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Economic Evaluation of Reamed versus Unreamed Intramedullary Nailing in Patients with Closed and Open Tibial Fractures: Results from the Study to Prospectively Evaluate Reamed Intramedullary Nails in Patients with Tibial Fractures (SPRINT)

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A B S T R A C T

Introduction: Recently, results from the large, randomized study to prospectively evaluate reamed intramedullary nails in patients with tibial fractures (SPRINT) trial suggested a benefit for reamed intramedullary nail insertion in patients with closed tibial shaft fractures largely based on cost-neutral autodynamizations and a potential advantage for unreamed intramedullary nailing in open fractures. We performed an economic evaluation to compare resource use and effectiveness of reamed and unreamed intramedullary nailing using a cost-utility analysis. **Methods:** We calculated quality-adjusted life years (QALYs) for each patient from a self-administered health utility index 3 questionnaire for the first 12 months following the intramedullary nailing. A convenience sample of 235 SPRINT patients provided data on costs associated with health care resource utilization. All costs are reported in Canadian dollars for the 2008 financial year. **Results:** We found incremental effects of −0.017 (95% confidence interval [CI] −0.021–0.058) and −0.002 (95% CI −0.060–0.062) QALYs for patients treated with reamed compared with unreamed intramedullary nails in closed and open fractures, respectively. The incremental costs for reamed compared with unreamed intramedullary nailing were $51 Canadian dollars (95% CI −$2298–$2400) in closed tibial fractures and $2546 Canadian dollars (95%CI −$1773–$6864) in open tibial fractures. Unreamed nailing dominated reamed nailing for both closed and open tibial fractures; however, the cost and the utility results had high variability. **Conclusion:** Our economic analysis from a governmental perspective suggests small differences in both cost and effectiveness with large uncertainty between reamed and unreamed intramedullary nailing.

Keywords: cost-utility analysis, economic analysis, reamed intramedullary nails, tibia fractures, unreamed intramedullary nails.

Introduction

Tibial fractures are the most common long bone fractures and constitute a major component of emergency operating room procedures in trauma centers. The National Center for Health Statistics reports an annual incidence of 492,000 fractures of the tibia and fibula per year in the United States [1]. Patients with tibial fractures remain in the hospital for a total of 569,000 hospital days and incur 825,000 physician visits per year, which imposes considerable cost to the health care system [1]. Although evidence favors the use of intramedullary nails to repair fractures of the tibia [2,3], the choice between two alternative operative approaches, reamed or unreamed intramedullary nailing, remains controversial [3–5].

A systematic search of the literature (MEDLINE, Cochrane Library, and HEED from March 1988 to November 2009) revealed only two economic evaluations of reamed versus unreamed intramedullary nailing [6,7]. The first analysis was a single center, observational study in 51 patients with open tibia fractures [6]. Conducted from the hospital perspective, it found a trend toward lower costs due to fewer secondary procedures with reamed intramedullary nailing while healing rates remained similar for the two approaches [6]. The second was a model-based analysis using data from small randomized clinical trials with methodological limitations; it explored the cost associated with the treatment of low-energy tibial shaft fractures and found that there were higher costs associated with treatment with unreamed intramedullary when compared to reamed intramedullary nailing [7].

Recently, results from the large, randomized study to prospectively evaluate reamed intramedullary nails in patients with tibial fractures (SPRINT) trial suggested a benefit for reamed intramedullary nail insertion in patients with closed tibial shaft fractures, largely due to fewer dynamizations, and a potential advantage for

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unreamed intramedullary nailing in open tibia fractures [8]. The objective of this economic evaluation was to compare resource use and effectiveness of reamed and unreamed intramedullary nailing in a cost-utility analysis. To meet this objective, we used utilities, resource utilization from the index hospital stay, and data on re-operations collected prospectively as part of the SPRINT trial. In addition, we collected data on other resources consumed during the 12 months' follow-up retrospectively from a sample of 235 SPRINT patients.

Methods

The SPRINT trial

This economic analysis was part of the SPRINT trial with collection of utilities and resource utilization data alongside the trial. The design, baseline findings, and primary results of SPRINT have been reported in detail [8,9]. Briefly, SPRINT (NCT00038129 at www.Clinicaltrial.gov) was a multicenter, blinded randomized controlled trial enrolling 1319 patients at 29 clinical sites in Canada, the United States, and The Netherlands from July 2000 to September 2005. Patients were followed for 12 months post-surgery. Eligible patients were skeletally mature and sustained a closed or open shaft fracture (Tscherne Type 0-3, Gustilo Type I-IIIB) [10–12] of the tibia amenable to operative fixation with an intramedullary nail. Patients with pathologic fractures or likely problems with maintaining follow-up were excluded. Since the main study results suggested different treatment effects for closed versus open tibial fractures (interaction $P = 0.01$), we included a stratified analysis by closed versus open fractures in this economic evaluation.

Perspective

This economic evaluation was performed from the viewpoint of the Ontario Provincial Ministry of Health. All costs are expressed in Canadian dollars for the 2008 financial year. While a comprehensive societal perspective is desirable, it was not feasible to reliably collect these data retrospectively (including out-of-pocket expenses and lost productivity for patients, family members, and other caregivers).

Utilities (quality-adjusted life years)

Utility is the preference or worth assigned to a particular health status, on an interval scale ranging from 0 (death) to 1 (perfect health) [13,14]. In order to estimate utility scores in SPRINT, participants were asked to complete the self-administered health utility index 3 (HUI3) questionnaire at 2 weeks after hospital discharge, and at 3 months, 6 months, and 12 months post-surgery [9]. We calculated quality-adjusted life years (QALYs) for each patient through conversion of corresponding HUI3 scores for the first 12 months following the intramedullary nailing.

Resource utilization and cost valuation

Data on resource utilization were collected from a convenience sample of 235 patients from six study centers with a high recruitment rate (three Canadian sites: St. Michael's Hospital, Toronto, ON; Hamilton Health Sciences – General Site, Hamilton, ON; and London Health Sciences, London, ON; and at three US sites: Boston Medical Center, Boston, MA; Wake Medical Center, Winston-Salem, NC; and The University of Oklahoma Health Science Center, Oklahoma City, OK). Data on the length of the index procedure, the length of the index hospital stay, complications during index hospitalization, and re-operations during the 12-month follow-up period were collected prospectively alongside the trial. Data on resources consumed during the 12-month follow-up period were collected retrospectively through a medical record review.

In an attempt to accurately reflect relative cost differences between groups, we focused on resource items that were potentially consumed to a different degree by the two groups as a consequence of the two different operative techniques. In other words, we did not attempt to comprehensively estimate absolute costs of intramedullary nailing procedures. Therefore, we considered only re-operations that were classified by the outcome adjudication committee as study events. Surgical procedures classified by the adjudication committee as nonevents were re-operations determined by the circumstances of the injury rather than by the different operative techniques (e.g., planned re-operations, re-operations in patients with a fracture gap greater than 1 cm). Along the same lines, we did not consider any after hours or weekend surcharges and considered material costs of intramedullary nails and locking screws only for re-operations such as implant exchanges.

Based on the collected data on resource utilization from all 6 centers we evaluated the costs as follows: Prices of operation and consultation fees were determined from the Physician's Schedule of Benefits (February, 2008) [15]. We used estimates from the Eclipsys T2 Case Costing System in London ON (based on data from 2007), for overhead costs of the operating room, fracture clinic, emergency room, and for the ward and rehabilitation institution costs. Prescription medication prices were obtained from the Ontario Drug Benefit Formulary [16]. Prices for drugs not listed on the formulary were obtained from drug distributors. Mark-ups and dispensing fees were added as appropriate. For material costs we contacted manufacturers.

Inpatient costs were derived from the following: 1) surgeon's fee depending on the type of operation; 2) the surgical assistant's fee depending on the type of operation; 3) the anesthetist's fee; 4) the fluoroscopy technician's fee; 5) operating room overhead including nursing staff, surgical supplies and infrastructure costs; 6) overhead ward room costs; and 7) drugs related to the tibial fracture and administered during hospital stay.

Outpatient costs included: 1) follow-up visits with the surgeon; 2) surgical procedures performed during follow-up visits (e.g., cast application, removal); 3) fracture clinic overhead; 4) outpatient diagnostic tests required (e.g., radiographs, ultrasound, bone density scan); 5) rehabilitation institution services; 6) nonorthopedic outpatient services (e.g., consultation with a plastic surgeon, emergency room consultation); and 7) drugs related to the tibial fracture and prescribed in outpatient clinics. Resource utilization of physiotherapy, occupational therapy, social workers, and blood tests were not systematically captured and were therefore excluded from the analysis.

Statistical analysis

The cost-utility analysis consisted of first determining whether one treatment dominated the other (i.e., lower costs and better outcomes) and, failing that, determining the trade-off between incremental costs and incremental effects calculated as the cost per QALY gained as

$$[(\textit{mean annual cost per patient})_R - (\textit{mean annual cost per patient})_{UR}] / [(\textit{mean QALY per patient})_R - (\textit{mean QALY per patient})_{UR}]$$

where UR is the unreamed group and R is the reamed group. To determine the effect of uncertainty around QALY point estimates, we conducted a bootstrapping analysis by performing a separate bootstrap of 1000 replications for each of the two strata, open tibial shaft fractures and closed tibial shaft fractures. We plotted the results on the incremental cost-effectiveness plane and estimated incremental cost-effectiveness acceptability curves for both open and closed fractures, using the bootstrap data to determine the probability that treatments are cost-effective according to various societal willingness-to-pay thresholds for health improvements (i.e., willingness-to-pay per QALY gained). The bootstrapping procedure was performed in S-PLUS version 8.0, (Insightful Corpora-

Table 1 – SPRINT patient demographics and fracture characteristics.

	Economic review patients				SPRINT patients not in economic review			
	Closed		Open		Closed		Open	
	Reamed N = 85	Unreamed N = 82	Reamed N = 33	Unreamed N = 35	Reamed N = 331	Unreamed N = 328	Reamed N = 173	Unreamed N = 159
Age, mean (SD)	44.1 (16.9)	40.6 (16.6)	34.5 (11.9)	36.8 (15.9)	38.9 (15.7)	39.9 (16.0)	37.7 (16.7)	40.1 (15.4)
Sex, n (%)								
Male	51 (60.0)	55 (67.1)	28 (84.8)	23 (65.7)	243 (73.4)	248 (75.6)	135 (78.0)	121 (76.1)
Female	34 (40.0)	27 (32.9)	5 (15.2)	12 (34.3)	88 (26.6)	80 (24.4)	38 (22.0)	38 (23.9)
Smoking history, n (%)*								
Non-smoker	57 (67.1)	47 (58.0)	18 (56.3)	24 (68.6)	195 (59.3)	180 (54.9)	94 (54.7)	96 (60.4)
Current smoker	20 (23.5)	19 (23.5)	13 (40.6)	8 (22.9)	107 (32.5)	123 (37.5)	60 (34.9)	56 (35.2)
Previous smoker	8 (9.4)	15 (18.5)	1 (3.1)	3 (8.6)	27 (8.2)	25 (7.6)	18 (10.5)	7 (4.4)
Leg fractured, n (%)								
Isolated								
Left	42 (49.4)	34 (41.5)	15 (45.5)	15 (42.9)	148 (44.7)	140 (42.7)	74 (42.8)	78 (49.1)
Right	41 (48.2)	48 (58.5)	17 (51.5)	18 (51.4)	178 (53.8)	187 (57.0)	92 (53.2)	77 (48.4)
Bilateral	2 (2.4)	0 (0)	1 (3.0)	2 (5.7)	5 (1.5)	1 (0.3)	7 (4.0)	4 (2.5)
Both open and closed fracture, n (%)	0 (0)	0 (0)	1 (3.0)	2 (5.7)	0 (0)	0 (0)	3 (1.7)	2 (1.3)
Isolated fractures, n (%)	59 (69.4)	61 (74.4)	19 (57.6)	23 (65.7)	234 (70.7)	221 (67.4)	106 (61.3)	102 (64.2)
Type of fracture†, n (%)								
Open	—	—	5 (15.2)	13 (37.1)	—	—	40 (23.1)	49 (30.8)
Type I			11 (33.3)	16 (45.7)			73 (42.2)	58 (36.5)
Type II			13 (39.4)	5 (14.3)			45 (26.0)	42 (26.4)
Type IIIA			4 (12.1)	1 (2.9)			15 (8.7)	10 (6.3)
Type IIIB			—	—			—	—
Closed*								
Tscherne 0–1	75 (88.2)	78 (95.1)			268 (81.2)	258 (78.7)		
Tscherne 2–3	10 (11.8)	4 (4.9)			62 (18.8)	70 (21.3)		
AO classification†, n (%)								
A (simple)	47 (55.3)	58 (70.7)	14 (42.4)	13 (37.1)	198 (59.8)	195 (59.5)	80(46.2)	82 (51.6)
B (wedge)	28 (32.9)	19 (23.2)	13 (39.4)	12 (34.3)	88 (26.6)	92 (28.0)	58 (33.5)	52 (32.7)
C (complex)	10 (11.8)	5 (6.1)	6 (18.2)	10 (28.6)	45 (13.6)	41 (12.5)	35 (20.2)	25 (15.7)
Bone loss in open fractures†, n (%)	—	—			—	—		
Yes			11 (33.3)	13 (37.1)			36 (20.8)	30 (18.9)
No			22 (66.7)	22 (62.9)			137 (79.2)	129 (81.1)

SD, standard deviation; SPRINT, study to prospectively evaluate reamed intramedullary nails in patients with tibial fractures.
* Some missing data.
† Based on most severe for bilateral fractures.

tion, Seattle, WA). All other analyses were performed in SAS version 9.1 (SAS Institute, Cary, NC).

Because uncertainty concerning quality of life and resource utilization is inherently part of the trial-based bootstrap analysis, we conducted a series of one-way sensitivity analyses to investigate the impact of varying unit costs by +/− 20%. In response to reviewers' comments, we additionally conducted a sensitivity analysis excluding rehabilitation costs and a stratified analysis of resource utilization stratified by Canadian and US centers.

Results

Patient characteristics

In SPRINT, 1226 patients (93% of 1319 enrolled patients) completed the final 1-year follow-up visit and were included in this and previous analyses [8]. Included patients were predominantly men with a mean age of about 40 years old (Table 1). Two-thirds of study patients had a closed tibia fracture and one-third had an open tibia fracture. The convenience sample of 235 patients (118 in reamed and 117 in unreamed group) included in the cost analysis was similar to patients not included in the cost analysis, and patients allocated to reamed intramedullary nailing were similar to patients allocated to unreamed intramedullary nailing with respect to key prognostic variables except for a larger proportion of patients with a grade III open fracture in the reamed compared with the unreamed group (Table 1).

Patient outcomes

The primary outcome of the SPRINT trial, which was a composite of re-operations including autodynamization, showed a benefit for reamed intramedullary nail insertion in patients with closed tibial shaft fractures largely due to fewer dynamizations, and a potential advantage for unreamed intramedullary nailing in open tibia fractures (Table 2). The mean utility scores (overall health) during the first 12 months following intramedullary nailing were similar in the unreamed group and the reamed groups for both open and closed tibia fractures (Table 2). Closed tibia fractures in general were associated with higher utility scores than open tibia fractures (Table 2).

Cost analysis

Table 3 summarizes health care resource utilization. Table 4 summarizes the unit costs for the hospitalization, clinic follow-up, and re-operations. Consumed resources during the index hospital stay and for re-operations were recorded at the time of trial conduct,

Table 2 – Outcomes for the entire SPRINT trial, N = 1226.

	Closed		Open	
	Reamed N = 416	Unreamed N = 410	Reamed N = 206	Unreamed N = 194
Re-operations (primary outcome of SPRINT)	45	68	60	46
Bone graft	2	2	7	6
Implant exchange	6	10	12	12
Re-operation due to local infection	9	7	19	16
Fasciotomy for compartment syndrome (in a procedure separate from the intramedullary nailing)	6	1	3	2
Fasciotomy for compartment syndrome (in the same procedure as the intramedullary nailing)	1	6	2	1
Removal of locking screws	1	0	0	0
Dynamization				
In operating room	8	16	17	13
In outpatient clinic	2	3	0	1
Autodynamization	12	29	9	8
Failure of construct (broken nail)	0	0	0	1
Utility scores from the health utilities index, mean (SD)				
Prior to injury	0.88 (0.19)	0.88 (0.22)	0.90 (0.16)	0.89 (0.18)
2 weeks	0.32 (0.25)	0.35 (0.27)	0.33 (0.29)	0.37 (0.26)
3 months	0.57 (0.29)	0.58 (0.28)	0.53 (0.32)	0.52 (0.29)
6 months	0.68 (0.29)	0.68 (0.31)	0.61 (0.31)	0.62 (0.30)
12 months	0.72 (0.30)	0.76 (0.29)	0.68 (0.30)	0.66 (0.31)

SD, standard deviation; SPRINT, study to prospectively evaluate reamed intramedually nails in patients with tibial fractures.

while other resource utilization was determined through medical chart review. In general, costs associated with open tibia fractures were higher than costs associated with closed tibia fractures (Table 5). Costs from the index procedure, from the index hospital stay, and from fracture-associated medications were similar in the reamed and unreamed treatment groups. However, the costs from re-operations were quite different between groups.

Mean costs from re-operations were similar for reamed patients with closed tibia fractures, but higher with open tibia fractures. The cost difference for "Other costs" (Table 5) between the reamed and the unreamed group with closed fractures was mainly driven by a considerable difference in costs from rehabilitation institutions. Six patients in the reamed group and two patients in the unreamed group went to rehabilitation institutions for a mean of 25 days (range, 2–80 days), resulting in a total of rehabilitation costs in the reamed group of $105,888 Canadian dollars and in the unreamed group of $15,600 Canadian dollars. Because of the small number of patients, the most likely explanation for the difference is chance.

According to the stratified description of resource utilization by Canadian and US centers (see Table 1 at: doi:10.1016/j.jval.2010.10.034), we did not find any differences between Canadian and US centers, except for orthopedic surgeon visits with open fractures for which there was a trend toward more orthopedic surgeon visits in US centers when compared with Cana-

Table 3 – Health care resource utilization, N=235.

	Closed		Open	
	Reamed N = 85	Unreamed N = 82	Reamed N = 33	Unreamed N = 35
Index hospital length of stay (days on an orthopedic ward)				
Mean (SD)	6.8 (5.6)	7.9 (9.2)	10.3 (6.6)	9.8 (8.9)
Median (IQR)	5 (4–8)	5 (4–9)	7 (6–16)	7 (5–10)
Index operating room time				
Mean (SD)	74.7 (41.7)	66.7 (26.6)	85.6 (30.8)	82.3 (40.5)
Median (IQR)	65 (48–90)	61 (45–85)	83 (60–110)	80 (55–115)
Number of orthopedic surgeon visits				
Mean (SD)	5.2 (1.5)	5.1 (1.4)	7.6 (4.2)	6.4 (3.0)
Median (IQR)	5 (5–6)	5 (4–6)	6 (5–8)	6 (5–7)
Number of x-rays				
Mean (SD)	4.4 (1.7)	4.3 (1.5)	5.4 (2.9)	4.6 (1.8)
Median (IQR)	4 (4–5)	4 (3–5)	5 (4–7)	5 (3–6)
Number of readmissions				
Mean (SD)	0.1 (0.4)	0.1 (0.3)	0.4 (0.7)	0.1 (0.4)
Total number	10	8	13	3

IQR, interquartile range; SD, standard deviation.

Table 4 – Unit costs of hospitalization, clinic visits, and surgical procedures.

Hospital and clinic costs	Costs	Data source
Day on orthopedic ward	$696	Eclipsys T2 Case Costing System, London, Ontario (2007)
Radiographs of the tibia (2 views)	$22	Physician Schedule of Benefits (February 2008)
Fracture clinic visit	$58	Eclipsys T2 Case Costing System, London, Ontario (2007) and Physician Schedule of Benefits (February 2008)
Emergency room visit		
Initial visit	$157	Eclipsys T2 Case Costing System, London, Ontario (2007) and Physician Schedule of Benefits (February 2008)
Follow-up visit	$102	
Surgical procedures		
Bone graft	$2224	Eclipsys T2 Case Costing System (2007) and Physician Schedule of Benefits (February 2008)
Implant exchange	$4520	Eclipsys T2 Case Costing System (2007) and Physician Schedule of Benefits (February 2008)
Re-operation due to local infection	$890	Eclipsys T2 Case Costing System (2007) and Physician Schedule of Benefits (February 2008)
Fasciotomy for compartment syndrome	$1655	Eclipsys T2 Case Costing System (2007) and Physician Schedule of Benefits (February 2008)
Removal of locking screws/dynamization		
In operating room	$1065	Eclipsys T2 Case Costing System (2007) and Physician Schedule of Benefits (February 2008)
In outpatient clinic	$70	

Costs expressed in Canadian dollars. Average exchange rate for 2008: $1 USD = $1.066 Canadian dollars.

dian centers; however, this trend was equally present for reamed and unreamed intra-medullary nailing.

Cost-utility analysis

In closed fractures, we found a mean increased incremental cost of $51 Canadian dollars (95% confidence interval [CI] −$2298–$2400) for patients treated with a reamed intramedullary nail compared to an unreamed nail (Table 6). In open fractures, we found a mean increased incremental cost of $2546 Canadian dollars (95% CI −$1773–$6864) for patients treated with a reamed intramedullary nail. The mean incremental effects on QALYs in reamed compared to unreamed intramedullary nailing were −0.017 (95% CI −0.058–0.017) and −0.002 (95% CI −0.062–0.060) in closed and open fractures, respectively. Considering only the point estimates for both cost and QALYs, unreamed intramedullary nailing was more effective and less costly than reamed intramedullary nailing in both closed and open fractures. The analyses of uncertainty based on the bootstrap replications are shown on the cost-effectiveness planes in Figure 1A for closed and Figure 1B for open fractures. Representing this uncertainty on cost-effectiveness acceptability curves (Fig. 2), shows that for all willingness to pay thresholds, unreamed nailing was more likely to be cost-effective at all decision-making thresholds for both closed and open fractures. However, there is considerable fragility of these results due to small differences in both cost and effectiveness associated with large standard errors.

To explore the impact of the higher proportion of patients with grade III open fractures in the reamed group on our results, we calculated total costs for open fractures stratified by grades I/II or grades IIIA/B in a *post-hoc* sensitivity analysis. The mean (range) of total costs for patients with open fractures grade I/II were $12,806 Canadian dollars ($4441 to $57,060) in the reamed, and $9999 Canadian dollars ($2959 to $35,509) in the unreamed group, and for patients with open fractures grade IIIA/B $12,717 Canadian dollars ($5068 to $31,832) in the reamed, and $11,257 Canadian dollars ($6612 to $19,766) in the unreamed group. Even if we assumed mean total costs of $11,257 Canadian dollars for all unreamed patients with open fractures we would still find a considerably lower point estimate for total costs in patients with unreamed compared with reamed open fractures.

Table 5 – Average costs based on SPRINT data.

	Closed		Open	
	Reamed N = 85	Unreamed N = 82	Reamed N = 33	Unreamed N = 35
Total cost, mean (range)	$8053 ($3023 to $63,894)	$8002 ($2692 to $51,036)	$12,760 ($4441 to $57,060)	$10,215 ($2959 to $35,509)
Cost for index surgery, mean (range)	$1649 ($1002 to $4840)	$1503 ($870 to $2703)	$1805 ($1002 to $2780)	$1741 ($870 to $2938)
Cost for index hospital stay excluding the index surgery, mean (range)	$4725 ($1392 to $32,712)	$5492 ($1392 to $48,720)	$7192 ($2088 to $18,792)	$6821 ($1392 to $32,016)
Cost for fracture-associated medications, mean (range)	$95 ($4 to $896)	$103 ($2 to $598)	$282 ($7 to $2242)	$245 ($1 to $2264)
Cost for re-operations (range)	$136 ($0 to $3153)	$347 ($0 to $12,312)	$1989 ($0 to $16,874)	$485 ($0 to $8000)
Other costs, mean (range)*	$1448 ($0 to $48,402)	$556 ($139 to $11,202)	$1492 ($241 to $28,141)	$923 ($161 to $8962)

Costs expressed in Canadian dollars. Average exchange rate for 2008: $1 USD = $1.066 Canadian dollar.
SPRINT, study to prospectively evaluate reamed intramedullary nails in patients with tibial fractures.
* Other costs comprised cost items such as outpatient fracture clinic visits, radiographs, computed tomography scans, magnetic resonance imaging, bone density scans, venous Doppler, cast applications, cast removals, air cast boots, rehabilitation institutions, emergency room consultations, and consultations with a plastic surgeon.

Table 6 – Cost-utility analysis results.

	Costs ($) mean (95% CI)	QALYs mean (95% CI*)	Incremental costs ($) mean (95% CI)	Incremental effects (QALYs) mean (95% CI*)	ICER
Closed					
Reamed	$8053 ($6255, $9851)	0.64 (0.61, 0.66)	$51 (−$2298, $2400)	−0.017 (−0.058, 0.021)	Unreamed dominates reamed
Unreamed	$802 ($6475, $9528)	0.65 (0.63, 0.68)			
Open					
Reamed	$12,760 ($9138, $16,383)	0.59 (0.55, 0.64)	$2546 (−$1773, $6864)	−0.002 (−0.062, 0.060)	Unreamed dominates reamed
Unreamed	$10,215 ($7644, $12,786)	0.59 (0.55, 0.63)			

Costs expressed in Canadian dollars. Average exchange rate for 2008: $1 USD = $1.066 Canadian dollar.
CI, confidence interval; ICER, incremental cost-effectiveness ratio; QALYs, quality-adjusted life years.
* 95% CI calculated from bootstrapping for QALYs and incremental effects.

In a series of one-way sensitivity analyses varying each of the unit costs listed in Table 4 by ±20% (Table 2 found at: doi:10.1016/j.jval.2010.10.034), we found that unreamed dominated reamed in all but one of these analyses, which is consistent with our primary result. When we assumed an increase of 20% in the per day cost on an orthopedic ward, the reamed group had a lower mean cost than the unreamed group ($9008 and $9124 Canadian dollars, respectively) for closed fracture patients.

Because we found a considerable difference in rehabilitation costs between groups for closed fractures which was most likely due to chance, we conducted a sensitivity analysis excluding rehabilitation costs from the analysis. This led to a lower mean cost for the reamed group compared with the unreamed group in closed fractures (Table 3 found at: doi:10.1016/j.jval.2010.10.034) underlining the fragility of our point estimate results.

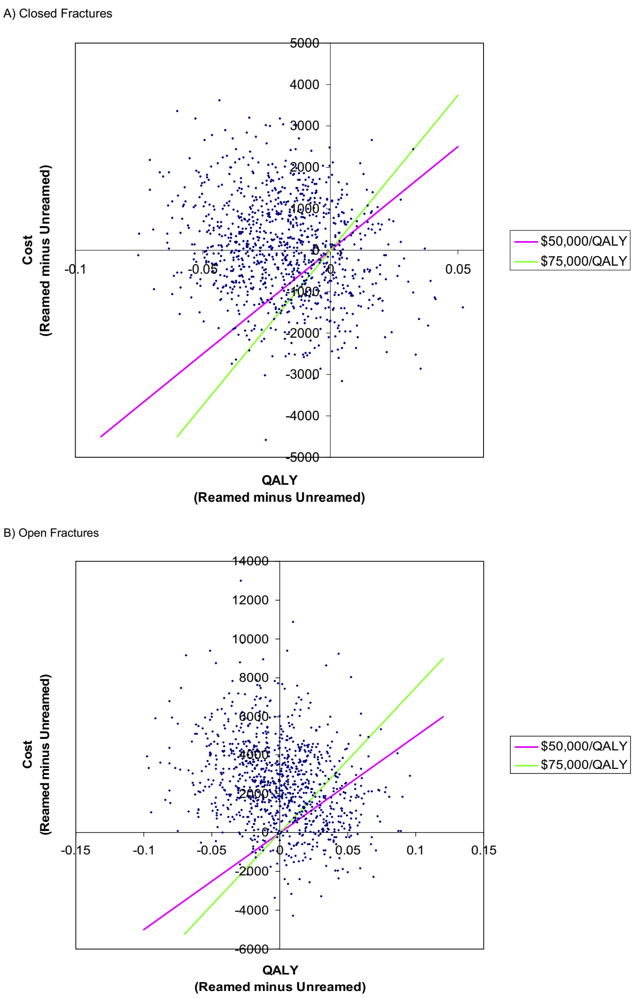

Fig. 1 – Incremental cost-effectiveness plane. (A) Closed fractures. (B) Open fractures. QALY, quality-adjusted life years.

Discussion

Waiting lists for surgical procedures are long in Canada [17] and health care costs continue to climb [18]. Therefore, means to prevent re-operations and reduce costs are important. We found small differences in both cost and effectiveness in favor of unreamed intramedullary nailing compared to reamed intramedullary nailing in both closed and open fractures. However, the con-

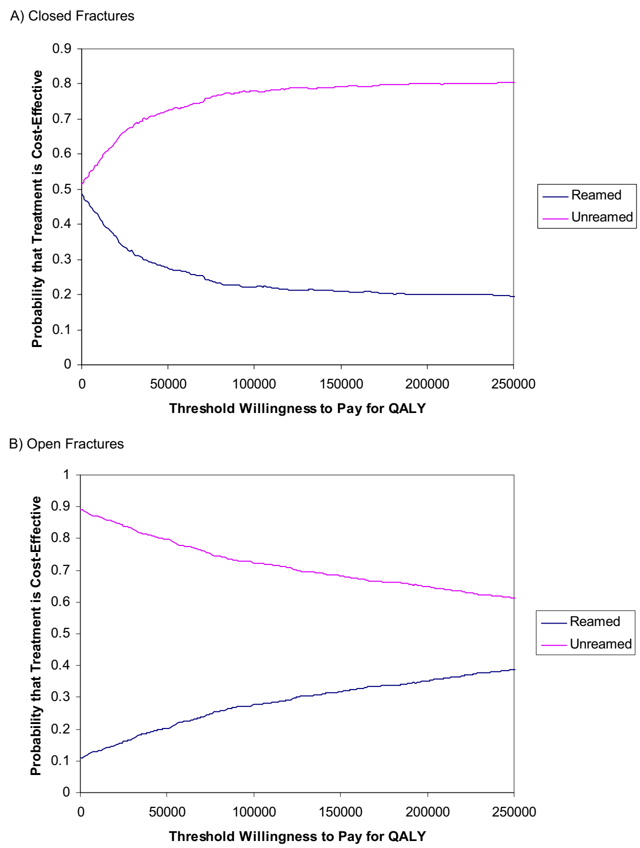

Fig. 2 – Incremental cost-effectiveness acceptability curves. (A) Closed fractures. (B) Open fractures. QALY, quality-adjusted life years.

fidence intervals surrounding the point estimates for both cost and effectiveness are wide, indicating a considerable amount of uncertainty and precluding firm conclusions regarding relative benefit and cost. Another interpretation of our results, in which for decision-making purposes probabilities for incremental cost-effectiveness are directly compared given the available data, could conclude that unreamed intramedullary nailing dominates reamed nailing for both closed and open tibial fractures; this approach, however, ignores the fragility of the results.

Strengths and limitations

The strengths of this study are the large sample size of the SPRINT trial; its high internal validity through strategies to reduce bias that include centralized randomization of patients to ensure concealment, and independent, blinded adjudication of outcome events; and its pragmatic nature: patients enrolled in SPRINT were typical of the normal case load, the operative approaches reflect current care, a wide range of end points was measured (e.g., different types of re-operations, patients' functional status, and quality of life), and the multiple participating surgeons and centers are fairly representative of the United States and Canada [8].

The hypothesis that effects differ in open and closed fractures was specified a priori, reflected in the decision to stratify randomization according to open and closed fractures [9]. Other factors supporting the credibility of a subgroup effect are the large difference in effect size of the primary outcome in this within-study comparison, the fact that it was statistically significant ($P = 0.01$), and that it is biologically plausible since preservation of the endosteal blood supply might be more important in open than in closed fractures.

We acknowledge the possibility of a short-term bias since our study was constrained to the trial period of 1 year. However, the time horizon of one year appears reasonable for this analysis because re-operations for tibial fractures typically occur within the first year following surgery, and closed tibia fractures usually heal at a mean of 3.9 months and open tibial fractures at a mean of 7 months [8]. Given this fact and our results, a follow-up beyond 1 year would have probably yielded little additional information about resource utilization and quality of life; although it is possible that a decision analytic model with a lifetime horizon could have yielded different results, we consider this unlikely.

Although this economic evaluation was planned from the initiation of the SPRINT trial and the most important data were collected during the trial conduct, part of the resource utilization data was collected retrospectively through review of medical records on a non-random sample of less than one-fifth of SPRINT patients. Resource items such as physiotherapy, occupational therapy, social workers, and blood tests were not systematically captured and were therefore omitted in the analysis. Further information sources such as family physicians were not contacted to complement information on consumed follow-up resources found in hospital charts. A trend toward more orthopedic surgeon visits in US centers when compared with Canadian centers was equally present for reamed and unreamed intra-medullary nailing and is therefore unlikely to have biased our results.

In order to optimize the signal-noise ratio, this analysis focused on relative cost differences between reamed and unreamed nail groups, and made no attempt to accurately reflect absolute costs of intramedullary nailing of tibia fractures. Therefore, surgical procedures classified by the adjudication committee as non-events (re-operations determined by the circumstances of the injury rather than by the different operative techniques) were not included in the analysis. Along the same lines, we did not include any after hours or weekend surcharges and we considered material costs of intramedullary nails and locking screws only for re-operations such as implant exchanges.

Finally, the generalizability of the study results is limited to the extent that peri-operative regimens were standardized in participating centers [9]. Although SPRINT was a pragmatic trial, these measures probably increased the internal validity of the trial but made it less representative of usual clinical practice.

Findings in relation to prior evidence

The SPRINT primary manuscript reported a benefit for reamed intramedullary nail insertion in patients with closed tibial shaft fractures, and a potential advantage for unreamed intramedullary nailing in open tibia fractures [8]. This economic evaluation found that unreamed intramedullary nailing was more effective and less costly when compared to reamed intramedullary nailing for both open and closed fractures. Confidence intervals around both cost and utility estimates were, however, wide, and neither approached conventional levels of statistical significance. The results from the primary SPRINT manuscript were largely driven by fewer dynamizations and autodynamizations [8] in the reamed group, but these had negligible impact on the cost-effectiveness because there is little or no cost associated with autodynamizations, and the differences in autodynamization did not appear to affect the results of the utility measures.

There has been limited economic research in this area. The results of a previously published economic evaluation of reamed versus unreamed intramedullary nailing in 51 patients with open tibia fractures reported fewer costs with reamed intramedullary nailing due to fewer secondary procedures while healing rates remained similar in the two groups [6]. This study is limited by the biases that accompany any observational study and by the small sample size. Similarly, Busse et al. [7] reported that from an economic standpoint, the reamed intramedullary nail is the treatment of choice for low energy tibia fractures. To develop their decision tree, Busse et al. [7] used data from small randomized clinical trials with methodological limitations. The prospective, randomized SPRINT trial with concealed 24-hour allocation of patients provides higher internal validity, and its results in favor of the unreamed technique for open tibia fractures may be a conservative estimate for a potential benefit since participating surgeons had superior skills in reamed nailing.

Conclusions

Our economic analysis from a governmental perspective found no convincing evidence of differences between reamed and unreamed nailing in either cost and effectiveness with wide confidence intervals. The uncertainty regarding the relative cost and utility of the procedures suggests that results based on point estimates, in which unreamed intramedullary nailing dominated reamed nailing for both closed and open tibial shaft fractures, should be viewed with great caution.

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Supplemental Materials

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