# The combined use of surgery and radiotherapy to treat patients with epidural cord compression due to metastatic disease: a cost-utility analysis

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Neoplastic metastatic epidural spinal cord compression is a common complication of cancer that causes pain and progressive neurologic impairment. The previous standard treatment for this condition involved corticosteroids and radiotherapy (RT). Direct decompressive surgery with postoperative radiotherapy (S + RT) is now increasingly being chosen by clinicians to significantly improve patients' ability to walk and reduce their need for opioid analgesics and corticosteroids. A cost-utility analysis was conducted to compare S + RT with RT alone based on the landmark randomized clinical trial by Patchell et al. (2005). It was performed from the perspective of the Ontario Ministry of Health and Long-Term Care. Ontario-based costs were adjusted to 2010 US dollars. S + RT is more costly but also more effective than corticosteroids and RT alone, with an incremental cost-effectiveness ratio of US\$250307 per qualityadjusted life year (QALY) gained. First order probabilistic sensitivity analysis revealed that the probability of S + RT being cost-effective is 18.11%. The cost-effectiveness acceptability curve showed that there is a 91.11%

probability of S + RT being cost-effective over RT alone at a willingness-to-pay of US\$1683000 per QALY. In practice, the results of our study indicate that, by adopting the S + RT strategy, there would still be a chance of 18.11% of not paying extra at a willingness-to-pay of US\$50000 per QALY. Those results are sensitive to the costs of hospice palliative care. Our results suggest that adopting a standard S + RT approach for patients with MSCC is likely to increase health care costs but would result in improved outcomes.

**Keywords:** cost-utility analysis, palliative care, radiotherapy, spine cancer, surgery.

etastatic spinal cord compression (MSCC) is one of the most dreaded complications of metastatic cancer that, if untreated, causes progressive pain and irreversible loss of neurologic function.<sup>1</sup> In a population-based study in Ontario, the estimated prevalence of MSCC was 0.23% at the time of diagnosis, which corresponds to an estimated 1700 new cases of MSCC at the time of diagnosis across Canada and approximately 17 000 new cases of MSCC in the United States annually.<sup>2</sup>

Until the past decade, nonoperative treatment of MESCC with corticosteroids and radiotherapy (RT) has been considered to be the standard of care, particularly

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in light of the failure of decompressive laminectomy to provide added benefit to RT in terms of pain control and neurological outcomes.<sup>3,4</sup> However, over the past 20 years, there has been a significant evolution in decompressive and reconstructive spinal techniques, which have been increasingly applied to the management of spine oncology.<sup>5</sup> Indeed, the beneficial impact of surgical resection and spinal reconstruction was recently shown in a randomized, multi-institutional trial comparing direct decompressive surgical resection, followed by RT (S + RT strategy), with the RT-only strategy in a selected group of patients.<sup>6</sup> In addition to the longer survival time in the S + RT group when compared with the RT-only group, the S + RT approach allowed more patients with MSCC to remain ambulatory and continent while also reducing pain and analgesic needs.<sup>6</sup>

Despite the apparent benefits of the S + RT approach to treat MESCC, these patients have a limited life expectancy, and thus, the cost-effectiveness of such an approach could be questioned. Health care costs have been increasing worldwide over the past decades, and palliative care is likely to represent a growing share of those expenditures that will necessitate economic evaluations of palliative care interventions to inform resource allocation decisions.<sup>7</sup> In a prior cost-effectiveness analysis, the results favor the S + RT strategy in comparison with the RT-only strategy regarding the cost per additional day of ambulation and the cost per life gained.<sup>8</sup> However, those results should be interpreted cautiously because of the lack of rigorous compliance with the criteria for high quality of the cost-effectiveness studies and limitations regarding their outcomes, data source, and regression modeling.<sup>8-10</sup> Because of this background, the present study aims to contribute to the body of evidence in spine oncology by undertaking a cost-utility analysis that compares the S + RT strategy with the RT-only strategy in the context of a publicly funded health care system.

## Methods

This analysis adopts the perspective of the public payer, the Ontario Ministry of Health and Long Term Care. An

analytic decision model was established to compare 2 strategies: S + RT versus RT alone (Fig. 1). After the decision node to select a particular treatment modality, there are 2 initial symmetric chance nodes for each therapeutic strategy that reflect the probability of having complications after each initial treatment (Fig. 1). All underlying initial health states that could influence outcomes are included in each branch of the decision tree (Fig. 1).<sup>11</sup> Subsequent chance nodes correspond to the possible consequences of each strategy within the first 60 days after the initial treatment (Fig. 1). The subsequent node for each branch representing discharge disposition of patients at 60 days from the initial treatment is a 9-state Markov node. A Markov model or state transition model is the optimal representation of decision trees in which events recur over time.<sup>12</sup> As shown in the bubble diagram representation, each Markov node is constructed in a 3-way factorial manner that includes 8 mutually exclusive health states based on placement (home or institution), mobility (ambulatory or not), and urinary function (continent or incontinent) (Fig. 2). In addition to these health states, a patient in the cohort could finish each 30-day cycle alive or dead, thus expanding the total number of health states to 9 in each Markov node (Fig. 2). The half-cycle correction was applied to our Markov model to avoid overestimating life expectancy.<sup>13</sup>

#### Clinical Information

The probabilities and rates of clinical events for this model are based on the data from Patchell et al.<sup>6</sup> The probability of discharge home is based on data from a cohort of patients with MSCC who underwent surgical treatment at the Toronto Western Hospital (Toronto, Ontario) from January 2001 through July 2005 (Table 1). University Health Network Research Ethics Board approval was obtained for this chart review. In addition, a prior publication and expert opinions from medical oncologists and radiation oncologists from the Grand River Regional Cancer Center (Kitchener, Ontario) were used to perform a sensitivity analysis.<sup>14</sup>



Fig. 1. Analytic decision model for cost-utility analysis comparing surgical decompression followed by radiotherapy (S + RT) versus RT-only strategy in the palliative care of patients with metastatic spinal cord compression (MSCC). The decision node (square) indicates a choice facing the clinician with regard to the available strategy options for the base case. In this decision tree, a chance node (circle) represents an event with 2 possible consequences that are not under the clinician's control. The 4 branches designated by (1) are symmetric and are followed by a Markov node (open circle with an "M" inside). For each Markov model, there are 9 Markov states. The terminal node (diamond) indicates that patients reached their life span.



Fig. 2. Bubble diagram representation of the Markov model with 3 mutually exclusive health states such that, in any cycle, a patient of the cohort is in only 1 of the 9 Markov states defined by the patient's health state and disposition (alive in home care, alive in a hospice, and dead).

Table 1	-	Baseline	data	for	our	decision	tree
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Values	Data source	
Percentage		
71%	Toronto Western Hospital	
Utilities		
0.35	HODaR <sup>20</sup>	
0.388	HODaR <sup>20</sup>	
0.949	HUC <sup>19</sup>	
0.555	HODaR <sup>20</sup>	
0.7	HUC <sup>19</sup>	
0.9	HUC <sup>19</sup>	
0.72	HUC <sup>19</sup>	
2010 US dollars		
\$10 360.30	OCCI	
\$1845.70	OCCI	
\$3634.66	OHIP schedules of benefits	
\$593.78	OHIP schedules of benefits	
\$1097.03	OCCI	
\$91.21	CCAC report	
	Values   Percentage   71%   Utilities   0.35   0.388   0.949   0.555   0.7   0.9   0.72   2010 US dollars   \$10 360.30   \$1845.70   \$3634.66   \$593.78   \$1097.03   \$91.21	

Abbreviations: OCCI, Ontario Case Costing Initiative; OHIP, Ontario Health Insurance Plan; HUC, Harvard University Catalogue; HODaR, Health Outcomes Data Repository Data; CCAC, Community Care Access Center.

#### Cost Information

The costs of both treatment strategies are composed of physician fees and hospital expenses. The physician fees for direct decompressive surgery included surgeons' consultation fees, surgeons' procedure fees, anesthesiologists' procedure fees, and surgical assistants' assisting fees. The physician fees for inpatient RT included radiation oncologists' consultation fees, weekly assessment fees, and RT treatment planning fees. All physician fees were obtained from the Ontario Health Insurance Plan schedules of benefits.<sup>15</sup> All costs were adjusted and converted to 2010 US dollars.

Hospital expenses were obtained from the Ontario Case Costing Initiative (OCCI), which was established in 1992 as a joint initiative of the Ontario Hospital Association and the Ontario Ministry of Health and Long Term Care (OMHLTC) to develop a cost database.<sup>16</sup> The hospital costs for both study arms were adjusted for the hospitalization time based on the original trial data.<sup>6</sup> With use of data from the OCCI, the daily costs for hospital admission with diagnosis of metastatic spinal cord tumor were estimated after excluding the costs related to surgical procedures and RT. Those costs correspond to the variable costs per diem for all hospitalizations, whereas the fixed costs for each study arm were calculated using the hospital costs related to surgical procedures and RT based on the data from the OCCI (Table 1).

The cost of medications included the cost of corticosteroids and opioids. It was assumed that the utilization of all other medications would not be influenced by whether surgery was performed. The total cost included the cost of drugs and the pharmacy-dispensing fee. The outpatient medication expenses were counted as costs in our model because all patients who receive home care would also obtain Community Care Access Center drug cards for reimbursement of outpatient medication costs from the public health care insurer.

For patients who are discharged home, we assumed that all of them would receive palliative home care services, because this represents the optimal clinical care for patients with MSCC. The cost of home care was estimated on the basis of previously reported data from the OMHLTC (Table 1).<sup>17</sup> The cost per patient-day of inpatient palliative care was estimated on the basis of the average cost of inpatient palliative care facilities according to the OCCI data (Table 1).

#### Utilities

The 2 extremes (or anchor states) for all the outcomes are expressed in single values of 0-1, in which a value of 0 represents "death" and 1 represents "full health." <sup>18</sup> Utilities were taken from the Harvard University Catalogue from the United States and in the Health Outcomes Data Repository Data–Health Utility list from the United Kingdom (Table 1).<sup>19,20</sup>

Because there are no published data on the specific utilities for each branch in the study decision tree, those specific utilities were estimated by multiplying the utilities associated with each branch by the period that the condition or procedure affects the patient's quality of life.<sup>18</sup>

#### Outcomes

The primary outcome of this cost-utility analysis was the incremental cost (in 2010 US dollars) per quality-adjusted life year (QALY) gained.

#### Baseline and Sensitivity Analyses

The baseline analysis included the most likely values of the probabilities, costs, and outcomes from a variety of sources to build the decision tree (Fig. 1). In addition to the baseline analysis, a series of sensitivity analyses were performed, including 1-way and 2-way sensitivity analyses, threshold analysis, and probabilistic sensitivity analysis. The main purpose of these sensitivity analyses was to test the robustness of the model, and thus, a range of values for the costs was used in both treatment arms to assess the extent to which the results are robust to changes in costs of 50%-150% of mean costs for each item. Furthermore, sensitivity analysis tested the range of probabilities and utilities of 0-1. The threshold analysis examines whether there was a value of variable at which preferred strategy changes.

With use of Monte Carlo simulations, the probabilistic sensitivity analysis was performed using the range and mean values of probability for discharge disposition, the various costs, and survival. All simulations were performed using first-order sensitivity analysis with 100 000 trials. The results of the simulation were used to generate an incremental cost-effectiveness ratio (ICER) scatterplot and a cost-effectiveness acceptability curve (CEAC).

Data analyses were performed using TreeAge Pro 2009 Suite software (TreeAge Software).

#### Results

The mean overall hospitalization costs within the first 60 days and subsequent mean monthly costs for each branch in both trial arms are shown in Tables 2 and 3. Although the S + RT strategy cost US\$1 215 514.01 per QALY gained, the RT-only approach cost US\$1 017 372.80 per QALY gained. Of importance, the expected effectiveness for the S + RT strategy (0.57 QALYs) was higher than the effectiveness for the RT-only strategy (0.46 QALY) (Fig. 3A). The ICER of S + RT when compared with RT alone is US\$250 307.30. However, the cost-effectiveness ratios for both strategies were located in the northeastern quadrant, which reveals that no strategy was dominant (Fig. 3A).

The baseline analysis suggests that the RT-only approach is more cost-effective than the S + RT strategy at a willingness-to-pay of US\$50 000 (Fig. 3A). The 1-way sensitivity analysis showed that S + RT becomes cost-effective with a willingness-to-pay threshold of US\$50 000 when the initial cost of S + RT within the

Table 2. Data of the branches (initia	60 days) for ou	ur analytic decision	and the results of the thresh	old sensitivity analysis
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Analytic Decision Branches	Mean survival time (days)	Mean overall costs (US dollars)	Cost threshold (US dollars)	Mean effectiveness (QALYs)	Effectiveness threshold (QALYs)
S + RT strategy with postoperative complications					
S and postoperative death	3	14524.81	_	0.0004	-
S + RT (with post-RT complication) and post-treatment death	36.9	43886.20	-	0.0379	-
S + RT (with post-RT complication) and survived at least 60 days	60	58649.10	-	0.1066	-
S + RT (no post-RT complication) and post-treatment death	36.9	43832.76	-	0.038	-
S + RT (no post-RT complication) and survived at least 60 days	60	58595.66	-	0.1068	-
S + RT strategy without postoperative complications					
S + RT (with post-RT complication) and post-treatment death	36.9	43638.87	-	0.0381	-
S + RT (with post-RT complication) and survived at least 60 days	60	58497.45	-	0.1071	-
S + RT (no post-RT complication) and post-treatment death	36.9	43585.43	-	0.0382	-
S + RT (no post-RT complication) and survived at least 60 days	60	58444.01	-29439.44	0.1072	-
RT-only strategy with post-RT complications					
RT (no SS) and post-RT death	25.3	20999.97	-	0.0174	-
RT (no SS) and survived at least 60 days	60	56057.11	-	0.115	-
RT + SS (with post-operative complications) and postoperative death	8	27391.62	-	0.0007	-
RT + SS (with post-operative complications) and cancer-related death	19.5	42568.73	-	0.0032	-
RT + SS (with post-operative complications) and survived at least 60 days	60	78280.39	-	0.0436	-
RT + SS (without post-operative complications) and cancer-related death	32	49165.66	-	0.0172	-
RT + SS (without post-operative complications) and survived at least 60 days	60	69035.12	-	0.0381	-
RT-only strategy without post-RT complications					
RT (no SS) and post-RT death	25.3	20946.53	-	0.0175	-
RT (no SS) and survived at least 60 days	60	56003.67	-	0.1151	-
RT + SS (with post-operative complications) and postoperative death	8	27338.18	-	0.0007	-
RT + SS (with post-operative complications) and cancer-related death	19.5	42515.29	-	0.0033	-
RT + SS (with post-operative complications) and survived at least 60 days	60	78226.95	-	0.0437	-
RT + SS (without post-operative complications) and cancer-related death	32	49112.22	-	0.0172	-
RT + SS (without post-operative complications) and survived at least 60 days	60	68981.67	_	0.0381	-

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Table 3. Data of the sub-branches (every 30 days) for our Markov model and the results of the threshold sensitivity analysis

Analytic Decision Sub-Branches	Mean survival time (days)	Mean overall costs (US dollars)	Cost threshold (US dollars)	Mean effectiveness (QALYs)	Effectiveness threshold (QALYs)
S + RT strategy					
S + RT (ambulatory with urinary continence in home care)	30	2777.29	_	0.074	_
S + RT (non-ambulatory with urinary continence in home care)	30	2777.29	_	0.0426	_
S + RT (ambulatory with urinary incontinence in home care)	30	3369.79	_	0.0501	_
S + RT (non-ambulatory with urinary incontinence in home care)	30	3369.79	-	0.0289	-
S + RT (ambulatory with urinary continence in a hospice)	30	32939.95	-20607.58	0.0518	_
S + RT (non-ambulatory with urinary continence in a hospice)	30	32939.95	- 19624.30	0.0298	_
S + RT (ambulatory with urinary incontinence in a hospice)	30	33532.45	-26161.38	0.0351	_
S + RT (non-ambulatory with urinary incontinence in a hospice)	30	33532.45	-31065.73	0.0202	+0.07
RT strategy					
RT (ambulatory with urinary continence in home care)	30	2810.88	_	0.0287	_
RT (non-ambulatory with urinary continence in home care)	30	2810.88	_	0.0165	_
RT (ambulatory with urinary incontinence in home care)	30	3403.38	_	0.0195	_
RT (non-ambulatory with urinary incontinence in home care)	30	3403.38	_	0.0112	_
RT (ambulatory with urinary continence in a hospice)	30	32958.67	+37621.59	0.0201	_
RT (non-ambulatory with urinary continence in a hospice)	30	32958.67	+38631.54	0.0116	_
RT (ambulatory with urinary incontinence in a hospice)	30	33551.17	_	0.0136	_
RT (non-ambulatory with urinary incontinence in a hospice)	30	33551.17	+37781.10	0.0078	_
RT + SS (ambulatory with urinary continence in home care)	30	2810.88	_	0.0738	_
RT + SS (non-ambulatory with urinary continence in home care)	30	2810.88	_	0.0426	_
RT + SS (ambulatory with urinary incontinence in home care)	30	3403.38	-	0.0501	-
RT + SS (non-ambulatory with urinary incontinence in home care)	30	3403.38	-	0.0289	_
RT + SS (ambulatory with urinary continence in a hospice)	30	32958.67	-	0.0518	_
RT + SS (non-ambulatory with urinary continence in a hospice)	30	32958.67	-	0.0298	_
RT + SS (ambulatory with urinary incontinence in a hospice)	30	33551.17	-	0.0351	_
RT + SS (non-ambulatory with urinary incontinence in a hospice)	30	33551.17	_	0.0202	_





Fig. 3. Graphic representation of the baseline analysis and 2-way sensitivity analyses comparing the strategy that combines surgical decompression and postoperative radiotherapy (S + RT strategy) with the standard of care (RT-only strategy). (A) Based on the baseline analysis, both strategies are located in the northeastern quadrant that is the nondominant, not-dominated quadrant. The S + RT strategy represents a more costly but more effective approach in comparison with the RT-only strategy. Two-way sensitivity analyses focused on (B) monthly overall costs and (C) effectiveness in quality-adjusted life years (QALYs) of hospice for non-ambulatory individuals with urinary incontinence reinforce the robustness of the model. Red signs indicate The S + RT strategy (the comparator) is identified by the solid area, whereas the RT-only approach (the baseline term) is shown in stripes. Asterisks indicate the actual results of the sensitivity analysis.

**Table 4.** Results from probabilistic sensitivity analysis at a willingness-to-pay of US\$50 000 using the Monte Carlo simulation (all costs in 2010 US dollars)

Strategy	RT-only	S + RT strategy		
	strategy			
Costs				
Mean overall costs	\$554 323.01	\$583 809.21		
95% confidence interval for costs	\$59 407.05 \$2 211 295.22	\$61 813.80 \$2 235 090.76		
Effectiveness				
Mean effectiveness value (in QALYs)	0.46	0.57		
95% confidence interval for QALYs	0.06 3.41	0.13 2.24		
Cost-Utility Analysis				
Cost-effectiveness ratios	\$1 215 514.01 per QALY	\$1 017 372.80 per QALY		
Incremental cost-effectiveness ratio (ICER)		\$250 307.30 per QALY gained (\$685.77 per quality adjusted life day gained)		

first 60 days is less than US\$29439.44 (Table 2). Furthermore, the hospice costs appear to be an important factor in distinguishing the 2 strategies (Table 3). The results of this 1-way sensitivity analysis reinforce the robustness of our model, because there is only one threshold value for this parameter (Tables 2 and 3). Using 2-way sensitivity analysis, the monthly hospice costs for each health state favors the RT-only approach, compared with the S + RT strategy (Fig. 3B). The 2-way sensitivity analysis also indicates that there is an extremely small chance of the utility for nonambulatory patients with urinary incontinence who underwent S + RT approach to experience higher utility than patients in the same health state treated with RT alone (Fig. 3C).

The results obtained from probabilistic sensitivity analysis using the Monte Carlo simulation approach are summarized in Table 4. The scatterplot shows that the northeastern and southeastern quadrants represented the majority of simulation results (68.5%), and, thus, the S + RT strategy is more effective than the RT-only strategy (Fig. 4A). The ICER fell into the dominant quadrant (or southeastern quadrant) 18.11% of the times in which the S + RT strategy would be more effective and less costly in comparison with the RT-only strategy. In addition, the S + RT strategy was more cost-effective in 24.02% of the simulations at a willingness-to-pay of US\$50 000. Nonetheless, the ICER fell into the dominated quadrant (or northwestern quadrant) in 30.15% of the simulations in which the S + RT strategy would be less effective and more costly than the RT-only strategy. Indeed, the acceptability curve never reached the upper limit (100%) (Fig. 4B). The acceptability curve also showed that 55.86% of the ICERs were under the limit of US\$100000 per additional QALY (Fig. 4B). The proportion of ICERs



Fig. 4. Comparisons of the strategy that combines surgical decompression and postoperative radiotherapy (S + RT strategy) with the standard of care (RT-only strategy). (A) In the incremental cost-effectiveness scatterplot for the probabilistic sensitivity analysis, the S + RT strategy was compared with the RT-only strategy that was set up as the baseline approach. Each dot represents a result of a Monte Carlo simulation. The ellipse delineates a 95% confidence interval, and the larger dotted line represents a willingness-to-pay of US\$50000. (B) In the acceptability curve, the willingness-to-pay was set from virtually zero dollars per QALY gained (a symbolic way to represent no willingness-to-pay for an extra effect) to US\$2000.000. The vertical dotted lines indicate the willingness-to-pay of US\$100 000, US\$500 000, and US\$1 604 800 which correspond to a proportion of cost-effectiveness of 55.86%, 64.98%, and a maximum of 91.11%, respectively.

covered by the willingness-to-pay reached a maximum value of 91.11% at the level of US\$1 604 800 per 1 additional QALY (Fig. 4B).

#### Discussion

This study for the first time, to our knowledge, examines the cost-utility ratios for a combined S + RT strategy

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compared with RT alone for patients with MSCC. The results of this study indicate that the S + RT strategy appears to be more costly and more effective than the RT-only strategy. The estimated ICER of the S + RT strategy in comparison with the RT-only strategy is US\$250 307 per QALY in this patient population. These results indicate that increased expenditures are needed to impact patients' quality of life for such a morbid clinical condition. Moreover, by adopting the S + RT strategy, there would still be a reasonable chance (approximately 18.11%) of not paying extra for 1 additional QALY gained at the willingness-to-pay of US\$50 000 according to our Monte Carlo simulations.

Although the practice of medicine is often driven by ability, availability, and affability, physicians need to better understand their practice cost of providing patient care in the present environment of cost containment.<sup>21,22</sup> At present, there is mounting pressure on clinicians to provide cost-effective care, especially when equivalent alternatives are available. Because cancer care represents approximately 9% of all health care spending, there is increased impetus to cost out care services on the basis of objective evidence and an increasing demand for greater in-depth understanding of the elative clinical cost efficiency of various treatment options.<sup>23,24</sup> In the context of spinal cancer care, however, there is still a paucity of high-quality studies focused on health economics. Brauer et al. reported a critical appraisal on articles published from 1976 to 2001 that focused on cost-utility analysis in orthopedic surgery for spinal cancer.<sup>25</sup> In their analysis of the literature, Brauer et al. found only 14 articles that focused on spine surgery and 5 articles that specifically dealt with spine tumors. Moreover, only 5 (4.3%) of the 116 studies that focused on orthopedic surgery satisfied the 4 key criteria for high quality cost-utility analysis, as recommended by the United States Panel on Cost-Effectiveness in Health and Medicine.9,10,25

To our knowledge, this is the first study to focus on a cost-utility analysis comparing stand-alone radiotherapy with S + RT to treat patients with MSCC. Our results suggest that the S + RT strategy is more costly and more effective than that of RT alone. From the perspective of a public health care insurer, it would cost an extra US\$ 250,307 to gain 1 additional QALY by adopting the S + RT strategy, compared with the costs and effects of the RT-only strategy. On the basis of the Monte Carlo simulation method, the probabilistic sensitivity analysis confirmed the robustness of our model. This also supports the results with regard to the acceptability curve that suggest that, for instance, by adopting the S + RT strategy, there is a 65% chance that S + RTstrategy is cost-effective, compared with RT alone, at a willingness-to-pay of US\$500 000 per OALY.

In terms of broader policy implications, the results also highlight that palliative care interventions are likely to generate high ICERs. This is because patients have short remaining life spans over which to benefit from any treatment. Furthermore, patients at the end of life tend to have low QALYs because of very poor health status, and it is difficult for treatments to generate large QALY increases under these circumstances. This raises the question of whether economic evaluations, even cost-utility analyses that attempt to take account of quality of life not just length of life, ought to use some adjustment that would give additional weight to gains to health occurring at the end of life. This is a question that perhaps merits investigation in future research.

#### Study Limitations

One potential limitation of this economic evaluation refers to the use of data from a single randomized trial that enrolled a selected group of patients.<sup>4,6</sup> Although those features may limit the generalizability of its conclusions and implications, that randomized trial has strong internal validity.<sup>4,6</sup> The conclusions of our study apply only to a highly selected population nonetheless.

Ideally, cost data would be more accurately obtained if the economic evaluation were being conducted along with the randomized study. Despite the advantages of more specific costs for both treatment strategies, there are multiple parties working as health care payers in the United States, where the original trial was conducted.<sup>6</sup> In contrast to this scenario, Ontario has a universal health care system with OMHLTC as the single payer. Although there are notable differences between the American and Ontario health care systems, the homogeneity of cost in Ontario appears to minimize the potential bias that may arise when using costs from a mixed health market with private insurers.

The most generalizable perspective in any health economic evaluation is the societal perspective. Nevertheless, the economic analysis under the societal perspective requires a variety of cost information, including productivity losses and loss of leisure time by patients and caregivers, which were unfortunately unavailable for this specific patient population in Ontario. Therefore, for feasibility, the perspective of a public health care insurer was adopted in this study.

We assume that the utilities of all health states involved in the studies are independent of each other so that we could apply multiplication of multiple utilities to derive the combined utilities for each of the arms of the analytic decision model. In reality, these utilities may not be independent of each other. Patients in this

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population may have adjusted to multiple symptoms arising from their cancers that may influence their reported utility. Furthermore, new symptoms may not necessarily decrease the utilities of their health state in an independent way.

Furthermore, our economic analysis did not consider other important clinical features, including stage of the disease and histopathological diagnosis. Given the sample size of 101 cases, any subgroup analysis would not have sufficient statistical power to draw relevant conclusions.

### Conclusions

Given the increasing focus on the provision of costeffective medical care, our results suggest that a change of the palliative treatment protocols for patients with MSCC toward S+RT is more likely to increase the health care costs. However, the gain in terms of patients' quality of life is relatively significant and should be considered by health care policy makers. Our results further suggest that economic evaluations should perhaps account for remaining life left in palliative care interventions. This may reduce the potential bias in economic evaluations away from interventions aimed at the very ill (at the end of life, with no hope of cure), to recognize that, although gains to health or QALYs for this group may be difficult to achieve, they are not necessarily less valuable from the patient's perspective.

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