**Supplemental Digital Material**

**Appendix A: Search Strategy**

|  |  |  |  |
| --- | --- | --- | --- |
|  | Description | Search terms | Results |
|  | MESCC terms | neoplasm metastasis[MeSH] OR epidural neoplasms[MeSH] OR spinal cord neoplasms[MeSH] OR spinal cord compression[MeSH] OR metastatic epidural spinal cord compression[MeSH] | 167,880 |
|  | Operative terms | decompression, surgical[MeSH] OR decompression[MeSH] OR spinal decompression[MeSH] OR microdecompression OR microdiscectomy OR open decompression OR laminectomy OR spinal cord compression, therapy[MeSH] OR spinal fusion/instrumentation[MeSH] OR kyphoplasty OR vertebroplasty | 27,585 |
|  | Radiotherapy terms | radiotherapy [MeSH] OR radiation, ionizing[MeSH]  | 236,343 |
|  |  | #2 OR #3 | 263,606 |
|  |  | #4 AND #1 | 12,765 |
|  | Economic terms | cost analysis[MeSH] OR cost benefit analysis[MeSH] OR cost utility OR incremental cost-effectiveness ratio OR cost per unit of outcome OR spinal cord compression/economics[MeSH] OR radiotherapy/economics[MeSH] OR neurosurgical procedures/economics[MeSH] OR epidural neoplasms/economics[MeSH] | 181,713 |
|  |  | #5 AND #6 | 38 |

**Limits**: Humans, Abstract available

**Appendix B: Critical Appraisal**

**Table B1. Quality of Health Economic Studies (QHES) scores for included studies**

|  |  |  |  |
| --- | --- | --- | --- |
| **Questions** | **Possible points** | **Furlan (2012)1** | **Thomas (2006)2** |
| 1. Was the **study** **objective** presented in a clear, specific, and measurable manner? | 7 | 7 | 7 |
| 2. Were the **perspective** of the analysis (societal, third-party payer, etc.) and reasons for its selection stated? | 4 | 4 | 4 |
| 3. Were **variable estimates** used in the analysis **from the best available source** (i.e. randomized controlled trial - best, expert opinion - worst)? | 8 | 8 | 8 |
| 4. If estimates came from a **subgroup analysis**, were the groups prespecified at the beginning of the study? | 1 | 1 | 1 |
| 5. Was **uncertainty** handled by (1) statistical analysis to address random events, (2) sensitivity analysis to cover a range of assumptions? | 9 | 9 | 9 |
| 6. Was **incremental analysis** performed between alternatives for resources and costs? | 6 | 6 | 6 |
| 7. Was the methodology for **data abstraction** (including the value of health states and other benefits) stated? | 5 | 0 | 0 |
| 8. Did the **analytic horizon allow time** for all relevant and important outcomes? Were benefits and costs that went beyond 1 year discounted (3% to 5%) and justification given for the discount rate? | 7 | 0 | 7 |
| 9. Was the **measurement of costs** appropriate and the methodology for the estimation of quantities and unit costs clearly described? | 8 | 8 | 8 |
| 10. Were the primary **outcome measure(s**) for the economic evaluation clearly stated and did they include the major short-term, long-term and negative outcomes?  | 6 | 6 | 0 |
| 11. Were the health outcomes **measures/scales valid** and reliable? If previously tested valid and reliable measures were not available, was justification given for the measures/scales used? | 7 | 7 | 7 |
| 12. Were the **economic model** (including structure), study methods and analysis, and the components of the numerator and denominator displayed in a clear, transparent manner? | 8 | 8 | 8 |
| 13. Were the choice of economic model, main **assumptions, and limitations** of the study stated and justified? | 7 | 7 | 7 |
| 14. Did the author(s) explicitly discuss direction and magnitude of potential **biases?** | 6 | 6 | 6 |
| 15. Were the **conclusions/recommendations** of the study justified and based on the study results? | 8 | 8 | 8 |
| 16. Was there a statement disclosing the **source of funding** for the study? | 3 | 3 | 0 |
| **TOTAL POINTS** | **100** | **88** | **86** |

1 Furlan, J. C., K. K. Chan, et al. (2012). "The combined use of surgery and radiotherapy to treat patients with epidural cord compression due to metastatic disease: a cost-utility analysis." Neuro Oncol **14**(5): 631-640.

2 Thomas, K. C., B. Nosyk, et al. (2006). "Cost-effectiveness of surgery plus radiotherapy versus radiotherapy alone for metastatic epidural spinal cord compression." Int J Radiat Oncol Biol Phys **66**(4): 1212-1218.

**Table B2. Class of Evidence for source of clinical effectiveness data**

|  |  |
| --- | --- |
| **Methodological Principle** | **Patchell (2005)1** |
| **Study design** |  |
| Randomized controlled trial | ✓ |
| Prospective cohort study |  |
| Retrospective cohort study |  |
| Case-control |  |
| Case-series |  |
| Random sequence generation\* | ✓ |
| Statement of concealed allocation\* |  |
| Intention to treat\* | ✓ |
| Independent or blind assessment |  |
| Co-interventions applied equally | ✓ |
| Complete follow-up of >80% | ✓ |
| Adequate sample size | ✓ |
| Controlling for possible confounding† | ✓ |
| **Evidence class** | II |

\*Applies only to randomized controlled trials

†Groups must be comparable on baseline characteristics or evidence of control for confounding presented

*Blank cells indicate that the criterion was either not met or that it could not be determined*

**1**Patchell RA, Tibbs PA, Regine WF, et al. Direct decompressive surgical resection in the treatment of spinal cord compression caused by metastatic cancer: a randomised trial. *Lancet.* 2005;366(9486):643-648.

**Appendix C: Detailed Data Abstraction Tables**

**Table C1: Detailed study characteristics and results for included studies**

|  |  |  |
| --- | --- | --- |
| **Author (year)** | **Furlan (2012)1** | **Thomas (2006)2** |
| **Type of economic evaluation** | Cost-utility | Cost effectiveness |
| **Country** | Canada | Canada |
| **Funding** | Lawson Postdoctoral Fellowship at the University Health Network and the Krembil Chair in Neural Repair and Regeneration | NR |
| **QHES** | 88 | 86 |
| **Objective** | To determine cost utility of surgery and radiotherapy (Cost-effectiveness ratio/QALY). | To determine the incremental cost-effectiveness ratio (ICER), from a societal perspective, of radical surgical decompression plus radiotherapy compared with radiotherapy alone. |
| **Model type** | Decision treeMarkov ModelMonte Carlo simulation | Weibull ModelMonte Carlo simulation |
| **Analytic perspective** | Publicly-funded healthcare system (Ontario Ministry of Health and Long-Term Care) | Societal  |
| **Time horizon** | Lifetime, but less than 1 year | Lifetime |
| **Clinical effectiveness** |
| **Effectiveness data source(s) CoE of data source** | RCT3 CoE: II | RCT3CoE: II |
| **Number of patients** | N=101 | N=101 |
| **Diagnosis** | Diagnosis of cancer (not of CNS or spinal column origin) and MRI evidence of MESCC | Diagnosis of cancer (not of CNS or spinal column origin) and MRI evidence of MESCC |
| **Interventions being compared** | Surgery + Radiotherapy (S+RT)Radiotherapy alone (RT-only) | Surgery + Radiotherapy (S+RT)Radiotherapy alone (RT-only) |
| **Demographics****Number of patients****Median age****Sex (% female)** | **S+RT**n= 50Median age: 60 yearsSex (% female): 34%**RT-only**n= 51Median age: 60 yearsSex (% female): 27% | **S+RT**n= 50Median age: 60 yearsSex (% female): 34%**RT-only**n= 51Median age: 60 yearsSex (% female): 27% |
| **Outcome measures used in model****Validated in disease population?** | Placement (home or institution)AmbulationContinenceSurvivalValidation: NR | Ambulation (baseline measure of effectiveness)Survival time until death (sensitivity analysis)Validation: Ambulatory status meets effectiveness criteria (clinical credibility, responsiveness to change, and a lack of bias in the efficacy estimate) and is an accepted measure of effectiveness forMESCC within the published literature. |
| **Timeframe of effectiveness outcomes included** | NR | Outcomes measured every 4 weeks until death |
| **Country of study** | USA | USA |
| **Type of organization** | Multiple hospitals | Multiple hospitals |
| **Costs** |
| **Currency (type and year)** | US Dollars (2010) | Canadian Dollars (2003) |
| **Costs included in analysis (Source)** | * Physician fees, which included surgeon consultation fees and procedure fees, anesthesiologist consultation fees and procedure fees, surgical assistant fees, radiation oncologist consultation fees, weekly assessment fees, and RT treatment planning fees (Ontario Health Insurance Plan schedules of benefits)
* Hospital expenses (Ontario Case Costing Initiative (OCCI)
* Palliative home care, cost of medication (Source NR)
* Cost of home care (Ontario Ministry of Health and Long Term Care)
* Cost per patient-day of inpatient palliative care (Ontario Case Costing Initiative)

  | * Diagnostic tests, treatment planning, surgery, hospital ward stay meals, necessary intravenous therapy (St. Paul’s Hospital Cost Model)
* Surgeon and anesthetist fees (British Columbia Medical Association Guide to Fees)
* Workload unit values of diagnostic tests (2002 Management Information Systems Guidelines)
* Pharmaceutical costs (2003 British Columbia Pharmacare Low Cost Alternative Drug Booklet)
* Costs of institutionalization (Hollander et al.)
* National average hourly costs of in-home nursing care (Statistics Canada)
* Costs for RT treatment (a published study concerning the cost of RT at an Ontario regional cancer center (Earle et al.), from a perspective of the government as payer in a universal health care system.)
* Resource use (data were collected from a prospective cohort of patients with spinal metastases treated by radical decompression and stabilization at Vancouver Hospital and Health Sciences Center.)
* Estimation of resource use for diagnostic tests, treatment planning, the probabilities of complications arising from radiotherapy along with treatment of both major and minor complications, probabilities of institutionalization as well as resource utilization of in-home care post-treatment, and necessary medication after acute treatment for the initial 12 weeks of follow-up (median responses given by two expert panels of spine surgeons and radiation oncologists, n=13).
 |
| **Timeframe of costs included** | NR | The lifetime of each cohort |
| **Discount rate** | No discounting because of short time horizon | No discounting because of short time horizon |
| **Utilities** |
| **Source(s)**  | Harvard University CatalogHealth Outcomes Data Repository | NA |
| **Health state utilities** | * Metastatic malignant neoplasm of bone: 0.35
* Spinal cord compression: 0.388
* Surgery: 0.949
* Radiotherapy: 0.555
* Hospital bed stay: 0.7
* Restricted activity, but ambulatory: 0.9
* Paralysis: 0.72
 | NA |
| **Sensitivity Analysis** |
| **Sensitivity analysis performed?** | Yes | Yes |
| **Type of sensitivity analysis** | 1-way and 2-way sensitivity analyses, threshold analysis, and probabilistic sensitivity analysis using Monte Carlo simulations | 1-way and 2-way sensitivity analyses, probabilistic sensitivity analysis using Monte Carlo simulations |
| **Variables evaluated in sensitivity analysis** | * 1-way and 2-way: costs, probabilities, utilities
 | * 1-way: cost of surgery, number of days spent in ICU or general care ward, hospital costs
* 2-way: estimates of mean survival, ambulation
 |
| **Results** |
| **Baseline analysis** | * Both strategies are located in northeastern quadrant (non-dominant, non-dominated quadrant)
* RT only approach is more cost-effective than the S+RT approach at a willingness to pay threshold of US $50,000
 | Baseline ICER* Ambulation: CAD $60.06
* Survival: CAD $87.76 ($30,940.16 per life-year gained)
 |
| **Results of sensitivity analysis** | 1-way sensitivity analysis* S+RT becomes cost-effective with a willingness to pay threshold of US $50,000 when the initial cost of S+RT within the first 60 days is less than US $29,439.44

2-way sensitivity analysis* Monthly hospice costs for each health state favors RT-only approach
* Very small chance of the utility for non-ambulatory patients with urinary incontinence who underwent S+RT to experience higher utility than patients with same health state treated with RT only

Probabilistic sensitivity analysis* *Costs (within first 60 days) (mean overall costs (95% CI))*

**S+RT**: $583,809.21 (61,813.80 – 2,235,090.76)**RT-only:** $554,323.01 (59,407.05 – 2,21,295.22)* *Effectiveness (mean effectiveness value in QALYs (95% CI))*

**S+RT**: 0.57 (0.13 – 2.24)**RT-only:** 0.46 (0.06 – 3.41)* *Cost-Utility (cost-effectiveness ratio)*

**S+RT**: $1,215,514.01 per QALY gained**RT-only:** $1,017,372.80 per QALY gained* *Incremental Cost-Effectiveness Ratio (ICER)*

$250,307.30 per QALY gained ($685.77 per quality adjusted life day gained* The northeastern and southeastern quadrants represented 68.5% of simulation results (S+RT is more effective than RT-only)
* The ICER was in the dominant quadrant (southeastern) in 18.11% of the simulations (S+RT is more effective and less costly)
* The ICER was in the dominated quadrant (northwestern) in 30.15% of the simulations (S+RT would be less effective and more costly)
* S+RT was more cost-effective in 24.02% of simulations at a willingness to pay of US $50,000
* The proportion of ICERs 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
 | Weibull model* *Expected days of survival (mean)*

**S+RT**: 377.06**RT-only**: 221.11* *Expected days of ambulation (mean)*

**S+RT**: 312.47**RT-only:** 92.341-way sensitivity analysis (ICER after varying a single cost parameter)* Cost of hospitalization (±25%): $46.37-$73.75
* Intensive care unit LOS (95% CI): $53.27-$66.87
* General care ward LOS (95% CI): $53.28-$66.87
* Surgery (95% CI): $56.64-$63.48
* Common post-hospitalization costs: $198.02
* Common treatment costs: $61.07

2-way sensitivity analysis (ICER after varying both ambulation and survival)* RT-only: survival/ambulation (P25, P75): $91.93-(-$138.50)
* S+RT: survival/ambulation (P25, P75): $54.60-$73.62

Probabilistic sensitivity analysis (ICER based on simulated data)* Median (95% CI): $56.89 (-$72.47-$309.44)
* 18% of all simulations fell in dominant quadrant (S+RT resulted in cost savings compared to RT-only)
* 50% of all generated ICERs were lower than $57, and 95% were lower than $242 per additional day of ambulation (95% CI of -$72.74 to 309.44, meaning that this intervention ranged from a financial savings of $72.74 to a cost of $309.44 per additional day of ambulation).
* When S+RT was not cost saving, 95% of the time the cost of an additional day of ambulation was less than $242.
 |
| **Study conclusion** | S+RT appears to be more costly but more effective than RT-only. | S+RT is cost-effective both in terms of cost per additional day of ambulation, and cost per life-year gained. |

CAD: Canadian dollars; CNS: central nervous system; CoE: class of evidence; ICER: incremental cost-effectiveness ratio; LOS: length of stay; MESCC: metastatic epidural spinal cord compression; MRI: magnetic resonance imaging; NR: not reported; QALY: quality-adjusted life years; QHES: quality of health economic studies; RCT: randomized controlled trial; RT: radiotherapy; S+RT: surgery plus radiotherapy;

1 Furlan, J. C., K. K. Chan, et al. (2012). "The combined use of surgery and radiotherapy to treat patients with epidural cord compression due to metastatic disease: a cost-utility analysis." Neuro Oncol **14**(5): 631-640.

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