

NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

INTERVENTIONAL PROCEDURES PROGRAMME

Interventional procedure overview of serial transverse enteroplasty procedure (STEP) for bowel lengthening in parenteral nutrition-dependent children

In children, some diseases may result in abnormally short bowel. This can cause severe nutritional problems because of insufficient absorption of food. Serial transverse enteroplasty is an operation where the bowel is cut and stapled in a zig-zag pattern in order to narrow and lengthen it.

Introduction

This overview has been prepared to assist members of the Interventional Procedures Advisory Committee (IPAC) in making recommendations about the safety and efficacy of an interventional procedure. It is based on a rapid review of the medical literature and specialist opinion. It should not be regarded as a definitive assessment of the procedure.

Date prepared

This overview was prepared in March 2007

Procedure name

- Serial transverse enteroplasty procedure (STEP) for bowel lengthening in total parenteral nutrition-dependent children

Specialty societies

- British Association of Paediatric Surgeons
- British Society of Paediatric Gastroenterology, Hepatology and Nutrition

Description

Indications

Short Bowel Syndrome (SBS) is a very rare but extremely serious condition in which patients display a rapid intestinal transit time which results in

malabsorption of enteral nutrition and commonly diarrhoea. The condition results in growth failure and malnutrition. The child may stay in hospital for many months before home parenteral nutrition is possible. Liver failure and recurrent sepsis which can result in death are complications associated with total parenteral nutrition. SBS is either structural, i.e. the jejuno-ileal length is anatomically shortened, or functional where intestinal mucosa is damaged or is dysfunctional such as by enteropathy. SBS is a dynamic condition and in a substantial number of patients intestinal autonomy is possible through intestinal adaptation particularly in children where intestinal growth can still occur, and thus symptoms may improve spontaneously.

The aetiology of SBS may relate to jejuno-ileal atresia, gastroschisis or omphalocele (congenital defects in the abdominal wall through which organs may protrude), Hirschsprung's disease, necrotising enterocolitis, or intestinal volvulus.

Current treatment and alternatives

Most patients with SBS are partially or totally dependent on parenteral nutrition. Other surgical procedures to improve bowel transit time include resection of dilated segments of the small intestine, tapering enteroplasty, intestinal placcation, or the Bianchi intestinal loop lengthening procedure which is technically difficult. Some patients require small bowel and liver transplants.

What the procedure involves

The Serial Transverse Enteroplasty (STEP) procedure is a surgical technique for bowel lengthening designed for patients with SBS. The aim of the procedure is to increase the length of the small intestine so that patients can benefit from enteral nutrition and eventually wean from IV nutrition.

The STEP procedure relies on the anatomic principle that the blood supply to the small bowel originates from the mesentery and traverses the bowel perpendicular to its long axis. Under general anaesthesia a small defect was created in the mesentery and a rubber catheter passed through this defect. One arm of an endoscopic stapling device is passed through the mesentery. The bowel is simultaneously stapled and dissected in a direction parallel to this plane. The small bowel is left with a zig-zag appearance from these staples lines.

Efficacy

Specialist Advisers considered the key efficacy outcomes of this procedure to be reduction in TPN dependence, increased bowel length, patient growth, improved intestinal motility, avoidance of small bowel and transplantation, less systemic infection, and improved biochemical markers of liver function (e.g. bilirubin)

Bowel length, girth and function

One case series of 5 patients undergoing STEP reported an increase in mean bowel length of 17 cm¹. A second case series showed a statistically significant increase in bowel length of 37 cm (82%) from 61 cm at baseline to 98cm immediately following the procedure ($p<0.01$)². A third case series of 27 patients with bowel length measured at baseline reported an increase of 69% in bowel length from 68 ± 44 cm to 115 ± 87 cm, ($p<0.0001$)⁶. This study also reported a statistically significant decrease in bowel width following STEP from 6.3 ± 3.9 cm to 2.1 ± 0.9 cm, ($p<0.0001$) among 30 patients with measurements both at baseline and 13 month follow up. A case report of a patient undergoing STEP for SBS and D-Lactic acidosis reported that a normal calibre bowel was achieved with 2.5 hour transit time, at 7 days follow up³.

One case series of 8 patients undergoing STEP or STEP in conjunction with another procedure found that cholestasis was present at the time of surgery in 25% (2/8) of patients. This resolved in 1 patient¹.

Parenteral nutrition dependency

One case series of five patients reported that 'more than 50%' were completely weaned off TPN and one patient had significantly decreased (not defined) dependency¹. A second case series with follow up to 17 months reported that the mean percentage of nutrition received enterally improved from 49% at baseline to 80% in three patients ($p<0.05$)². A third case series with follow up to 13 months reported an improvement from 31% at baseline to 67% in the same outcome ($p<0.01$)⁶. In two case reports STEP allowed for 75%³ and 100%⁴ of calorific intake to be achieved enterally at 11 and 7 months respectively.

Growth

One case series of reported that weight for age (as measured against common epidemiological distributions for children) improved from a score of -2.7 at baseline to -2.0 at 12 months follow up ($p=0.01$)⁵.

Safety

The important safety outcomes by which to evaluate this procedure were highlighted by Specialist Advisers to be death, leaks, adhesion obstruction, intestinal failure, and deteriorating liver function.

The rate of mortality and of transplant following STEP was 8% (3/38) in one case series with 13 months follow up⁶.

One patient in a case series of eight patients had cholestasis that could not be controlled which contributed to sepsis, liver failure, and subsequently death at 3 months follow up¹.

One case report identified the postoperative complication of requirement for naso-gastric fluid aspiration of 50 mL/day which was bilious at first but cleared over time⁴.

One case series of 5 patients followed up for 15 months², and one case report of a patient followed up for 7 months⁴ reported that there were no long term complications noted.

Literature review

Rapid review of literature

The medical literature was searched to identify studies and reviews relevant to Serial transverse enteroplasty procedure (STEP) for bowel lengthening. Searches were conducted via the following databases, covering the period from their commencement to 17/01/07: Medline, PreMedline, EMBASE, Cochrane Library and other databases. Trial registries and the Internet were also searched. No language restriction was applied to the searches. (See Appendix C for details of search strategy.)

The following selection criteria (Table 1) were applied to the abstracts identified by the literature search. Where these criteria could not be determined from the abstracts the full paper was retrieved.

Table 1 Inclusion criteria for identification of relevant studies

Characteristic	Criteria
Publication type	Clinical studies were included. Emphasis was placed on identifying good quality studies. Abstracts were excluded where no clinical outcomes were reported, or where the paper was a review, editorial, laboratory or animal study. Conference abstracts were also excluded because of the difficulty of appraising methodology.
Patient	Patients with short bowel syndrome requiring partial or total parenteral nutrition
Intervention/test	Serial transverse enteroplasty procedure (STEP)
Outcome	Articles were retrieved if the abstract contained information relevant to the safety and/or efficacy.
Language	Non-English-language articles were excluded unless they were thought to add substantively to the English-language evidence base.

List of studies included in the overview

This overview is based on three case series two with one report^{1,6} and one with two reports^{2,5}, and additionally, two case reports^{3,4}.

Other studies that were considered to be relevant to the procedure but were not included in the main extraction table (Table 2) have been listed in Appendix A.

Existing reviews on this procedure

There were no published reviews identified at the time of the literature search.

Related NICE guidance

Below is a list of NICE guidance related to this procedure. Appendix B details the recommendations made in each piece of guidance listed below.

Interventional procedures:

None

Technology appraisals:

None

Clinical guidelines:

None

Public health:

None

Table 2 Summary of key efficacy and safety findings on serial transverse enteroplasty procedure (STEP) for bowel lengthening in parenteral nutrition-dependent children

Abbreviations used: TPN – total parenteral nutrition,																													
Study details	Key efficacy findings	Key safety findings	Comments																										
Modi B P (2007)⁶ Case series International multicentre (19 sites) Study Period: Sept 2004 to Apr 2006 n = 38 Population: median age = 1.3 years, male = 53%. Intestinal atresia n = 13, gastroschisis (with or without volvulus) n=11, necrotising enterocolitis n= 7. Previous Bianchi procedure n= 3. Indications: Short bowel syndrome, n = 29, bacterial overgrowth n = 6, Neonatal obstruction with marginal bowel length n = 3. Technique: STEP procedure, no further details given. Follow-up: Median 13 months Conflict of Interest: none	Bowel dimensions Among the 27 patients with bowel length measured at baseline the STEP procedure increased length from 68 ± 44 cm to 115 ± 87 cm, an increase of 69% (p<0.0001). Among the 30 patients with bowel width measured at baseline the STEP procedure decreased the width from 6.3 ± 3.9 cm to 2.1 ± 0.9cm, (p<0.0001). Parenteral dependency Among the 21 patients where STEP was performed on patients with dependence on parenteral nutrition the STEP procedure increased the percentage of total calories tolerated enterally from 31 ± 31 % at baseline to 67 ± 37% at 12.6 months follow up an increase of 116% (p<0.01). This analysis excluded neonates, and patients who progressed to transplantation or death. 48% (10/21) of patients were completely weaned from parenteral nutrition. 3 patients who were listed for liver and intestine transplant were removed from the list following STEP and improvement in enteral tolerance. Bacterial symptoms Of the six patients who underwent STEP for bacterial overgrowth five reported complete resolution of their symptoms.	Complications <table><thead><tr><th>Outcome</th><th>Rate</th></tr></thead><tbody><tr><td><i>Intraoperative</i></td><td></td></tr><tr><td>Staple line leak</td><td>5% (2/38)</td></tr><tr><td>Aspiration leading to prolonged ITU stay for respiratory insufficiency</td><td>3% (1/38)</td></tr><tr><td><i>Postoperative</i></td><td></td></tr><tr><td>Bowel obstruction</td><td>5% (2/38)</td></tr><tr><td>Hypertension</td><td>3% (1/38)</td></tr><tr><td>Haematoma</td><td>3% (1/38)</td></tr><tr><td>Abscess</td><td>3% (1/38)</td></tr><tr><td>Pleural effusion</td><td>3% (1/38)</td></tr><tr><td><i>Late</i></td><td></td></tr><tr><td>Mortality (progressive liver failure and sepsis)</td><td>8% (3/38)</td></tr><tr><td>Transplant</td><td>8% (3/38)</td></tr></tbody></table> Authors state that the rate of mortality and transplant are less than those following the Bianchi procedure carried out at one of the participating institutions	Outcome	Rate	<i>Intraoperative</i>		Staple line leak	5% (2/38)	Aspiration leading to prolonged ITU stay for respiratory insufficiency	3% (1/38)	<i>Postoperative</i>		Bowel obstruction	5% (2/38)	Hypertension	3% (1/38)	Haematoma	3% (1/38)	Abscess	3% (1/38)	Pleural effusion	3% (1/38)	<i>Late</i>		Mortality (progressive liver failure and sepsis)	8% (3/38)	Transplant	8% (3/38)	Data from an internationally registry with voluntary registration but without mandatory enrolment of patients. So unclear whether this represents consecutive patients at all participating institutions. However authors state that they believe that full reporting has been achieved. Given the number of patients captured and the number of participating sites, it is likely that some sites will have undertaken only a small volume of procedures (1 to 10 each) and results may reflect a learning curve. No details provided of independence of outcome assessment.
Outcome	Rate																												
<i>Intraoperative</i>																													
Staple line leak	5% (2/38)																												
Aspiration leading to prolonged ITU stay for respiratory insufficiency	3% (1/38)																												
<i>Postoperative</i>																													
Bowel obstruction	5% (2/38)																												
Hypertension	3% (1/38)																												
Haematoma	3% (1/38)																												
Abscess	3% (1/38)																												
Pleural effusion	3% (1/38)																												
<i>Late</i>																													
Mortality (progressive liver failure and sepsis)	8% (3/38)																												
Transplant	8% (3/38)																												

Abbreviations used: TPN – total parenteral nutrition,			
Study details	Key efficacy findings	Key safety findings	Comments
Sudan A (2005)¹ Case series USA Study Period: Oct 2000 onwards n = 8 (5 STEP as monotherapy) Population: adults n = 3, children n = 2. Median remnant bowel length = 62 CM Indications: Short bowel syndrome, including short mesentery n = 2, dilated loop removal or fistula repair in previous Bianchi procedure n = 3, dilated small bowel segment n = 4. Technique: STEP procedure, no further details given. Follow-up: Median 2 years (for all patient not necessarily STEP) Conflict of Interest: not stated	Bowel length Mean increase in bowel length was 17cm in the 5 patients that underwent STEP only. From 62 to 79 cms. Parenteral dependency More than 50% of patients undergoing STEP procedures were weaned off their TPN completely and one had a significantly decreased need for TPN. Cholestasis was present at the time of surgery in 25% (2/8) patients which resolved in one patient.	Complications Cholestasis was unresolved in one patient and contributed to sepsis, liver failure, and death at 3 months follow up in one patient.	Patients were treated with a range of interventions following the instigation of a MDT intestinal failure programme. Overall 8 patients had STEP, although 3 had previous or subsequent Bianchi procedure. Data recorded here applies to either the 5 patients who has STEP alone or 8 patients including the 3 who had STEP plus Bianchi procedure. Authors state that STEP should be reserved for use as a secondary procedure in patients that dilate after undergoing the Bianchi procedure. They also state that timing of a surgical intervention is controversial, and the choice of waiting to see if full adaptation is achieved not universally recommended.

Abbreviations used: TPN – total parenteral nutrition,						
Study details		Key efficacy findings		Key safety findings	Comments	
Javid P J (2005) ² and Duggan C (2006) ⁵		Bowel length There was a statistically significant increase in mean bowel length of 37cm (82%) from 61cm (range 22 to 135cm) at baseline to 98cm (range 51 to 200 cm) (p<0.01) immediately following the procedure.		Complications There were no perioperative complications, and no postoperative complications to 15 months follow up.	Retrospective case chart study	
Case series		Parenteral dependency Postoperative nutritional data was available for 3 patients at 17 months follow up.		Mean hospital length of stay was 16 days (range 11 to 20).	No details provided for case selection criteria	
USA		The percentage of enteral nutrition improved significantly from 49% (range 10 to 70%) at baseline, to 80% (range 60 to 100%) (p<0.05).		There were no cases of intestinal leak, obstruction, or bowel motility delay on fluoroscopic study.	Operator experience not stated.	
Study Period: Feb 2002 - Mar 2004		One patient was completely weaned from TPN at 6 months follow up. One patient listed for liver-small bowel transplantation normalised their serological liver function test results within 6 months follow up.			High drop out rate for nutrition dependency outcome for a small series. No reasons provided why data not available for all patients.	
n = 5		Growth All patients gained weight following the procedure.			Authors stress the need for co-ordinated prospective data collection and have set up a registry. See link in 'issues for consideration by IPAC' section.	
Population: age = 12 months, Male = NR, STEP as primary therapy n = 4, previous Bianchi procedure n = 1. Gastroschisis / volvulus n = 2, malrotation / volvulus n = 1, necrotizing enterocolitis n = 1, gastroschisis / intestinal atresia n = 1. Mean bowel length = 61 cm.		More detailed nutritional outcomes data was recorded in 4 pf the patients at 12 months follow up				
Indications: Short bowel syndrome, not further described		Mean Z scores (calculated using Epi Info 2002), or % of standard size				
Technique: STEP procedure using a mean of 18 incisions/staplings.		Outcome	baseline	12 months	Difference (95% CI)	p=
Follow-up: 17 months		Weight for age	-2.7	-2.0	0.7 (0.2 to 1.3)	0.01
Conflict of Interest: not stated		Height for age	-2.3	-2.2	0.1 (-0.8 to 1.1)	0.77
		Weight for height	-0.8	-0.2	0.6 (0.3 to 0.9)	<0.0001
		Mid upper arm circumference %	90.1	103.2	13.1 (1.0 to 25.3)	0.03
		Mid arm muscle area	97.7	115.8	81.2 (-8.4 to 44.8)	0.18
		Triceps skin fold	62.6	87.1	24.5 (17.9 to 31.2)	<0.0001

Abbreviations used: TPN – total parenteral nutrition,			
Study details	Key efficacy findings	Key safety findings	Comments
Modi B P (2006)³ Case report USA Study Period: Not stated n = 1 Population: Male = 0% , Age = 18 years, previous Ladd procedure for malrotation, and bowel resection for intestinal volvulus. Gait instability and ataxia, irritability, fatigue, and slurred speech. 33% of energy intake from parenteral nutrition. Largely dilated duodenum with small bowel transit time of 5 hours. Small bowel = 32 cm, with 8cm proximal duodenum which was dilated. Indications: Short bowel syndrome, with D-Lactic Acidosis refractory to medical management. Technique: STEP procedure to taper the dilated duodenum to eliminate the focus of D-Lactate producing bacteria. 3 stapled incisions made. Follow-up: 11 months Conflict of Interest: not stated	Bowel length Gastrointestinal study on day 7 showed a normal calibre small bowel with a 2.5 hour transit time. Hospital stay The patient was discharged on the 11th postoperative day on a regular diet. Repeat admission Up to 11 months follow up the patient only required 1 admission of D-Lactic acidosis (at 8 months) compared to 6 admissions in 6 months prior to the procedure. Parenteral dependency The patient has maintained their weight, and at final follow up is receiving 75% of daily calories enterally. Quality of life The patient's quality of life has drastically improved and they have been able to return to college.	No details provided on safety outcomes.	Not clear how many cases had been undertaken for this indication at this institution, and why this particular case was published. Authors state that long term outcomes remain to be seen No details provided about changes to medication regimen.

Abbreviations used: TPN – total parenteral nutrition,			
Study details	Key efficacy findings	Key safety findings	Comments
Wales P W (2005)⁴ Case report Canada Study Period: Not stated n = 1 Population: Male = 100% , Age = 36 weeks gestation, bowel loops of 2.5 to 5 cm diameter, weight 2600g at caesarean section. Type IIIa proximal jejunal atresia. Proximal segment 30cm and 6 cm diameter, and distal segment 60 cm. Indications: Short bowel syndrome (jejunal atresia). Technique: STEP procedure performed to decrease the calibre of the atretic bowel. 14 stapled incisions made. Concomitant anastomosis of the proximal and distal bowel segments. Follow-up: 7 months Conflict of Interest: not stated	Bowel length 23.5 cm of dilated proximal jejunum was lengthened to 51.5 cm (120% lengthening) with an effective bowel diameter of 1.5 cm. An upper gastrointestinal and small bowel contrast study demonstrated a patent intestinal tract with no obstruction at 13 days follow up. Transit time to rectum was 50 minutes. Parenteral dependency Enteral feeds were initiated on the 13th postoperative day, and 8 days later the patient tolerated full-volume bottle feeds. At 7 months follow up the patient was thriving on full enteral feeds.	Complications Post operatively nasogastric aspirate was 50 ml/day and these were initially bilious, but cleared over time. There were no long term complications.	Not clear how many cases had been undertaken for this indication at this institution, and why this particular case was published. Difficult to determine the specific safety and efficacy profile of the STEP procedure as compared to the bowel anastomosis. Operator experience prior to this procedure is not stated. Authors state that spontaneous intestinal adaptation occurs in approximately 75% of patients with congenital or acquired causes of SBS

Validity and generalisability of the studies

- There are patients with a range of indications in addition to SBS included within the studies extracted in table 2
- Some patients received concomitant surgical interventions to STEP
- Few inclusion criteria for case selection are reported
- Studies include a range of patient ages, not all are specifically children, and outcomes for children and adults are not reported separately.
- As previously alluded, SBS in children is a dynamic condition, and some children will achieve weaning from TPN without any surgical intervention. This complicates judgements on efficacy in case series settings.

Specialist advisers' opinions

Specialist advice was sought from consultants who have been nominated or ratified by their Specialist Society or Royal College.

Mr M Jones, Mr B Jaffray, Mr B Davies, Mr I Sugarman, Prof A Pierro, Mr G Mackinlay.

- The Specialist Advisers thought that this procedure is intended to be a simple operation with low morbidity, aimed at improving the absorptive capacity of the bowel; it should be compared with the Bianchi tapering procedure, or bowel transplantation.
- Four out of five Specialist Advisers who commented on the current status of the procedure thought that it was novel and of uncertain safety and efficacy; the other Specialist Adviser considered it to be established.
- Adverse events reported in the literature or known anecdotally to the Specialist Advisers include late mortality, progression to transplant, staple-line leak, bowel obstruction, pleural effusion, hypertension, haematoma and abscess formation
- Additional theoretical complications relating to this procedure include further shortening of the bowel, formation of fistulae, bleeding, deteriorating bowel or liver function, worsening cholestasis, and septic complications.
- One Specialist Adviser had experience of a case where a repeat STEP was possible following initial lengthening.
- Results from operations carried out soon after birth are still unknown. Most of the specialist advisers suggested that the prognosis of SBS is uncertain. Some patients improve spontaneously without treatment.
- One Specialist Adviser commented that STEP is one of a range of surgical options, none of which has been shown convincingly to provide benefit.
- The Specialist Advisers thought that the procedure was not technically difficult but advised apprenticeship or observing an experienced surgeon.
- Patients need to be treated under multidisciplinary care.
- The impact of this procedure is likely to be low, as fewer than 100 patients per year in the UK are likely to require it; STEP would probably be provided by around 10 specialist centres in the UK.

Issues for consideration by IPAC

- An international multicentre registry with 19 participating sites has been set up which has collected 38 cases with a mean follow up of 11.5 months, to April 2006. www.stepoperation.org
- The bowel lengthening achieved in each patient is likely to be directly related to the number of stapled incisions made, and the intended lengthening may not have been the same across all studies.

References

- 1 Sudan D, DiBaise J, Torres C et al. (2005) A multidisciplinary approach to the treatment of intestinal failure. *Journal of Gastrointestinal Surgery* 9: 165–76.
- 2 Javid PJ, Kim HB, Duggan CP et al. (2005) Serial transverse enteroplasty is associated with successful short-term outcomes in infants with short bowel syndrome. *Journal of Pediatric Surgery* 40: 1019–23.
- 3 Modi BP, Langer M, Duggan C et al. (2006) Serial transverse enteroplasty for management of refractory D-lactic acidosis in short-bowel syndrome. *Journal of Pediatric Gastroenterology & Nutrition* 43: 395–7.
- 4 Wales PW, de Silva N, Kim JH et al. (2005) Neonatal short bowel syndrome: a cohort study. *Journal of Pediatric Surgery* 40: 755–62.
- 5 Duggan C, Piper H, Javid PJ et al. (2006) Growth and nutritional status in infants with short-bowel syndrome after the serial transverse enteroplasty procedure. *Clinical Gastroenterology & Hepatology* 4: 1237–41.
- 6 Modi BP, Javid PJ, Jaksic T et al. (2007) First report of the International Serial Transverse Enteroplasty Data Registry: Indications, Efficacy, and Complications. *Journal of the American College of Surgeons* 204: 365–371

Appendix A: Additional papers on serial transverse enteroplasty procedure (STEP) for bowel lengthening in parenteral nutrition-dependent children not included in summary Table 2

The following table outlines the studies that are considered potentially relevant to the overview but were not included in the main data extraction table (Table 2). It is by no means an exhaustive list of potentially relevant studies.

Article title	Number of patients/ follow-up	Direction of conclusions	Reasons for non- inclusion in Table 2
No additional relevant clinical studies were found			

Appendix B: Related published NICE guidance for serial transverse enteroplasty procedure (STEP) for bowel lengthening in parenteral nutrition-dependent children

Guidance programme	Recommendation
Interventional procedures	None applicable
Technology appraisals	None applicable
Clinical guidelines	None applicable
Public health	None applicable

Appendix C: Literature search for serial transverse enteroplasty procedure (STEP) for bowel lengthening in parenteral nutrition-dependent children

IP: 385 Serial transverse enteroplasty		
Database	Date searched	Version searched
Cochrane Library	17/01/07	2006, Issue 4
CRD databases (DARE & HTA)	17/01/07	2006, Issue 4
Embase	17/01/07	1980 to 2007 Week 02
Medline	17/01/07	1950 to January Week 2 2007
Premedline	17/01/07	January 17, 2007
CINAHL	17/01/07	1982 to December Week 2 2006
British Library Inside Conferences	18/01/07	-
NRR	18/01/07	2006 Issue 4
Controlled Trials Registry	17/01/07	-

The following search strategy was used to identify papers in Medline. A similar strategy was used to identify papers in other databases.

1	(serial adj3 transverse\$ adj3 enteroplast\$).tw.	12
2	((bowel or intestin\$) adj3 (length\$ or elongat\$ or taper\$)).tw.	1204
3	Surgical Stapling/	1400
4	(bowel\$ adj3 stapl\$).tw.	56
5	or/1-4	2642
6	Short Bowel Syndrome/	1621
7	(short\$ adj3 (bowel\$ or gut\$) adj3 syndrome\$).tw.	1718
8	sbs.tw.	733

9	or/6-8	2782
10	parenteral nutrition/	11102
11	(parenter\$ adj3 nutrition\$).tw.	11948
12	tpn.tw.	3140
13	(intravenous\$ adj3 (feed\$ or nutrition\$)).tw.	1211
14	or/10-13	19365
15	Enterocolitis/	1028
16	Typhlitis/	1
17	enterocolitis.tw.	5050
18	coloenteritis.tw.	1
19	(ileocecal adj3 syndrome\$).tw.	18
20	typhlitis.tw.	229
21	or/15-20	5631
22	Intestinal Atresia/	1490
23	(intestin\$ adj3 atresia).tw.	464
24	(small adj3 bowel adj3 atresia).tw.	89
25	(jejunal adj3 atresia).tw.	182
26	atretic.tw.	1610
27	or/22-26	3321
28	9 or 14 or 21 or 27	29758
29	5 and 28	333
30	infant/	486088
31	exp child/	1157620
32	adolescent/	1150199
33	(infant\$ or child\$ or youth or young or youngster or minor\$ or kid\$ or adolescen\$ or teenager\$).tw.	1299585
34	or/30-33	2499137
35	29 and 34	176
36	animals/	3957966
37	humans/	9496627
38	36 not (36 and 37)	3010245
39	35 not 38	167