Further Explanation of Methods

Apples study background

The Alberta Population-based Prospective Evaluation of the Quality of Life Outcomes and Economic Impact of Bariatric Surgery (APPLES) study was designed to assess the impact of extended wait-times for bariatric care and examine effectiveness of bariatric treatments on clinical, economic, and humanistic endpoints in the extremely obese. It was conducted via the Edmonton Weight Wise program, which is a comprehensive bariatric therapy program that was established in 2005. It provides integrated, patient-focused, evidence-based care in the Edmonton Zone, Alberta. This region is one of the largest integrated health delivery systems in Canada: the catchment population is approximately 1.6 million residents. Weight Wise includes a central, region-wide single-point-of-access referral system. Adult specialty services are offered to patients who were referred from a medical practitioner and that have a BMI greater than 35 kg/m². The program is structured such that patients progress from the wait-list to intensive medical management through to bariatric surgery, if indicated. When APPLES study was initiated in 2008, approximately 800 new patients were seen and with 200 surgeries performed annually: about 1500 adults were waitlisted for clinic entry, and the mean wait time was 2 years.^{1,2}

Consecutive patients aged 18–60 years with BMI levels of over 40 kg/m2 or 35 kg/m2 and an obesity-related comorbidity (ex, diabetes, sleep apnea) consented to be enrolled. The APPLES study was a naturalistic assessment of bariatric care: subjects were allowed to progress through the program over the 2-year study period and were not kept in their original study group for the

entire 2 years: wait-listed patients could progress to medical treatment and medically treated patients could progress to surgery. This necessitated the censoring of patients who crossed over into the next phase of treatment. Subjects who were pregnant or nursing, participating in obesity-related clinical trials, or who had absolute contraindications to bariatric surgery were excluded.² Absolute contraindications to surgery include pregnancy, uncontrolled psychiatric disease, active substance abuse or smoking, an active eating disorder (anorexia or bulimia), and high-risk for surgery medical status (e.g. severe coronary artery disease).

Wait-listed patients were advised to participate in community based group education sessions before clinic entry: otherwise they received no intervention. In contrast, medically managed patients received individualized intensive medical management consisting of 24–36 weeks of lifestyle counseling (diet, exercise, behavioral modification), with visits every 4–8 weeks by a multidisciplinary staff (internists, endocrinologists, family physicians, psychiatrists, dietitians, nurses, physiotherapists, occupational therapists, and psychologists) as per the current recommendations. Behavioral modification focuses on teaching skills to help identify and modify eating and activity behaviors. Key elements of behavioral modification include self-monitoring of weight, food intake and activity, stimulus control, and problem solving to help overcome barriers to weight loss.²

Surgical patients had already progressed through the wait listed and medical therapy stages of the Weight Wise clinic. As discussed in the main body of text, patients were educated on the

procedures offered and underwent either adjustable gastric band placement, sleeve gastrectomy or Roux-en-Y gastric bypass. All surgeries were conducted laparoscopically. ²

Transition Probabilities

The probability of resolution of comorbidities in the surgery arm was extrapolated from the primary data using parametric survival analysis. ³ In the remaining arms of the APPLES cohort, there were too few cases of comorbidity resolution to extrapolate a rate, and the rates of resolution were set to zero. The finding were supported by the results of the SOS study. ³

The APPLES study reported the prevalence of hypertension at 2 years, however *de novo* or recurrent hypertension may subsequently occur. The probability of acquiring hypertension was estimated using the externally validated Framingham risk regression model⁴, with risk increasing with age. The values estimated were compared to those published by the Public Health Agency of Canada (PHAC) and Shuger et al: the Framingham values were similar estimates.^{5,6}

The probability of acquiring diabetes in the surgical group was estimated from the average rate from the SOS and the Canadian population risk. Assuming this is the probability associated with class I obesity, the probability of acquiring diabetes for the medical and standard care groups was calculated by assuming patients experienced risk based on their class of obesity.⁷⁻¹⁰

The probability of death for each state was estimated using mortality rates for the Canadian population, adjusting for sex ratio and allowing the risk to increase with age in each successive Markov cycle. The relative risks associated with BMI and comorbidity, as published in the literature, were applied to these mortality rates accordingly. ^{5,8,9,11-13} The baseline risk of mortality was used for the surgical group, and conservative values for the increased risks associated with the BMI were congruently applied to the medical and standard care groups. This likely results in a conservative estimate of mortality. ¹⁴ The risk associated with the surgical health states was applied as the lowest bound for the plausible ranges of the medical and standard care parameters.

Costs

Publicly funded health care system perspective

To operationalize the publicly funded health care system costs, the costs of all hospitalizations, ambulatory care episodes, and physician billings obtained from linked administrative data were combined with patient out-of-pocket costs, including transport, assistance, household care, personal care, mobility aids, meal replacements, physical trainers, exercise/diet/nutrition programs, private nursing care, physical, occupational and respiratory therapy and other, as recorded at each study visit. Prescription and over-the-counter medication use was recorded and costs based on the lowest-cost formulary alternative were assigned.

Societal perspective

The friction cost was determined from the mean length of unemployment in Canada and mean wage, in 2016.¹⁵ If patients were unemployed for two separate periods in a year, only one friction

period was applied. A friction period was applied if the patient reported being unemployed or on short or long-term disability: for those on long-term disability, the friction cost was applied only once. For the standard care, medical and surgical groups, the percent of persons incurring a friction cost was 40%, 35% and 17%, respectively.

Cost Extrapolation beyond 2-year APPLES study

It was assumed that patients were discharged from the obesity management clinic after 2 years, and as such the ambulatory care and physician billings associated with the program ceased. As there were no deaths in the surgery arm, the cost associated with death in the medical therapy arm was applied. With regards to the SP costs, cost of income transfer payments occurred every year until the mean age of retirement in Canada¹⁵, after which incremental costs were solely health care costs. The costs acquired during the 2-year APPLES study were used as an initial cost, and annual costs were accrued each cycle.

- 1. Padwal RS, Majumdar SR, Klarenbach S, et al. The Alberta population-based prospective evaluation of the quality of life outcomes and economic impact of bariatric surgery (APPLES) study: background, design and rationale. *BMC Health Serv Res.* 2010;10:284.
- 2. Padwal RS, Rueda-Clausen CF, Sharma AM, et al. Weight loss and outcomes in waitlisted, medically managed, and surgically treated patients enrolled in a population-based Bariatric program: prospective cohort study. *Med Care*. 2014;52(3):208-215.
- 3. Sjostrom L. Bariatric surgery and reduction in morbidity and mortality: experiences from the SOS study. *Int J Obes (Lond)*. 2008;32 Suppl 7:S93-97.
- 4. Parikh NI, Pencina MJ, Wang TJ, et al. A risk score for predicting near-term incidence of hypertension: the Framingham Heart Study. *Ann Intern Med.* 2008;148(2):102-110.
- 5. Canada PHAo. Report from the Canadian Chronic Disease Surveillance System: Hypertension in Canada, 2010. Ottawa, Canada2010.
- 6. Shuger SL, Sui X, Church TS, Meriwether RA, Blair SN. Body mass index as a predictor of hypertension incidence among initially healthy normotensive women. *Am J Hypertens*. 2008;21(6):613-619.

- 7. Ganz ML, Wintfeld N, Li Q, Alas V, Langer J, Hammer M. The association of body mass index with the risk of type 2 diabetes: a case-control study nested in an electronic health records system in the United States. *Diabetol Metab Syndr*. 2014;6(1):50.
- 8. Canda PHAo. Report from the National Diabetes Surveillance System: Diabetes in Canada, 2009. Ottawa, Canada2009.
- 9. Canada PHAo. Diabetes in Canada: Facts and Figures from a Public Health Perscretive. In: Department of Health GoC, ed. Ottawa2011.
- 10. Altman DG BJ. Interaction revisited: the difference between two estimates. *BMJ*. 2003;326(7382):219.
- 11. Kitahara CM, Flint AJ, Berrington de Gonzalez A, et al. Association between class III obesity (BMI of 40-59 kg/m2) and mortality: a pooled analysis of 20 prospective studies. *PLoS Med.* 2014;11(7):e1001673.
- 12. Orpana HM, Berthelot JM, Kaplan MS, Feeny DH, McFarland B, Ross NA. BMI and mortality: results from a national longitudinal study of Canadian adults. *Obesity (Silver Spring)*. 2010;18(1):214-218.
- 13. Canada S. Probability of dying by age and sex, Canada, 2009/2011. http://www.statcan.gc.ca/pub/91-209-x/2013001/article/11867/fig/desc/desc04-eng.htm. Published 2011. Accessed 2016.
- 14. Padwal R, Majumdar SR, Leslie WD. Relationship Among Body Fat Percentage, Body Mass Index, and All-Cause Mortality. *Ann Intern Med.* 2016;165(8):604.
- 15. Canada Go. Statistics Canada. https://www.statcan.gc.ca/. Published 2016. Accessed 2016.