An economic evaluation of surgery versus collagen injection for the treatment of female stress urinary incontinence

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Objective: *To use data from a randomized controlled trial and update an earlier economic evaluation of surgery versus collagen injection for the treatment of female stress urinary incontinence (SUI).*

Materials and methods: *A decision tree model was developed using probabilities of success and complications from a randomized controlled trial. Resource use and cost data were taken from the earlier economic evaluation. The primary outcome was treatment success, which was defined as a negative 24 hour PAD test given 1 year post-treatment. The evaluation was conducted from the 'healthcare system' perspective and separate analyses were undertaken for Ontario and Québec. Sensitivity analyses were used to examine uncertainty in probabilities and costs.*

Results: *Surgery was generally more costly and more successful than collagen injection. Incremental cost effectiveness ratios indicated that the healthcare system would incur an additional cost of $121.08 to $341.35 per additional patient that was successfully treated with surgery. Sensitivity analyses showed that surgery would be less costly and more successful than collagen injection if the postoperative length of hospital stay was reduced to 1 day. Surgery might also be more cost effective than collagen injection if the number of injections used to treat patients were to increase beyond two for treatment successes and four for treatment failures.*

Conclusions: *Collagen injection is an outpatient procedure without risk of significant morbidity or complications. However, this does not readily translate into a clear cost effective advantage relative to surgery. In some cases, surgery may be more cost effective than collagen injection in the treatment of female SUI.*

Key Words: stress urinary incontinence, surgery, collagen, economic evaluation

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Introduction

Stress urinary incontinence (SUI) is an involuntary loss of urine due to increased intra-abdominal pressure. Prevalence estimates in females range from 10.3%[1] to 46.0%.[2] Total treatment costs for SUI in the United States (US) in 1995 were $10.5 billion.[3] Surgery is the preferred treatment when non-invasive therapies

(e.g., bladder retraining, pelvic floor exercises) or medications (e.g., oxybutynin, duloxetine)[4] fail to control the incontinence. In the US alone, the number of surgical procedures performed annually for SUI increased from 48,345 in 1979 to 103,467 in 2004.[5] These trends were recently reproduced in a study of US female Medicare beneficiaries.[6] Although surgery has a good cure rate (≥ 80%[7]), approximately 7% of women will have recurrent SUI following treatment.[8]

Injectable therapies have been studied as an alternative to surgery since the late 1930s.[9] These therapies are minimally invasive outpatient procedures that have fewer complications than surgery. One injectable therapy, collagen, was evaluated in at least 18 case series. Cure or improved rates varied widely in these series (dry: 9% to 83%; improved: 9% to 63%) and the durability of treatment was shown to decrease over time. However, approximately 50% of collagen-treated patients remained dry at 2 years post-treatment.[10] Findings from the Urologic Diseases of America Project indicated that collagen injection became the most common procedure to treat SUI in the US in the late 1990s, although there is some evidence that it has since been eclipsed by sling procedures.[6]

Since collagen is performed on an outpatient basis and has fewer complications than surgery, an economic evaluation was conducted in 2001 to examine the cost effectiveness of surgery versus collagen injection in the treatment of female SUI.[11] At the time of the economic evaluation, collagen had not yet been compared to surgery in a randomized controlled trial (RCT). In the absence of RCT data, the results of the economic evaluation showed that each additional patient who was successfully treated with surgery, in comparison to collagen, would cost the healthcare system between $1,388 and $6,814, depending on the province (Ontario or Quebec) and type of surgery.[11]

Two years after the economic evaluation was published in 2003, the first RCT[12] comparing surgery and collagen injection to treat female SUI appeared in the literature. The publication of the RCT led to the objective of this study, which was to update the initial economic evaluation with data from the RCT and assess whether the results would change when data from a single source (i.e., the RCT) were used to replace data from multiple sources (i.e., meta analysis, case series, and expert opinion).

Materials and methods

The initial and updated economic evaluations of surgery versus collagen injection were decision analyses,[13] where decision tree models were used to calculate the expected costs of both treatments. A decision tree model is composed of nodes and branches. Two or more branches flow from each node and each branch has a cost and probability attached to it. A single series of branches is known as a pathway, which leads to a patient outcome (e.g., cure and no complications, cure and a single minor complication). The probabilities define the chance that each outcome will occur. Once the decision tree has been fully populated with nodes, branches, probabilities, and costs, the expected cost of a pathway can be calculated by multiplying the cost attached to each branch in the pathway by the probability attached to that branch. The expected costs of all of the pathways are summed to obtain the total expected cost of treatment (often simply called the 'expected cost').[13]

In the initial economic evaluation,[11] collagen injection was compared to three types of surgery: retropubic suspension, transvaginal suspension, and sling procedure. Definitions of these surgeries were based on a meta analysis published by Leach et al.[7] A separate decision tree was developed for each surgery-collagen comparison in the initial evaluation. Probabilities for the success of surgery came from the meta analysis,[7] while probabilities for the success of collagen came from published case series and expert opinion.[14] Probabilities for the incidence of surgery- or collagen-related complications came from case series.

The initial economic evaluation was conducted from the 'healthcare system' perspective, which required the collection of data on resources used by the public healthcare provider to treat SUI with surgery or collagen. This included resources that incurred direct costs for the Ministry of Health (e.g., physician services, lab tests), but not resources that incurred costs for patients (e.g., hospital parking) or society (e.g., lost productivity due to recuperation from treatment).

In the updated economic evaluation, all probabilities came from the RCT, Table 1.[12] Patients who were randomized to surgery in the trial were analyzed as one group and there were no subgroup analyses by type of surgery. Consequently, probabilities of success were not provided for specific operations in the RCT.

Treatment success in the initial and updated economic evaluations was defined to match the definition of the primary outcome in the RCT, namely a negative 24 hour pad test at 1 year post-treatment.

In the updated economic evaluation, probabilities of treatment success were based on the intention-to-treat results from the RCT. The time horizon for the economic evaluation was the 1 year period post-treatment.

TABLE 1. **Probabilities from surgery collagen incontinence trial**

	Surgery		Collagen	
	Probability	**95% confidence interval**	**Probability**	**95% confidence interval**
Success				
Intention-to-treat	0.55	0.43 to 0.67	0.52	0.39 to 0.64
Complications				
Complete retention	0.20	NR	0.05	NR
Transient difficulty voiding	0.53	NR	0.55	NR
Urinary infection	0.09	NR	0.00	NR
Transient hematuria	0.18	NR	0.40	NR

NR = not reported.
Source: Corcos J, Collet JP, Shapiro S, Herschorn S, Radomski SB, Schick E, Gajewski JB, Benedetti A, Macramallah E, Hyams B. Multicentre randomized clinical trial comparing surgery and collagen injections for treatment of female stress urinary incontinence. Urology 2005;65(5):898-904.

Cost data from the initial economic evaluation were used in the updated evaluation, although the cost of surgery in the updated evaluation was calculated as a weighted average of the cost of the three surgeries in the initial economic analysis. The weights were based on the proportion of patients in the RCT who received each type of surgery.

The results of the economic evaluations were reported as incremental cost effectiveness ratios (ICERs), with the numerator being the difference in expected cost between surgery and collagen and the denominator being the difference in the probability of success between the two treatments. The general form of the ICERs was as follows:

$$\text{ICER} = \left[\frac{\text{Surgery}_{\text{expected cost}} - \text{Collagen}_{\text{expected cost}}}{\text{Surgery}_{\text{probability of success}} - \text{Collagen}_{\text{probability of success}}} \right]$$

Differences in cost were divided by differences in success to obtain costs-per-success of surgery versus collagen.

Two sets of ICERs were calculated in the initial and updated economic analyses. Base case ICERs were computed using a single value for each cost and probability; these ICERs are said to represent the 'average' female with SUI. The second set of ICERs was calculated after the costs and probabilities were allowed to vary in sensitivity analyses (see below). Both sets of ICERs were calculated separately for the provinces of Ontario and Quebec.

One-way and probabilistic sensitivity analyses were used to investigate uncertainty in the base case ICERs. One-way sensitivity analysis involves varying each probability or cost estimate in the base case one at a time to examine the impact on results.[15]

One-way sensitivity analyses were performed on treatment success and complication rates, length of hospital stay for surgery, and the mean number of collagen injections. Point estimate success rates were varied by the 95% confidence intervals reported in the RCT. Complication rates were varied by adding or subtracting 0.05 from the point estimate probabilities reported in the RCT (lower bounds were truncated at 0.00 when subtraction led to a probability of < 0.00). Length of stay was reduced to 1 day, and the mean number of collagen injections was changed from a combination of two for treatment successes and four for treatment failures in the base case to the following success/failure combinations: two/five, three/four, three/five.

While one-way sensitivity analysis can be used to highlight the impact of variables that have a strong influence on the results, it does not account for the fact that several variables usually act simultaneously to determine an ICER. Probabilistic sensitivity analysis is a method of accounting for all of this variability at once by assigning a distribution (e.g., normal, beta, gamma) to all of the parameters in the decision tree.[13] When expected costs are calculated, a computer simulation will select a value at random from the distribution associated with each parameter. Thus, unlike the base case calculation of expected costs, which use point estimates of probabilities and costs and therefore will always produce the same results, the calculation of expected costs using distributions will be likely to produce a different result each time the model is run. A model run 10,000 times will produce as many as 10,000 ICERs. These ICERs may be plotted on a cost effectiveness plane,[15] which is used to depict the differences in cost and effectiveness between competing treatments.

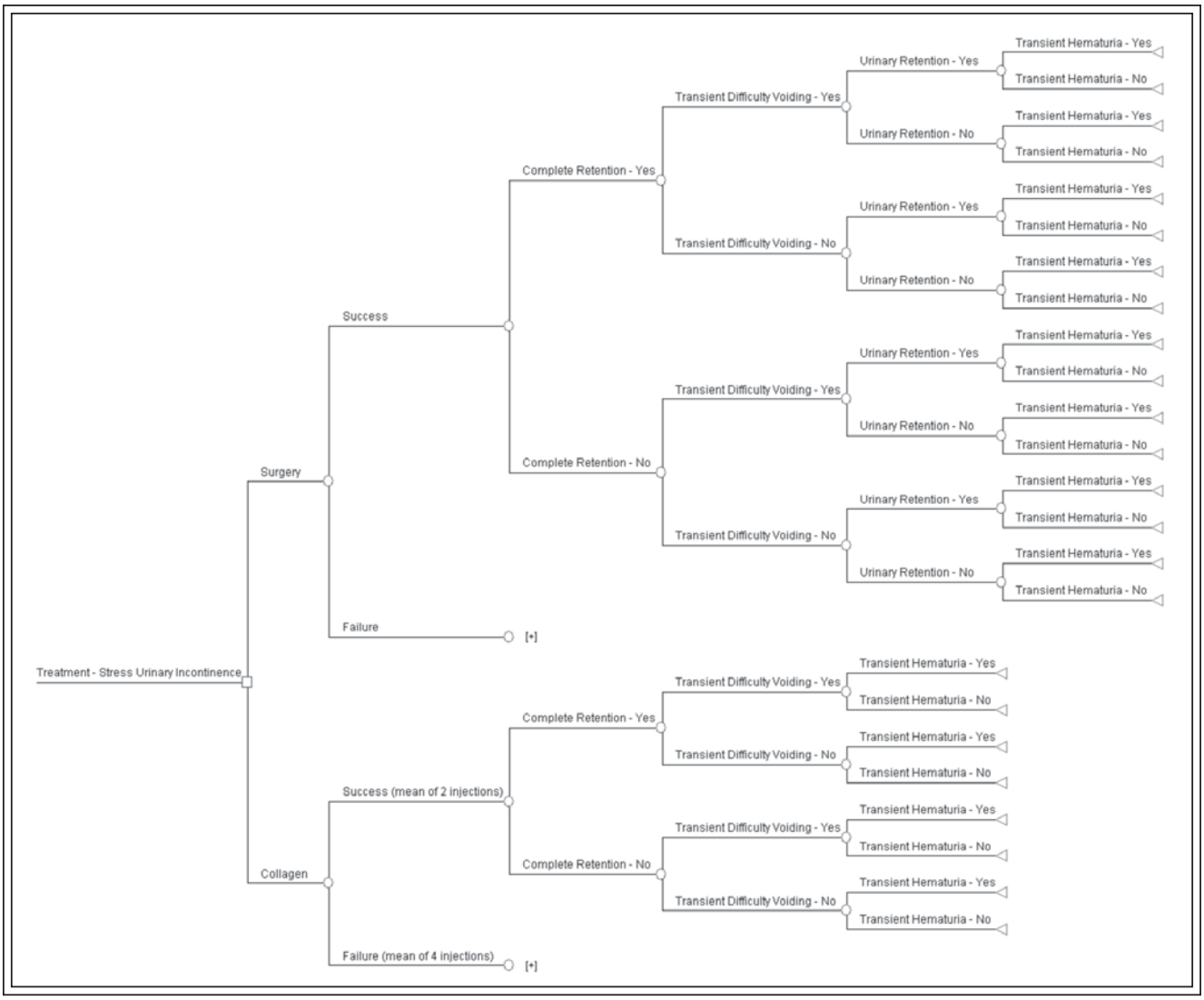

Figure 1. Decision tree – updated economic analysis of surgery versus collagen injection to treat female stress urinary incontinence.
[+] = Hidden subtree that is equivalent to the subtree emanating from the 'success' branch immediately above.

For the probabilistic sensitivity analysis, a Monte Carlo simulation with 10,000 iterations was used to obtain one ICER per iteration.[16] The distributions (e.g., normal) assigned to each of the variables in the probabilistic sensitivity analysis are available from the authors upon request. ICERs were plotted on cost effectiveness planes.

All cost data are reported in 1998 Canadian dollars, which was the currency used in the initial economic analysis. Using monthly Consumer Price Index data, dollar values from 1998 can be multiplied by 1.27 to obtain the equivalent value in 2010 dollars.[17] Data 3.0 (TreeAge Software Inc., Williamstown, MA), Crystal Ball 7.0 (Decisioneering Inc., Denver, CO), and SAS 9.2 (The SAS Institute, Cary, NC) were used for all analyses. The decision tree that was developed for the updated economic evaluation is shown in Figure 1.

Results

The base case analysis for the updated economic evaluation indicated that surgery had an additional cost-per-success relative to collagen (i.e., ICER > 0). These additional costs were larger in Ontario than Quebec, Table 2.

One-way sensitivity analyses indicated that, in Ontario, surgery remained more costly per success than collagen over all possible ranges of probabilities of success for either treatment. In Quebec, surgery was more costly per success than collagen when the

TABLE 2. **Incremental cost effectiveness ratios (ICERs*)**

	Ontario	Quebec
Base case	$341.35	$121.08
LOS = 1 day	Dominate	Dominate
Injections = 2/5†	$244.59	Dominate
Injections = 3/4†	$238.65	$12.97
Injections = 3/5†	$141.62	$19.46

LOS = length of hospital stay post-surgery;
$ = 1998 Canadian dollars.
*Calculation of ICER: (expected cost surgery – expected cost collagen)/((probability of success surgery – probability of success collagen) x 100). ICER > 0 means surgery is more costly and more successful than collagen. 'Dominate' means surgery is less costly and more successful than collagen.
†Expected number of injections per treatment success/expected number of injections per treatment failure (base case = 2/4).
Notes: Ontario: expected cost of surgery = $3,913; expected cost of collagen = $2,650; Québec: expected cost of surgery = $3,138; expected cost of collagen = $2,690.

probability of success for collagen was above 0.48. When the probability of success for collagen was below 0.48, surgery was less costly per success than collagen (surgery could be said to 'dominate' collagen when it is less costly and more successful than the injectable). The cost-per-success of surgery relative to collagen was unaffected by varying the probabilities of the occurrence of complications. When the length of post-surgery hospital stay was reduced to 1 day, surgery dominated collagen in Ontario and Quebec, Table 2. When the mean number of injections for collagen was varied, ICERs decreased in magnitude relative to the base case, but surgery was still shown to be more successful and more costly than collagen. In one instance in Quebec, though, changing the mean number of collagen injections led surgery to dominate collagen, Table 2.

The probabilistic sensitivity analysis for Ontario showed that a majority of the ICERs were in the northeast quadrant of the cost effectiveness plane (indicating an additional cost per additional success for surgery, Figure 2). Only 5% of all ICERs were in the southeast quadrant of the cost effectiveness plane (where surgery dominates collagen).

Turning to the probabilistic sensitivity analysis for Quebec, a majority of the ICERs were also in the northeast quadrant, Figure 3, but a larger number of ICERs (i.e., 18%) were in the southeast quadrant relative to the Ontario results.

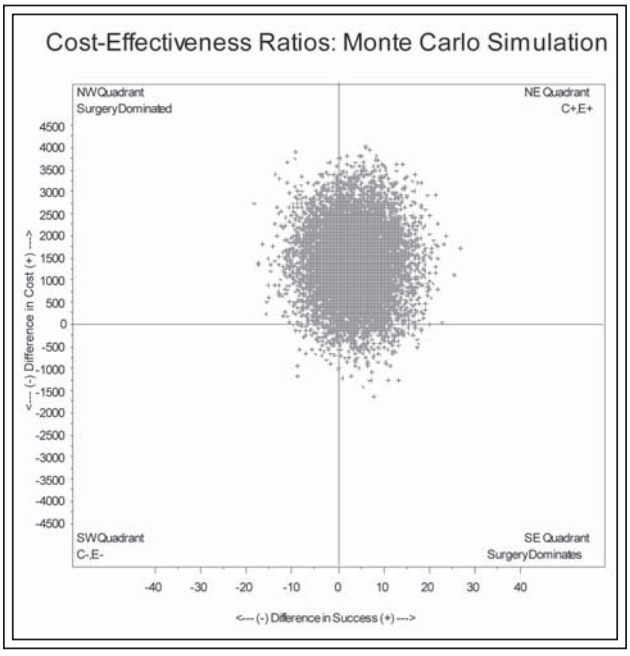

Figure 2. Cost effectiveness plane – surgery versus collagen (Ontario).
C = cost; E = effectiveness; NE = northeast;
NW = northwest; SE = southeast; SW = southwest;
+ = cost or effect of surgery is greater than collagen;
- = cost or effect of surgery is less than collagen.

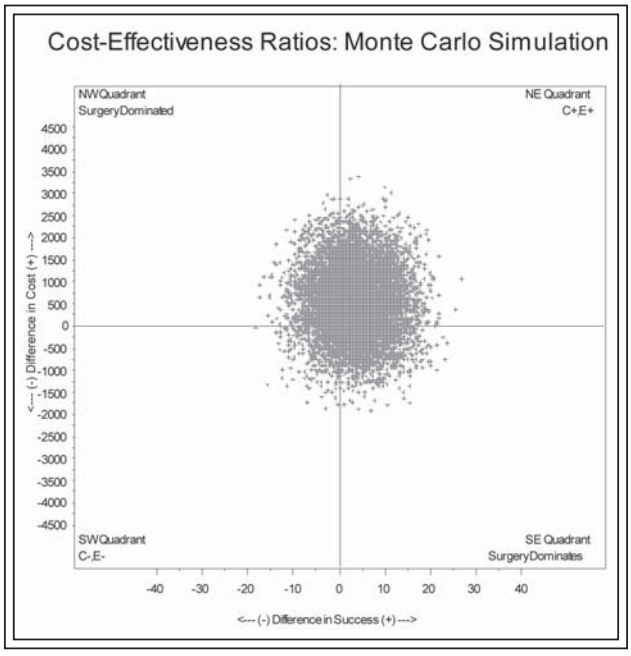

Figure 3. Cost effectiveness plane – surgery versus collagen (Québec).
C = cost; E = effectiveness; NE = northeast;
NW = northwest; SE = southeast; SW = southwest;
+ = cost or effect of surgery is greater than collagen;
- = cost or effect of surgery is less than collagen.

Discussion

Overall, surgery was found to be more costly and more successful than collagen in the base case analyses. The primary factors that would reduce the cost-per-success of surgery were a decreased length of postoperative hospital stay, an increased number of collagen injections, and (in Quebec) a probability of success that is less than 0.48 for collagen. Surgery was more likely to be the optimal treatment choice in Quebec because the cost of surgical procedures for SUI was lower in Quebec than in Ontario.[11] Hence, the ICERs were of a lower magnitude in Québec and more Québec ICERs were located within the southeast quadrant of the cost effectiveness plane.

The results of the updated economic evaluation agree with the findings of the initial cost effectiveness analysis. In the initial analysis, base case results demonstrated that surgery had a higher cost-per-success than collagen (cost-per-success in Ontario: $1,824 to $6,814; cost-per-success in Québec: $1,388 to $3,008).[11] One-way sensitivity analyses in the initial economic evaluation showed that surgery would dominate collagen if the length of postoperative hospital stay was reduced to 1 day or less. Additionally, one type of surgery in each province (Ontario: retropubic suspension; Québec: sling procedure) dominated collagen when three injections were needed to successfully treat a patient or when five injections were used in patients for whom collagen did not work.

The magnitude of the ICERs in the updated economic evaluation was smaller than in the initial evaluation because of the different source of probabilities for the decision tree. Further differences in magnitude may have resulted from the fact that three surgical procedures were modelled as one treatment in the updated evaluation, while these procedures were modelled separately in the initial analysis.

The results of the updated economic evaluation must be considered in light of the fact that they are based on resource use and cost data from 1998. Over time, changing practice patterns may have altered the type or quantity of resources used in the treatment of SUI. These changes would not be reflected in the results of the updated evaluation. Additionally, the updated economic evaluation was conducted using data that were collected prior to the advent of newer surgical procedures such as transobturator or midurethral slings. These slings have supplanted some of the procedures used in the updated economic evaluation.

From a clinical and patient perspective, collagen injection appears to be a viable alternative to surgery because it is an outpatient procedure that does not involve a hospital stay and patients may resume normal activities shortly after leaving the doctor's office. From a health policy perspective, collagen's lower average probability of success relative to surgery, the variable number of injections needed to complete treatment, and the move to reduce lengths of hospital stay postsurgery, suggest there are few (if any) cost savings to be realized by instituting public health coverage of collagen treatment. Although the ICERs in the updated economic evaluation suggested surgery would cost more than collagen for each successfully treated patient, the additional cost increment was rather minimal in comparison to other economic findings in the field of urology. For example, in an analysis of three treatments for overactive bladder—once daily controlled release oxybutynin, immediate release oxybutynin, and twice daily tolterodine—ICERs measuring the cost-per-success of the optimal therapy (controlled release oxybutynin) ranged from $3,079 to $9,326,[18] following conversion from published values in 1999 US dollars to 2009 Canadian dollars.[17,19]

Future investigations of the cost effectiveness of surgery versus collagen injection could focus on time horizons of greater than 1 year. This would allow for an investigation of what might happen to persons in whom treatment fails. The issue is whether these persons should be given a repeat treatment with the same therapy or switched to the other therapy. A recent chart review showed that collagen had some clinical utility as a second line treatment in women with persistent SUI following surgical failure.[20] However, the most cost effective approach to treatment failures is currently unknown. Future investigations should also include treatments such as transobturator and midurethral slings, as well as indirect cost data on lost workplace productivity and leisure time during recuperation.

Conclusion

Collagen injection is an outpatient procedure without risk of significant morbidity or complications. However, this does not readily translate into a clear cost effective advantage relative to surgery. In some cases, surgery may be more cost effective than collagen injection in the treatment of female SUI. □

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