

## Cardiovascular risk factors: when should we treat?

*We need to derive absolute cardiovascular risk functions based on contemporary Australian data*

THE ACCURATE ESTIMATION of risk for future disease events is critical to the determination of the benefit–risk ratio and the most cost-effective use of preventive therapies (Box 1). This is particularly relevant for cardiovascular diseases (CVD), which are the leading cause of deaths in Australia (40% of total deaths), and in 1993–1994 accounted for the largest proportion (12%, or \$3.9 billion) of total annual recurrent health expenditure.<sup>3</sup> (This proportion is now almost certainly greater.) Expenditure on cardiovascular drugs under the Pharmaceutical Benefits Scheme totals \$1.2 billion annually, \$629 million of this on lipid-lowering drugs, especially statins.<sup>4</sup> Accurate assessment of the likelihood of future events would optimise resource allocation by targeting patients at higher risk.<sup>5</sup>

In this context, the work of Simons et al, reported in this issue of the Journal (*page 113*),<sup>6</sup> is very important. In their ongoing Dubbo Study (which commenced in 1988 and involved 2805 men and women aged 60 years and older when first assessed), the authors evaluated a risk function for coronary heart disease (CHD) prediction developed from a longitudinal cohort study in Framingham, Massachusetts — the Framingham Study. They also derived a risk function for future CVD events, including stroke as well as CHD, by modelling data from the Dubbo cohort.

The Framingham risk functions<sup>7–9</sup> are widely used and form the basis of a New Zealand cardiovascular risk calculator,<sup>10</sup> itself proposed as the absolute risk measurement tool in the recent lipid guidelines of the National Heart Foundation/Cardiac Society of Australia and New Zealand.<sup>11</sup>

The Framingham cohort consists primarily of white, middle-class individuals. The equation was derived from calculations based on age, sex, cigarette smoking status, diabetes status, and blood pressure, cholesterol and HDL cholesterol levels only. The Framingham measurements were also made some time ago before the dramatic increase in the prevalence of diabetes,<sup>12</sup> and indeed Framingham included low numbers of people with diabetes.

In essence, the study by Simons et al determined the applicability of observations made in another time and another place to an Australian population. They showed that the Framingham equation accurately predicted overall 10-year incidence of “hard” CHD endpoints (myocardial infarction or coronary death). This supports previous validation work with the Framingham equation in the Busselton study.<sup>13</sup> However, the Busselton study is now over 20 years old, while the Dubbo cohort included only older individuals.

Therefore, while these validation studies are important, it would be more relevant to derive predictive equations from data obtained from a representative and contemporary Australian cohort. This would acknowledge the variety of ethnic groups in Australia and the current mix of known and unknown risk factors. As the Framingham equation correctly predicts risk in only about 80% of cases,<sup>14</sup> there is

### 1: Why focus on absolute risk of cardiovascular disease?

- Individuals with levels which fall in the highest decile for systolic blood pressure, cholesterol and body mass index account for only 20%–30% of the total number of cases of stroke, ischaemic heart disease and diabetes.<sup>1</sup>
- Interventions based on elevated levels of a single risk factor may allocate treatment to individuals with little chance of gain because of low absolute risk.<sup>2</sup>
- Absolute risk is the likelihood of developing an event(s) over a particular time period.
- Absolute risk equations acknowledge the multifactorial causation of cardiovascular disease, the sex difference in risk and the steep increase in risk with ageing.
- Epidemiological studies have shown a continuum of risk for increasing levels of risk factors, such as blood pressure, total cholesterol and HDL cholesterol levels, which is acknowledged in absolute risk equations.

### 2: Recommendations for current guidelines, practice and research in cardiovascular disease

- Treatment guidelines should place greater emphasis on absolute risk estimation in those without manifest cardiovascular disease (CVD).
- Linking estimates of the likely absolute benefit of interventions with calculation of absolute risk should reinforce the rationale for lifestyle measure for all individuals and pharmacological treatment for those at higher risk.
- Prediction of overall CVD risk over 5 (or 10) years should be the endpoint, as opposed to risk of coronary heart disease alone.
- Components of a composite CVD endpoint should be re-examined and possibly restricted to “hard” outcomes such as CVD death, non-fatal myocardial infarction and non-fatal stroke.
- Agreement on and adoption of a standardised approach would facilitate implementing absolute risk prediction in Australia.
- Future studies should include variables that might further improve risk prediction (eg, waist circumference, microalbuminuria, high-sensitivity C-reactive protein).
- Absolute risk assessment is likely to be implemented most effectively using electronic tools which can link to other national initiatives.
- Absolute risk assessment will not only optimise health gains, but will result in more cost-effective treatment and prevention.

considerable interest in “novel” risk factors (eg, high sensitivity C-reactive protein) and techniques for imaging the arterial wall. Future research must examine the degree to which these elements might improve the ability to correctly identify those at risk.

With the shift of treatment guidelines from individual risk thresholds for treatment to decisions based on multivariable absolute risk, the logical extension of this is to estimate treatment efficacy or effectiveness in terms of absolute treatment benefit. For example, the benefits of cholesterol lowering in terms of improving average life expectancy have previously been estimated.<sup>15</sup> This approach would provide

more meaningful information to both patients and clinicians, as well as allowing the non-cardiovascular benefits of modifying risk factors such as tobacco smoking, physical inactivity, and unhealthy diet to be taken into account.

Data such as those from the Dubbo study have important implications for current Australian guidelines and practice (Box 2). Treatment decisions based on individual risk-factor thresholds are inadequate. The Dubbo study assesses the validity of the Framingham risk prediction equations in the elderly and provides an Australian risk equation for the same age group. Further work should be done to validate these equations in a wider contemporary population and to determine the extent to which new risk factors may improve assessment of risk. This should not, however, preclude swift measures to implement the use of absolute risk, as well as consideration of absolute treatment benefit, as ways of guiding treatment decisions in clinical practice.

**Andrew M Tonkin**

Director, Health, Medical and Scientific Affairs  
National Heart Foundation of Australia, West Melbourne, VIC  
and Adjunct Professor, Department of Epidemiology and Preventive Medicine  
Monash University, Melbourne, VIC

**Stephen S Lim**

Lecturer and PhD Scholar

**Henrik Schirmer**

Visiting Postdoctoral Research Fellow  
Department of Epidemiology and Preventive Medicine  
Monash University, Melbourne, VIC  
andrew.tonkin@heartfoundation.com.au

1. Law M, Wald NJ. Risk factor thresholds: their existence under scrutiny. *BMJ* 2002; 324: 1570-1576.
2. Forge BH, Briganti EM. Lipid lowering and coronary heart disease risk: how appropriate are the national guidelines? *Med J Aust* 2001; 175: 471-475.
3. Australian Institute of Health and Welfare. National cardiovascular disease database online, 2001. Available at: <http://www.aihw.gov.au/> (accessed Oct 2002).
4. Pharmaceutical Benefits Scheme expenditure report, April 2001 to March 2002. Available at: <http://www.health.gov.au/pbs/stats.htm> (accessed Oct 2002).
5. Lim S, Vos T, Peeters A, et al. Cost-effectiveness of prescribing statins according to Pharmaceutical Benefits Scheme criteria. *Med J Aust* 2001; 175: 459-464.
6. Simons LA, Simons J, Friedlander Y, et al. Risk functions for prediction of cardiovascular disease in the Australian elderly: the Dubbo study. *Med J Aust* 2002; 178: 113-116.
7. Kannel WB, McGee D, Gordon T. A general cardiovascular risk profile: the Framingham Study. *Am J Cardiol* 1976; 38: 46-51.
8. Anderson KM, Wilson PW, Odell PM, Kannel WB. An updated coronary risk profile. A statement for health professionals. *Circulation* 1991; 83: 356-362.
9. Wilson PW, D'Agostino RB, Levy D, et al. Prediction of coronary heart disease using risk factor categories. *Circulation* 1998; 97: 1837-1847.
10. New Zealand Guideline Group risk calculator. Available at: [http://www.nzgg.org.nz/library/gl\\_complete/bloodpressure/index.cfm#contents](http://www.nzgg.org.nz/library/gl_complete/bloodpressure/index.cfm#contents) (accessed Nov 2002).
11. Lipid Management Guidelines – 2001. National Heart Foundation of Australia and Cardiac Society of Australia and New Zealand. *Med J Aust* 2001; 175 (Suppl 5 November). Available at: [http://www.heartfoundation.com.au/prof/docs/lipid\\_guide\\_2001.pdf](http://www.heartfoundation.com.au/prof/docs/lipid_guide_2001.pdf) (accessed Dec 2002).
12. Dunstan DW, Zimmet PZ, Welborn TA, et al. The rising prevalence of diabetes and impaired glucose tolerance: the Australian Diabetes, Obesity and Lifestyle Study. *Diabetes Care* 2002; 25: 829-834.
13. Knuiman MW, Vu HT. Prediction of coronary heart disease mortality in Busselton, Western Australia: an evaluation of the Framingham, National Health Epidemiologic Follow-up Study, and WHO ERICA risk scores. *J Epidemiol Community Health* 1997; 51: 515-519.
14. D'Agostino RB, Grundy S, Sullivan LM, Wilson P, for the CHD Risk Prediction Group. Validation of the Framingham coronary heart disease prediction scores. Results of a multiple ethnic groups investigation. *JAMA* 2001; 286: 180-187.
15. Bonneux L. Cholesterol-lowering therapy for smokers and non-smokers: a life-table analysis. *Lancet* 2000; 356: 2004-2006. □

## time capsule

### Emergency medicine — no longer a casualty

The ageing population already has been mentioned as a factor in the increase in the severity of illness that is being seen. With bed shortages this has brought about a phenomenon which governments and the community have not yet been able to accommodate — the “placement problem”. The population is getting older, as are the patients whom we are treating. This increases the work-load of emergency departments in a number of ways. Elderly patients, in general, do not have “simple” illnesses. If elderly patients who are suffering from an acute illness are sent home, they often require considerable support from community organizations such as Home Help, Meals on Wheels, social workers, occupational therapists and physiotherapists. These support agencies and personnel take time to organize and often cannot be accessed after hours, which results in these patients spending prolonged periods in emergency departments.

These difficulties are yet another reflection of the deficiency that is consequent upon society’s inability to provide, and to fund adequately, decent respite, residential and custodial facilities for the growing number of infirm elderly patients. However, a lack of inpatient facilities does not affect elderly persons only: regrettably, even the most acutely-ill patients have to wait for definitive placement.

Excerpt from:  
*Med J Aust* 1989; 150: 546-548

