Treating to target: ready, fire, aim

Adrienne J. Lindblad ACPR PharmD Mark Makowsky ACPR PharmD G. Michael Allan MD CCFP

Clinical question

Can we achieve guideline-specified surrogate marker targets (SMTs) in primary care (PC)?

Bottom line

Even in ideal settings, less than 25% of carefully selected patients achieve multiple SMTs. However, clinical outcomes improve with proven interventions (eg, statins, metformin, ACEIs) without achieving targets. Clinicians should focus more on using proven therapies than attaining exact SMTs.

Evidence

- Multiple cohort studies found PC patients did not achieve SMTs (ie, cholesterol, blood pressure [BP], glycated hemoglobin [HbA_{1c}]).
  -Of 1706 patients with diabetes mellitus (DM), 7.3% achieved 3 targets (HbA_{1c} <7%, BP <130/80 mm Hg, and cholesterol <5.18 mmol/L)[1]; of 1701 Canadians, 24% had low-density lipoprotein (LDL) levels of <2 mmol/L[2]; and of 3167 patients with coronary artery disease (CAD), 16% achieved 3 targets (BP <130/80 to 85 mm Hg, LDL <2.2 mmol/L, and acetylsalicylic acid use).[3]
- Some RCTs have found achieving targets difficult (despite intense care, maximum doses, and multiple therapies).
  -In a meta-analysis of 7 RCTs (29 395 patients), less than 50% attained LDL levels of less than 2 mmol/L with maximum statin dose.[4]
  -In 3 RCTs of DM patients with CAD (5034 patients), about 23% achieved 4 targets (LDL <2.5 mmol/L, systolic BP <130 mm Hg, HbA_{1c} <7%, and not smoking).[5]
  -In the Steno-2 RCT (160 DM patients), at 13 years, 1% hit 5 targets (HbA_{1c} <6.5%, cholesterol <4.5 mmol/L, triglyceride <1.7 mmol/L, SBP <130 mm Hg, DBP <80 mm Hg).[6]
- Despite not achieving targets, proven therapies (eg, statins, ACEIs, metformin) improved clinical outcomes. Statins reduced CAD (eg, number needed to treat [NNT] of 27 for low-moderate dose and 91 for high dose over low dose).[7] Proven therapies in Steno-2 study reduced death (NNT=5) and cardiovascular disease (NNT=4).[6]

Context

- Targets in guidelines are primarily based on expert opinion (about 50%) and on lower-level evidence (about 40%) and rarely on RCTs.[8]
- Multiple comorbidities are common in PC, particularly in older adults,[9,10] but rare in clinical trials or guidelines, making application difficult.[11]
- Some newer guidelines are relaxing (hypertension[12] and DM[13]) or removing targets (cholesterol[14]).

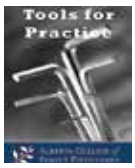
Implementation

Small deviations from SMTs are of little clinical importance, and intensifying care exposes patients to side effects and increases costs.[15] Using treatment targets as performance measures for clinicians does not account for these issues nor for patient preferences.[16] Some guidelines now discourage use of target attainment as a performance measure.[17] Some have suggested that "[o]nly when those who promulgate measures are held personally responsible for their decisions should they hold physicians on the front line personally responsible for their implementation."[16]

Dr Lindblad is Knowledge Translation and Evidence Coordinator with the Alberta College of Family Physicians. **Dr Makowsky** is Associate Professor at the Faculty of Pharmacy and Pharmaceutical Sciences and **Dr Allan** is Associate Professor in the Department of Family Medicine, both at the University of Alberta in Edmonton.

References

1. Saydah SH, Fradkin J, Cowie CC. Poor control of risk factors for vascular disease among adults with previously diagnosed diabetes. *JAMA* 2004;291(3):335-42.
2. Joffres M, Shields M, Tremblay MS, Connor Gorber S. Dyslipidemia prevalence, treatment, control, and awareness in the Canadian Health Measures Survey. *Can J Public Health* 2013;104(3):e252-7.
3. Brown TM, Voeks JH, Bittner V, Brenner DA, Cushman M, Goff DC Jr, et al. Achievement of optimal medical therapy goals for U.S. adults with coronary artery disease: results from the REasons for Geographic And Racial Differences in Stroke (REGARDS) study. *J Am Coll Cardiol* 2014;63(16):1626-33. Epub 2014 Feb 26.
4. Josan K, Majumdar SR, McAlister FA. The efficacy and safety of intensive statin therapy: a meta-analysis of randomized trials. *CMAJ* 2008;178(5):576-84.
5. Farkouh ME, Boden WE, Bittner V, Muratov V, Hartigan P, Ogdie M, et al. Risk factor control for coronary artery disease secondary prevention in large randomized trials. *J Am Coll Cardiol* 2013;61(15):1607-15.
6. Gaede P, Lund-Andersen H, Parving HH, Pedersen O. Effect of a multifactorial intervention on mortality in type 2 diabetes. *N Engl J Med* 2008;358(6):580-91.
7. Allan GM, Mannarino M. *How does high dose statin compare to low dose in people with heart disease.* In: Tools for Practice [website]. Edmonton, AB: ACFP; 2012. Available from: **www.acfp.ca/Portals/0/docs/TFP/20120522_090852.pdf**. Accessed 2014 Mar 25.
8. Tricoci P, Allen JM, Kramer JM, Califf RM, Smith SC Jr. Scientific evidence underlying the ACC/AHA clinical practice guidelines. *JAMA* 2009;301(8):831-41.
9. Fortin M, Bravo G, Hudon C, Vanasse A, Lapointe L. Prevalence of multimorbidity among adults seen in family practice. *Ann Fam Med* 2005;3(3):223-8.
10. Britt HC, Harrison CM, Miller GC, Knox SA. Prevalence and patterns of multimorbidity in Australia. *Med J Aus* 2008;189(2):72-7.
11. Tinetti ME, Bogardus ST Jr, Agostini JV. Potential pitfalls of disease-specific guidelines for patients with multiple conditions. *New Engl J Med* 2004;351(27):2870-4.
12. James PA, Oparil S, Carter BL, Cushman WC, Dennison-Himmelfarb C, Handler J, et al. 2014 Evidence-based guideline for the management of high blood pressure in adults: report from the panel members appointed to the Eighth Joint National Committee (JNC 8). *JAMA* 2014;311(5):507-20.
13. Imran SA, Rabasa-Lhoret R, Ross S. Clinical practice guidelines: targets for glycemic control. *Can J Diabetes* 2013;37(Suppl 1):S31-S34.
14. Stone NJ, Robinson J, Lichtenstein AH, Bairey Merz CN, Lloyd-Jones DM, Blum CB, et al. 2013 ACC/AHA guidelines on the treatment of blood cholesterol to reduce atherosclerotic cardiovascular risk in adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol* 2013 Nov 7. Epub ahead of print.
15. Hayward RA. All-or-nothing treatment targets make bad performance measures. *Am J Manag Care* 2007;13(3):126-8.
16. Pogach L, Aron DC. Sudden acceleration of diabetes quality measures. *JAMA* 2011;305(7):709-10.
17. Inzucchi SE, Bergenstal RM, Buse JB, Diamant M, Ferrannini E, Nauck M, et al. Management of hyperglycemia in type 2 diabetes: a patient-centered approach: position statement of the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). *Diabetes Care* 2012;35(6):1364-79.



Tools for Practice articles in *Canadian Family Physician (CFP)* are adapted from articles published on the Alberta College of Family Physicians (ACFP) website, summarizing medical evidence with a focus on topical issues and practice-modifying information. The ACFP summaries and the series in *CFP* are coordinated by **Dr G. Michael Allan**, and the summaries are co-authored by at least 1 practising family physician and are peer reviewed. Feedback is welcome and can be sent to **toolsforpractice@cfpc.ca**. Archived articles are available on the ACFP website: **www.acfp.ca.**