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Reducing CVD risk

Integration of clinical and laboratory criteria

Background
Recent updates to National Heart Foundation of Australia (NHFA) *Lipid management guidelines* and Pharmaceutical Benefits Scheme (PBS) criteria for subsidised lipid lowering therapy have resulted in greater alignment between the two documents. However, several recommendations, such as the need to focus on low density lipoprotein cholesterol level rather than total cholesterol, while well supported in the literature, may initially create confusion for both patients and clinicians.

Objective
This article summarises the likely pathology reporting changes that will occur as a result of a recent review of NHFA guidelines by the Australian Pathology Lipid Interest Group; compares current PBS criteria for subsidised lipid lowering therapy to the NHFA high risk categories and treatment targets; and provides an algorithm for treatment based on the PBS criteria integrating risk factors and lipid levels.

Discussion
Although pathology testing plays an important role in the assessment of risk in patients, it is ultimately the clinician who must determine the patient's absolute risk based on all relevant previous and current clinical information before the initiation or review of appropriate treatment.

Cardiovascular disease (CVD) remains a major cause of morbidity and mortality in Australia. Plasma lipid levels are one of the major factors which contribute to CVD risk.[1] Successive lipid management guidelines developed by the National Heart Foundation of Australia (NHFA) emphasise the detection and treatment of patients at higher risk of CVD. These guidelines identify target levels for patient management[2,3] whereas the Pharmaceutical Benefits Scheme (PBS) criteria for lipid lowering therapy provide thresholds to ensure that patients at a sufficiently high risk can receive subsidised treatment.[4] The confusion created by the differing target values and thresholds in the respective documents was in part resolved by the update of the PBS criteria in October 2006.[5]

Reporting by pathology services

Pathology services strive to add value to the analyses they perform by providing appropriate interpretive comments. Theoretically, they are well placed to define the relationship between lipid values: total cholesterol (TC), triglycerides (TG), high density lipoprotein cholesterol (HDL-C), low density lipoprotein cholesterol (LDL-C) and the appropriate response for an individual patient based on current recommendations. Unfortunately, the amount of patient specific information required for such a response exceeds that usually provided on the test request form. A recent review of changes to the NHFA *Lipid management guidelines* has formulated recommendations for the reference limits and comments that should be provided on laboratory reports.[6,7] If these recommendations are incorporated into pathology reporting, they are likely to impact on clinical management. The proposed changes include:

- no clinical decision limit for TC on pathology reports, but a comment which highlights the NHFA position that TC alone is insufficient for CVD risk assessment
- a comment to recommend a full lipid profile including the assessment of HDL-C and LDL-C when only TC and TG, either together or alone, have been requested

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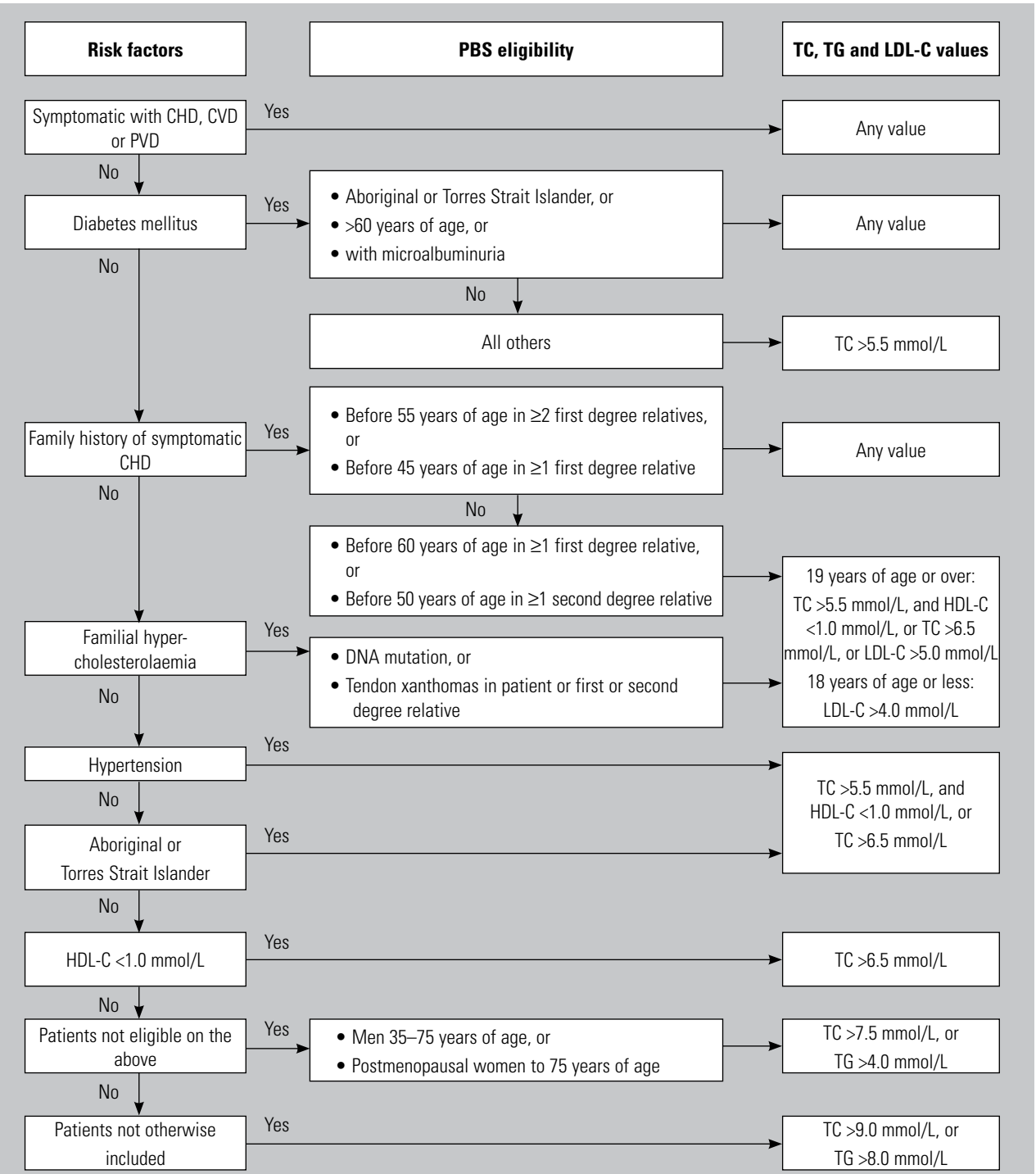
Figure 1. PBS criteria for the initiation of lipid lowering therapy



CHD = coronary heart disease, CVD = cerebrovascular disease, PVD = peripheral vascular disease
Microalbuminuria = urinary albumin excretion rate >20 µg/min or urinary albumin to creatinine ratio of >2.5 for males, >3.5 for females

Table 1. Comparison of PBS eligibility criteria for lipid lowering agents vs. NHFA/CSANZ high risk categories and targets

Category of patients at higher risk	PBS initiation criteria4	NHFA recommended targets postintervention and management statements[3]
Any patient with clinical evidence of vascular disease (coronary heart disease, cerebrovascular disease or peripheral vascular disease)	• Any TC value	• High risk – LDL-C target <2.0 mmol/L • Management: – statin therapy for patients with clinical evidence of vascular disease – fibrate therapy in combination with statins, particularly in patients with likely metabolic syndrome
Diabetes mellitus	• Any TC value if diabetes mellitus: – with microalbuminuria (defined as urinary albumin excretion rate of >20 µg/min or urinary albumin to creatinine ratio of >2.5 for males, >3.5 for females) – in Aboriginal or Torres Strait Islander patients – in patients aged 60 years or over, or if – TC >5.5 mmol/L in any other patient	• High risk – LDL-C target <2.0 mmol/L • Management – after lifestyle and glucose interventions consider: – statin therapy for LDL-C >2.5 mmol/L – fibrate therapy for TG>2.0 mmol/L
Kidney failure/kidney transplantation and patients with chronic kidney disease or impairment	• No specific PBS criteria for this group – consider other categories	• High risk – LDL-C target <2 mmol/L • Management – pending trial results, initiation of statins for patients with kidney impairment to be considered on an individual basis
Familial hypercholesterolaemia (FH)	• Patients with FH identified by either DNA mutation or tendon xanthomas in the patient or first or second degree relative • If 19 years or over: – TC >5.5 mmol/L and HDL-C <1.0 mmol/L, or – TC >6.5 mmol/L or LDL-C >5.0 mmol/L • 18 years or under: – LDL-C >4.0 mmol/L	• High risk – LDL-C target <2.0 mmol/L • Management – statin therapy recommended
Family history of coronary heart disease (CHD)	• Any TC value if the patient has a family history of symptomatic CHD either: – before 55 years of age in ≥2 first degree relatives, or – before 45 years of age in ≥1 first degree relative • If the patient has a family history of symptomatic CHD either: – before 60 years of age in ≥1 first degree relative, or – before 50 years of age in ≥1 second degree relative	• High risk – LDL-C target <2.0 mmol/L • Management – lipid lowering therapy is indicated in those with: – absolute risk of 10–15% of a CVD event in the next 5 years, and – a family history of premature CHD (first degree relative who developed CHD before 60 years of age)

	• If 19 years or over: – TC >5.5 mmol/L and HDL-C <1.0 mmol/L, or – TC >6.5 mmol/L, or – LDL-C >5.0 mmol/L • 18 years or less: – LDL-C >4.0 mmol/L	
Aboriginal or Torres Strait Islander patients	• TC >6.5 mmol/L, or • TC >5.5 mmol/L, and • HDL-C <1.0 mmol/L	• High risk – LDL-C target <2.0 mmol/L • Management – commence screening for lipid levels at 18 years of age and consider statins if LDL-C >2.5 mmol/L after lifestyle modifications
Hypertension	• TC >6.5 mmol/L, or • TC >5.5 mmol/L, and • HDL-C <1.0 mmol/L	• Blood pressure is considered within the calculation of absolute risk (see below)
Patients with HDL cholesterol <1.0 mmol/L	• TC >6.5 mmol/L	• HDL is considered within the calculation of absolute risk (see below)
Patients not eligible under the above: • men 35–75 years of age • postmenopausal women up to 75 years of age	• TC >7.5 mmol/L, or • TG >4.0 mmol/L	
Patients not otherwise included	• TC >9.0 mmol/L, or • TG >8.0 mmol/L	
Absolute risk	• No specific PBS criteria for this group – consider other categories	• High risk – LDL-C target <2.0 mmol/L • Management – lipid lowering therapy is indicated in those with either: – ≥15% risk of a CVD event in the next 5 years, or – 10–15% of a CVD event in the next 5 years, plus either: – a family history of premature CHD (first degree relative who developed CHD before 60 years of age) – patient has metabolic syndrome

- comments, triggered by HDL-C and LDL-C values, in relation to NHFA 2005 guidelines and PBS guidelines
- possible deletion of ratios such as TC:HDL-C, as this is not recommended but will remain optional.

Some of these changes may initially be problematic for clinicians. For example, absence of a reference interval or target values for TC may require adaptation by clinicians who have used TC to track progress or treatment efficacy.[8] Similarly, using LDL-C >2.0 mmol/L to trigger a comment may result in a significant increase in the number of comments that only recommend lifestyle changes.[9] Finally, omission of ratios such as TC:HDL-C may require the clinician to access these individual components separately when using tools such as the New Zealand cardiovascular risk calculator. These issues reflect the need for pathology providers to strike a balance between current guidelines and previous practice.

PBS criteria for lipid lowering therapy

In conjunction with this review, the current PBS criteria for lipid lowering therapy can be presented in a fashion that simplifies the response to individual pathology reports. An algorithm was developed to assist primary care physicians to assess the eligibility of their patients for lipid lowering therapy. The algorithm is based on a patient centred approach involving clinical decision points: clinical diagnosis, PBS definition of each risk category, and pathology results (*Figure 1*).

The classifications of high risk recommended by the PBS criteria are now more consistent with those included in the NHFA 2005 update but they are not identical. These subtle differences may cause some confusion to primary care physicians as might the continued use of TC by the PBS guidelines verses the NHFA focus on LDL-C. In addition, the values required for initiation of lipid lowering therapy (PBS criteria) must be taken in context with the 'target' values recommended by the NHFA 2005 guidelines. A comparison of the PBS criteria and NHFA recommendation is presented in *Table 1*.

Discussion

The current NHFA *Lipid management guidelines* reflect worldwide acceptance of the impact of dyslipidaemia on the risk for CVD. While there are inherent limitations of any guidelines,[7] recent updates to NHFA guidelines and PBS criteria have resulted in greater alignment, which also reflects the evolving needs of the Australian population. However, several recommendations, such as the need to focus on LDL-C rather than TC, while well supported in the literature, may initially be a challenge in terms of acceptance by both clinicians and their patients. Pathology services are in a position to support this shift in focus. The use of expert commenting systems in many pathology laboratories will assist in providing relevant comments more appropriate to the individual patient's lipid profile. Although pathology testing plays an important role in the assessment of risk in patients, ultimately it is the clinician who must determine the patient's absolute risk based on all relevant previous and current clinical information before the initiation or review of appropriate treatment.

The December 2005 update of the NHFA *Lipid management guidelines* highlights the importance of follow up. Currently, some patients are lost to follow up despite being identified with significant lipid abnormalities. This problem is common to many chronic disorders, especially those that are asymptomatic in their early stages. It is therefore important to have in place treatment plans with: clear goals to reach target values, and regular review cycles to ensure motivation for compliance and tracking of benefit.

Conflict of interest: none declared.

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