The Real World Cost-effectiveness of Bariatric Surgery for the Treatment of Severe Obesity

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ABSTRACT

Background: Extreme obesity is associated with adverse health outcomes and increased mortality. The 'real-word' cost-utility of obesity therapy, from the publicly funded health care system and societal perspectives, is infrequently assessed.

Methods: Decision and Markov models compared medical, surgical and standard care therapies. Primary granular data from a prospective observational cohort of 500 severely obese adults in a regional obesity program over 2 years was extrapolated to 10-year and lifetime models, validated and supplemented with literature sources. Deterministic and probabilistic sensitivity analyses were performed.

Results: From a publicly funded health system perspective, compared to standard care therapy, at 2 years surgical therapy demonstrated an ICUR of $54,456/QALY. Over a lifetime, it had an ICUR of 14,056/QALY. From the societal perspective, at 2 years surgical therapy demonstrated an ICUR of $340/QALY: over a lifetime, it was the dominant option. The results were robust to sensitivity analysis.

Conclusions: From a public health care perspective, surgery is cost effective. When approached from a societal perspective, surgery becomes cost saving. These findings, using real-world data, support using surgical therapy for severe obesity, and fill a deficit within the health economic and clinical literature with regards to robust analysis from the social perspective.

INTRODUCTION

Extreme obesity, defined as a body mass index greater than 35 kg/m^2, is associated with adverse health outcomes [1-4], increased health care resource use, and reduced home and workforce productivity. Numerous approaches to treat obesity have been developed, including lifestyle modifications, pharmacotherapies, and surgical interventions.[5-10] Bariatric surgery has emerged as one of the most clinically effective options, with numerous studies demonstrating its effectiveness.[3,11]

While many studies have examined cost-effectiveness from the health payer perspective, a broader perspective that fully captures all the costs and consequences of obesity and its treatment is lacking.[3,12] Failing to consider the societal perspective can underestimate opportunity costs and misdirect resource allocation; this is especially relevant when assessing interventions that increase productivity in a working age patient population, and quality of life. Further, most analyses use data that are estimated from multiple sources, which may not reflect pragmatic, real-world resource use and outcomes. Failure to incorporate factors such as compliance or outcomes of treatment programs outside of a rigorous study protocol may lead to biased estimates of the cost-effectiveness of bariatric treatment programs.

Using prospective, empirical data from a regional bariatric program, we conducted an economic evaluation of surgical and medical therapy compared with standard care from both the public health care system and societal perspectives over 2 years, and extrapolated to 10-year and lifetime time horizons. This rigorously collected data from a pragmatic clinical treatment program coupled with a broad perspective facilitates the real-world assessment of treatment.

METHODS

Data from The Alberta Population-based Prospective Evaluation of the Quality of Life Outcomes and Economic Impact of Bariatric Surgery (APPLES) study was used to inform this cost-utility analysis. A detailed study protocol, approved by the University of Alberta Health Research Ethics Board (Pro00003594), has been previously published.[5] The 500 obese (BMI > 35 kg/m^2) adult patients were allocated to three groups: medical therapy, surgical therapy or standard care (a wait-listed standard care group with no direct weight-loss therapy administered, serving as a control group). All patients were deemed surgical candidates, as per the NIH guidelines.[13] Data were captured prospectively at 6, 12, 18 and 24 months after respective therapy commencement, including demographics, anthropometrics, health-related quality of life, medication use, detailed health care resource use through linkage with administrative data, and patient and societal costs including transportation needs, out-of-pocket health related purchases, attendance at work and enrollment in government support programs, captured through patient surveys.

Statistical Analysis

Models

Outcomes at two years were assessed using primary data from the APPLES study by treatment group.

Markov models using 10-year and lifetime time horizons were created. Patients were allocated to the health states of death, diabetes, hypertension, diabetes and hypertension or no obesity related comorbidity as per the results of the 2-year cohort study, and could transition between states during each one-year cycle. (Figure 1) Baseline characteristics for each treatment arm at the completion of the APPLES study are reported in Table 1, and were applied to the respective health states.

Transition probabilities between health states were obtained from primary data where possible, and otherwise informed by focused literature review (supplementary file 1). The approach to determining probabilities is outlined in supplementary file 2.

Utility

For the 2-year assessment, utility values from the APPLES cohort were used. These were measured using the EQ-5D-3L survey and derived via the USA valuation system.[14] For the 10-year and lifetime models, utility measurements were extrapolated by performing multivariable analysis on the APPLES data and using the resultant regression equation to calculate the utility associated with each health state by age. The values calculated were validated by comparison to the values collected by the Health Quality Council of Alberta: the values from the APPLES data were minimally and consistently lower than those from the HCQA. While the HCQA data did not differentiate comorbidities, this finding increased our confidence in the extrapolation.

Costs

The publicly funded health care system (HCP) and societal perspectives (SP) were defined as per the Canadian Agency for Drugs and Technologies in Health (CADTH) guidelines. [15] The former includes costs to the publicly funded health care system, patients and their families: details concerning cost determinations are contained in supplementary file 2.

The SP is defined by CADTH as the components of the HCP combined with the direct costs to publicly funded services (other than health care) and productivity costs.[15] This was operationalized by adding, to the HCP cost, the costs of income transfer payments (income for disabled persons, disability and employment insurance benefits), as well as cost of productivity loss, as measured by the friction method: details pertaining to these cost determinations are outlined in supplementary file 2.[16]

Beyond 2 years, the cost of each health state was extrapolated using APPLES data, assuming costs observed for a health state in the second year would persist. Assumptions associated with the cost extrapolation are outlined in supplementary file 2.

All costs were expressed in 2016 Canadian dollars. Where health care related costs required adjustment, the health specific CPI was employed.[17] Other costs were adjusted using the Bank of Canada Inflation Calculator.[18]

Sensitivity Analysis

In the 2-year model, probabilistic sensitivity analysis (PSA) was conducted using patient level costs and its distributions. Transition probabilities were applied to beta distributions.

In the 10-year and lifetime model, all variables were assessed via one-way sensitivity analysis, comparing surgical or medical therapy to the reference group (standard care) using the ranges displayed in supplementary files 1-3. PSA was also conducted.

PSA was conducted using Monte Carlo simulation with 1000 iterations. Costs and effects were assessed at a discount rate of 5%, with 3% and 0% in sensitivity analysis. All modeling was conducting using Treeage Pro (2018) [19], and all statistical analysis using Stata 13.[20] Face, internal and external validity were assessed.[21]

RESULTS

The annual HCP and SP costs and utility estimates for patients by health state are reported in supplementary files 3 and 4 respectively.

The incremental cost utility ratio (ICUR) are reported with standard care as the comparator group. At 2 years, the absolute QALYs were 1.37, 1.56 and 1.69 for standard care, medical and surgical therapy respectively (supplementary file 5). From the HCP, the mean cost of therapy over the 2-year cohort for standard care, medical and surgical therapy was 8037, 10591 and 25463 respectively. When compared to standard care therapy, surgical therapy demonstrated an ICUR of $54,456/QALY. The cost effectiveness acceptability curve (CEAC) is reported in Figure 2, and indicates that at a willingness-to-pay(WTP) value of $30,000 and above medical therapy is favoured.

From the SP, mean costs were 51,016, 39,358 and 51,125 for standard care, medical and surgical therapy respectively (supplementary file 5). Surgical therapy demonstrated an ICUR of $340/QALY. When compared to standard care, medical therapy was dominant (led to more QALYs with lower costs). The CEAC (Figure 2) indicates that at a WTP value of $5,000 and above medical therapy is favoured.

Results in the 10-year time horizon model are reported in supplementary file 4. From a HCP, standard care was the lowest cost option. When compared to standard care, medical therapy had an ICUR of $27,199/QALY, and surgical therapy had an ICUR of $19,989/QALY.

The results were robust to most parameter changes in 1-way sensitivity analysis. The 15 variables inducing the greatest change in 1-way sensitivity analysis are displayed via tornado diagrams in supplementary file 5. Comparing surgery to standard care, the model is sensitive to the cost of the health states of diabetes and hypertension in standard care patients. The model is also sensitive to the mean initial QALY level of surgical patients, which is obtained directly from the APPLES data. When comparing medical therapy to standard care, the model is most sensitive to changes in the cost of standard care patients with both diabetes and hypertension.

In PSA of the 10-year model, surgical therapy is favoured at WTP thresholds above $15,000 (Figure 3).

When a SP was used in the 10-year model, medical therapy was the lowest cost option. Standard care was dominated (had higher costs and worse health outcomes), and surgery and medical therapy dominated.

This model was robust to most parameter changes in 1-way sensitivity analysis. Overall results were impacted by the cost of surgical group with no comorbidities: as the cost the care in this group increased, the ICUR for surgery became positive. A similar relationship was seen in the medical patients with both diabetes and hypertension. The results of the deterministic sensitivity analysis are displayed in supplementary file 5.

In PSA, surgical therapy is favoured at WTP thresholds above $20,000 (Figure 3).

Results in the lifetime horizon model are reported in supplementary file 5. Considering health system costs, the lowest cost option was standard care, however this resulted in the least QALYs. Compared to standard care, surgery had an ICUR of 14,056/QALY, and medical therapy was dominated by surgery (most costly and less effective than surgery).

In 1-way sensitivity analysis the model was sensitive to the cost of having both diabetes and hypertension in the standard care group. When comparing surgery to standard care, surgery became the dominating approach with minimal increases in the cost of this heath state. The results of the deterministic sensitivity analysis are displayed in supplementary file 6.

In PSA, from the HCP surgical therapy was preferred at WTP threshold above $12,000 (Figure 4).

Using a SP, surgery was the lowest cost option, with medical and standard care dominated.

In deterministic sensitivity analysis, when comparing surgery to standard care, increasing cost of having no comorbidities in the surgery arm altered the results from surgery dominating to having a positive ICUR. The results of the deterministic sensitivity analysis are displayed in supplementary file 6.

In PSA (Figure 4), surgical therapy is preferred at all WTP values.

INTERPRETATION

Using prospectively collected real world data, we calculated the cost and utility of surgical therapy, medical therapy and standard care for the treatment of extreme obesity, from both the public health care system and societal perspectives. We have demonstrated that the perspective taken alters the results of this comparison, with surgical and medical treatment becoming more attractive from the societal perspective. This is most pronounced in the short run; as time progresses, the overarching results begin to converge and surgery emerges as the most cost effective method across a wide range of WTP thresholds. From the societal perspective, surgery becomes the lowest cost option, dominating medical therapy and standard care. Surgery also exhibits the highest level of utility gains, and therefore increases quality of life more than medical or standard therapy.

Our finding that bariatric surgery is either cost effective or cost saving is congruent with previous published reports.[11,12,22-26] However, many previous studies do not consider the societal perspective; as obesity has effects on many facets of life, failing to take into account the breadth of this impact reduces the applicability of these studies. [3,11,25,26] Moreover, many studies do not consider comparative therapies or real-world data, making this study more informative and valuable for decision makers. [11,12]. Finally, application of a lifetime time horizon better reflects the long-term impact of obesity interventions, an approach often not pursued in previous studies.[11]

By creating a 2-year model that directly reflects prospectively collected data, and utilizing each individual's data points in custom distributions, the model incorporates real world heterogeneity and variability, including the costs of surgical complications. This reduces parameter and model uncertainty and increases the validity of the PSA results. In using real-world data to inform long-term models, and sources such as the Framingham risk score and the HCQA to externally validate parameter estimates, parameter uncertainty is reduced.[27]

Conservative assumptions, with regards to the long-term effects of surgery and the impact of untreated or ineffectively treated obesity, likely reduced the magnitude of difference in mortality and comorbidity rates between bariatric surgery and the other treatment arms. This was supported by the deterministic sensitivity analysis: while rarely altering the direction of the

ICUR, the magnitude was often sensitive to mortality rates, with at minimum 2 mortality rates presenting in the top 15 most sensitive model parameters in each tornado diagram. Conservative assumptions likely underestimate the cost-effectiveness of bariatric surgery relative to comparators.

The overarching results were generally insensitive to parameter changes. It is noteworthy that the cost of having hypertension and diabetes in the standard care group was, in every one-way sensitivity analysis, either the first or second most sensitive parameter in the model. As reported in supplementary file 2, this parameter has a range of $53 to $182,264, with a mean value of $9513, as calculated from the APPLES data. This mean value is notably higher than most other non-death states, and the broad plausible range likely contributes to its impact on ICUR. From a conceptual standpoint, this emphasizes the impact of the cost of comorbidities on overall costs: reduction in the prevalence of hypertension and diabetes via therapy reduces both health care and societal costs.

LIMITATIONS

Several limitations of this work merit consideration. The friction approach was taken to calculate societal costs, as per the CADTH guidelines.[15] Relative to the human capital approach, this may underestimate societal costs: particularly in the standard care and medical groups, as there were greater levels of disability and unemployment in those groups.

Hypertension and diabetes were chosen as health states, as they have been illustrated to be drivers of cost and morality[28,29]. The study omits numerous other health states; for example, sleep apnea or coronary artery disease. As these, and other diagnosis, were present in the population, and the costs of all health care delivery was utilized, it is logical to assume that the costs associated with these diagnoses are included in the analysis, and exist in each treatment arm at the rate that they would coexist with hypertension and/or diabetes. Given the multifaceted nature of obesity, it is impractical to label each possible comorbidity, and the iterative combinations, as health states. Furthermore, the number of probability estimations would increase uncertainties in the model.[30]

The APPLES study was conducted prior to the introduction of pharmaceuticals such as combination naltrexone/bupropion and liraglutide: these will likely impact both cost and outcomes in medical and surgical groups, as they are being used perioperatively and instead of surgery. Future studies will be needed to understand the long-term clinical and economic impact of these technologies.[31-33]

This study was conducted using single center data. While this institution uses up-to-date, multidisciplinary approaches with outcomes comparable to those in the literature, this study does not take into account variation in practise between centers, which may influence cost and outcome.

CONCLUSION

Bariatric surgery resulted in the greatest health-related quality of life gains. From a HCP, surgery is cost effective. From a SP, surgery becomes cost saving. These findings, using real-world data, support using surgical therapy for severe obesity, and fill a deficit within the literature with regards to robust analysis from the social perspective.

DATA-SHARING STATEMENT

The APPLES data is proprietary: please contact the corresponding author with questions. All other data points were open source.

FUNDING STATEMENT

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There are no conflicts of interest to declare.

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Table 1: Baseline characteristics of treatment groups upon completion of APPLES study (entrance into 10-year and lifetime Models)

	Standard Care (n=150)	Medical Therapy (n=200)	Surgical Therapy (n=150)	All (n=500)
Age (mean SD)	45.64 (9.18)	45.95 (10.01)	45.53 (9.49)	45.73((9.60)
BMI (mean SD) kg/m2	48.83(8.04)	46.54(8.17)	36.36(7.57)	44.77(9.03)
Sex (%) female	90.67	87.00	87.33	88.20
Hypertension (%)	64.00	59.00	44.00	56.00
Diabetes (%)	47.33	41.50	22.00	37.40

Figure 1: 10-year to lifetime time horizon

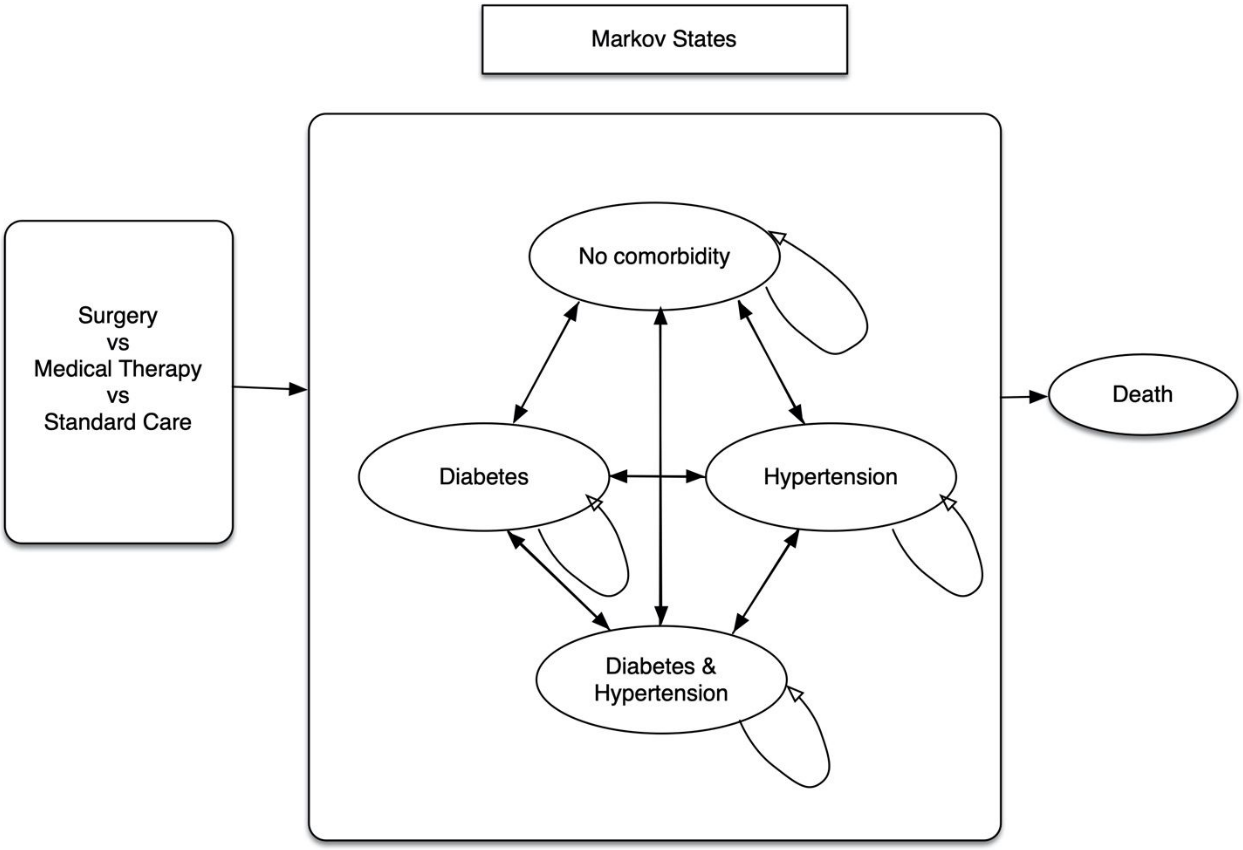
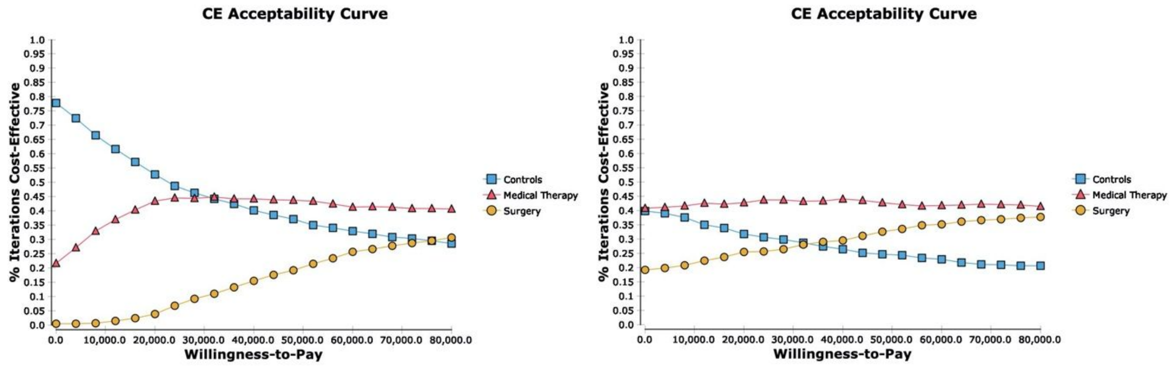
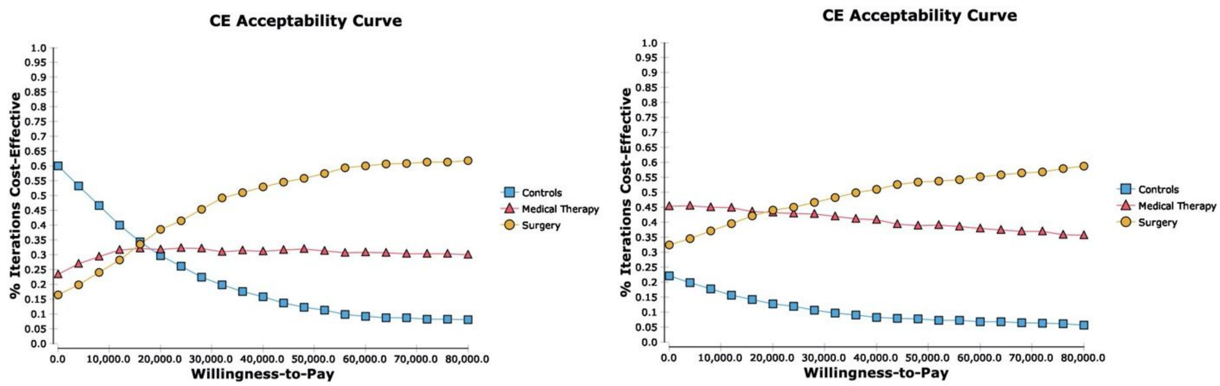


Figure 2: CEAC for 2-year time horizon from the a) publicly funded health care system and b) societal perspective



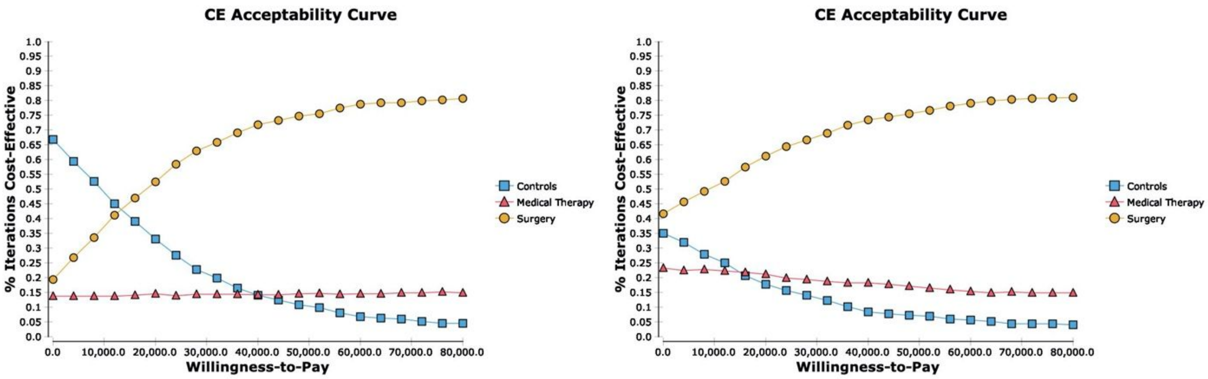
a) publicly funded health care system b) societal perspective

Figure 3: CEAC for 10-year time horizon from the a) publicly funded health care system and b) societal perspective



a) publicly funded health care system b) societal perspective

Figure 4: CEAC for lifetime time horizon from the a) publicly funded health care system and b) societal perspective



a) publicly funded health care system b) societal perspective

Table 2: Transition Probabilities for 10-year and Lifetime Models; values listed at age 45 (mean age at first cycle Markov model)

	Risk per annum, value assigned at age 45*	Plausible range	Variables used in determination	Source	Distribution
Mortality with no comorbidity					
Surgical	0.00137	0.00130-0.00190	Age, sex	[4, 22, 23]	Lognormal
Medical	0.00191	0.00137-0.00455	Age, sex	[4, 22, 23]	Lognormal
Standard Care	0.00274	0.00137-0.0980	Age, sex	[4, 22, 23]	Lognormal
Mortality with Diabetes					
Surgical	0.00274	0.00274-0.00821	Age, sex	[19, 20, 23]	Lognormal

Medical	0.00383	0.00274-0.0138	Age, sex	19, 20, 23	Lognormal
Standard Care	0.00547	0.00274-0.588	Age, sex	19, 20, 23	Lognormal
Mortality with Hypertension					
Surgical	0.00274	0.00274-0.0038	Age, sex	16, 23, 25, 50	Lognormal
Medical	0.00383	0.00274-0.00460	Age, sex	16, 23, 25, 50	Lognormal
Standard Care	0.00548	0.00274-0.196	Age, sex	16, 23, 25, 50	Lognormal
Mortality with Diabetes and Hypertension					
Surgical	0.00548	0.00548-0.164	Age, sex	16, 19, 20, 23, 50	Lognormal
Medical	0.00767	0.00548-0.0276	Age, sex	16, 19, 20, 23, 50	Lognormal
Standard Care	0.0110	0.00548-1.18	Age, sex	16, 19, 20, 23, 50	Lognormal
Diabetes					

acquisition					
Surgical	0.0077	0.0073-0.077	Age	[14, 18-20]	Beta
Medical	0.0111	0.0077-0.200	Age, BMI	[14, 19, 20] [18]	Lognormal
Standard Care	0.0157	0.0077-0.200	Age, BMI	[14] [18-20]	Lognormal
Diabetes Resolution					
Surgical	0.0162	0-0.0162	Age, sex	[5, 14]	Lognormal
Medical	0	0-0.0162	-	[5, 14]	-
Standard Care	0	0-0.0162	-	[5, 14]	-
Hypertension acquisition					
Surgical	0.0245	0.0186-0.0245	Age, sex, blood pressure, smoking status, BMI	[15, 16, 41] [14, 17]	Weibull
Medical	0.0808	0.023-0.85	Age, sex, blood pressure, smoking	[14-17, 41]	Weibull

			status, BMI		
Standard Care	0.0917	0.023-0.85	Age, sex, blood pressure, smoking status, BMI	[15-17, 41]	Weibull
Hypertension Resolution					
Surgical	4.813 $x10^{-5}$	0-4.813 $x10^{-5}$	Age, sex	[5, 14]	Logistic
Medical	0	0-4.813 $x10^{-5}$	-	[5, 14]	-
Standard Care	0	0-4.813 $x10^{-5}$	-	[5, 14]	-

* Rates are determined by evidence found in the literature and informed by the primary APPLES data. For instance, mortality tables from Statistics Canada were employed to determine mortality rates, adjusting for the sex, BMI and comorbidity states as determined from the APPLES data. Using the same tables, the rate of mortality increased with increasing age.

Supplementary file 2: Further Explanation of Methods

Transition Probabilities

The probability of resolution of comorbidities in the surgery arm was extrapolated from the primary data using parametric survival analysis. [14] 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. [14]

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 model[15], 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.[16,17]

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.[18-21]

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. [4,16,19,20,22,23] 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. [24] 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.[28] 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 Canada[17], 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.

Table 3: Annual cost estimates for 10-year and Lifetime Models; values listed at age 45 (mean age at first cycle of Markov model)

Estimate	Publicly Funded Health Care System Costs (CDN)	Plausible Range	Societal Perspective Value Assigned (CDN)	Plausible Range	Distribution
Standard care group no comorbidity	3236	156-6487	6587	119-20594	Gamma
Standard care group diabetes	6017	767-43772	25002	602-190926	Gamma
Standard care group hypertension	4130	669-8260	8504	1137-14936	Gamma
Standard care group Diabetes and hypertension	9513	53-182264	38686	204-245017	Gamma
Standard care group death	13385	22915-37788	31367	31367-54763	Gamma

Medical Therapy no comorbidity	7876	85-15627	8938	198-51125	Gamma
Medical Therapy diabetes	7654	646-10208	10133	735-67097	Gamma
Medical Therapy hypertension	9502	1011-30269	9830	1295-43490	Gamma
Medical Therapy Diabetes and hypertension	9513	346-37918	12540	346-65370	Gamma
Medical Therapy death	27296	22915-37788	45602	40296-54763	Gamma
Surgical Therapy no comorbidity	7795	270-54717	12982	381-98949	Gamma
Surgical Therapy diabetes	6996	1446-47999	13703	890-55539	Gamma

Surgical Therapy hypertension	6488	347-25003	10977	1034-59779	Gamma
Surgical Therapy Diabetes and hypertension	7560	744-16137	10594	901-27783	Gamma
Surgical Therapy death	27296	22915-37788	45602	40296-54763	Gamma

Table 4. Utility estimates for 10-year and Lifetime Models; values listed at age 45 (mean age at first cycle Markov model)

Utility	Value assigned	Plausible range	Distribution
Standard care group no comorbidity	0.694	0.308-1.00	Beta
Standard care group diabetes	0.642	0.376-1.00	Beta
Standard care group hypertension	0.724	0.204-1.00	Beta
Standard care group Diabetes and hypertension	0.683	0.167-1.00	Beta
Medical Therapy no comorbidity	0.782	0.678-1.00	Beta
Medical Therapy diabetes	0.765	0.378-1.00	Beta
Medical Therapy hypertension	0.782	0.263-1.00	Beta

Medical Therapy Diabetes and hypertension	0.765	-0.0402-1.00	Beta
Surgical Therapy no comorbidity	0.838	0.463-1.00	Beta
Surgical Therapy diabetes	0.821	0.271-1.00	Beta
Surgical Therapy hypertension	0.838	0.271-1.00	Beta
Surgical Therapy Diabetes and hypertension	0.821	0.204-1.00	Beta
Death	0	0	-

Table 5: 2-year, 10 year and lifetime time horizon results, with standard care as the comparator

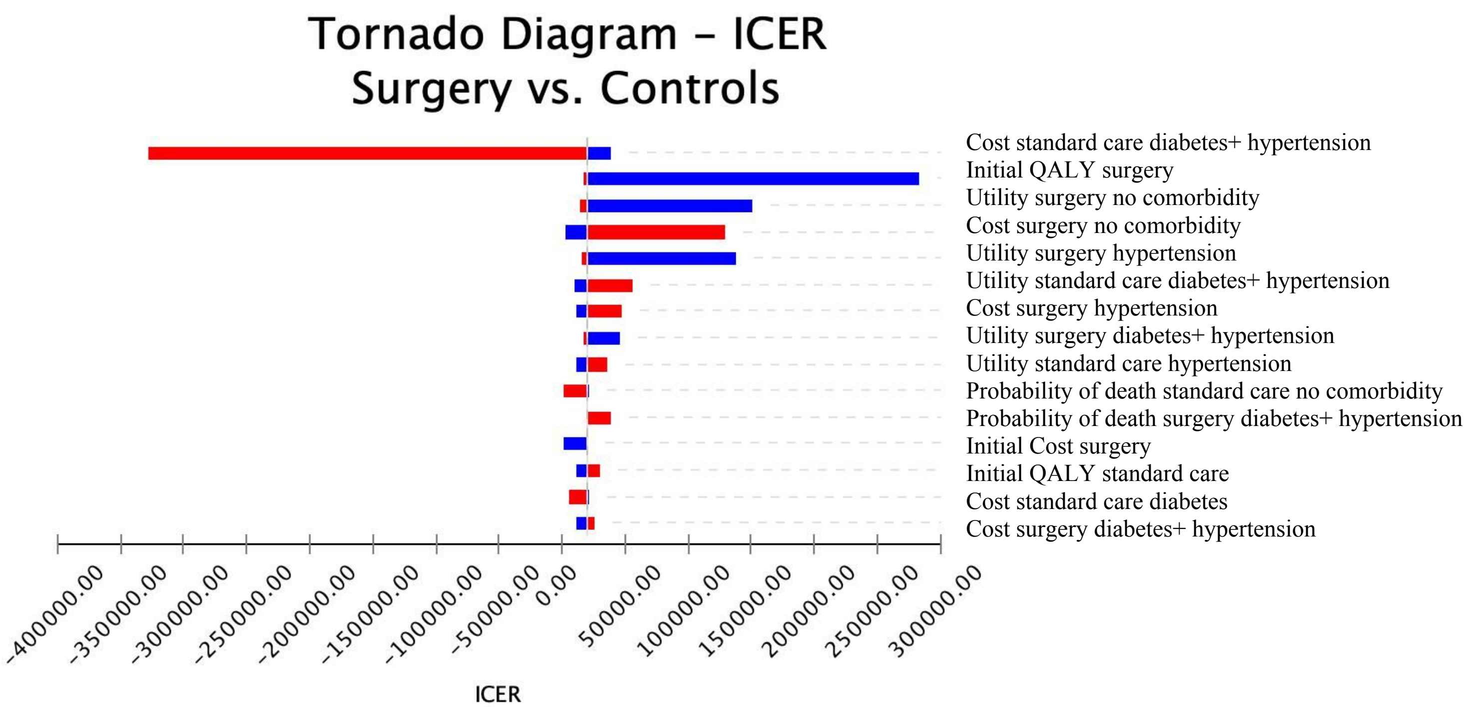
	Absolute Cost	Incremental Cost	Absolute QALY gain	Incremental QALY gain	ICUR
2-year Time Horizon					
Publicly Funded Health Care System Perspective					
Standard Care	8037	-	1.37	-	-
Medical Therapy	10591	2554	1.56	0.19	13,442
Surgical Therapy	25463	17426	1.69	0.32	54,456
Societal Perspective					
Standard Care	51,016	-	1.37	-	-
Medical Therapy	39,358	-11,658	1.56	0.19	Dominates (less costly and more effective)
Surgical Therapy	51,125	109	1.69	0.32	340
10-year Time Horizon					

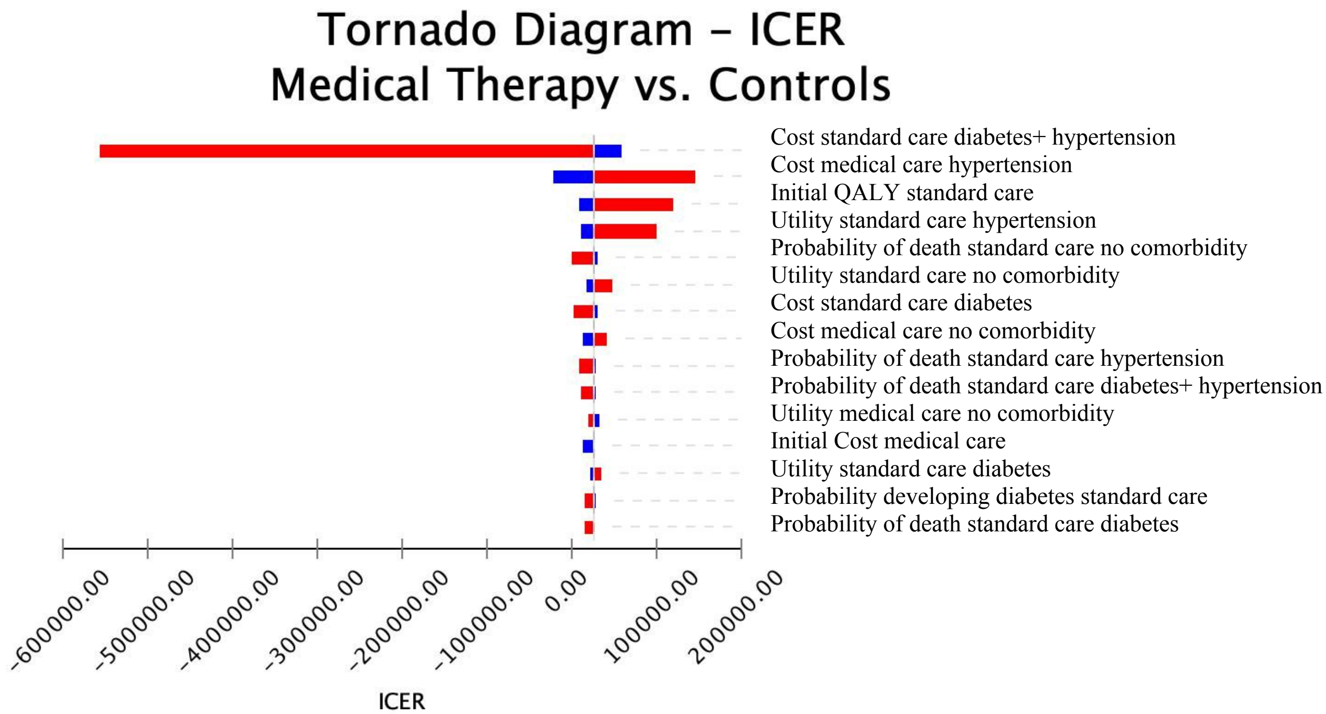
Publicly Funded Health Care System Perspective					
Standard Care	53,514	-	5.85	-	-
Medical Therapy	75,332	21,818	6.66	0.8	27199
Surgical Therapy	80,498	26,984	7.20	1.35	19,989
Societal Perspective					
Standard Care	204,103	-	5.88	-	
Medical Therapy	117,603	-86,500	6.68	0.8	Dominant
Surgical Therapy	134,582	-69,521	7.21	1.33	Dominant
Lifetime Time Horizon					

Publicly Funded Health Care System Perspective					
Standard Care	168,217	-	10.41	-	-
Medical Therapy	260,905	92,688	12.49	2.08	44,561
Surgical Therapy	227,634	59,417	14.63	4.22	14,056
Societal Perspective					
Standard Care	436,488	-	10.41		
Medical Therapy	330,770	-105,718	12.49	2.08	Dominant
Surgical Therapy	313,162	-123,326	14.63	4.22	Dominant

Supplementary file 6

10 year Health Care Perspective




Tornado Diagram – ICER
Medical Therapy vs. Controls
Cost standard care diabetes+ hypertension
Cost medical care hypertension
Initial QALY standard care
Utility standard care hypertension
Probability of death standard care no comorbidity
Utility standard care no comorbidity
Cost standard care diabetes
Cost medical care no comorbidity
Probability of death standard care hypertension
Probability of death standard care diabetes+ hypertension
Utility medical care no comorbidity
Initial Cost medical care
Utility standard care diabetes
Probability developing diabetes standard care
Probability of death standard care diabetes
-600000.00
-500000.00
-400000.00
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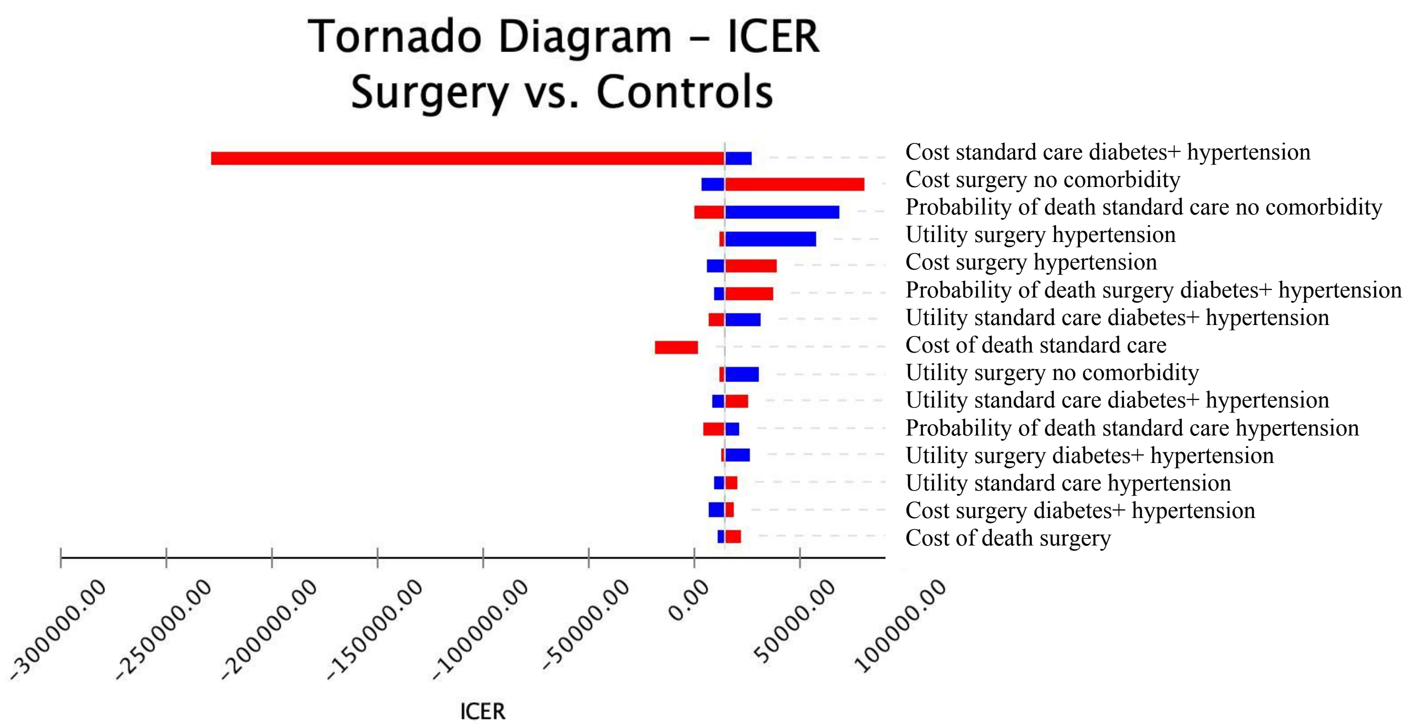
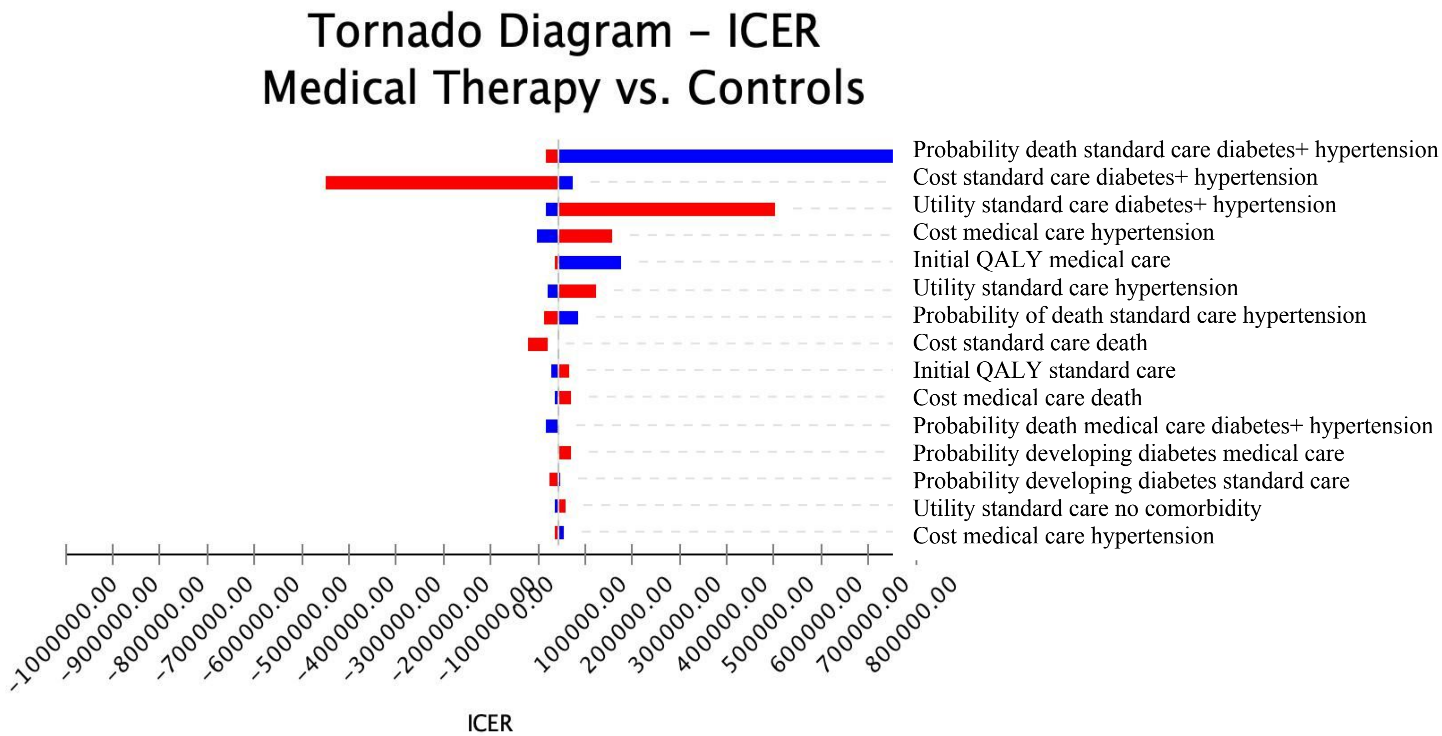
ICER

Lifetime Health Care Perspective




Tornado Diagram – ICER
Medical Therapy vs. Controls
Probability death standard care diabetes+ hypertension
Cost standard care diabetes+ hypertension
Utility standard care diabetes+ hypertension
Cost medical care hypertension
Initial QALY medical care
Utility standard care hypertension
Probability of death standard care hypertension
Cost standard care death
Initial QALY standard care
Cost medical care death
Probability death medical care diabetes+ hypertension
Probability developing diabetes medical care
Probability developing diabetes standard care
Utility standard care no comorbidity
Cost medical care hypertension
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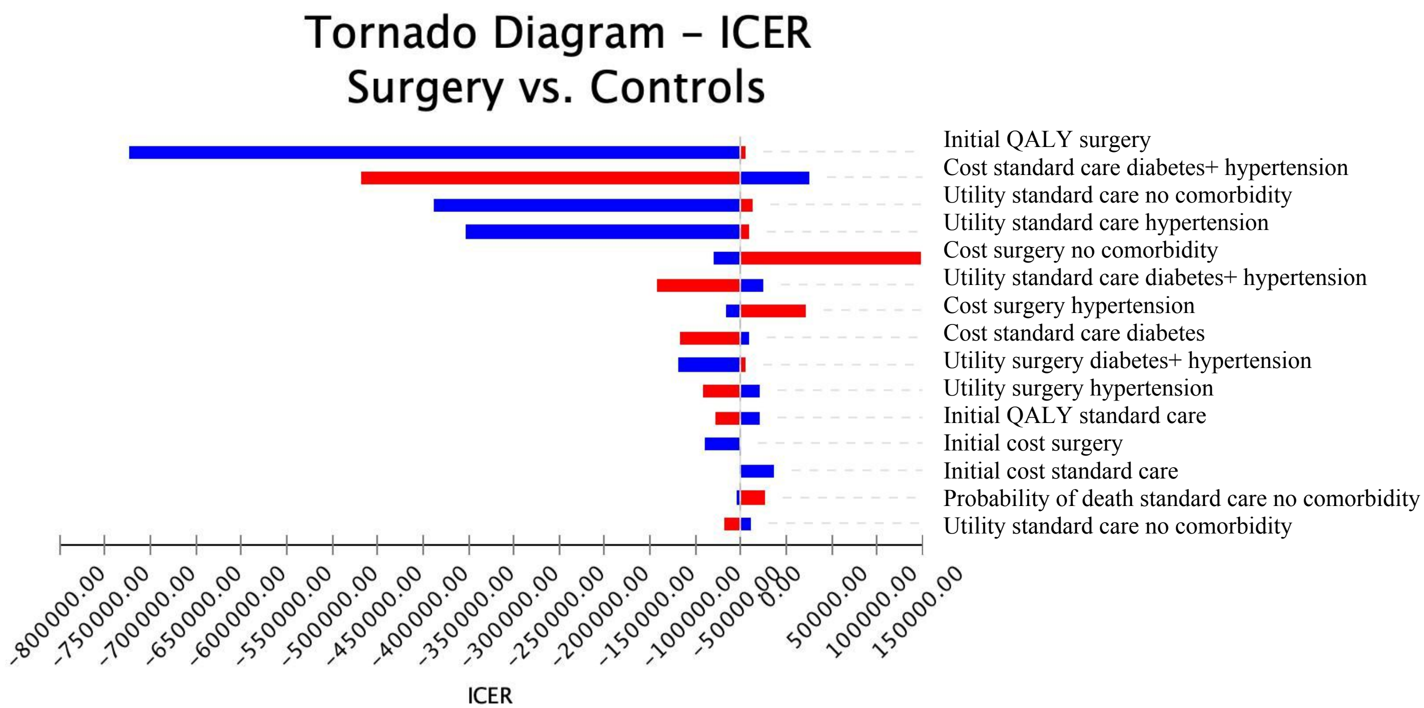
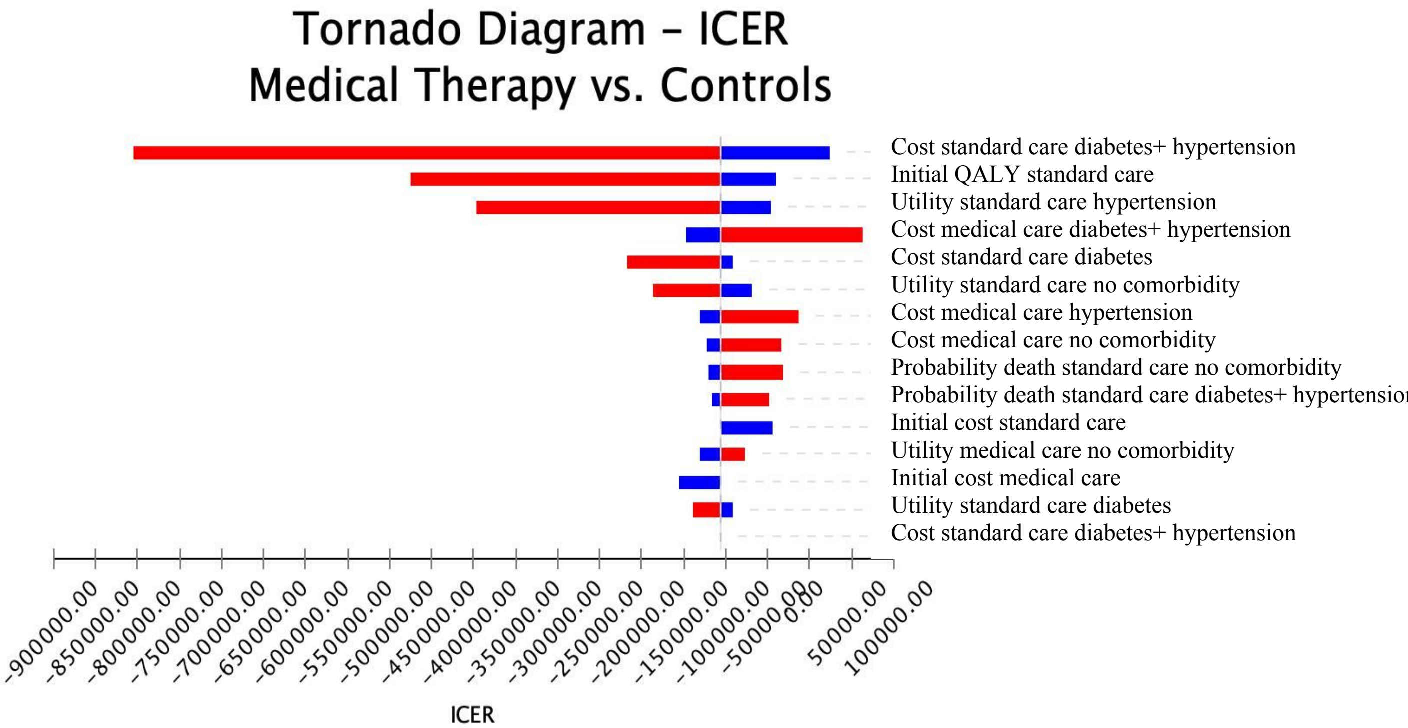
10 year Societal Perspective

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Initial cost standard care
Utility medical care no comorbidity
Initial cost medical care
Utility standard care diabetes
Cost standard care diabetes+ hypertension
-900000.00
-850000.00
-800000.00
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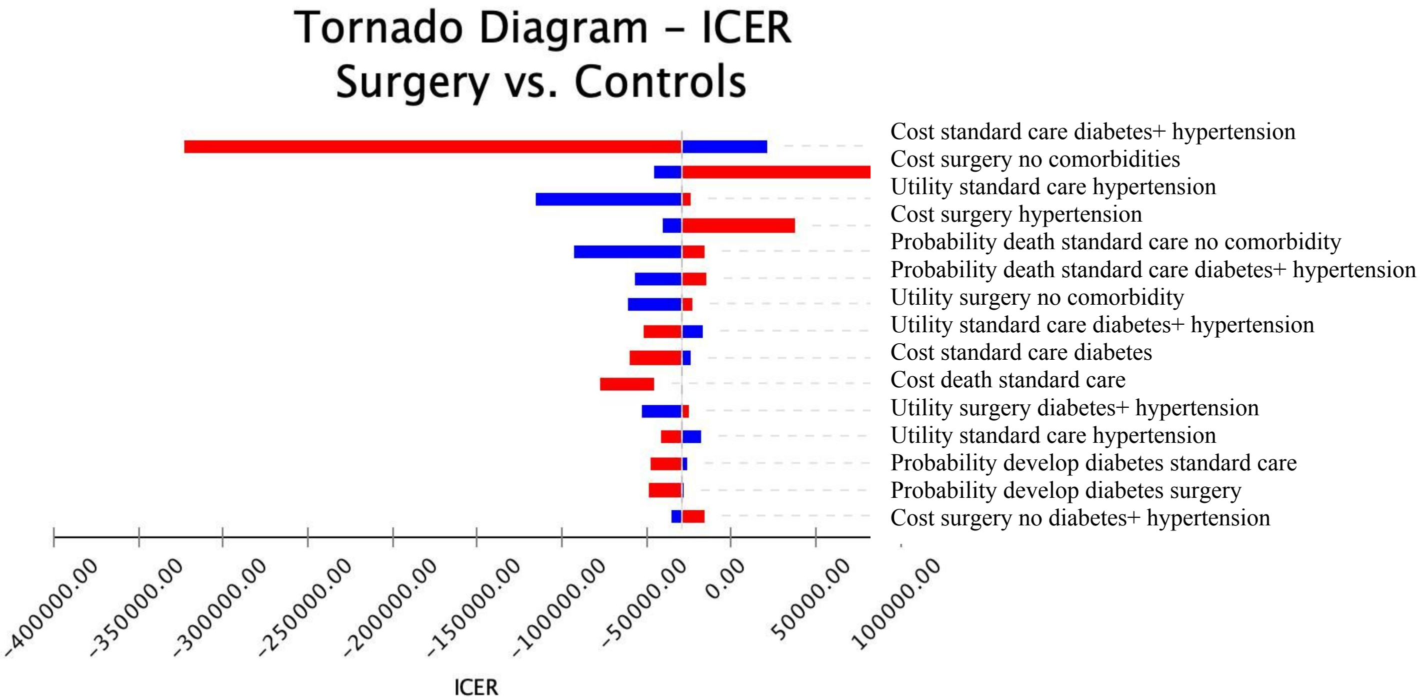
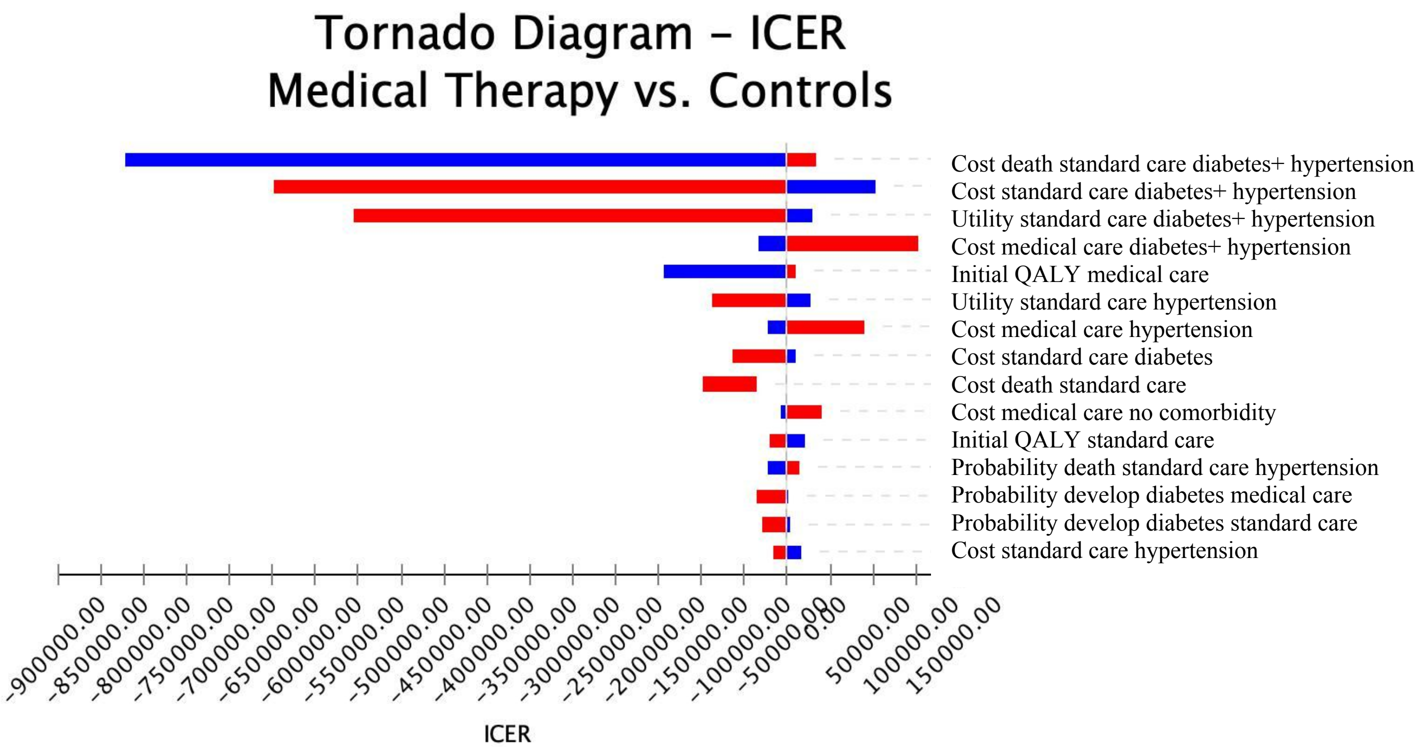
ICER

Lifetime Societal Perspective




Tornado Diagram – ICER
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Cost death standard care diabetes+ hypertension
Cost standard care diabetes+ hypertension
Utility standard care diabetes+ hypertension
Cost medical care diabetes+ hypertension
Initial QALY medical care
Utility standard care hypertension
Cost medical care hypertension
Cost standard care diabetes
Cost death standard care
Cost medical care no comorbidity
Initial QALY standard care
Probability death standard care hypertension
Probability develop diabetes medical care
Probability develop diabetes standard care
Cost standard care hypertension
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