REVIEW

Rapid Magnetic Resonance Imaging for Diagnosing Cancer-related Low Back Pain

A Cost-effectiveness Analysis

William Hollingworth, PhD, Darryl T. Gray, MD, ScD, Brook I. Martin, BS, Sean D. Sullivan, PhD, Richard A. Deyo, MD, MPH, Jeffrey G. Jarvik, MD, MPH

OBJECTIVES: This study compared the relative efficiency of lumbar x-ray and rapid magnetic resonance (MR) imaging for diagnosing cancer-related low back pain (LBP) in primary care patients.

DESIGN: We developed a decision model with Markov state transitions to calculate the cost per case detected and cost per quality-adjusted life year (QALY) of rapid MR imaging. Model parameters were estimated from the medical literature. The costs of x-ray and rapid MR were calculated in an activity-based costing study.

SETTING AND PATIENTS: A hypothetical cohort of primary care patients with LBP referred for imaging to exclude cancer as the cause of their pain.

MAIN RESULTS: The rapid MR strategy was more expensive due to higher initial imaging costs and larger numbers of patients requiring conventional MR and biopsy. The overall sensitivity of the rapid MR strategy was higher than that of the x-ray strategy (62% vs 55%). However, because of low pre-imaging prevalence of cancer-related LBP, this generates <1 extra case per 1,000 patients imaged. Therefore, the incremental cost per case detected using rapid MR was high (\$213,927). The rapid MR strategy resulted in a small increase in quality-adjusted survival (0.00043 QALYs). The estimated incremental cost per QALY for the rapid MR strategy was \$296,176.

CONCLUSIONS: There is currently not enough evidence to support the routine use of rapid MR to detect cancer as a cause of LBP in primary care patients.

KEY WORDS: low back pain; decision analysis; cost-effectiveness analysis; magnetic resonance imaging; radiography.

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Low back pain (LBP) is a leading reason for patients to consult primary care physicians. On occasion primary or metastatic cancer may be the cause of LBP, but in most populations this is rare.¹ Early detection of cancer-related LBP is important in order to prevent the onset of debilitating symptoms. Back pain is the first symptom in over 95% of patients who go on to develop epidural cord compression.² Therapy may be most effective for patients who have cancer-related pain as the only symptom of the underlying disease.³⁻⁶ In contrast, when sensory and motor deficits exist before therapy is instigated, the prognosis is much worse. For example, mobility is restored in only 10% to 30% of cases in which the patient is already paretic.⁷

Cancer is, therefore, an important diagnostic consideration for physicians evaluating patients with LBP. Many physicians cite the need to rule out rare diseases like cancer as the primary rationale for requesting radiography among patients with LBP.⁸ In the United States, about 46% of patients with back pain are referred for lumbar radiography during the acute-care episode.^{9,10} However, radiographs are not highly sensitive or specific in the detection of spinal malignancies¹¹ and they identify many minor abnormalities that may be coincidental to the patient's symptoms.¹² Furthermore, radiography engenders costs to the healthcare system as well as potential risks to the patient from exposure to ionizing radiation. Consequently, it is unlikely that indiscriminate use of lumbar radiography is cost-effective.

Previous research¹ has identified several clinical and laboratory findings associated with cancer-related back pain. These include history of cancer, weight loss, advanced age, failure to improve with conservative therapy and elevated erythrocyte sedimentation rate (ESR). These "red flags" have been subsequently incorporated into a variety of clinical guidelines for the management of LBP.¹³

Received from the Departments of Radiology (JGJ, WH), Pediatrics (DTG), Pharmacy (SDS), Internal Medicine (BIM, RAD), Health Services (DTG, SDS, RAD, JGJ), Neurosurgery (JGJ), and the Center for Cost and Outcomes Research (all authors) University of Washington School of Medicine, Seattle, Wash.

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Address correspondence and requests for reprints to Dr. Hollingworth: Center for Cost and Outcomes Research, University of Washington, 146 N. Canal St., Suite 300, Seattle, WA 98103 (e-mail: willh@u.washington.edu).

Such diagnostic algorithms should promote cost-effective use of imaging in the detection of cancer-related back pain, but this is hard to prove. A randomized trial would have to recruit a huge number of patients in order to detect a difference in a rare endpoint such as cancer-related back pain. No such trial has been conducted.

An alternative approach is to use the best available evidence to model the cost-effectiveness of diagnostic strategies using decision analysis.¹⁴ Joines et al.¹⁵ recently compared the cost-effectiveness of various strategies for diagnosing cancer in primary care patients with LBP. They concluded that a strategy whereby all patients with any of the “red flags” listed above are imaged with x-ray and more advanced imaging would detect 70% of patients with cancer at an incremental cost per case detected of \$91,000. The objective of our paper was to extend the analysis of Joines et al. in 2 distinct ways.

First, we aimed to widen the analysis to examine the cost-effectiveness of a new imaging modality, rapid magnetic resonance (MR) imaging. Rapid MR is a quicker and less expensive version of conventional MR imaging.^{16–18} Rapid MR is limited to selected sequences with slightly reduced image resolution when compared to conventional MR, but provides more accurate anatomical information than x-ray. Due to the large numbers of lumbar x-rays performed, it is important to quickly determine the viability of rapid MR imaging as a potential replacement for x-ray.

Second, we aimed to extend previous analyses by going beyond the intermediate endpoint of cost per case detected. Studies that measure cost per case of cancer detected are difficult to interpret and compare because the outcome is not a unique metric. Clearly the benefit of detecting a case of cancer will depend on the site, stage, histology, and numerous other prognostic indicators. This is particularly relevant for patients with cancer-related back pain, because the majority will have metastatic disease and most therapy is palliative. Therefore our second objective was to extend the analysis to the more definitive endpoint of quality-adjusted survival.

METHODS

General Assumptions

We employed several assumptions in modeling the efficiency of rapid MR versus x-ray in the detection of cancer-related LBP (Fig. 1). We assumed that the clinical and laboratory work-up patients receive prior to imaging referral would only influence our results through its effect on cancer prevalence. In other words, a clinician who carefully selects high-risk patients for referral to x-ray or rapid MR would observe a high prevalence of cancer among imaged patients in comparison to a less discerning clinician.

We assumed that all patients with x-ray or rapid MR findings indicating malignancy would subsequently have a whole-spine conventional MR examination and, if malignancy was not ruled out, a CT-guided percutaneous biopsy for confirmation and tumor typing. In practice, not all patients are suitable for conventional MR¹⁹ and, as an alternative, whole-body bone scan may be useful if metastases to other sites are suspected. Furthermore, some patients with known primary tumors and poor prognosis may require no further investigations. However, studies have shown conventional MR to be more sensitive and specific than bone scan for vertebral metastases^{11,20,21} and conventional MR has been advocated as the initial study of choice in patients with suspected metastatic spinal disease.^{11,22} Even if a tumor is well visualized on x-ray, conventional MR may be required to plan therapy.^{19,23}

In our model, we assumed that the accuracy of imaging did not depend on the primary tumor type. Breast, pulmonary, and prostate cancer are the most frequent primary tumors found in patients with vertebral metastases.^{7,24} However, a wide variety of primary and secondary lesions may occur in the vertebrae and intradural space. Studies that have evaluated diagnostic accuracy for different tumor types have demonstrated some variation by primary malignancy site and by location within the spinal cord or vertebral bodies.¹⁶ Rather than

FIGURE 1. Decision tree: cost per case detected.

modeling each tumor type separately, we used the mean sensitivity and specificity of x-ray and rapid MR in detecting all tumor types combined. We assumed that the diagnostic accuracy of all tests were conditionally independent of each other and independent of the likely range of cancer prevalence observed in clinical practice.²⁵

Parameter Estimates

Prevalence of Cancer. In primary care populations, the prevalence of cancer-related back pain is likely to be low. In a study of 1,975 consecutive primary care patients with back pain, Deyo and Diehl¹ reported that the prevalence of cancer-related pain was 0.66%. In mixed primary and secondary care settings the prevalence may be slightly higher.¹⁸ With careful use of clinical signs and laboratory findings, physicians can select the patients with the highest risk of underlying cancer for referral to imaging. Joines et al.¹⁵ compared 11 selection strategies, finding that even with the most stringent referral strategy, the prevalence of cancer-related back pain in the subset of patients referred for imaging would only reach 3.4%. In our analysis, we assigned a base case value for cancer prevalence of 1% (Table 1).

X-ray. The sensitivity (0.70) and specificity (0.95) of x-ray can be estimated from the Deyo and Diehl cohort (Table 1). However, because of the small numbers of patients who had subsequently confirmed cancer as the cause of their back pain, the uncertainty surrounding the sensitivity estimate was large. A more recent study²⁶ that examined the accuracy of lumbar radiography for metastatic disease in selected patients with a high prevalence of cancer indicated similar sensitivity (0.73) and specificity (0.95).

Conventional Magnetic Resonance Imaging. Few studies have measured the sensitivity and specificity of conventional magnetic resonance imaging (MRI) for cancer-related back pain.^{27,28} This is largely due to the difficulty in defining a gold standard for comparison. Using an amalgamated gold standard of myelographic, surgical, autopsy, and compelling clinical findings, Li and Poon²⁸ estimated the sensitivity (0.93) and specificity (0.97) of conventional MR (Table 1).

Rapid MR. Rapid MR imaging is not yet widely used and no studies have assessed its diagnostic accuracy for detecting spinal tumors in relevant primary care populations. Kim et al. examined diagnostic performance in selected patients with a high clinical suspicion of malignant spinal cord compression.¹⁶ Their study compared a rapid MR T₁-weighted sagittal sequence against a conventional MRI protocol. The reported sensitivity and specificity of rapid MR interpreted by an experienced radiologist for vertebral, epidural, and cord-compressing lesions combined were 0.78 and 0.92

respectively. We used these estimates in our base case analysis, but they should be interpreted cautiously. Specificity is likely to be higher in primary care populations in which the preimaging suspicion of cancer is low.²⁵ Likewise, the addition of limited axial pulse sequences could increase sensitivity. Therefore, we included a wide range of possible values for the sensitivity and specificity of rapid MR (Table 1).

Biopsy. The sensitivity of percutaneous biopsy in detecting malignancy depends on several factors. These include the method of guidance (fluoroscopy or computerized tomography [CT]), the access route, the trocar diameter, the tumor type, and the skill of the radiologist and pathologist.^{29,30} The number of unsatisfactory or inadequate biopsy specimens is higher among patients with no clinical history of malignancy.²⁹ False-positive biopsy results are possible, but rarely reported. As in the decision analysis by Joines et al.,¹⁵ we assumed that biopsy had a sensitivity of 0.85 and a specificity of 1.00 in the base case analysis (Table 1).

Cost of Diagnosis. We included costs to health care purchasers in the model. To accurately estimate the true resource cost of rapid MR and plain films, we conducted an activity-based cost analysis.³¹ In brief, the cost analysis tracked consumables (e.g., film), radiologist, technologist, and patient imaging room time for a series of LBP patients randomized to rapid MR or x-ray. Staff time was multiplied by compensation rates, while equipment time was valued using the amortized capital cost plus consumable and overhead costs. We used the 2001 nationwide average Medicare fee schedule reimbursement to estimate the technical and professional cost of whole-spine conventional MR, percutaneous biopsy with CT guidance, and pathology.³² To acknowledge the uncertainty regarding the accuracy of reimbursement as a proxy for true cost and to account for any additional costs of identifying the site of the primary tumor, we included a wide range of costs in the sensitivity analysis (Table 1).

Disease States. We excluded the potential but unproven impact of rapid MR imaging on patients with other causes of LBP (e.g., herniated discs, spinal stenosis) and considered only patients with cancer-related back pain. We used a Markov model³³ to predict the clinical course of patients. The model tracks the progress of patients through prespecified disease states over time. Markov models condense the infinite number of disease states that a patient may experience to a tractable number. We simplified the analysis to 5 possible states: (a) cancer-related back pain successfully treated – “No pain”; (b) persistent cancer-related back pain – “Pain”; (c) patient ambulant with mild paraparesis – “Mild spinal cord compression (SCC)”; (d) Patient unable to walk, with severe paraparesis or paraplegia – “Severe SCC”; (e) “Dead.”

Table 1. Parameter Estimates for the Decision Analysis

Parameter	Base Case	Favors Rapid MR	Favors X-ray
Cost per case detected			
Prevalence of cancer-related LBP, %	1*	5	0.35 [†]
Sensitivity of x-ray	0.70 [‡]	0.63	0.77
Specificity of x-ray	0.95 [‡]	0.93	0.97
Sensitivity of rapid MR	0.78 [‡]	0.93	0.70
Specificity of rapid MR	0.92 [‡]	0.97	0.87
Sensitivity of conventional MR	0.93 [§]	0.99 [§]	0.81 [§]
Specificity of conventional MR	0.97 [§]	1.00 [§]	0.83 [§]
Sensitivity of biopsy	0.85*	0.90	0.80
Specificity of biopsy	1.00*	1.00*	1.00*
Cost of x-ray, \$	44	66 [¶]	22 [¶]
Cost of rapid MR, \$	126	63 [¶]	189 [¶]
Cost of whole-spine conventional MR, \$	1,705 [#]	853 [¶]	2,558 [¶]
Cost of biopsy with CT guidance, \$	786 [#]	393 [¶]	1,179 [¶]
Cost per QALY			
Survival, %**			
6-Month survival	71	88	47
12-Month survival	56	77	23
36-Month survival	28	50	7
State at 2 mo: false negatives, %			
Pain only	66 ^{††}	55	75
Mild SCC	15 ^{††}	16 ^{††}	8 ^{††}
Severe SCC	4 ^{††}	14 ^{††}	2 ^{††}
Dead	15 ^{**}	15 ^{**}	15 ^{**}
Quality of life (utility)			
No pain	0.86 ^{§§}	0.86	0.76
Pain/bone pain only	0.64	0.64	0.54
Mild SCC	0.47 ^{¶¶}	0.27	0.47
Severe SCC	0.39 ^{##}	0	0.39
Dead	0	0	0
Cost per month, \$			
Initial care (false negative)	2,980 ^{***}	4,470	1,490
No pain	673 ^{***}	336	1,010
Pain/bone pain only	1,572	786	1,684
Mild SCC	2,470	3,705	1,684
Severe SCC	3,369 ^{***}	5,054	1,684
Discount rate, %	3	0	7
Lifetime risk of x-ray-induced death	9.5/100,000	19/100,000 ^{†††}	0

* Based on Joines et al.¹⁵[†] Based on Deyo and Diehl¹[‡] Based on Kim et al.¹⁶[§] Based on Li and Poon.²⁸^{||} Based on Gray et al.³¹[¶] ± 50%.[#] Based on average nationwide Medicare reimbursement.³²^{**} Weibull function fitted on survival data reported by Tatsui et al.²⁴^{††} Derived from Kienstra et al.³⁶^{†††} Proportion of SCC patients with severe symptoms from Maranzano and Latini.⁴^{§§} Mobility scale (MOB) 5, physical activity scale (PAC) 4, social activity scale (SAC) 5, taking medication for health reasons.³⁴^{|||} MOB 5, PAC 4, SAC 3, pain, stiffness, or other discomfort.³⁴^{¶¶} MOB 4, PAC 3, SAC 2, pain, stiffness, or other discomfort.³⁴^{##} MOB 2, PAC 1, SAC 1, paralyzed.³⁴^{***} Derived from Fireman et al.³⁵^{†††} Derived from United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR) attained age model.³⁷

SCC, spinal cord compression.

We assumed that patients with evidence of myelopathy or cauda equina syndrome would be urgently referred for specialist assessment rather than routine radiography. Therefore, patients with cancer-related back pain detected by the x-ray or rapid MR imaging strategies would initially have localized or radicular pain with no symptoms of cord or

cauda equina compression. However, delays in referral and treatment are inherent in health care systems³⁸ and a small percentage of patients might develop cord compression before treatment was instigated. In the base case analysis, we estimated that 2% of patients with cancer-related back pain would have mild SCC before treatment (Table 1).

Some patients with cancer-related back pain will be overlooked (false-negative) by the imaging strategies. Many of these patients have tumors that already encroach on the epidural space.³⁹ Husband³⁸ reported a median delay of about 2 months between the onset of back pain and the onset of spinal cord compression, but tumor dissemination is highly variable. In the base case analysis, we assumed a 2-month delay in diagnosis. During those 2 months, a proportion of patients would die due to systemic disease. Of the remainder, some patients would have deteriorated to mild SCC or severe SCC before the underlying disease was recognized. We used evidence from a prospective study of primary and secondary care patients with a history of cancer and recently developed back pain to estimate the proportion of patients who typically present with symptoms of SCC³⁶ (Table 1).

Survival. We assumed that therapy instigated by the discovery of cancer-related LBP would be palliative and would not improve survival.⁷ Therefore, survival only affected our results through its influence on the time that patients spend in various disease states. Tatsui et al.²⁴ published the 3-year survival of 425 patients with metastatic spinal cancer detected by scintigraphy. Their cohort included a mix of patients with good (41% with primary cancer of the breast or prostate) and poor (42% with pulmonary or gastric cancer) prognoses. Mortality in our model was based on the survival observed in the cohort of Tatsui et al. (Table 1). Arguably this method overestimates the survival of patients with disease detected by plain films or rapid MR due to lead-time bias; scintigraphy can detect metastases several months earlier than radiographs. However, patients who have their symptoms monitored in primary care may represent survivors with slowly disseminating disease and consequently longer survival.⁴⁰ We examined these issues in the sensitivity analysis by varying survival.

Disease State Transition and Treatment Effectiveness. We modeled the proportion of patients in each of the 5 disease states every month up to 3 years. Monthly transition probabilities between states are presented in Table 2. The probability of developing SCC during any month was estimated from the 0.07 events per patient per year reported in the control arm of a large randomized trial in women with advanced breast cancer and bone lesions.⁴¹ We estimated that 48% of these incident cases of cord compression would be severe at presentation.⁴

Surgery, radiotherapy, and chemotherapy are all used to palliate symptoms. We based our estimates of treatment effectiveness on a systematic review⁴² of radiotherapy for the palliation of painful bone metastases and a large prospective study of clinical outcomes for patients with spinal cord compression.⁴³ We estimated that substantial pain relief would be achieved in 42% of patients⁴² within 1 month of the start of radiotherapy (Table 2). Thereafter, the proportion of patients experiencing pain relief

diminishes; by 1 year, 70% of survivors have substantial pain relief. Bone pain at the initial or a new location was estimated to recur in 75% of patients during the course of a year.⁴¹

The success of treatment for SCC is dependent on the pretreatment ambulatory status of the patient. Only a small proportion of nonambulatory patients (severe SCC) recover normal (18%) or assisted (11%) gait.⁴³ If cord compression is treated while the patient is still ambulatory, most patients (75%) regain or maintain normal gait, while only a small proportion (14%) progress to a nonambulatory state⁴³ (Table 2).

Quality of Life. There is growing interest in assessing quality of life and utility scores for patients with advanced cancer.⁴⁶ However, no studies have measured utility scores for patients with cancer-related LBP or cord compression. Therefore, we subjectively assigned the 5 Markov disease states described above to the most relevant level of mobility, physical activity, social activity, and symptoms defined by the Quality of Well-Being (QWB) scale.³⁴ The QWB uses category scaling to assign preference weights to disease states on a scale ranging from 0 (death) to 1 (full health). These preference weights are combined with patient survival to estimate quality-adjusted life years (QALYs). The estimated preference weight for each disease state is described in Table 1.

Somatic Effects of Radiation. The harmful effects of ionizing radiation may influence the choice between rapid MR and x-ray. Technological advances have decreased radiation exposure from x-rays over the years. Typically the effective radiation dose associated with a lumbar x-ray is minimal (1.8 milliSieverts (mSv)), less than the average annual per caput dose from natural background radiation (2.4 mSv).⁴⁷

Table 2. Monthly Transition Probabilities*

Prior Disease State	End Disease State				
	No Pain	Pain	Mild SCC	Severe SCC	Dead
No pain	#	0.1091	0.0031	0.0029	†
Pain	0.4250	#	0.0031	0.0029	†
Mild SCC	0.0460	0.0622	#	0.0124	†
Severe SCC	0.0068	0.0092	0.0095	#	†
Dead	0	0	0	0	1

* All transition probabilities converted into monthly probabilities⁴⁴ with half cycle correction, and varied by $\pm 10\%$ in the sensitivity analysis.

† Monthly mortality modeled using a Weibull function.⁴⁵ The probability of death declines in the base case analysis from 0.09 in month 1 to 0.02 in month 36.

‡ It is estimated that 42.5% of patients experience substantial pain relief in the first month of therapy.⁴² Thereafter the probability of moving from pain to no pain diminishes to 0.057 per month.

Represents the residual probability needed in order to make the probability in each row sum to 1.
SCC, spinal cord compression.

However, there may be no dose threshold below which radiation exposure is risk free. Quantification of risk is largely conjectural and depends upon the organs exposed to radiation, patient gender and age, and assumptions about the linearity of the relationship between low-dose exposure and risk. Based on the United Nations³⁷ estimate of risk of exposure-induced death in the United States of 1% per 0.1 Sievert, and assuming a linear dose-response relationship with no threshold, the lifetime mortality risk of solid cancer and leukemia attributable to a lumbar x-ray is 19 deaths per 100,000 people imaged. Because this estimate relates to whole-body exposure, we used it as the upper bound for radiation-induced risk. We assumed that radiation-induced tumors are associated with a 10-year loss of life expectancy,⁴⁷ on average 20 years after exposure. This equated to 4.1 discounted QALYs per radiation-induced cancer avoided (Table 1).

Cost of Treatment. The cost of care was derived from published provider perspective cost estimates for remote-stage breast, lung, and prostate cancer patients³⁵ (Table 1). These data attribute costs to the initial, continuing, and terminal stages of care. We assumed that the resources used during 6 months of terminal stage of care (\$20,214) would approximate the cost of caring for patients with severe SCC. The cost of continuing care for 6 months (\$4,035) was used to estimate costs for patients in remission from bone pain. The monthly cost of patients with mild SCC and bone pain was assumed to fall between these extremes (Table 1). All costs are in year 2001 dollars. Costs and effects beyond 1 year were discounted at 3%.⁴⁸ All analyses were conducted using DATA 3.5 for Healthcare (Treeage Software Inc., Williamstown, Mass).

RESULTS

The initial estimate of cost per case detected is presented in Table 3. The rapid MR strategy was more expensive than x-ray partly due to lower specificity and,

consequently, larger numbers of patients requiring conventional MR and biopsy to confirm or rule out disease. For every 1,000 patients imaged with rapid MR, 87 were referred for conventional MRI, of whom 10 also required a biopsy. Approximately 20% of biopsies following rapid MR were conducted on patients who did not have cancer-related back pain. The average cost per patient of the rapid MR strategy was \$282 compared to \$147 for the x-ray strategy. The overall sensitivity of the rapid MR strategy was 62% compared to 55% for the x-ray strategy. However, because of the low preimaging prevalence of cancer-related LBP, MRI detects <1 extra case of cancer per 1,000 patients screened. The incremental cost per case detected is more relevant to policy makers than is the average cost per case detected, because the incremental measure directly compares the extra costs and benefits of replacing x-ray with rapid MR. In our model, the incremental cost per case detected of rapid MR strategy was relatively high at \$213,927.

Table 4 details the prevalence of the 5 Markov disease states at selected time intervals for those patients who have cancer-related LBP. At 6 months, the model estimated that only 3% of patients with cancer-related LBP detected by the rapid MR or x-ray screening strategies (true positives) developed cord compression, while 31% obtained substantial relief from bone pain. In comparison, patients missed by the primary care screening process (false negatives) had higher rates of cord compression (12%) and pain (45%). The high mortality rate and the frequent recurrence of bone pain ensured that the benefit of early detection of cancer-related LBP diminished quickly. By 24 months, the prevalence of pain and dysfunction in each group was similar. By our prior assumption, the median survival was the same in both groups (14 months) but quality-adjusted survival varied (Table 4). True-positive patients had accumulated a mean of 1.05 QALYs by 3 years compared to 0.98 QALYs in false-negative patients. Most of this difference accrued in the first year of treatment. The net cost of treating true-positive patients was lower because of

Table 3. Base Case Results*

Strategy	Number of Conventional MRIs per 1,000	Number of Biopsies per 1,000	Cost per Patient, \$	Incremental Cost, \$	Effectiveness	Incremental Effectiveness	Average C/E Ratio, \$	Incremental C/E Ratio, \$
Cost per case detected								
X-ray	57	8 (1) [†]	147		0.00553		26,496	
Rapid MRI	87	10 (2) [†]	282	135	0.00617	0.00063	45,720	213,927
Cost per QALY								
X-ray	57	8 (1) [†]	406		0.00982 QALY		41,390	
Rapid MRI	87	10 (2) [†]	535	128	0.01025 QALY	0.00043 QALY	52,161	296,176

* All costs rounded to the nearest dollar, all effects rounded to five decimal places. Due to rounding, the reported cost-effectiveness (C/E) ratios do not exactly equal the ratio of reported costs and effects.

[†] Number in parentheses represents the number of biopsies conducted on patients who do not have cancer-related LBP. MRI, magnetic resonance imaging; QALY, quality-adjusted life year; LBP, low back pain.

Table 4. Predicted Disease State, Cost, and QALYs up to 36 Months Postimaging

Month	Disease State													
	True Positive							False Negative						
	No Pain, %	Pain, %	Mild SCC, %	Severe SCC, %	Dead, %	Net Cost, \$	Net QALY	No Pain, %	Pain, %	Mild SCC, %	Severe SCC, %	Dead, %	Net Cost, \$	Net QALY
2	37	46	2	1	15	2,888	0.13	0	66	15	4	15	6,856	0.12
6	31	37	2	1	29	6,526	0.31	13	45	8	4	29	11,857	0.27
12	24	29	1	2	44	11,028	0.53	18	31	4	4	44	17,330	0.47
24	17	19	1	2	61	17,819	0.85	15	19	1	3	61	24,804	0.78
36	12	14	1	2	72	22,501	1.05	11	13	1	3	72	29,711	0.98

SCC, spinal cord compression; QALY, quality-adjusted life year.

the lower morbidity levels associated with the early diagnosis. Over the course of 3 years, the estimated mean cost of treatment was \$22,501 for true-positive patients compared to \$29,711 for false-negative patients.

In the cost-per-QALY model (Table 3), the incremental costs of treatment were overshadowed by the incremental costs of diagnosis. This was because <1 in 1,000 patients had their palliative treatment altered as a result of being in the rapid MR rather than the x-ray strategy. Therefore, the incremental cost difference in the cost-per-QALY model (\$128) was only fractionally less than the difference in the cost-per-case-detected model (\$135). Furthermore, when effectiveness is estimated in terms of QALYs rather than cases detected, the estimated incremental effectiveness of the rapid MR strategy was slightly lower (0.00043 QALYs). Only 10% of the incremental effectiveness of rapid MR was due to reduced morbidity from cancer-related back pain. The remaining 90% arose from the avoidance of the radiation-induced tumors inherent in the x-ray strategy. Overall the estimated incremental cost per quality-adjusted life year was \$296,176.

A series of 1-way sensitivity analyses revealed that the incremental cost-effectiveness ratio (ICER) was most dependent upon assumptions about the probability of x-ray-induced cancers (Fig. 2). If the low dose exposure of a lumbar x-ray carried no risk, then the ICER for rapid MR would be greater than \$2.8 million. However, even if the risk of x-ray-induced cancer increased to 19 in 100,000, the incremental cost per QALY would still be high (\$153,421). The discount rate was also influential because the potential risk of induced cancers is not manifest until 20 years after the initial imaging. Therefore, if health in future years is given weight equal to that given current health (i.e., 0% discount rate), then the incremental cost-effectiveness of rapid MR improved to \$145,090 per QALY.

The baseline prevalence of cancer and the cost and diagnostic accuracy of rapid MR were also important determinants. In particular, as the specificity of rapid MR approached that achieved by conventional MRI (0.97), the incremental cost per QALY fell to \$98,681. If, as would be the case in carefully selected patients, the prevalence of cancer approaches 5% and the sensitivity and specificity of rapid MR were simultaneously high then, at \$8,816 per

QALY, rapid MR would be a more efficient method of screening for cancer-related back pain than x-ray. Other diagnostic parameters relating to subsequent conventional MRI and percutaneous biopsy investigations had much less impact on our results (Fig. 2). Estimates of the survival, quality of life, and treatment costs for patients with cancer-related LBP did not greatly influence our findings despite the wide ranges tested in the sensitivity analyses. The incremental cost-effectiveness was \$277,031 even under the assumption that 30% of false-negative patients would develop spinal cord compression by 2 months after the initial missed diagnosis.

DISCUSSION

Our results demonstrate that there is insufficient evidence to support the routine use of rapid MR as a cost-effective screening tool for cancer-related LBP in primary care patients. Furthermore, the results from our cost-per-QALY analysis indicate that studies that only measure cost per case detected are likely to overvalue the importance of imaging because of the short life expectancy and high morbidity of patients with cancer-related LBP. These conclusions are subject to a number of caveats and may be modified as new evidence becomes available.

Primary care physicians may prefer rapid MR imaging for reasons that are not captured in this cost-effectiveness analysis. Rapid MR is likely to be more sensitive than x-ray in detecting other causes of low back pain such as herniated disc, infection, and inflammatory disorders. In previous work, we have demonstrated that rapid MR increased physicians' diagnostic confidence and provided greater reassurance about the absence of serious disease than did plain films.⁴⁹ However, the same study suggested that this greater diagnostic certainty did not result in improved patient outcomes. Furthermore, the extra diagnostic confidence provided by rapid MR should be weighed against the possibility that more advanced imaging will lead to over-diagnosis and unnecessary surgery for low back pain.⁵⁰ This is an important consideration, given the small mortality risk associated with lumbar surgery.

The potentially harmful somatic effects of low-dose radiation are difficult to quantify. The risks, if they exist at

all, are too small for epidemiological studies to detect with any precision. Despite this, we felt it was important to include an estimate of these potential risks in our analysis, because they are of concern to physicians and patients alike. We did not model any hereditary effects of radiation that might be relevant to younger patients with LBP. We believe that any such risk would fall within the range of risks assessed in our sensitivity analysis. Because rapid MR resulted in only a small benefit to the few patients with cancer-related back pain, the effect of radiation became relatively influential in the model. However, rapid MR was not cost-effective even with a high estimated risk attributed to low-dose radiation. It is important to note that the risks of somatic and mutagenic effects from radiation are inversely related to age at exposure.⁵¹ Therefore, physicians might consider the use of rapid MR to be more justified for younger patients.

Primary care physicians have some control over the prevalence of cancer-related back pain among patients referred for x-ray or rapid MR. Physicians should make judicious use of clinical and laboratory findings such as history of cancer, unexplained weight loss, failure of conservative therapy, and elevated ESR before referral for imaging, thereby maximizing positive predictive values and

the efficiency of the diagnostic process. While careful selection of patients suitable for imaging is essential, our findings suggest that these selective strategies, in isolation, are unlikely to render rapid MR a cost-effective alternative to x-ray in typical primary care settings. Despite this, in specific subgroups with very high prevalence, for example breast cancer patients with nonspecific back pain and known metastases to bone, rapid MR might be more valuable. In our model, the incremental cost per QALY of rapid MR was less than \$100,000 when the prevalence of cancer-related back pain was greater than 13%.

Further research is needed to clarify the sensitivity and specificity of rapid MR imaging in primary care populations. The one study that measured the sensitivity and specificity of rapid MR for metastatic spinal disease was based on patients with a high clinical suspicion of malignant disease.¹⁶ While these data are valuable, specificity will probably be higher when rapid MR is used in primary care populations.²⁵ If higher specificity can be achieved, rapid MR might become a viable alternative to x-ray for primary care patients. If the specificity of rapid MR reached 0.97 then the extra cost of the rapid MR strategy would decrease to \$43 per patient and the incremental cost per QALY would fall below \$100,000. A further increase in

FIGURE 2. Sensitivity analysis.

the specificity of rapid MR to 0.985 would reduce the cost per QALY ratio to \$39,432. Specificity will be driven, in large part, by the advancing technical capabilities of rapid MR. In addition, radiologists can increase specificity by careful interpretation and reporting of results to primary care physicians.⁵² Technical advances leading to improvements in the sensitivity of rapid MR will not have as large an impact on efficiency as will improvements in specificity. In our model, even if rapid MR is assumed to be perfectly sensitive, the incremental cost-effectiveness ratio remains in excess of \$200,000. Further reductions in the cost of rapid MR are constrained by the high capital cost of MR equipment. Therefore, improvements in the specificity of rapid MR provide the most likely means for making rapid MR more cost-effective.

Prompt and effective treatment of vertebral metastases is important and appears to benefit patients.⁴³ However, due to the low prevalence and high mortality rate associated with cancer-related back pain in primary care, none of our estimates of treatment costs and effects had a large impact on our results (Fig. 2). Over the 3-year period modeled, 70% of patients with cancer-related back pain died and, on average, each accumulated only 1 QALY. Because rapid MR only identified 1 extra case of cancer-related LBP per 1,000 patients screened, changes in assumptions relating to treatment effectiveness were relatively unimportant. Furthermore, in the base case analysis, the potential detrimental effects of x-ray radiation were as important as the beneficial effects of rapid MR screening. This emphasizes the need for physicians to carefully consider the risks and benefits to patients before ordering diagnostic tests.

Our results did not depend significantly upon the cost or the diagnostic parameters of subsequent conventional MRI and biopsy tests (Fig. 2). Therefore, we believe that our results would be essentially the same even if, in routine practice, some patients do not require biopsy, CT, or nuclear studies to further clarify the diagnosis. Similarly, diagnostic accuracy and treatment efficacy will vary to some extent by tumor type and location. We believe the mean estimates presented here are most relevant for primary care physicians.

In many situations, a randomized controlled trial will provide the best evidence about the cost-effectiveness of a new technology. In certain circumstances, such as cancer-related back pain in primary care patients, where the primary outcome occurs infrequently, even a large trial may not be useful unless it is sufficiently powered. In this situation, a decision analysis can aid the decision-making process by collating the evidence, identifying important variables requiring further research, and making tentative policy recommendations pending the results of a large trial. We have used a combined approach to evaluate rapid MR. We conducted a randomized trial to assess the impact of rapid MR on the treatment and patient outcomes of common causes of LBP⁵³ in combination with this decision analysis to assess the impact on cancer-related LBP.

Our findings suggest that the benefits of using rapid MR instead of x-ray for detecting cancer-related back pain do not currently justify the extra costs, even when the potentially harmful effects of radiation are accounted for. Further research measuring the specificity of various rapid MR protocols in primary care populations should be prioritized. If specificity for detecting cancer-related LBP is proven to be high, then rapid MR coupled with careful imaging selection criteria might be a cost-effective alternative to plain films.

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