Efficacy and cost-effectiveness of a gentamicin-loaded collagen sponge as an adjuvant antibiotic prophylaxis for colorectal surgery

Report Number 41

April 28, 2010

Report available at www.mcgill.ca/tau/
Invitation.
This document was developed to assist decision-making in the McGill University Health Centre. All are welcome to make use of it. However, to help us estimate its impact, it would be deeply appreciated if potential users could inform us whether it has influenced policy decisions in any way.

E-mail address:

maurice.mcgregor@mcgill.ca  nandini.dendukuri@mcgill.ca
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- **Dr. Barry Stein**
- **Dr. Patrick Charlebois**
  Department of Colorectal Surgery
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  External Consultant – French Translation

TIMELINES

Report requested September 2009 by Gary Stoopler, Administrative Director, Surgery, Medicine, Cancer Care, Mental Health & Women’s Health, MUHC

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<table>
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<th>Abbreviation</th>
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<tr>
<td>AETMIS</td>
<td>L’Agence d’évaluation des technologies et des modes d’intervention en santé</td>
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<tr>
<td>CADTH</td>
<td>Canadian Agency for Drugs and Technologies in Health</td>
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<tr>
<td>CDC</td>
<td>Centers of Disease Control and Prevention, United States</td>
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<tr>
<td>CG</td>
<td>Control group</td>
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<tr>
<td>CoNS</td>
<td>Coagulase-negative staphylococci</td>
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<tr>
<td>CRD</td>
<td>Centre for Reviews and Dissemination, York University, United Kingdom</td>
</tr>
<tr>
<td>CUSM</td>
<td>Centre universitaire de santé McGill</td>
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<tr>
<td>ECIG</td>
<td>Éponges de collagène imbibes de gentamicine</td>
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<td>GCS</td>
<td>Gentamicin-loaded collagen sponge</td>
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<tr>
<td>IG</td>
<td>Intervention group</td>
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<tr>
<td>INAHTA</td>
<td>International Network of Agencies for Health Technology Assessment</td>
</tr>
<tr>
<td>LOS</td>
<td>Length of stay</td>
</tr>
<tr>
<td>NICE</td>
<td>National Institute of Clinical Excellence, United Kingdom</td>
</tr>
<tr>
<td>RCT</td>
<td>Randomized controlled trials</td>
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<tr>
<td>RR</td>
<td>Risk ratio</td>
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<td>SSI</td>
<td>Surgical site infection</td>
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PRINCIPAL MESSAGES

- Gentamicin loaded collagen sponge can lower infection rates after colorectal surgery even in patients receiving prophylactic antibiotic, by an amount that will depend on the base rate.

- Evidence at the MUHC indicates a relatively high base rate.

- It is recommended that the risk of surgical site infection at the MUHC be re-estimated during strict adherence to a standard antibiotic protocol and that routine use of the gentamicin-loaded collagen sponge be re-examined as these details are available.
EXECUTIVE SUMMARY

Background
There is an interest in decreasing the risk of surgical site infections following non-laparoscopic colorectal surgery at the McGill University Health Centre (MUHC). The GI division has proposed the use of gentamicin-loaded collagen sponge (GCS) as an antibiotic prophylaxis.

Objective
Evaluate the clinical efficacy of GCS for the prevention of surgical site infection following colorectal surgery, and to estimate its cost-effectiveness and potential budget impact from the point of view of the MUHC.

Methods
A systematic literature search was performed using major online databases of the medical literature and health technology assessments, with the purpose of identifying studies that estimated the efficacy of GCS. The quality of the selected randomized controlled trials was assessed using the Jadad scale. Results from comparable studies were pooled using meta-analysis.

Results
Clinical Efficacy: Eight randomized controlled trials reporting the use of GCS in colorectal surgeries were identified. These trials covered various types of surgeries including resectable rectal cancer, loop-ileostomy, hernia, flap repair, and pilonidal sinus. Except for two studies of pilonidal sinus, all included studies examined the benefit of GCS over and above the routine use of an oral or intravenous antibiotic prophylaxis. Based on the meta-analysis, there was an average reduction of risk of 56% across the five included trials (Risk ratio 0.44 (95% confidence interval = 0.25-0.75)). GCS also appears to promote surgical wound healing with an average 18% increased chance of healing (pooled risk ratio = 1.18, 95% confidence interval = 0.99-1.40). There were no reports of complications related to the use of GCS.
**Budget impact:** The gross cost per patient of using CGS is estimated to be $600. Assuming 300 procedures per year, the gross annual budget impact would be $180,000. Following this procedure at the MUHC has been estimated at 15% and the cost per patient of a case of surgical site infection following a non-laparoscopic colorectal surgery was estimated at $1,628. With these assumptions, the cost of hospitalization due to surgical site infection would be $488,250. Assuming that the risk of surgical site infection decreases by 56% with GCS use, the number of surgical site infection cases would decrease from 45 to 20 and the total cost of hospitalization of these patients would fall to $217,000. With these assumptions, there would be a net budget saving of $91,250. (Since the liberated beds would undoubtedly be used for other patients this would not result in actual saving but rather in increased efficiency). Sensitivity analyses suggest that in order for GCS to result in a net negative budget impact the initial risk of surgical site infection at the MUHC must be at least 10%.

**CONCLUSIONS**

A gentamicin-loaded collagen sponge appears to be promising in preventing surgical site infection following colorectal surgery, though there is a paucity of high-quality RCTs demonstrating this. It is possible that improved adherence to the oral and intravenous antibiotic protocol at the MUHC might lower the infection rate from the assumed value of 15% to a negligible risk that eliminates the need for further intervention. The cost-effectiveness of GCS depends on the assumed risk of infection.

- There is strongly suggestive evidence that use of gentamicin loaded collagen sponge is capable of lowering surgical site infection rates following colorectal surgery in patients already receiving prophylactic antibiotic treatment.

- The extent of the benefit that can be expected from the use of Collatamp will depend on the base rate of post-operative infections.
When last examined, the use of prophylactic antibiotic for colorectal surgery at the MUHC was below optimal while the base infection rate was high (15%).

RECOMMENDATIONS

- It is recommended that the risk of surgical site infection at the MUHC be re-estimated during a period of strict adherence to a standard antibiotic protocol.

- The routine use of the gentamicin-loaded collagen sponge as an adjuvant antibiotic prophylaxis for colorectal surgery be re-examined as soon as these data are available.
SOMMAIRE

Contexte
Le Centre universitaire de santé McGill (CUSM) est soucieux de diminuer les risques d’infection du site chirurgicale suivant une chirurgie colorectale non-laparoscopique et dans cet ordre d’idée, le service de gastroentérologie a proposé l’utilisation d’éponges de collagène imbibées de gentamicine (ECIG) comme prophylaxie antibiotique.

Objectif
L’objectif de ce rapport est d’évaluer l’efficacité clinique des ECIG pour la prévention des infections du site chirurgicale suivant une chirurgie colorectale et d’évaluer son coût-efficacité ainsi que son impact budgétaire sur le fonctionnement du CUSM.

Méthodologie
Une revue systématique de la littérature fut menée à partir des bases de données importantes de la littérature médicale et de l’évaluation des technologies pour identifier les études évaluant l’efficacité des ECIG. La qualité des études randomisées retenues fut évaluée à partir de l’échelle Jadad. Enfin, les résultats d’études comparables furent regroupés à partir de méta-analyses.

Résultats
Efficacité clinique : Huit études randomisées traitant de l’utilisation des ECIG lors de chirurgies colorectales furent identifiées. Ces études concernaient différentes chirurgies incluant le cancer rectal opérable, l’iléostomie en boucle, la cure d’hernie ou de lambeaux et l’excérèse de sinus pilonidaux. À l’exception de deux études portant sur l’excérèse du sinus pilonidal, toutes les études retenues examinaient les bénéfices des ECIG en sus de l’utilisation routinière de la prophylaxie antibiotique orale ou intraveineuse. Les méta-analyses montrèrent une réduction moyenne des risques de 56% parmi les 5 études retenues (RR 0.44 (95% CI = 0.25-0.75)). Les ECIG semblent aussi favoriser la cicatrisation des plaies chirurgicales en augmentant de 18% les
chances de guérison (RR 1.18 (95% CI = 0.99-1.40)). Aucune complication n’a été rapportée suite à l’utilisation des ECIG.

**Impact budgétaire :** Le coût brut par patient pour utiliser les ECIG est évalué à 600 $. En supposant que 300 procédures par année sont effectuées, l’impact budgétaire brut serait de 180 000 $ par année. Au CUSM, le risque et le coût d’une infection du site chirurgical suite à une chirurgie colorectale non-laparoscopique ont été évalués à 15% et 1 628 $, respectivement, par patient. En se basant sur ces hypothèses, le coût d’hospitalisation suite à des infections du site chirurgical serait de 488 250 $. Si l’on suppose que le risque d’infection du site chirurgical diminue de 56% suite à l’utilisation des ECIG, le nombre de cas d’infection passerait de 45 à 20, avec un coût d’hospitalisation correspondant de 217 000 $. À partir de ces hypothèses, il y aurait des économies budgétaires nettes de 91 250 $. Puisque les lits libérés seraient sûrement utilisés par d’autres patients, ceci ne se traduirait pas par des économies réelles mais plutôt par une augmentation de l’efficacité. Les analyses de sensibilité suggèrent que le risque initial d’infection du site chirurgical soit au moins de 10% pour que l’utilisation des ECIG se traduise par un impact budgétaire négatif au CUSM.

**CONCLUSIONS**

- Il est fortement suggéré que l’utilisation des éponges de collagène imbibées de gentamicine peut diminuer les taux d’infections du site chirurgical suite à une chirurgie colorectale chez les patients déjà sous prophylaxie antibiotique.
- L’importance des bénéfices découlant de l’utilisation du Collatamp dépendra du niveau d’infection post-opératoire existant.
- Selon les dernières données, la prophylaxie antibiotique pour la chirurgie colorectale était sous-utilisée au CUSM tandis que le taux d’infection de base était élevé (15%).
RECOMMANDATIONS

❖ Il est recommandé que le risque d’infection du site chirurgical soit révisé de façon urgente au CUSM suite à une adhésion stricte à un protocole antibiotique standard.
❖ L’utilisation de routine des éponges de collagène imbibées de gentamicine comme adjuvant à une prophylaxie antibiotique pour la chirurgie colorectale doit être réexaminée aussitôt que les données précédentes sont disponibles.
Efficacy and cost-effectiveness of a gentamicin-loaded collagen sponge as an adjuvant antibiotic prophylaxis for colorectal surgery

BACKGROUND
The gastrointestinal lining harbors various groups of normal microflora, which may cause infectious complications if they spread to areas other than their usual sites. There is a high risk of such complications following clean-contaminated surgeries, such as colorectal surgeries. In the 2005 Healthcare Cost and Utilization Project by de Lissovoy et al.\(^1\) (of the United States' Agency for Healthcare Quality and Research) that collected data accounting for 90% of all US hospital discharges, the surgical site infection (SSI) rate for colorectal surgery was estimated at 4.11%, the highest of seven surgical categories studied (including cardiovascular and gastrointestinal).\(^1\) The study by de Lissovoy et al.\(^1\) also indicated an average increase of 8.9 days of hospital stay in SSI patients, which roughly translated into an incremental cost of $17,955.00 per case of SSI to be treated. In 2006-2007, the National Nosocomial Infections Surveillance System (NNIS)\(^2\) in the United States reported the risk of surgical site infection in four groups of colorectal surgery patients defined according to degree of wound contamination, surgical indication, and duration of surgery (See Appendix 1). The risk ranged from 3.57% to 12.88% in the lowest to the highest risk category. Laparoscopic procedures were not included in this report.\(^2\) The report was based on voluntary reporting from nearly 300 US hospitals.

A recent Cochrane review\(^3\) on pre-operative oral or intravenous antibiotic prophylaxis for colorectal surgery, meta-analyzed 182 clinical trials that studied 50 antibiotics (including 17 cephalosporins) in 30,880 patients. Results indicated that the use of any pre-operative antibiotic regimen vs. placebo or no treatment was associated with a relative risk (RR) of 0.3 (95% CI = 0.22-0.41), i.e. it significantly reduced the risk of surgical site infections. Furthermore, combined intravenous and oral antibiotic...
treatment was significantly more effective in lowering infection rate than intravenous or oral administration alone.³

Because of the generally satisfactory prophylactic outcome via the intravenous and oral routes, the usefulness of topical antibiotic has received little attention. A more recent, innovative alternative for antibiotic prophylaxis is the local application of a gentamicin-loaded collagen sponge (GCS), which was first described by Ascheral et al.⁴ in 1986, for the treatment of osteomyelitis. In this report we examine whether the use of GCS can further reduce the risk of SSI over and above the reduction achieved with oral and intravenous antibiotic prophylaxis.

**Gentamicin-loaded collagen (GCS)**
Collatamp-G is the brand name of the GCS manufactured by Schering-Plough Inc. in Canada.⁵ It contains 1.3 mg gentamicin base per cm² of collagen. The same product is marketed in other countries under the names Sulmycin (Austria, Germany), Garacol (the Netherlands), Garamycin Schwamm (Eastern Europe, Switzerland), and Septocoll (Germany), just to list a few. The manufacturer’s (Schering-Plough Inc.’s) product information sheet recommended that up to 3 pieces of Collatamp-G could be used as an adjuvant agent for antibiotic prophylaxis in surgeries.⁵ A recent study indicated serum toxicity (defined at 2mg/L) after 24 hours of application when more than 4 units (Garacol) were used in patients undergoing total hip replacement.⁶
Surgical site infection at the MUHC
The colorectal SSI risk at the MUHC was estimated at 14.5% for 2008-09. The average duration of hospitalization for patients without any infectious complications was 11.5 days (Minimum = 1.8, Maximum = 32), while for patients who had a SSI it was 42.8 days (Minimum = 7, Maximum = 292) (Doris Dubé, MUHC surgical and hospital stay data).

Antibiotic prophylaxis in colorectal surgery at the MUHC
The current protocol of antibiotic prophylaxis requires that the following criteria be met:7

- Appropriate choice of antibiotic: metronidazole + cefazolin or clindamycin + gentamycin (penallergic) (+/- vancomycin if MRSA), ciprofloxacin/metronidazole accepted (protocol);
- Appropriate dose of antibiotic: cefazolin 1-2 g, metronidazole 500 mg, ciprofloxacin 750 mg PO (400 mg IV), vancomycin 1 g, clindamycin 600 or 900 mg;
- Appropriate timing: antibiotic started within 60 minutes prior to incision.
- Intra-operative dose: if surgery lasted more than 3 hours;
- Duration: antibiotics given for a maximum of 24 hours post-operative.

A recent chart review of 72 patients who had undergone colorectal surgeries at the MUHC (April 2008 – June 2009), indicated only 30% had met all criteria of the
protocol. The criteria that were least likely to be complied with were timing of the first dose given to patients (57% non-compliance), and intra-operative dose being given when needed (30% non-compliance).

OBJECTIVE

- To determine the efficacy and safety of a gentamicin-loaded collagen sponge for lowering risk of surgical site infection
- To determine the budget impact of routine use of Collatamp-G, and its cost-effectiveness for lowering risk of surgical site infection

METHODS

A systematic literature search was performed in the Ovid MEDLINE and EMBASE databases. Six major online publishers of health technology assessment (HTA) reports (INAHTA, NICE, AETMIS, Cochrane, CADTH, CRD) were also searched. Keywords used in the search were: “gentamicin,” “collagen,” “infection OR antibiotic prophylaxis,” “colorectal,” and “perineal OR abdominal.” Studies were selected according to the following inclusion criteria:

- clean-contaminated surgery in the colon/rectum/perineal vicinity (see Appendix 2 for a detailed description of types of infections following colorectal surgery)
- duration of operation longer than two hours
- surgery not for upper gastrointestinal tract indications
- not a laparoscopic surgery
- non-urgent surgery

The selected studies were reviewed by both authors. Summary statistics on patients’ age and sex, oral or intravenous antibiotic prophylaxis and post-operative infection rates were extracted from the selected citations. The two primary outcomes of interest were: surgical site infection and wound healing.

Study quality was assessed using the Jadad scale for randomized controlled trials (RCTs). The Jadad score assesses study quality based on whether the study was randomized (1 point) or double blinded (1 point). Additional points are assigned if the
method of randomization and the method of blinding were reported (1 point each), and the reasons for withdrawals and attrition was reported (1 point). Possible values of the Jadad score range from 0 to 5, 0 being the lowest and equivalent to poorest study quality and 5 being the highest and best study quality.

Random effects meta-analysis was performed to pool risk ratios (RR) across comparable RCTs using the inverse-variance method. For the outcome of SSI, a risk ratio less than 1 was interpreted as evidence of a beneficial effect of GCS. For the outcome of percentage of primary healing, a risk ratio greater than 1 was interpreted as evidence of a beneficial effect of GCS.

**CLINICAL RESULTS**

The literature search returned 92 unique citations (Appendix 3). Eight randomized controlled trials, one cohort, and one case-series were retained for analysis and detailed discussion in this report. A variety of different types of colorectal surgeries were considered in these eight studies including resectable colon cancer, repair of anal fistula, loop-ileostomy, hernia, pilonidal sinus, and all types of clean-contaminated elective colorectal surgery.

To estimate the efficacy of GCS over and above routine oral and intra-venous antibiotic prophylaxis, we estimated the pooled risk ratios for the two primary outcomes: post-operative infection rate and percentage of primary healing. We did not include the two studies on surgery for pilonidal sinus in this analysis as antibiotic prophylaxis was not part of their protocol.

**Characteristics of patients in the included studies**

The shortest follow-up period was 1 month and the longest 12 months. All studies used one unit of GCS, except for Gruessner et al., who used three units in patients undergoing abdominoperineal resection for rectal cancer. Patients' average age across the included studies was highly variable due to the difference in the target population for each surgical indication. Most patients were between 40-60 years old, and more than 50% of the patients were male (Table 1).
**Study quality**

The average Jadad score for study quality was 2.4 (range 1-5). Haase et al.’s study\(^{13}\) is the only RCT that achieved the full Jadad score with an adequate and appropriate method of treatment allocation concealment (Table 1).

**Impact of GCS on post-operative surgical site infection, percentage of primary healing, and LOS**

The SSI rate in control groups across the included studies, where routine antibiotic prophylaxis was used, ranged from 2.1% to 21%.\(^{10, 11, 13, 14, 17}\) In the three studies that reported on the primary wound healing rate, the rate in the control group ranged from 35-75% (Table 2).\(^{10, 12, 16}\)

Most of the studies indicated lower SSI rate with the use of GCS,\(^{10-12, 14, 17}\) although most studies had an insufficient sample size with only one study reporting statistical significance.\(^{17}\) The latter had the highest SSI rate of 21% in the control group among all studies (Table 2). The study by Haase et al,\(^{13}\) which had the highest quality score on the Jadad scale, found no benefit due to GCS. The pooled RR for SSI risk across RCTs measuring this outcome was 0.44 (95% CI = 0.25, 0.75) (Figure 1a). When limiting the analysis to only those studies that had a Jadad score of 2 or more (i.e. the studies by Gruessner et al.\(^{10},\) Haase et al.\(^{13}\) and Musella et al.\(^{14}\)) we found that the pooled RR did not change much but was no longer statistically significant (RR 0.42 (95% CI = 0.15, 1.16)). In both analyses, the heterogeneity between studies was relatively low as indicated by the I\(^2\) statistic - 7% when including all studies and 28% when including only higher quality studies.

The study by Gustafsson et al.\(^{12}\) indicated that GCS has no significant impact on the percentage of primary healing at both early (1-3 months) and late (12 months) follow-up after surgical repair of anal fistula. However, when pooled with the study by Gruessner, the overall risk ratio suggested a possible small, beneficial effect (Figure 2).

Both non-RCT studies\(^ {18, 19}\) (Table 3) reported significantly lower SSI rate in the GCS group. In a study\(^ {18}\) from Germany 41 patients who received ileo- or colostomata were prospectively recruited and treated with GCS. This case-series was compared with a historical control group of 77 patients who were similar in terms of age, risk factors
and pre-operative preparation. Among patients who received GCS the SSI rate was 12% compared to 42% in a group of historical controls, (z-test p=0.00173). A cohort study\textsuperscript{19} from an institute in The Netherlands compared patients who received GCS with those who did not over the same 4-year period. The authors reported an SSI rate of 16% in the GCS group vs. 30% in the control group, p=0.0016. In addition, de Bruin et al.\textsuperscript{18} reported significantly higher primary wound healing in the GCS group (84% GCS vs. 43% control, p=0.01).

Finally, with regard to GCS’s impact on hospital length of stay three RCTs found a marginally lower median or mean length of stay in the GCS group\textsuperscript{11, 17}. In the case series of De Bruin et al.\textsuperscript{18} there was a significantly shorter hospitalization in the GCS group (15 vs. 25 days, p=0.04), the control group having a longer mean length of stay that was similar to the value reported in the study by de Lissovoy.\textsuperscript{1}

**Open wound procedures**

Two included studies\textsuperscript{15, 16} investigated the usefulness of GCS for open wound healing and infection prevention in pilonidal sinus.

A 73% primary healing with GCS and wound closure was reported by Holzer et al.,\textsuperscript{15} but the authors failed to provide the result for the control group for comparison. It was also observed that the time to healing was significantly shorter in the GCS group (GCS 17 vs. Control 68 days, p=0.0001). Vogel et al.\textsuperscript{16} reported 35% and 87.5% primary healing in their control and GCS group (p<0.001), respectively. Holzer et al.\textsuperscript{15} reported mean LOS of 9 vs. 10 days for GCS and control groups, respectively.

**Complications and mortality**

No particular GCS-related adverse event was reported in any study. The post-operative complication rate was comparable in the GCS and control groups and ranged from 0% to 37.5% depending on surgery type. The highest rates of post-operative complications were associated with resectable colorectal cancer\textsuperscript{10, 11} and loop-ileostomy.\textsuperscript{13} In general, adverse events or incidence of complications were unrelated to the application of GCS.

One RCT that studied rectal cancer patients reported a significantly lower post-operative complication rate in the GCS group (21% vs. 38%, p=0.0441).\textsuperscript{11} They also
indicated a significantly lower cancer recurrence rate (both local recurrence and metastasis) in the GCS group (14% vs. 32%, p=0.03) at three-year post-operative. However, the authors could not provide a rationale for this result.11

ECONOMIC ANALYSIS

Budget Impact
Each unit of Collatamp-G costs CAD$200. Up to three pieces could be used for one patient.5 Approximately 300 non-laparoscopic colorectal surgeries (including for resectable cancer) are performed annually at the MUHC. Therefore, the upper limit for the gross budget impact due to GCS is roughly CAD$180,000.

Cost-effectiveness analysis
We compared 2 different scenarios (i) No Collatamp use, ii) Collatamp used for all patients based on the following assumptions:

- Number of non-laparoscopic colorectal surgeries/year at the MUHC = 300
- Risk of surgical site infection in colorectal surgery patients following a non-laparoscopic procedure, after adhering to the current antibiotic prophylaxis protocol = 15% (based on MUHC infection rate for 2008-9)
- Number of units of Collatamp needed for each surgery = 3 ($600, based on literature from Schering-Plough)
- Expected reduction in rate of infection = 56% (Figure 1)
- Additional length of stay due to SSI following non-laparoscopic colorectal surgery=31 days (Doris Dubé, Quality Assessment, MUHC)
- Cost of hospitalization on a surgical ward was assumed to be $350/day (Department of Finance, MUHC).
- Increased length of stay was assumed to be the only source of increased cost due to SSI.

The results of the cost-effectiveness analysis are presented in Table 4. Based on these assumptions, the use of Collatamp-G is cost-saving by at least $91,250. This theoretical cost-saving would be due to a reduction in bed usage associated with lower infection
rates. Since the liberated beds would undoubtedly be used for other patients this would not result in actual saving but rather in increased efficiency).

**Sensitivity analysis**

We carried out univariate sensitivity analyses modifying the assumptions regarding: i) the number of GCS units needed (1-4), ii) the expected risk ratio for surgical site infections following Collatamp use (0.3-1), iii) the current risk of surgical site infection at the MUHC in the absence of Collatamp use (0.05-0.25), and iv) increase in length of stay due to surgical site infection (0-60).

The results of the sensitivity analyses are given in Figure 3. We found that there will be a net cost-saving with Collatamp-G provided the risk ratio is 0.6 or lower (i.e. SSI rate is decreased by at least 40%), if the average additional length of hospital stay for infected patients is over 15 days and if the initial risk of surgical site infection remains at 10% or more despite adherence to an oral/intravenous antibiotic prophylaxis protocol. The maximum number of Collatamp-G units that could be used while maintaining cost-saving exceeds the maximum number allowed to avoid serum toxicity as recommended by the manufacturer.

**CONCLUSIONS**

- There is strongly suggestive evidence that use of a gentamicin loaded collagen sponge is capable of lowering surgical site infection rates following colorectal surgery in patients already receiving prophylactic antibiotic treatment.

- The extent of the benefit that can be expected from use of Collatamp will depend on the base rate of post-operative infections.

- When last examined, the use of prophylactic antibiotic for colorectal surgery at the MUHC was below optimal while the base infection rate was high (15%).
RECOMMENDATIONS

- It is recommended that the risk of surgical site infection at the MUHC be urgently re-estimated during a period of strict adherence to a standard antibiotic protocol.

- The routine use of the gentamicin-loaded collagen sponge as an adjuvant antibiotic prophylaxis for colorectal surgery be re-examined as soon as these data are available.
## TABLES

Table 1: Summary of included randomized controlled trials’ study characteristics

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<th>Surgical indication; Wound infection</th>
<th>Target population</th>
<th>Control Group n=; Age, mean/median (range, SD); % Female; Antibiotic Prophylaxis</th>
<th>Intervention Group n=; Age, mean/median (range, SD); % Female; Antibiotic Prophylaxis</th>
<th>Funding source</th>
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<td>Gruessner, 2001; Germany, Austria; 8 weeks; [3]</td>
<td>Rectal cancer, APR; Abdominal/Perineal wound infection;</td>
<td>age≥18, undergoing APR</td>
<td>n=48; Age 63.2 (41-90); NR; Routine: Orthograde intestinal lavage + single dose parenteral 2 g cefazoline + single dose parenteral 500 mg metronidazole</td>
<td>n=49; Age 61.9 (44-83); NR; Routine + 3 Septocoll (5 × 8 cm) fleeces, 210 mg gentamicin base equivalent evenly inserted into sacral wound cavity</td>
<td>NR</td>
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<td>Gustafsson, 2006; Sweden; 12 months; [3]</td>
<td>Anal fistula surgery, advancement flap repair; Percentage of primary healing</td>
<td>Patients scheduled for endoanal advancement flap repair for anal fistula</td>
<td>n=41; Age 46(17-67); 42% ; Routine: Preoperative prophylaxis and/or postoperative treatment (no details provided)</td>
<td>n=42; Age 51 (27-71); 33%; Routine + 1 Collatamp-G (5 × 5 cm), 2.0 mg/cm² gentamicin sulphate) sponge, ½ placed under flap then sutured &amp; ½ placed deep in external wound</td>
<td>Swedish Research Council, project no. K2002-73X-14221-01A</td>
</tr>
<tr>
<td>Haase, 2005; Germany; 1 month; [5]</td>
<td>Loop-ileostomy; Subcutaneous wound infection</td>
<td>Patients undergoing ileostomy</td>
<td>n=40; Age 64.8(9.9); 38%; Routine: Parenteral 1.5 g cefuroxime &amp; 0.5 g metronidazole + Placebo collagen implant</td>
<td>n=40; Age 65.8(11.5); 40%; Routine + 1 gentamycin implant (Sulmycin) placed subcutaneously</td>
<td>NR</td>
</tr>
<tr>
<td>Holzer, 2003; Austria; 24 weeks; [1]</td>
<td>Pilonidal sinus; Time to wound healing; Perineal wound infection</td>
<td>Patients undergoing surgical treatment for pilonidal sinus</td>
<td>n=52; Age 26 (18–53); 12%; No primary closure of wound; wound left to granulate.</td>
<td>N=51; Age 25 (17–67); 18%; 1 Septocoll (5 × 8 cm, 35 mg gentamicin base, Merck Biomaterial GmbH, Darmstadt, Germany)</td>
<td>NR</td>
</tr>
<tr>
<td>Musella, 2001; Italy; 6 months; [2]</td>
<td>Prosthetic repair of groin hernias; Subcutaneous</td>
<td>Groin hernia repairs</td>
<td>n=284; Age 51.4; 5%; Routine: cefriaxone 2 g systemically 1 h before and 12 h later</td>
<td>n=293; Age 53.2; 5%; Routine + 1 Collatamp G placed in front of prosthetic mesh</td>
<td>NR</td>
</tr>
<tr>
<td>Study</td>
<td>Procedure</td>
<td>Intervention</td>
<td>n, Age, and %</td>
<td>Antibiotic Prophylaxis</td>
<td></td>
</tr>
<tr>
<td>----------------------------</td>
<td>----------------------------------</td>
<td>-------------------------------------------------------------------------------</td>
<td>---------------</td>
<td>--------------------------------------------------------------------------------------</td>
<td></td>
</tr>
<tr>
<td>Nowacki, 2005; Poland; 30 days; [1]</td>
<td>Resectable rectal cancer; Perineal wound infection;</td>
<td>Rectal cancer resected by TME technique</td>
<td>n=112; Age 63 (25-89); 46%;</td>
<td>Routine: Intravenous metronidazole 500 mg tid with cefuroxime 1,500 mg tid</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Routine + 1 Garamycin Schwamm (10 × 10 × 0.5 cm): Shering Plough, Kenilworth, NJ, USA, containing 280 mg purified bovine tendon collagen type I and 130 mg gentamicin, placed in the presacral area, always below the peritoneal reflection</td>
<td></td>
</tr>
<tr>
<td>Rutten, 1997; The Netherlands; NR; [1]</td>
<td>Colorectal surgery; Perineal wound infection</td>
<td>Colorectal surgery</td>
<td>n=114;</td>
<td>Routine: Either intravenous ceftriaxone 1g and metronidazole 1g single dose OR gentamicin 120mg and metronidazole 500mg bid within 24hr following induction of anaesthesia</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Routine + 1 Garacol</td>
<td></td>
</tr>
<tr>
<td>Vogel, 1992; Germany; 12 months; [2]</td>
<td>Pilonidal sinus; Primary healing of subcutaneous wound</td>
<td>NR</td>
<td>n=40</td>
<td>No primary closure of wound; wound left to granulate.</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>n=40</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: APR=Abdominoperineal resection; n=Sample size; SD=Standard deviation; IV=Intravenous; CABG=Coronary artery bypass grafting; CG=Control group; IG=Intervention group; NR=Not reported, N/A=Not applicable.

Jadad score 0= poorest quality. Score 5 = highest quality; * 10% of patients in the control group and 16.7% of patients in the treatment group did not receive the routine antibiotic prophylaxis.
Table 2: Summary of clinical outcomes from RCTs

<table>
<thead>
<tr>
<th>First author, year; Country(s); Total n=; Follow-up period</th>
<th>Surgical wound infection, n= (%)</th>
<th>Primary wound healing: Time to healing (days), or n/N (%) healed</th>
<th>Length of hospital stay, day(s) mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Control</td>
<td>Intervention</td>
<td>95% C.I. of group difference</td>
</tr>
<tr>
<td>Gruessner, 2001; Germany, Austria; n=97; 8 weeks</td>
<td>n=10/48 (21%)</td>
<td>n=3/49 (6%)</td>
<td>(0.0089, 0.2872)</td>
</tr>
<tr>
<td>Gustafsson, 2006; Sweden; n=83; 12 months</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Haase, 2005; Germany; n=80; 1 month</td>
<td>n=4/40 (10%)</td>
<td>n=4/40 (10%)</td>
<td>(-0.0799, 0.1854)</td>
</tr>
<tr>
<td>Holzer, 2003; Austria; n=103; 6 months</td>
<td>NR</td>
<td>n=2/51 (3.9%)</td>
<td>-</td>
</tr>
<tr>
<td>Musella, 2001; Italy; n=508; 6 months</td>
<td>n=6/284 (2.1%)</td>
<td>n=1/293 (0.3%)</td>
<td>(-0.0017, 0.0421)</td>
</tr>
<tr>
<td>Nowacki, 2001; n=218; 1 month</td>
<td>n=9/112 (6.4%)</td>
<td>n=6/106 (5.7%)</td>
<td>(-0.0482, 0.0958)</td>
</tr>
<tr>
<td>Rutten, 1997; The Netherlands; n=221; NR</td>
<td>n=21/114 (18.4%)</td>
<td>n=6/107 (5.6%)</td>
<td>(0.0423, 0.2146)</td>
</tr>
<tr>
<td>Vogel, 1992; Germany; n=80; 12 months</td>
<td>Abscess n=20/40 (50%)</td>
<td>Abscess n=3/40 (7.5%)</td>
<td>(0.2321, 0.5810)</td>
</tr>
</tbody>
</table>

*Patients discharged next day of surgery.

**Median (Range).

Abbreviations: n=Sample size; SD=Standard deviation; CG=Control group; IG=Intervention group; NR=Not reported; N/A=Not applicable.
### Table 3: Summary of included non-randomized controlled study characteristics and results

<table>
<thead>
<tr>
<th>First author, Year; Country(s); Study design</th>
<th>Target population</th>
<th>Control group n=; Age, mean(SD); % Female; Treatment</th>
<th>Gentamicin group n=; Age, mean(SD); % Female; Treatment</th>
<th>Study outcome</th>
<th>Control</th>
<th>Gentamicin</th>
<th>Difference (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>De Bruin, 2008; The Netherlands; Case-series</td>
<td>Rectal cancer patients who had received one course of short-term radiotherapy</td>
<td>n=19; Age 71 (10); 36.8%; Routine: amoxicillin with clavulanate 1,000/200mg</td>
<td>n=21; Age 69 (9); 38%; Routine + 3 Garacol (EUSA Pharma, Europe, the Magdalen Centre, Oxford Science Park, UK)</td>
<td>Primary wound healing</td>
<td>9 (43%)</td>
<td>16 (84%)</td>
<td>41% (-4.33%, 55.41%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Superficial wound infection</td>
<td>6 (29%)</td>
<td>2 (11%)</td>
<td>18% (-6.62%, 48.19%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Deep wound infection/abscess</td>
<td>6 (29%)</td>
<td>1 (5%)</td>
<td>24% (2.66%, 49.57%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Hospital stay (days), mean (SD)</td>
<td>25 (18)</td>
<td>15 (8)</td>
<td>13 (4.23, 21.77)</td>
</tr>
<tr>
<td>Fischer, 1996; Germany; Prospective cohort</td>
<td>Patients underwent ileo-/colostomata for various indications</td>
<td>Historical control n=77; Routine: Either - perioperative antibiotic prophylaxis or postoperative antibiotic treatment</td>
<td>n=41; NR; 36.7%; Routine + 1 GCS</td>
<td>Superficial wound infection</td>
<td>32 (42%)</td>
<td>5 (12%)</td>
<td>27% (10.95%, 43.4%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Percentage of primary healing</td>
<td>-</td>
<td>36 (88%)</td>
<td>-</td>
</tr>
</tbody>
</table>

*Article in German, English abstract used for data extraction.

Abbreviations: APR=Abdominoperineal resection; n=Sample size; SD=Standard deviation; IV=Intravenous; CAGB=Coronary artery bypass grafting; CG=Control group; IG=Intervention group; NOS=Newcastle-Ottawa Scale; NR=Not reported, N/A=Not applicable.
Table 4: Summary of cost-analysis

<table>
<thead>
<tr>
<th>Scenario</th>
<th>Expected number of SWI cases per 300 patients</th>
<th>Cost per patient ($)</th>
<th>Budget Impact</th>
<th>Net Budget Impact</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Additional hospitalization due to SWI</td>
<td>GCS</td>
<td></td>
</tr>
<tr>
<td>No GCS</td>
<td>45</td>
<td>$1,628</td>
<td>0</td>
<td>$488,250</td>
</tr>
<tr>
<td>GCS for all patients</td>
<td>20</td>
<td>$723</td>
<td>600</td>
<td>$397,000</td>
</tr>
</tbody>
</table>
FIGURES

Figure 1a: Pooled risk ratio for SSI in RCTs of colorectal surgery

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>GCS Events</th>
<th>Control Events</th>
<th>Total Events</th>
<th>Weight</th>
<th>Risk Ratio IV, Random, 95% CI</th>
<th>Risk Ratio IV, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gruessner 2001</td>
<td>3</td>
<td>49</td>
<td>10</td>
<td>48</td>
<td>18.0% 0.29 [0.09, 1.00]</td>
<td></td>
</tr>
<tr>
<td>Haase 2005</td>
<td>4</td>
<td>40</td>
<td>4</td>
<td>40</td>
<td>15.8% 1.00 [0.27, 3.72]</td>
<td></td>
</tr>
<tr>
<td>Musella 2001</td>
<td>1</td>
<td>293</td>
<td>6</td>
<td>284</td>
<td>6.4% 0.16 [0.02, 1.33]</td>
<td></td>
</tr>
<tr>
<td>Nowacki 2005</td>
<td>6</td>
<td>106</td>
<td>9</td>
<td>112</td>
<td>26.2% 0.70 [0.26, 1.91]</td>
<td></td>
</tr>
<tr>
<td>Rutten 1997</td>
<td>6</td>
<td>107</td>
<td>21</td>
<td>114</td>
<td>33.6% 0.30 [0.13, 0.73]</td>
<td></td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>595</td>
<td>598</td>
<td></td>
<td>100.0%</td>
<td>0.44 [0.25, 0.75]</td>
<td></td>
</tr>
<tr>
<td>Total events</td>
<td>20</td>
<td>50</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: Tau² = 0.03; Chi² = 4.32, df = 4 (P = 0.36); I² = 7%
Test for overall effect: Z = 3.01 (P = 0.003)

IV: Inverse Variance method

GCS: Gentamicin-Collagen Sponge; IV: Inverse Variance method

Note: A risk ratio for surgical site infection that is less than 1 indicates beneficial effect of GCS.

Figure 1b: Pooled risk ratio for SSI, including only studies with a Jadad score of 2 or more

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>GCS Events</th>
<th>Control Events</th>
<th>Total Events</th>
<th>Weight</th>
<th>Risk Ratio IV, Random, 95% CI</th>
<th>Risk Ratio IV, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gruessner 2001</td>
<td>3</td>
<td>49</td>
<td>10</td>
<td>48</td>
<td>42.4% 0.29 [0.09, 1.00]</td>
<td></td>
</tr>
<tr>
<td>Haase 2005</td>
<td>4</td>
<td>40</td>
<td>4</td>
<td>40</td>
<td>38.7% 1.00 [0.27, 3.72]</td>
<td></td>
</tr>
<tr>
<td>Musella 2001</td>
<td>1</td>
<td>293</td>
<td>6</td>
<td>284</td>
<td>18.9% 0.16 [0.02, 1.33]</td>
<td></td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>382</td>
<td>372</td>
<td></td>
<td>100.0%</td>
<td>0.42 [0.15, 1.15]</td>
<td></td>
</tr>
<tr>
<td>Total events</td>
<td>8</td>
<td>20</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: Tau² = 0.22; Chi² = 2.78, df = 2 (P = 0.25); I² = 28%
Test for overall effect: Z = 1.69 (P = 0.09)

IV: Inverse Variance method

GCS: Gentamicin-Collagen Sponge; IV: Inverse Variance method

Note: A risk ratio for surgical site infection that is less than 1 indicates beneficial effect of GCS.

Figure 2: Meta-analysis results for post-operative percentage of primary healing

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>GCS Events</th>
<th>Control Events</th>
<th>Total Events</th>
<th>Weight</th>
<th>Risk Ratio IV, Random, 95% CI</th>
<th>Risk Ratio IV, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gruessner 2001</td>
<td>43</td>
<td>49</td>
<td>36</td>
<td>48</td>
<td>79.5% 1.17 [0.96, 1.42]</td>
<td></td>
</tr>
<tr>
<td>Gustafsson 2006</td>
<td>26</td>
<td>42</td>
<td>21</td>
<td>41</td>
<td>20.5% 1.21 [0.83, 1.77]</td>
<td></td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>91</td>
<td>89</td>
<td></td>
<td>100.0%</td>
<td>1.18 [0.99, 1.40]</td>
<td></td>
</tr>
<tr>
<td>Total events</td>
<td>69</td>
<td>57</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: Tau² = 0.00; Chi² = 0.02, df = 1 (P = 0.88); I² = 0%
Test for overall effect: Z = 1.86 (P = 0.06)

IV: Inverse Variance method

GCS: Gentamicin-Collagen Sponge; IV: Inverse Variance method

Note: A risk ratio for post-operative percentage of primary healing that is greater than 1 indicates beneficial effect of GCS.
Figure 3: Change in cost of treating surgical site infections according to different assumptions

- **Hospital cost (in 1000 $CAD)**
  - Risk ratio
    - Horizontal line = Cost without Collatamp, $488,250; Sloped line = Cost with Collatamp ∆ with risk ratio
  - Additional length of stay due to SSI (day)
    - Cost changes with the change in average total days of hospitalization of infected patients –
      - Dashed line = Cost without Collatamp; Solid line = Cost with Collatamp
  - SSI rate
    - Cost changes with the change in the estimated surgical site infection rate at the MUHC –
      - Dashed line = Cost without Collatamp; Solid line = Cost with Collatamp

- **No. GCS unit**
  - Sloped line = Cost with Collatamp ∆ with number of GCS required
APPENDICES
Appendix 1: NNIS risk index

The NNIS risk index\textsuperscript{20} is operation-specific and applied to prospectively collected surveillance data. The index values range from 0 to 3 points and are defined by three independent and equally weighted variables. One point is scored for each of the following when present:

(1) American Society of Anesthesiologists (ASA) Physical Status Classification\textsuperscript{21, 22} of >2 (i.e. a classification of 3: patient has a severe systemic disease that is not incapacitating, 4: Patient with an incapacitating systemic disease that is a constant threat to life or 5: Moribund patient who is not expected to survive for 24 hours with or without operation). The ASA class is a surrogate for the patient’s underlying severity of illness (host susceptibility) and has the advantage of being readily available in the chart during the patient’s hospital stay.

(2) Either contaminated or dirty/infected wound classification, and

(3) Length of operation >T hours, where T is the approximate 75th percentile of the duration of the specific operation being performed.
## Appendix 2: Classification of infection for colorectal surgery [USA Centers of Disease Control and Prevention]

**Operative category:** Colorectal  
**Category description:** **COLO** [Colon surgery: Incision, resection, or anastomosis of the large intestine; includes large-to-small and small-to-large bowel anastomosis; does not include rectal operations], **REC** [Rectal surgery: operations on rectum]

### Classification of infectious complications:

<table>
<thead>
<tr>
<th>Category</th>
<th>Description</th>
</tr>
</thead>
</table>
| **Superficial** | A superficial incisional SSI (Primary or secondary) must meet one of the following criteria:  
- Infection occurs within 30 days after the operative procedure  
- Involves only skin and subcutaneous tissue of the incision  
- Patient has at least one of the following:  
  a. Purulent drainage from the superficial incision.  
  b. Organisms isolated from an aseptically obtained culture of fluid or tissue from the superficial incision.  
  c. At least one of the following signs or symptoms of infection: pain or tenderness, localized swelling, redness, or heat, and superficial incision is deliberately opened by surgeon, and is culture-positive or not cultured. A culture-negative finding does not meet this criterion.  
  d. Diagnosis of superficial incisional SSI by the surgeon or attending physician. |
| **Deep** | A deep incisional SSI (Primary or secondary) must meet one of the following criteria:  
- Infection occurs within 30 days after the operative procedure if no implant is left in place or within one year if implant is in place and the infection appears to be related to the operative procedure  
- Involves deep soft tissues (e.g. fascial or muscle layers) of the incision  
- Patient has at least one of the following:  
  a. Purulent drainage from the deep incision but not from the organ/space component of the surgical site.  
  b. A deep incision spontaneously dehisces or is deliberately opened by a surgeon and is culture-positive or not cultured when the patient has at least one of the following signs or symptoms of infection: pain or tenderness. A culture-negative finding does not meet this criterion.  
  c. Abscess or other evidence of infection involving the deep incision is found on direct examination, during reoperation, or by histopathologic or radiologic examination. |
d. diagnosis of deep incisional SSI by the surgeon or attending physician.

<table>
<thead>
<tr>
<th>Organ/space</th>
<th>GIT-Gastrointestinal tract (esophagus, stomach, small and large bowel, and rectum) excluding gastroenteritis and appendicitis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Gastrointestinal tract infections, excluding gastroenteritis and appendicitis, must meet at least 1 of the following criteria:</td>
</tr>
<tr>
<td></td>
<td>1. Patient has an abscess or other evidence of infection seen during a surgical operation or histopathologic examination.</td>
</tr>
<tr>
<td></td>
<td>2. Patient has at least 2 of the following signs or symptoms with no other recognized cause and compatible with infection of the organ or tissue involved: fever (&gt;38°C), nausea, vomiting, abdominal pain, or tenderness and</td>
</tr>
<tr>
<td></td>
<td>at least 1 of the following:</td>
</tr>
<tr>
<td></td>
<td>a. organisms cultured from drainage or tissue obtained during a surgical operation or endoscopy or from a surgically placed drain</td>
</tr>
<tr>
<td></td>
<td>b. organisms seen on Gram’s or KOH stain or multinucleated giant cells seen on microscopic examination of drainage or tissue obtained during a surgical operation or endoscopy or from a surgically placed drain</td>
</tr>
<tr>
<td></td>
<td>c. organisms cultured from blood</td>
</tr>
<tr>
<td></td>
<td>d. evidence of pathologic findings on radiographic examination</td>
</tr>
<tr>
<td></td>
<td>e. evidence of pathologic findings on endoscopic examination (eg, Candida esophagitis or proctitis).</td>
</tr>
</tbody>
</table>
Appendix 3. Flow of Included Studies

Potentially relevant citations identified and screened for retrieval (n=92)

Citations excluded, with reasons (n=76)
- Animal study, n=2
- Basic science – biochemistry, n=7
- Basic science – microbiology, n=11
- Basic science – pharmacokinetics, n=2
- Case report, n=4
- Duplicates, n=5
- Irrelevant to colorectal surgery, n=28
- Non-English publication, n=4
- Paediatrics, n=2
- Review irrelevant to colorectal surgery, n=2
- Survey, n=1
- Treatment irrelevant to colorectal surgery, n=9

Citations retrieved for more detailed evaluation (n=15)

RCT (n=8)
- Relevant review, n=1
- GCS as treatment for infection, n=3
- Cohort study – no useful data, n=1

Non-RCT (n=7)
- Citation retained for discussion (n=4)

Citation with relevant information (n=10)
- RCT, n=8
- Cohort study, n=2
- Relevant review, n=1
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treatment in advancement flap repair for anal fistula. Br J Surg 2006;93:1202-
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gentamicin collagen fleece (Septocoll) after surgical treatment of a pilonidal sinus.
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1992;63(9):748-753.

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by local application of a gentamicin-containing collagen sponge. Eur J Surg
1997;Suppl 578:31-35.

(18) de Bruin A, Gosselink M, Wijffels N, Coene P, van der Harst E. Local gentamicin
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(19) Fischer A, Fleck U, Lunstedt B. Local antibiotic prophylaxis of high risk wounds
after closure of colostomata by a collagen sponge loaded with gentamicin [article
in German]. Aktuelle Chirurgie 1996;31(5):312-315.


infection rates by wound class, operative procedure, and patient risk index.
3B):153S-157S.

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