



# Incidence and predictors of postoperative ileus after loop ileostomy closure: a systematic review and meta-analysis

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## Abstract

**Introduction** Postoperative ileus (POI) is regarded as the most clinically significant morbidity following loop ileostomy closure; however, its incidence remains poorly understood. Our objective was therefore to determine the pooled incidence of POI after loop ileostomy closure and identify risk factors associated with its development.

**Methods** We systematically searched MEDLINE (via Ovid and PubMed), Embase, the Cochrane Library, Biosis Previews, and Scopus to identify studies reporting the incidence of POI in patients who underwent loop ileostomy closure. Two independent reviewers extracted data and appraised study quality. Cumulative incidence proportions were pooled across studies using a random-effects meta-analytic model.

**Results** Sixty-seven studies, including 9528 patients, met our inclusion criteria. The pooled estimate of POI was 8.0% (95% CI 6.9–9.3%;  $I^2 = 74%$ ). The estimated incidence varied by POI definition: studies with a robust definition of POI ( $n = 8$ ) demonstrated the highest estimate of POI (12.4%, 95% CI 9.2–16.5%;  $I^2 = 79%$ ) while studies that did not report an explicit POI definition ( $n = 38$ ) demonstrated the lowest estimate (6.7%, 95% CI 5.3–8.3%;  $I^2 = 61%$ ). Small bowel anastomosis technique (hand-sewn) and interval time from ileostomy creation to closure (longer time) were the factors most commonly associated with POI after loop ileostomy closure. However, most comparative studies were not powered to examine risk factors for POI.

**Conclusions** POI is an important complication after loop ileostomy closure, and its incidence is dependent on its definition. More research aimed at studying this complication is required to better understand risk factors for POI after loop ileostomy closure.

**Keywords** Postoperative ileus · Ileostomy · Systematic review · Stoma closure · Postoperative morbidity

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A loop ileostomy is constructed to protect a distal colorectal or ileoanal anastomosis, and is used to decrease both the rate and sequelae of anastomotic leak [1, 2]. However, it comes at the price of requiring a second operation to restore intestinal continuity, which carries its own risk for complications. Among all postoperative morbidities following loop ileostomy closure, postoperative ileus (POI) is perhaps the most significant in terms of impact and frequency [3, 4]. POI is associated with increased length of stay, increased risk for nosocomial infections and associated morbidities, and higher healthcare costs [5, 6].

Despite loop ileostomy closure being a relatively short operation with minimal surgical stress and bowel manipulation, POI appears to be common. Even among contemporary publications studying enhanced recovery protocols (ERPs) specific to ileostomy closure, POI was observed in over 20% of cases [7]. It is also the leading cause of 30-day hospital

readmission following loop ileostomy closure [8, 9], which will continue to be problematic as the use of ERPs increases and length of stay decreases. Some groups are even advocating for same-day discharge protocols after loop ileostomy closure [10, 11], and POI is likely the greatest hindrance to their successful widespread implementation.

Although POI is recognized as an important complication after loop ileostomy closure, the cumulative incidence of POI reported in previous studies has varied greatly. To our knowledge, data on POI after loop ileostomy closure have not been synthesized via systematic review and meta-analysis. Our objective was therefore to systematically review the literature reporting on POI after loop ileostomy closure, to determine the pooled incidence of POI, and to describe factors associated with its development. Secondly, we aimed to determine if there were any differences in the estimate of POI by definition used. Our a priori hypothesis was that studies using a more robust definition of POI would report a higher incidence of POI.

## Methods

This systematic review and meta-analysis was conducted according to a pre-specified protocol (PROSPERO 2018 CRD42018087884; registered February 6, 2018) and is reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [12]. Internal Review Board approval was waived at our institution given the study design.

### Search strategy

We systematically searched for published reports of POI after loop ileostomy closure using the following databases: MEDLINE (via Ovid 1946 to December 18, 2017; via PubMed December 13, 2017 to December 19, 2017); Embase Classic + Embase (via Ovid 1947 to December 18, 2017); BIOSIS Previews (via Ovid 1969–2017 Week 51); The Cochrane Central Register of Controlled Trials (via The Cochrane Library, to issue 12 of 12, December 2017); The Database of Abstracts of Reviews of Effects (via The Cochrane Library, to issue 2 of 4, April 2015); the Cochrane Database of Systematic Reviews (via The Cochrane Library, to issue 11 of 12, November 2017); the NHS Economic Evaluation Database (via The Cochrane Library, to issue 2 of 4, April 2015); and Scopus (via Elsevier). The search strategy used text words and relevant indexing to identify relevant reports. The full MEDLINE strategy (Appendix 1) was applied to all databases, with modifications to search terms as necessary. No language limits were applied in the search. Further studies were identified in Web of Science and Scopus (May 24, 2018) by carrying out citation searches

for studies citing included studies, as well as by examining their reference lists. An updated MEDLINE search was run prior to data analysis (June 5, 2018), and additional relevant studies were included.

### Study selection

The title and abstract of each record were screened in duplicate (R.G., P.S.), and publications were retained if they met the following criteria: (1) published after January 1, 2000; (2) reported on patients who underwent ileostomy closure; and (3) included any postoperative outcomes. Each retained record was then assessed independently by two reviewers (R.G., P.S.) for eligibility. Disagreements were resolved by consensus, and a third author (M.B.) was consulted if no agreement could be achieved. During full-text review, studies were retained for inclusion if they (1) included patients who underwent loop ileostomy closure, alone or as a discrete treatment group; and (2) reported on the incidence of POI and/or factors associated with the development of POI. Exclusion criteria were (1) studies that reported on patients who underwent multiple types of ostomy closure, and in which loop ileostomy closure patients could not be separated and analyzed independently; (2) studies in which all patients were managed in an experimental or non-standard of care manner (e.g., ileostomy closure under spinal anesthesia, or the use of nasogastric tubes (NGT) until return of bowel function); and (3) studies that reported on small bowel obstruction (SBO) and not POI. Studies in which POI and SBO were reported together as a single outcome (“POI/SBO”) were included only if those patients who underwent reoperation could be readily identified and excluded. Furthermore, each of these studies was discussed by both independent reviewers (R.G., P.S.) and the arbitrator (M.B.), who had to all be in agreement that this outcome likely reflected POI and not SBO. Randomized controlled trials (RCTs) and observational studies (cohort and case-control) were included; case series < 10 patients, case reports, and conference abstracts were excluded. There were no language restrictions. Finally, systematic reviews and meta-analyses were excluded but were reviewed for individual studies that met our inclusion criteria, and these studies were added if not already captured in our electronic search.

### Data extraction and synthesis

Data for each record were extracted independently by two reviewers (R.G., P.S.) using a standardized data extraction form, with disagreements resolved by consensus or by a third author (M.B.) when needed. The following study characteristics were systematically extracted: author, year, country of origin, study design, and exposure (if comparative study design). Patient characteristics were also extracted,

including age, sex, indication for ileostomy, intersurgery length (defined as length of time, in days, between ileostomy creation and ileostomy closure), operative time, and anastomotic technique. The incidence of POI was extracted, as was the definition of POI used in each study. For comparative studies in which the exposure was considered experimental or non-standard of care (Table 1), only POI data from the control arm were pooled. Data were extracted as means with standard deviations, medians with ranges, count data, or proportions with 95% confidence intervals (CI), as reported. For factors associated with POI, effect size and measures of statistical significance were extracted when provided.

## Quality assessment

Study quality was assessed using the Methodological Index for Non-Randomized Studies (MINORS) instrument for observational studies [13], or the Cochrane Collaboration Risk of Bias Tool for RCTs [14], where appropriate. The MINORS instrument includes eight items for all studies, and an additional four items for comparative studies. Each item is scored 0 (not reported), 1 (reported but inadequate), or 2 (reported and adequate). As such, the total denominator for each study is either 16 or 24.

## Statistical analysis

We estimated the pooled 30-day cumulative incidence proportion and 95% CI of POI after loop ileostomy closure using a DerSimonian and Laird random-effects model with inverse-variance weighting and a logit transformation. An  $I^2$  value was estimated to describe the amount of between-study heterogeneity that was present. We then performed stratified analyses to assess the influence of POI definition on the pooled estimate of POI, comparing (1) the presence or absence of a reported definition of POI; and (2) the robustness of the definition. Robustness was loosely based on the consensus definition of POI provided by Vather et al. [15], which included three components: symptoms of absent

bowel function (e.g., nausea/vomiting, obstipation), time element for the persistence of symptoms (e.g., criteria met on or after postoperative day 4), and radiologic confirmation. We added a fourth component—insertion of a NGT—given that it is commonly used in research settings to define POI retrospectively. Studies that included > 2 of the 4 components as part of their definition were considered robust. Due to the combination of study designs and the non-comparative nature of many included studies, predictive factors associated with POI were described qualitatively via systematic review only. All statistical analyses were performed using R v3.5.1 (R Development Core Team. 2017. *R: A Language and Environment for Statistical Computing*. Vienna, Austria).

## Results

### Search results

The electronic search yielded 2187 publications for review after excluding duplicates (Fig. 1). After title and abstract screening, 205 publications were retrieved for full-text review. Of these, 67 met the inclusion criteria for our systematic review.

### Study characteristics and quality assessment

Of the 67 studies included, 10 were RCTs and 57 were observational studies (50 cohort studies and 7 case-control studies) (Table 2) [3, 4, 7, 9–11, 16–76]. Sample sizes ranged from 10 to 944 patients, and 40 studies evaluated an exposure–outcome association with POI. Only 28 of 67 studies reported their definition of POI, and among these, eight definitions (29%) were considered robust. The methodological quality of included studies is presented in Table 2.

### Patient and operative characteristics

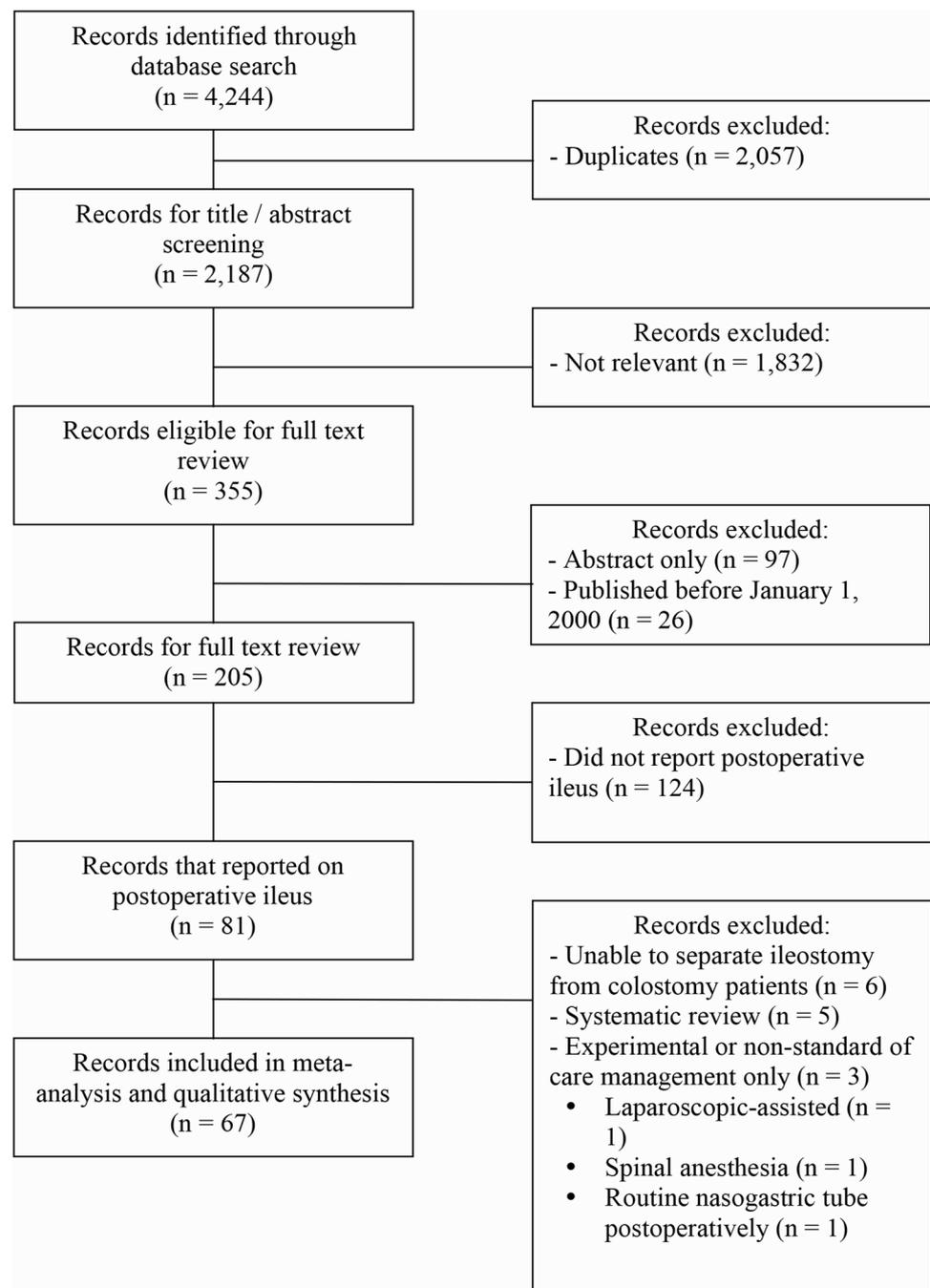
Patient and operative characteristics are displayed in Supplemental Table 1. Data were not available in every study, often because loop ileostomy closure patients only made up a fraction of the total study population. The mean or median age of patients ranged from 31 to 71 years, and most studies (54/59) had a majority male sample. Colorectal cancer was the most common underlying pathology necessitating ileostomy creation in 48 of the 59 studies that reported this information. Intersurgery length differed in each study and was often related to institutional protocol. Hand-sewn anastomosis was the preferred technique to restore intestinal continuity in 27 of 45 studies.

**Table 1** Summary of experimental or non-standard of care interventions that precluded the inclusion of intervention-group patients for pooled estimate of postoperative ileus

Intervention
Adhesion barrier ( $n = 324$ patients) [25, 31, 46, 69]
Laparoscopic assisted ( $n = 89$ patients) [53, 63]
Early ileostomy closure < 14 days ( $n = 77$ patients) [47, 62, 65]
Routine NGT until return of bowel function ( $n = 64$ patients) [66]
Preoperative bowel stimulation ( $n = 35$ patients) [54]
Umbilical ileostomy ( $n = 10$ patients) [70]

NGT nasogastric tube

**Fig. 1** PRISMA diagram of included studies reporting on postoperative ileus after loop ileostomy closure



### Pooled estimate of POI

Our meta-analysis included 67 studies that enrolled a total of 9528 patients. When data were pooled across studies, the 30-day cumulative incidence proportion of POI after loop ileostomy closure was 8.0% (95% CI 6.9–9.3%;  $I^2 = 74\%$ ) (Fig. 2). Of the 67 included studies, 60 reported POI and 7 reported POI/SBO, but no patients included from the latter studies underwent reoperation [3, 4, 9, 24, 27, 45, 72]. A sensitivity analysis excluding these seven studies

demonstrated similar results (pooled estimate of POI = 7.8%; 95% CI 6.4–9.1%;  $I^2 = 74\%$ ). A stratified analysis comparing studies that provided a definition of POI in their methods ( $n = 28$ ) to those that did not ( $n = 39$ ) revealed a higher pooled estimate of POI when a definition was provided (9.5%; 95% CI 7.8–11.6%;  $I^2 = 80\%$  vs. 6.7%; 95% CI 5.3–8.3%;  $I^2 = 61\%$ ) (Fig. 3). Among studies that provided a definition of POI, studies with a robust definition of POI ( $n = 8$ ) revealed a higher pooled estimate of POI than did those with a non-robust definition ( $n = 20$ ) (12.4%; 95% CI

**Table 2** Characteristics of studies reporting the cumulative incidence of POI after loop ileostomy closure

Study ID	Design	Sample size <sup>a</sup>	Exposure	POI criteria <sup>b</sup>	Quality
Amin 2001 [16]	Cohort	67	None	None	7/16
Swain 2001 [17]	Cohort	53	None	None	11/16
Hallbook 2002 [18]	Cohort	213	None	None	11/16
Kairaluoma 2002 [19]	Cohort	28	None	None	11/24
Kalady 2003 [10]	Cohort	58	23-h protocol	None	16/24
Garcia-Botello 2004 [20]	Cohort	109	None	None	12/16
Bell 2005 [21]	Cohort	20	None	None	17/24
Gastinger 2005 [22]	Cohort	407	None	S; T	12/24
Haase 2005 [23]	RCT	80	Gentamycin implant	none	Unclear ROB
Perez 2006 [24]	Cohort	93	None	None	11/16
Salum 2006 [25]	RCT	64	Adhesion barrier	None	High ROB
Thalheimer 2006 [26]	Cohort	120	Chemoradiotherapy	None	13/24
Flikier-Zelkowicz 2008 [27]	Cohort	62	None	None	11/16
Joh 2008 [28]	Cohort	42	None	S; T	11/16
Kaiser 2008 [29]	Cohort	56	None	None	16/24
Mansfield 2008 [30]	Cohort	123	None	None	7/16
Tjandra 2008 [31]	RCT	21	Adhesion barrier	None	Low ROB
Akiyoshi 2010 [32]	Case-control	125	None	S; R	12/16
Baraza 2010 [33]	Cohort	80	None	None	8/16
Courtier 2010 [34]	Cohort	54	None	S; T; NGT	10/16
Horisberger 2010 [35]	Cohort	128	SBA	S; T; NGT	16/24
Ihedioha 2010 [36]	Cohort	100	None	None	10/16
Shelygin 2010 [37]	RCT	119	SBA	None	Low ROB
D'Haeninck 2011 [38]	Cohort	197	Time to closure, SBA, index operation	S; T	16/24
Luglio 2011 [3]	Cohort	944	SBA	S; R; T	18/24
Mennigen 2011 [39]	Cohort	89	None	None	19/24
Peacock 2011 [40]	Cohort	138	None	None	9/16
Worni 2011 [41]	Cohort	134	Time to closure	NGT	16/24
Chun 2012 [42]	Case-control	94	None	S; NGT	11/16
Cipe 2012 [43]	Case-control	255	None	None	13/24
El-Hussuna 2012 [44]	Case-control	159	SBA	S; T	16/24
Gustavsson 2012 [45]	Cohort	351	SBA	S; R	17/24
Memon 2012 [46]	Cohort	32	Adhesion barrier, time to closure	None	12/24
Omundsen 2012 [47]	Cohort	74	Time to closure	S	15/24
Dusch 2013 [48]	RCT	84	Skin closure	None	Unclear ROB
Hiranyakas 2013 [49]	Cohort	351	Index operation approach	S; T; NGT	15/24
Klink 2013 [50]	Cohort	140	Skin closure	None	15/24
Loffler 2013 [4]	RCT	328	SBA	S; T; NGT	Low ROB
Marcet 2013 [51]	Cohort	27	Liposome bupivacaine analgesia	None	20/24
Peacock 2013 [52]	Cohort	23	None	None	11/16
Royds 2013 [53]	RCT	34	Laparoscopic assistance	S; R	High ROB
Abrisqueta 2014 [54]	RCT	35	Bowel stimulation	S; R; T; NGT	High ROB
Keller 2014 [9]	Cohort	332	None	S; T	9/16
Perez Dominguez 2014 [55]	Case-control	86	None	None	9/16
Rubio-Perez 2014 [56]	Cohort	93	SBA	None	10/16
Saito 2014 [57]	Case-control	82	None	S; R	12/16
Vallribera 2014 [58]	Cohort	167	SBA	S; T	17/24
Bhalla 2015 [11]	Cohort	15	None	None	12/16
Bracey 2015 [59]	Cohort	145	ERP	None	15/24
Figueiredo 2015 [60]	Cohort	259	Time to closure	S	17/24

**Table 2** (continued)

Study ID	Design	Sample size <sup>a</sup>	Exposure	POI criteria <sup>b</sup>	Quality
Markides 2015 [61]	Cohort	108	SBA	S; R; T; NGT	16/24
Robertson 2015 [62]	Cohort	61	Time to closure	None	17/24
Young 2015 [63]	Cohort	80	Laparoscopic assistance	S; NGT	16/24
Ihnat 2016 [64]	Cohort	78	None	S	18/24
Lasithiotakis 2016 [65]	RCT	10	Time to closure	None	High ROB
Mahla 2016 [66]	RCT	64	Early feeding	S; T	High ROB
Man 2016 [67]	Case-control	213	Age	S; T	11/16
Zhou 2016 [68]	Cohort	176	Time to closure	None	17/24
Bertoni 2017 [69]	Cohort	147	Adhesion barrier	None	16/24
Lam 2017 [70]	Cohort	10	Umbilical ileostomy	None	12/24
Li 2017 [71]	Cohort	358	Time to closure	None	19/24
Luglio 2017 [72]	Cohort	298	SBA	S; R; T	13/24
Zhen 2017 [73]	Cohort	148	SBA	None	20/24
Zhou 2017 [74]	Cohort	123	Time to closure	None	15/24
Lob 2018 [75]	Cohort	558	Surgeon experience	S; NGT	16/24
Park 2018 [76]	Cohort	71	None	None	11/16
Slieker 2018 [7]	Cohort	143	ERP	NGT	18/24

POI postoperative ileus, RCT randomized controlled trial, ERP enhanced recovery protocol, SBA small bowel anastomosis, ROB risk of bias

<sup>a</sup> number of subjects eligible for inclusion for pooled estimate of postoperative ileus

<sup>b</sup> S symptoms, R radiology, T time element, NGT nasogastric tube insertion

9.2–16.5%;  $I^2 = 79\%$  vs. 8.3%; 95% CI 6.4–10.8%;  $I^2 = 80\%$ ) (Fig. 4).

### Factors associated with POI

Of the 40 comparative studies, the primary endpoint was bowel recovery in only six of them, while the majority were aimed at assessing all postoperative morbidities collectively. The most common exposures assessed were small bowel anastomosis and time to ileostomy closure. One RCT found no difference in POI with hand-sewn anastomosis compared to stapled, albeit a numerically higher absolute incidence with hand-sewn anastomosis (16.0% vs. 9.1%,  $p = \text{NS}$ ) [4]. A large observational study of 944 patients found higher rates of POI with hand-sewn anastomosis with bowel resection compared to fold-over sutured anastomosis (without bowel resection) and stapled anastomosis with bowel resection (20.9% vs. 13.9% vs. 6.7%,  $p < 0.001$ ) [3]. Several other studies reported a higher incidence of POI with hand-sewn anastomosis to varying degrees of statistical significance [35, 37, 38, 44, 45, 61, 68], with only one study demonstrating the opposite trend [58]. Earlier time to closure appeared to have a protective association with POI, but different time cutoffs in studies precluded definitive conclusions from being drawn. D’Haeninck et al. observed less POI in patients closed < 84 days after the index operation (3.5% vs. 14.3%,  $p = 0.02$ ) [38]. Worni et al. demonstrated a potential dose–response association between intersurgery

length and POI, and reported an adjusted odds ratio for POI of 8.2 (95% CI 0.9–73.6) and 10.0 (95% CI 1.0–97.8) for closures that occurred 84–126 days and > 126 days after ileostomy creation, respectively, compared to those that occurred before 84 days [41]. However, the wide confidence intervals demonstrate a lack of power and precision in their findings. Three studies evaluated the impact of very early closure (< 14 days) and demonstrated no differences in POI [47, 62, 65].

The use of ERPs was evaluated in two studies, and both showed no protective effect for POI [7, 59]. Single observational studies reported trends towards increased POI with an open surgical approach for the index resection (13.6% vs. 9.0%) [49] and with the administration of adjuvant therapy in the intersurgery period (10.9% vs. 3.1%) [26], but no inferential statistics were presented. One study demonstrated age > 80 years as a risk factor for POI, but suffered from multiple testing and no clear hypothesis [67]. Skin closure technique (linear vs. purse-string) [48, 50], surgeon experience [75], gentamycin wound implants [21], and the use of liposome bupivacaine-based analgesia [51] had no impact on POI after loop ileostomy closure.

Among those exposures considered experimental or non-standard of care, only preoperative bowel stimulation was shown to reduce POI in a small RCT (2.9% vs. 20.0%,  $p = 0.024$ ) [54]. The use of adhesion barriers [25, 31, 46, 69], laparoscopic assistance at the time of closure [53, 63], early feeding [66], and position of ileostomy (umbilical vs.

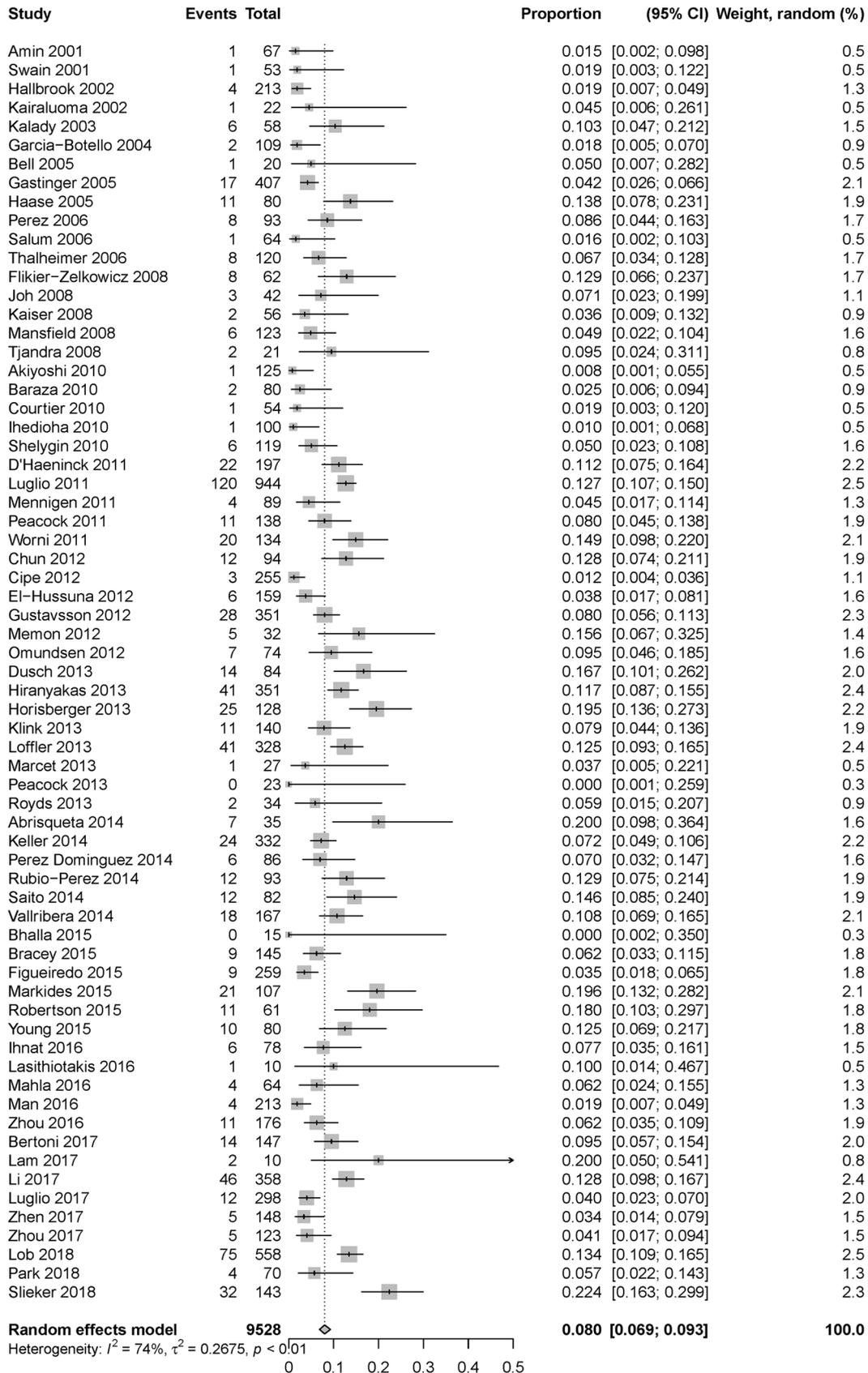
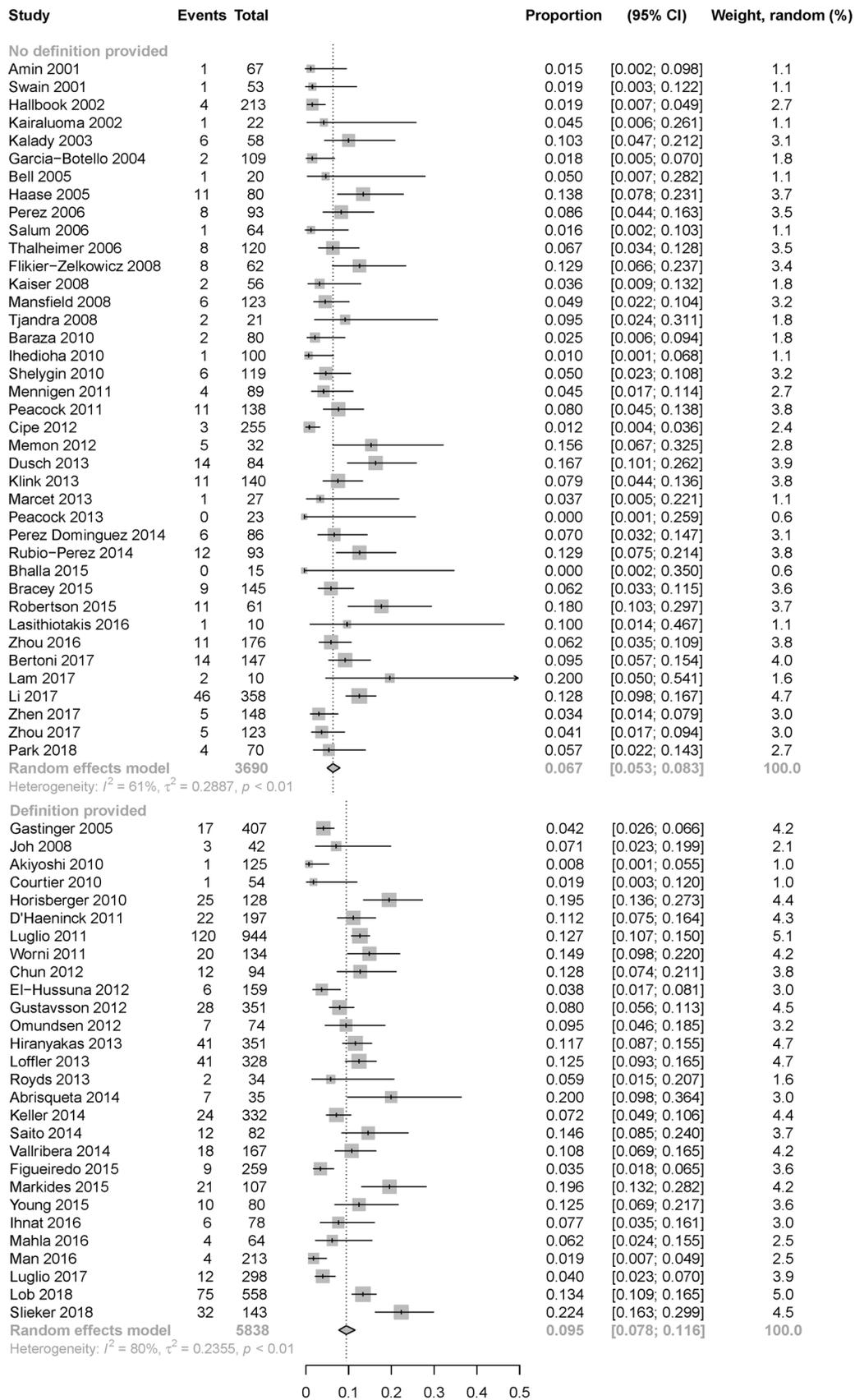


Fig. 2 Forest plot of incidence of postoperative ileus after loop ileostomy closure in included studies



**Fig. 3** Forest plot of incidence of postoperative ileus after loop ileostomy closure in included studies, stratified by the presence or absence of reported definition for postoperative ileus

traditional) [70] had no impact on POI after loop ileostomy closure.

## Discussion

This study is, to our knowledge, the first systematic review and meta-analysis to synthesize the literature on the development of POI after loop ileostomy closure, to estimate a pooled cumulative incidence of POI, and identify risk factors for its development. POI is often regarded as the most important complication following loop ileostomy closure [4, 7, 54], both clinically and economically, with authors concluding that all efforts should be made to better understand and decrease its incidence [7]. In addition to an increased length of stay, POI is associated with increased risk for other morbidities and higher healthcare costs [6].

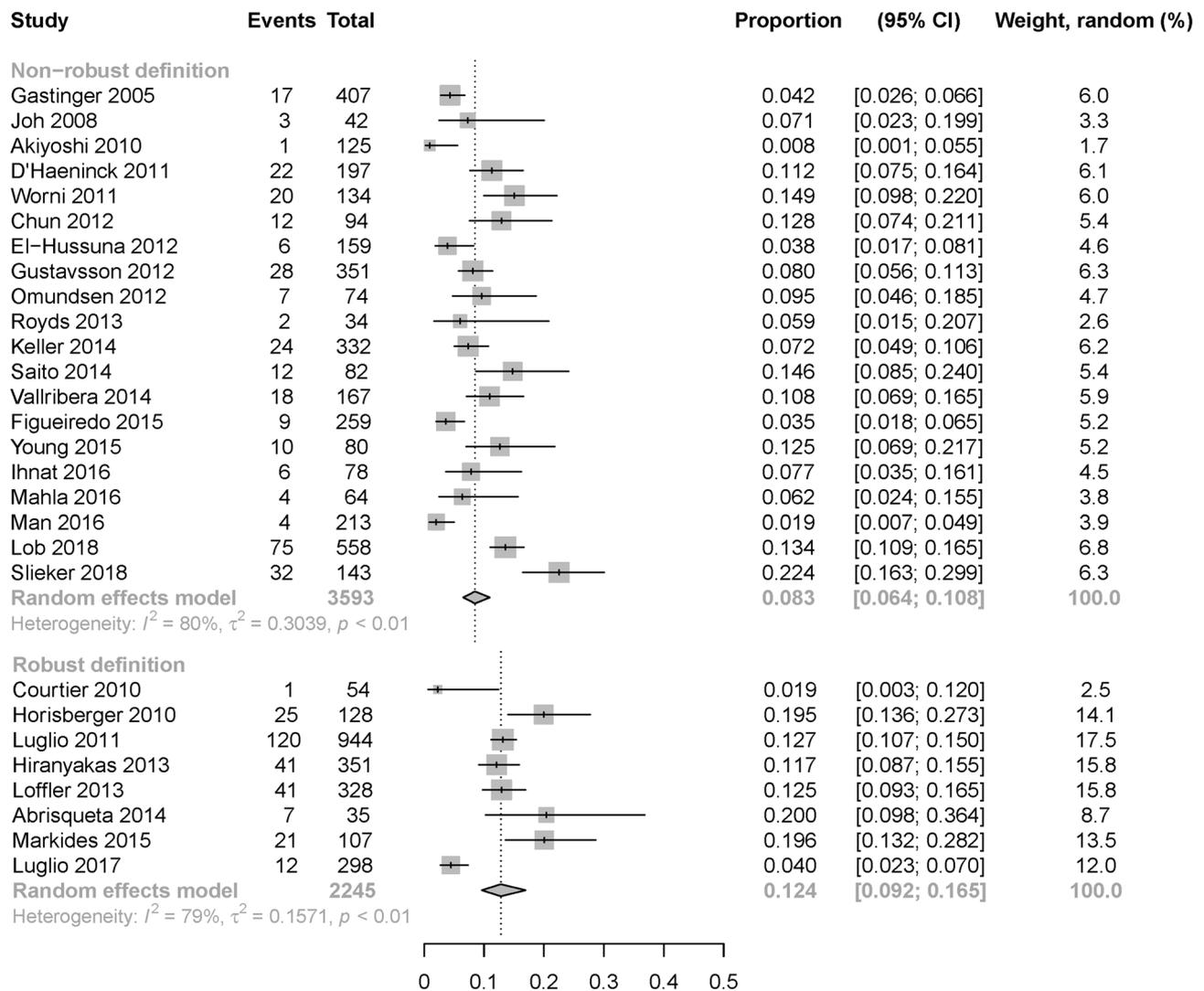
Our primary objective was to conduct a meta-analysis of proportions to better understand the risk for POI after loop ileostomy closure. We used a random-effects model given the expected clinical heterogeneity in patient populations between studies. The overall pooled estimate of POI was 8.0% (95% CI 6.9–9.3%), but important heterogeneity was present ( $I^2 = 74\%$ ). We also found that studies that lacked a clear definition of POI had the lowest incidence (6.7%; 95% CI 5.3–8.3%), perhaps reflecting a lower quality study for the given outcome. Among studies that did report a definition, a more robust definition resulted in the highest incidence of POI (12.4%; 95% CI 9.2–16.5%), which is consistent with findings from a recent systematic review of POI after colorectal resections [77]. Clinically, this is intuitive, as a more inclusive definition better reflects the spectrum of POI that is observed in practice. A recent joint consensus statement from the American Society for Enhanced Recovery and the Perioperative Quality Initiative proposed symptom-score-based definitions for postoperative gastrointestinal dysfunction, based on tolerance to diet, nausea, vomiting, distension, and duration of symptoms [78]. Such a definition better reflects the variable clinical manifestations of POI, while the use of more restrictive definitions may miss some clinically relevant cases.

One issue that may have contributed to an underestimation in the pooled estimate of POI is the overlap of POI and postoperative SBO in the surgical literature. SBO, a rarer entity than POI following ileostomy closure, may mimic POI in its presentation and response to conservative management in most cases. Some studies were excluded from the present study for reporting SBO only [79, 80], despite their study definition of SBO resembling what most surgeons would

consider POI (i.e., absent bowel function with radiologic confirmation of bowel dilatation but with no mention of mechanical obstruction or transition point seen on imaging). Consequently, some potentially relevant studies may have been excluded. Furthermore, many included studies reported very high rates of early postoperative SBO that rivaled that of POI, and there is likely a degree of misclassification of POI as partial SBO. While the initial clinical management of these patients may be similar (barring the need for reoperation), this event misclassification may impact the estimation of the true incidence of POI. We did include seven studies that reported on POI/SBO; however, based on their study definitions for POI/SBO and the absence of patients undergoing reoperation for this outcome, we felt that these studies were most likely capturing POI. This is supported by the results of a sensitivity analysis that produced similar estimates of POI when these studies were excluded. Postoperative nausea and vomiting and gastroparesis are two other entities with similar presentation to POI; however, these outcomes were seldom reported in the included studies.

This study highlights the importance of POI after loop ileostomy closure. The pooled estimate of POI was similar to that estimated in a systematic review of POI after colorectal resections [77]. This is noteworthy, given that loop ileostomy closure does not share many of the traditional POI risk factors associated with these larger-scale colorectal operations, such as large open incisions, epidurals, long operations, increased fluid administration, and major blood loss. In contrast, this operation carries its own set of risk factors unique to loop ileostomy closure patients, such as being the second operation of a two-stage procedure, varying time periods of bowel defunctionalization between ileostomy creation and closure, and a small bowel anastomosis, emphasizing the need for research into POI in this specific population.

The most consistent risk factors for POI were hand-sewn anastomosis and later time to closure. Hand-sewn anastomosis has previously been associated with increased risk of SBO after loop ileostomy closure in small RCTs and meta-analyses [80–82]. The HASTA trial, designed specifically to answer this question, failed to demonstrate a statistical difference in POI/SBO with hand-sewn anastomosis (16% vs. 9%), but did not rule out clinically relevant differences due to its modest size [4]. Several other observational studies also reported a higher incidence of POI with a hand-sewn anastomosis [35, 37, 38, 44, 45, 61, 68]. This observation may be due to the relatively narrow lumen and increased bowel wall edema caused by a hand-sewn anastomosis compared to the wide-open anastomosis with a stapled side-to-side reconfiguration. However, among patients undergoing a hand-sewn anastomosis, the fold-over technique may result in less POI compared to a small bowel resection and end-to-end anastomosis [3],



**Fig. 4** Forest plot of incidence of postoperative ileus after loop ileostomy closure in included studies with a definition, stratified by robustness of reported definition for postoperative ileus. Robust

definition for POI=includes > 2 of the following four components: description of symptoms, radiological criteria, time element for the development of symptoms, and insertion of a nasogastric tube

as an enterectomy necessitates more dissection, bowel manipulation, and possible myenteric nerve disruption. Time to ileostomy closure is interesting, as it is an actionable risk factor in many respects. If POI is truly associated with longer intersurgery length, surgeons should attempt to operate on patients who are deemed fit for intestinal continuity as soon as is suitable. Among those patients who are delayed for medical reasons, a novel intervention exists to potentially reduce POI after ileostomy closure. Abrisqueta et al. hypothesized that the defunctioned segment of bowel undergoes a series of structural and functional changes that leave it functionally unprepared for intestinal content, perhaps contributing to POI upon ileostomy closure. They proposed that preoperative bowel stimulation via the efferent limb may reverse some of these changes,

and demonstrated reduced rates of POI among stimulated patients (20% vs. 3%) in a small RCT [54].

Unlike many prior studies investigating risk factors for POI after colorectal surgery [83, 84], not one included study in the current review made use of a large database, which often affords the sample size required to precisely determine associations between an exposure and an outcome. The American College of Surgeons National Surgical Quality Improvement Program is one such database that was created as a quality control program to measure 30-day surgical outcomes. It would be ideal to answer the current question within this database as all variables, including POI, are recorded prospectively, with rigorous pre-defined definitions and standardized criteria. Unfortunately, POI is only recorded as a variable in the colectomy datasets, and

ileostomy closure is not included as a procedure within this subgroup. If ileostomy closure could be included in the colectomy-specific dataset, predictors of POI after this procedure could be better understood [85].

Our systematic review has some potential limitations. There was significant heterogeneity between studies, which can be explained in part by differences in study populations. Heterogeneity is often a limitation in meta-analyses of observational data, particularly when the outcome (e.g., POI) is defined inconsistently across studies. We used a random-effects model, which does consider both within- and between-study variability; however, the use of this approach may not fully mitigate the issue of heterogeneity. Furthermore, the majority of included studies were retrospective observational studies designed to assess a composite outcome of all postoperative morbidities following loop ileostomy closure rather than POI alone. As such, many of these studies were not properly powered to examine risk factors for POI. In addition, most studies also did not use any statistical approaches to adjust for confounding, limiting the strength of the conclusions that can be drawn. There is also a possibility of publication bias in any systematic review; however, given that the pooled estimate was a proportion and not a measure of association, publication bias is unlikely to have had a major impact on the results of the present study.

## Conclusions

POI is a frequent complication after loop ileostomy closure that merits our attention to better understand its etiology and risk factors. From the existing literature, the pooled 30-day cumulative incidence of POI was 8%; however, this estimate was dependent on the study definition of POI, as studies with a robust definition had a higher pooled incidence. Hand-sewn small bowel anastomosis and a longer intersurgery length may be associated with POI, but very few studies were designed to study POI specifically, which limits the conclusions that can be drawn from this literature. Lastly, this study underscores the challenges in conducting research on POI. The use of a consistent definition of POI in future research in this area is essential to allow for meaningful comparisons and pooling of the existing literature.

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## Compliance with ethical standards

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## Appendix 1—Full MEDLINE strategy of systematic review search

- 1 Ileostomy/ (6912)
- 2 Ostomy/ (1385)
- 3 Surgical Stomas/ (1696)
- 4 1 or 2 or 3 (9620)
- 5 Abdominal Wound Closure Techniques/ (596)
- 6 (closure or reversal).tw,kf. (168566)
- 7 5 or 6 (168748)
- 8 4 and 7 (928)
- 9 ((ileostom\* or ostom\* or stoma\*) adj5 (closure or reversal)).tw,kf. (3616)
- 10 8 or 9 (3802)
- 11 exp Ileus/ (5496)
- 12 Intestinal Obstruction/ (30689)
- 13 limit 12 to yr="1968 - 2003" (16593)
- 14 Morbidity/ (29418)
- 15 Postoperative complications/ (362621)
- 16 Reoperation/ (85728)
- 17 (complicat\* or ileus or morbidity).tw,kf. (1362026)
- 18 POI.tw,kf. (1053)
- 19 11 or 13 or 14 or 15 or 16 or 17 or 18 (1643244)
- 20 10 and 19 (1444)
- 21 Animals/ not Humans/ (4771261)
- 22 (animals or animal or canine\* or cat or cats or dog or dogs or feline or hamster\* or mice or monkey or monkeys or mouse or murine or pig or pigs or piglet\* or porcine or primate\* or rabbit\* or rats or rat or rodent\* or sheep or veterinar\*).ti,jw. (2438914)
- 23 21 or 22 (5204283)
- 24 20 not 23 (1430)
- 25 (exp child/ or exp infant/ or adolescent/) not exp adult/ (1875013)
- 26 (adolesc\* or baby or babies or boy\* or child\* or fetus or fetal or foet\* or girl\* or juvenile\* or kid or kids or infan\* or newborn\* or new-born\* or neonat\* or neo-nat\* or paediatr\* or pediatr\* or preadolesc\* or prepubesc\* or preteen\* or pubescen\* or teen\* or toddler\* or youth\*).ti,jw. (1884656)
- 27 25 or 26 (2538655)

28 24 not 27 (1245)  
 29 remove duplicates from 28 (1048)

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