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**MESTRADO INTEGRADO EM MEDICINA**

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Pedro Felgueiras Loureiro

Laparoscopic versus Robotic gastric cancer surgery: Short-term Outcomes.  
Systematic Review and Meta-analysis of 25 521 patients

Março, 2023

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# Laparoscopic versus Robotic gastric cancer surgery: Short-term Outcomes. Systematic Review and Meta-analysis of 25 521 patients

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Laparoscopic versus Robotic gastric cancer surgery

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**Keywords:** Gastrectomy; Gastric Cancer; Robotic surgery; Laparoscopy; Short-term outcomes

## Abstract

**Background:** Gastric cancer has the third highest cancer-related mortality worldwide. There is no consensus regarding the optimal surgical technique to perform curative resection surgery.

**Objective:** Compare laparoscopic and robotic gastrectomy regarding short-term outcomes in patients with gastric cancer.

**Materials and Methods:** This systematic review was conducted according to the PRISMA guidelines. We searched the following topics: “Gastrectomy”, “Laparoscopic” and “Robotic Surgical Procedures”. The included studies compared short-term outcomes between laparoscopic and robotic gastrectomy. Individual risk of bias was assessed with the MINORS scale.

**Results:** There were no significant differences between robotic gastrectomy (RG) and laparoscopic gastrectomy (LG) regarding conversion rate, reoperation rate, mortality, overall complications, anastomotic leakage, distal and proximal resection margin distances, and recurrence rate. However, mean blood loss (mean difference – MD – -19.43 mL,  $p < 0.00001$ ), length of hospital stay (MD -0.50 days,  $p = 0.0007$ ), time to first flatus (MD -0.52 days,  $p < 0.00001$ ), time to oral intake (MD -0.17 days,  $p = 0.0001$ ), surgical complications with a Clavien-Dindo grade  $\geq$  III (relative risk – RR – 0.68,  $p < 0.0001$ ), and pancreatic complications (RR 0.51,  $p = 0.007$ ) were significantly lower in the RG group. Furthermore, the number of retrieved lymph nodes was significantly higher in the RG group. Nevertheless, the RG group showed a significantly higher operation time (MD 41.19 min,  $p < 0.00001$ ) and cost (MD 3684.27 US Dollars,  $p < 0.00001$ ).

**Conclusion:** This meta-analysis supports the choice of robotic surgery over laparoscopy concerning relevant surgical complications. However, longer operation time and higher cost remain crucial limitations. Randomized clinical trials are required to clarify the advantages and disadvantages of RG.

## Introduction

Nowadays, gastric cancer is the fifth most common cancer worldwide, with its highest prevalence being in Mongolia, Japan, and South Korea. Moreover, WCRF International, in 2020, demonstrated that gastric cancer has the third highest cancer-related mortality rate (7.7/100 000) and it is the fifth most incident tumour in the entire world (11.1/100 000).<sup>1,2</sup>

Despite the development of new surgical techniques and medical devices, prognosis remains poor.<sup>3</sup> Therefore, it is necessary to improve screening methods to achieve earlier diagnosis and improve the odds of finding a resectable tumour, so as to reduce its burden.<sup>4,5</sup>

There are two approaches to treat localized gastric cancer: endoscopic resection or radical gastrectomy. The first one is used for gastric cancer classified as stage IA (T1 N0 M0), according to the TNM classification. On the other hand, radical gastrectomy is used for stage IB-III gastric cancers (>T1 and/or ≥N0 M0), and is associated with a simultaneous D2 lymphadenectomy. To increase the probability of a curative resection, this treatment requires neoadjuvant and adjuvant chemotherapy, in order to reduce pre-operative tumour size and probability of recurrence, respectively.<sup>6</sup>

Currently, the main surgical approaches are minimally invasive, including laparoscopic surgery and robotic surgery.<sup>5</sup>

The largely used conventional laparoscopic gastrectomy (LG) has shown several advantages, when compared with open gastrectomy, such as better surgical safety, less trauma, lower operative morbidity and faster recovery, with similar overall survival, oncologic outcomes and relapse-free survival.<sup>6,7</sup>

On the other hand, robotic gastrectomy (RG) yields high-resolution three-dimensional images, wrist instruments that offer freedom, tremor filtering technology and less fatigue. These features are expected to overcome some drawbacks of laparoscopic surgery.<sup>5</sup>

There are several studies which reported the advantages of the RG, when compared with LG, on the following short-term outcomes in patients with gastric cancer: less blood loss, higher number of harvested lymph nodes, less time to first flatus, shorter length of hospital stay and less post-operative complications.<sup>8</sup> However, the cost and the operative time related to the expensive instruments and the low experience in performing robotic surgery are still relevant limitations to its current utilization.<sup>5,9</sup>

Therefore, our systematic review includes the most recent observational studies and the current literature about the comparison of the short-term outcomes between LG and RG for gastric cancer patients in order to clarify the feasibility and efficiency of robotic surgery, as it is predicted to be more prevalent in the coming years.<sup>10</sup>



## Materials and methods

### 2.1 Search strategy / Information sources

We conducted our meta-analysis according to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines. Literature search was performed independently by two reviewers, on the following databases: PubMed, Web of Science and Cochrane Library. The query used in PubMed was: “Search (((laparoscopic gastrectomy) OR (“Gastrectomy” [Majr:NoExp]) AND “Laparoscopy” [Mesh])) OR (((“Gastrectomy” [Majr:NoExp]) AND “Robotic Surgical Procedures” [Mesh])) OR robotic gastrectomy”. In the Web of Science and Cochrane Library, we used the following query: “(“Gastrectomy” AND “Laparoscopy”) OR (“Laparoscopic Gastrectomy”) AND (“Robotic Surgery” OR “Robotic Surgical Procedures” OR “Robotic Gastrectomy”)”. Existing systematic reviews were also consulted for additional papers.

### 2.2 Study selection and eligibility criteria

The researchers screened the literature and selected articles based on their titles and abstracts. In accordance with previous reviews, we included observational clinical studies that compared short-term outcomes between the two surgical approaches (RG and LG), in patients with gastric cancer who underwent curative-intent surgery.<sup>8,11,12</sup>

Then, the authors reviewed the full texts and excluded articles which met the following exclusion criteria: (1) articles which also reported comparison of two robotic systems, (2) proximal gastrectomy comparison only and (3) D1 lymphadenectomy only. One article was excluded due to the impossibility of obtaining an English version.

### 2.3 Data extraction

Two reviewers independently read and interpreted every original study. Data extraction comprised: study information (author, region, published year, study period, study design, sample size, surgical extension, level of lymphadenectomy and reconstruction options), patients’ characteristics (age and gender) and short-term outcomes, which included three groups: surgical outcomes (operating time, blood loss, conversion rate, reoperation rate and mortality rate), postoperative outcomes (length of hospital stay, time to first flatus, time to oral intake, overall complications, surgical complications according to Clavien-Dindo Grade, anastomotic leakage, pancreatic complication and cost of operation) and oncological outcomes (distal resection margin distance, proximal resection margin distance, recurrence rate and number of retrieved lymph nodes). These variables were chosen in accordance with previous systematic reviews.<sup>8,9,11,12</sup> (Table 1)(Table 2)

### 2.4 Quality assessment

In our meta-analysis, we used the MINORS (Methodological Index for Non-Randomized Studies) scale to assess the quality and individual risk of bias of our non-randomized studies. The final version of the MINORS scale comprises 12 items, which identify whether the included studies contained a clearly stated aim, included all

potentially fit patients, involved prospective collection data, had appropriate endpoints according to the aim of the study, had blind evaluation of objectives and subjective endpoints, had an appropriate follow-up period, loss of follow-up under 5% and prospective calculation of the study size. Furthermore, the MINORS scale also evaluates additional criteria for comparative studies such as the control group, the time period of both groups, their baseline equivalence and an adequate statistical analysis. Each item is scored as 0 (not reported), 1 (reported but inadequate) or 2 (report and adequate). The total score, in comparative studies, is 24 points.<sup>13</sup>

## **2.5 Statistical analysis**

We performed our meta-analysis using Review Manager (Version 5.4.1).

For dichotomous outcomes, we presented the results as risk ratios (RR) with 95% confidence intervals (CI), by using the Mantel-Haenszel method. For continuous outcomes, we presented the results as mean differences with 95% CI, by using the generic inverse variance method. Some studies presented their outcomes as median and range. Therefore, we applied a method described by Hozo et al.<sup>14</sup> in order to estimate the mean and standard deviation. We used an alpha ( $\alpha$ ) level of 0.05 for statistical significance. The Chi-squared ( $\chi^2$ ) test and the I-squared ( $I^2$ ) measure were used to assess heterogeneity. We applied a random effects model because of the clinical heterogeneity of the included studies. We assessed the existence of publication bias among included studies using funnel plots, provided as supplemental file no.1.

## **2.6 Subgroup analysis**

In our systematic review, 22 studies used Propensity Score-Matching (PSM) in order to minimize baseline differences that usually contribute to bias in the interpretation of the results. The remaining 31 studies did not perform PSM. Hence, we conducted a subgroup analysis to understand whether PSM had any effect in the association between the surgical approach and the studied outcomes.

# **Results**

## **3.1 Studies selected and characteristics**

We selected 2848 articles from our research on PubMed, Web of Science and Cochrane Library. After reading their titles and abstracts, we selected 82 full-text articles to assess for eligibility. No additional studies from other sources were deemed relevant. From these articles, we excluded 29 because they did not fulfil the inclusion criteria. Then, for our systematic review, we included 53 studies in the quality assessment and quantitative analysis (Figure 1). These studies include a total of 25 521 participants, of which 8154 underwent RG and 17367 underwent LG. All studies were retrospective observational studies.<sup>15-67</sup>

## **3.2 Quality assessment**

The median score in the MINORS scale was 22, with a range of 19 to 23. Therefore, all included studies were considered adequate to be included in the quantitative analysis.

### **3.3 Meta-analysis**

A synthesis of every meta-analytical measure is presented in figure 2. (Figure 2) We provide the results of each individual meta-analysis as forest plots in supplemental file no.2.

#### **Surgical outcomes:**

##### **Operative time**

Our meta-analysis included fifty studies which reported the operation time. It was significantly shorter in laparoscopic gastrectomy group, when compared with the robotic surgery group [MD 41.19,  $p < 0.00001$  (95%CI: 33.47, 48.92),  $I^2 = 98\%$ ,  $p < 0.00001$ ]. Mean operation time was 269.22 minutes in the robotic surgery group and 225.65 in the laparoscopic surgery group. (Figure 3)

##### **Blood loss**

Blood loss was reported in forty-six studies. The mean blood loss was 90.72 mL in the RG group and 108.2 mL in the LG group. This difference was statistically significant [MD -19.43,  $p < 0.00001$  (95%CI: -25.23, -13.62),  $I^2 = 92\%$ ,  $p < 0.00001$ ].

##### **Conversion**

This outcome was included in thirty-three studies and demonstrated no statistically significant difference between the two groups [RR 0.68,  $p = 0.09$  (95% CI: 0.43, 1.07),  $I^2 = 0\%$ ,  $p = 0.50$ ]. Conversion rate to open surgery was 0.59% (26/4390) in the RG group and 0.89% (69/7730) in the LG group.

##### **Reoperation**

Eighteen studies reported reoperation rate. There was no statistically significant difference between both surgical approaches, regarding reoperation [RR 0.89,  $p = 0.57$  (95% CI: 0.59, 1.34),  $I^2 = 0\%$ ,  $p = 0.72$ ]. Reoperation rate was 1.38% (37/2677) in the RG group and 1.56% (68/4366) in the LG group.

##### **Mortality**

Thirty-nine studies were included, and mortality was comparable between both groups [RR 1.20,  $p = 0.37$  (95% CI: 0.81, 1.77),  $I^2 = 0\%$ ,  $p = 0.98$ ]. Mortality rate was 0,6% (40/6708) in the RG group and 0,59% (64/10776) in the LG group. (Figure 4)

#### **Postoperative outcomes:**

##### **Length of Hospital Stay**

This outcome was reported in fifty-two studies. The mean length of hospital stay was 8.74 days in the robotic surgery group and 9.38 days in the laparoscopic surgery group.

The robotic surgery group displayed a significantly shorter hospital stay [MD -0,50,  $p=0.0007$  (95% CI -0,79, -0,21),  $I^2=85\%$   $p<0.00001$ ].

### **Time to first flatus**

There were twenty-five studies which reported time to first flatus. The robotic surgery group showed a significantly shorter time to first flatus [MD -0.52,  $p<0.00001$  (95%CI -0.55, -0.50),  $I^2=98\%$   $p<0.00001$ ].

### **Time to oral intake**

Twenty-seven studies included this outcome. Time to oral intake was significantly shorter in the robotic surgery group [MD -0.17,  $p=0.0001$  (95%CI -0.25, -0.08),  $I^2=53\%$   $p=0.0008$ ].

### **Overall complications**

The overall complication rate was 12.97% (873/6732) in the RG group and 13.11% (1504/11469) in the LG group. There were fifty-one studies reporting this outcome, and the meta-analysis did not demonstrate a statistically significant difference [RR 0.93,  $p=0.15$  (95% CI 0.85, 1.03),  $I^2=18\%$ ,  $p=0.14$ ].

### **Surgical complications (Grade $\geq$ III in the Clavien-Dindo Classification)**

Thirty-one studies reported this outcome. Our study showed that the robotic surgery group had a significantly lower number of surgical complications [RR 0.68,  $p<0.0001$  (95% CI 0.57, 0.82),  $I^2=7\%$ ,  $p=0.35$ ], with a rate of 3.88% (212/5464) in the RG group and 6.4% (467/7303) in the LG group. (Figure 5)

### **Anastomotic leakage**

Thirty-three studies included this outcome. The rate of anastomotic leakage was 1.72% (91/5289) in the RG group and 1.93% (168/8721) in the LG group. This difference was not significant [RR 1.06,  $p=0.71$  (95% CI 0.78, 1.45),  $I^2=16\%$ ,  $p=0.21$ ].

### **Pancreatic complications**

This outcome was included in twenty-one studies. The rate of pancreatic complications was 0.64% (22/3445) in the RG group and 1.42% (78/5497) in the LG group. This difference was statistically significant [RR 0.51,  $p=0.007$  (95% CI 0.31, 0.83),  $I^2=0\%$ ,  $p=0.60$ ]. (Figure 6)

### **Cost**

Cost was reported in eight studies. On average, the total cost of robotic surgery was 3684.27 US dollars (3442.99 Euros), significantly higher than that of laparoscopic surgery [MD 3684.27,  $p<0.00001$  (95%CI 2986.11, 4382.44),  $I^2=90\%$   $p<0.00001$ ]. (Figure 7)

### **Oncological outcomes:**

#### **Distal resection margin distance**

Fourteen studies reported this outcome. The mean distal resection margin distance was 6.9 cm in the robotic surgery group and 6.82 cm in the laparoscopic surgery group. The difference was not statistically significant [MD 0.16,  $p=0.37$  (95%CI -0.19, 0.51),  $I^2=76%$   $p<0.00001$ ].

#### **Proximal resection margin distance**

Fifteen studies reported this outcome. The mean proximal resection margin distance was 4.35 cm in RG and 4.24 cm in LG. The difference was not statistically significant [MD 0.06,  $p=0.29$  (95%CI -0.05, 0.18),  $I^2=0%$   $p=0.52$ ].

#### **Recurrence**

Eleven studies reported this outcome. The recurrence rate was 9.9% (134/1358) in the RG group and 10.6% (215/2024) in the LG group. There were no statistically significant differences [RR 0.95,  $p=0.61$  (95% CI 0.77, 1.17),  $I^2=0%$ ,  $p=0.91$ ].

#### **Number of retrieved lymph nodes**

The number of retrieved lymph nodes was reported in forty-nine studies. The mean number of retrieved lymph nodes was 36.7 in the RG group and 35.61 in the LG group. The robotic surgery group had a significantly higher number of retrieved lymph nodes [MD 1.69,  $p=0.001$  (95%CI 0.68, 2.70),  $I^2=93%$   $p<0.00001$ ]. (Figure 8)

### **3.4 Subgroup analysis:**

#### **Surgical outcomes:**

##### **Operative Time**

Both subgroups demonstrated a significantly longer operative time in the robotic surgery group. Heterogeneity was high and statistically significant. Additionally, regarding subgroup differences,  $I^2=73.5%$  and  $p=0.05$ . (Figure 3)

##### **Blood Loss**

There was a significantly lower blood loss in the robotic surgery group in studies with and without PSM. This difference was more evident in the PSM subgroup. There were no significant differences between groups ( $I^2=0%$ ,  $p=0.76$ ) and heterogeneity was similar.

##### **Conversion**

The PSM subgroup presented a stronger association between surgical approach and conversion rate, with the robotic surgery group being lower in both subgroups. However, neither subgroup had a statistically significant result ( $p=0.06$  for studies with PSM and  $p=0.61$  for studies without PSM). There were no significant differences between subgroups ( $I^2=0%$ ,  $p=0.63$ ) and no significant heterogeneity in either.

##### **Reoperation**

The subgroups showed opposite results, both without statistical significance. Inside each subgroup, heterogeneity was not significant. There were no significant differences between subgroups either ( $I^2=68.4\%$ ,  $p=0.08$ ).

### **Mortality**

There were no significant differences between subgroups ( $I^2=0\%$ ,  $p=0.98$ ) and neither displayed significant heterogeneity. Both favour the laparoscopic surgery group, although these results are not statistically significant. (Figure 4)

### **Postoperative complications:**

#### **Length of Hospital Stay**

The PSM subgroup displayed a significantly lower length of hospital stay in the robotic surgery group, whereas there was no significant difference in studies without PSM, despite both favouring the robotic surgery group. Heterogeneity in both subgroups was significantly high. Between subgroups, there were no significant differences, with  $I^2=0\%$ ,  $p=0.84$ .

#### **Time to first flatus**

Both subgroups showed a significantly shorter time to first flatus in the robotic surgery group, although there was significant heterogeneity. There was a significant difference between subgroups ( $I^2=99.8\%$ ,  $p<0.00001$ ). The PSM subgroup displayed lower heterogeneity.

#### **Time to oral intake**

The robotic surgery group had a significantly lower time to oral intake in both subgroups. Heterogeneity was significant in the non-PSM subgroup ( $I^2=71\%$ ,  $p=0.0008$ ). There were no significant differences between subgroups ( $I^2=0\%$ ,  $p=0.32$ ).

### **Overall complications**

There was no significant difference in either subgroup. The PSM subgroup favoured the robotic surgery group, but  $p=0.06$ . Differences between subgroups were not statistically significant ( $I^2=56\%$ ,  $p=0.13$ ).

### **Surgical complications (Grade $\geq$ III in the Clavien-Dindo Classification)**

The PSM subgroup demonstrated a significantly lower rate of surgical complications in the robotic surgery group when compared to the laparoscopic surgery group (3.9% and 5.76%, respectively;  $RR = 0.66$ ,  $p<0.0001$ ). Additionally, both subgroups revealed low heterogeneity and there were no significant differences between them ( $I^2=0\%$ ,  $p=0.97$ ). (Figure 5)

### **Anastomotic Leakage**

In the PSM subgroup, anastomotic leakage was lower in the robotic surgery group. However, the results were not statistically significant ( $RR=0.73$ ;  $p=0.11$ ). In both

subgroups, heterogeneity was not significant. The differences between them were statistically significant ( $I^2=80.8\%$ ,  $p=0.02$ ), as they showed opposite results.

### **Pancreatic Complications**

Both subgroups favoured the robotic surgery group, but the results were not statistically significant. There was no significant heterogeneity. Moreover, the two subgroups were similar ( $I^2=0\%$ ,  $p=0.64$ ). (Figure 6)

### **Cost**

Both subgroups significantly favoured laparoscopic surgery. Heterogeneity was high and significant in both subgroups. There were no significant differences between subgroups ( $I^2=4.4\%$ ,  $p=0.31$ ). (Figure 7)

### **Oncological outcomes:**

#### **Distal and proximal resection margin distances**

Regarding distal resection margin, both subgroups were similar ( $I^2=0\%$ ,  $p=0.73$ ). In studies without PSM, there was significant heterogeneity ( $I^2=85\%$ ,  $p<0.00001$ ). For the proximal resection margin, there were no significant differences between subgroups ( $I^2=23.6\%$ ,  $p=0.25$ ) and neither subgroup displayed significant heterogeneity.

### **Recurrence**

None of the subgroups showed a significant difference in recurrence rate between the two approaches, and heterogeneity was not significant. There were no significant differences between subgroups ( $I^2=0\%$ ,  $p=0.36$ ).

### **Number of harvested lymph nodes**

The two subgroups showed a significantly higher number of retrieved lymph nodes in the robotic surgery group. They appeared to be similar concerning subgroup differences ( $I^2=0\%$ ,  $p=1.00$ ), and they both showed high values of heterogeneity, individually. (Figure 8)

## **Discussion**

This meta-analysis, which, as far as we know, is the largest one on the subject so far, provides insights into the comparison of short-term outcomes between robotic and laparoscopic gastrectomies in patients with gastric cancer. *Marano L. et al.*<sup>9</sup> aggregated fourteen meta-analyses published until December 2019 and showed better results in favour of robotic surgery, regarding blood loss, length of hospital stay, recovery of bowel function, distal resection margin distance and number of retrieved lymph nodes. However, not all represented an acceptable level of evidence, concerning the high percentage of heterogeneity of some outcomes. Hence, it is still unclear if robotic gastrectomy is more feasible and safer than laparoscopic gastrectomy.

Our results demonstrated that both surgical techniques are similarly effective in term of conversion rate, reoperation rate, mortality, overall complications, anastomotic leakage, distal and proximal resection margin distances, and recurrence rate.

Operative time and cost favour the laparoscopic approach, while blood loss, length of hospital stay, time to first flatus, time to oral intake, surgical complications (Clavien-Dindo grade  $\geq$  III), pancreatic complications and the number of retrieved lymph nodes favour the robotic approach.

### **Surgical outcomes:**

- **Operative Time**

This meta-analysis shows a similar result to previous studies, which demonstrated that operative time is significantly longer in robotic gastrectomy when compared with laparoscopic gastrectomy.<sup>9,11,12</sup>

Some studies have suggested that the learning curve associated with the use of robotic technology and the need for instrument exchange during the procedure may contribute to the longer operative time seen in the robotic surgery group.<sup>68</sup>

As *Gong S. et al.*<sup>8</sup> refer, the majority of studies did not discriminate the several steps of the surgery, regarding the operative time. *Nishi*<sup>40</sup> and *Ye*<sup>65</sup> divided the operative time into different steps of the surgery, which demonstrated that robotic surgery is not inferior regarding the effective operative time. However, the total operative time, which includes the effective time and “junk time” (setup, docking, and adjustment of surgical instruments), remains longer in robotic surgery due to the latter.<sup>65,69</sup>

There were two studies demonstrating a shorter operative time in the robotic surgery group. One of them (*Omori*) with a statistically significant difference.<sup>40,45</sup> *Omori et al.*<sup>45</sup> applied relevant techniques to shorten the “junk” time, such as the standardization of the setup and the use of MBS and SPIDER techniques which reduce pancreatic manipulation during lymphadenectomy.

So, the early standardization of the setup as well as the surgical team’s experience could contribute to similar results between both technical approaches.<sup>26,40</sup> On the other hand, there appear to be more possible factors that influence the operative time, rather than the docking time<sup>46</sup>, such as the more accurate and delicate lymphadenectomy provided by the robotic platform.<sup>15,45</sup>

- **Blood Loss**

The mean blood loss was significantly lower in the robotic surgery group, compared to the laparoscopic surgery group. This result was also observed in previous systematic reviews.<sup>9</sup> The majority of studies included in our meta-analysis demonstrate a tendency to a lower blood loss in robotic surgery. However, there were some studies that showed the opposite and stated that robotic surgery still has some instrumental limitations.<sup>22,55</sup>



The reasons for the significant difference in intraoperative blood loss could be due to reduction of the physiologic tremor, increased surgical field with 3D view, which provides greater instrument dexterity and more precise and less damaging dissection. These allow for a more accurate lymphadenectomy, less blood loss, less pancreatic damage, and less muscle trauma.<sup>65,70</sup>

- **Conversion/ Reoperation/Mortality**

Conversion, reoperation, and mortality were found to be comparable between the two groups. There was a tendency to favour the robotic surgery group, regarding conversion and reoperation, and previous studies also presented similar results with no statistically significant difference.<sup>8,11,12</sup> There were four studies that demonstrated more cases of conversion to open gastrectomy in the robotic surgery group, with the following causes: intraabdominal bleeding, serosa involvement, massive abdominal adhesion, damage to adjacent organs with the insertion of trocars, inadequate surgical margins and anatomical and dissection difficulties.<sup>20,33,47,48</sup> Some studies reported the causes of reoperation, such as anastomotic or intra-abdominal bleeding, pancreatic complications (post-operative pancreatic fistula) and intestinal obstruction.<sup>34,65</sup>

The mortality rate was also found to be similar between the two groups. This holds true in this study, with the laparoscopic surgery group displaying a mortality of 0.59%, and the robotic surgery group displaying a value of 0.60%. These findings are consistent with previous studies.<sup>9</sup>

**Perioperative outcomes:**

- **Length of Hospital Stay/Time to first flatus/Time to oral intake**

The length of hospital stay, time to first flatus and time to oral intake are outcomes associated with a faster recovery as well as lower probability of intrahospital complications and better patient well-being.

This study showed significant results favouring robotic surgery, which appears to cause less damage to adjacent organs, less blood loss and fewer postoperative complications. This finding supports the intrinsic advantages of the robotic platform, resulting in less trauma and, therefore, shorter time to recovery.

The mean of length of hospital stay was 8.74 days in the robotic surgery group and 9.38 days in the laparoscopic surgery group. Similar results can be seen in *Hu LD et al.*, without significant heterogeneity.<sup>71</sup>

In fact, *Liu et al.* correlate the shorter hospital stay in the robotic surgery group with a better bowel function recovery and a faster shift from liquid to soft diet. Additionally, the surgical operation area and the inflammatory response can influence gastrointestinal recovery, due to surgical manipulation of internal organs.<sup>37,65</sup> Moreover, *Guerrini et al.* referred the importance of early oral feeding in accelerating the recuperation process.<sup>12</sup>

- **Overall complications**

Regarding overall complications, they did not differ considerably between both surgical approaches, despite a tendency for lower overall complications in the robotic surgery group. These results were also observed in other meta-analyses.<sup>8,12</sup> However, *Jin T. et al.* claimed to be the first meta-analysis to demonstrate fewer overall complications in the robotic surgery group with statistical significance.<sup>11</sup> Nevertheless, it remains unclear the possible cause of this observation. They still add that this could be related with the statistically significant result in pancreatic complications.<sup>11</sup>

*Omori et al.* demonstrated, by multivariate analysis, that laparoscopic surgery is an independent risk factor for postoperative complications.<sup>45</sup>

- **Surgical complications (Grade  $\geq$  III in the Clavien-Dindo Classification)**

Several studies applied the Clavien-Dindo (CD) classification to highlight the most severe complications, which have the most impact in postoperative morbidity and mortality. In fact, *Guerrini et al.* emphasized the importance of separate medical and surgical complications, because of a direct relation between surgical complications and postoperative recovery and prognosis.<sup>12</sup> *Tian et al.* showed that surgical complications CD grade III-IV are independent prognostic factors for both overall survival and relapse-free survival.<sup>59</sup>

Furthermore, *Hikage et al.* established, according to their multivariate analysis, that laparoscopic surgery is an independent risk factor for postoperative complications with a CD grade of III or higher.<sup>22</sup> In this article, these surgical complications were significantly lower in the robotic surgery group, with only 7% heterogeneity ( $p$  value=0.35). The rates of the surgical complications were 3.88% in the robotic surgery group and 6.39% in the laparoscopic surgery group. These observations are consistent with those of *Guerrini's* meta-analysis. However, our results presented slightly lower rates of surgical complications.<sup>12</sup> Hence, robotic gastrectomy results in less relevant morbidity.

- **Anastomotic Leakage**

This study did not show a statistically significant difference in anastomotic leakage, which is congruent with previous studies.<sup>12</sup>

- **Pancreatic complications**

Pancreatic morbidity is relatively rare. Nevertheless, it represents a real threat to the patient.<sup>72</sup> One of the main concerns of gastrectomy is pancreatic manipulation during lymphadenectomy.<sup>58</sup>

*Jin T. et al.* and *Gong S. et al.* showed that pancreatic complications were significantly lower in the robotic surgery group.<sup>8,11</sup> These results are consistent with our meta-analysis. Additionally, *Jin T. et al.* discuss the influence of the extension of lymphadenectomy on pancreatic complications as an unexpected inverse relationship between the number of harvested lymph nodes and pancreatic morbidity.<sup>11</sup> In fact, these results support the efficacy and efficiency of the abovementioned characteristics

of the robotic surgery, which lead to minimization of the pressure on the pancreas as well as reduction on parenchymal injury.<sup>16,58,72</sup>

*Omori et al.* used the SPIDER and MBS techniques to optimize the removal of the suprapancreatic lymph nodes with an internal organ retractor, which held the pancreas, and a bipolar soft-coagulation forceps which minimizes thermal damage.<sup>45</sup>

- **Cost**

The cost of robotic surgery remains an important drawback to this technique. On average, the total cost of robotic surgery was 3684.27 US dollars (3442,99 Euros) significantly higher than that of laparoscopic surgery. Our meta-analysis includes 8 studies that reach the same conclusion: that the cost of the laparoscopic surgery is significantly lower, compared to that of robotic surgery.<sup>9,12</sup>

Some studies suggest that the fewer postoperative complications and the faster recovery and hospital stay can compensate for the higher costs associated with robotic surgery.<sup>9,59</sup> Moreover, other studies predict a reduction in the cost of robotic surgery over time with an increase in competition and technological improvement.<sup>12,19,34</sup>

#### **Oncological outcomes:**

- **Distal and proximal resection margin distances**

Our systematic review mainly includes studies on short-term outcomes. Therefore, it becomes difficult to analyse oncological variables, which demand a longer follow-up. To overcome this problem, we used distal and proximal resection margin distances as predictors for oncologic prognosis.<sup>12</sup>

This article did not show a significant difference in either resection margin distance, but there was a small tendency to favour the robotic approach. The mean distal resection margin distance was 6.9 cm in the robotic surgery group and 6.82 cm in the laparoscopic surgery group. Regarding the proximal resection margin distance RG had a mean of 4.35 cm and LG had a mean of 4.24 cm.

- **Recurrence**

Overall, the recurrence rate was comparable between the robotic and laparoscopic techniques (9.9% and 10.6%, respectively), although it appears to be lower in the robotic surgery group. Only one of the recent included studies analyses recurrence, particularly within 5 years after surgery, and it reported 7 cases of recurrence in 58 patients who underwent LG and 3 cases in 36 patients who underwent RG, with no locoregional recurrence in the robotic surgery group.<sup>22</sup> *Han et al.*<sup>21</sup> did not report any case of recurrence and the mean follow-up for both surgical groups were less than 2 years, when recurrence is more common.<sup>73</sup> In fact, recurrence rate can happen in more than half of gastric cancer patients after surgical treatment.<sup>74,75</sup> Furthermore, lymphovascular invasion, lymph node metastases, and tumour stage are independent risk factors of early recurrence ( $\leq 12$  months) after curative resection.<sup>76</sup>

- **Number of harvested lymph nodes**

Lymphadenectomy is part of the standard treatment, and it is one of the main steps of the surgery, regarding the difficulty on managing and dissecting around critical organs, such as the pancreas, and an important predictor of the oncological prognosis, as they determine the extent of the tumour, according the TNM classification.

In our meta-analysis, the number of retrieved lymph nodes was significantly higher in the robotic surgery group, when compared with the laparoscopic surgery group, as demonstrated in previous meta-analysis.<sup>8,11,12</sup> All of these studies, including ours, showed a significant heterogeneity, which puts the external validity of their results into question.

In fact, some studies<sup>40,59</sup> revealed a significantly higher number of harvested lymph nodes in the robotic surgery group, particularly caused by the retrieval of the supra-pancreatic lymph nodes.<sup>59</sup> They attribute these results to the better surgical field, with 3D vision and endowrist movements, and the reduction of the surgeon's physiologic tremor that the robotic platform provides.<sup>40,59</sup> Moreover, these differences were more evident in advanced gastric cancer<sup>59</sup> and *Jin T. et al.* demonstrated a preference for performing robotic surgery in patients whose BMI was under 25 kg/m<sup>2</sup>, whose age was under 65, and who had a tumour with a longest diameter above 5 cm.<sup>11</sup>

Several studies defined that an adequate number of retrieved lymph nodes was more than 15.<sup>34,49-51</sup> *Roh C. 2020.*<sup>49</sup> showed that there was an inadequate number of retrieved lymph nodes (<16) in the laparoscopic surgery group and the surgical success, which included this outcome, was significantly higher in the robotic surgery group. Nevertheless, it remained unclear what the real cause of these results was. This robotic surgery had a firefly system that was used for achieving a real time fluorescence image, during lymphadenectomy, to detect lymphatic drainage and optimise the dissection and retrieval of the lymph nodes with more accuracy. On the other hand, despite the good results of the SPIDER and MBS techniques in reducing pancreatic damage, *Omori et al.*<sup>45</sup> found that laparoscopic and robotic surgeries are comparable concerning the number of retrieved lymph nodes, as shown in a randomized control trial.<sup>77</sup> In opposition, another RCT described a significantly higher number of harvested lymph nodes.<sup>78</sup>

### **Subgroup Analysis**

There were significant subgroup differences in the following outcomes: operative time, time to first flatus and anastomotic leakage. Regarding operative time, while both subgroups favoured robotic surgery, studies without PSM showed more pronounced differences.

The mean difference of time to first flatus was higher in the non-PSM subgroup, when compared to that of the PSM subgroup. However, the first subgroup showed higher heterogeneity. These findings demonstrated that propensity score-matching reduced both heterogeneity and difference between the robotic and laparoscopic surgery groups. The same happened in the following outcomes: conversion, time to oral

intake, surgical complications (Clavien-Dindo Grade  $\geq$ III), cost, and distal resection margin distance. Therefore, this method allows for a better understanding of each comparison and a more accurate approximation of reality.

Concerning anastomotic leakage, the significant subgroup differences appear to be due to opposite results. The meta-analysis showed that, in the PSM subgroup, there is a tendency for lower anastomotic leakage when performing robotic surgery. There were other outcomes which also showed results favouring robotic surgery in the PSM subgroup, in comparison with those in the non-PSM subgroup, such as blood loss, reoperation, overall complications, proximal resection margin distance and recurrence. However, none of these outcomes demonstrated any significant difference between subgroups.

There were also outcomes where the PSM method did not reduce the heterogeneity of the included studies. In fact, there were higher values of heterogeneity in the PSM subgroup regarding operative time, length of hospital stay, overall complications, pancreatic complications and number of retrieved lymph nodes.

Additionally, length of hospital stay and surgical complications with a Clavien-Dindo Grade  $\geq$ III showed a significant difference only in the PSM subgroup.

On the one hand, PSM subgroups were more consistent and did not emphasize the differences between both surgical approaches. On the other hand, in certain outcomes, these subgroups demonstrated results that were more supportive of robotic surgery, highlighting its advantages when compared with laparoscopic surgery.

The demographic characteristics of the people that underwent propensity score-matching were not equal in every study. Therefore, it is still possible that there are variables that did not undergo PSM and are affecting the validity of the results, in terms of heterogeneity.

## Limitations

The present study also has some limitations: first, we included non-randomized comparative studies; second, several outcomes demonstrated a high percentage of heterogeneity, which may put the validity of the results into question. These differences between studies could be explained by discrepancies in the surgical team's experience in performing robotic surgery; third, about half of the studies included did not perform propensity score-matching, contributing to the influence of confounding factors on the results and conclusions about the outcomes in study; fourth, there was one article which we could not access, resulting in a slight reporting bias; fifth, the majority of the included studies are from Southeast Asia (Japan, China and Korea), which may not be representative of the global reality; sixth, postoperative inflammatory reaction and drain amylase levels, which could improve the assessment of pancreatic damage, were not included.

## Conclusion

In conclusion, we believe that our results demonstrate that robotic gastrectomy is a safe and feasible procedure, when compared with laparoscopic gastrectomy.

Overall, robotic surgery presented better results regarding blood loss, length of hospital stay, time to first flatus, time to oral intake, relevant surgical complications, pancreatic complications and the number of retrieved lymph nodes. However, operative time and financial cost remain the main drawbacks to its widespread use. Further studies are needed to understand mechanisms to minimize these downsides, aiming for a more efficient use of the robotic platform in gastric cancer curative-intent surgery.

Moreover, randomized clinical trials are also desired in contemplation of a better comprehension of the advantages in performing robotic gastrectomy.

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## Authorship confirmation/contribution statement

Pedro Loureiro: Conceptualization (equal); Data curation (equal); Formal analysis (equal); Investigation (Lead); Validation (equal); Visualization (Lead); Writing – original draft (Lead); Writing – review & editing (equal)

José Pedro Barbosa: Data curation (equal); Formal analysis (equal); Investigation (Supporting); Resources (Lead); Supervision (Supporting); Validation (equal); Visualization (Supporting); Writing – original draft (Supporting); Writing – review & editing (equal)

José Barbosa: Conceptualization (equal); Investigation (Supporting); Supervision (Lead); Visualization (Supporting); Writing – review & editing (Supporting)

## Conflicts of interest

The authors have no conflicts of interest to disclose.

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# Tables

Table 1: Summary of studies included in the Meta-analysis

No.	Author	Region	Year	Study period	Study design	Sample size		Surgical extension	Level of LND	Reconstruction	MINORS
						RG	LG				
1	Aktas et al. 2020	Turkey	2020	2013-2018	OCS (P)	30	64	D, P, T, EJG	D2	RY	21
2	Alhoassaini et al. 2020	Korea	2019	2005-2017	OCS (R)	25	30	T	NA	BI, BII	23
3	Cianchi et al. 2016	Italy	2016	2008-2015	OCS (P)	30	41	D	D1+a/b, D2	BII, RY	21
4	Eom et al. 2012	Korea	2011	2009-2010	OCS (P)	30	62	D	D1+b, D2	BII	22
5	Gao, G. et al. 2022	China	2022	2015-2021	OCS (R)	441	723	D	D2	BI, BII, RY	21
6	Gao, Y. et al. 2019	China	2018	2011-2014	OCS (P)	163	339	D, P, T	D1+, D2	BI, BII, RY	21
7	Han et al. 2015	Korea	2015	2008-2013	OCS (R)	68	68	PPG	D1 + b	GG	23
8	Hikage et al. 2022	Japan	2022	2013-2020	OCS (P)	36	58	T	D1 +, D2	EJJ	21
9	Hong et al. 2016	Korea	2016	2008-2015	OCS (P)	232	232	D	D1+a/b, D2	BI, BII, RY	22
10	Huang et al. 2014	Taiwan	2014	2008-2014	OCS (P)	72	73	D, T	D1+a/b, D2	BI, RY	22
11	Hyun et al. 2013	Korea	2013	2009-2010	OCS (P)	38	83	D, T	D1+a/b, D2	BI, BII, RY	22
12	Isobe et al. 2021	Japan	2021	2018-2020	OCS (R)	69	88	D	D1, D1+, D2	BI, BII, RY	21
13	Junfeng et al. 2014	China	2014	2010-2013	OCS (R)	120	394	D, P, T	D1, D2	BI, BII, RY	23
14	Kang et al. 2012	Korea	2012	2008-2011	OCS (P)	100	282	D, T	D1+a/b, D2	BI, BII, RY	22
15	Kim, H.I. et al. 2016	Korea	2013	2003-2009	OCS (P)	172	481	D, T	D1+a/b, D2	BI, BII	22
16	Kim, H.I. et al. 2014	Korea	2016	2011-2012	OCS (P)	185	185	D, T	D1+a/b, D2	BI, BII, RY	23
17	Kim, K.M. et al. 2012	Korea	2012	2005-2010	OCS (P)	436	861	D, T	D1+a/b, D2	BI, BII, RY	23
18	Kim, M.C. et al. 2010	Korea	2010	2007-2008	OCS (P)	16	11	D	D1 + b, D2	BI, BII	22
19	Kim, Y.W. et al. 2016	Korea	2015	2009-2001	OCS (P)	87	288	D	D1, D2	NA	20
20	Kong et al. 2020	China	2020	2014-2017	OCS (R)	294	750	D, P, T	D2, D2+	BI, BII, RY	21
21	Lee et al. 2015	Korea	2015	2003-2010	OCS (P)	133	267	D	D2	BI, BII, RY	21
22	Liu et al. 2018	China	2018	2017-2017	OCS (R)	100	135	D, T	D1+a/b, D2	BII, RY	21
23	Li et al. 2018	China	2018	2013-2017	OCS (P)	112	112	D, T	D2	BI, BII, RY	23
24	Lu et al. 2018	China	2018	2016-2017	OCS (P)	101	303	D, T	D1 +, D2	BI, BII, RY	20
25	Nakauchi et al. 2016	Japan	2016	2009-2012	OCS (R)	84	437	D, T	D1+a/b, D2	BI, BII, RY	23
26	Nishi et al. 2022	Japan	2022	2005-2020	OCS (R)	83	368	D, P, T, PPG	D1, D2	BI, RY	21
27	Noshiro et al. 2014	Japan	2014	2010-2012	OCS (P)	21	160	D	D1+a/b, D2	BI, BII, RY	22
28	Obama et al. 2018	Korea	2017	2005-2009	OCS (P)	315	525	D, T	D1+a/b, D2	BI, BII, RY	23
29	Okabe et al. 2021	Japan	2021	2012-2020	OCS (P)	110	256	D, P, T	D1 +, D2	BI, RY	22
30	Okumura et al. 2016	Japan	2016	2003-2010	OCS (P)	370	132	D, T	D1+a/b, D2	BI, BII, RY	22
31	Omori et al. 2022	Japan	2022	2014-2019	OCS (P)	210	979	D, P, T, EJG	D1 +, D2	BI	22
32	Parisi et al. 2017	Italy	2017	2015-2016	OCS (P)	151	151	D, T	D2	BI, BII, RY	21
33	Park et al. 2015	Korea	2015	2009-2011	OCS (P)	145	612	D, T	D1 + a/b	BI, BII, RY	19
34	Pugliese et al. 2010	Italy	2010	2000-2009	OCS (R)	16	48	D	D2	RY	21
35	Roh, C.K. et al. 2020	Korea	2020	2015-2017	OCS (R)	56	152	D	D1 +	BI, BII	21
36	Roh, C.K. et al. 2021	Korea	2021	2009-2018	OCS (P)	74	321	T	D1 +, D2	RY	22
37	Ryan et al. 2020	USA	2020	2010-2014	OCS (P)	631	1262	T, ST	NA	NA	22
38	Seo et al. 2015	Korea	2014	2004-2009	OCS (P)	40	40	D	D1+b, D2	BI, BII, RY	20
39	Shen et al. 2016	China	2016	2011-2014	OCS (R)	93	330	D, T	D1+a/b, D2	BI, BII, RY	21
40	Shibasaki et al 2020	Japan	2020	2009-2019	OCS (P)	359	1042	D, P, T	D1+, D2	BI, BII, RY	22
41	Song et al. 2009	Korea	2008	2005-2006	OCS (P)	20	20	D	D1+a/b, D2	BI	21
42	Son, S-Y. et al. 2012	Korea	2012	2007-2011	OCS (R)	21	42	D, P, T	D1 + b, D2	BI, BII, RY	19
43	Son, T. et al. 2014	Korea	2014	2003-2010	OCS (P)	51	58	T	D2	RY	22
44	Suda et al. 2015	Japan	2015	2009-2012	OCS (R)	88	438	D, T	D1+a/b, D2	BI, BII, RY	22
45	Tian et al 2022	China	2022	2014-2019	OCS (P)	463	877	T, ST	D1 +, D2	BI, BII, RY	22
46	Uyama et al. 2012	Japan	2012	2009-2010	OCS (P)	25	225	D	D2	BI	21
47	Wang et al. 2019	China	2018	2016-2018	OCS (P)	223	223	D, T	D2	BII, RY	23
48	Woo et al. 2011	Japan	2011	2005-2009	OCS (P)	236	591	D, T	D1+a/b, D2	BI, BII, RY	23
49	Yang, S.Y. et al. 2017	Korea	2017	2009-2015	OCS (P)	173	511	D, T	D1+a/b, D2	BI, BII, RY	21
50	Yang, C. et al. 2020	China	2020	2010-2017	OCS (P)	126	257	T	D2	RY	22
51	Ye et al. 2020	China	2020	2014-2019	OCS (R)	325	358	D	D2	BI, BII, RY	21
52	Yoon et al 2012	Korea	2011	2009-2011	OCS (R)	36	65	T	D1+a/b, D2	BI, BII	23
53	Zheng-Yan et al. 2021	China	2020	2010-2019	OCS (P)	519	957	D	D1, D2	BI, BII, RY	22

RG: Robotic Gastrectomy; LG: Laparoscopic Gastrectomy; LND: Lymphadenectomy; MINORS: Methodological Index for Non-Randomized Studies; OCS: Observational Clinical Study; P: prospectively collected data; R: retrospectively collected data; D: Distal; P: Proximal; T: Total; EJG: Esophagogastric Junction; PPG: Pylorus-preserving Gastrectomy; ST: Sub-Total; BI: Billroth I; BII: Billroth II; RY: Roux-en-Y; GG: gastro-gastro anastomosis; EJJ: Esophagojejunostomy; NA: Not Available

Table 2: Patients' characteristics.

No.	Author	Year	Age (RG)		Age (LG)		Sex (RG)			Sex (LG)		
			Mean	Sd	Mean	Sd	M	F	Pt	M	F	Pt
1	Aktas et al. 2020	2020	55	8	59	10,5	18	12	30	41	23	64
2	Alhoassaini et al. 2020	2019	54	15	60	15	17	8	25	22	8	30
3	Cianchi et al. 2016	2016	73	10,25	74	11,75	14	16	30	19	22	41
4	Eom et al. 2012	2011	52	11,5	57	11	21	9	30	41	21	62
5	Gao, G. et al. 2022	2022	60	11	60	11	284	126	410	301	109	410
6	Gao, Y. et al. 2019	2018	60	10	59	11	121	42	163	201	138	339
7	Han et al. 2015	2015	50	8	49	11	31	37	68	32	36	68
8	Hikage et al. 2022	2022	72	10,25	71	12,5	26	10	36	46	12	58
9	Hong et al. 2016	2016	53	11	55	13	154	78	232	156	76	232
10	Huang et al. 2014	2014	67	15	66	13	40	32	72	42	31	73
11	Hyun et al. 2013	2013	54	12	60	12	25	13	38	55	28	83
12	Isobe et al. 2021	2021	70	1	70	1	31	19	50	34	16	50
13	Junfeng et al. 2014	2014	54	10	55	11	90	30	120	276	118	394
14	Kang et al. 2012	2012	53	12	58	12	63	37	100	191	91	282
15	Kim, H.I. et al. 2016	2013	55	13	61	11	103	69	172	294	187	481
16	Kim, H.I. et al. 2014	2016	53	11	56	11	113	72	185	113	72	185
17	Kim, K.M. et al. 2012	2012	54	12	58	12	265	171	436	550	311	861
18	Kim, M.C. et al. 2010	2010	53	15	57	13	10	6	16	10	1	11
19	Kim, Y.W. et al. 2016	2015	54	12	60	11	46	41	87	170	118	288
20	Kong et al. 2020	2020	58	11	59	10	197	69	266	383	149	532
21	Lee et al. 2015	2015	53	13	59	11	85	48	133	154	113	267
22	Liu et al. 2018	2018	58	2,83	58	2,5	79	21	100	101	34	135
23	Li et al. 2018	2018	55	11	56	11	78	34	112	79	33	112
24	Lu et al. 2018	2018	NA	NA	NA	NA	73	28	101	212	91	303
25	Nakauchi et al. 2016	2016	64	8,67	68	9	48	36	84	307	130	437
26	Nishi et al. 2022	2022	67	12	67	11	62	21	83	243	125	368
27	Noshiro et al. 2014	2014	66	10	69	12	14	7	21	102	58	160
28	Obama et al. 2018	2017	54	12	59	11	189	126	315	327	198	525
29	Okabe et al. 2021	2021	69	8	70	7,83	62	31	93	57	36	93
30	Okumura et al. 2016	2016	NA	NA	NA	NA	227	143	370	83	49	132
31	Omori et al. 2022	2022	66	1	66	1	152	58	210	153	57	210
32	Parisi et al. 2017	2017	68	12	65	14	70	81	151	66	85	151
33	Park et al. 2015	2015	54	11	58	11	75	70	145	369	243	612
34	Pugliese et al. 2010	2010	NA	NA	NA	NA	NA	NA	16	NA	NA	48
35	Roh, C.K. et al 2020	2020	58	11	58	11	27	24	51	27	24	51
36	Roh, C.K. et al 2021	2021	54	12	55	13	42	32	74	42	32	74
37	Ryan et al. 2020	2020	65	12	65	12	449	182	631	906	356	1262
38	Seo et al 2015	2014	51	4	55	5	19	21	40	20	20	40
39	Shen et al 2016	2016	56	10	57	11	75	18	93	249	81	330
40	Shibasaki et al 2020	2020	67	9,83	70	5	233	126	359	740	302	1042
41	Song et al. 2009	2008	51	12	55	5	8	12	20	13	7	20
42	Son, S-Y. et al. 2012	2012	52	13	52	13	14	7	21	26	16	42
43	Son, T. et al. 2014	2014	55	12	58	12	23	28	51	36	22	58
44	Suda et al. 2015	2015	68	9	64	11,5	51	37	88	307	131	438
45	Tian et al 2022	2022	59	11	60	10	330	126	456	310	146	456
46	Uyama et al. 2012	2012	61	11	62	9	14	11	25	156	69	225
47	Wang et al. 2019	2018	57	10	57	11	183	40	223	180	43	223
48	Woo et al. 2011	2011	54	12	58	11	136	100	236	364	227	591
49	Yang, S.Y. et al. 2017	2017	NA	NA	NA	NA	98	75	173	335	176	511
50	Yang, C. et al. 2020	2020	60	9	61	9	105	21	126	100	26	126
51	Ye et al. 2020	2020	57	8	57	9	189	96	285	186	99	285
52	Yoon et al 2012	2011	53	11	56	12	18	18	36	31	34	65
53	Zheng-Yan et al. 2021	2020	55	10	55	12	354	162	516	333	184	516

RG: Robotic Gastrectomy; LG: Laparoscopic Gastrectomy; SD: Standard Deviation; M: Male; F: Female; Pt: Patients; NA: Not Available

# Figures



## PRISMA 2009 Flow Diagram

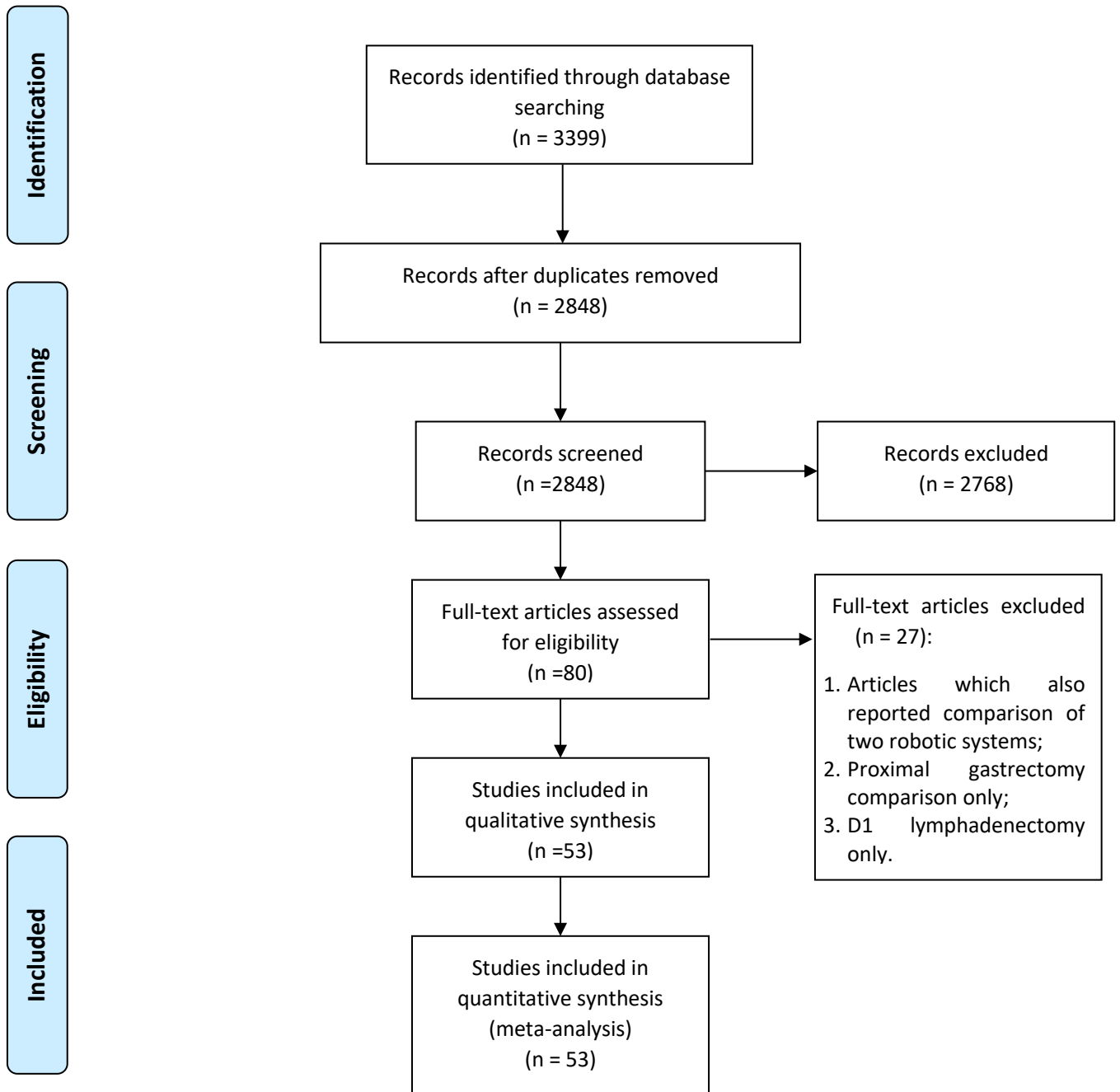


Figure 1: Flow Diagram according to the PRISMA Guidelines

Outcomes	No. of studies	No. patients		Overall effect size (MD1/RR)	95% CI of overall effect	P value	Heterogeneity (I <sup>2</sup> , P)
		RG	LG				
<b>Surgical Outcomes:</b>							
Operative Time	50	6950	11651	41.19	33.47, 48.92	p< 0.00001	I <sup>2</sup> = 98%, p< 0.00001
Blood Loss	46	6734	11856	-19.43	-25.23, -13.62	p< 0.00001	I <sup>2</sup> = 92%, p< 0.00001
Conversion	33	4390	7730	0.68	0.43, 1.07	p= 0.09	I <sup>2</sup> = 0%, p= 0.50
Reoperation	18	2677	4366	0.89	0.59, 1.34	p= 0.57	I <sup>2</sup> = 0%, p= 0.72
Mortality	39	6708	10776	1.20	0.81, 1.77	p= 0.37	I <sup>2</sup> = 0%, p= 0.98
<b>Perioperative Outcomes:</b>							
Length of Hospital Stay	52	7621	12953	-0,50	-0,79, -0,21	p= 0.0007	I <sup>2</sup> = 85%, p< 0.00001
Time to First Flatus	25	4002	5623	-0,52	-0,55, -0,50	p< 0.00001	I <sup>2</sup> = 98%, p< 0.00001
Time to Oral Intake	27	4602	6296	-0,17	-0,25, -0,08	p= 0.0001	I <sup>2</sup> = 53%, p= 0.0008
Overall complications	51	6732	11469	0.93	0.85, 1.03	p= 0.15	I <sup>2</sup> = 18%, p= 0.14
Surgical complications	31	5464	7303	0.68	0.57, 0.82	p< 0.0001	I <sup>2</sup> = 7%, p= 0.35
Anastomotic leakage	33	5289	8721	1.06	0.78, 1.45	p= 0.71	I <sup>2</sup> = 16%, p= 0.21
Pancreatic comp.	21	3445	5497	0.51	0.31, 0.83	p= 0.007	I <sup>2</sup> = 0%, p= 0.60
Cost	8	1683	2184	3684.27	2986.11, 4382.44	p< 0.00001	I <sup>2</sup> = 90%, p< 0.00001
<b>Oncological Outcomes:</b>							
Distal Resection MD2	14	2184	3973	0.16	-0.19, 0.51	p= 0.37	I <sup>2</sup> = 76% p< 0.00001
Proximal Resection MD2	15	2235	4031	0.06	-0.05, 0.18	p= 0.29	I <sup>2</sup> = 0%, p= 0.52
Recurrence	11	1358	2024	0.95	0.77, 1.17	p= 0.61	I <sup>2</sup> = 0%, p= 0.91
No. retrieved lymph nodes	49	7292	11622	1.69	0.68, 2.70	p= 0.001	I <sup>2</sup> = 93% p< 0.00001

Figure 2: Results of the Meta-Analysis: RG: Robotic Gastrectomy; LG: Laparoscopic Gastrectomy; MD1: Mean Difference; RR: Risk Ratio; CI: Confidence Interval; comp.: complications; MD2: Margin Distance



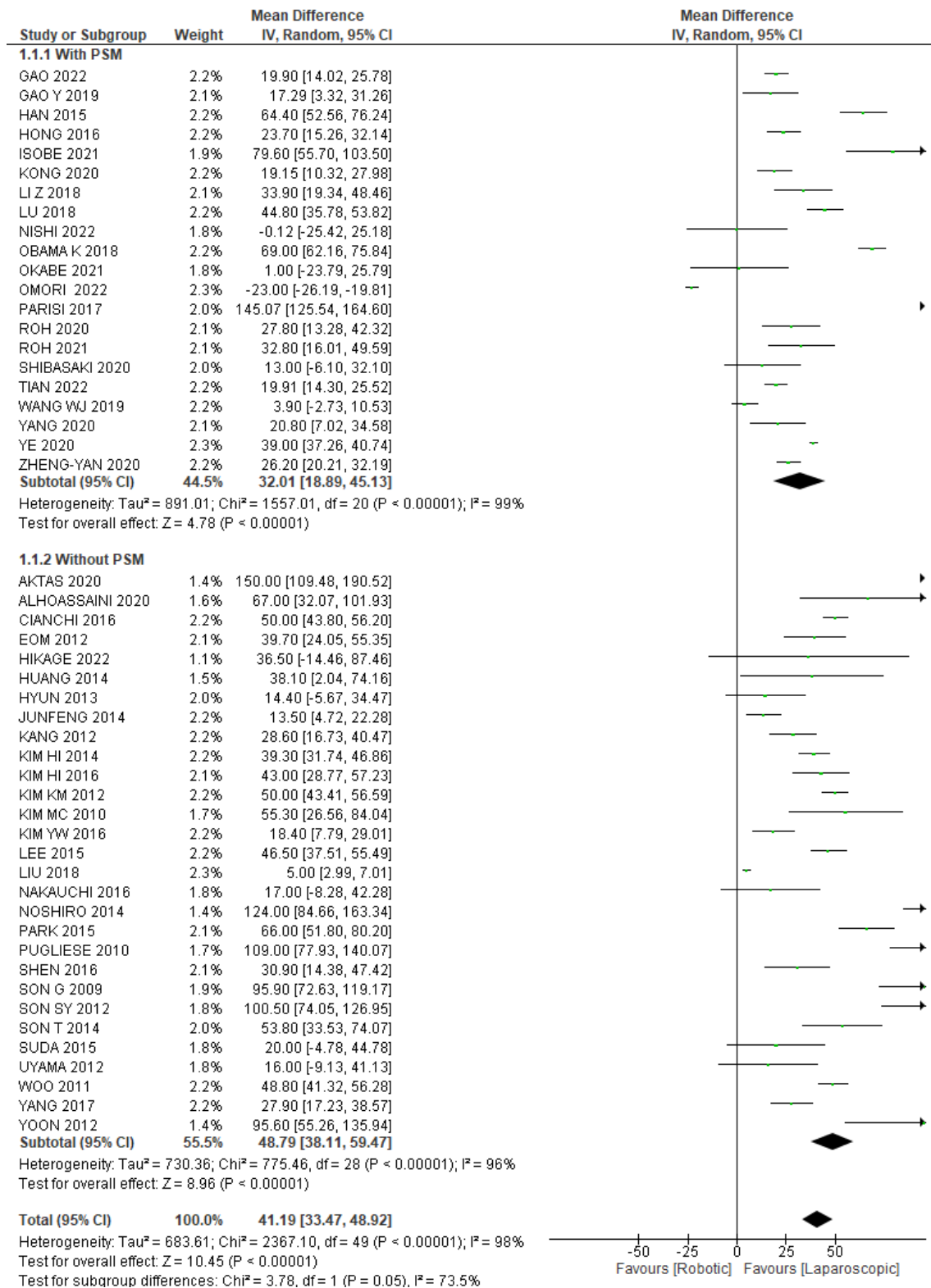


Figure 3: Operative Time

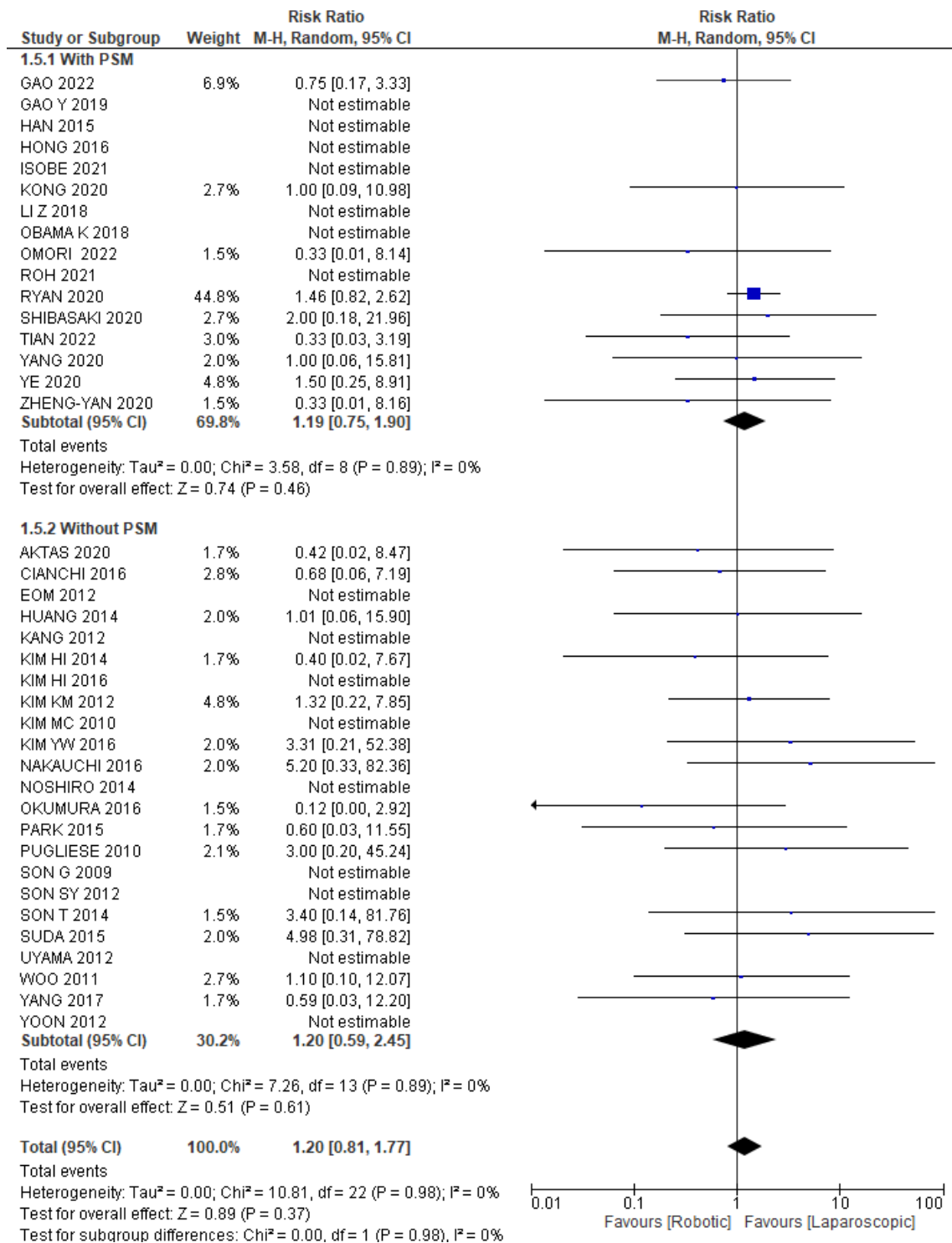


Figure 4: Mortality

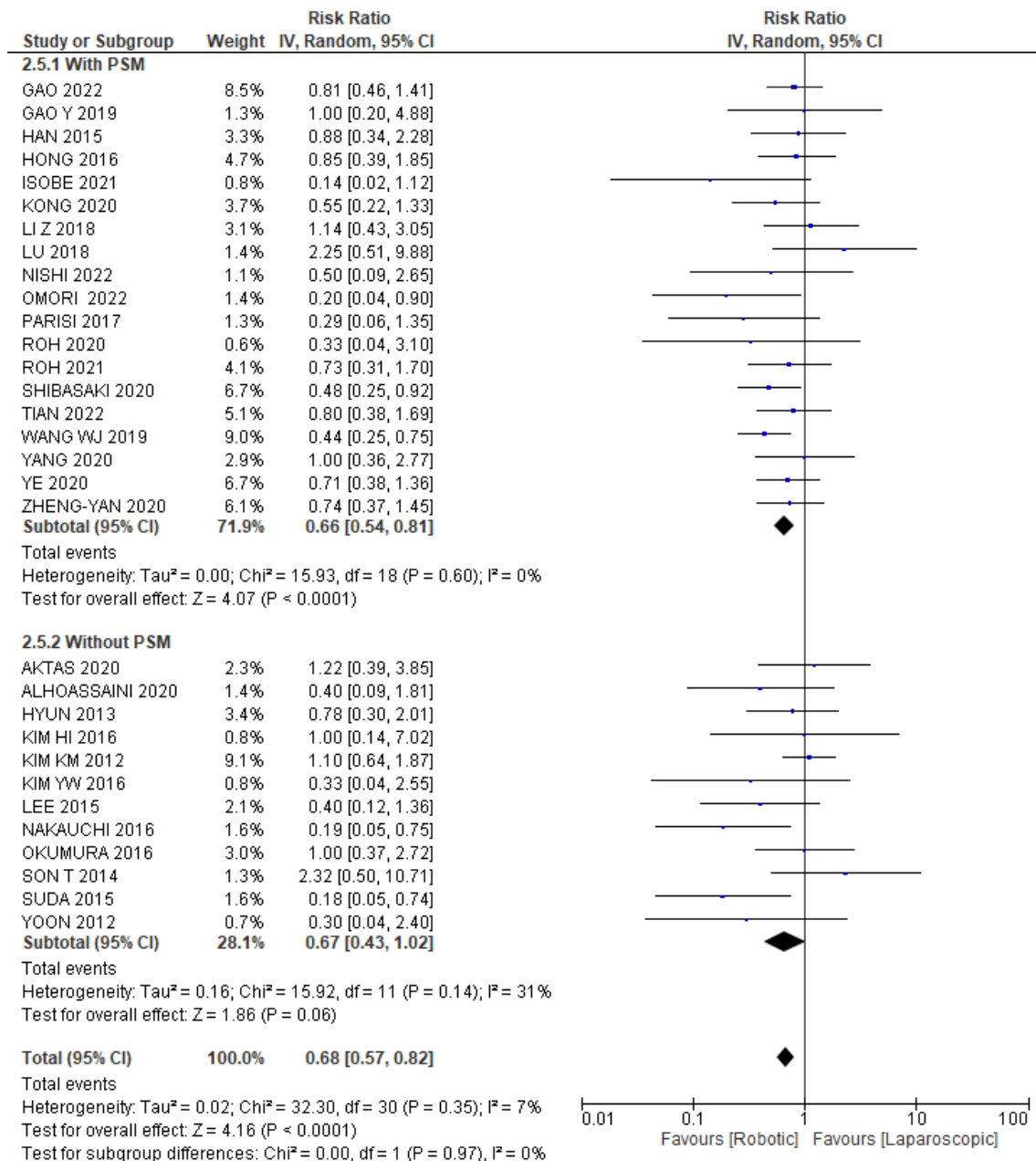


Figure 5: Surgical complications (Grade  $\geq$  III in the Clavien-Dindo Classification)

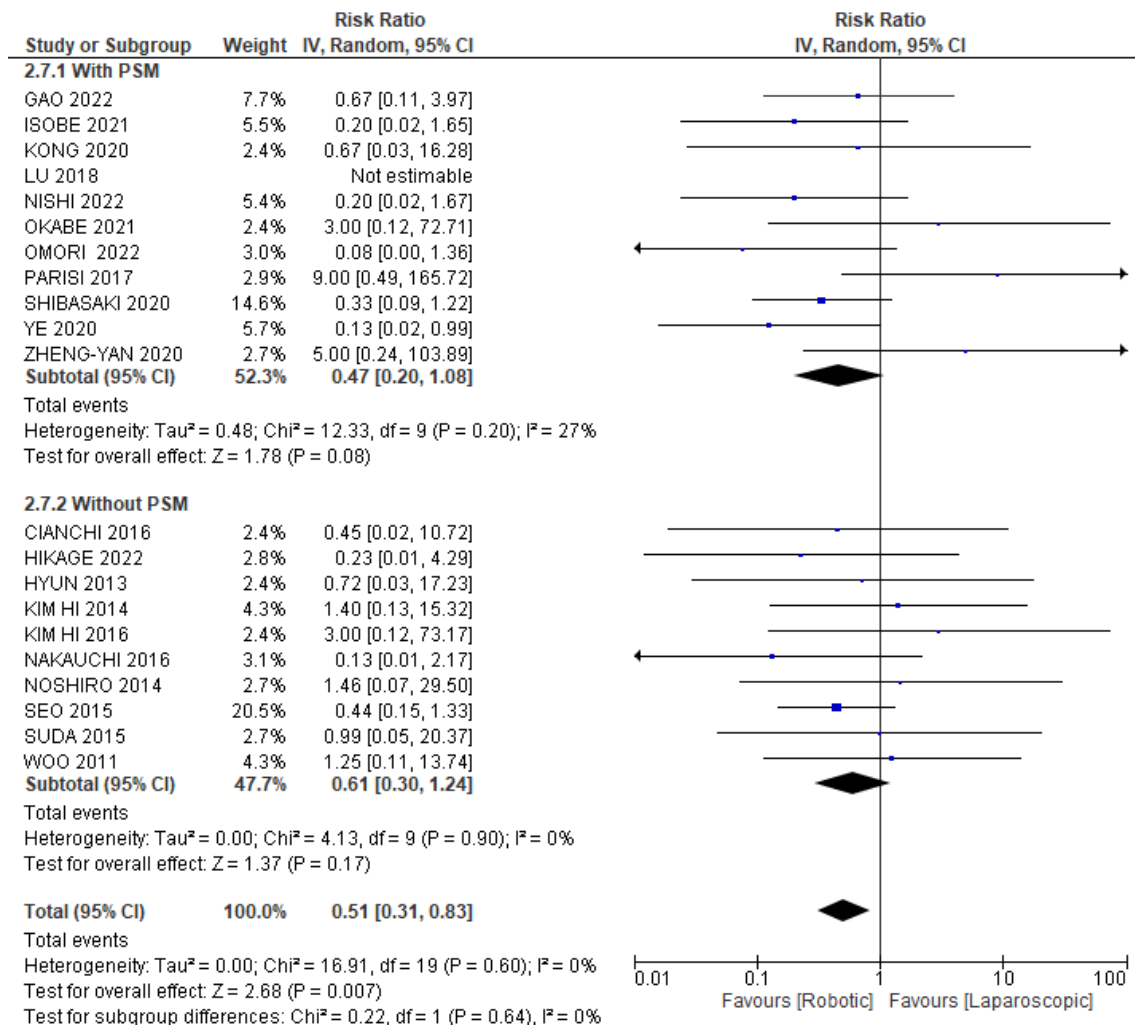


Figure 6: Pancreatic Complications

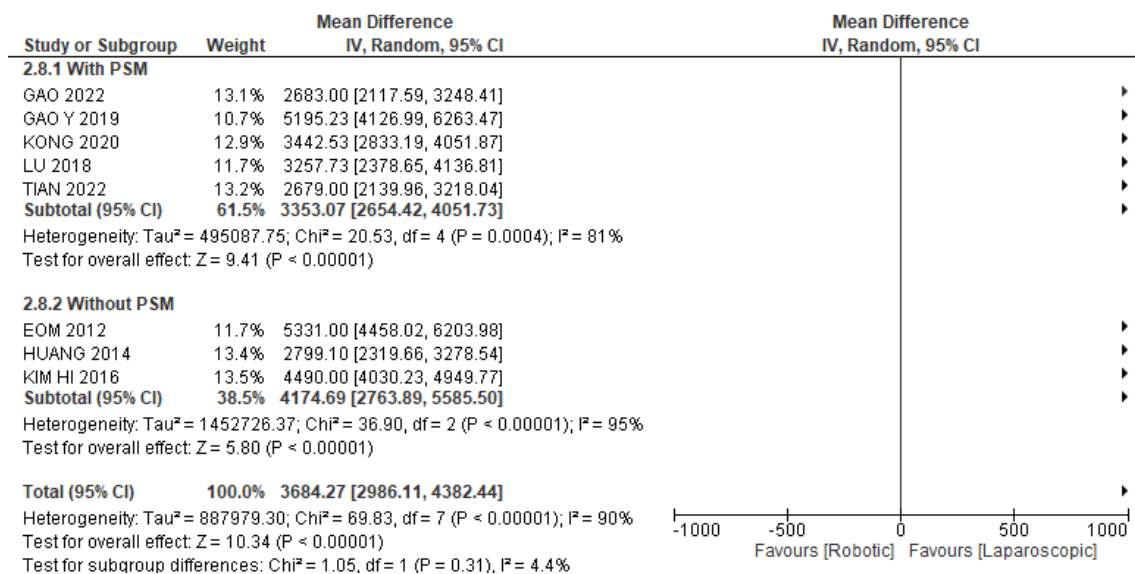


Figure 7: Cost

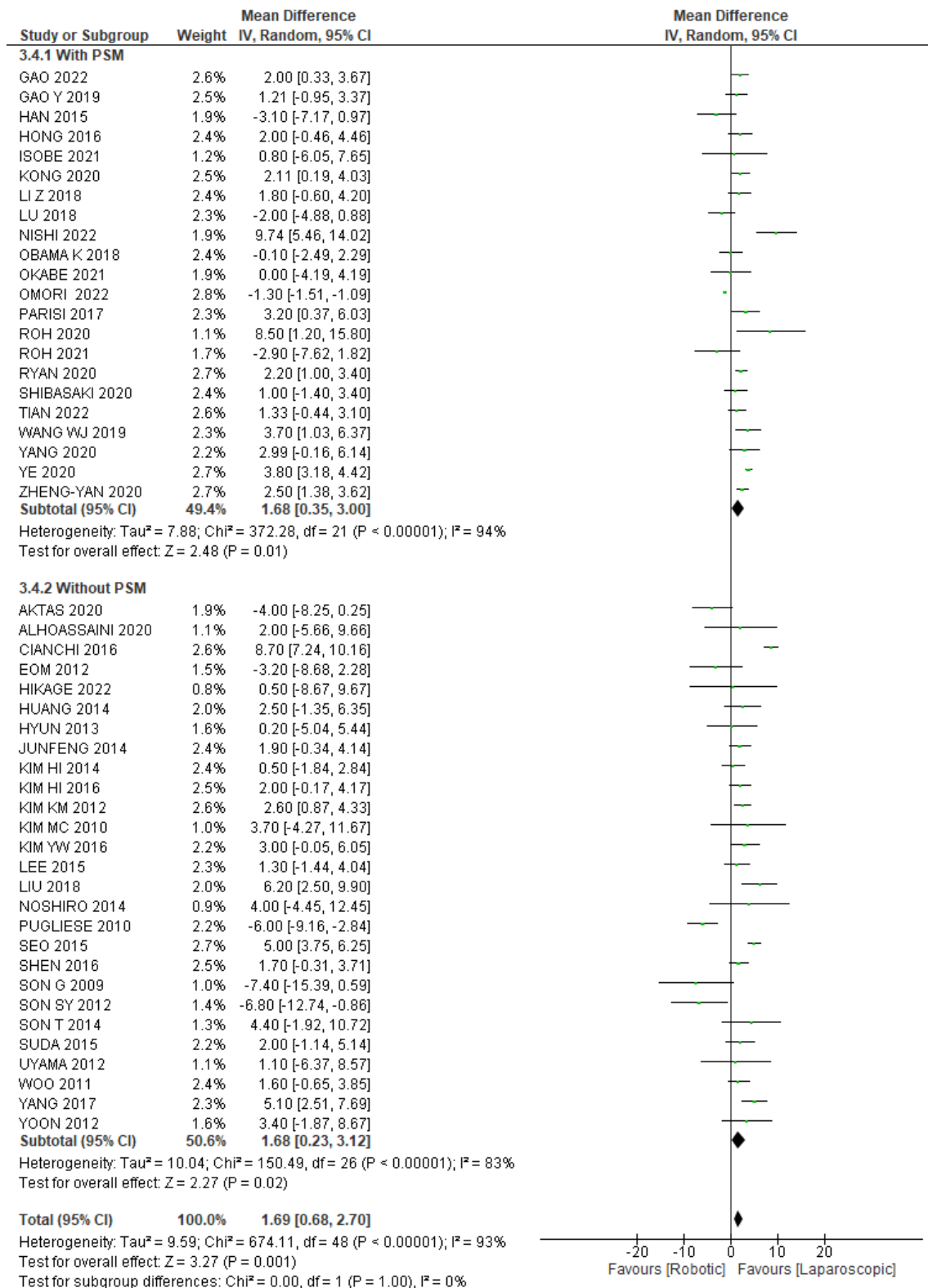
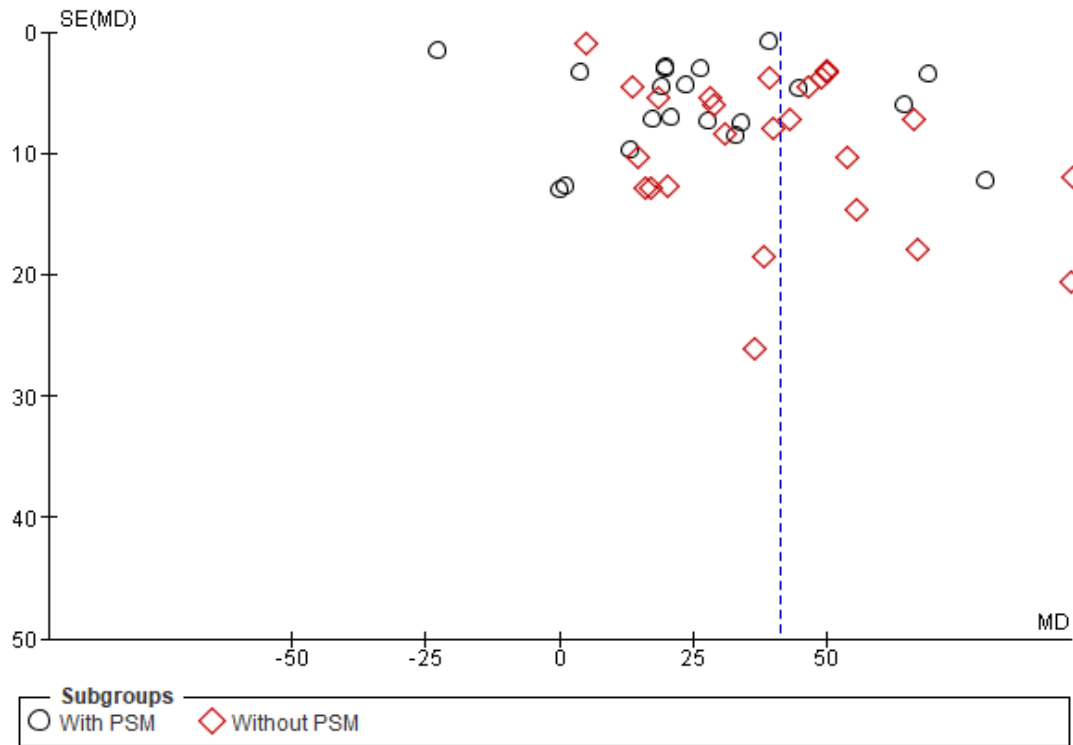


Figure 8: Number of Retrieved Lymph Nodes

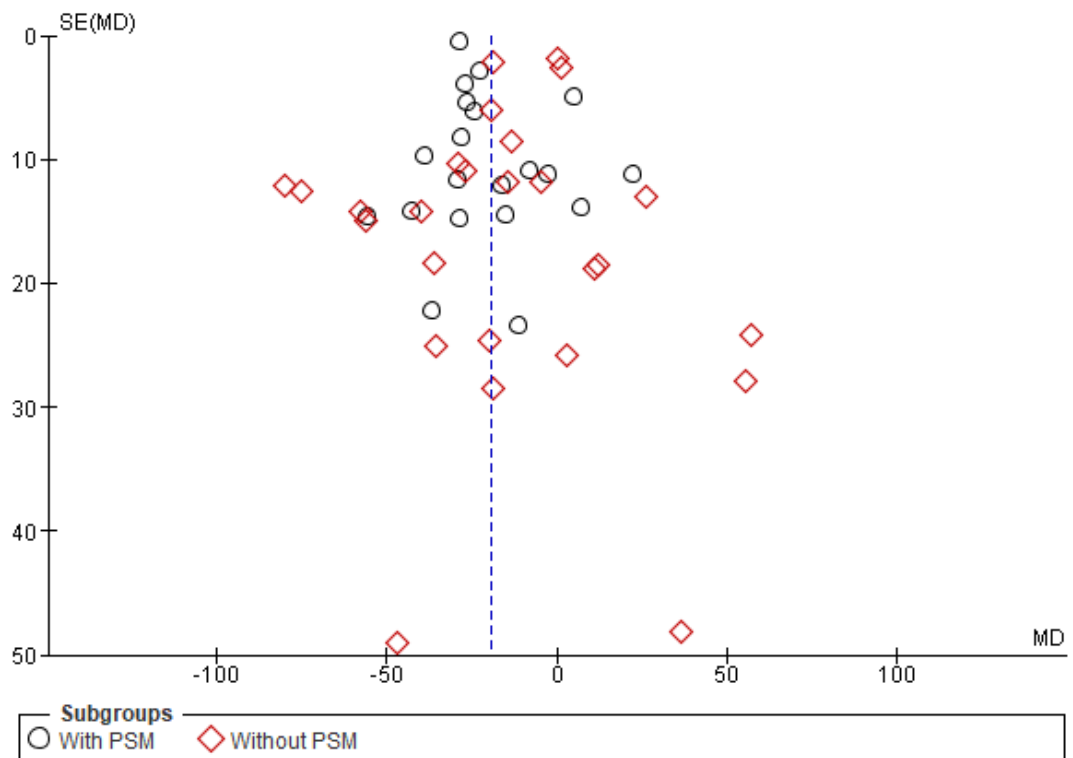
# Supplemental Files

## Supplemental File no.1 - Funnel Plots

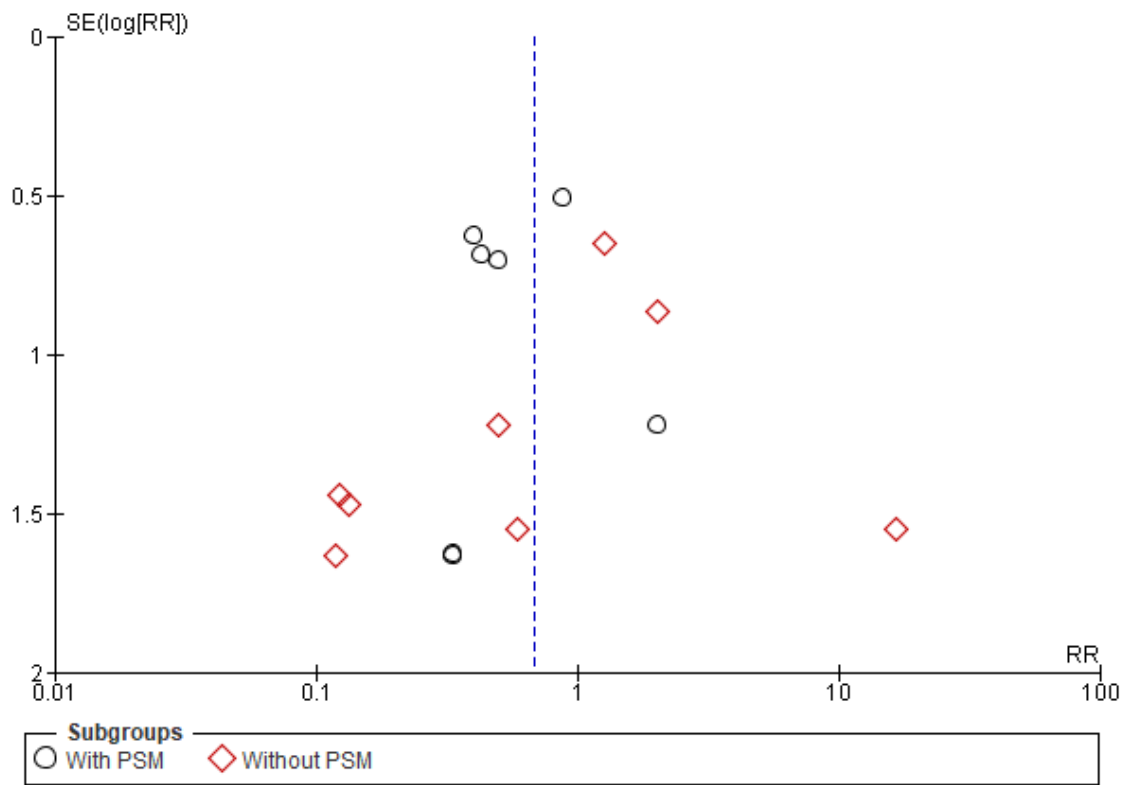
### • Operative Time



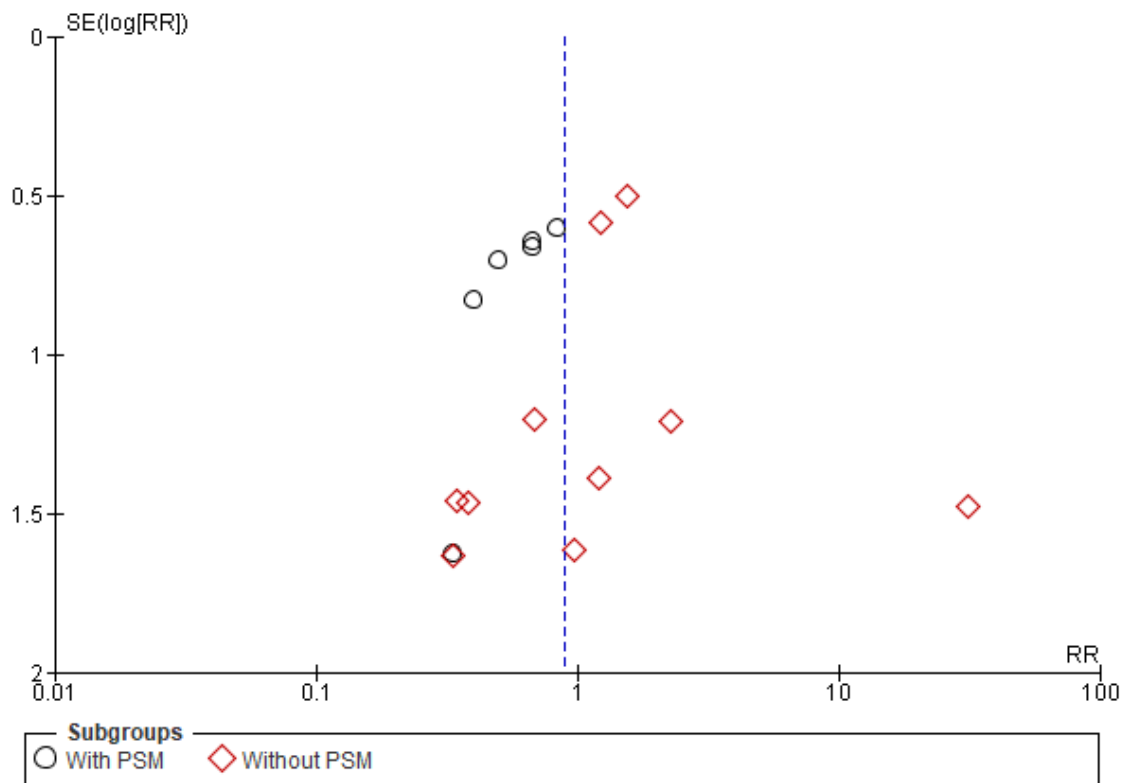
### • Blood Loss



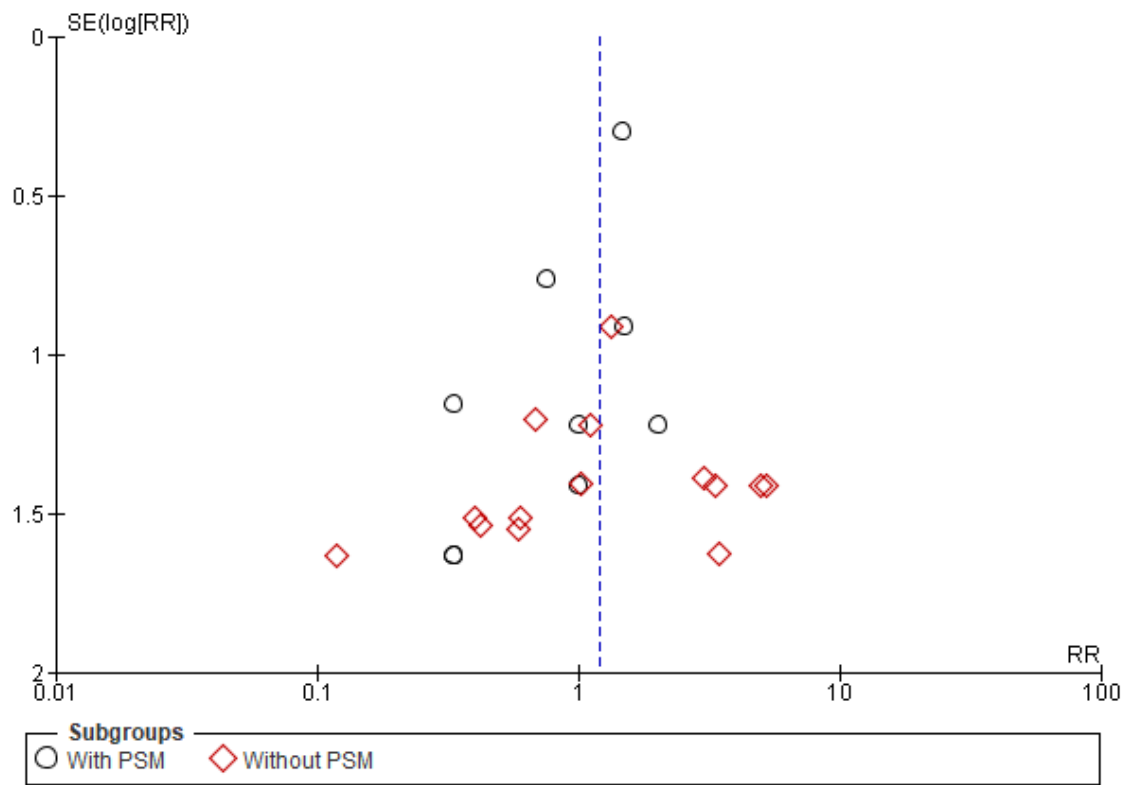
- Conversion



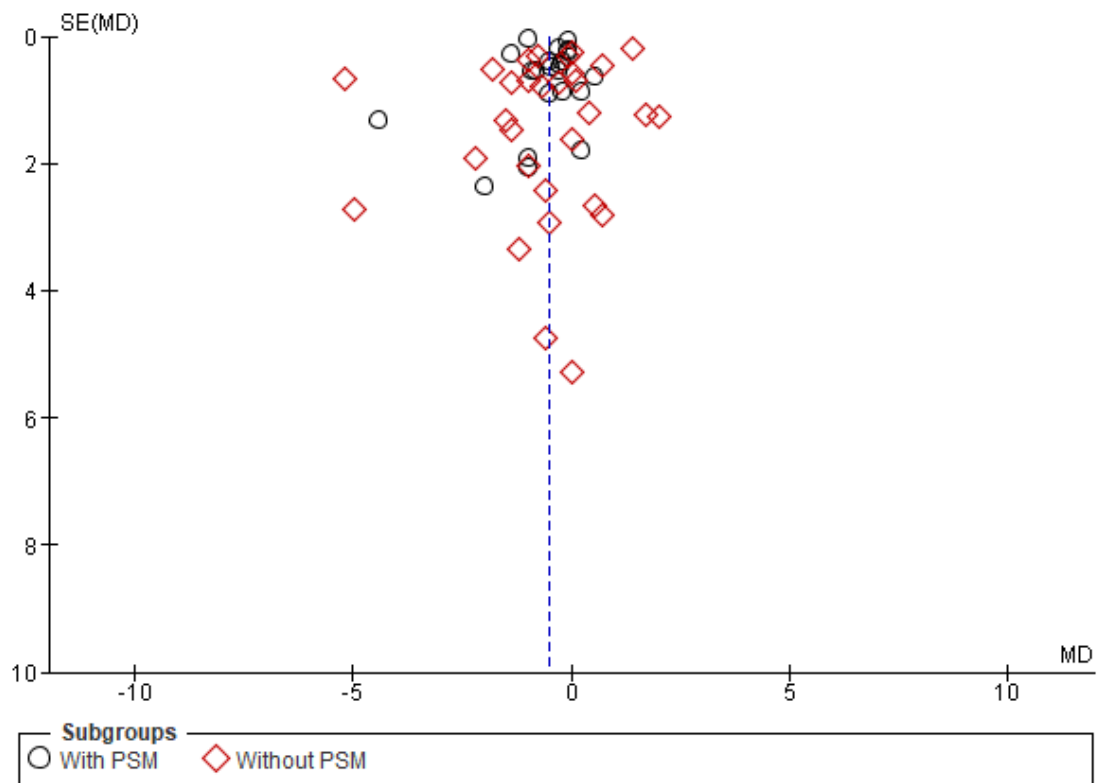
- Reoperation



- **Mortality**

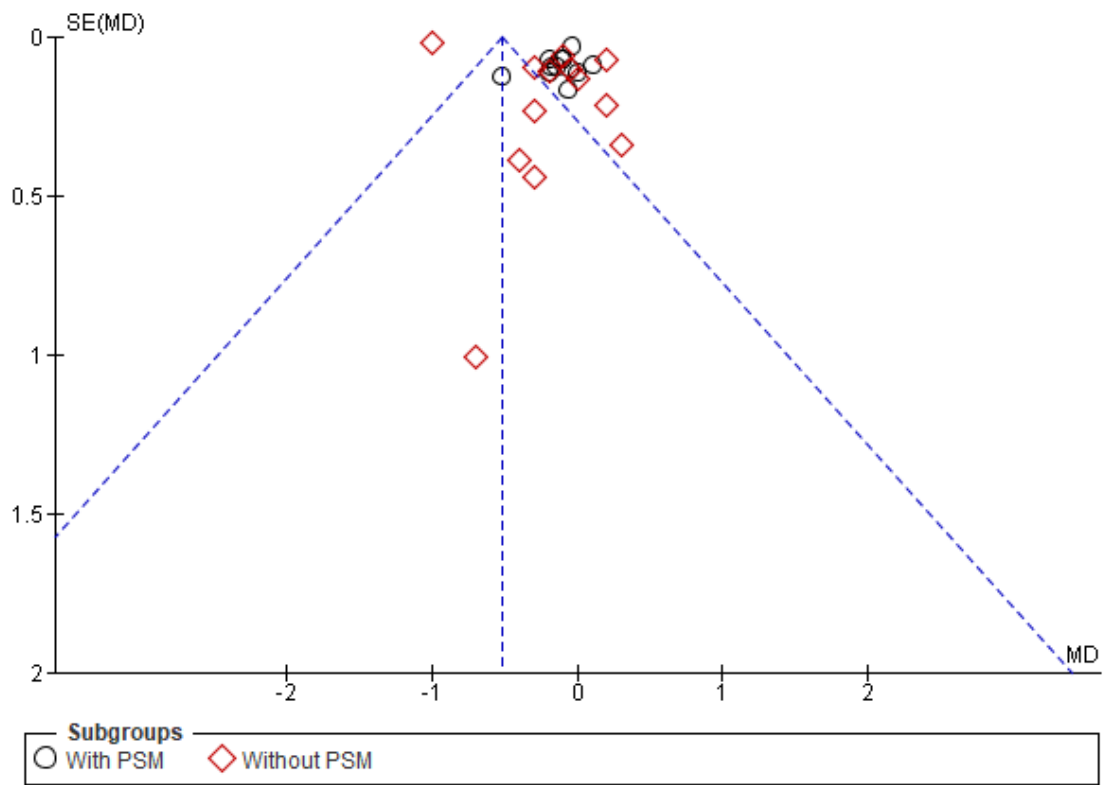


- **Length of Hospital stay**

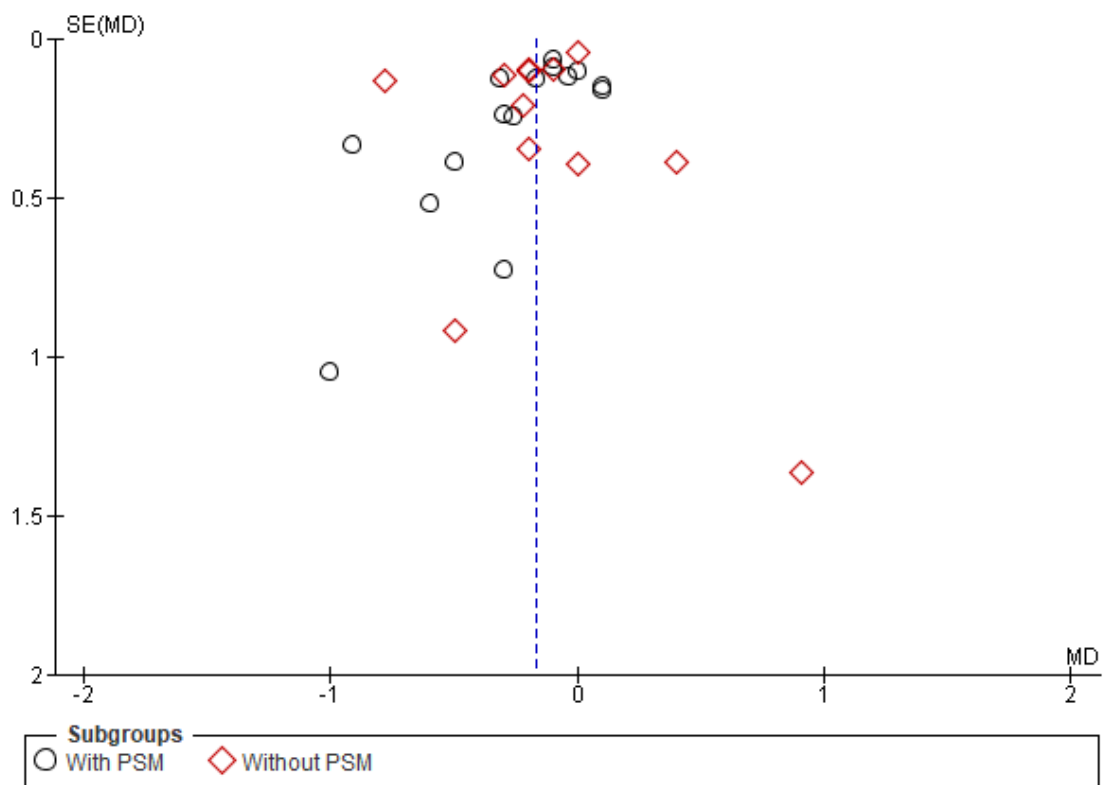




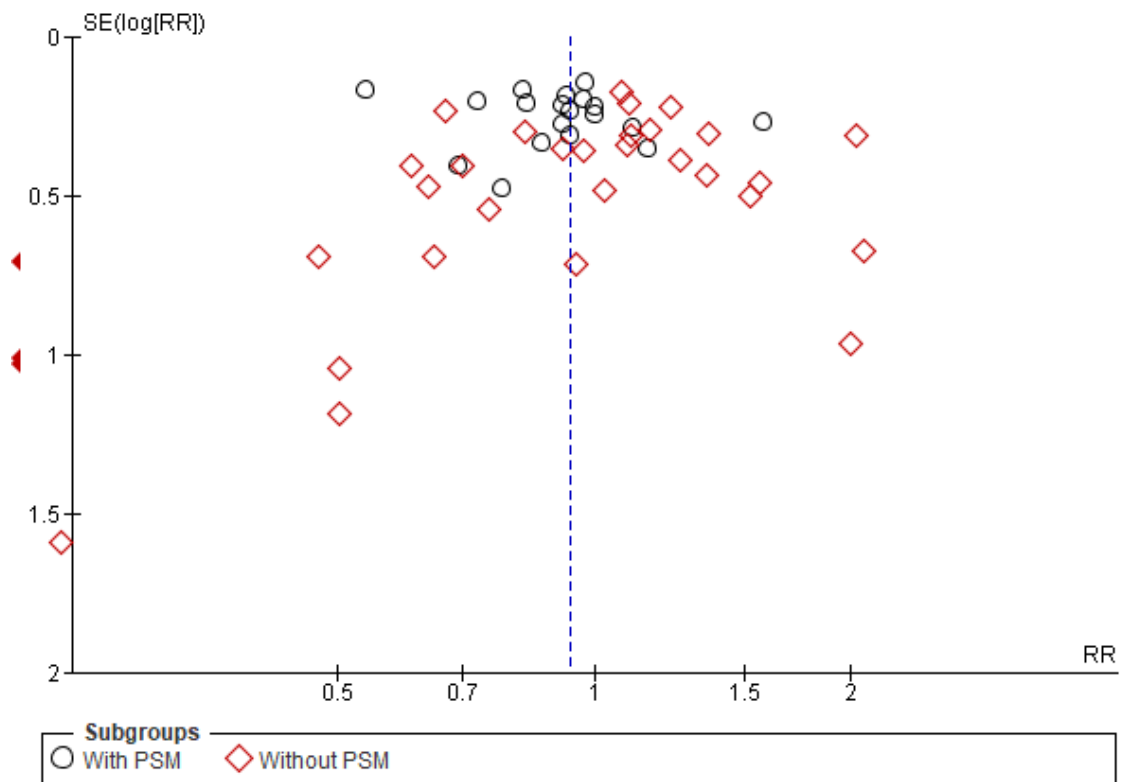
• **Time to First Flatus**



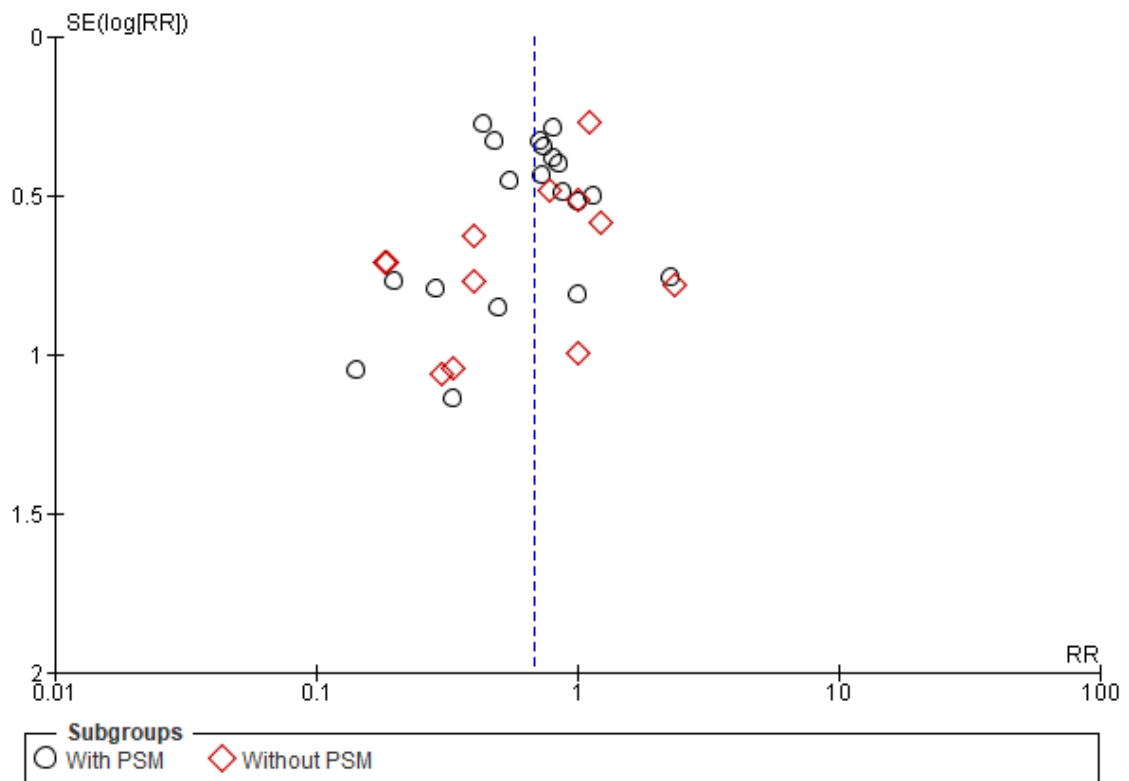
• **Time to oral intake**



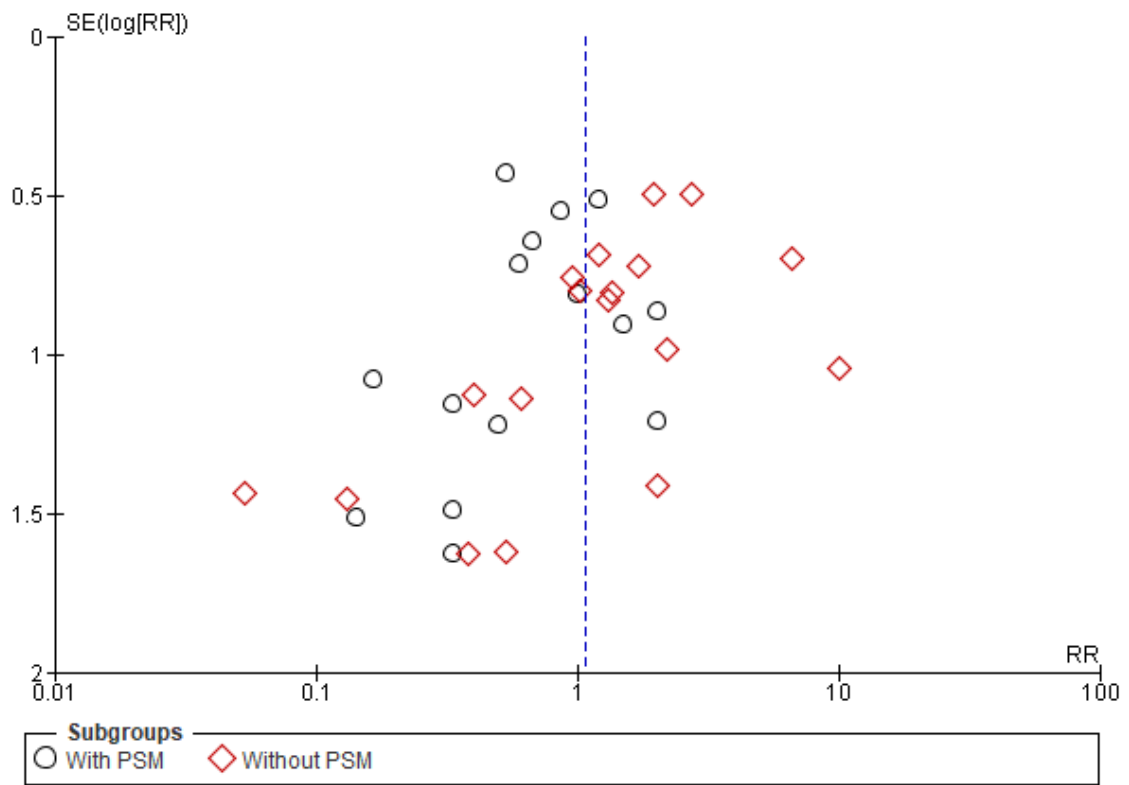
- Overall Complications



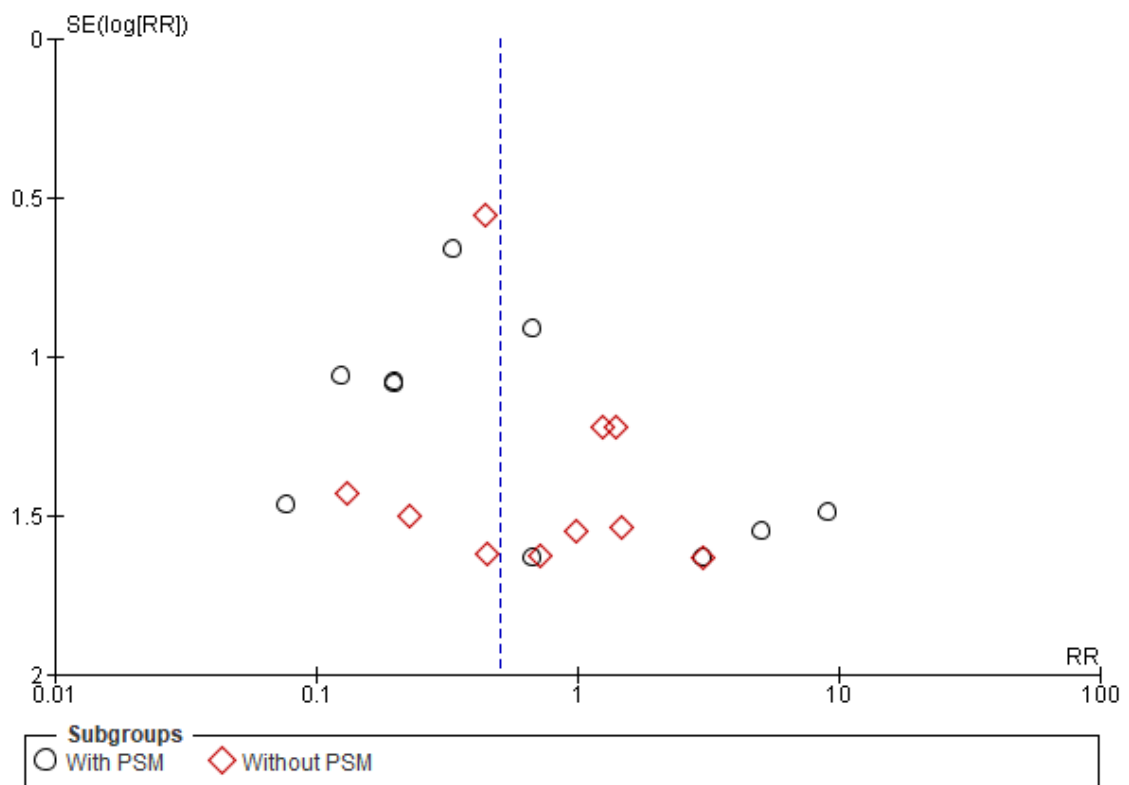
- Surgical complication according to Clavien-Dindo Grade  $\geq$  III



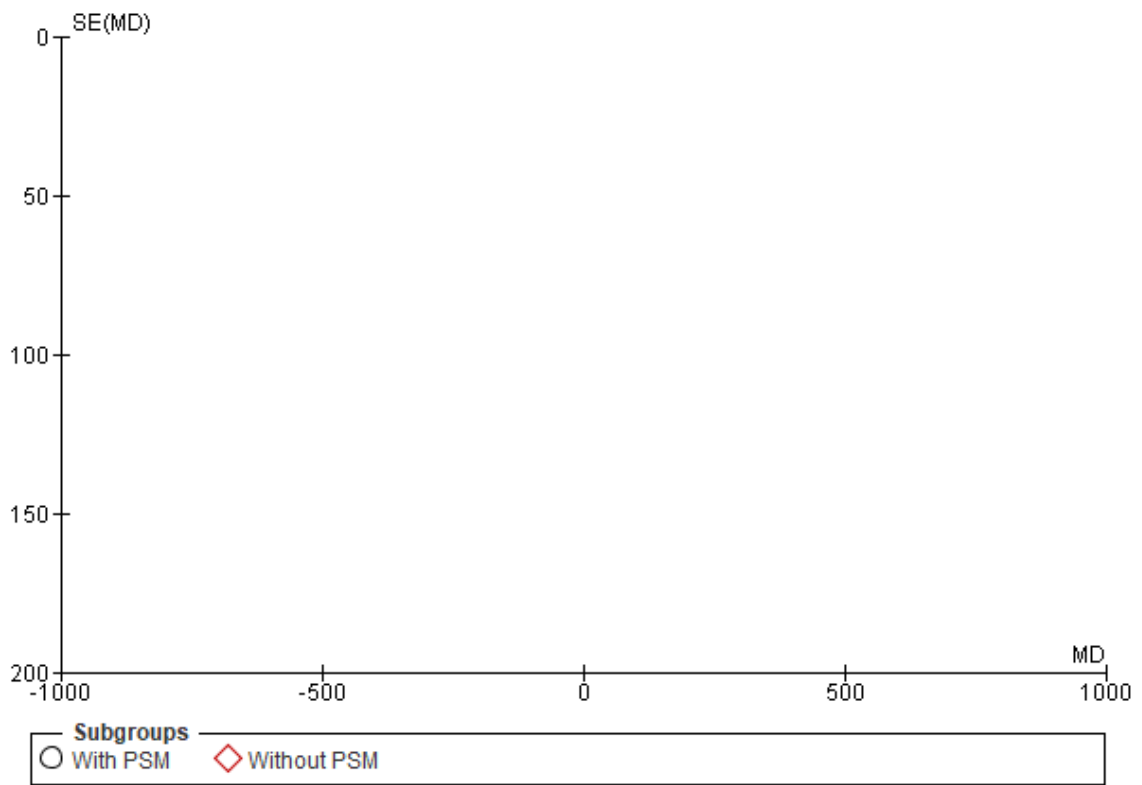
- **Anastomotic Leakage**



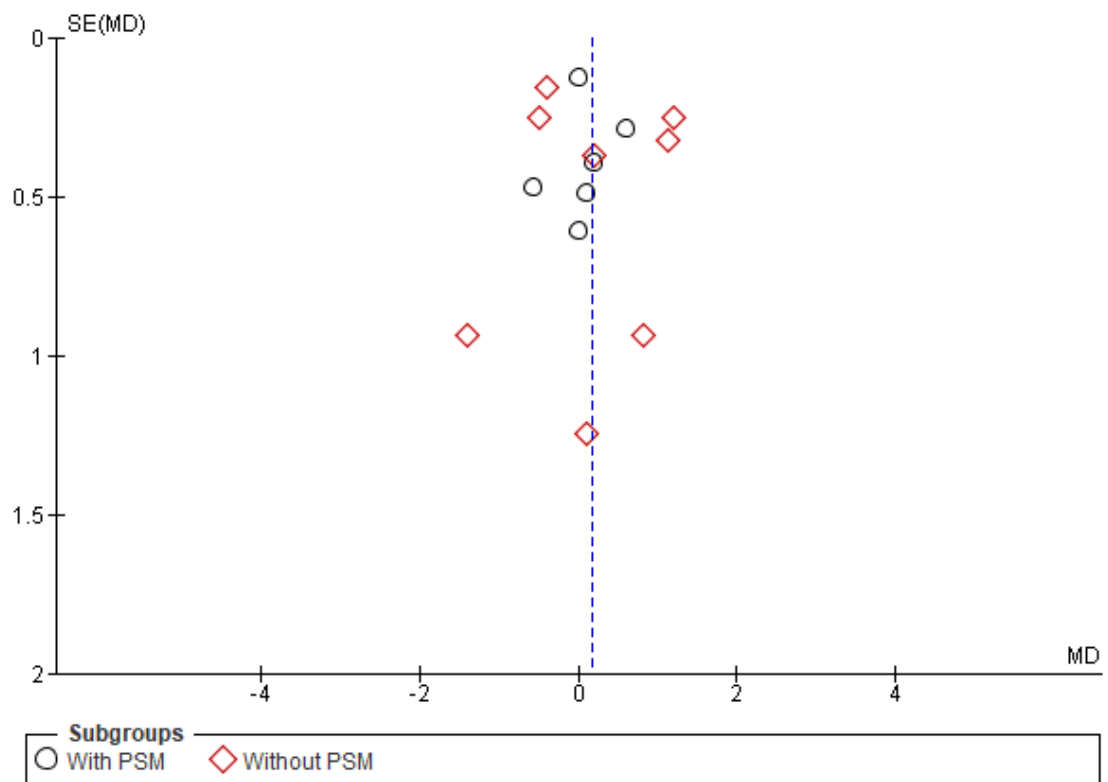
- **Pancreatic Complications**



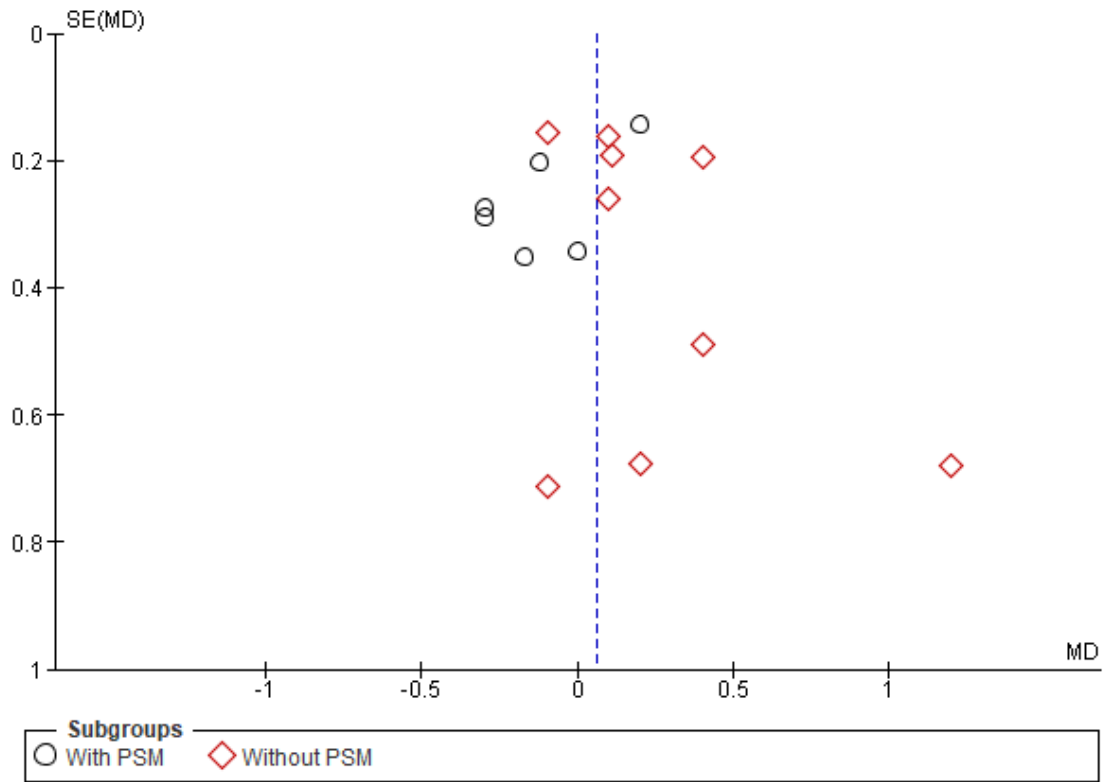
- **Cost**



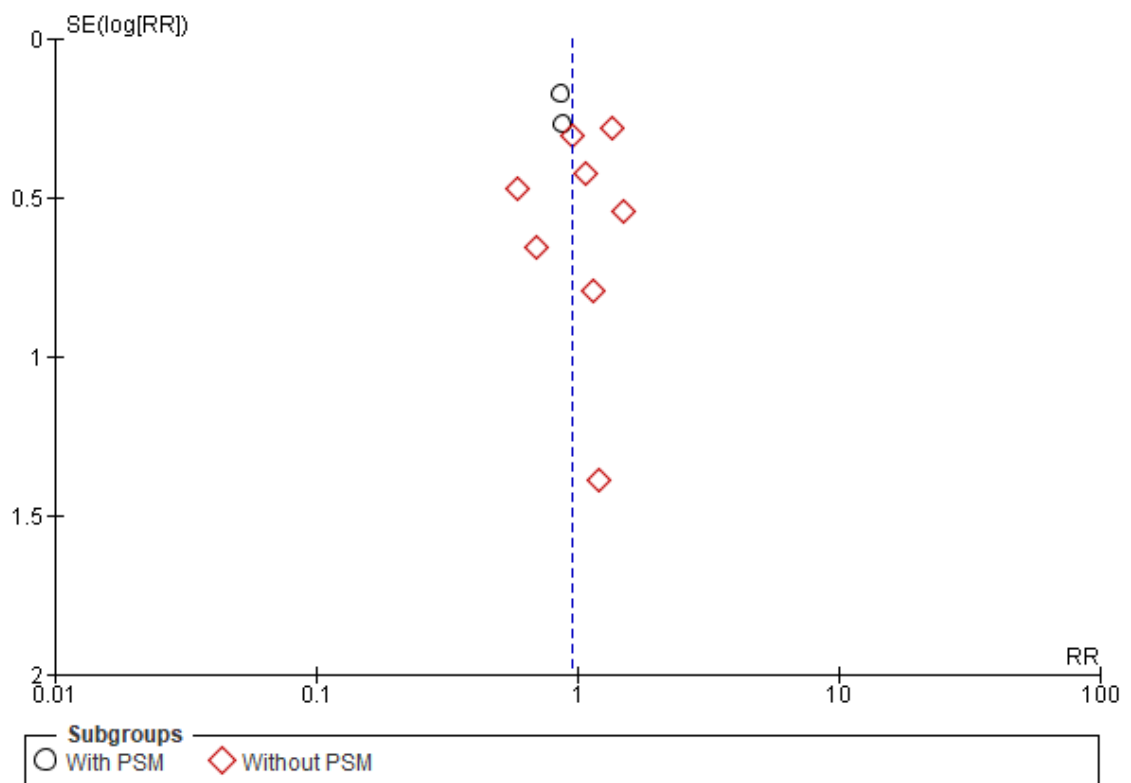
- **Distal resection margin distance**



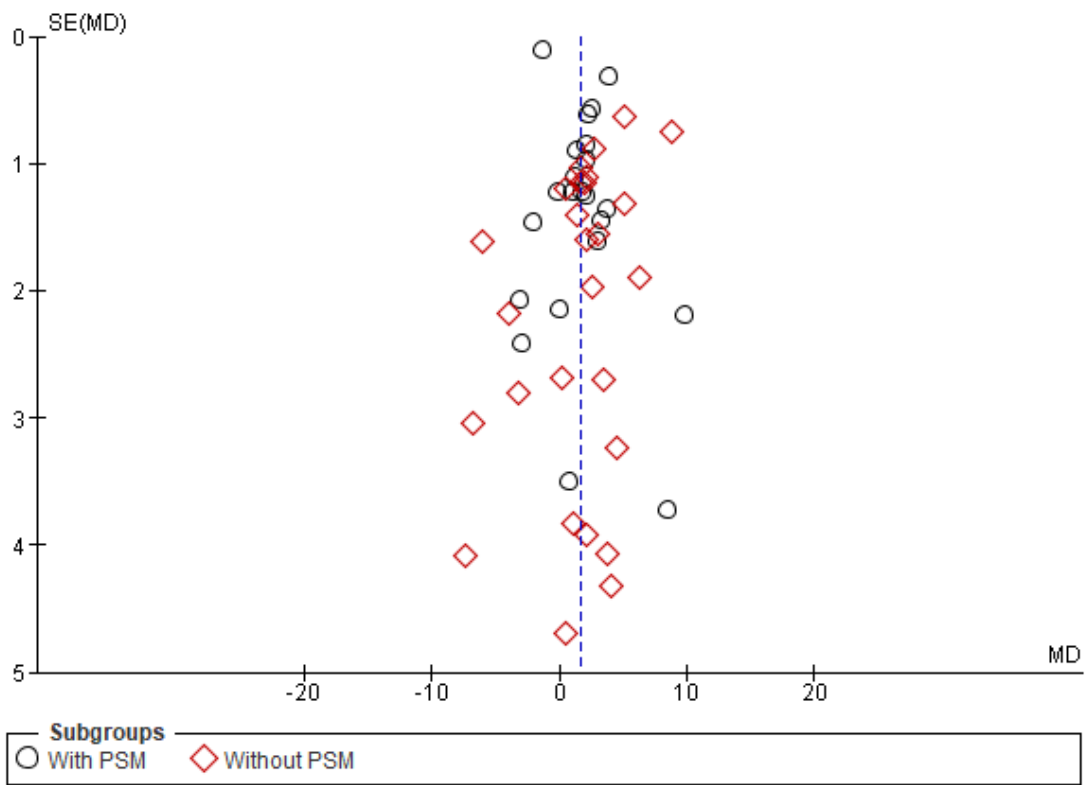
- Proximal resection margin distance



- Recurrence

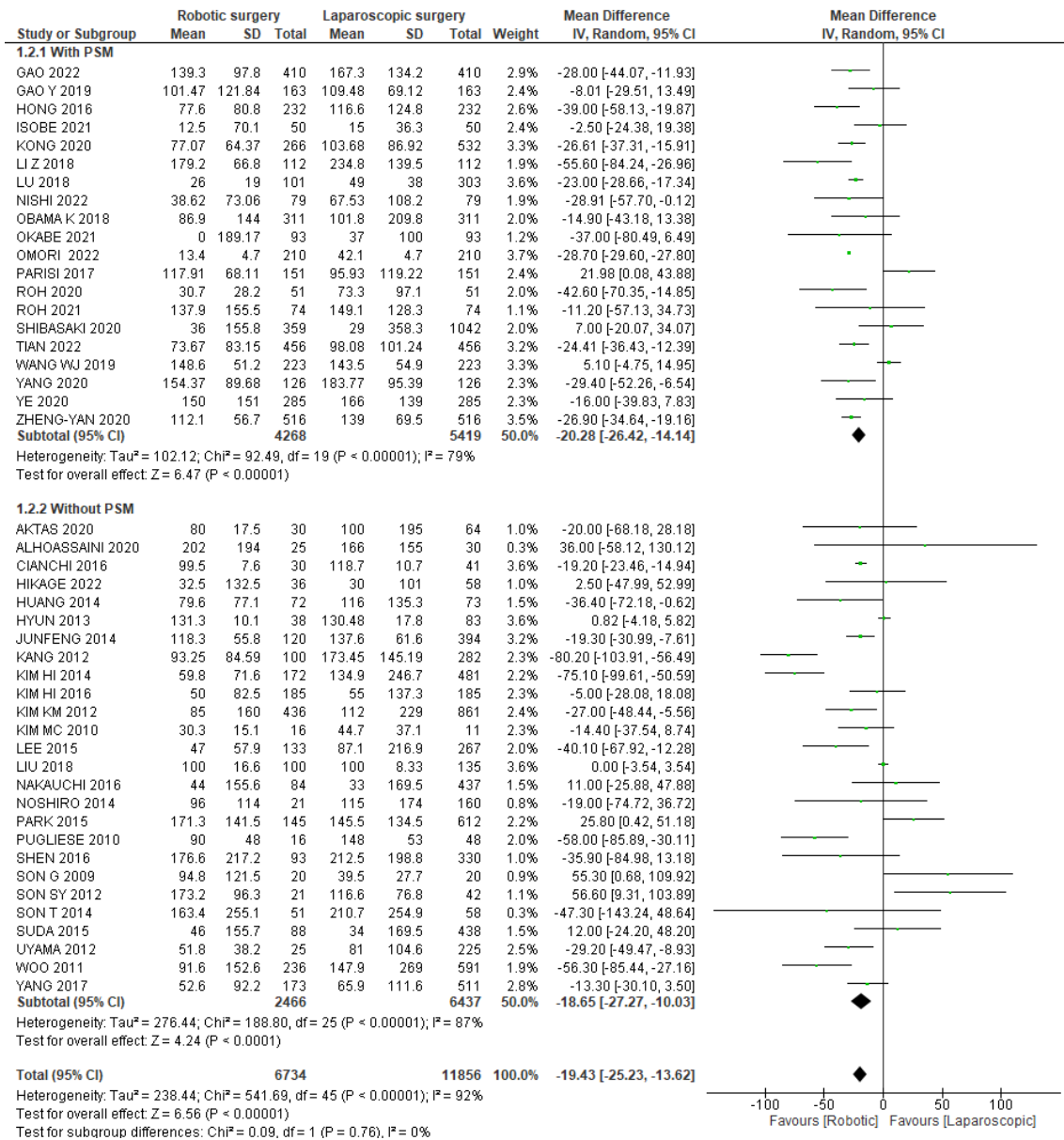


- **Number of retrieved lymph nodes**

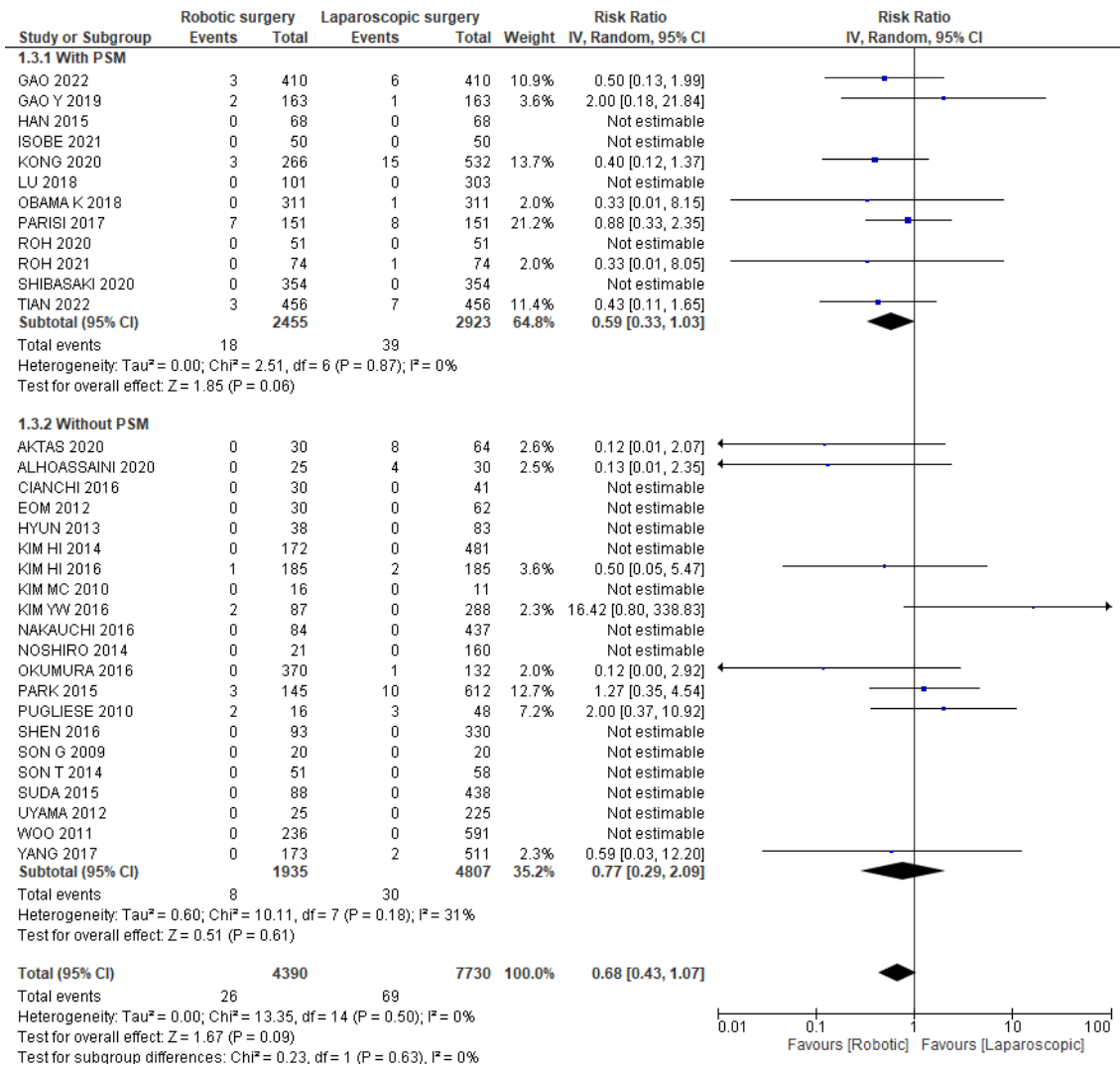


## Supplemental File no.2 - Forest Plots:

- **Blood Loss**

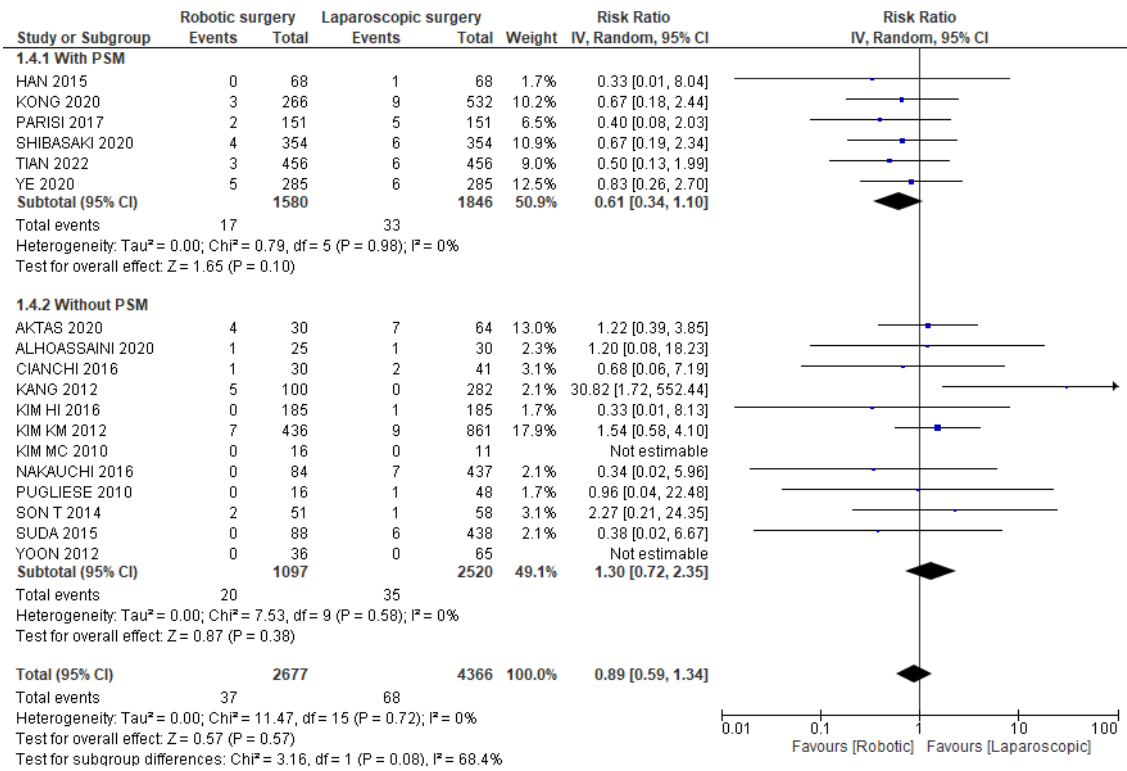


- Conversion

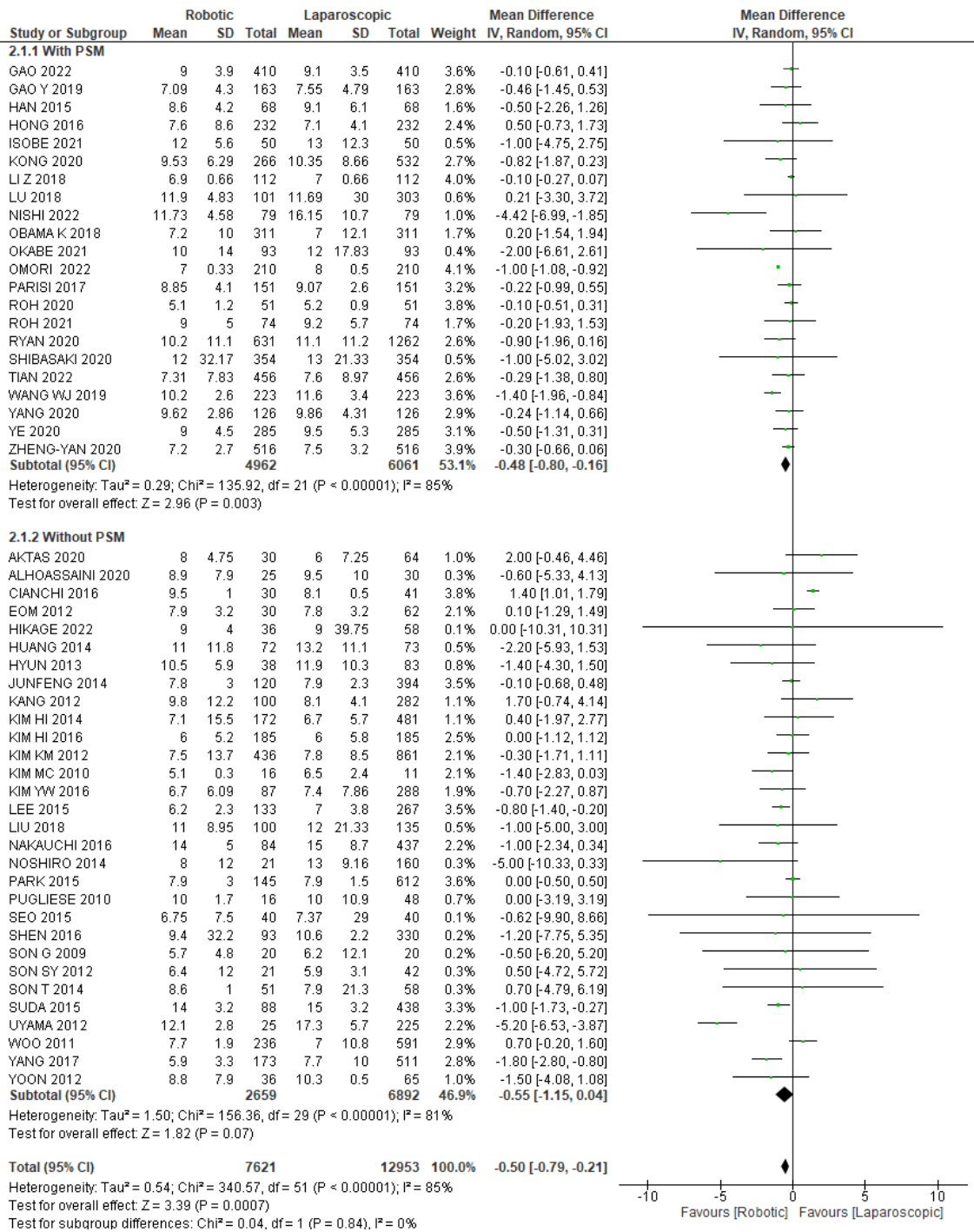




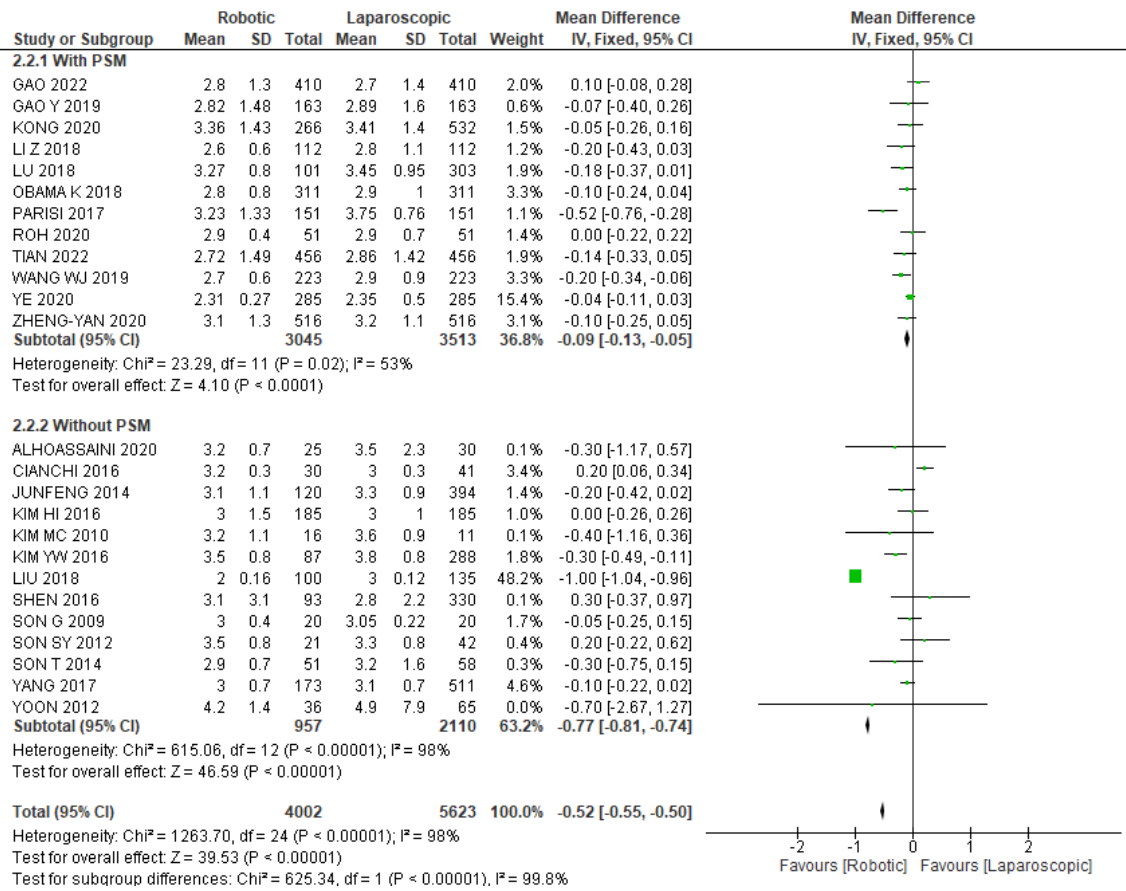
- Reoperation



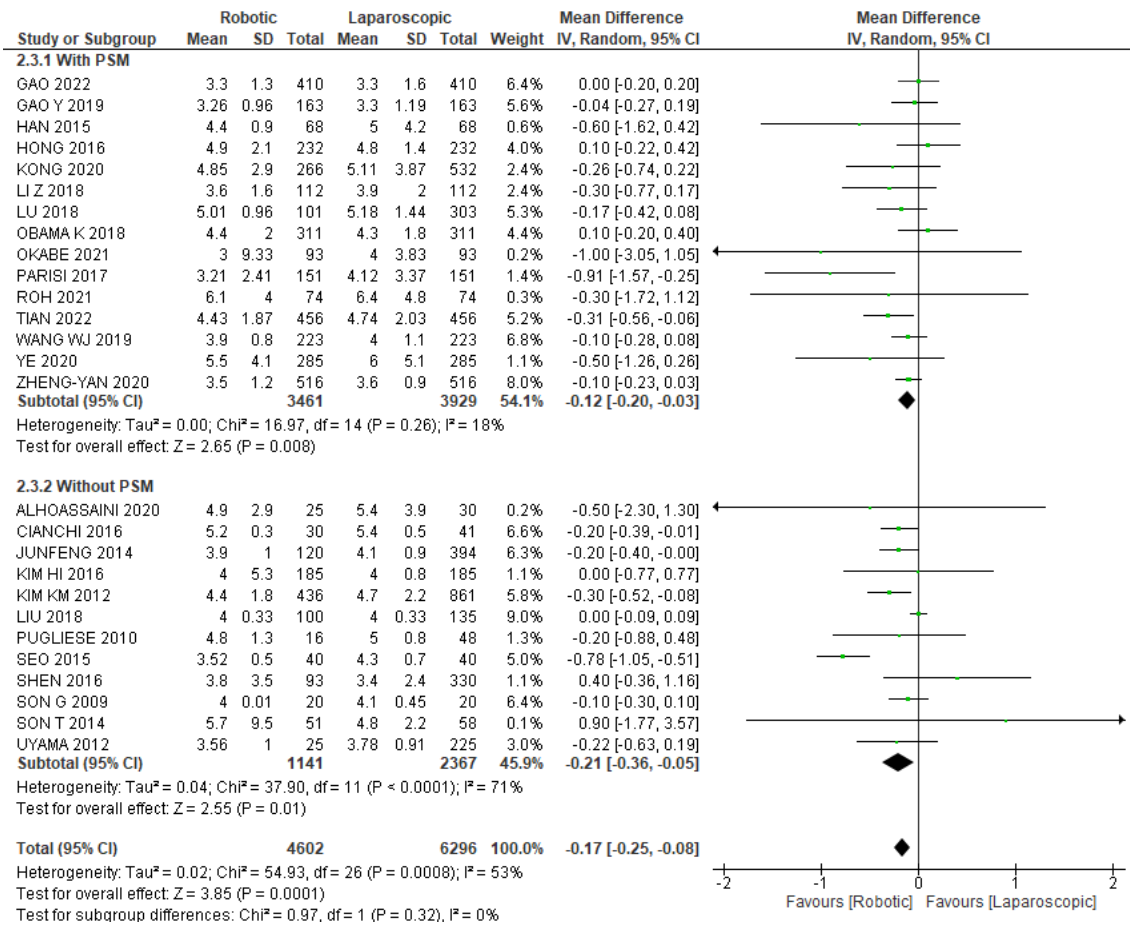
• Length of Hospital Stay



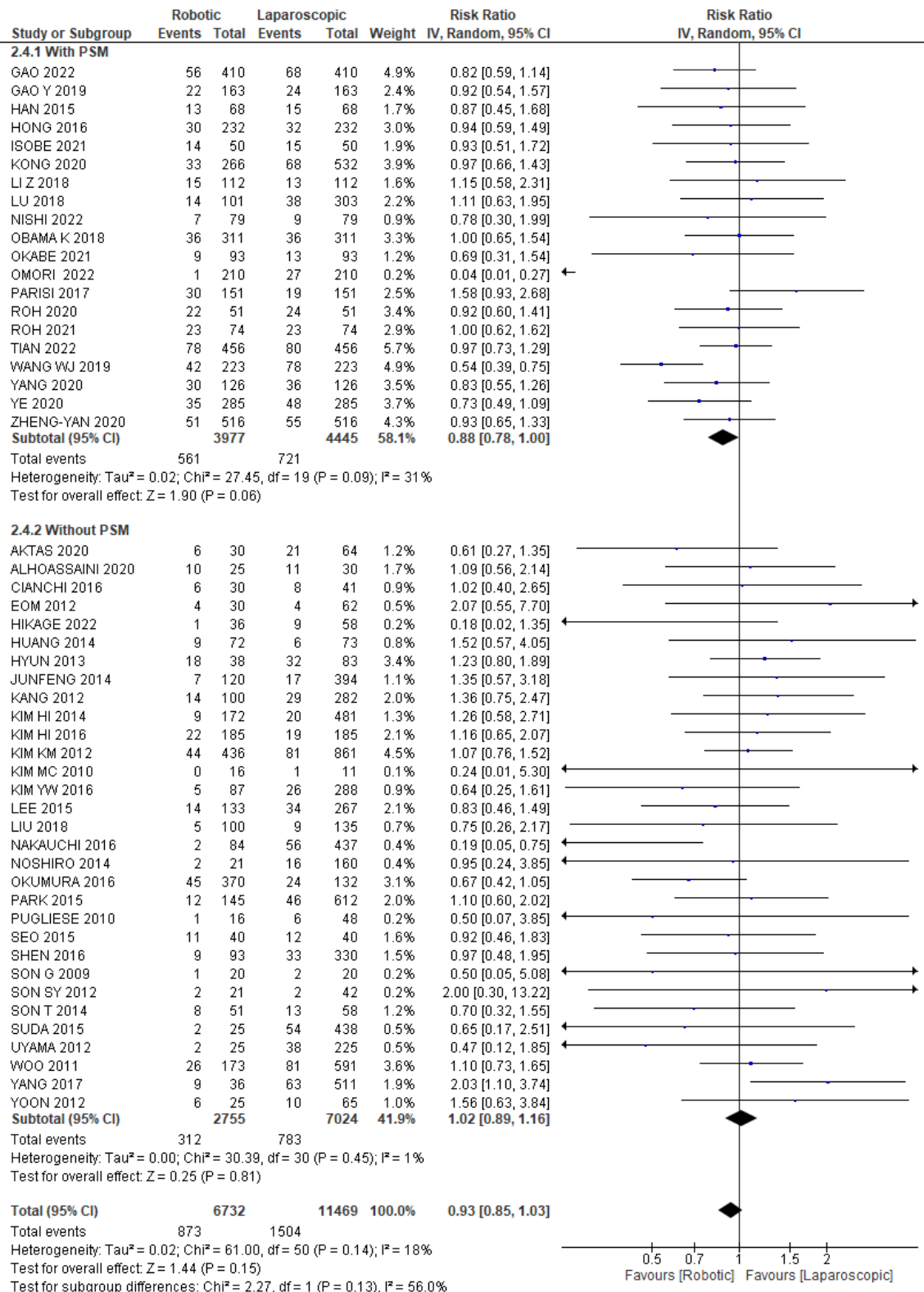
- Time to First Flatus



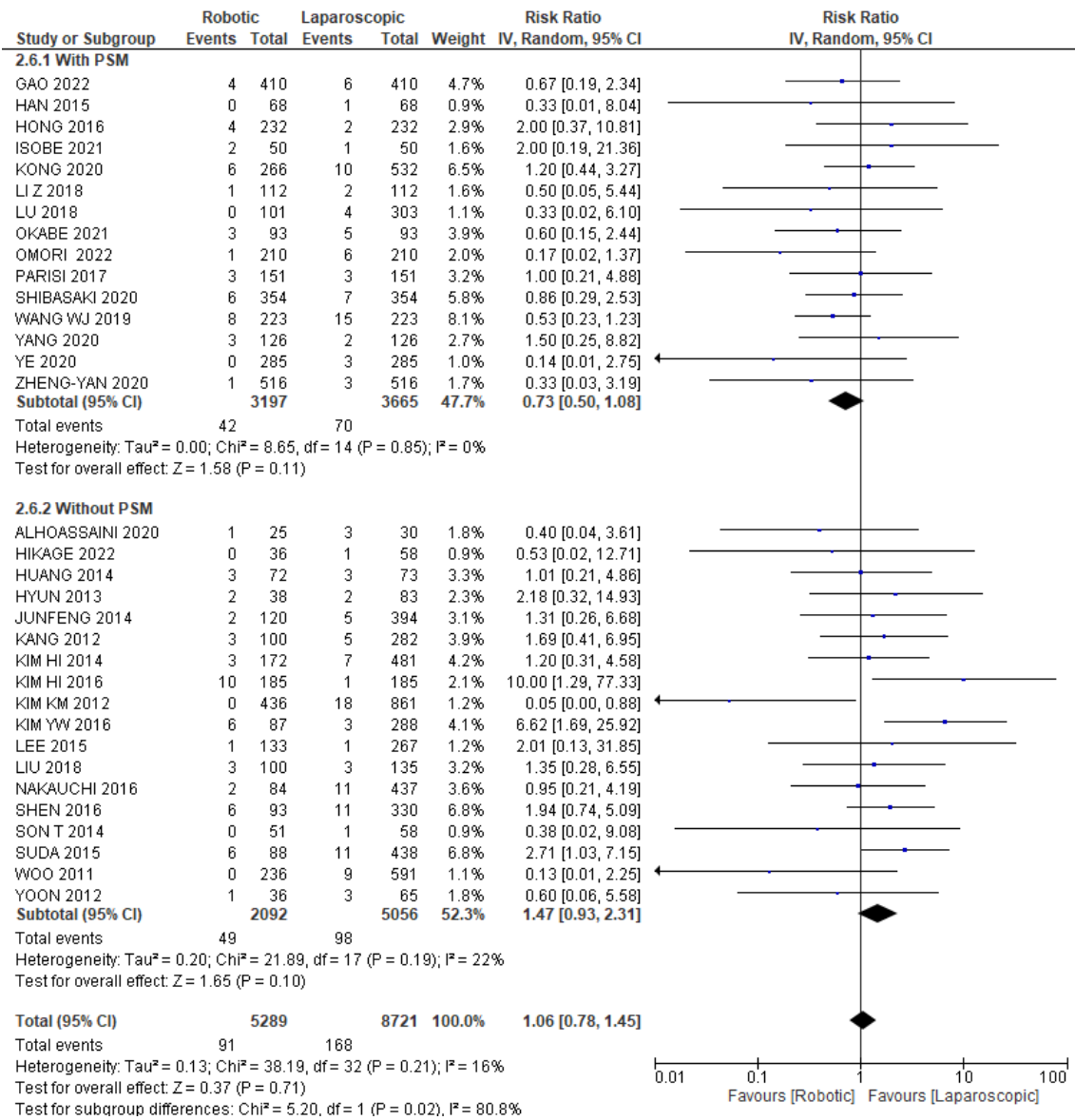
- Time to Oral Intake



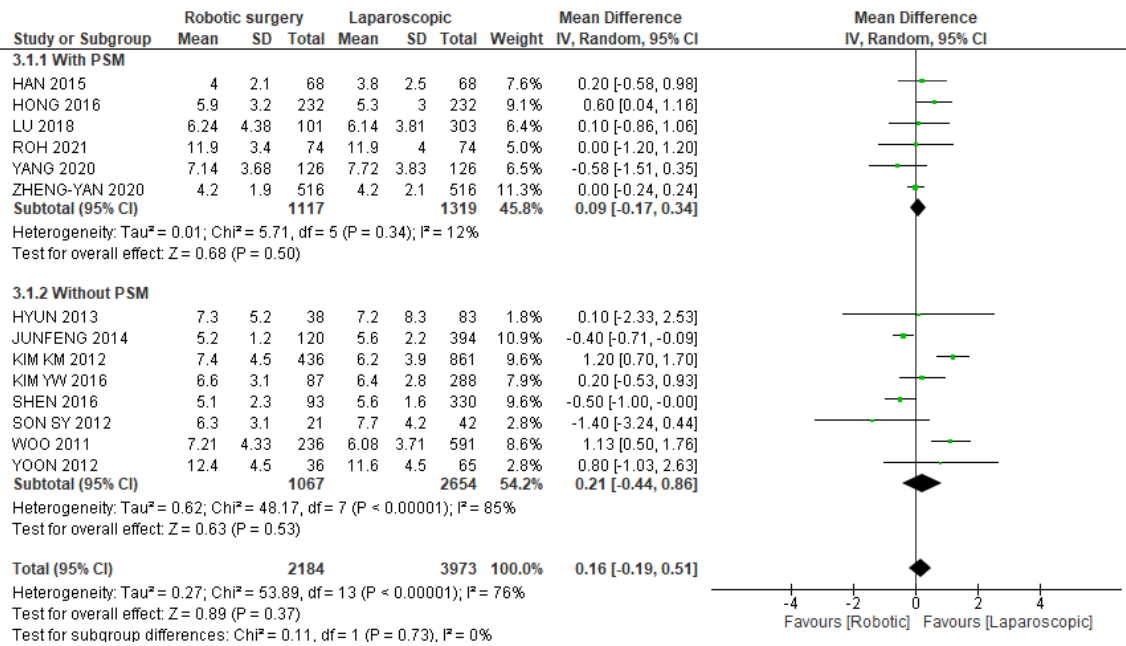
- Overall Complications



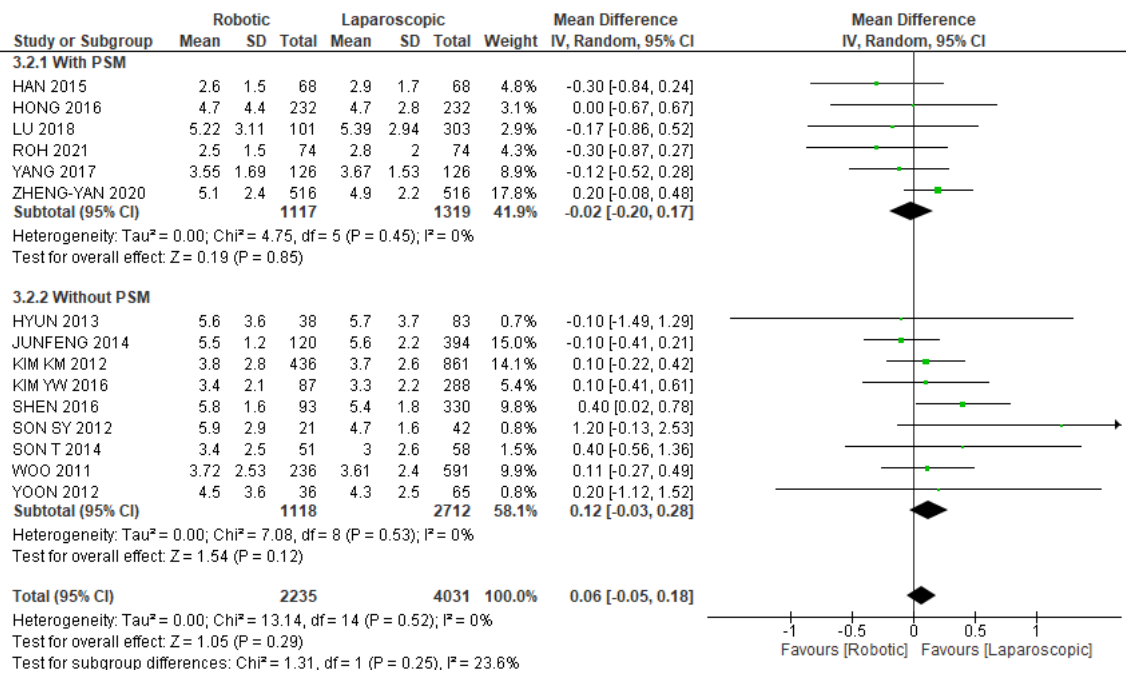
- Anastomotic Leakage



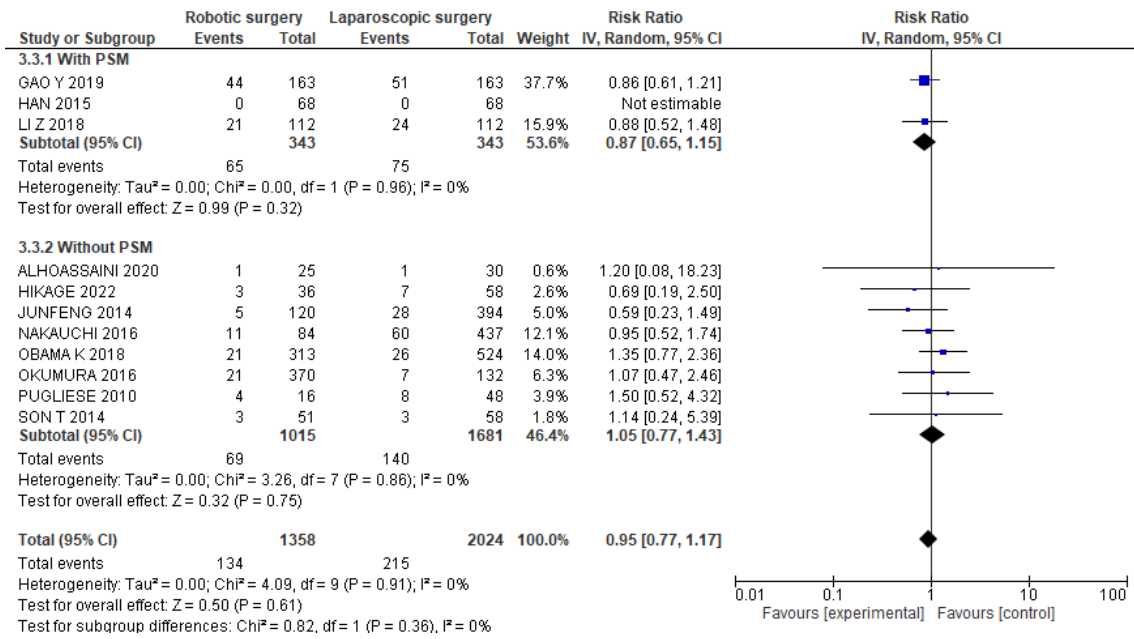
- **Distal resection margin distance**



- **Proximal resection margin distance**



- Recurrence





## Reporting Guidelines



# PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page and paragraph/ table #
<b>TITLE</b>			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	Page 1 (paragraph 1): “Laparoscopic versus Robotic gastric cancer surgery: Short-term Outcomes. Systematic Review and Meta-analysis of 25 521 patients”
<b>ABSTRACT</b>			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	Page 2 (paragraph 1-5): “Background: (...) There is no consensus regarding the optimal surgical technique to perform curative resection surgery”; “Objective: Compare laparoscopic and robotic gastrectomy regarding short-term outcomes in patients with gastric cancer.”; “Materials and Methods: (...) We searched the following topics: “Gastrectomy”, “Laparoscopic” and “Robotic Surgical Procedures”. (...)”; “Results: There were no significant differences between robotic gastrectomy (RG) and laparoscopic gastrectomy (LG) regarding conversion rate, reoperation rate, mortality, overall complications, anastomotic leakage, distal and proximal resection margin distances and recurrence rate. (...)”; “Conclusion: This meta-analysis supports the choice of robotic surgery over laparoscopy concerning relevant surgical complications. (...)”
<b>INTRODUCTION</b>			
Rationale	3	Describe the rationale for the review in the context of what is already known.	Page 3 (paragraph 1; 2 and 8): “Nowadays, gastric cancer is the fifth most common cancer worldwide (...) has third highest cancer-related mortality rate (7.7/100 000) and it is the fifth most



## PRISMA 2009 Checklist

			incident tumour in the entire world (11.1/100 000).” “Currently, the main surgical approaches are minimally invasive, including laparoscopic surgery and robotic surgery”;
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	Page 3 (paragraph 3-8): “Therefore, our systematic review includes the most recent observational studies and the current literature about the comparison of the short-term outcomes between LG and RG for gastric cancer patients in order to clarify the feasibility and efficiency of robotic surgery, as it is predicted to be more prevalent in the coming years.”
<b>METHODS</b>			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	Not reported.
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	Page 4 (paragraph 2 and 3): “(…) we included observational clinical studies that compared short-term outcomes between the two surgical approaches (RG and LG), in patients with gastric cancer who underwent curative-intent surgery.”
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	Page 4 (paragraph 1): “(…), on the following databases: PubMed, Web of Science and Cochrane Library.”



## PRISMA 2009 Checklist

Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Page 4 (paragraph 1): “The query in the PubMed was: “Search (((laparoscopic gastrectomy) OR (“Gastrectomy” [Majr:NoExp]) AND “Laparoscopy” [Mesh])) OR (((“Gastrectomy” [Majr:NoExp]) AND “Robotic Surgical Procedures” [Mesh]) OR robotic gastrectomy)”.”
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	Page 4 (paragraph 2 and 3): “The researchers screened the literature and selected articles based on their titles and abstracts”; “Then, the authors reviewed the full texts and excluded articles which met the following exclusion criteria (...)”
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	Page 4 (paragraph 4): “Two reviewers independently read and interpreted every original study.”
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	Page 4 (paragraph 4): “Data extraction comprised: study information (...), patients’ characteristics (...) and short-term outcomes (...)”
Risk of bias in individual studies / Risk of bias across studies	12/ 15	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	Page 4 (paragraph 5): “In our meta-analysis, we used the MINORS (Methodological Index for Non-Randomized Studies) scale to assess the quality and individual risk of bias of our non-randomized studies.”
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	Page 5 (paragraph 1 and 2): “For dichotomous outcomes, we presented the results as risk ratios (RR) with 95% confidence intervals (CI), by using the Mantel-Haenszel method. For



## PRISMA 2009 Checklist

			continuous outcomes, we presented the results as mean differences with 95% CI, by using the generic inverse variance method.”
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I <sup>2</sup> ) for each meta-analysis.	Page 5 (paragraph 1 and 2): “We performed our meta-analysis using Review Manager (Version 5.4.1).”; “The Chi-squared ( $\chi^2$ ) test and the I-squared (I <sup>2</sup> ) measure were used to assess heterogeneity. We applied a random effects model because of the clinical heterogeneity of the included studies.”
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	Page 5 (paragraph 3): “Hence, we conducted a subgroup analysis to understand whether PSM had any effect in the association between the surgical approach and the studied outcomes.”
<b>RESULTS</b>			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	Page 5 (paragraph 4): “Then, for our systematic review, we included 53 studies in the quality assessment and quantitative analysis (Figure 1).”
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	Page 5 (paragraph 4): “These studies include a total of 25 521 participants, of which 8154 underwent RG and 17367 underwent LG. All studies were retrospective observational studies.”
Risk of bias within and across studies	19/ 22	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	Page 6 (paragraph 1): “The median score in the MINORS scale was 22, with a range of 19 to 23. Therefore, all included studies were considered adequate to be included in the quantitative analysis.”



# PRISMA 2009 Checklist

Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	Page 6 (paragraphs 3-8); page 7 and 8 (paragraph 1-4): Operation Time: “Our meta-analysis included fifty studies which reported the operative time. It was significantly shorter in laparoscopic gastrectomy group, when compared with the robotic surgery group [MD 41.19, p<0.00001 (95%CI: 33.47, 48.92), I2=98%, p<0.00001]. Mean operation time was 269.22 minutes in the robotic surgery group and 225.65 in the laparoscopic surgery group. (Figure 3)”
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	Page 6 (paragraph 2): Operation Time: “Our meta-analysis included fifty studies which reported the operative time. It was significantly shorter in laparoscopic gastrectomy group, when compared with the robotic surgery group [MD 41.19, p<0.00001 (95%CI: 33.47, 48.92), I2=98%, p<0.00001]. Mean operation time was 269.22 minutes in the robotic surgery group and 225.65 in the laparoscopic surgery group. (Figure 3)”
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	Page 8 (paragraph 5-7); page 9 and 10 (paragraph 1-5): Subgroups Analysis – Operation Time: “Both subgroups demonstrated a significant longer operative time in the robotic surgery group. Heterogeneity was high and statistically significant. Additionally, regarding subgroup differences, I2=73.5% and p= 0.05. (Figure 3)”
<b>DISCUSSION</b>			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	Page 10 (paragraph 6-7); page 11-15 and 16 (paragraph 1): “Operative time and cost favor the laparoscopic approach, while blood loss, length of hospital stays, time to first flatus, time to oral intake, surgical complications (Clavien-Dindo grade ≥ III), pancreatic complications and the number of retrieved lymph nodes favors the robotic approach.”;



## PRISMA 2009 Checklist

			Operative Time: “This meta-analysis shows a similar result to previous studies, which demonstrated that operative time is significantly longer in robotic gastrectomy when compared with laparoscopic gastrectomy.”
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	Page 16 (paragraph 2): “The present study also has its limitations: first, we included non-randomized comparative studies; second, several outcomes demonstrated a high percentage of heterogeneity, which may put the validity of the results into. These differences between studies could be explained by the discrepancies in the surgical team’s experience in performing robotic surgery;(...)”
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	Page 16 (paragraph 3-5): “In conclusion, we believe that our results demonstrate that robotic gastrectomy is a safe and feasible procedure, when compared with laparoscopic gastrectomy.”; “Moreover, randomized clinical trials are also desired in contemplation of a better comprehension of the advantages in performing robotic gastrectomy.”
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	No funding.

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

## Submission Guidelines



# Manuscript Submission Guidelines and Policies for *Journal of Laparoendoscopic & Advanced Surgical Techniques*

Last updated 7/20/2022 12:31:13 PM

## Journal Information

- **Manuscript Submission Site:** <https://mc.manuscriptcentral.com/lap>
- Editorial Office Contact: [jlast1@verizon.net](mailto:jlast1@verizon.net)
- Support Contact: [prosupport@liebertpub.com](mailto:prosupport@liebertpub.com)
- Journal Model: Hybrid (Open Access option)
- Blinding: Single Blind
- File formatting requirement stage: Upon submission
- Instant Online Option (immediate publication of accepted version): No
- Submission Fee: None
- Average time to initial decision: 15 days

## Manuscript Types and Guidelines

Full Original Reports-Research Articles	3,000-word limit Structured abstract of no more than 250 words Maximum total of ten (10) figures and/or tables
Full Reports-Review Articles	8,000-word limit Structured abstract of no more than 250 words Maximum total of ten (10) figures and/or tables
Technical Reports	3,000-word limit Structured abstract of no more than 250 words Maximum total of ten (10) figures and/or tables

Perspectives	1,500-word limit Unstructured abstract of no more than 200 words Maximum total of two (2) figures and/or tables
Research Briefs	1,200-word limit No abstract Section headings are not required Maximum total of two (2) figures and/or tables
Editorials	1,000-word limit No abstract No figures or tables
Letters to the Editor	500-word limit May include one figure OR table Reference citations are identical in style to those of full original articles, but should not exceed five (5).

Word limits do NOT pertain to the abstract, disclosure statements, author contribution statements, funding information, acknowledgments, tables, figure legends, or references.

## References

*Journal of Laparoscopic & Advanced Surgical Techniques* uses Mary Ann Liebert's **Vancouver** reference format. Templates are available in [Zotero](#) and through the [CSL Style Repository](#). An [Endnote template](#) is also available.

Liebert Vancouver Style: Order of Citation

- Reference List: Prepared in sequential order as cited in text.
- In-text Citations: All references must be cited in text in numerical order, set in superscript Arabic numerals outside of any punctuation. Do not set reference numbers in parentheses or brackets. To cite several references at once, use commas to separate non-sequential citations and use dashes to separate sequential citations; do not include spaces. Ex: 3,7,12–15
- Journal titles should follow the abbreviation style of PubMed/Medline.
- Include among the references any articles that have been accepted but have not yet published; identify the name of publication and add "In Press." If the reference has been published online, provide the DOI number in place of the page range.

Style Examples for Reference List:

Type of Reference	Punctuation and Order of Elements in Reference List
Journal article with 1-3 authors	Wang Q, Nambiar K, Wilson JM. Isolating natural adeno-associated viruses from primate tissues with a high-fidelity polymerase. <i>Hum Gene Ther</i> 2021;32(23-24):1439-1449; doi: 10.1089/hum.2021.055 [insert article-specific DOI if available].

Journal article with more than 3 authors	Pfister EL, DiNardo N, Mondo E, et al. Artificial miRNAs reduce human mutant Huntington throughout the striatum in a transgenic sheep model of Huntington's disease. <i>Hum Gene Ther</i> 2018;29(6):663–673; doi: 10.1089/hum.2017.199 [insert article-specific DOI if available].
Edited Book	Herzog RW, Zolotukhin S, (eds). <i>A Guide to Human Gene Therapy</i> . World Scientific Publishing Co. Pte. Ltd.: Singapore; 2010.
Chapter in an Edited Book	Nicklin SA, Baker AH. Adenoviral Vectors. In: <i>A Guide to Human Gene Therapy</i> . (Herzog RW, Zolotukhin S. eds.) World Scientific Publishing Co. Pte. Ltd.: Singapore; 2010; pp. 21-36.
Authored Book	Isaacson W. <i>The Code Breaker: Jennifer Doudna, Gene Editing, and the Future of the Human Race</i> . Simon & Schuster: New York, NY; 2021.
Website	Last name, first/middle initial(s) of author(s) [if available]. U.S. Food and Drug Administration. <i>What is Gene Therapy?</i> Silver Spring, MD; 2018. Available from: <a href="https://www.fda.gov/vaccines-blood-biologics/cellular-gene-therapy-products/what-gene-therapy">https://www.fda.gov/vaccines-blood-biologics/cellular-gene-therapy-products/what-gene-therapy</a> [Last accessed: month/date/year].
Personal communications	References that are unpublished (ie: personal communications, emails, letters) are not to be included in the reference list. Instead, insert "Personal communication; [name], date" parenthetically at the point of citation within text.
Using previously published images or tables as a reference	Reused/adapted images, tables, or any published material must be officially cited as a reference in the reference list, and the author(s) of the submitted work must obtain written permission from the copyright holder. Verbal approvals are not acceptable. Any fees associated with the reuse or adaptation of any material is the sole responsibility of the author(s).

## Other

### Supplemental Video Submission

*Journal of Laparoscopic & Advanced Surgical Techniques* welcomes supplement videos demonstrating cutting-edge minimally invasive surgical techniques. The videos must serve as an accompaniment and amplification of a full manuscript. Please follow the guidelines below for submission:

- The video may be up to 10 minutes in duration.
- Videos may be uploaded in the following formats:
  - WMV
  - MPEG
  - AVI

- MOV
- Video dimensions must be at least 640 x 840 or higher for the best results. The video must also be in the NTSC format (the European PAL format is not supported).

## PaperPal Preflight

**The Paperpal Preflight service is available for this journal.** PaperPal Preflight allows authors to check their **Original Research** manuscripts for common errors prior to submitting a manuscript for consideration. Please note that this does not guarantee that your paper will pass all submission or other checks, nor that it will be considered for review.

The checks are configured for Original Research manuscripts only and may not be applicable to other manuscript types. There may be additional requirements for submission. Please review the full instructions for authors for guidelines.

The basic service is free. PaperPal preflight offers an *optional* fee-based service that will provide a report showing tracked changes and potential modifications. Please note that if this service is used, a clean copy of the manuscript must be uploaded to the submission system.

There is no obligation to use either the free or paid service. No editorial, review, nor any other decisions will be dependent on its use.

All manuscripts must be submitted through the journal's ScholarOne Manuscripts site.

# General Manuscript Submission Guidelines and Policies for Mary Ann Liebert Journals

Last updated 1/30/2023 3:32:12 PM

## Submission Preparation

All manuscripts must be prepared in accordance with the Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly Work in Medical Journals ([icmje.org](http://icmje.org)). Please consult your specific journal's requirements for additional information.

All Mary Ann Liebert, Inc. journals follow the standards, guidelines, and best practices set forth by the Committee on Publication Ethics (COPE; [publicationethics.org](http://publicationethics.org)), the International Committee of Journal Medical Editors (ICJME; [www.icmje.org](http://www.icmje.org)), the World Medical Association (WMA); [www.wma.net](http://www.wma.net)), and the American Medical Association ([www.ama-assn.org](http://www.ama-assn.org)).

Mary Ann Liebert, Inc. recommends that submissions follow standard relevant reporting guidelines. Please consult [TheEquator Network](http://TheEquatorNetwork) for more information.

### PaperPal Preflight

The PaperPal Preflight service is available for most journals. PaperPal Preflight allows authors to check their **Original Research** manuscripts for common errors prior to submitting a manuscript for consideration. Please note that this does not guarantee that your paper will pass all submission or other checks, nor that it will be considered for review.

There may be additional requirements for submission. Please review the full instructions for authors for guidelines.

The basic service is free. PaperPal preflight offers an *optional* fee-based service that will provide a report showing tracked changes and potential modifications. Please note that if this service is used, a clean copy of the manuscript must be uploaded to the submission system.

There is no obligation to use either the free or paid service. No editorial, review, nor any other decisions will be dependent on its use.

All manuscripts must be submitted through the journal's ScholarOne Manuscripts site. Please refer to the individual journal's instructions for more information and to access the service.

# Manuscript Formatting

Please check your journal's requirements for file formatting. Many journals require formatting compliance only on revision; however, unless stated, the file formatting should comply with the following requirements on submission.

## Manuscript Files

The main text file, figure legends, and tables should be prepared in Microsoft Word. Some journals may accept LaTeX. Please consult your individual journal instructions for guidance.

## File Naming

- All file names should be in English and contain only alphanumeric characters.
- Do not include spaces, symbols, special characters, dashes, dots, or underscores.
- Title each file with the type of content contained in the file (e.g., manuscript.doc, tables.doc, FigureLegends.doc, Fig1.tif, SupplementalData.pdf, etc.).

## Figures

- Submission of high resolution .TIFF or .EPS figure files is preferred. Please upload as individual files. Cite figures consecutively in text within parentheses.
- Images should not reveal the name of a patient or a manufacturer.
- Note: Figures that will not be reproduced in color must be readable and interpretable in black and white.

## Figure Legends

- A legend should be provided for each supplied figure. All legends should be numbered consecutively.
- Figure legends may be included at the end of the main text file or uploaded as a separate, double-spaced
- Word file.
- In each legend, provide explanations for any abbreviations or symbols that appear in the figure.
- If the figure is taken from a copyrighted publication, permission must be secured by the author(s) and supplied at the time of submission with appropriate credit listed in the legend. Permissions and associated fees are the responsibility of the author.

## Tables

- Tables may be included after the references at the end of the main text file, or uploaded as a single, separate Word file. All tables should be editable.

- Provide a title for each supplied table.
- Cite tables sequentially in text within parentheses.
- Explain abbreviations used in the body of the table in footnotes using superscript letters, not symbols.
- If a table is taken from a copyrighted publication, permission must be secured by the author(s) and supplied at the time of submission with appropriate credit listed in the legend. Permissions and associated fees are the responsibility of the author.

## Supplemental Files

- Supplemental files should be uploaded as individual files. Most text, photo, graphic, and video formats are accepted. Ensure that patient identities are not revealed.
- Supplemental Information will not be copyedited or typeset; it will be posted online as supplied.
- For journals that publish accepted versions of papers prior to copyediting and typesetting, supplemental files will not be posted with the paper until after production has been completed.

## Manuscript Structure

Specific journal requirements will vary, however the general order of elements in each manuscript should be

- Title page\* with full manuscript title, all contributing authors' names and affiliations, a short running title, a denotation of the corresponding author, and a list of 4-6 keywords/search terms,
- Abstract,
- Main text without embedded figures or tables and with appropriate section headings, if applicable. Most research papers should be organized as follows: Introduction, Materials and Methods, Results, Discussion, and Conclusions.
- Acknowledgments,
- Authorship confirmation/contribution statement (CRediT format is preferred)
- Author(s)' disclosure (Conflict of Interest) statement(s), even when not applicable,
- Funding statement, even when not applicable,
- References,
- Tables included in the text or as a separate document,
- Figure legends at the end of the main text or in a separate Word file,
- Figures uploaded as individual high-resolution files,
- Supplemental files uploaded as individual files.

\*Double-blinded journals require a separate title page with the title, all contributing authors' names and affiliations, a denotation of the corresponding author, author acknowledgements, disclosures, and related identifying information.

Your individual journal may require

- An Institutional Review Board (IRB) approval (or waiver) statement and statement of patient consent as a separate paragraph after the methods section,
- Other relevant ethics attestations (see [icmje.org](http://icmje.org) for further guidance),
- Data sharing statement,
- Specific abstract and content sections, depending on manuscript type,
- Word count limits, tables/figure limits, and reference format requirements.

Please note that paragraphs should be no longer than 15 lines once typeset.

## Pre-Publication Policies

### Funding

Upon manuscript submission, the submitting agent will have an opportunity to enter funding/grant information. If funding information is entered correctly, the publisher will deposit the funding acknowledgements from the article as

part of the standard metadata to Funder Registry. The entered information should include funder names, funder IDs (if available), and associated grant numbers. Special care should be taken when entering this information to ensure total accuracy. Funding information must also be provided within the manuscript.

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