to change her diet and come back in a year for a follow up test.

After travelling and working as a chef overseas, Maja had a follow up blood test in March 2020 after returning to Australia. This test showed a significant jump in her cholesterol, with her LDL-C levels at 3.2mmol/L. However, Maja had just recovered from COVID-19 and it was thought that perhaps this was affecting her cholesterol levels. She had another test a month later which again showed her LDL-C levels at 3.2mmol/L. If her GP had not been diligent about regular monitoring and testing, Maja may have gone undiagnosed.

Despite her age, Maja was not shocked when she was informed of her high cholesterol, it did run in her family after all. Both her mother and father have high cholesterol, and her maternal grandfather has had a number of cardiovascular events, which resulted in him requiring a pacemaker.

Maja would encourage everyone to be diligent in knowing their cholesterol levels and getting tested annually, no matter how young they may be. **"We need to be more diligent in informing people about the dangers of elevated cholesterol, and that the disease does not discriminate, no matter your lifestyle or age."**

Her next steps in treatment will depend on the results of her next cholesterol test, due in six months' time, but in the meantime, she is working to change her diet, and increasing her physical activity by running, cycling and yoga.

Adrian Davidson | **43**

Canberran Adrian Davidson, 43, never imagined he would be impacted by cardiovascular disease. Adrian always prioritised living a healthy lifestyle – he ate well, worked out at the gym 5-6 times per week and did not have a family history of high cholesterol or cardiovascular disease.

Despite this, at the age of 39, at work one day, Adrian experienced a slight fever and discomfort in his chest. A few hours later, Adrian couldn't breathe and his family called an ambulance. Adrian was having a heart attack. Tests revealed three blocked arteries, one completely blocked and two others about 80 per cent blocked. A stent was inserted and open heart surgery scheduled in a few weeks' time. Time was not on Adrian's side. Five days later Adrian, suffered a stroke, leaving him partially paralysed.

About six months prior, Adrian's GP tested his cholesterol, and it was only slightly elevated. It was higher at the time of his CVD events. Through diligent management, his cholesterol levels are now under control, however he still lives with one artery that is completely blocked.

Adrian's heart attack and stroke have significantly impacted his life. Adrian has reduced cognitive function and tires quickly, and as a result hasn't been able to return to work or participate in family outings, in the same capacity as before. Adrian is working at restoring his strength, building up to going to the gym two days per week and working on his ability to enjoy his hobbies again, such as reading books.

He would like everyone to know that often cardiovascular disease comes as a surprise, so it's important to be proactive and get your cholesterol checked regularly. He also says to all the workaholics out there – the stress isn't worth it.

The impact of improving CVD outcomes

An economic model was developed to enable a quantitative assessment of the costs and benefits of the recommended solutions. The approach used to estimate CVD death, CVD events and associated health system related costs was an economic evaluation based on a discrete event simulation (DES) model. The model is based on the CVD and CVD death, risk equations first developed by Anderson et al and published in 1991 and based on analysing data from the Framingham Heart Study (38). Further detail on the approach to the economic analysis is included in Appendix B.

Solutions one and two have been modelled to reveal the benefits, cost and impact to patients, and the health system more broadly. Enabling solutions three to five, with no cost to Government, and variable impact were not included in the analysis.

Analysis of solutions one and two increased the number of patients with an ongoing annual LDL-C result to ninety per cent, thereby increasing the associated program costs.

Program costs

At a program level, the costs of ensuring that a majority of patients have a lipid profile test undertaken every twelve months, including establishing the baseline measurements, is estimated to be **$226 million or $197 per patient over a five year period**.

Test and treat – the impact

1

Lives saved and CVD events avoided

Implementation of an annual 'test and treat' cycle results in 20,704 fewer CVD deaths and 64,411 non-fatal CVD events avoided over a lifetime.

In the first five years of implementation, 3,221 CVD deaths and 7,591 non-fatal CVD events will be avoided.

2

More patients at or below target

Successful implementation of these solutions will shift the population of high-risk patients towards target lipid levels, resulting in a 28 per cent increase in patients with an LDL-C level at target or below (Figure 2).

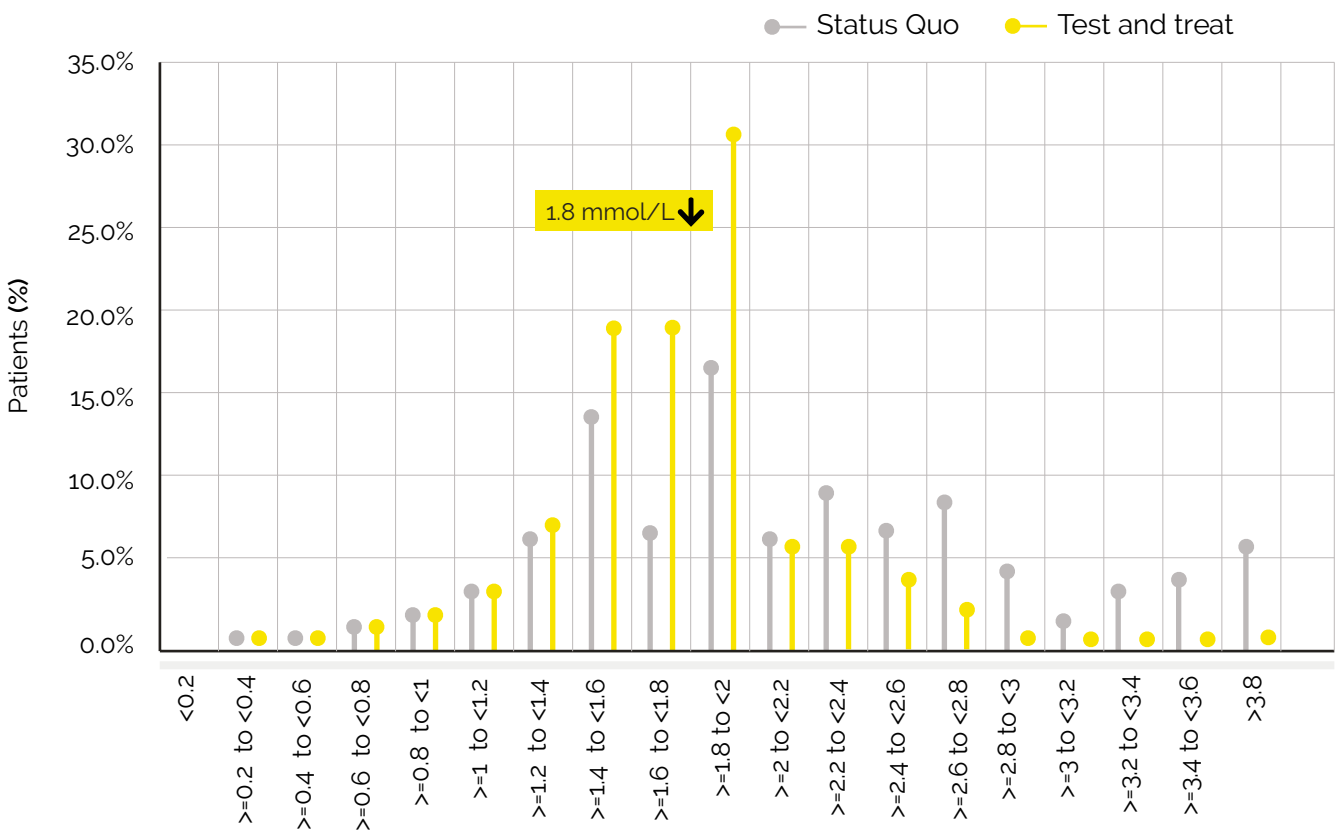


Figure 2 Distribution of patients by LDL-C category

3 More patients on treatment

The analysis demonstrates that more patients are on appropriate lipid lowering treatment, including combination therapy following the implementation of an annual test and treat program. This includes some patients who were previously on no treatment at all, based on data in the CODE RED report. (Figure 3)

Importantly, there is a **significant (70 per cent) reduction** in the patients who were not on any treatment compared with the status quo, as identified in the CODE RED report.

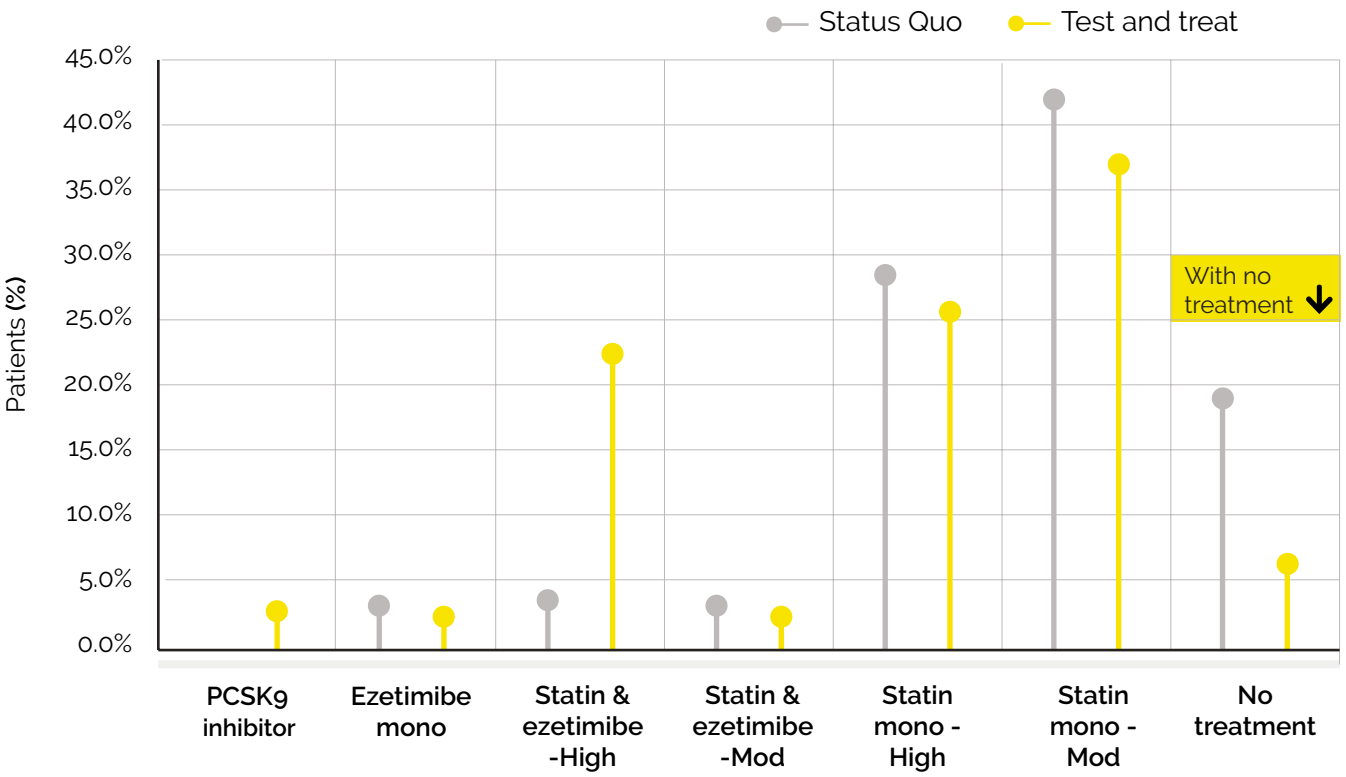
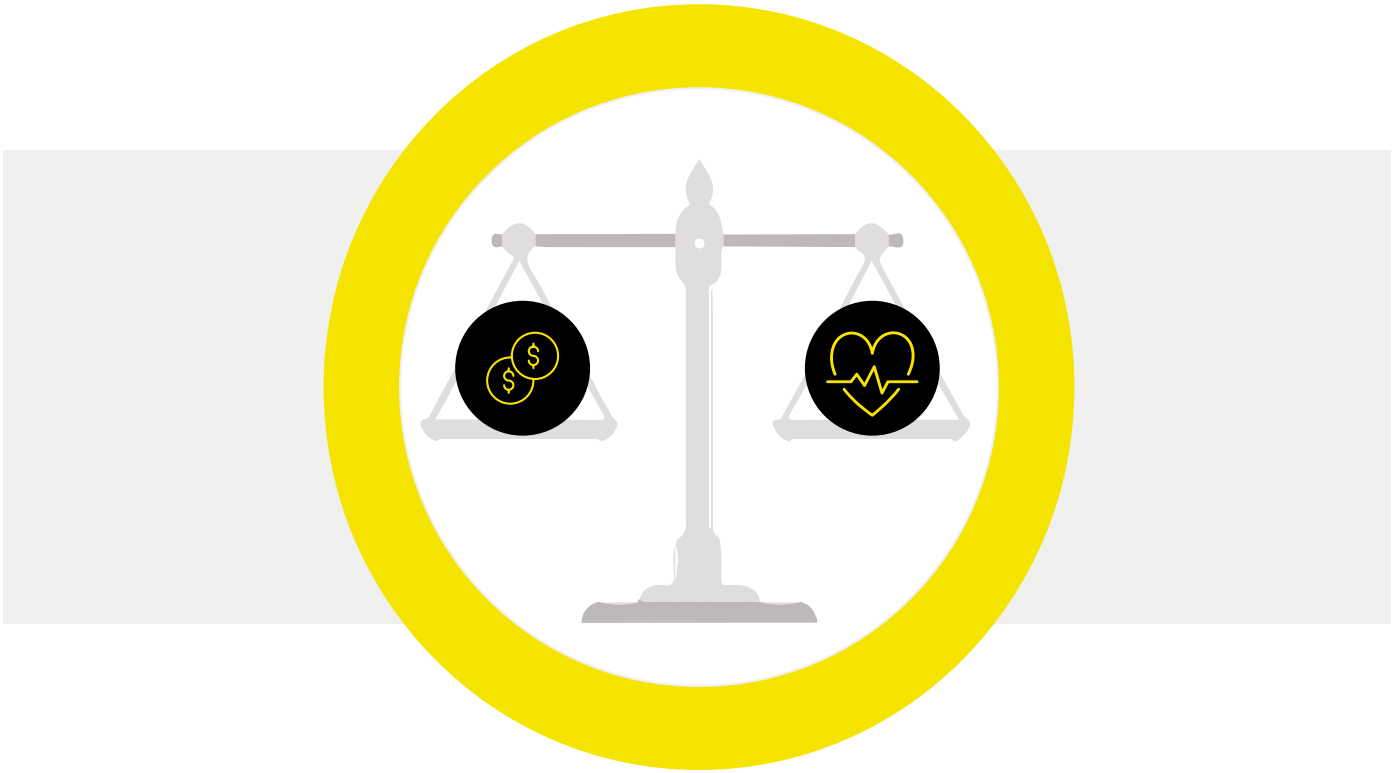


Figure 3 Distribution of patients by treatment at end of study

This analysis demonstrates that the solutions in this report result in almost **65,000 patients** avoiding a non-fatal CVD event and approximately **20,000 fewer** lives lost over a lifetime.

Are these solutions cost-effective?



In order to test if the solutions are cost-effective to Government, a robust methodology consistent with that used by the federal Health Technology Assessment Committees, the Pharmaceutical Benefits Advisory Committee (PBAC) and the Medical Services Advisory Committee (MSAC) was applied (see Appendix B).

This resulted in an **Incremental cost-effectiveness ratio (ICER) of $26,210 per death or CVD event avoided.**

This is well within the range considered cost-effective by these committees. The outcome is also considered conservative as additional benefits such as reduced patient quality of life associated with non-fatal CVD events and the wider implications of costs borne by patients and carers were not captured.

The detailed solutions

Solution One

Ensure all high-risk Australians know their LDL-C level

Implement a national quality improvement program, leveraging existing policy infrastructure to ensure all high-risk and at-risk Australians have their LDL-C level measured and treated as appropriate.

Overview

While it is encouraging to see that a number of patients do have their LDL-C measured (2) we can, and must do more to ensure that a higher number of patients' LDL-C levels are at or below the target level of <1.8 mmol/L. The first step is to determine how many high-risk and at-risk patients (see Appendix A) have had a test within the previous twelve months. Establishing a baseline of LDL-C levels will support embedding an annual 'test and treat' cycle into clinical practice.

There is an opportunity to align this solution with current health policy, specifically the Federal Government's PIPQI for general practice. This program includes two core components:

- participation in continuous quality improvement activities in partnership with the local Primary Health Network (PHN); and
- provision of the PIP eligible data set to the local PHN.

Quarterly data collection and payment for PIPQI is managed through Australia's network of PHNs. The quality activity needs to be informed by data and meet the needs of the population. With almost 500,000 Australians above the recommended LDL-C target of <1.8 mmol/L (2) it is anticipated that most general practices across Australia will have patients who meet the criteria for inclusion.

We are recommending that this activity of annual testing, and subsequent treatment, of LDL-C for high-risk and at-risk patients is aligned with either PIPQI measure eight, 'Proportion of patients with the necessary risk factors assessed to enable CVD assessment' or a quality improvement activity not aligned with PIPQI (39).

This QI activity must focus on targeting high-risk and at-risk patients annually for five years to achieve the greatest impact.

Benefits

With an enhanced focus on secondary prevention through the PIPQI, this provides a simple solution that will fit within current Government policy, at minimal cost, to enhance clinical decision support for general practice to improve lipid management in high-risk and at-risk patients.

Cost

The cost of this program in the economic model includes a Medicare Benefits Schedule (MBS) Consultation B and MBS lipid test (MBS 66512) and is $181 per patient over five years or $208 million. The impact of this policy intervention is summarised below.

IMPACT

18,403 CVD deaths avoided over a lifetime[3*];

60,731 non-fatal CVD events avoided over a lifetime*;

* For Solution one when implemented as stand-alone policy.

Actions required

1.1 | Ensure that the PIPQI measures measure 8 is updated to explicitly include QI activities related to secondary prevention of CVD.

1.2 | Update PIPQI measure 8, to explicitly include the requirement for clinicians to obtain a patient's full lipid profile, including LDL-C.

1.3 | Engage with PHNs on the need for QI activities in secondary prevention of CVD. This would also include providing information with regards to collection of data on a patient's full lipid profile, including LDL-C.

1.4 | Evaluate QI activity uptake, via PHNs, to ensure that there is an equitable spread of activity across metropolitan, regional and rural areas.

1.5 | Develop an example QI activity focused on two key patient variables:
- those meeting the criteria for high-risk and at-risk as noted in appendix A; and then,
- absence of a valid full lipid profile, including LDL-C from the previous twelve months.

1.6 | Develop an example QI activity similar to that listed in 1.5 that is culturally appropriate for inclusion in primary care practices focused on the delivery of health to Aboriginal and Torres Strait Islander people.

1.7 | Develop a campaign targeted at general practice on the benefits of conducting an annual quality improvement activity focused on obtaining a lipid profile for high-risk and at-risk patients over a five-year period. This campaign would include the example QI activity developed under 1.5.

1.8 | Provide information to relevant patient groups on the benefit of supporting this solution.

Solution Two

Embed annual LDL-C tests for all high-risk Australians.

Using the baseline established through solution one, embed an annual 'test and treat' cycle for all high-risk and at-risk Australians. Ensuring that these patients have their LDL-C measured annually and are treated as per best practice guidelines. This will be supported by a consumer awareness campaign to 'know your number'.

Overview

Annual testing of lipid profile for high-risk and at-risk patients forms an integral part of best practice care (36). Solution two seeks to further embed the annual 'test and treat' cycle into ongoing standard clinical practice.

For those practices that seek to implement a QI activity under solution one, this annual test will continue beyond the proposed five years. For the other practices, the annual testing will commence in the first year.

Targeted campaigns and messages that drive the patient to understand their lipid levels will support the 'test and treat' cycle outlined in solutions one and two. This 'know your number' campaign should be aimed at creating an informed patient who is able to seek best practice care from their clinician. It should also include messaging targeted at vulnerable population groups, such as the elderly, so that those who are unable to be active participants in their care are not forgotten.

Benefits

When implemented with the baseline LDL-C QI activity under solution one, this annual 'test and treat' intervention results in significant reduction in non-fatal CVD events and associated deaths. Further, this measure will deliver greater support for clinical decision making for general practice and enhance awareness of elevated LDL-C including target for high-risk and at-risk groups.

This measure is directly aligned with current Government policy, allowing for ease of implementation at a minimal cost to Government.

Cost

The clinical cost of this program has been modelled in addition to the cost of solution one and is $16 per patient over five years or $18 million. Supporting the measure with a 'know your number' campaign is also critical. This campaign is estimated to cost between $5-10 million over 5 years. It has not been modelled.

The impact of this policy intervention is summarised below. However, the full benefit of this solution will only be realised if it is implemented in conjunction with solution one.

IMPACT

An additional **2,301 deaths avoided** over a lifetime*

An additional **3,680 non-fatal CVD events avoided** over a lifetime *

* For solution two when implemented as a stand-alone policy

Actions required

2.1 | Align with solution one.

2.2 | Ensure that clinicians have access to full lipid profiles to inform clinical decision-making.

2.3 | Ensure appropriate pathology comments to flag patients requiring further investigation for possible FH.

2.4 | Adapt clinical information systems to allow for patient tracking and annual recall.

2.5 | Include specific treatment algorithm within Clinical Information System to support appropriate patient treatment.

2.6 | Create a multi-layered 'know your number' campaign targeted at informing all relevant cohorts of CVD patients at risk of future CVD events to increase awareness of the benefits of optimising lipid therapy.

2.7 | Design a complementary campaign for GPs to inform them of the benefits of an annual 'test and treat' cycle including the benefits and funding (if made available) under solution one and two.

2.8 | Both of the campaigns in 2.6 and 2.7 will need to be adapted and delivered annually to support at least the first five years of the intervention detailed at solution one.

Solution Three

Standardise lipid profile reporting across Australia

Coordinate national implementation of the work undertaken by the Australasian Association of Clinical Biochemists to harmonise lipid reporting across Australia.

Overview

This report has highlighted the need for clinicians and patients to have access to a standardised full lipid profile that includes LDL-C, no matter where they live in Australia. Such access will support effective clinical decisions leading to better outcomes for patients.

Fortuitously, work has commenced on this in Australia. In 2018 the Australasian Association of Clinical Biochemists (AACB) endorsed a range of recommendations on the harmonisation of lipid reporting across Australia. These included:

- samples being collected as fasting or non-fasting, and marked appropriately;
- the full lipid panel contains 5 tests: total cholesterol, triglycerides, HDL-C, LDL-C and non-HDL-C; and
- a range of clinical support flags against each of the tests (40).

It is recommended that the Federal Government facilitate standardised roll out to ensure that all clinicians in Australia have access to effective clinical decision support.

Benefits

Altering the standard methods of cholesterol reporting to ensuring each cholesterol test delivers the full lipid profile, including LDL-C levels, enables the optimisation of management and supports more Australians to reach the target of <1.8mmol/L LDL-C or below. It will also support improved clinical decision making, early diagnosis of FH and increase referral to specialist care for lipid management where appropriate.

Cost

There is no anticipated cost to Government, this solution can be actioned within additional resourcing.

Actions required

3.1 Seek input from the Royal College of Pathologists, clinicians (chemical pathologists, cardiologists and GPs), pathology networks and representative bodies to continue work on standardised lipid profile reporting as commenced by AACB.

3.2 Undertake an audit of the current state of lipid profile reporting across Australia.

3.3 Facilitate the rollout of standardised lipid profile reporting, consistent with the solutions formulated by the stakeholders in action 3.1.

Solution Four

Update the guidelines to reflect best practice for secondary prevention of CVD

Establish updated guidelines to reflect best practice management for secondary CVD prevention, particularly for high-risk and at-risk patients.

Overview

Ensuring that patient care is consistent with clinical guidelines leads to better outcomes, such as reduced emergency department (ED) visits and admissions (41) (42). CVD is a complex multifactorial disease and patients often present with multiple risk factors and co-morbidities. Evidence suggests that patient complexity can lead to less consistency with best practice care (43).

In Australia, the most relevant guidelines for patients at risk of a secondary event are 'Reducing risk in heart disease – an expert guide to clinical practice for secondary prevention of coronary heart disease' (44). These guidelines were last updated in 2012.

Whilst the guidelines note the targets for LDL-C of <1.8 mmol/L, they do not include all pharmacologic therapies currently available for patients in Australia nor the current pathway to diagnosis and treatment of FH patients, and their families.

In addition to developing guidelines, a range of mechanisms can be utilised to ensure that guidance is embedded into clinical practice, these include:

- individual audit and peer feedback on guideline uptake;
- sending out reminders to clinicians,
- educational seminars with opinion leaders;
- having dedicated nurses / allied health professionals to assist physicians operationalise the recommendations;
- reimbursement incentives; and
- Support (financial and institutional) for performing any additional administration.

Benefits

Ensuring that all clinicians have access to updated guidelines to provide best practice care to CVD patients is critical to drive improved patient outcomes. Additionally, a structured implementation plan that includes incentives for administration and feedback mechanisms, will ensure that the guidelines are reflected in real world clinical practice. This will drive:

- a standardised approach to lipid management for secondary prevention;
- increased focus on secondary prevention of CVD; and
- importance of LDL-C management in secondary prevention of CVD.

Cost

There is no anticipated cost to Government, this solution can be actioned within current resourcing.

Actions required

4.1 | Establish a multi-disciplinary working group, including representatives of key clinical groups and patients to develop an updated national guideline document for secondary prevention of CVD.

4.2 | Once developed, ensure that this guideline is available in a range of accessible formats, including digital.

4.3 | Ensure that the guideline is relevant and supported by a range of mechanisms to ensure that it is embedded in clinical practice.

4.4 | Schedule mechanisms for review so that the guideline remains up to date with respect to current evidence and clinical practice.

Solution Five

Enhance the role of cardiac rehabilitation across Australia

Coordinate national implementation of the recommendations proposed by the Australian Cardiovascular Health and Rehabilitation Association to ensure a standardised approach to quality comprehensive cardiac rehabilitation across Australia.

Overview

Cardiac rehabilitation is a medically supervised program for patients who have had an acute CVD event or surgical intervention, most often at discharge from the tertiary setting. When patients participate in cardiac rehabilitation (CR) they have fewer hospital admissions, better medication adherence and overall improved survival (45, 50).

In fact, there is a 16 per cent reduction in mortality and 18 per cent reduction in hospital re-admissions leading to $25.5 million annual savings in health care costs according to the Australian Cardiovascular Health and Rehabilitation Association (ACRA) (8). CR programs that include medication adherence programs reduce all-cause mortality by 65 per cent compared with programs that do not (46).

Unfortunately, in Australia, CR participation is poor with just 1 in 3 patients referred at discharge (8). Of those referred, patients in rural Australia, as well as those with multiple comorbidities, are less likely to attend (45). CR attendance is also low for Aboriginal and Torres Strait Islander people (47).

Additionally, there is no standard approach, monitoring or clear measurement of the quality of care offered by CR service providers in Australia. CR providers vary widely in terms of program delivery, modality and the types of health professional care. To resolve this issue, ACRA has proposed a set of national indicators (51). This is a necessary first step in supporting the delivery of quality CR care. These evidence-based indicators are also appropriate for the Australian context (46).

Benefits

The benefits of focusing on standardised quality CR care reach far beyond optimising lipid management. It is important though, in the context of this report, to support an enhanced role for CR in the secondary prevention of CVD. The broader benefits of CR include:

- consistent delivery of care;
- improved transition and continuity of care from tertiary to primary setting; and
- enhanced access for some patient cohorts, including those in regional and rural Australia

Cost

There is no anticipated cost to Government, this solution can be actioned within current resourcing.

Table 1 - Summary of impact from solution (8)

IMPACT		
65 per cent improvement in medication adherence comparatively;	**26 per cent reduction** in mortality; and	**18 per cent reduction** in hospital readmission. (8).

Actions required

5.1 Endorse the establishment of nationally consistent and standard framework, focused on quality indicators, nationally developed by ACRA.

5.2 Establish guidelines that encompass the ACRA framework that include evidence-based content across a range of modalities including digital and face-to-face. These guidelines would need to include the following elements:

- Evidence-based guidance on the intensity, frequency and duration of CR;
- Inclusion of practice elements to address potential cultural and gender barriers; and
- Options to reduce the transport burden associated with CR which can lead to poorer attendance particularly amongst some socio-economic groups.

5.3 Ensure that the delivery of CR supports individual patient care including mode of delivery and services offered.

5.4 Utilise enhanced telehealth acceptance and uptake resulting from the COVID-19 pandemic.

5.5 Ensure that CR services are made available to all Australians irrespective of age, culture, socioeconomic status and locality.

Conclusion

While Australia has been successful over the years in addressing the burden of CVD, it is clear that there is a significant population of Australians, considered to be at high-risk of a CVD event, who are not currently having their 'bad cholesterol', or LDL-C, tested and treated appropriately.

This provides a real opportunity for the Federal Government to implement several simple, actionable solutions, designed to fit within the current health system infrastructure, that will significantly impact on outcomes for these Australians. The call to action is clear, to save lives we must:

1. Ensure all high-risk Australians know their LDL-C level
2. Embed annual LDL-C tests for all high-risk Australians
3. Standardise lipid profile reporting across Australia
4. Update the guidelines to reflect best practice for secondary prevention of CVD
5. Enhance the role of cardiac rehabilitation across Australia

Abbreviations

Abbreviations	Description
AACB	Australasian Association of Clinical Biochemists
ACRA	Australian Cardiovascular Health and Rehabilitation Association
ACS	Acute Coronary Syndrome
AIHW	Australian Institute of Health and Welfare
ARC	Absolute Risk Calculator
ASCVD	Atherosclerotic Cardiovascular Disease
CR	Cardiac rehabilitation
COVID-19	Coronavirus Disease 2019
CVD	Cardiovascular disease
DLCNS	Dutch Lipid Clinic Network Score
ED	Emergency Department
eGFR	Estimated Glomerular Filtration Rate
ESC	European Society of Cardiology
FH	Familial hypercholesterolaemia
GP	General Practitioner
HDL-C	High density lipoprotein cholesterol
LDL-C	Low density lipoprotein cholesterol
MSAC	Medical Services Advisory Committee
Non-HDL-C	Non high-density lipoprotein cholesterol
PBAC	Pharmaceutical Benefits Advisory Committee
PBS	Pharmaceutical Benefits Scheme
PCSK9	Proprotein convertase subtilisin/kexin type 9
PHN	Primary Health Network
PIPQI	Practice Incentive Program Quality Improvement
RCPA	Royal College of Pathologists of Australia
TC	Total cholesterol
T1DM	Type 1 Diabetes Mellitus

Appendix A

Definitions used in this report

For the purposes of this report, a definition of high-risk and at risk-patients has been developed. This is based on the ESC Guidelines for the management of dyslipidaemias (28). It has also been validated with the project Advisory Committee and includes expert input from committee members to ensure that it meets the specific needs of this report.

High-risk	People who have suffered a primary CVD event, are not on optimised lipid therapy and have: • Documented atherosclerotic CVD (ASCVD), either clinical or unequivocal on imaging; or • Unequivocally documented ASCVD on imaging includes those findings that are known to be predictive of clinical events, such as significant plaque on coronary angiography or CT scan (multivessel coronary disease with two major epicardial arteries having >50% stenosis), or on carotid ultrasound. • Diabetes Mellitus with target organ damage, a or at least three major risk factors, or early onset of T1DM; or • Chronic Kidney Disease (eGFR≤ 60ml/min/1.73m2 with or without albuminuria); or • Markedly elevated LDL-C, in particular TC >8 mmol/L (>310 mg/dL), LDL-C >4.9 mmol/L (>190 mg/dL), or BP >_180/110 mmHg; or • Patients with FH (with or without major risk factors).
At risk	People who have suffered a primary CVD event, are not on optimised lipid therapy and have an elevated LDL-C between 1.8mmol/L and 4.9 mmol/L.

Appendix B
Detail of economic analysis

An economic model was developed to enable a quantitative assessment of the costs and benefits of the recommended policy interventions by modelling the impact of improved lipid treatment adherence and escalation of the intensity of lipid.

The approach used to estimate CVD death, CVD events and associated health system related costs was an economic evaluation based on a discrete event simulation (DES) model. The model is based on the CVD and CVD death, risk equations first developed by Anderson et al and published in 1991 and based on analyzing data from the Framingham Heart Study (38). To ensure the model produced results that are relevant to a higher risk / secondary prevention population the model was then calibrated using data from the Cholesterol Treatment Trialist Collaboration (CTTC) meta analyses of 26 trials and 170,000 patients (48). This ensured that the DES model could replicate closely the yearly risks of those patients in the CTTC meta-analyses.

An additional element of the model was to ensure that the baseline LDL-C levels and population characteristics of the model match those of the current Australian population being considered in this report. The population characteristics and LDL distributions from the MedicineInsight data set (as used in the CODE RED report) (n = 107,664) was used for this purpose to ensure the baseline model was applicable to the Australian context. The model was populated with relevant Australian health care resource item and cost data using published data (MBS, PBS, Australian DRGs and other Australian publications), including cost of events such as Myocardial infarction or Ischaemic stroke, pathology and medicine reimbursement costs and healthcare professional costs.

The baseline model used the LDL-C treatment (statin monotherapy, statin combination with ezetimibe, ezetimibe monotherapy, PCSK9 inhibitor) distributions from the Medicine Wise dataset from the CODE RED report. The CODE RED report showed that a significant proportion of that dataset were also not on recommended therapy. It was assumed that the MedicineInsight population had an adherence rate to LDL-C lowering therapy that amounted to 60% based on a population of patients post MI studied by Colantonio et al (49).

The analysis modelled improvements in adherence rate (up to 80%) and also increased intensity of LDL-C lowering treatment. If a person was not on therapy, depending on LDL-C level they could have a maximum of 5 escalations in therapy to achieve LDL control defined as 1.8mmol/L or below. The escalations in therapy that such a patient could receive include:

Step 1 | statin monotherapy moderate intensity

Step 2 | statin monotherapy high intensity if LDL-C above 1.8mmol/L

Step 3 | add in ezetimibe therapy moderate intensity statin if LDL-C above 1.8mmol/L

Step 4 | add in ezetimibe therapy high intensity statin if LDL-C above 1.8mmol/L

Step 5 | add in / move to PCSK9 inhibitor if LDL-C above 2.6mmol/L despite optimised therapy with statins and ezetimibe.

Patients already on treatment will be limited to escalations that provide superior LDL-C lowering than current therapy provides.

The results from the discrete event simulation were extrapolated to represent those that would be seen in the 1,150,200 Australians which are high risk / secondary CVD prevention. The results include CVD events (MI, stroke, revascularisation) and CVD death.

The cost effectiveness is calculated in terms of cost per event avoided. In the life-time analyses using the DES model the cost effectiveness associated with the solutions detailed in this report was $26,210 per CVD event avoided.

This can be considered cost effective given the significant nature of the events considered (death, stroke, MI, revascularisation) and that the average age of the population was 64 years old which infers that a considerable number of life years saved would accrue when deaths are avoided. The analysis can also be considered conservative because quality of life decrements were not included in the analysis and these would most likely be considerable post CVD events.

Finally, the impact of CVD events or death was not considered more broadly on society in terms of productivity lost or in terms of impact on family and carers.

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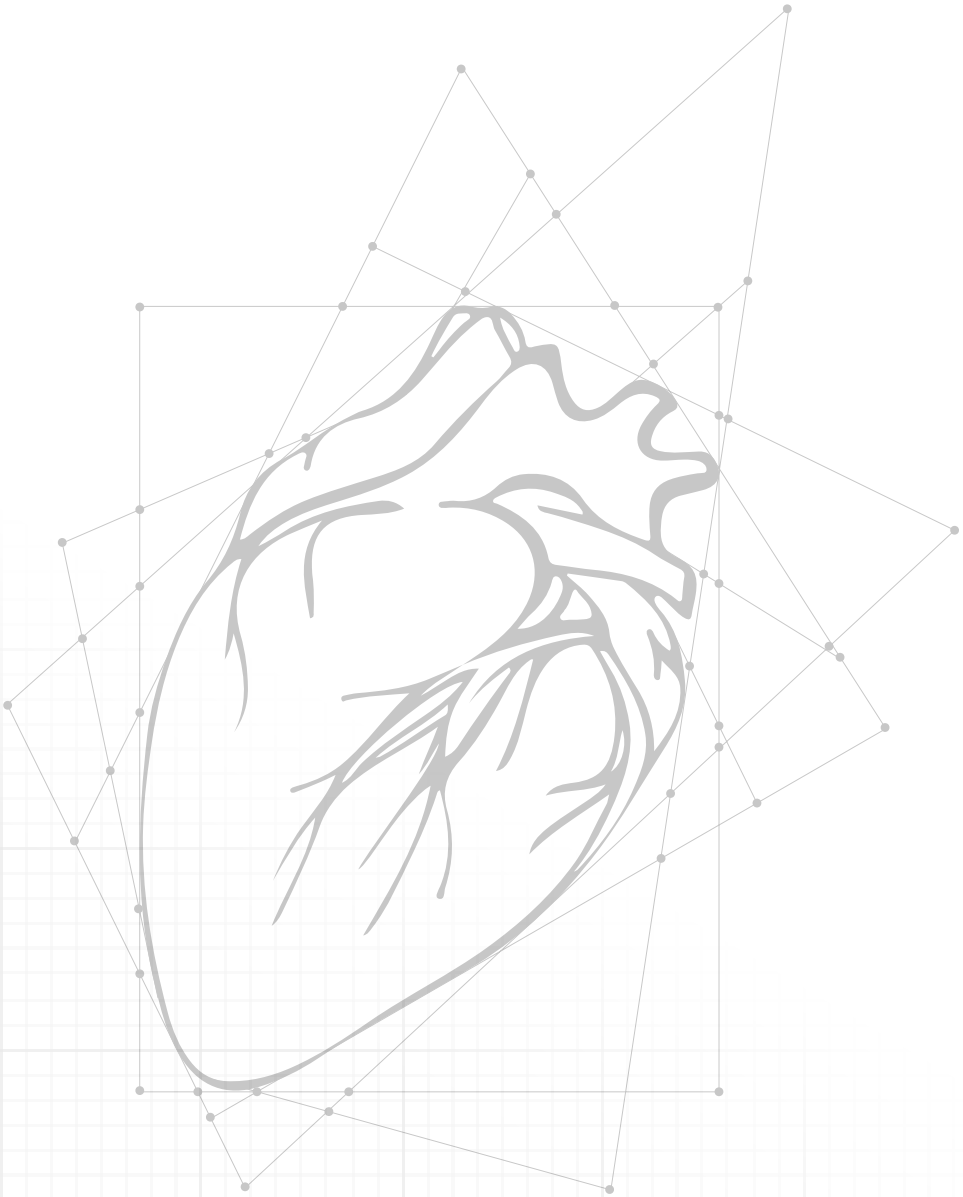

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