


Financial burden of postoperative complications following colonic resection

A systematic review

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Abstract

Background: Colonic resection is a common surgical procedure that is associated with a high rate of postoperative complications. Postoperative complications are expected to be major contributors to hospital costs. Therefore, this systematic review aims to outline the health costs of postoperative complications following colon resection surgery.

Methods: MEDLINE, Excerpta Medica database, Cochrane, and Economics literature medical databases were searched from 2010 to 2019 to identify English studies containing an economic evaluation of postoperative complications following colonic resection in adult patients. All surgical techniques and indications for colon resection were included. Eligible study designs included randomized trials, comparative observational studies, and conference abstracts.

Results: Thirty-four articles met the eligibility criteria. We found a high overall complication incidence with associated increased costs ranging from \$2290 to \$43,146. Surgical site infections and anastomotic leak were shown to be associated with greater resource utilization relative to other postoperative complications. Postoperative complications were associated with greater incidence of hospital readmission, which in turn is highlighted as a significant financial burden. Weak evidence demonstrates increased complication incidence and costlier complications with open colon surgery as compared to laparoscopic surgery. Notably, we identified a vast degree of heterogeneity in study design, complication reporting and costing methodology preventing quantitative analysis of cost results.

Conclusions: Postoperative complications in colonic resection appear to be associated with a significant financial burden. Therefore, large, prospective, cost-benefit clinical trials investigating preventative strategies, with detailed and consistent methodology and reporting standards, are required to improve patient outcomes and the cost-effectiveness of our health care systems.

Abbreviations: LOS = length of stay, RCT = randomized controlled trial, SIGN = Scottish Intercollegiate Guidelines Network, SSI = surgical site infection, USD = United States dollar.

Keywords: colon surgery, complication, cost, cost analysis

1. Introduction

1.1. Rationale

Cost-effective health care, particularly in the hospital setting, is crucial for the sustainability of our health care systems. On the international level, health care expenditure has increased at a faster annual rate than economy growth between the years 2000

and 2016.^[1] Rising health care costs combined with the continual necessity for high quality care, has resulted in growing demand by policy makers for high quality health economic assessments.

Vonlanthen et al^[2] report that postoperative complications are the strongest indicators of in-hospital costs. These findings were reinforced by a systematic review demonstrating increased hospital costs from surgical complications after major surgery.^[3]

Editor: Young-Kug Kim.

The authors have no funding and conflicts of interest to disclose.

Supplemental Digital Content is available for this article.

The datasets generated during and/or analyzed during the current study are not publicly available, but are available from the corresponding author on reasonable request. The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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How to cite this article: Louis M, Johnston SA, Churilov L, Ma R, Christophi C, Weinberg L. Financial burden of postoperative complications following colonic resection: a systematic review. *Medicine* 2021;100:27(e26546).

Received: 9 January 2021 / Received in final form: 20 May 2021 / Accepted: 14 June 2021

<http://dx.doi.org/10.1097/MD.00000000000026546>

Limitations of this review were that it failed to report colorectal complications. Given that colon resection surgery is a common procedure with a high rate of postoperative adverse events relative to other major surgeries,^[4,5] it is expected to be a major contributor to hospital costs. The development of cost-effective management strategies targeting colon resection surgery is dependent on accurate financial data and a deep understanding of the relationship between postoperative complications and the drivers of increased hospital costs.

1.2. Objectives

The primary aim of this systematic literature review is to outline the health costs of postoperative complications in adult patients who undergo colon resection surgery. We highlight the importance of evaluating the components of healthcare cost profiles relevant to patients undergoing colon resections and consider the quality of the studies with reference to how they measure and report costing data.

2. Materials and methods

2.1. Protocol and registration

We conducted a systematic review of the literature in accordance with Cochrane guidelines^[6] and reported under the guidance of the preferred reporting items for systematic reviews and meta-analyses statement.^[7] The protocol of this review was registered in PROSPERO, an international prospective register of systematic reviews, and is available from: http://www.crd.york.ac.uk/PROSPERO/display_record.php?ID=CRD42019128618. The Austin Health Research Ethics Committee waived the requirement for ethics approval as collection of data did not involve patient contact or patient data.

2.2. Eligibility criteria

We included studies containing a full or partial economic evaluation of postoperative complications in adult patients (≥ 18 years of age) undergoing any form of colonic resection. Colon resection was defined as complete excision of any part of the large bowel (excluding rectum). Studies that did not report the cost of colon resection specifically were excluded.

Eligible study designs included randomized controlled trials (RCTs), non-RCTs, comparative observational studies and conference abstracts. Letters, opinion papers and editorials were excluded. Only studies in the English language were considered and no restriction by country or currency was applied.

Enhanced recovery after surgery^[8] was established globally and adopted by many hospitals as a uniform approach to minimizing variability of perioperative care. Taking this recent advancement into account, we included studies published from January 2010 until February 2019 in order to retrieve up to date cost data.

2.3. Primary outcome

Total hospital costs associated with complications following colonic resection surgery

2.4. Secondary outcomes

(1) The costs of individual complications after colonic surgery (e.g., anastomotic leak, surgical site infection [SSI] etc)

- (2) The association of severity of complications and hospital costs.
- (3) The impact of complication on length of hospital stay, mortality and 30-day readmission rates.
- (4) Costs associated with postoperative complications by surgical technique.
- (5) Costs associated with postoperative complications by indication for surgery.
- (6) Costs associated with postoperative complications by surgical urgency (emergent or elective).

2.5. Information sources and search

A detailed search strategy was constructed based on the topic title. The search was conducted by one author (ML) and applied to Economics literature (EBSCOhost; January 2010–present), MEDLINE (Ovid; 2010 - present), Excerpta Medica database (Ovid; 2010 - present) and The Cochrane Library (Wiley Online Library; 2010 - present). The last search was run on 19/02/2019. The search strategy is described in Table S1, Supplemental Digital Content, <http://links.lww.com/MD2/A259>. Medical subject Headings terms and free-text terms on costs, health economics, colonic resections and complications were used. An additional manual search of the bibliographies of all identified studies and review articles was also performed.

2.6. Study selection

The titles and abstracts of all retrieved studies were screened by 2 authors (ML and SJ) in an independent and blinded manner. The full texts of eligible studies were retrieved and independently evaluated for eligibility by 3 authors (ML, SJ, and LW). Disagreements were resolved by a fourth author (RM) and by consensus.

2.7. Data collection process and data items

Data from included studies was extracted in an independent manner by 2 authors (ML and SJ) into a predetermined data extraction table. Extracted data included study characteristics, colon resection procedure and technique, population demographics, complication incidence, cost of complications, length of stay (LOS), mortality, 30-day readmission, indication for colonic resection, and urgency status. A copy of the data extraction table is presented in Tables S2 and S3, Supplemental Digital Content, <http://links.lww.com/MD2/A260>, <http://links.lww.com/MD2/A261>.

2.8. Risk of bias in individual studies

Risk of bias of the included studies were assessed by 2 authors (ML and SJ) using the Cochrane Collaboration's risk of bias tool to assess randomized controlled trials (RCTs) and the Scottish Intercollegiate Guidelines Network (SIGN) Checklist for Cohort Studies to assess cohort studies. Discrepancies were resolved by consensus following review by a third author (LW).

2.9. Summary measures and synthesis of results

Findings are reported in the form of a narrative synthesis. This is structured around the type of complications and their hospital costs. Cost of complications was derived from either the stated value within the study or by calculation of the cost difference

between the group with and the group without complications. Costs were converted to United States dollar (USD) (\$) based on the annual average conversion rate^[9] of the specified base currency year or the year of publication if a currency year was not reported. Costs were then inflated to February 2019 from January of the specified or assumed cost year using the Bureau of Labor Statistics Consumer Price Index inflation calculator.^[10]

We referenced complication costs to the complication type, complication severity, surgical technique, indication for surgery, surgical urgency, readmissions, mortality, and LOS. A critical review of the data showed significant discrepancies in economic environment and hospital characteristics of the included studies resulting in significant heterogeneity of the studies, therefore a meta-analysis could not be performed.

2.10. Risk of bias across studies

Homogenous effect sizes across studies were unavailable. Therefore, formal assessment of publication bias using a funnel plot was not presented. Each of the reported study's outcomes and results were compared to assess for selective reporting bias.

2.11. Additional analyses

Subgroup analyses were undertaken for resource utilization measure, readmissions, surgical technique, number and severity of complications and type of complication.

3. Results

3.1. Study selection

The search strategy resulted in a total of 2289 articles being sourced. Twelve additional studies were identified by manual searching of bibliographies. Thirty-four articles^[11–44] met the eligibility criteria. The preferred reporting items for systematic reviews and meta-analyses flow diagram^[7] representing the selection of studies is presented in Figure 1.

3.2. Study characteristics

All included studies were reported in English and had publication dates between 2010 and 2018. Thirty-one studies were retrospective cohort studies,^[11–13,15–28,30–33,35–44] with the remaining studies consisting of a cross-sectional cohort study,^[34] an RCT^[29] and a randomized clinical trial^[14]. Twenty-five studies were full reports^[11,12,14,16–20,22,24,25,27–29,31,32,34,35,37,38,40–44] and 9 were conference abstracts.^[13,15,21,23,26,30,33,36,39] Study characteristics and outcome measures are presented in Tables S2 and S3, Supplemental Digital Content, <http://links.lww.com/MD2/A260>, <http://links.lww.com/MD2/A261>.

3.3. Population

Number of participants ranged from 46 patients^[29] to 217,939 patients.^[41] Reported mean and median patient age ranged from 49.9 years^[24] to 78.5 years.^[43] Most studies incorporated broad inclusion criteria, including all colon resections performed within the specified time frame. Details on patient demographics are presented in Table S2, Supplemental Digital Content, <http://links.lww.com/MD2/A260>.

3.4. Primary outcome

Twenty-one studies^[11,13,15–22,25–28,33,36,38–41,44] evaluated cost of complications in colonic resection as one of their key outcomes. Thirteen articles^[12,14,23,24,29–32,34,35,37,42,43] did not study the cost of complications as a key outcome but contained sufficient complication and financial data to meet inclusion criteria.

3.5. Defining currency

Twenty-nine studies^[11–13,15–25,27,28,30–34,36–38,40–44] reported costs using USD (\$), three used Euro (€)^[14,26,29] and one used New Zealand Dollars (\$) ^[35]. One study^[39], a conference abstract, did not report the currency used. This was assumed to be USD due to the study being conducted in New York, USA. Only 8 studies^[16–18,27,31,34,40,41] reported the base currency year.

3.6. Defining hospital resource utilization

Nineteen studies^[11,13–15,17,19–22,25,28–30,32,33,35,36,40,41] reported hospital costs, with twelve studies^[12,16,23,24,27,31,34,38,39,42–44] reporting total hospital reimbursements, two studies^[18,37] reporting hospital charges and one study^[26] reporting negative Diagnosis Related Groups based cost coverage. Where multiple hospital resource utilization measures were reported, hospital costs were extracted. The definition of hospital resource for each study is presented in Table S2, Supplemental Digital Content, <http://links.lww.com/MD2/A260>.

3.7. Risk of bias within studies

Thirty-one out of the thirty-four included studies were retrospective cohort studies with their retrospective nature preventing them from being considered “high quality” evidence based on the SIGN cohort study checklist. All twenty-two retrospective cohort full paper publications^[11,12,16–20,22,24,25,27,28,31,32,35,37,38,40–44] were of “acceptable quality” with clear focused research questions. The risk of bias in the nine conference abstracts^[13,15,21,23,26,30,33,36,39] was not formally assessed due to the incomplete nature of their reporting. The cross-sectional cohort study^[34] was deemed of “acceptable quality” as it is classified as a database study by the SIGN cohort study checklist. The overall risk of bias for the randomized controlled^[14] and the randomized clinical trial^[29] was judged to be low with satisfactory randomization and no evidence of selection bias.

3.8. Risk of bias across studies

Noninclusion of grey literature in this review may have resulted in publication bias. In addition, inclusion of studies only in the English language may have resulted in a language bias. The principally objective nature of the financial and clinical outcomes assessed in this review makes outcome measurement an unlikely bias. Conference abstracts are at a high risk of selective reporting bias and this was considered in our data synthesis.

Synthesis of results: all costs are presented as: study reported costs (adjusted USD cost).

3.9. Incidence and cost of complications

Postoperative complication incidence varied greatly between the studies ranging from 6.0%^[32] to 66.0%^[35] (Fig. 2). This variance can be attributed to the different definitions of complications

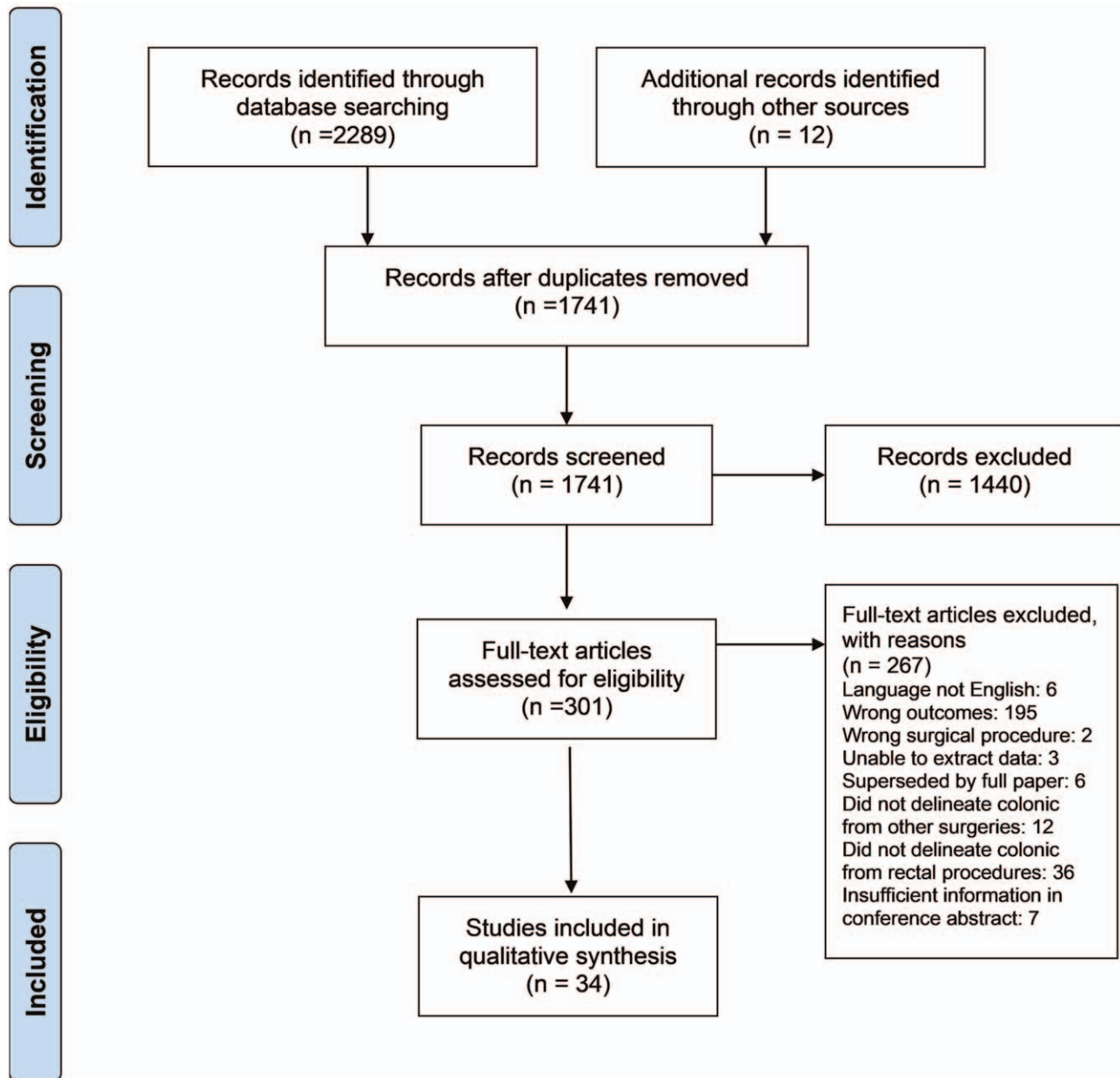


Figure 1. PRISMA flow diagram summarizing the study selection process of the systematic review. PRISMA = preferred reporting items for systematic reviews and meta-analysis.

adopted by the studies. Studies reporting hospital costs were analyzed separately to studies reporting hospital charges or hospital reimbursements. Postoperative complications resulted in a substantial increase in hospital costs across all studies (Fig. 3). The additional costs of complications varied from €1478.63 [\$2290]^[14] to \$39,306 [\$43,146],^[21] this is in part due to the heterogenous definitions of hospital costs adopted by the different studies as well as the different complication types reported. Asgeirsson et al^[11] and Knechtel et al^[25] further demonstrate a positive correlation between the count of complications and the additional cost incurred by the hospital. All studies reporting hospital charges and hospital reimbursements demonstrated a positive increase in hospital resource utilization with postoperative complications (Table S2, Supplemental Digital Content, <http://links.lww.com/MD2/A260>).

3.10. Complication severity

Asgeirsson et al^[11] demonstrated an increase in the additional cost of SSI from \$22,730 [\$24,563] for superficial SSIs to \$30,733 [\$33,211] for deep SSIs. Fukuda et al,^[18] demonstrated similar increases in hospital charges with increasing SSI severity. Widmar et al^[39] analyzed the impact of complication severity on Medicare reimbursements by utilizing the Clavien-Dindo classification. Thirty-day hospital reimbursements increased from \$3520 [\$3756] for no complication to \$5570 [\$5943] and \$7,610 [\$8119] for grade I and grade II complications, respectively.^[39] There was an exponential rise in reimbursements to \$17,124 [\$18,270] for grade III+ complications.^[39] Despite this, grade I and grade II complications remain a significant health care burden due to their high prevalence rates (29% and 49%, respectively).^[39]

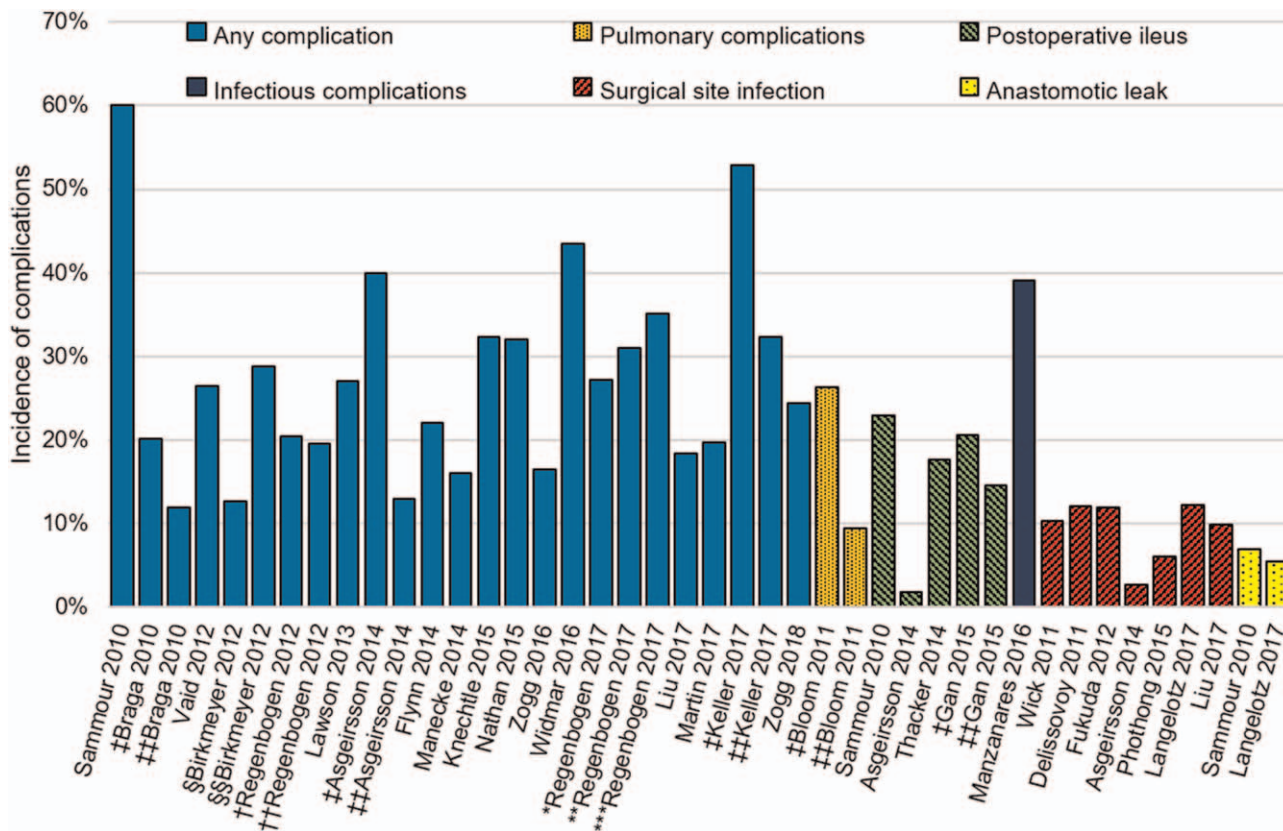


Figure 2. The incidence of postoperative complications (%) following colonic resection surgery, stratified by complication type when available, compared across studies †Open, ‡Laparoscopic; Surgical volume: †Low, ††High; Hospital quality: ‡Lowest, §Highest; Hospital length of stay: * ≤3, ** 4–6, *** ≥7 days.

3.11. Cost by complication type

SSI, postoperative ileus, and anastomotic leak were the most commonly reported postoperative complications. Results and outcome metrics of studies reporting the financial burden of these complications are presented in Table 1. SSI and anastomotic leak were associated with the greatest financial burden amongst postoperative complications in colon resection surgery. The additional hospital cost of SSI varied greatly across studies (Table 1). This significant variation in costs for SSI can be attributed to the geographic differences in health care systems. Asgeirsson et al^[11] was the only study directly comparing SSI with postoperative ileus demonstrating significantly higher additional costs in the presence of SSI than with postoperative ileus (Table 1).

3.12. Cost of surgical technique

Nine studies^[11,13,14,18,19,22,30,37,40] reported the cost of complications in open and laparoscopic surgery, however only one study^[37] compared the two groups as its primary outcome. Postoperative complications in open surgery were shown to be associated with higher hospital costs than postoperative complications in laparoscopic surgery across all included studies except Kashimura et al^[22] (Table S3, Supplemental Digital Content, <http://links.lww.com/MD2/A261>). In addition, the incidence of complications was consistently higher in open surgery as compared to laparoscopic surgery in all studies, but only reached statistical significance in six studies.^[11,18,24,37,38,40]

The risk of selection bias due to the retrospective nature of the studies and existence of uncertainty around the statistical significance of data reported in some studies means that these findings are supported by weak evidence.

3.13. Cost of readmissions

Incidence of readmissions ranged from 6.6%^[23] to 28.4%^[44] with greater readmission rates for patients who experienced postoperative complications in the index admission as compared to patients who had an uncomplicated admission (Fig. 4). Reimbursement for readmissions varied greatly across the studies, from \$1322 [\$1474]^[12] to \$29,802 [\$32,234]^[16] (Fig. 4).

3.14. Length of stay

Postoperative complications resulted in an increased hospital LOS across all studies with additional LOS ranging from 1.5 days^[38] to 19 days.^[26] In addition, the greater the cumulative number of complications a patient experienced, the greater their hospital LOS.^[25] Increasing SSI severity was also associated with increased hospital LOS.^[18] No study assessed the direct cost impact of LOS.

3.15. Mortality

Three studies^[28,36,40] reported increased mortality rates associated with incidence of postoperative complications. No study reported the cost impact of mortality.

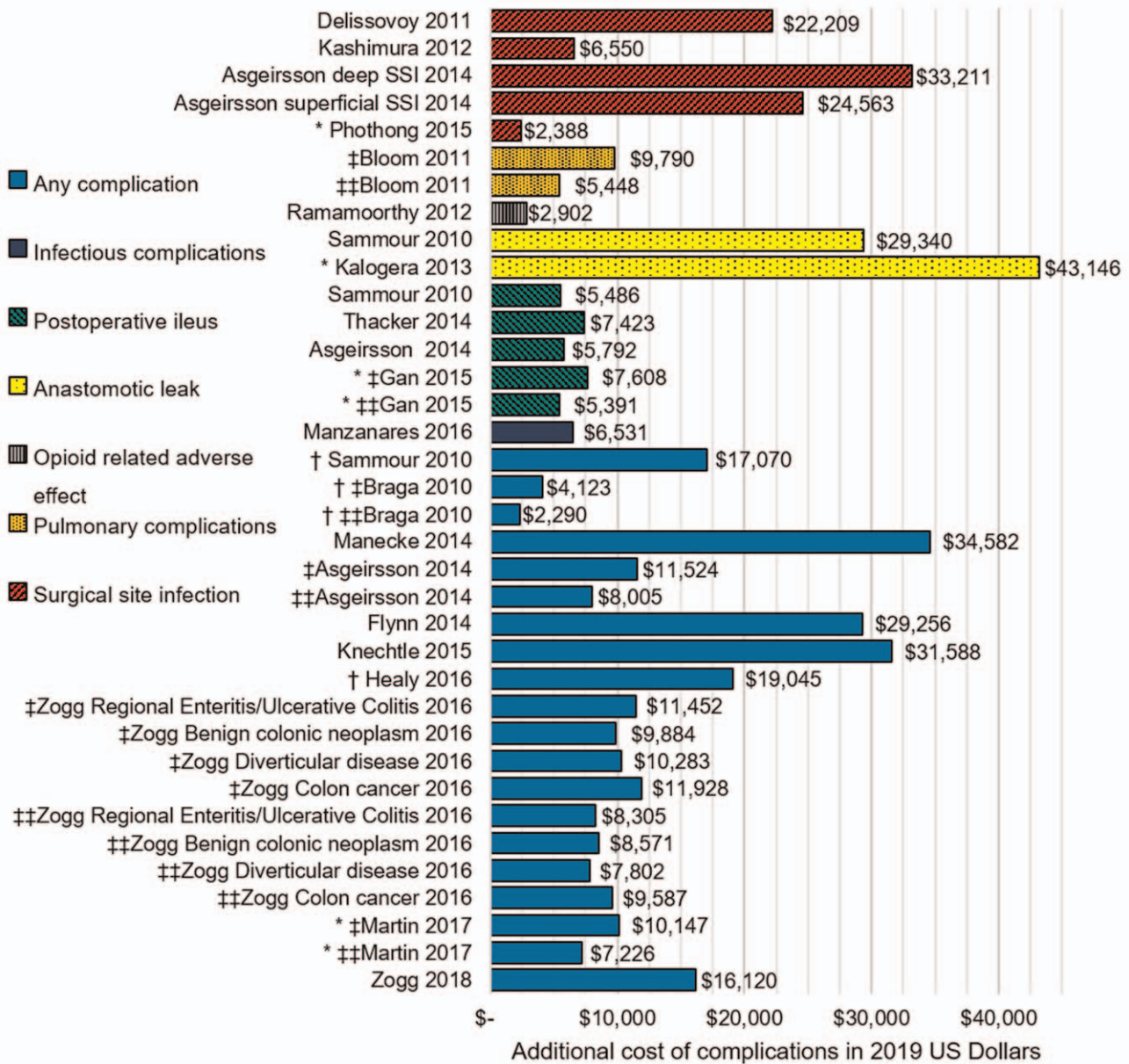


Figure 3. The increase in hospital costs due to postoperative complications following colonic resection surgery, stratified by complication type when available, compared across studies. Costs are reported in 2019 USD (\$) and are presented as mean unless otherwise stated * Median, †Unclear; ‡Open, ‡‡Laparoscopic.

3.16. Indication for surgery

Impact of indication for surgery on incidence of complications was inconclusive across all studies.^[18,38,40] Zogg et al^[40] was the only study assessing the cost impact of indication for surgery demonstrating increased costs associated with patients with colon cancer experiencing postoperative complications.

3.17. Surgical urgency

Impact of surgical urgency on incidence and cost of complications is inconclusive across all studies.^[11,17] Fukuda et al^[18] reported no statistical association between surgical urgency and risk of SSI. However, Asgeirsson et al^[11] reported higher complication

incidence and hospital costs with urgent/emergent admissions as compared to elective admissions.

3.18. Cost breakdown

Only two studies^[32,38] reported the financial burden associated with complications broken down into different hospital cost centers (Table S2, Supplemental Digital Content, <http://links.lww.com/MD2/A260>). Both studies explored the costs associated with SSI, demonstrating the greatest cost difference in inpatient costs^[38] and “room,” “operative,” and “other” hospital costs, which included the combined cost of nursing, medication, laboratory, and radiology services.^[32] These increased costs can

Table 1

Summary of studies evaluating the financial burden of surgical site infection, postoperative ileus and anastomotic leak following colonic resection surgery.

| Author, year, reference number | Study design | Country, currency and price year | Patients (n) and dates of patient sample | Surgery | Outcome definition | Incidence and cost of complications |
|----------------------------------|---|---|--|--|---|--|
| Delissovoy et al ^[15] | Multicenter retrospective cohort study utilizing the Premier Perspective Comparative Database (<i>Conference abstract</i>) | USA; USD (\$) assumed 2011 | Number of patients undergoing colon procedures not reported; 2007–2010 | Colon resection; Surgical technique not specified | Costs: Hospital costs. Definition not reported. Postoperative complications SSI was identified by a combination of postoperative infection diagnosis codes, or postoperative prescription of selected antimicrobial drugs with treatment duration ≥ 5 days. | Incidence (95%CI) of SSI = 12.0%, (11.78–12.2%) Mean (95%CI) additional cost of SSI = \$19,349 (19,315–19,383) [\$22,209] |
| Wick et al ^[38] | Multicenter retrospective cohort study utilizing Blue Cross and Blue Shield insurance plan claims database | USA, USD (\$) assumed 2011 | 7020 patients undergoing partial or total colectomy, January 2002–December 2008 | Laparoscopic colon resection = 1273 (18.1%) Open colon resection = 5747 (81.9%) | Costs: Hospital reimbursements defined as payments to hospitals from day of operation to 90 days postoperatively. Postoperative complications SSI was identified using ICD-9-CM codes. | Incidence of SSI = 726/7020 (10.3%) Mean (95%CI) reimbursement for SSI: With SSI = \$31,933 (29,607–34,298) [\$36,653] Without SSI = \$14,608 (14,018–15,197) [\$16,767] ; <i>P</i> -value < .001 |
| Fukuda et al ^[9] | Multicenter retrospective cohort study utilizing the Diagnosis Procedure Combination/Per-Diem Payment System and Japan Nosocomial Infections Surveillance databases | Japan; USD (\$) 2010 Converted and adjusted from Yens (US\$1 = ¥122.1) | 1817 patients out of which 1308 patients were undergoing colon resection; September 2007 to December 2010 <i>Only 1108 colon resection patients had data for postoperative resource consumption</i> | Laparoscopic colon resection = 381 (29.1%) Open colon resection = 927 (70.9%) | Costs: Hospital charges defined as expenditure incurred between the first day postoperatively and the day of discharge (surgery charges on the day of operation were not included) calculated by multiplying the volume of resources consumed per patient by the official unit price. Postoperative complications: SSI was identified using the standard Centers for Disease Control and Prevention National Nosocomial Infections Surveillance System criteria. | Incidence of SSI = 156/1308 (11.9%) • Superficial SSI = 73/1108 (6.6%) • Deep SSI = 15/1108 (1.4%) • Space/organ SSI = 9/1108 (0.8%) Mean (95% CI) charge of SSI • With SSI = \$4189 (411.4–4266) [\$4,887] • Without SSI = \$2,973 (2919–3033) [\$3,468] ; <i>P</i> -value < .001 Mean (95%CI) additional charge of SSI = \$1216 (1196–1240) [\$1419] |
| Kashimura et al ^[22] | Multicenter retrospective-matched cohort study | Japan; USD (\$) assumed 2012 | 334 patients out of which 204 patients underwent colon resection; April 2006–March 2008 | Open colon resection = 154 (75.5%) laparoscopic colon resection = 50 (24.5%) | Costs: Hospital costs, defined as cost of index admission postsurgery, plus any costs incurred during readmission secondary to SSI. Costs were calculated using the fee-for-service calculation method. Postoperative complications SSI was identified using Centers for Disease Control and prevention criteria. | Case-matched population with 102 patients with SSI Mean (SD) cost of SSI • With SSI = \$10,152 (13,474) [\$11,322] • Without SSI = \$4279 (2945) [\$4,772] Mean (95%CI) additional cost of SSI = \$5873 (3166–8579) [\$6550] |
| Asgerfsson et al ^[11] | Single-center retrospective cohort study | USA; USD (\$) assumed 2014 | 1422 patients undergoing segmental colectomy; July 2008–June 2012 | Laparoscopic segmental colectomy = 654 (46.0%) Open Segmental colectomy = 768 (54.0%) | Costs: Hospital costs derived from the institutional cost accounting system for 30 days postsurgery Postoperative complications: SSI was defined as superficial, deep, and organ space (in the absence of anastomotic leak). | Incidence of SSI = 39/1422 (2.7%) • Superficial Site Infection = 12/1422 (0.8%) • Deep Surgical Site Infection/Organ space = 27/1422 (1.9%) Mean (SD) additional cost of SSI • Superficial SSI = \$31,899 (14,705) [\$34,471] • Deep SSI/Organ space = \$39,902 (27,911) [\$43,119] Incidence of SSI = 6/100 (6.0%) <i>Cost data available for SSI in open surgery group only</i> Median (range) cost of SSI • With SSI = \$4348 (\$2185–\$11,509) [\$4703] • Without SSI = \$2140 (\$1379–\$6277) [\$2315] ; <i>P</i> -value = 0.004 |
| Phothong et al ^[62] | Single-center retrospective cohort study | Thailand; USD (\$) assumed 2015 | 100 case-matched patients undergoing sigmoidectomy; January 2008–September 2013 | Hand-assisted laparoscopic sigmoidectomy = 50 (50%) Open sigmoidectomy = 50 (50%) | Costs Hospital costs including room charges, operating room costs, anesthesia costs, instrument costs and other hospital costs. Postoperative complications SSI definition not reported. | Incidence of SSI = 56/460 (12.2%) Median negative cost coverage effect of complications |
| Langelotz et al ^[26] | Single-center retrospective cohort study utilizing the Institute for the Hospital Remuneration-System | Germany, Euro (€) assumed 2017 | 460 patients undergoing colonic resections; 2010–2015 | Colonic resection; surgical technique not specified | Costs: Cost coverage effect of complications. Cost definition not reported. Postoperative complications SSI were identified using DRG codes. | Incidence of SSI = 56/460 (12.2%) Median negative cost coverage effect of complications |

(continued)

Table 1
(continued).

| Author, year, reference number | Study design | Country, currency and price year | Patients (n) and dates of patient sample | Surgery | Outcome definition | Incidence and cost of complications |
|--|---|--|--|--|---|--|
| Liu et al ^[27] | (Germany) database (<i>Conference abstract</i>) Multi-center retrospective cohort study utilizing the ACS-NSQIP and the Medicare Provider Analysis and Review databases. | USA; USD (\$) 2012 | 19,089 patients undergoing elective colectomy; 2009–2012 | Colectomy; Surgical technique not specified | Costs: Payments to hospitals by Centers for Medicare and Medicaid Services based on MS-DRG categories. Payments not directly related to care were excluded. Postoperative complications Complications were identified using ACS-NSQIP criteria. | Without SSI = -668€ [-\$786] With SSI only = -6823€ [-\$8026] Incidence of SSI = 9.8% Mean (95%CI) reimbursement for SSI With SSI = \$16,257.21 (15,940.01–16,580.72) [\$18,130] Uncomplicated = \$13531.16 (13,390.63–13,673.15) [\$15,090] Additional reimbursement for SSI = \$2726.05 [\$3040] |
| Postoperative ileus Sammour et al ^[35] | Single-center retrospective cohort study ERAS group was collected prospectively Control group was collected retrospectively | New Zealand, NZD (\$) assumed 2010 | 100 patients undergoing elective colonic surgery; • ERAS program: 50 consecutive patients (December 2005–March 2007) • Pre-ERAS program: 50 consecutive patients (September 2004–September 2005) | Open and laparoscopic colon resection techniques included and analyzed as one group | Costs: Hospital costs defined as cost of index hospital stay excluding cost of day stay and readmissions. Postoperative complications POI definition not reported. | Incidence of POI = 23/100 (23.0%) Additional cost of POI = \$6517.37 [\$5,486] |
| Asgerisson et al ^[11] | Single-center retrospective cohort study | USA; USD (\$) assumed 2014 | 1422 patients undergoing segmental colectomy; July 2008–June 2012 | Laparoscopic colectomy = 654 (46.0%) Open colectomy = 768 (54.0%) | Costs: Hospital costs derived from the institutional cost accounting system for 30 days post-surgery Postoperative complications: Postoperative ileus definition not reported. | Incidence of POI = 26/1422 (1.8%) Mean (SD) additional cost of POI = \$14,529 (12,953) [\$15,700] |
| Thacker et al ^[36] | Multicenter retrospective cohort study utilizing the Premier research database (US) (<i>Conference abstract</i>) Multicenter retrospective cohort study utilizing The Premier Research Database | United Kingdom; USD (\$) assumed 2014 | 84,722 patients undergoing elective colon surgery; January 2008–June 2012 | Colon surgery; Surgical technique not specified. | Costs: Hospital costs Definition not reported Postoperative complications POI identified using ICD-9-CM codes. | Incidence of POI = 14,972 (17.7%) Mean (SD) total hospital costs With POI = \$20,734 (14,506) [\$22,406] Without POI = \$13,865 (8,315) [\$14,983] ; <i>P</i> -value < .001 |
| Gan et al ^[9] | Single-center retrospective cohort study utilizing The Premier Research Database | USA; USD (\$) assumed 2015 | 138,068 patients out of which 57,948 patients were undergoing colon resection; September 2008 – August 2010 | Open colon resection = 40,250 (69.5%) Laparoscopic colon resection = 17,638 (30.5%) | Costs: Hospital costs derived from all billed items at the individual patient level. Postoperative complications POI identified using ICD-9-CM codes. | Incidence of POI = 10,880/57,948 (18.8%) Median cost for laparoscopic colon resection: With POI = \$17,505 [\$18,933] Without POI = \$12,521 [\$13,543] ; <i>P</i> -value < .001 Median cost for open colon resection: • With POI = \$24,078 [\$26,043] • Without POI = \$17,044 [\$18,435] ; <i>P</i> -value < .001 |
| Anastomotic Leak Sammour et al ^[35] | Single-center retrospective cohort study ERAS group was collected prospectively Control group was collected retrospectively | New Zealand, NZD (\$) assumed 2010 | 100 patients undergoing elective colonic surgery; • ERAS program: 50 consecutive patients (December 2005–March 2007) • Pre-ERAS program: 50 consecutive patients (September 2004–September 2005) | Open and laparoscopic colon resection techniques included and analyzed as one group | Costs: Hospital costs defined as cost of index hospital stay excluding cost of day stay and readmissions. Anastomotic leak definition not reported. | Incidence of anastomotic leak = 7/100 (7.0%) Additional cost of anastomotic leak = \$34,853.26 [\$29,340] |
| Kalogera et al ^[21] | Single-center retrospective cohort study (<i>Conference abstract</i>) | USA, USD (\$) assumed 2013 | 42 Anastomotic leak cases matched with 84 no-leak controls undergoing large bowel resection for primary | Large bowel resection; Surgical technique not specified | Costs: Hospital costs excluding outpatient cost data. Postoperative complications Anastomotic leak definition not reported. | Case-matched population with 42 patients with anastomotic leaks Median (IQR) cost of anastomotic leak at 30 days • With anastomotic leak = \$72,760.4 (52,858.9–104,449.2) [\$79,868] |

(continued)

Table 1
(continued).

| Author, year, reference number | Study design | Country, currency and price year | Patients (n) and dates of patient sample | Surgery | Outcome definition | Incidence and cost of complications |
|---------------------------------|---|----------------------------------|--|---|--|--|
| Langelitz et al ^[26] | Single-center retrospective cohort study utilizing the Institute for the Hospital Remuneration System database (Conference abstract) | Germany, Euro (€) assumed 2017 | ovarian cancer; 1994–2011 460 patients undergoing colonic resections; 2010–2015 | Colonic resection; surgical technique not specified | Costs: Cost coverage effect of complications. Cost definition not reported. Postoperative complications. Anastomotic insufficiency was identified using DRG codes. | <ul style="list-style-type: none"> Without anastomotic leaks = \$33,453.7 (27,081.0–41,743.0) [\$36,722]; P-value < .001 Incidence of anastomotic insufficiency = 25 (5.4%) Median negative cost coverage effect of complications: Without anastomotic insufficiency = –668€ [–\$786] With anastomotic insufficiency only = –2659€ [–\$3128] |

Costs in bold, [**\$\$\$**], have been converted and inflated to February 2019 \$USD from assumed cost year.

95% CI = 95% confidence interval, ACS-NSQIP = American College of Surgeons-National Surgical Quality Improvement Project, DRG = diagnosis related group, ERAS = enhanced recovery after surgery, ICD-9-CM = International Classification of Diseases, Ninth Revision, Clinical Modification, IQR = interquartile range; MS-DRG = Medicare Severity - Diagnosis Related Group, NZD = New Zealand Dollar, POI = postoperative ileus, SD = Standard Deviation, SSI = surgical site infection, USD = United States Dollar.

be directly attributed to the increased LOS associated with SSI.^[32,38]

4. Discussion

In an updated systematic review of thirty-four studies, we demonstrate strong evidence of high overall complication incidence arising from colonic resection surgery with associated increased costs and resource utilization. We found a considerable degree of heterogeneity among studies in factors such as study design, defining and reporting on complications, and methodology used to calculate “cost” and associated outcomes. Despite these limitations, our findings confirm that hospital readmissions are associated with significant financial burden, and postoperative complications are associated with greater incidence of hospital readmissions. We found weaker evidence that postoperative SSI and anastomotic leak are associated with greater costs and resource utilization relative to other postoperative complications.

Our review highlights significant shortcomings in defining and reporting of hospital resource utilization in economic studies of postoperative complications in colon resection surgery. First, the measure of hospital resource utilization adopted by the studies varied and was poorly defined in many. Second, the currency year was not reported in most of the studies thus had to be assumed to be the publication year. Thirdly, reporting of costs using means and medians varied, impeding on direct comparison between studies.

Hospital costs, hospital charges and hospital reimbursements are 3 resource use measures that represent different financial aspects of health economics.^[45,46] Hospital charges for a given service may differ greatly between hospitals and health care systems and are considered a poor representation of hospital costs.^[47] Similarly, hospital reimbursement systems demonstrate significant geographical variation in their coding classification and payment value.^[48] In the USA, and many European countries, hospital reimbursements are predetermined and based on DRG codes^[48,49] with cost variation within DRG codes acting as a source of uncertainty. As such, the most reliable measure of hospital costs involves recording actual resource consumption for each admission.^[47] Secondary to this, studies should clearly define and report the utilized hospital resource use measure to enable accurate analysis of a study’s results.

Poorly defined and inconsistent reporting of hospital resources acts as a barrier to accurate comparison of cost and clinical outcomes between studies. Hospital costs consists of fixed direct, variable direct and indirect costs.^[46] Inclusion or exclusion of specific hospital cost components resulted in variation in total financial burden of complications amongst the included studies as presented in Figure 3. Furthermore, many studies in our review failed to report the cost currency and currency year which is essential in allowing comparison of cost data. The reporting of health cost studies should adhere to a minimal standard of reporting including the definition of hospital cost components analyzed including any adjustments for inflation that the authors performed. In addition, skewed distributions are expected in medical costing data,^[50] therefore it is recommended that both mean and median costs are reported to avoid misinterpretation of results.^[50]

Most of the included studies reported the cost of a specific complication type improving the clinical relevance of these studies. However, complication definitions were inconsistent

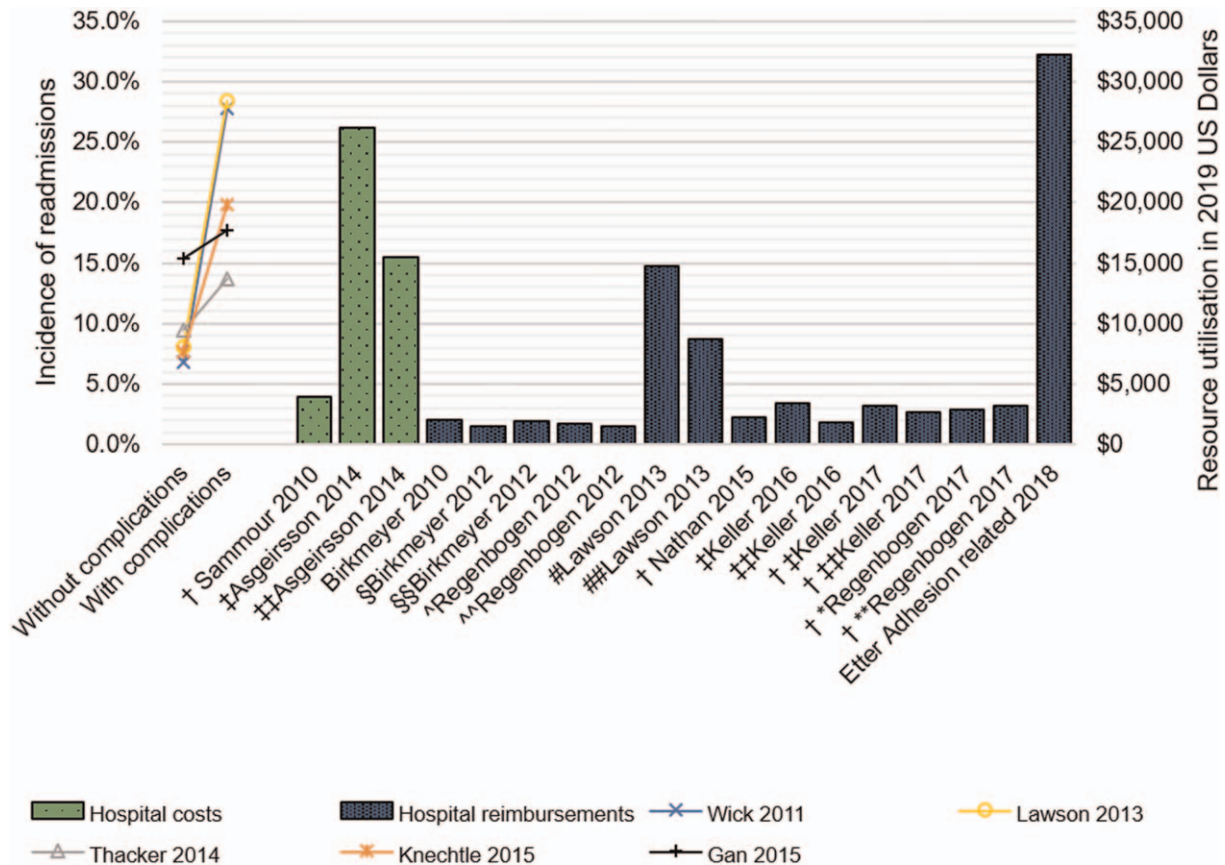


Figure 4. The incidence of readmissions in the presence and absence of postoperative complications following colonic resection surgery with readmission resource utilization compared across studies. Resource utilization is reported in 2019 USD (\$) and is presented as mean unless otherwise stated †Unclear; ‡Open, ‡‡Laparoscopic; Surgical volume: ^Low, ^^High; Hospital quality: §Lowest, §§Highest; Hospital length of stay: *≤3, **≥7 days, Complication: #Yes, ##No.

across studies limiting the ability to compare complication types. Many studies utilized local institutional definitions or the definitions of the national databases they analyzed. Only seven studies^[19,24,36–38,40,41] specified the use of the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) codes to classify complications. Reporting on postsurgical complications should be aligned with established international standards for definitions and use of outcome measures, designed for clinical effectiveness research in perioperative medicine.^[51]

Additionally, only three studies^[11,18,39] assessed the cost impact of complication severity with only one^[39] of these utilizing a prevalidated complication severity grading system (the Clavien-Dindo classification system). Our results demonstrated greater hospital resource use with greater complication severity, and as such management and outcomes of complications are heavily reliant on complication severity. Therefore, complication severity is an important factor to analyze and should be reported using internationally validated grading systems such as the Clavien-Dindo classification system.^[52]

Our review also highlights hospital readmissions as a significant source of costs. This has been recognized internationally. Specifically, in the USA, the hospital readmissions reduction program was introduced which penalizes hospitals who demonstrate high 30-day readmission rates for specific conditions/procedures.^[53] This initiative creates a significant financial

incentive for hospitals to introduce measures that reduce readmissions. Our review demonstrated increased readmission rates in patients who experience postoperative complications, highlighting the financial benefit of reducing postoperative complication rates. We also recommend that the reporting of readmissions should be standardized to at least 30 days post discharge.

Prevention strategies that aim to mitigate risk factors for complications following colorectal surgery are well described.^[54] These include preoperative weight loss,^[54] nutritional optimization through immunonutrition^[55] and early postoperative enteric nutrition,^[56] intraoperative blood loss and blood transfusion minimization,^[57,58] and use of laparoscopic surgery if feasible.^[59,60,61] Incorporation of these strategies and others into enhanced recovery after surgery management programs has been shown to be associated with reduced postoperative complications,^[60] reduced hospital LOS and costs.^[62] Despite this, there is a paucity of studies analyzing the cost-benefit outcomes of these strategies. Therefore, large, prospective cost-benefit clinical trials investigating interventions aimed at reducing postoperative complications are still required to improve patient outcomes and the cost-effectiveness of our health care systems.

Our review has several limitations. Notably our review includes a high number of retrospective studies with few high-quality detailed cost outcome studies. Despite an exhaustive search strategy, noninclusion of grey literature may subject our

review to a risk of publication bias. In addition, the significant heterogeneity of the included studies prevented a quantitative analysis of the cost results, however the large number of articles identified allowed direct comparison of studies of similar characteristics. High quality prospective economic studies are needed to evaluate the cost of complications arising from colonic resection surgery.

Our systematic review has important clinical implications. We have demonstrated a high prevalence of complications following colon resection surgery and a substantial financial burden associated with complications. Therefore, large, prospective cost-benefit analysis trials investigating strategies aimed at reducing surgical complications and their associated costs are required. Given the significant heterogeneity identified in our review, we propose a standardized approach for future costing studies of postoperative complications. Studies should follow a detailed and consistent methodology with the use of validated economic study guidelines^[63] and must report, as a minimum, the following variables: complication definition, complication severity (reported using internationally validated grading systems such as the Clavien-Dindo classification system), follow-up duration for each outcome of interest, mortality reported at 90 days postoperatively and ideally at 1 year in clinical effectiveness research, readmissions standardized to at least 30 days post discharge, hospital cost definition (clearly define and report the utilized hospital resource use measure and the hospital cost components analyzed), cost currency, cost year adjusted for inflation, mean and median cost, confidence intervals and interquartile range as skewed distributions are expected in medical costing data.

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References

- Xu K, Soucat A, Kutzin J et al. Public Spending on Health: A Closer Look at Global Trends. Geneva: World Health Organization; 2018 (WHO/HIS/HGF/HFWorkingPaper/18.3). Licence: CC BY-NC-SA 3.0 IGO. Available from: <http://www.who.int/iris/handle/10665/276728>. Accessed April 6, 2019
- Vonlanthen R, Slankamenac K, Breitenstein S, et al. The impact of complications on costs of major surgical procedures: a cost analysis of 1200 patients. *Ann Surg* 2011;254:907–13.
- Patel AS, Bergman A, Moore BW, et al. The economic burden of complications occurring in major surgical procedures: a systematic review. *Appl Health Econ Health Policy* 2013;11:577–92.
- Schilling PL, Dimick JB, Birkmeyer JD. Prioritizing quality improvement in general surgery. *J Am Coll Surg* 2008;207:698–704.
- de Silva S, Ma C, Proulx MC, et al. Postoperative complications and mortality following colectomy for ulcerative colitis. *Clin Gastroenterol Hepatol* 2011;9:972–80.
- Higgins JPT, Green S (eds). *Cochrane Handbook for Systematic Reviews of Interventions* Version 5.1.0 [updated March 2011]. The Cochrane Collaboration, 2011. Available from: www.handbook.cochrane.org. Accessed February 4, 2019
- Moher D, Liberati A, Tetzlaff J, et al. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Med* 2009;6:e1000097.
- Encare. ERAS Definition: Encare; 2019. Available from: <https://www.encare.net/eras-definition>. Accessed April 13, 2019.
- OFX Group Ltd, Yearly average rates. Available from: <https://www.ofx.com/en-au/forex-news/historical-exchange-rates/yearly-average-rates/>. Accessed April 22, 2019.
- Bureau of Labor Statistics, CPI Inflation Calculator. United States Department of Labor. Available from: https://www.bls.gov/data/inflation_calculator.htm. Accessed April, 2019.
- Asgeirsson T, Jrebi N, Feo L, et al. Incremental cost of complications in colectomy: a warranty-guided approach to surgical quality improvement. *Am J Surg* 2014;207:422–6. discussion 5–6.
- Birkmeyer JD, Gust C, Dimick JB, et al. Hospital quality and the cost of inpatient surgery in the United States. *Ann Surg* 2012;255:1–5.
- Bloom JD, Agarwal SJ, Erslon MG, et al. Attributable incidence and costs of postoperative pulmonary complications following common abdominal surgical procedures. *Surg Endosc* 2011;1:S355.
- Braga M, Frasson M, Zuliani W, et al. Randomized clinical trial of laparoscopic versus open left colonic resection. *Br J Surg* 2010;97:1180–6.
- Delissovoy G, Pan F, Patkar AD, et al. Surgical site infection incidence and burden assessment using multi-institutional real-world data. *Value in Health* 2011;14:A271–2.
- Etter K, Sutton N, Wei D, et al. Impact of postcolectomy adhesion-related complications on healthcare utilization. *ClinicoEcon* 2018;10:761–71.
- Flynn DN, Speck RM, Mahmoud NN, et al. The impact of complications following open colectomy on hospital finances: a retrospective cohort study. *Perioper Med (Lond)* 2014;3:1.
- Fukuda H, Morikane K, Kuroki M, et al. Impact of surgical site infections after open and laparoscopic colon and rectal surgeries on postoperative resource consumption. *Infection* 2012;40:649–59.
- Gan TJ, Robinson SB, Oderda GM, et al. Impact of postsurgical opioid use and ileus on economic outcomes in gastrointestinal surgeries. *Curr Med Res Opin* 2015;31:677–86.
- Healy MA, Mullard AJ, Campbell DA, et al. Hospital and payer costs associated with surgical complications. *JAMA Surg* 2016;151:823–30.
- Kalogeria E, Haas L, Borah B, et al. A cost-analysis of anastomotic leak vs. prophylactic bowel diversion at the time of large bowel resection for primary ovarian cancer. *Gyn Onc* 2013;130:e62.
- Kashimura N, Kusachi S, Konishi T, et al. Impact of surgical site infection after colorectal surgery on hospital stay and medical expenditure in Japan. *Surg* 2012;42:639–45.
- Keller D, Fitch K, Bochner A, et al. Overall value of laparoscopy in colon cancer-benefits for payers and patients. *Dis Colon Rectum* 2016;59:e247–8.
- Keller DS, Senagore AJ, Fitch K, et al. A new perspective on the value of minimally invasive colorectal surgery-payer, provider, and patient benefits. *Surg Endosc* 2017;31:2846–53.
- Knechtle WS, Perez SD, Medbery RL, et al. The association between hospital finances and complications after complex abdominal surgery: deficiencies in the current health care reimbursement system and implications for the future. *Ann Surg* 2015;262:273–9.
- Langelotz C, Hammerich R, Muller V, et al. Negative effects of surgical site infections after colonic resections on clinical course and costs are worse than anastomotic insufficiency. *Eur Surg Res* 2017;58 (Supplement 1):45–6.
- Liu JB, Berian JR, Chen S, et al. Postoperative complications and hospital payment: implications for achieving value. *J Am Coll Surg* 2017;224:779–86. e2.
- Manecke GR, Asemota A, Michard F. Tackling the economic burden of postsurgical complications: would perioperative goal-directed fluid therapy help? *Crit Care* 2014;18(no pagination):566.
- Manzanares Campillo MDC, Martín Fernández J, Amo Salas M, et al. A randomized controlled trial of preoperative oral immunonutrition in

- patients undergoing surgery for colorectal cancer: hospital stay and health care costs. *Cir* 2017;85:393–400.
- [30] Martin L, Yu JX, Gawron A, et al. Elective colectomy for the treatment of benign colon polyps: National surgical trends, outcomes and cost analysis. *Am J Gastroenterol* 2017;112(Supplement 1):S47.
- [31] Nathan H, Atoria CL, Bach PB, et al. Hospital volume, complications, and cost of cancer surgery in the elderly. *J Clin Oncol* 2015;33:107–14.
- [32] Phothong N, Akaraviputh T, Chinswangwatanakul V, et al. Cost-effective and potential benefits in three-port hand-assisted laparoscopic sigmoidectomy. *J Med Assoc Thai* 2015;98:864–70.
- [33] Ramamoorthy S. Impact of opioid-related adverse events (ORAE) on length of stay (LOS) and hospital costs in patients undergoing a laparoscopic colectomy. *Gastroenterol* 2012;1:S1053.
- [34] Regenbogen SE, Cain-Nielsen AH, Norton EC, et al. Costs and consequences of early hospital discharge after major inpatient surgery in older adults. *JAMA Surg* 2017;152:e170123.
- [35] Sammour T, Zargar-Shoshtari K, Bhat A, et al. A programme of enhanced recovery after surgery (ERAS) is a cost-effective intervention in elective colonic surgery. *N Z Med J* 2010;123:61–70.
- [36] Thacker J, Mountford W, Mythen M, et al. An updated evaluation of postoperative ileus in colon surgery—associations and outcomes. *Dis Colon Rectum* 2014;57:e306.
- [37] Vaid S, Tucker J, Bell T, et al. Cost analysis of laparoscopic versus open colectomy in patients with colon cancer: results from a large nationwide population database. *Am Surg* 2012;78:635–41.
- [38] Wick EC, Hirose K, Shore AD, et al. Surgical site infections and cost in obese patients undergoing colorectal surgery. *Arch Surg* 2011;146:1068–72.
- [39] Widmar M, Strombom P, Keskin M, et al. Burden of surgical complications: contribution of long-term costs by Clavien-Dindo classification. *J Am Coll Surg* 2016;223(4 Supplement 1):e90.
- [40] Zogg CK, Najjar P, Diaz AJ, et al. Rethinking priorities: cost of complications after elective colectomy. *Ann Surg* 2016;264:312–22.
- [41] Zogg CK, Ottesen TD, Kebaish KJ, et al. The cost of complications following major resection of malignant neoplasia. *J Gastrointest Surg* 2018;22:1976–86.
- [42] Birkmeyer JD, Gust C, Baser O, et al. Medicare payments for common inpatient procedures: implications for episode-based payment bundling. *Health Serv Res* 2010;45(6 Pt 1):1783–95.
- [43] Regenbogen SE, Gust C, Birkmeyer JD. Hospital surgical volume and cost of inpatient surgery in the elderly. *J Am Coll Surg* 2012;215:758–65.
- [44] Lawson EH, Hall BL, Louie R, et al. Association between occurrence of a postoperative complication and readmission: implications for quality improvement and cost savings. *Ann Surg* 2013;258:10–8.
- [45] Arora V, Moriates C, Shah N. The challenge of understanding health care costs and charges. *AMA J Ethics* 2015;17:1046–52.
- [46] Rubin GD. Costing in radiology and health care: rationale, relativity, rudiments, and realities. *Radiology* 2017;282:333–47.
- [47] Finkler SA. The distinction between cost and charges. *Ann Intern Med* 1982;96:102–9.
- [48] Busse R, Geissler A, Aaviksoo A, et al. Diagnosis related groups in Europe: moving towards transparency, efficiency, and quality in hospitals? *BMJ* 2013;346:f3197.
- [49] Quentin W, Scheller-Kreinsen D, Blumel M, et al. Hospital payment based on diagnosis-related groups differs in Europe and holds lessons for the United States. *Health Aff (Project Hope)* 2013;32:713–23.
- [50] Bang H, Zhao H. Cost-effectiveness analysis: a proposal of new reporting standards in statistical analysis. *J Biopharm Stat* 2014;24:443–60.
- [51] Jammer I, Wickboldt N, Sander M, et al. Standards for definitions and use of outcome measures for clinical effectiveness research in perioperative medicine: European Perioperative Clinical Outcome (EPCO) definitions: a statement from the ESA-ESICM joint taskforce on perioperative outcome measures. *Eur J Anaesthesiol* 2015;32:88–105.
- [52] Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. *Ann Surg* 2004;240:205–13.
- [53] Readmissions Reduction Program [Internet]. Maryland: Centers for Medicare and Medicaid Services; 2019 [updated 2019 Jan 16]. Available from: <https://www.cms.gov/Medicare/Medicare-Fee-for-Service-Payments/AcuteInpatientPPS/Readmissions-Reduction-Program.html>. Accessed April 27, 2019.
- [54] Kirchoff P, Clavien PA, Hahnloser D. Complications in colorectal surgery: risk factors and preventive strategies. *Patient Saf Surg* 2010;4:5.
- [55] Xu J, Sun X, Xin Q, et al. Effect of immunonutrition on colorectal cancer patients undergoing surgery: a meta-analysis. *Int J Colorectal Dis* 2018;33:273–83.
- [56] Osland E, Yunus RM, Khan S, et al. Early versus traditional postoperative feeding in patients undergoing resectional gastrointestinal surgery: a meta-analysis. *JPEN J Parenter Enteral Nutr* 2011;35:473–87.
- [57] Saleh A, Ihedioha U, Babu B, et al. Is estimated intra-operative blood loss a reliable predictor of surgical outcomes in laparoscopic colorectal cancer surgery? *Scott Med J* 2016;61:167–70.
- [58] Bernard AC, Davenport DL, Chang PK, et al. Intraoperative transfusion of 1 U to 2 U packed red blood cells is associated with increased 30-day mortality, surgical-site infection, pneumonia, and sepsis in general surgery patients. *J Am Coll Surg* 2009;208:931–7. 937.e1-2; discussion 938-9.
- [59] Compliance ERAS, Group . The impact of enhanced recovery protocol compliance on elective colorectal cancer resection: results from an international registry. *Ann Surg* 2015;261:1153–9.
- [60] Ripollés-Melchor J, Ramírez-Rodríguez JM, Casans-Francés R, et al. POWER Study Investigators Group for the Spanish Perioperative Audit and Research Network (REDGERM) Association Between Use of Enhanced Recovery After Surgery Protocol and Postoperative Complications in Colorectal Surgery: The Postoperative Outcomes Within Enhanced Recovery After Surgery Protocol (POWER) Study. *JAMA Surg* 2019;154:725–36.
- [61] Vlug MS, Wind J, Hollmann MW, et al. LAFA study group Laparoscopy in combination with fast track multimodal management is the best perioperative strategy in patients undergoing colonic surgery: a randomized clinical trial (LAFA-study). *Ann Surg* 2011;254:868–75.
- [62] Liska D, Novello M, Cengiz BT, et al. Enhanced recovery pathway benefits patients undergoing nonelective colorectal surgery. *Ann Surg* 2021;273:772–7.
- [63] Drummond MF, Jefferson TO. Guidelines for authors and peer reviewers of economic submissions to the BMJ. The BMJ Economic Evaluation Working Party. *BMJ* 1996;313:275–83.