Determining the cost effectiveness of peri-operative statin use for preventing adhesion related complications

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Background

- Post-operative adhesions frequently occur following intra-abdominal or pelvic surgery.
- Adhesion related complications (ARCs), such as small bowel obstruction (SBO) or need for adhesiolysis, are a serious public health and economic burden that currently lack successful strategies for prevention.
- Prior in vivo studies in murine models and a recent retrospective cohort study have shown that HMG-CoA reductase inhibitors, i.e. statins, possess anti-fibrotic properties and could serve as a potential novel therapy to prevent ARCs.
- We aimed to assess the cost-effectiveness of peri-operative statin use in order to prevent post-operative ARCs.

Methods

- We employed a Markov Model to assess the cost-effectiveness of peri-operative statin administration in patients undergoing various types of intra-abdominal and pelvic surgeries including:
  - Cholecystectomy
  - Liver surgery
  - Retroperitoneal surgery
  - Appendectomy
  - Colon surgery
  - Hysterectomy
- Two treatment strategies were compared in this model (Figure 1):
  - Statin Exposure : All individuals could either tolerate statins or not, before undergoing the index surgery.
  - Statin Non-exposure: All individuals undergo the index surgery.
- Statin use was assumed to be for 1 month prior to the surgical event.
- Individuals receiving statins had the potential to not tolerate the medication, defined by prior retrospective cohorts.
- For both options, all individuals transitioned to a post-surgery state, continuously exposed to the risk of SBO.
- SBOs could be managed surgically or non-surgically, and recovery from SBO resulted in an increased risk of recurrence.
- SBO related complications included inadvertent enterotomy or mortality.

Model Inputs

- SBO rates in the non-statin arm were surgery specific and derived from the SCAR-3 trial.
- The hazard ratio of an SBO when using statins was derived from our retrospective study.
- Utilities and costs were derived from the Nationwide Inpatient Sample, Truven Redbook, and published estimates.
- Quality adjusted life-year (QALY) estimates were derived from previously published estimates.

Analyses

- Mean costs, quality adjusted life years (QALYs), and incremental cost-effectiveness ratios (ICERs) were calculated via First order Monte Carlo simulation of 100 trials of 100,000 individuals.
- Willingness-to-pay thresholds of $50,000 were assessed.
- A one month cycle length and time horizon of 1 year was used for all analyses.
- Secondary sensitivity analyses explored 3 and 5 year time horizons.
- Probabilistic and one-way sensitivity analyses were performed varying all transition probabilities, QALYs, and cost estimates by +/-50%.
- Threshold analyses were conducted to determine the specific hazard ratio for statin efficacy at which they would no longer be cost-effective.

Model Structure

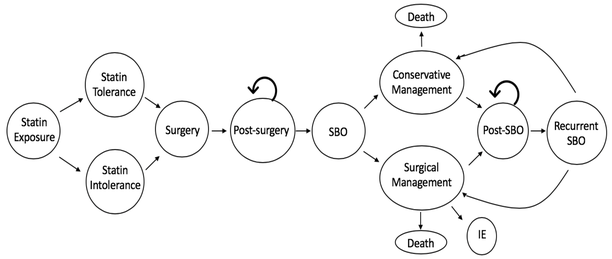

Figure 1: Markov Model structure for stain arm, with option for statin intolerance. The non-statin arm is identical with the exception of statin exposure. SBO, small bowel obstruction; IE, inadvertent enterotomy.

Model Inputs

Table 1. Key model transition probabilities, QALY estimates, and costs.

TRANSITION PROBABILITY	VALUE	SOURCE
Annual rate of SBO following cholecystectomy	0.00254	1
Annual rate of SBO following liver surgery	0.00577	1
Annual rate of SBO following retroperitoneal surgery	0.00904	1
Annual rate of SBO following appendectomy	0.00443	1
Annual rate of SBO following colon surgery	0.01997	1
Annual rate of SBO following hysterectomy	0.00579	1
Statin intolerance	0.0206	4
Surgical management for index SBO	0.199	1
Surgical management for recurrent SBO	0.153	1
30 day Inadvertent enterotomy	0.17518	6
Recurrent SBO	0.019	5
30 day all cause mortality for SBO after conservative management	0.06161	7
30 day all cause mortality for SBO after surgical management	0.06564	7
Hazard ratio for probability of SBO after statin use	0.81	§§
QALY ESTIMATES		
SBO	0.56	8
Inadvertent enterotomy	0.3	9
Disutility of SBO managed surgically compared to surgically	0.1	10,11
Statin intolerance	0.012	12
Index surgery	0.25	13
COSTS (In US dollars)		
Single dose of rosuvastatin 5mg	0.31	14
Appendectomy	41,083.01	15
Cholecystectomy	82,086.37	15
Colon surgery	170,433.50	15
Liver surgery	198,966.50	15
Retroperitoneal surgery	130,326.40	15
Hysterectomy	40,946.86	15
Non-surgical management of SBO	31,712.98	15
Surgical management of SBO	91,884.83	15

Table 1 Caption: Primary inputs related to medications, surgeries, and adverse events in the model.

Results

- Peri-operative statin use yielded both greater QALYs and reduced costs at 1,3, and 5 years compared to non-statin use (Table 2).
- The preference for statin use was only sensitive to variation of model inputs for cholecystectomies, where statins were no longer dominant if intolerance rates increased above 28% the baseline rate, or if the HR for statin efficacy was 0.90 or greater with a 1 year time horizon.

Results

Table 2. Mean costs, efficacy, and incremental cost-effectiveness ratios across surgery types when considering peri-operative statin use at 1, 3, and 5 years.

Surgery Type	Cost (in USD)		Incremental cost	Effectiveness (in QALYs)		Incremental effectiveness	ICER
	Statin exposure	Statin non-exposure		Statin exposure	Statin non-exposure		
Cholecystectomy							
1 year	82,257.78	82,284.58	-26.80	0.9763	0.9762	<0.0001	*
3 years	82,620.53	82,731.75	-111.22	2.8666	2.8664	0.0001	*
5 years	82,963.88	83,152.10	-188.22	4.6234	4.6230	0.0004	*
Liver							
1 year	199,339.91	199,413.60	-73.69	0.9761	0.9761	<0.0001	*
3 years	200,160.78	200,420.57	-259.79	2.8655	2.8652	0.0003	*
5 years	200,932.03	201,362.16	-430.13	4.6211	4.6202	0.0009	*
Retroperitoneal							
1 year	130,906.40	131,026.11	-119.71	0.9759	0.9759	0.0001	*
3 years	132,184.76	132,593.40	-408.64	2.8648	2.8642	0.0006	*
5 years	133,385.47	134,054.69	-669.22	4.6188	4.6174	0.0014	*
Appendectomy							
1 year	41,372.65	41,427.31	-54.66	0.9762	0.9761	0.0000	*
3 years	42,003.82	42,199.28	-195.46	2.8660	2.8657	0.0002	*
5 years	42,600.41	42,930.94	-330.53	4.6219	4.6212	0.0007	*
Colon							
1 year	171,704.75	171,979.32	-274.57	0.9755	0.9753	0.0002	*
3 years	174,469.46	175,351.01	-881.54	2.8617	2.8604	0.0013	*
5 years	177,073.77	178,501.72	-1,427.95	4.6115	4.6086	0.0029	*
Hysterectomy							
1 year	41,318.30	41,394.37	-76.07	0.9761	0.9761	0.0000	*
3 years	42,142.87	42,403.99	-261.12	2.8656	2.8653	0.0003	*
5 years	42,931.16	43,366.93	-435.77	4.6212	4.6203	0.0009	*

* Denotes strong dominance by statin arm. Negative ICERs not presented as per standard modeling convention.

Conclusions

- Based on this cost-effectiveness model, peri-operative statin use would be a cost-effective method to prevent ARCs for most surgeries.
- Future clinical trials are warranted to assess the effectiveness and economic impact of peri-operative statin use to prevent post-operative ARCs.

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