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Preliminary Results of a Cost-Utility Analysis of a Fracture Liaison Service Based on Health Services Indicators

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INTRODUCTION

- Fracture Liaison Services (FLSs) are secondary fracture prevention programs aiming to improve fragility fracture (FF) care and decrease the care gap in osteoporosis.
- Trajectory groups of patients following similar trajectories of care have been previously identified (see poster **PMS51-T16**).

Objective: This study aimed to assess the cost-utility of a high-intensity FLS according to patients' systematic follow-up compliance trajectories.

METHODS

The intervention

- This is a prospective cohort study of 532 women and men.
- FF patients (40 years or older) were recruited in two hospital-based outpatient orthopedic clinics in Montreal (Canada) and systematically followed in a FLS.
- Clinical data was collected during the study visits with patient testimony, medical files, pharmacy lists, radiological assessment and blood tests.
- Administrative data on health services, hospitalizations and pharmaceutical services was retrieved from the Régie de l'Assurance Maladie du Québec (RAMQ-Med-Echo, ReMed). Data was available for the duration of the study and up to 5 years (medical health services, hospitalizations) or 1 year (pharmaceutical services) before baseline.
- Participants were clinically assessed for bone fragility using bone mineral density (BMD), spine X-rays, blood testing and the FRAX tool for fracture risk assessment.
- When applicable, osteoporosis therapy along with calcium and vitamin D supplements were prescribed.
- FLS nurses monitored alcohol and tobacco use, physical activity, comorbidities, co-medication, adverse drug reactions and patient-reported adherence to therapy during systematic follow-up visits with patients.
- Quality of life, functional capacity and pain were monitored using self-administered questionnaires.

Trajectory groups of follow-up visit compliance

- Three trajectories of care were predicted using group-based trajectory modeling: 48.4% of patients were **high followers (HF)**, 28.1% were **intermediate followers (IF)**, and 23.5% were **low followers (LF)**. These results are currently under revision by the journal BMC Health Services Research.

Cost-utility analysis

- Comparing the costs and quality-adjusted life years (QALYs) between follow-up compliance trajectory groups and a simulated usual care (UC) cohort (drawn from literature). Analyses were also performed for the entire FLS (three trajectory groups combined).
- Main FLS data used to build the model: probability of BMD investigation, probability of treatment and probability of persistence to treatment among trajectory groups.
- Markov analytic models were used to measure the incremental cost-utility ratio (ICUR).
- Perspective of a healthcare system, lifetime horizon, two-year cycles and a $50,000 per QALY gained threshold were used for reference.

Decision analytic model

- Markov model: 11 health states, starting age of 63 years (mean age for the cohort) up to death or 105 years (21 cycles). Two subsequent FF allowed (Fig. 1).
- Assumptions: 1) first FF in time, 2) subsequent FF of the hip, humerus or wrist, which are representative of other categories of fracture, 3) no vertebral fractures accounted for in the model (hard to manage in clinical practice), 4) treated with oral bisphosphonates (alendronate/risedronate), 5) two cycles of persistence to treatment and residual effect of treatment up to 5 cycles (only treated and persistent patients), 6) patients persistent to treatment assumed to have optimal adherence.
- Modeled using TreeAge Pro Healthcare Module 2019 (TreeAge Software Inc., Williamstown, MA).
- Model inputs are shown in Table 1. Costs were expressed in 2018 Canadian dollars. Costs and benefits were discounted at 1.5%.

Sensitivity analyses

- In order to validate the simulated UC group, we used the LF trajectory group as reference in the cost-utility analysis, minus the FLS costs. This was done because we found similar probabilities and costs for these groups.
- One-way deterministic sensitivity analyses were performed for significant clinical parameters: 1) increasing the initial proportion of hip FF to 10% to simulate an older group, 2) doubling and tripling the cost of osteoporosis drugs to see the impact of the prescription of injectable alternate therapies, 3) the use of a minimal risk reduction effect of treatment (RR of 0.7), 4) the reduction of 25% of FLS costs because it is plausible to assume that real-life FLSs will be less intensive, 5) shorter time horizons (10, 20, 30 years).
- A probabilistic sensitivity analysis was performed with a Monte-Carlo simulation of 5000 iterations. Results were presented as acceptability curves.

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FIGURE I: Markov model.

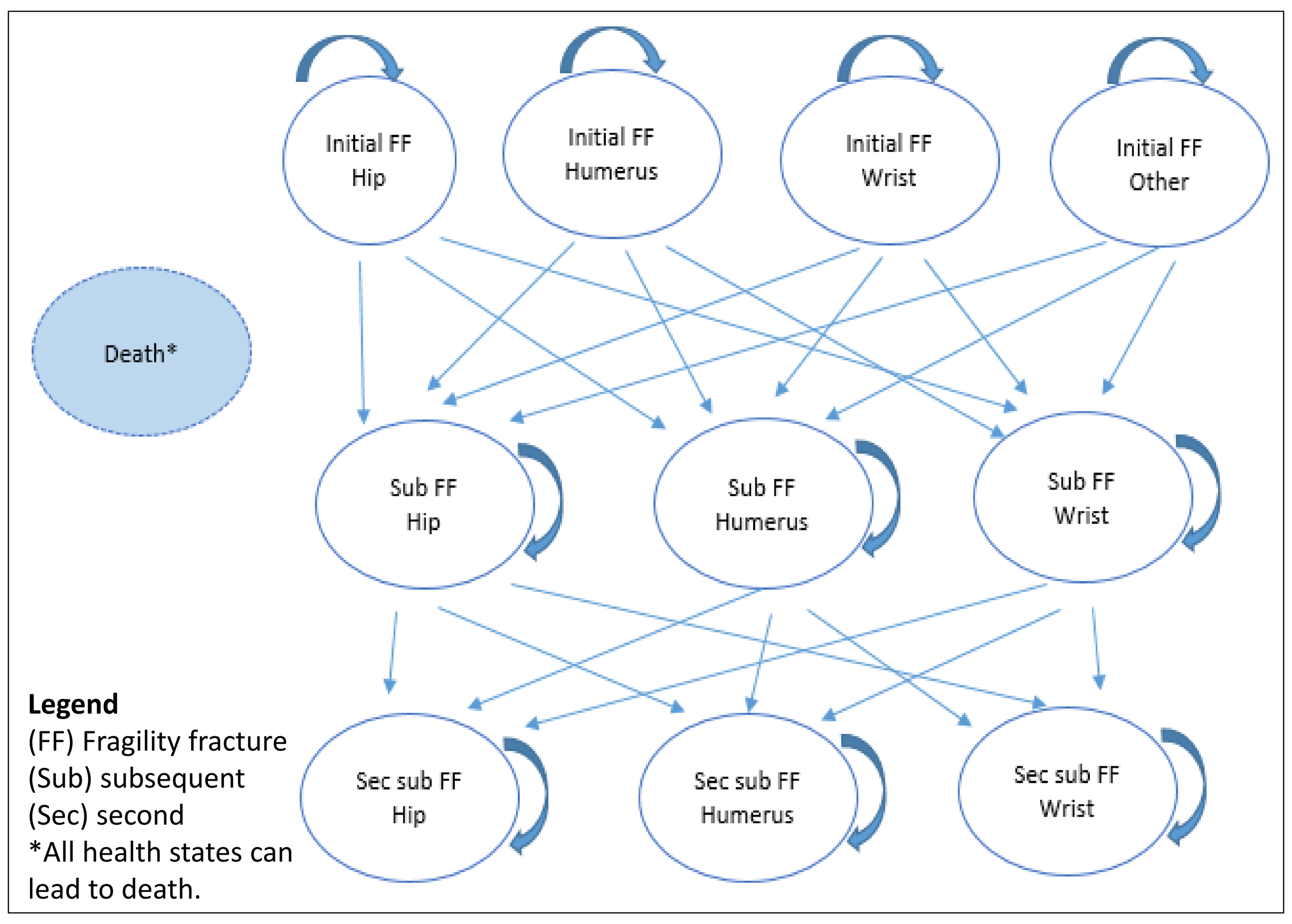


TABLE 2: Results of the health economic analysis according to each follow-up compliance trajectory group and the entire FLS compared to usual care

	Avg costs	Avg QALYs	Inc. costs	Inc. QALYs	ICURs	Avg Sub. Hip FF	Avg Sub. FF	Inc. Sub. Hip FF	Inc. Sub. FF
UC	$13,139	13.89	Reference			0.136	0.335	Reference	
LF	$13,554	13.89	$415	0.01	$74,000	0.134	0.331	0.002	0.004
IF	$13,530	13.91	$391	0.02	$22,000	0.131	0.322	0.005	0.013
HF	$13,286	13.93	$147	0.04	$3,600	0.123	0.306	0.013	0.029
FLS	$13,381	13.92	$242	0.03	$8,500	0.127	0.315	0.009	0.020

Abbreviations: (Avg) average, (FF) fragility fracture, (FLS) fracture liaison service, (HF) high followers, (ICUR) incremental cost-utility ratio, (IF) intermediate followers, (Inc.) incremental, (LF) low followers, (QALY) quality-adjusted life years, (Sub.) subsequent, (UC) usual care. All estimates were rounded. Differences and ratios were calculated using all decimals (not shown).

FIGURE 2: Deterministic sensitivity analysis for increased osteoporosis (OP) drug costs

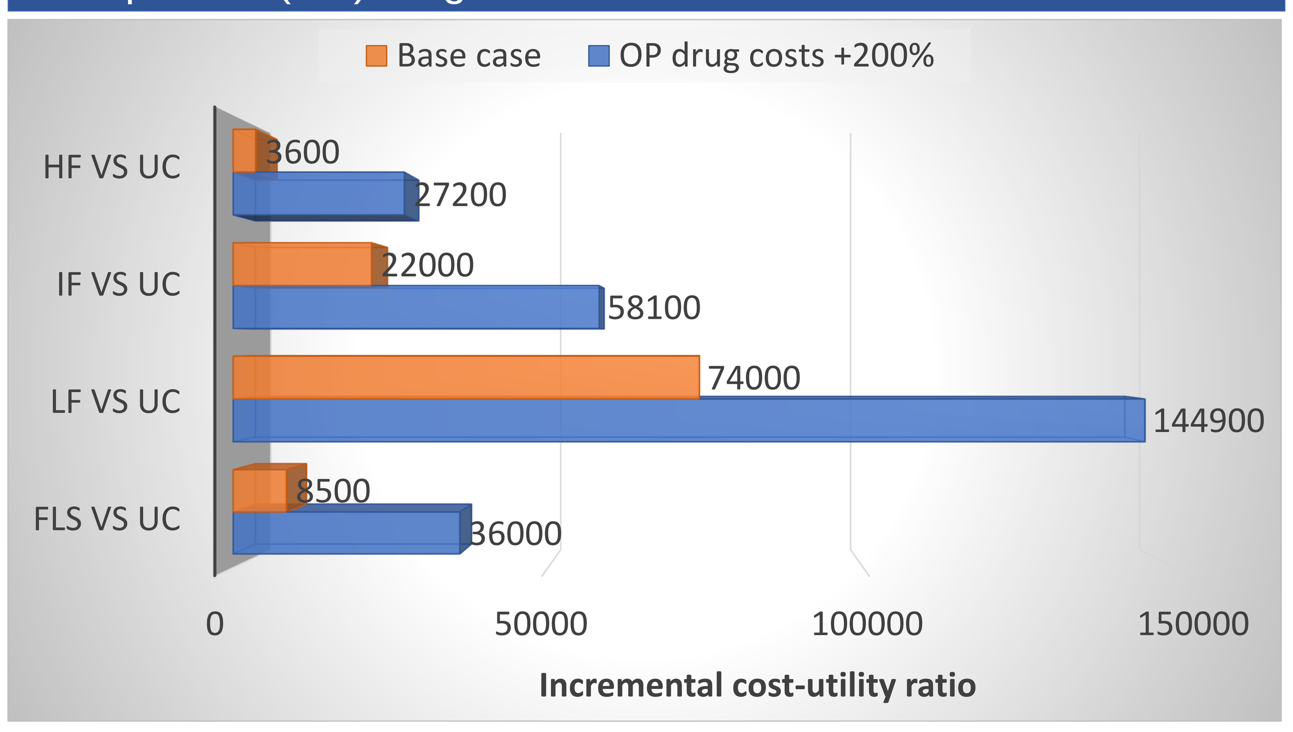
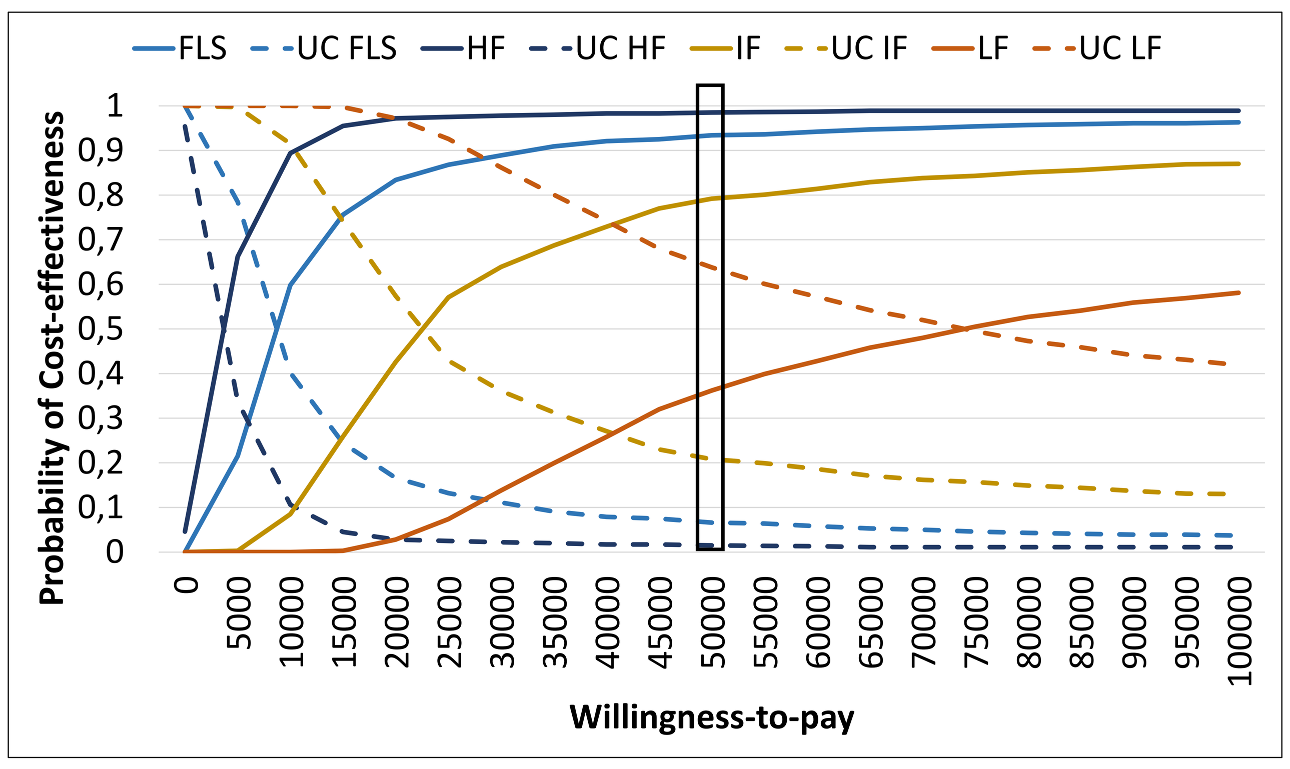


FIGURE 3: Acceptability curves according to trajectory groups



RESULTS

- Regardless of the trajectory group, BMD investigation, treatment initiation and persistence rates were superior to the simulated UC cohort, except for the LF group where parameters were similar to those of the UC group (Table 1).
- FLS mean costs varied between $300 and $446 CA per patient for two years of intervention.
- ICURs for the HF, IF and LF trajectory groups compared to UC were $3,600, $22,000 and $74,000 per QALY gained, respectively ($8,500 per QALY gained for the FLS) (Table 2).
- For every 1000 patients, 20 fragility fractures, of which 9 hips, were prevented in the FLS compared to UC.
- Sensitivity analysis showed similar ICURs using the LF group without FLS costs as reference, validating the UC group (data not shown).
- Increasing drug costs (+200%) led to important variation in the estimates (Fig. 2).
- According to acceptability curves (Fig. 3), >75% of simulations were cost-effective for the HF, IF and the entire FLS compared to UC, but only 40% for the LF group with a $50,000 per QALY threshold.

TABLE I: Model parameters.

Parameters	Estimate (SE)†	Dist.	Source
Mean age	63	Fixed	LB-FLS
Initial fracture site distributions			LB-FLS
Hip	0.038 (0.008)	Beta	
Humerus	0.133 (0.015)	Beta	
Wrist	0.387 (0.021)	Beta	
Other	0.442 (0.021)	Beta	
FLS trajectories distributions			LB-FLS
HF	0.484 (0.021)	Beta	
IF	0.281 (0.019)	Beta	
LF	0.235 (0.018)	Beta	
Probability of treatment – UC	0.350 (0.042)	Beta	Fraser et al. Osteoporos Int. 2011;22(3):789-96.
Probability of treatment – FLS			LB-FLS
HF	0.878 (0.027)	Beta	
IF	0.797 (0.052)	Beta	
LF	0.686 (0.065)	Beta	
FLS	0.822 (0.024)	Beta	
Probability of DXA – UC	0.280 (0.016)	Beta	Bessette et al. Osteoporos Int. 2008;19(1):79-86
Probability of DXA – FLS			LB-FLS
HF	0.966 (0.013)	Beta	
IF	0.968 (0.018)	Beta	
LF	0.598 (0.043)	Beta	
FLS	0.859 (0.017)	Beta	
Probability of persistence - two years – UC	0.399 (0.001)	Beta	INESSS. Portrait of osteoporosis drug use in Quebec, Canada. 2014.
Probability of persistence - two years – FLS			LB-FLS
HF	0.669 (0.039)	Beta	
IF	0.428 (0.071)	Beta	
LF	0.298 (0.078)	Beta	
FLS	0.556 (0.032)	Beta	
RR (95% CI) of fracture reduction with treatment	0.59 (0.49-0.73)	LN	Saito et al. Osteoporos Int. 2017;28(12):3289-3300
Residual effect from treatment after discontinuation	Up to 3 cycles.	Fixed	Ensrud et al. J Bone Miner Res. 2004;19(8): 1259-69.
Prob. of re-fracture - two years			Balasubramanian et al. Osteoporos Int. 2019;30(1):79-92. Hansen et al. Osteoporos Int. 2015;26(2):513-519.
Hip (index event)			
Hip	0.090 (0.001)	Beta	
Humerus	0.030 (0.0005)	Beta	
Wrist	0.029 (0.0005)	Beta	
Humerus (index event)			
Hip	0.054 (0.001)	Beta	
Humerus	0.059 (0.001)	Beta	
Wrist	0.044 (0.001)	Beta	
Wrist (index event)			
Hip	0.046 (0.001)	Beta	
Humerus	0.033 (0.001)	Beta	
Wrist	0.060 (0.001)	Beta	
Other site (index event)			
Hip	0.101 (0.001)	Beta	
Humerus	0.059 (0.0005)	Beta	
Wrist	0.064 (0.0005)	Beta	
Probability of death			Quebec Statistics Institute. Mortality rates, 2018 Ioannidis et al. CMAJ. 2009;181(5):265-271
General population	Varies with time	Beta	
Adjusted HR (95% CI) after hip fx	3.52 (1.54-8.03)	LN	
FLS costs – mean for two years			LB-FLS
HF	446.15 (2.32)	Gamma	
IF	376.80 (3.24)	Gamma	
LF	304.51 (3.02)	Gamma	
FLS	388.68 (3.12)	Gamma	
DXA exam cost - FLS	91.64	Fixed	LB-FLS
Physician fee-for-service treatment of FF – mean for two years			LB-FLS
Hip	634.41 (213.78)	Gamma	
Humerus	256.91 (83.86)	Gamma	
Wrist	204.92 (40.61)	Gamma	
Other	242.53 (38.81)	Gamma	
Osteoporosis drug cost			LB-FLS
Persistent	21.60 (0.13)/ mo	Gamma	
Non-persistent	Less 50%	Fixed	
Acute care hospital costs (±SD)			Ontario Case Costing Initiative. Ontario, Canada, 2018
Hip	14,951±17,514	Gamma	
Humerus	10,472±14,332	Gamma	
Wrist	6,262±8,570	Gamma	Bessette et al. Osteoporos Int. 2012;23(6):1757-68.
	(0.31 prob.)	Beta	
Utilities (95% CI)			
Age groups			Si et al. Osteoporos Int. 2014;25(1):51-60. Peasgood et al. Osteoporos Int. 2009;20(6):853-868. Hiligsmann et al. Calcif Tissue Int. 2008;82(4):288-292.
60-69	0.78 (0.74-0.81)	Beta	
70-79	0.74 (0.70-0.78)	Beta	
≥80	0.73 (0.67-0.78)	Beta	
Fracture multipliers			
Hip first year	0.70 (0.64-0.77)	Beta	
Hip subsequently	0.80 (0.68-0.96)	Beta	
Wrist	0.96 (0.86-1.00)	Beta	
Other (includes humerus)	0.91 (0.88-0.94)	Beta	
Discount rate for costs and QALYs	1.5%	Fixed	INESSS submission guide, Qubec, Canada, 2018

Abbreviations: (CI) confidence interval, (Dist.) distribution, (DXA) dual-energy x-ray absorptiometry, (FLS) Fracture Liaison Service, (fx) fracture, (HF) high followers, (HR) hazard ratio, (IF) intermediate followers, (LB) Lucky Bone™, (LF) low followers, (LN) lognormal, (QALY) quality-adjusted life years, (SD) standard deviation, (SE) standard error.
†Standard error, except when stated otherwise.

CONCLUSION

- ✓ The results of this study suggest that a FLS with a systematic follow-up is cost-effective when considering a $50,000 threshold.
- ✓ Having a pattern of low compliance to care led to not cost-effective scenarios.
- ✓ Limitations: the LB-FLS has no randomized evidence, the usual care cohort was simulated, societal costs not considered, lack of external validity (outpatient setting and urban population from Quebec, Canada).
- ✓ Results highlight the importance of better understanding what predicts patient retention into FLS program since patients have important risk of subsequent fractures.