

## Commentary

# Improving Outcomes After Acute Coronary Syndrome With Rehabilitation and Secondary Prevention

Tom Briffa, PhD<sup>1,2</sup>; Clara K. Chow, PhD<sup>2</sup>; Alexander M. Clark, RN, PhD<sup>2,3</sup>; and Julie Redfern, PhD<sup>2</sup>

<sup>1</sup>School of Population Health, University of Western Australia, Perth, Australia; <sup>2</sup>The George Institute for Global Health, University of Sydney, Sydney, Australia; and <sup>3</sup>Faculty of Nursing, University of Alberta, Edmonton, Canada

### ABSTRACT

**Background:** International studies suggest almost half of all major coronary episodes annually occur in survivors of acute coronary syndrome (ACS).

**Objective:** A greater focus on medium- and long-term ACS management and adherence to proven therapies is essential if out-of-hospital reductions in mortality and morbidity are to be optimized.

**Methods:** A national panel of clinical and research opinion leaders in ACS care met for 2 days to set future priorities in health care delivery.

**Results:** Lifestyle, control of risk factors, and prescription of pharmacological therapies can improve the course of coronary heart disease (CHD) by reducing all-cause and cardiovascular mortality by 15% to 25%. All ACS patients stand to benefit from rehabilitation and systematic secondary prevention, however, underutilization and suboptimal adherence to rehabilitation and secondary prevention measures persist globally.

**Results:** A range of new initiatives in Australia and elsewhere indicate that time is ripe for change to improve the uptake of preventative treatments in patients after ACS. Key universal drivers of delivering best evidence practice for medium- to long-term care after ACS are economics and locality.

**Conclusions:** Health-service redesign involving all stakeholders will be integral to increasing access, uptake, and adherence to lifestyle, control of risk factors, and pharmacologic therapies shown to improve cardiovascular outcomes. (*Clin Ther.* 2013;35:1076–1081) © 2013 Elsevier HS Journals, Inc. All rights reserved.

**Key words:** Acute coronary syndrome, secondary prevention, cardiac Rehabilitation, health outcomes.

### ACUTE CORONARY SYNDROME IN PERSPECTIVE

The burden of acute coronary syndrome (ACS) has never been greater,<sup>1</sup> but can we meet the challenge of improving evidence, access, and outcomes? International studies suggest almost half of all major coronary episodes annually occur in survivors of ACS,<sup>2,3</sup> particularly in the year after a nonfatal event.<sup>4,5</sup> Progress has been made with improvements in in-hospital ACS care,<sup>6</sup> such as reperfusion therapies (eg, fibrinolysis, primary percutaneous coronary intervention) and evidence-based medical therapy leading to low in-hospital mortality.<sup>7</sup> Yet, a greater focus on medium- and long-term ACS management and adherence to proven therapies will be essential if out-of-hospital reductions in mortality and morbidity are to be optimized. This should involve each patient receiving a written discharge care plan referring them to cardiac rehabilitation where available and ongoing secondary prevention, including proven lifestyle interventions and pharmacotherapy, all underpinned by periodic assessment and medical follow-up.<sup>8,9</sup>

### Benefits of Secondary Prevention

These core recommendations follow because there is substantial and contemporary evidence that across various settings, a range of rehabilitation and secondary prevention therapies are associated with reduced all-cause and cardiovascular mortality from 15% to 25%.<sup>10,11</sup> A recent exception to these findings is the

Accepted for publication July 24, 2013.

<http://dx.doi.org/10.1016/j.clinthera.2013.07.426>  
0149-2918/\$ - see front matter

© 2013 Elsevier HS Journals, Inc. All rights reserved.

RAMIT (Rehabilitation After Myocardial Infarction Trial),<sup>12</sup> the findings of which are discussed in other controversies. In addition, ACS patients who engage in rehabilitation and ongoing prevention initiatives have a 3 times lower risk of death with healthy behavioral change compared with nonparticipants,<sup>13</sup> and have fewer unplanned and costly readmissions, such as nonfatal myocardial infarction (MI) and coronary artery revascularization procedures.<sup>10,14–16</sup> Lifestyle, control of risk factors, and prescription of pharmacological therapies can improve the course of CHD (Table I).

All of these proven measures and treatments should be implemented and considered as potential performance indicators for the medium- to long-term management of ACS.<sup>18</sup> ACS survivors represent a substantial and readily identifiable target population that has the most to gain from rehabilitation and systematic secondary prevention.

Participation in rehabilitation or attendance at a secondary prevention clinic can improve patient adherence with the overall therapeutic regimen. The former strategy is strongly recommended to patients with a complicated ACS (eg, in-hospital GRACE [Global Registry of Acute Coronary Event] score >140<sup>19</sup> or pragmatically exceed median length of stay), those with poor psychosocial well being, or those in whom the care team believe direct tertiary supervision is warranted.<sup>20</sup> Indirect support for the degree of benefit associated with secondary prevention measures was documented in a nonrandomized post-hoc analysis of patients from the OASIS-5 (The Fifth Organization to Assess Strategies in Acute Ischemic Syndromes 5 trial) trial.<sup>13</sup> In this study, patients with non-ST segment MI or unstable angina (termed *non-ST segment elevation acute coronary syndrome* [NSTE-ACS]) were encouraged to adhere to healthy eating, regular physical activity, and smoking cessation 30 days after onset of symptoms. Patients who adhered to both healthy eating and physical

activity showed a relative risk reduction (RRR) of 54% for MI, stroke, or death (odds ratio [OR] = 0.46; 95% confidence interval [CI], 0.38–0.57;  $P < 0.001$ ), and for those who quit smoking, an RRR of 43% for MI (OR = 0.57; 95% CI, 0.36–0.89;  $P < 0.014$ ).<sup>13</sup> These outcomes from OASIS-5, in the Australian subset, were reportedly achieved by 67% of smokers having ceased, 56% of patients self reported adhering to their recommended healthy eating plan, and 60% engaging in 30 minutes of moderate physical activity 3 or more times a week. Other ACS studies have shown that the contribution of secondary prevention measures is equivalent to the deaths averted from acute in-hospital treatment.<sup>21,22</sup>

### Challenge of Underutilization and Low Adherence

All ACS patients stand to benefit from rehabilitation and systematic secondary prevention, however, underutilization and suboptimal adherence to rehabilitation and secondary prevention measures persist globally.<sup>23–25</sup> Patients with an ACS diagnosis of ST segment elevation MI are most likely to receive all therapies, and those with NSTE-ACS are less likely to get all therapies. Studies have shown those assessed to be at the highest risk are less likely to receive prevention treatments.<sup>5,10,23</sup> Other subgroups, such as older people, women, lower socioeconomic status, and indigenous people are less likely to receive treatments.<sup>10</sup>

### Other Controversies

Despite these potential benefits, there are many challenges to providing effective rehabilitation and secondary prevention after ACS. Among the more recent examples are 2 international randomized controlled trials of rehabilitation and secondary prevention therapy,<sup>12,26</sup> data from the International Reduction of Atherothrombosis for Continued Health (REACH) Registry,<sup>27</sup> and a secondary analysis of Australian Choice of

Table I. Recommended therapies and potential performance indicators in acute coronary syndrome.<sup>17</sup>

|  |
|--|
| Referral and uptake of rehabilitation or systematic secondary prevention   |
| Counsel and support active smokers and recent quitters to achieve complete abstinence  |
| Initiate and maintain healthy eating, ie, reduce saturated, <i>trans</i> -fatty fats, foods high in salt, and adjust kilojoules to counter obesity   |
| Achieve 30 minutes of moderate physical activity daily, totaling > 150 min/week  |
| Unless contraindicated and while in hospital commence statin; aspirin second or alternate antiplatelet agent; angiotension-converting enzyme inhibitor (or angiotension receptor blocker); $\beta$ blocker |

Health Options in Prevention of Cardiovascular Events (CHOICE) study.<sup>28</sup>

The RAMIT<sup>12</sup> concluded that cardiac rehabilitation was ineffective, as there were no differences in mortality at any time point during follow-up between intervention and control groups, culminating in 245 versus 243 deaths at 7 to 9 years. Equally, there were no major effects on cardiac or psychological morbidity, risk factors, health-related quality of life, or physical activity. These null mortality and surrogate end-point findings suggest suboptimal delivery of cardiac rehabilitation or recruitment of a low-risk patient sample. Critically, there was a high risk of bias in these findings due to early termination of the trial and possible contamination among controls having been exposed to secondary prevention. A better and more complete description of rehabilitation and the study methods in general would advance our understanding of what RAMIT contributes to the evidence base for preventing disease recurrence. Pooling the RAMIT findings with the existing randomized controlled trial data continues to show a mean reduction in all-cause mortality of 11% with cardiac rehabilitation compared with usual care (pooled relative risk = 0.89; 95% CI, 0.79–1.00).<sup>26</sup>

The full coverage for preventive medications after myocardial infarction (or MI FREEE) trial in patients younger than 65 years old showed that covering the cost of guideline-recommended pharmacotherapy (averaged about \$50 per month) was still associated with a low overall adherence.<sup>27</sup> Adherence with all 3 drug classes was increased from 38.9% with usual funding to 44.3% with full funding ( $P < 0.001$ ). However, there was no difference between the 2 groups in the primary outcome of a first major vascular event or coronary revascularization. The total cost to insurers was comparable for the 2 groups.

Data from the 2,873 Australian participants in the International Secondary Prevention REACH Registry confirm the scope to improve the use of guideline-recommended medication.<sup>28</sup> Only about one third of patients were taking the recommended combination of aspirin, a statin, and either an angiotension-converting enzyme inhibitor or angiotensin-receptor blocker, highlighting the well-recognized gap between trial evidence and routine practice.

There is also scope to improve follow-up of patients. The Australian CHOICE study compared individualized secondary prevention strategies with usual care in patients after ACS and found that the brief patient-

centered lifestyle and behavior intervention significantly improved risk-factor control after 1 year, with benefits sustained at 4 years.<sup>29,30</sup> However, a hypothesis-generating analysis suggested that more-frequent medical follow-up, assessed by the number of consultations with a general practitioner or cardiologist, did not improve multiple risk factors in the absence of systematic secondary prevention care.<sup>31</sup>

### Momentum for Change

A range of new initiatives locally and globally indicate that time is ripe for change to improve the uptake of preventative treatments in patients after ACS.<sup>31</sup> Among the key developments are strengthening of the evidence recommendations; uniting all stakeholders to develop solutions; defining minimum standards for secondary prevention; and devising key performance indicators for monitoring and quality-improvement initiatives. The structure and drivers behind these initiatives are broadly applicable to the medium- and long-term management of ACS in advanced health care systems.

Professional societies and organizations worldwide, in recognition of the variation in ACS care, have promulgated evidence recommendations with periodic updates in efforts to address the management gap. In Australia, a National Acute Coronary Syndrome Implementation Forum was convened by the Heart Foundation in collaboration with the Cardiac Society of Australia and New Zealand and the Australasian College for Emergency Medicine in 2007. It aimed to advise the Heart Foundation about priority interventions to improve the management of ACS in Australia. Its recommendations included better access to cardiac rehabilitation and expanded secondary prevention programs.<sup>32</sup> Recommended local actions included implementation of effective models of secondary prevention and collection of data to inform quality-improvement and practice-improvement programs. The forum was prompted by the emergence of national and international guidelines for the management of ACS, all of which have been updated recently.<sup>33–37</sup>

### Solutions Are Emerging

In the pursuit of finding solutions to the evidence-practice gaps around utilization and adherence, and following the recommendations of a 2007 forum, an inaugural National Secondary Prevention of Coronary Disease Summit was convened in Sydney in December 2011.<sup>18</sup> Forty opinion leaders in secondary prevention, representing 35 organizations around Australia, attended

Table II. Consensus recommendations from the National Secondary Prevention of Coronary Disease Summit.<sup>32</sup>

|  |
|--|
| <p>Develop and implement a national approach that is inherently flexible and adaptable according to available resources and individual patient needs and values.</p> <p>Narrow the divide between hospital and primary health care.</p> <p>Increase awareness of service availability, possibly via the production of a national inventory or “map” of secondary prevention initiatives to increase cohesion and utilization.</p> <p>Develop a primary key performance indicator with hospital readmission or death from cardiovascular disease emerging as the most practical and appropriate option at the current time.</p> <p>Implement a national advocacy program that links state and federal government, Medicare locals and stakeholders to develop sustainable funding.</p> <p>Establish a national secondary prevention taskforce to implement the recommendations resulting from the secondary prevention consensus meeting.</p> |
|--|

the December 2011 Summit. Consumers, policy makers, government, health professionals (including cardiology, general practice, nursing, and allied health), stakeholders such as the Heart Foundation, and private health insurance, were represented and participants were actively engaged during the Summit.

The Summit addressed the following major issues: (1) minimum standards: identify and agree on the key features that should be included in all CHD secondary prevention programs, including cardiac rehabilitation; (2) enabling strategies: identify and agree on enabling strategies for implementation within existing resources at individual, health-service, and policy levels; (3) data and monitoring: identify means to monitor and evaluate at a national level; and (4) future steps: agree on next steps for improving implementation of and access to effective secondary prevention strategies.

There was overwhelming consensus for a patient-centered approach in which the chronological journey after ACS is defined by the patient not by the system. The most significant systematic gap identified by the Summit was poor coordination and integration of tertiary, secondary, and primary care. Other systematic challenges included the often ad-hoc and didactic communication between health professionals and consumers; the lack of a national framework for delivering secondary prevention care; the absence of a defined minimum standard of care; the absence of a national framework for monitoring and maintaining quality; and limited public awareness of the life-long nature of CHD and the need for continued secondary prevention.

Six key recommendations arose from the meeting (Table II). A full report of the Summit is available at

The George Institute Web site ([www.georgeinstitute.org.au](http://www.georgeinstitute.org.au)) and a brief report has been published in the *Medical Journal of Australia*.<sup>18</sup>

#### FUTURE DIRECTIONS

Key universal drivers of delivering best-evidence practice for medium- to long-term care after ACS are economics and locality. Economic factors currently restrict funding of secondary prevention and cardiac rehabilitation, despite the high return on investment in these activities. We need to encourage appropriate funding in all health jurisdictions. As for location, primary care is likely to provide the majority of secondary prevention. The concept of a “medical home” is important, providing patients with long-term comprehensive care. Creating a “silo” for secondary prevention of ACS is unlikely to be efficient or effective.

The Summit has resulted in the establishment of a national task force and a 2-year program of work aimed at developing an action plan and implementing its recommendations. Strategies will be encouraged to embed training in secondary prevention into continuing education programs for health professionals, and to improve secondary prevention through activity-based funding or incentive schemes.

#### CONCLUSIONS

Survivors of ACS account for about half of all major coronary events each year and, as such, should be targeted for an effective and efficient means of preventing future events, while recognizing the essential and continuing role of primary prevention. Registry

data suggest that, at best, half of individuals with known CHD are on appropriate drug therapy, participate in rehabilitation, and make lifestyle changes. Secondary prevention is clearly important, but is not being translated into clinical practice in the long term for the majority of people. Health-service redesign involving all stakeholders will be integral to increasing access, uptake, and adherence to lifestyle, control of risk factors, and pharmacological therapies shown to improve cardiovascular outcomes.

## ACKNOWLEDGMENTS

Dr. Chow is supported by a National Health and Medical Research Council of Australia Career Development Fellowship (1033478) co-funded by the Heart Foundation and a Sydney Medical Foundation Chapman Fellowship. All authors contributed equally to the literature review, synthesis, interpretation, and writing of the manuscript. Dr. Briffa was responsible for preparing the first draft of the manuscript.

## CONFLICTS OF INTEREST

The authors have indicated that they have no conflicts of interest regarding the content of this article.

## REFERENCES

1. Briffa TG, Nedkoff LJ, Knuiman M, et al. Downward trend in the prevalence of hospitalisation for atherothrombotic disease. *Int J Cardiol.* 2013;164:185–192.
2. Briffa TG, Hobbs MS, Tonkin A, et al. Population trends of recurrent coronary heart disease event rates remain high. *Circ Cardiovasc Qual Outcomes.* 2011;4:107–113.
3. Kerr J, Broad J, Wells S, et al. Should the first priority in cardiovascular risk management be those with prior cardiovascular disease. *Heart.* 2009;95:125–129.
4. Kontos MC, de Lemos JA, Ou FS, et al. Troponin-positive, MB-negative patients with non-ST-elevation myocardial infarction: an undertreated but high-risk patient group: results from the National Cardiovascular Data Registry Acute Coronary Treatment and Intervention Outcomes Network—Get With the Guidelines (NCDR ACTION-GWTG) Registry. *Am Heart J.* 2010;160:819–825.
5. Chew DP, Amerena JV, Coverdale SG. the ACACIA Investigators. Invasive management and late clinical outcomes in contemporary Australian management of acute coronary syndromes: observations from the ACACIA registry. *Med J Aust.* 2008;188:691–697.
6. McManus DD, Gore J, Yarzebski J, et al. Recent trends in the incidence, treatment, and outcomes of patients with STEMI and NSTEMI. *Am J Med.* 2011;124:40–47.
7. Gale CP, Cattle BA, Woolston A, et al. Resolving inequalities in care? Reduced mortality in the elderly after acute coronary syndromes. The Myocardial Ischaemia National Audit Project 2003–2010. *Eur Heart J.* 2012;33:630–639.
8. Anderson JL, Adams CD, Antman EM, et al. 2011 ACCF/AHA Focused Update Incorporated Into the ACC/AHA 2007 Guidelines for the Management of Patients With Unstable Angina/Non-ST-Elevation Myocardial Infarction: A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *Circulation.* 2011;123:e426–e579.
9. Redfern J, Maiorana A, Neubeck L, et al. Achieving Coordinated Secondary Prevention of Coronary Heart Disease for All in Need (SPAN). *Int J Cardiol.* 2011;146:13.
10. Clark AM, Hartling L, Vandermeer B, McAlister FA. Secondary prevention program for patients with coronary artery disease: a meta-analysis of randomized control trials. *Ann Intern Med.* 2005;143:659–672.
11. Taylor RS, Brown A, Ebrahim S, et al. Exercise-based rehabilitation for patients with coronary heart disease: systematic review and meta-analysis of randomized controlled trials. *Am J Med.* 2004;116:682–692.
12. West RR, Jones DA, Henderson AH. Rehabilitation After Myocardial Infarction Trial (RAMIT): multi-centre randomised controlled trial of comprehensive cardiac rehabilitation in patients following acute myocardial infarction. *Heart.* 2012;98:637–644.
13. Chow CK, Jolly S, Rao-Melacini P, et al. Association of diet, exercise, and smoking modification with risk of early cardiovascular events after acute coronary syndromes. *Circulation.* 2010;121:750–758.
14. McAlister FA, Stewart S, Ferrua S, McMurray JJ. Multidisciplinary strategies for the management of heart failure patients at high risk for admission: a systematic review of randomized trials. *J Am Coll Cardiol.* 2004;44:810–819.
15. Lawler PR, Filion KB, Eisenberg MJ. Efficacy of exercise-based cardiac rehabilitation post-myocardial infarction: a systematic review and meta-analysis of randomized controlled trials. *Am Heart J.* 2011;162:571–584.
16. Lam G, Snow R, Shaffer L, et al. The effect of a comprehensive cardiac rehabilitation program on 60-day hospital readmissions after an acute myocardial infarction. *J Am Coll Cardiol.* 2011;57:597–604.
17. National Heart Foundation of Australia and the Cardiac Society of Australia and New Zealand. Reducing Risk in Heart Disease: An Expert Guide to Clinical Practice for



- Secondary Prevention of Coronary Heart Disease. Melbourne: National Heart Foundation of Australia; 2012.
18. Redfern J, Chow CK. Secondary prevention of coronary heart disease in Australia: a blueprint for reform. *Med J Aust.* 2013;198:70–71.
  19. Bueno H, Fernandez-Aviles F. Use of risk scores in acute coronary syndromes. *Heart.* 2012;98:162–168.
  20. Briffa TG, Kinsman L, Maiorana AJ, et al. An integrated and coordinated approach to preventing recurrent coronary heart disease events in Australia. *Med J Aust.* 2009;190:683–686.
  21. Chew DP, Huynh LT, Liew D, et al. Potential survival gains in the treatment of myocardial infarction. *Heart.* 2009;95:1844–1850.
  22. Ford ES, Ajani UA, Croft JB, et al. Explaining the decrease in US deaths from coronary disease, 1980–2000. *N Engl J Med.* 2007;356:2388–2398.
  23. Chew DK, French JF, Briffa TG, et al. Acute coronary syndrome care across Australia and New Zealand: the SNAPSHOT ACS study. *Med J Aust.* 2013;199:1–7.
  24. Piepoli MF, Corra U, Adamopoulos S, et al. Secondary prevention in the clinical management of patients with cardiovascular disease. Core components, standards and outcome measures for referral and delivery. *Eur J Prev Cardiol.* 2012 Jun 20. [Epub ahead of print].
  25. Smith AC, Benjamin EJ, Bonow RO, et al. AHA/ACCF secondary prevention and risk reduction therapy for patients with coronary and other atherosclerotic vascular disease: 2011 update: a guideline from the American Heart Association and American College of Cardiology Foundation. *Circulation.* 2011;124:2458–2473.
  26. Taylor RS, 2011 Cochrane review authors. The RAMIT trial: its results in the context of 2012 Cochrane review. *Heart.* 2012;98:672–673.
  27. Choudhry NK, Avorn J, Glynn RJ, et al. Full coverage for preventive medications after myocardial infarction. *N Engl J Med.* 2011;365:2088–2097.
  28. Reid CM, Ademi Z, Nelson MR, et al. Outcomes from the REACH Registry for Australian general practice patients with or at high risk of atherothrombosis. *Med J Aust.* 2012;196:193–197.
  29. Redfern J, Briffa T, Ellis E, Freedman SB. Choice of secondary prevention improves risk factors after acute coronary syndrome: one year follow-up of the CHOICE (Choice of Health Options In prevention of Cardiovascular Events) randomized controlled trial. *Heart.* 2009;95:468–475.
  30. Neubeck L, Freedman SB, Briffa T, et al. Four year follow-up of the CHOICE (Choice of Health Options In Prevention of Cardiovascular Events) randomised controlled trial. *Eur J Cardiovasc Prev Rehabil.* 2011;18:278–286.
  31. Redfern J, Menzies M, Briffa T, Freedman SB. Impact of medical consultation frequency on modifiable risk factors and medications at 12 months after acute coronary syndrome in the CHOICE randomised controlled trial. *Int J Cardiol.* 2010;145:481–486.
  32. Redfern J, Chow CK, Brieger D, et al. National secondary prevention of coronary disease summit. Technical report July 2012. <http://www.georgeinstitute.org.au/projects/secondary-prevention-of-coronary-heart-disease>. Accessed August 4, 2013.
  33. Chew DP, Aroney CN, Aylward PE, et al. 2011 Addendum to the National Heart Foundation of Australia/Cardiac Society of Australia and New Zealand Guidelines for the Management of Acute Coronary Syndromes (ACS) 2006. *Heart Lung Circ.* 2011;20:487–502.
  34. Anderson JL, Adams CD, Antman EM, et al. 2012 ACCF/AHA Focused Update Incorporated Into the ACCF/AHA 2007 Guidelines for the Management of Patients With Unstable Angina/Non-ST-Elevation Myocardial Infarction: A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *Circulation.* 2013;61:e179–e347.
  35. Christian W, Hamm CW, Bassand J-P, et al. ESC guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation. The Task Force for the management of acute coronary syndromes (ACS) in patients presenting without persistent ST-segment elevation of the European Society of Cardiology (ESC). *Eur Heart J.* 2011;32:2999–3054.
  36. Steg PG, James SK, Atar D, et al. ESC guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation. Task Force on the management of ST-segment elevation acute myocardial infarction of the European Society of Cardiology (ESC). *Eur Heart J.* 2012;33:2569–2619.
  37. O’Gara PT, Kushner FG, Ascheim DD, et al. 2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *Circulation.* 2013;127:e362–e425.

**Address correspondence to:** Tom Briffa, PhD, BPhyEd, MPhyEd, School of Population Health, University of Western Australia (M431), 35 Stirling Highway Crawley, WA 6009 Australia. E-mail: Tom.Briffa@uwa.edu.au