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Primary Repair or Anastomosis Versus Enterostomy for Spontaneous Intestinal Perforation in Preterm Neonates: A Systematic Review.

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ABSTRACT

Background: Spontaneous intestinal perforation (SIP) is a distinct gastrointestinal emergency of prematurity that predominantly affects very low birth weight and extremely low birth weight infants. It differs from necrotizing enterocolitis in pathogenesis, intraoperative findings, and postoperative course. The optimal operative strategy remains uncertain, particularly whether primary repair or primary anastomosis offers advantages over enterostomy in selected infants.

Methods: A systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 statement. PubMed/MEDLINE, Embase, Scopus, Web of Science, the Cochrane Library, and Google Scholar were searched from inception to 4 April 2026. Comparative studies of preterm neonates with SIP, including cohorts described as focal intestinal perforation or isolated intestinal perforation, were eligible if they compared primary repair or anastomosis with enterostomy. Mixed-population comparator studies involving isolated intestinal perforation and/or combined necrotizing enterocolitis-SIP cohorts were reviewed separately as supplementary evidence.

Results: Four SIP-specific retrospective comparative cohort studies formed the primary evidence base. Three studies provided directly verifiable sample sizes, comprising 105 infants in total. Across the studies with extractable numerical data, no consistent mortality advantage was demonstrated for either operative strategy. In Brisighelli et al., mortality was 23% after primary anastomosis and 33% after stoma formation. In Dübbers et al., mortality was 13.3% after primary anastomosis and 8.3% after enterostomy. Potential advantages of a non-stoma strategy were reported for discharge weight, length of hospital stay, parenteral nutrition duration, and number of procedures under general anesthesia. However, the evidence base was limited to retrospective studies and was vulnerable to confounding by indication [4-6,9].

Conclusions: Primary repair or primary anastomosis appears feasible in carefully selected preterm neonates with SIP, but current evidence does not establish superiority over enterostomy. The main potential advantages of a non-stoma strategy appear to relate to treatment burden and recovery rather than mortality. Better multicenter comparative studies are needed...

Keywords: spontaneous intestinal perforation; focal intestinal perforation; isolated intestinal perforation; preterm neonate; enterostomy; primary anastomosis; neonatal surgery.

INTRODUCTION

Spontaneous intestinal perforation is a serious gastrointestinal emergency of prematurity that occurs predominantly in very low birth weight and extremely low birth weight infants. It is generally regarded as a clinicopathological entity distinct from necrotizing enterocolitis, with differences in disease mechanism, bowel involvement, intraoperative findings, and postoperative course [1,2,7,10]. This distinction is important because combining SIP and necrotizing enterocolitis in the same surgical analysis can obscure disease-specific operative questions and weaken clinical interpretation [1,2].

The operative management of SIP remains controversial. In infants requiring laparotomy, the surgeon must decide between a non-stoma strategy, such as primary repair or resection with primary anastomosis, and bowel diversion with enterostomy. Enterostomy has traditionally been favored in fragile preterm infants because it may be perceived as safer when bowel viability is uncertain or the infant is physiologically unstable. However, diversion also carries important disadvantages, including fluid and electrolyte losses, skin complications, stoma prolapse or retraction, impaired growth, and the need for a second operation for stoma closure [2,5-7].

Over the last two decades, several observational studies have questioned whether enterostomy should remain the default strategy in all cases of SIP. Early comparative work in neonatal intestinal perforation was followed by more focused studies.

in isolated, focal, or spontaneous intestinal perforation [3-9]. These cohorts suggest that primary repair or primary anastomosis may be feasible in selected infants, with some studies reporting comparable mortality and possible advantages in discharge weight, length of hospital stay, duration of parenteral nutrition, or number of procedures under general anesthesia [5,6,9]. At the same time, these studies are retrospective, involve small numbers, and are vulnerable to confounding by indication because infants selected for enterostomy may be smaller, less stable, or have more compromised bowel at operation [4-6,8,9]...

Interpretation of the literature is further complicated by inconsistent terminology. Authors have used the terms spontaneous intestinal perforation, focal intestinal perforation, and isolated intestinal perforation to describe overlapping neonatal populations [1,4-7]. In addition, some studies classify the non-stoma group as primary anastomosis alone, whereas others combine suturing and anastomosis into a single one-stage surgery group [5,6,9]. A focused systematic review restricted to SIP is therefore justified. The aim of the present review was to evaluate the comparative evidence on primary repair or anastomosis versus enterostomy for spontaneous intestinal perforation in preterm neonates, with particular attention to mortality, reoperation, postoperative complications, nutritional recovery, and treatment burden.

MATERIALS AND METHODS

Protocol and registration

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 statement [11]. A review protocol was developed before study selection. This review was not prospectively registered.

Eligibility criteria

Studies were eligible if they: (1) included preterm neonates with spontaneous intestinal perforation or clinically comparable cohorts described as focal intestinal perforation or isolated intestinal perforation [1,4-7]; (2) compared a non-stoma strategy, defined as primary repair/suturing and/or resection with primary anastomosis, with enterostomy or stoma formation [4-9]; (3) reported at least one relevant clinical outcome; and (4) were comparative studies, including retrospective comparative cohort studies, prospective comparative studies, or case-control studies. Studies were excluded if they focused primarily on necrotizing enterocolitis, gastric perforation, meconium-related perforation, intestinal atresia, volvulus, Hirschsprung disease, anorectal malformations, or Meckel's diverticulum unless SIP data were reported separately [1,2,7]; compared only peritoneal drainage with laparotomy without a separable comparison between primary repair/anastomosis and enterostomy [8]; or were case reports, non-comparative case series, review articles, editorials, letters, or abstract-only publications without extractable comparative data.

Information sources and search strategy

A systematic literature search was performed in PubMed/MEDLINE, Embase, Scopus, Web of Science, the Cochrane Library, and Google Scholar from database inception to 4 April 2026. Reference lists of included studies and relevant review articles were also hand-searched to identify additional eligible studies [11]. The search strategy combined disease-specific, population, and operative terms, including: ("spontaneous intestinal perforation" OR "spontaneous bowel perforation" OR "focal intestinal perforation" OR "isolated intestinal perforation") AND (neonate* OR newborn* OR preterm OR premature OR "very low birth weight" OR VLBW OR "extremely low birth weight" OR ELBW) AND ("primary repair" OR sutur* OR "primary anastomosis" OR anastomos* OR enterostomy OR ileostomy OR stoma OR ostomy).

Study selection

Records were screened by title and abstract, followed by full-text assessment of potentially relevant studies. SIP-specific direct comparator studies were included in the primary synthesis. Mixed-population studies involving isolated intestinal perforation and/or combined necrotizing enterocolitis-SIP cohorts were retained for supplementary discussion if they addressed the same operative comparison. The current PRISMA flow diagram reflects the final study set used in this manuscript.

Data extraction

Data extracted included study design, recruitment period, sample size, terminology used for SIP, gestational age, birth weight, operative details, mortality, reoperation, major complications, parenteral nutrition duration, time to full feeds, length of stay, discharge weight, and treatment burden [4-9].

Risk of bias assessment

Risk of bias was assessed descriptively using the Newcastle-Ottawa framework for cohort studies [12]. Particular attention was paid to selection bias, comparability of groups, confounding by indication, and outcome assessment.

Data synthesis

A narrative synthesis was performed. Meta-analysis was not undertaken because of heterogeneity in terminology, operative grouping, and incomplete harmonization of reported outcomes [4-6,9].

RESULTS

Study selection

Four SIP-specific retrospective comparative cohort studies met the primary inclusion criteria: de Haro Jorge et al. 2016, Brisighelli et al. 2018, Dübbers et al. 2021, and Genet et al. 2025 [4-6,9]. Three additional mixed-population comparator studies were identified and retained for supplementary discussion: Singh et al. 2006, Calisti et al. 2004, and Alzamrooni et al. 2025 [3,13,14]. Figure 1 shows the PRISMA 2020 flow diagram for the final evidence set used in this review.

Study characteristics

All SIP-specific included studies were retrospective comparative cohorts. Three studies provided directly verifiable sample sizes totaling 105 infants. de Haro Jorge et al. included 23 preterm infants with isolated intestinal perforation, comparing 14 primary anastomoses with 9 ileostomies [4]. Brisighelli et al. included 40 very low birth weight infants with focal intestinal perforation, comparing 22 primary anastomoses with 18 stoma openings [5]. Dübbers et al. included 42 infants weighing less than 1000 g with spontaneous intestinal perforation, comparing 30 primary anastomoses with 12 enterostomies [6]. Genet et al. reported a bi-centric comparative cohort of extremely preterm infants undergoing primary anastomosis or suturing versus enterostomy, although the full sample size was not provided in the indexed report used for this synthesis [9].

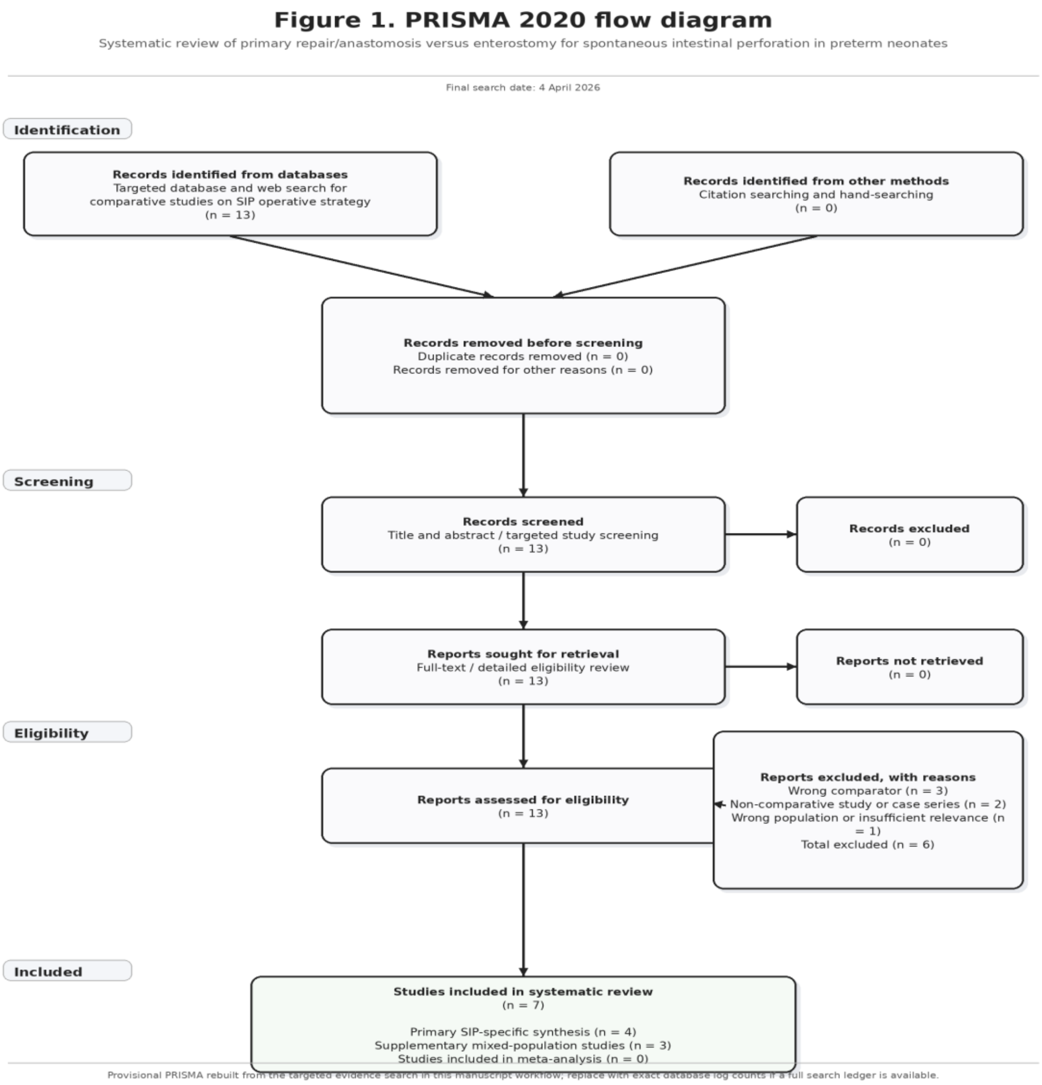

Figure 1. PRISMA 2020 flow diagram of study selection.

Table 1. Characteristics of included comparative studies.

Study	Design	Population	Non-stoma group	Enterostomy group	Verified numerical details
de Haro Jorge et al., 2016 [4]	Retrospective comparative cohort	Preterm infants with isolated intestinal perforation	Primary anastomosis	Ileostomy	Total 23 infants: 14 primary anastomosis, 9 ileostomy; median gestational age 27 weeks; median birth weight 883 g; overall mortality 30.4%
Brisighelli et al., 2018 [5]	Retrospective comparative cohort	VLBW infants with focal intestinal perforation	Primary anastomosis	Stoma opening	Total 40 infants: 22 primary anastomosis, 18 stoma; mean birth weight 865 g vs 778 g; mean gestational age 26.1 vs 25.6 weeks
Dübbers et al., 2021 [6]	Retrospective comparative cohort	Infants <1000 g with SIP	Primary anastomosis	Enterostomy	Total 42 infants: 30 primary anastomosis, 12 enterostomy; median gestational age 24.3 weeks; median birth weight 640 g
Genet et al., 2025 [9]	Retrospective bi-centric comparative cohort	Extremely preterm infants with SIP	Primary anastomosis or suturing	Enterostomy	Initial one-stage surgery associated with shorter parenteral nutrition duration and fewer procedures under general anesthesia; full sample size not provided in indexed report

Abbreviations: SIP, spontaneous intestinal perforation; VLBW, very low birth weight.

Risk of bias

All included SIP-specific studies had a high overall risk of bias. The main threats were retrospective design, treatment-selection bias, confounding by indication, and incomplete adjustment for baseline differences [4-6,9]. In de Haro Jorge et al., the choice of operative strategy depended on surgeon judgment [4]. In Dübbers et al., operative strategy changed by treatment era, introducing era bias [6]. In Genet et al., the one-stage group combined suturing and anastomosis, increasing procedural heterogeneity [9].

Table 2. Risk of bias assessment.

Study	Main bias concerns	Overall risk of bias
de Haro Jorge et al., 2016 [4]	Retrospective design; surgeon judgment used for operative choice; no protocolized allocation	High
Brisighelli et al., 2018 [5]	Retrospective single-center design; small sample; possible treatment-selection differences	High
Dübbers et al., 2021 [6]	Retrospective design; treatment strategy changed by era; confounding by indication	High

Genet et al., 2025 [9]	Retrospective bi-centric design; mixed non-stoma arm; likely center and selection effects	High

Primary outcomes

Mortality was directly extractable from Brisighelli et al. and Dübbers et al. In Brisighelli et al., mortality was 5/22 (23%) after primary anastomosis and 6/18 (33%) after stoma formation [5]. In Dübbers et al., mortality was 4/30 (13.3%) after primary anastomosis and 1/12 (8.3%) after enterostomy [6]. These data do not show a consistent mortality advantage for either strategy.

In Brisighelli et al., 5/22 (23%) infants initially treated with primary anastomosis later required stoma opening because of complications [5]. In Dübbers et al., complication-related reoperations occurred in 10/30 infants in the primary anastomosis group and 4/12 in the enterostomy group [6]. These findings indicate that one-stage surgery is feasible but does not eliminate the need for further intervention. Complication reporting was heterogeneous. In Brisighelli et al., the clearest extractable complication-related endpoint was later stoma creation after initial anastomosis in 23% of cases [5]. In Dübbers et al., revision burden was present in both groups [6]. De Haro Jorge et al. suggested a higher risk of life-threatening complications after primary anastomosis, although exact event counts were not provided in the indexed report [4].

Secondary outcomes

Dübbers et al. reported a median length of stay of 110.5 days after primary anastomosis versus 124 days after enterostomy [6]. Dübbers et al. also reported a higher median discharge weight after primary anastomosis: 2258 g versus 1880 g after enterostomy (p = 0.036) [6]. Genet et al. reported that one-stage surgery was associated with shorter parenteral nutrition duration and fewer procedures under general anesthesia than enterostomy [9]. All diversion strategies inherently involved stoma care and later closure, and the reduced number of procedures under general anesthesia in the Genet cohort supports a lower treatment burden with successful one-stage surgery [9].

Table 3. Summary of outcomes reported in included studies.

Study	Mortality	Reoperation / revision	Major complications	PN / feeding outcomes	Length of stay	Growth / discharge weight	Authors' conclusion
de Haro Jorge et al., 2016 [4]	Overall mortality 30.4%; exact group-specific counts not provided in indexed report	Not fully reported	Higher life-threatening complications after primary anastomosis suggested	Not fully reported	Not fully reported	Not fully reported	Ileostomy appeared safer than primary anastomosis in this cohort
Brisighelli et al., 2018 [5]	5/22 (23%) primary anastomosis vs 6/18 (33%) stoma	5/22 (23%) later required stoma	Conversion to stoma in 23% of primary anastomosis group	Not fully reported	Not fully reported	Not fully reported	Both procedures were feasible; primary anastomosis reduced reinterventions when successful
Dübbers et al., 2021 [6]	4/30 (13.3%) primary anastomosis vs 1/12 (8.3%) enterostomy	10/30 primary anastomosis vs 4/12 enterostomy	Similar revision burden across groups	Not fully reported	Median LOS 110.5 vs 124 days	Median discharge weight 2258 g vs 1880 g (p = 0.036)	Primary anastomosis was feasible and may improve recovery-related outcomes

Genet et al., 2025 [9]	Not provided in indexed report	Not provided in indexed report	Not provided in indexed report	Shorter PN duration with one-stage surgery	Not fully reported	Not fully reported	One-stage surgery appeared viable and reduced treatment burden

Abbreviation: PN, parenteral nutrition

Supplementary mixed-population evidence

Three additional comparative studies were identified but not pooled with the main SIP-specific synthesis because of clinical heterogeneity. Singh et al. included 68 neonates undergoing laparotomy for intestinal perforation, including 20 with isolated intestinal perforation, and compared anastomosis with stoma-based approaches [3]. Calisti et al. evaluated mixed neonatal intestinal perforation, including isolated intestinal perforation and necrotizing enterocolitis, and reported more favorable results with diversion than primary anastomosis [13]. Alzamrooni et al. studied 132 extremely low birth weight infants with combined necrotizing enterocolitis and SIP, including 40 primary anastomoses and 92 stoma procedures, and reported similar mortality but shorter hospital stay and faster progression to feeds with primary anastomosis, while noting baseline differences in illness severity [14].

DISCUSSION

This systematic review identified a small but clinically relevant body of comparative evidence addressing the operative management of spontaneous intestinal perforation in preterm neonates. The available SIP-specific studies suggest that primary repair or primary anastomosis is feasible in selected infants, but current evidence does not demonstrate a consistent mortality advantage for either a non-stoma strategy or enterostomy [4-6,9].

A major strength of this review is its restriction to SIP-specific evidence for the primary synthesis. SIP is distinct from necrotizing enterocolitis in pathology and operative context, and combining the two diseases would weaken the interpretability of the surgical comparison [1,2,7,10]. For that reason, mixed-population studies were considered supplementary rather than part of the main evidence base [3,13,14].

The mortality findings do not support a clear survival advantage for one operative strategy. In Brisighelli et al., mortality was 23% after primary anastomosis and 33% after stoma formation, whereas in Dübbers et al., mortality was 13.3% after primary anastomosis and 8.3% after enterostomy [5,6]. These differences likely reflect baseline case mix and operative selection rather than a direct treatment effect. The lack of consistent mortality separation across cohorts suggests that operative choice may influence recovery burden more than survival.

The most clinically relevant potential advantages of a non-stoma strategy appear to relate to recovery and treatment burden. Dübbers et al. reported shorter hospitalization and higher discharge weight after primary anastomosis [6]. Genet et al. reported shorter parenteral nutrition duration and fewer procedures under general anesthesia with one-stage surgery [9]. These findings are important because the disadvantages of enterostomy extend beyond the initial operation and include diversion-related morbidity, prolonged stoma care, and later closure.

At the same time, one-stage surgery is not without risk. In Brisighelli et al., 23% of infants initially treated with primary anastomosis later required stoma formation [5]. In Dübbers et al., reoperations for complications occurred in both groups [6]. These data support a selective rather than universal approach.

This review has important limitations. All included SIP-specific studies were retrospective cohorts and therefore vulnerable to confounding by indication and selection bias [4-6,9]. Terminology was inconsistent, and the non-stoma group was not uniformly defined across studies. In addition, some numerical outcomes remained incompletely available in indexed reports, especially for de Haro Jorge et al. and Genet et al. [4,9]. These limitations reduce the strength of inference and justify the decision not to perform meta-analysis.

The supplementary mixed-population studies are directionally informative but should not drive the main conclusion. Singh et al. and Calisti et al. included intestinal perforation populations broader than SIP alone [3,13]. Alzamrooni et al. combined necrotizing enterocolitis and SIP in extremely low birth weight infants and found no mortality difference but some recovery advantages with primary anastomosis [14]. These studies reinforce the need to keep SIP-specific conclusions separate from mixed-cohort findings.

Overall, the available evidence suggests that primary repair or primary anastomosis is a reasonable option in carefully selected preterm neonates with spontaneous intestinal perforation, particularly when bowel involvement is localized and the operative field is favorable. Enterostomy remains a valid strategy in more unstable infants or where bowel condition is less suitable for one-stage repair. Better multicenter comparative studies with clearer disease definitions and standardized outcome reporting are needed.

CONCLUSIONS

Spontaneous intestinal perforation should be assessed separately from necrotizing enterocolitis when operative strategies are evaluated in preterm neonates [1,2,7,10]. The available comparative evidence suggests that primary repair or primary anastomosis is feasible in selected infants, but current data do not demonstrate a consistent mortality advantage over enterostomy [4-6,9]. The main potential benefits of a non-stoma strategy appear to relate to treatment burden and recovery rather than survival [6,9]. Current evidence supports individualized operative decision-making rather than routine preference for either strategy.

Additional Information

Human subjects: Not applicable.

Animal subjects: Not applicable.

Conflicts of interest: The authors have declared that no competing interests exist.

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