Heart, Lung and Circulation (2015) **24,** 495–502
1443-9506/04/$36.00
http://dx.doi.org/10.1016/j.hlc.2014.12.009

ORIGINAL ARTICLE

Clinical Guidelines on Hyperlipidaemia: Recent Developments, Future Challenges and the Need for an Australian Review

D.R. Sullivan [a*], G.F. Watts [b], S.J. Nicholls [c], P. Barter [d], R. Grenfell [e], C.K. Chow [f], A. Tonkin [g], A. Keech [h]

[a]Department of Chemical Pathology, Royal Prince Alfred Hospital, Camperdown, NSW
[b]Department of Medicine, University of Western Australia, Perth, WA
[c]South Australian Health and Medical Research Institute, University of Adelaide, Adelaide, SA
[d]Centre for Vascular Research, University of NSW, Sydney NSW
[e]National Heart Foundation Director of Cardiovascular Health, Melbourne Vic
[f]The George Institute for International Health, University of Sydney, Camperdown, Sydney NSW
[g]Cardiovascular Research Unit, Department of Epidemiology and Preventive Medicine, Monash University, Melbourne, Vic
[h]NHMRC Clinical Trials Centre, University of Sydney and Royal Prince Alfred Hospital, University of Sydney, NSW

Online published-ahead-of-print 25 December 2014

Large reductions in cardiovascular disease (CVD) mortality have been achieved over the last 50 years in developed countries. The health policies that have contributed so much to this success have largely been coordinated by means of expert guidelines for the management of the classic modifiable risk factors such as blood pressure, diabetes and blood lipids. National and international guidelines for lipid management have demonstrated a high degree of consistency between numerous sets of recommendations. It has been argued that some important components of the consensus that has been established over the past decade have been challenged by the latest guidelines of the American Heart Association - American College of Cardiologists (AHA-ACC). Clinicians can be reassured that continued reliance on extensive scientific evidence has reaffirmed the importance of lipid metabolism as a modifiable risk factor for atherosclerotic cardiovascular disease. On the other hand, the recent AHA-ACC guidelines suggest changes in the strategies by which metabolic risk factors may be modified. This small number of important changes should not be sensationalised because these differences usefully reflect the need for guidelines to evolve to accommodate different contexts and changing perspectives as well as emerging issues and new information for which clinical trial evidence is incomplete. This article will consider the recent policies and responses of national and supranational organisations on topics including components of CVD risk assessment, sources of CVD risk information and re-appraisal of lipid-lowering interventions. Timely review of Australian lipid management guidelines will require consideration of these issues because they are creating a new context within which new guidelines must evolve.

Keywords Cardiovascular disease • Guidelines • Blood lipids • Lipid-lowering therapy • Australia

Introduction

The recent release of the AHA-ACC Lipid Guidelines [1] has stimulated much discussion, and has prompted strong responses from both supporters and opponents. There has also been much discussion of how these AHA-ACC guidelines differ from the European Society of Cardiology – European Atherosclerosis Society (ESC-EAS) Guidelines [2] and the International Atherosclerosis Society (IAS) recommendations [3]. Despite the unfortunate focus on differences in

*Corresponding author at: Department of Chemical Pathology, Royal Prince Alfred Hospital, Missenden Rd, Camperdown NSW 2050 Australia.
Tel.: +61 2 95158832; fax: +61 2 95156186/+61 427952996(Mob)., Email: david.sullivan@sswahs.nsw.gov.au

many of these discussions, it is important to note that the recommendations from all three groups agree on almost all important points, with the remaining differences representing fine-tuning rather than major disagreements. This article will examine these issues from an Australasian perspective.

The aetiology underlying atherosclerotic CVD is multi-factorial. Overarching guidelines which address all major modifiable CVD risk factors are required as the basis for an integrated primary care strategy. The Australian National Vascular Disease Prevention Alliance (NVDPA) guidelines allow general practitioners to engage with CVD prevention without the need to refer to three or four separate (and possibly conflicting) risk factor-specific guidelines [4]. The NVDPA primary prevention guidelines provide a patient-centred approach that is based on the impact of all major CVD risk factors on an individual's absolute risk of a CVD event within a five-year timeframe. The resultant emphasis on individuals at greatest risk favours cost-effective CVD prevention in primary care. Individual risk factors for CVD such as hypertension, hyperglycaemia and hyperlipidaemia are continuous, so the paradigm of a group of separate disease states at levels above arbitrary cutpoints is outdated. Consequently, full implementation of a multi-factorial approach still requires substantial reorganisation of the current system in which single risk factor clinics predominate.

On the other hand, single risk factor-specific guidelines remain necessary to meet the requirement amongst non-expert clinicians and specialists from other fields for greater expertise in particular circumstances. Furthermore, risk factors such as dyslipidaemia may take on particular significance in population subgroups including the elderly, children, women of child-bearing age, patients receiving anti-retroviral therapy, transplant recipients and others. Logistically, clinical lipid management needs to be provided by cardiologists, hypertension physicians and diabetologists, and to some extent by renal physicians, vascular surgeons and interested primary care and occupational health doctors.

The evolution of successive generations of Australian lipid management guidelines has reflected an extensive and advancing body of evidence based on a foundation of experimental investigations, epidemiological and observational studies and culminating in Level A meta-analyses [5] and systematic reviews of randomised controlled trials. These lines of evidence confirm that effective recognition and management of lipid disorders is fundamental to the prevention of CVD [6].

Lipid guidelines have been at the forefront of the use of absolute risk assessment in patient management. Despite efforts to promote a multiple risk factor approach to CVD prevention, suboptimal professional awareness has meant that patients have not always received appropriate management [7]. Even greater understanding of lipid metabolism and management principles will become necessary as newly developed lipid-modifying drugs become available. The National Heart Foundation (NHF) updated their Guidelines for Lipid Management in 2005 [8] and although many components of the NHF Guidelines remain robust, a comprehensive review of new developments and emerging issues is appropriate. In an era of limited resources it is instructive to consider the conclusions reached by expert groups in other developed countries that have recently undertaken the exhaustive process of guideline development based on essentially identical bodies of evidence [1–3,9]. Topics that have arisen include a) components of CVD risk assessment, such as ethnicity, family history, alternatives to low-density lipoprotein cholesterol (LDL-C), novel biomarkers and non-invasive imaging; b) sources of CVD risk information, such as reference populations, qualifying events and time-frames; and c) re-appraisal of lipid-lowering interventions in terms of target levels, non-statin drugs, costs and side effects. An appraisal of the similarities and differences that identify important guiding principles in a changing clinical environment [10].

Scope and Foundations for Lipid Management Guidelines

Lipid management guidelines need to address all forms of dyslipidaemia that affect diverse groups of people and that result from disturbances in the metabolism of low-density lipoproteins (LDL), triglyceride-rich lipoproteins and high-density lipoproteins (HDL). The aim is to identify and diagnose these disorders and recommend safe and cost-effective treatment to mitigate risk of end-organ damage, including CVD, pancreatitis and hepatic steatosis. Integration of all available evidence should be used to make graded recommendations, based on the quality of evidence, to best inform the medical consultation with the patient. With respect to coronary disease and CVD, the data may derive from several sources, including cell biology, animal experiments, genetic studies, case series, epidemiological observations and intervention trials employing imaging techniques and clinical endpoints, as well as integrated assessments such as systematic reviews and meta-analyses. Given that intervention trials cannot be undertaken to cover all clinical scenarios and are only carried out over a short period in the life of a patient, the totality of evidence needs to be considered. Lipid management guidelines must relate specifically to the population in which they will be employed.

Components of CVD Risk Assessment

It has been suggested that since clinical trials of statins have not employed estimates of global risk as a criterion for recruitment, such estimates may be unnecessary in deciding whether to introduce drug therapy. On the other hand, the event rates in the placebo arms of clinical trials have provided estimates of risk in these studies. Guidelines for the prevention of prevalent problems, such as CVD, need to be directed towards the population in question. It has become evident that data obtained in a particular population or era may not be fully applicable in other circumstances [11]. There