Case study: Collatamp-G gentamicin-collagen sponge for reducing risk of sternal wound infections

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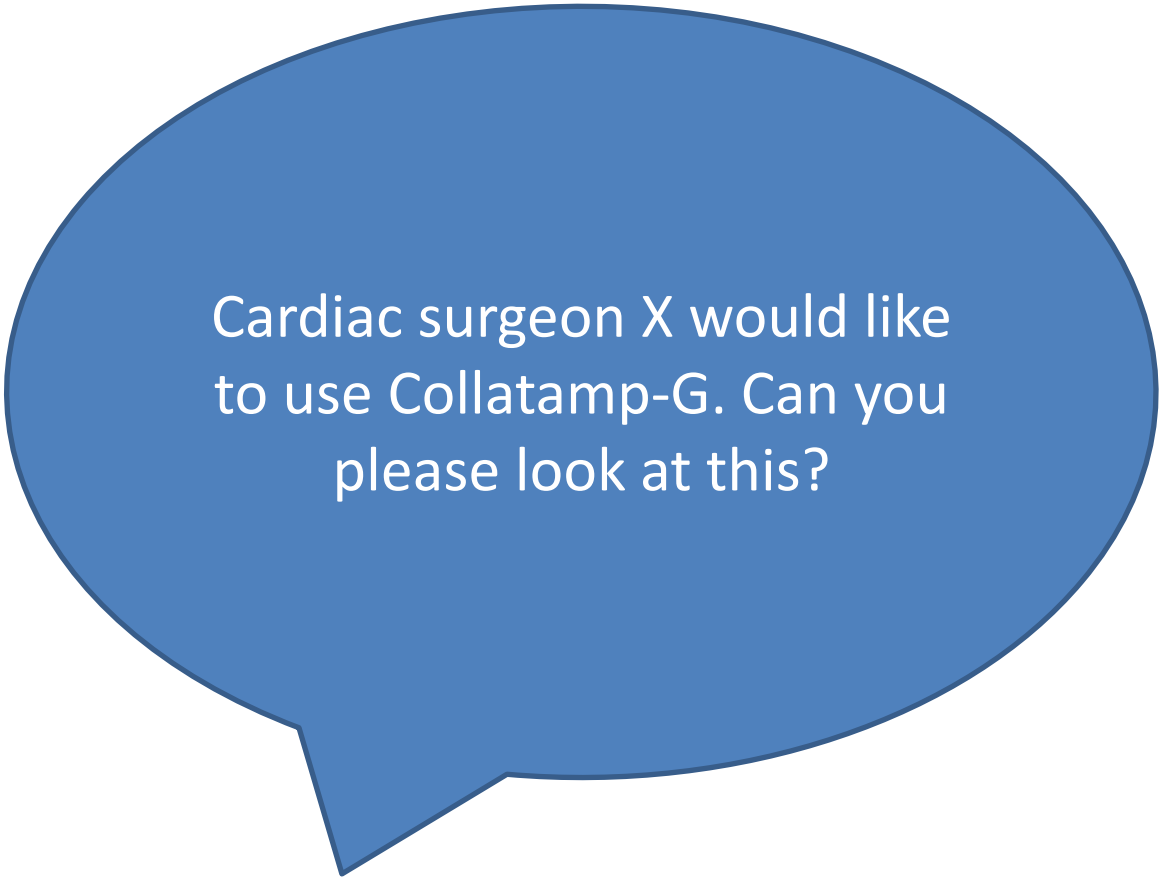
McGill University Health Centre's Technology Assessment Unit

- Established in 2000
- Completed 70+ reports to date
- Requests for HTAs originate from:
  - Cardiology, surgery, neurology, in-house, …
- TAU has 3 full-time research personnel (with degrees in Epidemiology, Health Economics and Medicine), 2 part-time senior researchers, 1 administrative technician

Question posed to TAU



Chief of Surgical Mission

Refining the question

- Health professional who requested the technology asked to complete a request form for a Health Technology Assessment explaining
  - What is the technology?
  - What is the target population?
  - What is the advantage to the hospital?
  - Is it already in the hospital?
  - Can you share key articles? Or keywords to aid in a literature search?
  - Who is our local expert?

Refining the question

- Carry out scoping search based on request form
- Consult with local expert (the cardiac surgeon) to make sure to understand local perspective
- Rephrase the question in terms of:
  - Efficacy: Does this technology work?
  - Effectiveness: Will it work in our hospital?
  - Safety: Are there any important safety concerns?
  - Cost: What is the budget impact? Cost-utility?

Refining the question on Collatamp-G

- The technology: Collatamp-G:
  - a type of gentamicin-loaded collagen sponge (GCS) that can be inserted in the wound at the time of surgery
  - Reported to reduce risk of sternal wound infections
- The target: Sternal wound infections (SWIs) are associated with serious morbidity and increased hospitalization costs due to prolonged length of stay
- The population of interest: All cardiac surgery patients, though possible a sub-group will benefit most

Burden of Sternal Wound Infection at McGill University Health Centre (MUHC) in 2008-2009

Type of sternal wound infection	n (%)	ICU stay (days) Median	Ward stay (days) Median
Superficial sternal wound infection	13 (1.4%)	1	15
Deep sternal wound infection	11 (1.2%)	2	32
Mediastinitis (no re-operation)	5 (0.5%)	3	28
Mediastinitis (required re-operation)	13 (1.4%)	6	35
No sternal wound infection	893 (95.5%)	1	5
TOTAL	935 (100%)		

Refining the question on Collatamp-G

- Is there evidence that Collatamp-G or a similar GCS is an efficacious, effective, safe and cost-effective intervention to reduce risk of sternal wound infections?

- Is there any advantage to using GCS in a sub-group of patients at high risk of SWI? What would be the characteristics of this sub-group?

Specific objectives for HTA

i. To systematically review the literature on efficacy of GCS in preventing SWI

ii. To review literature on risk factors for SWI

iii. To estimate frequency of SWI at the MUHC and influence of putative risk factors

iv. To determine the budget impact and cost-utility of GCS in the MUHC setting

Methods

- Systematic literature search of major online databases of medical literature, HTA reports
- Study quality was assessed using standard scales
- Meta-analysis models were used to combine risk ratios across selected randomized controlled trials (RCTs)
- Review of literature on risk of SWI. Carried out nested case-control study at MUHC
- Cost analysis and cost-utility analysis

Results of literature review

- We identified two RCTs and two cohort studies on efficacy of GCS
  - All studies reported a reduction in risk of SWI following use of GCS, with an average reduction in absolute risk ranging from 1.15% to 5.30%
  - Only 1 high quality RCT. It concluded that benefit was only for superficial SWI

Results of literature review

First author, Year	Sample size Control/GCS	Jadad Score for RCTs	Type of Infection	Sternal wound infection n (%)	
				Control	Intervention
Friberg, 2005	967/983	5	All SWI Superficial SWI Deep SWI Mediastinitis	87 (9.0%) 55 (5.68%) 17 (1.75%) 15 (1.55%)	42 (4.3%) 19 (1.93%) 10 (1.01%) 13 (1.32%)
Eklund, 2005	270/272	3	All SWI Superficial SWI Deep SWI Sternum osteitis Mediastinitis	16 (5.9%) 8 (2.96%) 2 (0.74%) 1 (0.37%) 5 (1.85%)	11 (4.0%) 6 (2.21%) 2 (0.74%) 0 (0%) 3 (1.10%)
Schersten, 2007	935/1091	-	Mediastinitis	18 (1.9%)	8 (0.75%)
Friberg, 2009	967/1359	-	All SWI Superficial SWI Deep SWI Mediastinitis	87 (9.0%) 55 (5.68%) 17 (1.75%) 15 (1.55%)	50 (3.7%) 30 (2.20%) 6 (0.44%) 14 (1.03%)

Results of meta-analysis

Outcome	Overall risk ratio from meta-analysis* [95% Confidence Interval]
Any SWI	0.51 [0.37; 0.70]
Superficial SWI	0.44 [0.21; 0.90]
Deep SWI	0.62 [0.30; 1.28]
Mediastinitis	0.79 [0.41; 1.52]

Results of meta-analysis

Thus, the beneficial impact of GCS depends on the baseline risk of SWI, and the proportion of superficial SWI

Other results from literature review

- From other studies, correspondence with Friberg
  - Higher SWI risk observed due to follow-up being extended beyond the end of the first admission
  - Among high SWI risk patients, benefit of GCS is at all levels of infection
  - Cost analyses suggest cost was reduced in GCS compared to control patients

Safety of GCS

- One study found that early reoperation due to bleeding was more common in the GCS group (4.0% vs. 2.3%, p=0.03).

- No other side effect or complication was reported regarding GCS use

Risk factors for sternal wound infection

- Based on the literature, the main risk factors for SWI are diabetes, obesity, COPD and smoking. All appear to increase SWI risk more than two fold.

- Three of these appear to be risk factors in MUHC patients as per our nested case-control study

	Prevalence			
	Diabetes	Obesity	COPD	Smokers
Matched controls (n=42)	19%	7%	7%	31%
SWI cases (n=42)	62%	9.5%	2%	41%
Risk ratio (95% CI)	6.9 (2.6, 18.6)	1.4 (0.3, 6.5)	0.3 (0.03, 3.2)	1.5 (0.6, 3.7)

Assumptions for cost-utility analysis

- 20% of cardiac surgery patients are at high risk for SWI (based on nested-case control study and expert input)
- Risk is doubled among these patients
- Costs:
  - GCS: $400/patient
  - ICU $1,200/day
  - Surgical ward $400/day
- Estimates of efficacy of GCS obtained from meta-analysis

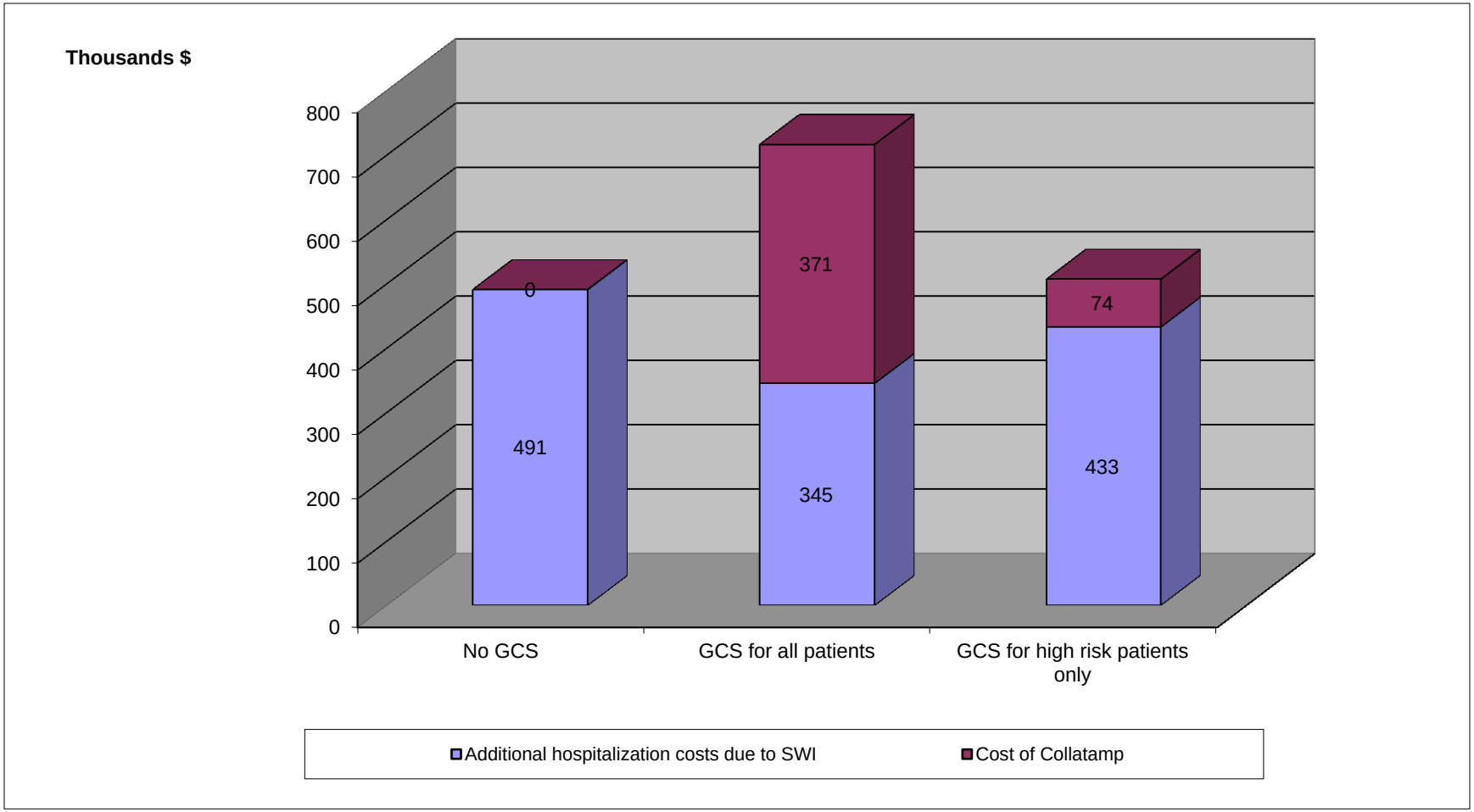
Cost of SWI

Type of sternal wound infection	Cost per patient
Superficial SWI	$4,175
Deep SWI	$12,490
Mediastinitis (without re-operation)	$12,038
Mediastinitis (with re-operation)	$18,614

Results of cost analysis

Scenario	Gross cost	Budget impact
GCS for all patients	$716,470	$225,460
GCS for high risk patients only	$506,954	$15,944

Illustration of budget impact



Results of cost-utility analysis (cost per SWI prevented)

Scenario (comparison is no GCS for all patients)	Cost-utility ratio
GCS for all patients	$15,031 per SWI prevented
GCS for high risk patients only	$2,657 per SWI prevented

Recommendations

- Though promising, evidence of the benefit of GCS is insufficiently strong to justify a recommendation that it should be used on a permanent ongoing basis.

- However, the evidence of possible benefit and the likelihood that it may lower hospital costs enough to largely offset the costs of its use strongly suggests that an effort to procure better evidence would be justified.

- The Department of cardiac surgery should be encouraged to conduct research with two objectives:
  1) To determine the risk factors predictive of SWI at the MUHC and their frequency, and
  2) To determine the effectiveness of GCS in lowering the incidence of SWI through an RCT.

Timeline

- Report requested on June 4, 2009 by Administrative Director, Surgical Mission, MUHC
- Work commenced: June 11, 2009
- Completed: November 6, 2009
- Approved: December 1, 2009

Peculiarities of hospital HTA

- Promising technology. Limited evidence. But, decision required

- Political issues peculiar to hospital HTAs:
  - Technology may be onsite
  - Cost of the technology may be covered in part (e.g. capital costs sponsored by private funds but maintenance and cost of disposables are the hospital's responsibility)

- Recommendations need follow-up
  - When follow-up required (e.g. creation of registry or update of literature review), clear path of responsibility is required

Lessons learnt at MUHC TAU

- Keep report brief – but not at the cost of rigour of scientific methods.
  - Use 1:3:30 format and relegate details to Appendix
- Use request form requiring approval by head of department
- Use a report template with items not to be forgotten:
  - Who requested, date of request, details of literature search, budget impact, cost benefit analyses
- Close collaboration with expert
- Executive committee is key in providing peer review and ensuring transparency
- Publish final report on web