SUPPLEMENTAL MATERIAL TO

Functional gastrointestinal disorders and related signs and symptoms in infants: discrepancies between actual and estimated costs of recommended treatments in England

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This document presents the results of the systematic review.

Abbreviations

AACP	Acupuncture Association of Chartered Physiotherapists
ALSPAC	Avon Longitudinal Study of Parents and Children
AWMA	Academy of Western Medical Acupuncture
BMAS	British Medical Acupuncture Society
BMJ	British Medical Journal
CAM	Complementary and Alternative Medicine
CEA	Cost Effectiveness Analysis
CMP	Cows' Milk Protein
COI	Cost of Illness
COL	Cost of living
CRD	Centre for Reviews and Dissemination
DARE	Database of Abstracts of Reviews of Effects
EED	Economic Evaluation Database
ESPGHAN	European Society for Pediatric Gastroenterology, Hepatology, and Nutrition
FGID	Functional Gastrointestinal Disorder
GER	Gastro-esophageal Reflux
GERD	Gastro-esophageal Reflux Disease
GOR	Gastroesophageal Reflux
GORD	Gastroesophageal Reflux Disease
GSRS	Gastrointestinal Rating Scale
HSCIC	Health and Social Care Information Centre
HTA	Health Technology Assessment
IBS	Irritable Bowel Syndrome
ISPOR	International Society for Pharmacoeconomics and Outcomes Research
JAMA	Journal of the American Medical Association
NASPGHAN	North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition
NHS	National Health Service
NICE	National Institute for Health and Care Excellence
OTC	Over the Counter
PLOS	Public Library of Science
PPI	Proton Pump Inhibitor
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
RCT	Randomised Controlled Trial
REPEC	Research Papers in Economics
REST	Reassurance, Empathy, Support, Time out
USA	United States of America
YHEC	York Health Economics Consortium

Section 1: Results of the Systematic Review

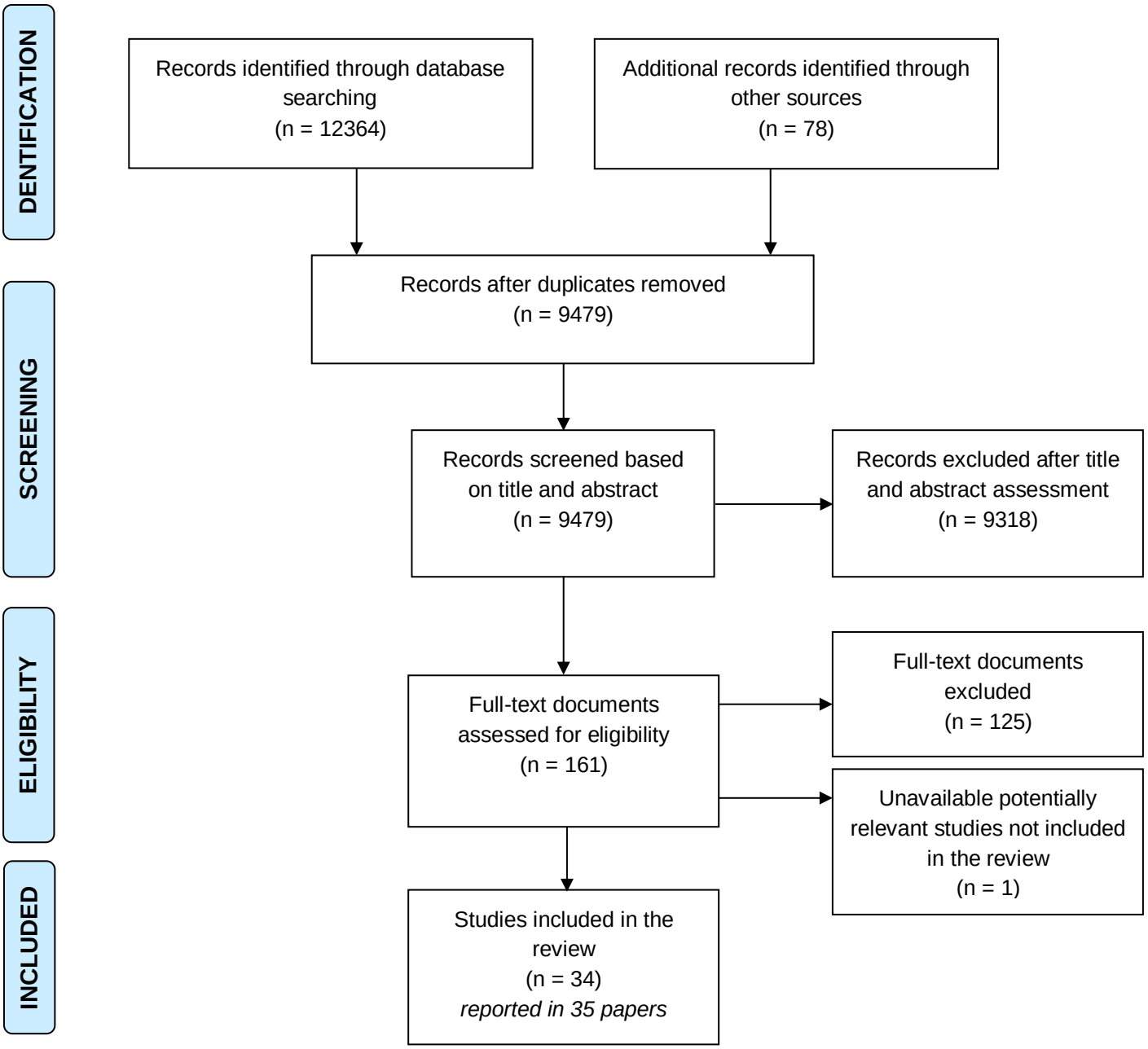
1.1 LITERATURE SEARCH RESULTS

The searches identified 12,442 records (Table 1.1). Following deduplication 9,479 records were assessed for relevance.

Table 1.1: Literature search results by resource

Resource or study identification method	Number of records identified
MEDLINE and MEDLINE In-Process	2793
PubMed (for non-MEDLINE records only)	1395
Embase	6500
PsycINFO	746
NEXIS	528
Database of Abstracts of Reviews of Effects (DARE)	109
Health Technology Assessment Database (HTA Database)	11
NHS Economic Evaluations Database (NHS EED)	25
CEA Registry	0
NHS Evidence Search	16
OAISTER	240
RePEc	1
Conference hand-searches	24
Contacting conference abstract authors	8
Checking reference lists	45
Other	1
Total number of records	**12,442**
Total number of records following deduplication	**9,479**

Figure 1.1: Record selection process (PRISMA)



1.2 STUDY CHARACTERISTICS

34 studies (reported in 35 documents) were identified reporting treatments for FGIDs and as well as related signs and symptoms, in infants younger than one year of age. One study was reported in two documents [1, 2]. Full details of the study characteristics of the included studies are reported in Table 1.2.

1.2.1 Study design

26 of the 34 studies (77%) were RCTs [2-27], including two crossover trials [4, 7] and a quasi-randomised trial [19]. Three of the studies [28-30] were cost of illness studies, although only of specific aspects of interventions for infant FGID. The remaining five studies were cohort, case series and cross sectional studies [31-35].

1.2.2 Study location

Almost half (15/34) [2, 7, 8, 11-13, 19, 21-25, 27, 33, 34] of the included studies were conducted in Europe, including three in the UK [8, 13, 34]. Seven studies were conducted in the USA [6, 10, 15, 20, 28-30] ; three in Australia [14, 16, 26]; three in Turkey [3, 5, 32]; and one each in China [17], Brazil [4] , Israel [31], Canada [9], Iran [18] and Nigeria [35].

1.2.3 Perspective

Of the 34 included studies, the majority assessed data from a patient/parent and healthcare perspective (32/34, 94%). Two studies assessed data from only the patient/parent perspective [19, 32].

1.2.4 Study objectives

Study objectives varied across the 34 included studies, but the majority sought to evaluate an intervention in infants with colic or functional constipation.

Table 1.2: Systematic review: Study characteristics

Study reference	Country	Study design	Perspective	Primary study objectives	Study duration	Inclusion criteria
Akcam 2006 [3]	Turkey	RCT	Patient and healthcare provider	To study efficacy of 30% glucose solution in the treatment of infant colic	Mar – Dec 2003	"Typical infant colic" – minimum of 3h crying per day, 3 days per week for the last 3 weeks
Alves 2012 [4]	Brazil	RCT	Patient and healthcare provider	To compare the efficacy of Mentha piperita with simethicone in the treatment of infant colic	Mar – Dec 2011	Infants aged 15 to 60 days, exclusively breastfeeding. IC was characterised as paroxysmal attacks or irritability, restlessness, or crying for at least 3 hours a day, and occurring more than 3 days a week for a period of 3 weeks
Arikan 2008 [5]	Turkey	RCT	Patient and healthcare provider	To evaluate the effectiveness of massage, sucrose solution, herbal tea or hydrolysed formula, each used individually in the treatment of infantile colic	Jan – Jun 2005	Infant between 4–12 weeks of age with typical infantile colic as defined by Wessel et al.; born at term or preterm (gestational age 37–42 weeks) with a birth weight between 2.5 and 4 kg; appropriate gain in weight, length and head circumference and normal psychomotor development on paediatric physical examination
Aviner 2010 [31]	Israel	Case series	Patient and healthcare provider	To report on 11 infants who presented with an apparent life-threatening event after ingestion of Gali-col Baby, a homeopathic agent indicated for "infantile colic"	Jan 2005 – Aug 2008	A computerised search was conducted for admissions with 1 of the following diagnoses: apparent life-threatening event, apnea, choking, cyanotic spell or episode, and sudden infant death syndrome (of these 11 patients were found to have taken Gali-col)
Berseth 2009 [6]	USA	RCT	Patient and healthcare provider	To examine the effects of a partially hydrolysed cow's milk protein, low lactose formula or a soy-based lactose-free formula on infant fussiness (defined as general irritability, discontentment, or discomfort that is difficult to soothe) and other symptoms of formula intolerance (crying, gas, occurrences of spit-up, diarrhoea, constipation, and	NR	Singleton births, 7-63 days of age, with a minimum birth weight of 2500 g, solely received a full-lactose, intact cow's milk protein formula for 7 days before randomisation, and were parent-identified as very fussy or extremely fussy in the baseline tolerance evaluation

Study reference	Country	Study design	Perspective	Primary study objectives	Study duration	Inclusion criteria
				stool patterns) in term infants parent identified as very or extremely fussy		
Bongers 2007 [7]	The Netherlands	RCT	Patient and healthcare provider	To examine the effects of a new infant formula in constipated infants	Apr 2002 – Jan 2004	Otherwise healthy, term infants with constipation, between 3 – 20 weeks of age, who received at least 2 bottles of milk-based formula per day
Browning 2008 [8]	UK	RCT	Patient and healthcare provider	To compare the short-term effects of chiropractic spinal manipulation and occipito-sacral decompression in the treatment of infant colic	NR	Less than 8 weeks of age, born with birth weight equal to or more than 2500 g, born at or after 38 weeks gestation, cry for 3 h or more per day with one or more inconsolable crying episodes for at least four of the previous 7 days and show typical restless behaviour (i.e. motor unrest, flexing knees against abdomen, extending the trunk, neck, and extremities). The parent/guardian had to be fluent and literate in the English language.
Chau 2015 [9]	Canada	RCT	Patient and healthcare provider	To investigate the effectiveness of Lactobacillus reuteri DSM 17938 for the treatment of infantile colic in breastfed infants, compared with placebo	Feb 2012 – Apr 2014	Diagnosis of infantile colic (i.e, crying or fussy/gassy episodes ≥3 hours/day for ≥3 days/7 days, as defined by a modified definition of Wessel criteria); age 3 weeks to 6 months; exclusively breastfed; term delivery (≥37 weeks gestation at birth); 5-minute Apgar score ≥7; and birth weight ≥2500 g
Ciftci 2007 [32]	Turkey	Cross sectional	Parents	To assess the methods used by mothers to eliminate colic in their infants and to determine the efficacy of the various methods	Jan –Feb 2005	Infants aged 1–3 months registered at a primary health centre
Cirgin 2006 [10]	USA	RCT	Patient and healthcare provider	To examine the effect of using Dr. Brown's Natural Flow baby bottles to feed the colicky infant on the mean time per day the infant spent crying, fussing, and sleeping	NR	7 months old or less and receiving the majority of their feedings by bottle
Coccorullo	Italy	RCT	Patient and	To evaluate the beneficial	Jan – Dec	Formula-fed infants >6 months of age referred

Study reference	Country	Study design	Perspective	Primary study objectives	Study duration	Inclusion criteria
2010 [11]			healthcare provider	effects of Lactobacillus reuteri (DSM 17938) in infants with functional chronic constipation	2008	for functional chronic constipation to the Gastrointestinal Endoscopy and Motility Unit of the Department of Pediatrics, University ‘‘Federico II’’ of Naples
Dupont 2010 [12]	France	RCT	Patient and healthcare provider	To evaluate the nutritional adequacy, the gastrointestinal tolerance and the effect on colic of an α-lactalbumin-enriched and probiotic-supplemented infant formulae, in infants with colic	NR	Infants had to be born at term, aged 3 weeks to 3 months, weaned, with normal growth and with more than 3 weeks of crying periods, at least 3 h per day, 3 days per week (Wessel et al., 1954 [36]), with or without abdominal distension, gas and regurgitation
Hayden 2006 [13]	UK	RCT	Patient and healthcare provider	To investigate the effect of cranial osteopathic manipulative treatment on the pattern of increased crying, irritability and disturbed sleep associated with infantile colic	NR	Infants between 1 and 12 weeks of age, not been previously treated osteopathically, exhibited signs of infantile colic and no signs or symptoms indicative of other disease
Hill 2005 [14]	Australia	RCT	Patient and healthcare provider	To evaluate the effect of a hypoallergenic maternal elimination diet on persistent crying among breastfed infants presenting with colic	2000 – 2002	Exclusively breastfed infants <6 weeks of age with colic; well, term infants (gestational age of 37 weeks) who were the result of a normal singleton pregnancy
Infante Pina 2008 [33]	Spain	Cross sectional	Patient and healthcare provider	To assess the effectiveness of dietetic treatment with the Novalac range of formulas specifically developed for mild gastrointestinal disorders.	NR	Infants up to four months of age fed with artificial milk formulas; the presence of mild gastrointestinal disorders; the possibility of feeding the infants with some product of the Novalac line of formulas; continuation of these formulas on an exclusive basis for at least 30 days.
Keefe 2006 [15]	USA	RCT	Patient and healthcare provider	To evaluate an individualized intervention program for infant irritability or colic	NR	Full term, healthy low-risk infants between the ages of 2 and 6 weeks, and living within a 2-hour radius of the metropolitan area.
Kianifar 2014 [16]	Australia	RCT	Patient and healthcare provider	To determine efficacy of synbiotic in reducing average infant crying time at day 7 and day 30 after starting	NR	Healthy breastfed infants aged 2 weeks to 4 months with infant colic defined as per Wessel’s criteria based on care giver’s symptom records diary.

Study reference	Country	Study design	Perspective	Primary study objectives	Study duration	Inclusion criteria
				intervention		
Landgren 2010 [2]	Sweden	RCT	Patient and healthcare provider	To investigate whether acupuncture reduces the duration of crying in infants with colic	Nov 2005 – Feb 2007	Healthy infants, born after gestational week 36, not treated with dicyclomine and fulfilling the modified Wessel criteria for colic: 'crying/fussing for at least 3 hrs a day, occurring 3 days or more in the same week'
Mi 2015 [17]	China	RCT	Patient and healthcare provider	To explore the role which L. reuteri could play in the management of infant colic	Feb 2013 – Apr 2014	Infants less than 4 months of age weighing between 2.5 and 4kg and exclusively or predominantly breastfed
Miller 2012 [34]	UK	Cohort	Patient and healthcare provider	To determine any possible justification of the use of three priori clinically determined categories of excessively crying infants, based on differences in parent reported outcomes after a course of chiropractic treatment	Jul 2007 – Mar 2008	All babies between the ages of one day and 18 weeks who presented with excessive crying to a UK chiropractic teaching clinic between July 2007 and March 2008 Infants included if they could be categorised using clinical signs and symptoms into one of the three classification groups; infant colic, irritable Infant syndrome of musculoskeletal origin or inefficient feeding crying infant with disordered sleep.
Moravej 2010 [18]	Iran	RCT	Patient and healthcare provider	To investigate the value of skin prick testing (SPT) in the diagnosis of cow's milk allergy in patients with infantile colic	NR	Breast-fed infants with history of infantile colic (diagnosed based on the Wessel criteria) between the ages of 3 weeks and 3 months
Oshikoya 2009 [35]	Nigeria	Cross sectional	Patient and healthcare provider	To determine the knowledge of Nigerian mothers about colic, their home-based management, extent of self-medication for the infants with colic and the types of medicines involved	Apr – Sep 2006	Mothers who brought their infants for vaccination to a primary health care centre
Park (2015)	USA	COI (retrospective database analysis)	Healthcare provider	To analyze the inpatient burden of common childhood FGIDs including constipation, abdominal pain, IBS, dyspepsia, abdominal	1997-2009	All infants in whom constipation, abdominal pain, dyspepsia, IBS, abdominal migraine, fecal incontinence was the primary discharge diagnosis from 1997, 2000, 2003, 2006 and 2009

Study reference	Country	Study design	Perspective	Primary study objectives	Study duration	Inclusion criteria
				migraine, and fecal incontinence		
Reinthal 2008 [19]	Sweden	RCT	Patient	To evaluated the effects of light needling on crying and the pain related behaviour in children with infantile colic	NR	New born, breastfed children with infantile colic (as described by Wessel et all, 1954 [36]) diagnosed by doctors and registered at one of 21 Child Welfare Clinics within an area of western Sweden.
Salisbury 2012 [20]	USA	RCT	Patient and healthcare provider	To examine the effectiveness of a unique model of integrated care for the treatment of infant colic.	NR	Participants were largely self-referred after seeing brochures in the office of their healthcare provider or were referred from a Specialty Clinic. Infants were required to be: singleton, born at or after 37 weeks gestational age, aged 4 to 8 weeks of age at the time of enrolment, had no more than 4 days of special nursery care after birth, no congenital anomalies, no exposure to illegal drugs in utero, and no suspicion of foetal alcohol syndRome. The family needed to be English-speaking and have a working telephone in the home. Mothers were over 17 years old and had no history of psychiatric hospitalization or involvement with Child Protective Services. The infant needed to be otherwise healthy, and meet the "Wessel Rule of 3s" criteria by parent report at the time of the call: crying for at least 3 hr a day for at least 3 days a week for at least 3 weeks.
Savino 2015 [21]	Italy	RCT	Patient and healthcare provider	To evaluate the efficacy of orally administered L. reuteri DSM 17938 with vitamin D3 from the age of ten days in reducing parental discomfort due to infantile colic in a population of otherwise healthy infants.	2012 - 2013	New borns aged less than 10 days of life, with gestational age between 37 and 42 weeks, birth weight from 2,500 to 4,300 g, and normal physical examination
Savino	Italy	RCT	Patient and	To test the efficacy of	2008 - 2009	Breast fed infants diagnosed with infantile colic

Study reference	Country	Study design	Perspective	Primary study objectives	Study duration	Inclusion criteria
2010 [22]			healthcare provider	Lactobacillus reuteri on infantile colic and to evaluate its relationship to the gut microbiota		according to the following modified Wessel's criteria: episodes of fussy crying that lasted 3 hours a day and episodes that lasted for 3 days in the 1 week before enrolment. All were born at term, adequate for gestational age (birth weight: 2500 – 4000 g), and aged 2 to 16 weeks at recruitment. Only exclusively breastfed infants were enrolled to prevent variability in the intestinal microbiota caused by diet.
Savino 2006 [23]	Italy	RCT	Patient and healthcare provider	To confirm the role of new formula in colicky infants with a randomized prospective controlled trial.	2002 - 2003	Gestational age between 37 and 42 weeks, normal birth weight (>2500 g), regular weight gain (>=150 g/week) and normal physical examination
Savino 2007 [24]	Italy	RCT	Patient and healthcare provider	To test the hypothesis that oral administration of Lactobacillus reuteri in a prospective randomized study would improve symptoms of infantile colic.	2004 - 2005	Breastfed infants with a diagnosis of infantile colic Patients 21 to 90 days of age, appropriate for gestational age with birth weights between 2500 and 4000 g, with colic symptoms (3 hours of crying on 3 days in the week) with debut 6 +/-1 days before enrolment
Sethi (2014)	USA	COI (retrospective database analysis)	Heatlhcare provider	To evaluate patient admission rates, length of stay and costs for constipation in the USA	1997-2010	Any admission with ICD-9-CM primary diagnostic codes 564.0-564.9
Skjeie 2013 [25]	Norway	RCT	Patient and healthcare provider	To test the hypothesis that acupuncture treatment has a clinically relevant effect for infant colic	2009 - 2012	Fulfilled Wessel's criteria [36] and were born at full term.
Sommers (2015)	USA	COI (retrospective database analysis)	Heatlhcare provider	To evaluate ED visits and costs for constipation in the USA	2006-2011	Any admission with ICD-9-CM primary diagnostic codes 564.0-564.9
Sung 2014 [26]	Australia	RCT	Patient and healthcare provider	To determine whether the probiotic Lactobacillus reuteri DSM 17938 reduces crying or fussing in a broad community	2011 - 2012	Healthy term infants less than 13 weeks of age with infant colic, defined by modified Wessel's criteria of crying or fussing for three hours or more a day for three days or more over seven

Study reference	Country	Study design	Perspective	Primary study objectives	Study duration	Inclusion criteria
				based sample of breastfed infants and formula fed infants with colic aged less than 3 months		days. Fussing was defined as “behaviour that is not quite crying but not awake and content either.”
Szajewska 2013 [27]	Poland	RCT	Patient and healthcare provider	To determine whether administration of Lactobacillus reuteri (L reuteri) DSM 17938 is beneficial in breastfed infants with infantile colic	2010 - 2011	Full term infants aged <5 months with infantile colic (defined as crying episodes lasting 3 or more hours per day and occurring at least 3 days per week within 7 days prior to enrolment), who were exclusively or predominantly (>50%) breastfed.
Key: ED – Emergency department; RCT: Randomised controlled trial; USA: United States of America; CMP: Cows’ Milk Protein; COI: Cost of illness						

1.3 PARTICIPANTS' CHARACTERISTICS

1.3.1 Number of trial participants

Of the 26 RCTs [2-27], nine [3, 4, 7, 8, 10, 11, 13, 17, 19] included fewer than 50 participants; ten trials [2, 9, 12, 16, 18, 20, 22, 24, 25, 27] included between 50 and 100 participants and seven trials [5, 6, 14, 15, 26, 32, 34] included between 101 and 200 participants.

Of the five case series studies, study numbers ranged from 11 [31] to 1441 [33]. Two case series studies included between 150 and 190 patients [32, 34] and another included 800 patients [35].

1.3.2 Age

All included studies were required to investigate treatments, signs and symptoms in infants less than 12 months old. The youngest participant was one day old, and the eldest was 12 months old. One COI study included patients aged over 12 months but data for patients under 12 months of age could be isolated in the analysis [30].

1.3.3 Sex

Among the studies that reported the number of males overall, the percentage of males ranged from 36% [31] to 79% [13] with an average percentage of males of 53%.

Among the studies that reported the number of males for treatment and control groups separately, treatment groups ranged from 44% [26] to 65% [19, 27] males, while control groups had from 48% [20, 21, 23] to 59% [26] males.

Four studies did not report the number of males [4, 12, 16, 18].

1.3.4 FGID description

The majority of studies (27/34, 80%) included participants with infantile colic. Four studies included participants with constipation [7, 11, 28, 29], one had participants with a range of FGIDs including constipation and dyspepsia [30] and one trial described participants as having mild gastrointestinal disorders including colic, regurgitation, diarrhoea and constipation [33].

1.3.5 ROME criteria met

Seventeen of the 34 included studies met the ROME III criteria (17/34, 50%) [4, 7-9, 11, 12, 14, 20, 22-26, 28-30], seventeen studies did not explicitly meet the ROME III criteria.[2, 3, 5, 6, 10, 13, 15-18, 21, 31, 33-35].

Full details of the participants' characteristics are reported in Table 2.3..

Table 1.3: Systematic review: Participants' characteristics

Study ID	Number of participants	Age		Sex	FGID description	ROME III criteria
		Min age	Max age	% = Male		
Akcam 2006 [3]	25 Randomised 28 Analysed (16 Treatment, 12 Control)	NR	NR	Overall: 48%	Infantile Colic	No
Alves 2012 [4]	30	8 days	56 days	NR	Infantile Colic	Yes
Arikan 2008 [5]	175 (35 x 4 treatment groups, 35 control)	4 weeks	12 weeks	Overall: 55%	Infantile Colic	No
Aviner 2010 [31]	11 Treatment, 11 matched controls	14 days	49 days	Overall: 36%	Infantile Colic	No
Berseth 2009 [6]	159 (82 Treatment A, 77 Treatment B)	7 days	63 days	Overall: 48%	Infantile Colic	No
Bongers 2007 [7]	38 (20 Treatment, 18 Control)	0.7 months	5 months	Overall: 50%	Constipation	Yes
Browning 2008 [8]	43 (22 Treatment A, 21 Treatment B)	NR	8 weeks	Overall: 63%	Infantile Colic	Yes
Chau 2015 [9]	52 (24 Treatment, 28 Control)	31 days	51 days	Overall: 48%	Infantile Colic	Yes
Ciftci 2007 [32]	186	1 month	3 months	Overall: 52%	Infantile Colic	Unclear
Cirgin 2006 [10]	36	NR	7 months	Overall: 48%	Infantile Colic	No
Coccorullo 2010 [11]	44 (22 Treatment, 22 Control)	6 months	NR	Overall: 55%	Constipation	Yes
Dupont 2010 [12]	66 Randomised, 47 Analysed (23 Treatment, 24 Control)	3 weeks	3 months	NR	Infantile Colic	Yes

Study ID	Number of participants	Age		Sex	FGID description	ROME III
Hayden 2006 [13]	28 Randomised, 26 Analysed (14 Treatment, 12 Control)	10 days	83 days	Overall: 79%	Infantile Colic	No
Hill 2005 [14]	107 Randomised, 90 Analysed (47 Treatment, 43 Control)	2.9 weeks	8.6 weeks	Overall: 60%	Infantile Colic	Yes
Infante Pina 2008 [33]	1441	1 week	4 months	Overall: 52%	Mild-gastrointestinal disorders including colic, regurgitation, diarrhoea and constipation	No
Keefe 2006 [15]	121	2.6 weeks	7.7 weeks	Overall: 50%	Infant irritability; Colic	No
Kianifar 2014 [16]	50 (26 Treatment, 24 Control)	2 weeks	4 months	NR	Infantile Colic	No
Landgren 2010 [2]	90 Randomised (46 Treatment, 44 Control) 81 Analysed (43 Treatment, 38 Control)	2 weeks	8 weeks	Overall: 52%	Infantile Colic	No
Mi 2015 [17]	42 Randomized (21 Treatment 21 Placebo); 39 Analysed (20 Treatment, 19 Placebo)	Mean: 29.7 days	4 months	Overall: 56%	Infantile Colic	No
Miller 2012 [34]	158 (Colic = 77; Infant syndrome of musculoskeletal origin = 56; inefficient feeding crying infant with disordered sleep	1 day	18 weeks	Overall: 57%	Infant colic, irritable Infant syndrome of musculoskeletal origin or inefficient feeding crying infant with disordered sleep	No

Study ID	Number of participants	Age		Sex	FGID description	ROME III
	= 25)					
Moravej 2010 [18]	77 (35 Treatment, 42 controls)	3 weeks	3 months	NR	Infantile Colic	No
Oshikoya 2009 [35]	800	Mothers: 15 years old Infants: 1 day	Mothers: 40 years old Infants: 12 months	Overall: 52%	Infantile Colic	No
Park (2015) [30]	4,436,817 discharges in 1997; 4,600,709 discharges in 2009	0 to 12 months		51% (all ages)	Functional GI disorders: chronic constipation, abdominal pain, irritable bowel syndrome, dyspepsia, abdominal migraine, fecal incontinence	Yes
Reinthal 2008 [19]	40 (20 Treatment, 20 Control)	Treatment: 1 week Control: 3 weeks	Treatment: 11 weeks Control: 25 weeks	Treatment: 65% Control: 55%	Infantile Colic	No
Salisbury 2012 [20]	62 (31 Treatment, 31 Control)	4.1 weeks	10.5 weeks	Treatment: 57% Control: 48%	Infantile Colic	Yes
Savino 2015 [21]	105 (51 Treatment, 54 Control)	NR	Overall: <10 days	Treatment: 49% Control: 48%	Infantile Colic	No
Savino 2010 [22]	50 (25 Treatment, 25 Control)	NR: median treatment: 32.5 days (21) Control: 28.5 days (21)	NR	Treatment: 60% Control: 56%	Infantile Colic	Yes

Study ID	Number of participants	Age		Sex	FGID description	ROME III
Savino 2006 [23]	267 Randomised, 199 Analysed (96 Treatment, 103 Control)	Treatment: mean 1.39 months (±0.84) Control: mean 1.29 months (±0.77)	NR	Treatment: 52% Control: 48%	Infantile Colic	Yes
Savino 2007 [24]	90 Randomised 83 Analysed (41 Treatment, 42 Control)	Treatment: 11 days Control: 14 days	Treatment: 80 days Control 74 days	Treatment: 56% Control: 50%	Infantile Colic	Yes
Sethi 2014 [29]	20% of admitted population in 12 months	0-12 months		38% 1997 39% 2010	Constipation (ICD-9-CM codes 564.0-564.9)	Yes
Skjeie 2013 [25]	84 (44 Treatment, 40 Control)	Treatment: 3 weeks Control: 3 weeks	Treatment: 13 weeks Control: 9 weeks	Treatment: 50% Control: 50%	Infantile Colic	Yes
Sommers 2015 [28]	20% of all ED visits in 12 months	0-12 months		NR	Constipation (ICD-9-CM codes 564.0-564.9)	Yes
Sung 2014 [26]	167 Randomised (85 Treatment, 82 Control); 127 Analysed	Treatment: mean 7.5 weeks (±2.9) Control: mean 6.9 weeks (±2.5)	NR	Treatment: 44% Control: 59%	Infantile Colic	Yes
Szajewska 2013 [27]	80 (40 Treatment, 40 Control)	Treatment: 16 days Control: 17 days	Treatment: 81 days Control: 69 days	Treatment: 65% Control: 55%	Infantile Colic	Yes
Key: NR: Not reported						

1.4 INTERVENTIONS AND COMPARATORS

1.4.1 Intervention

Several different interventions were investigated across the 31 included studies that considered interventions.

- Ten studies investigated the impact of probiotic supplementation [9, 11, 12, 16, 17, 21, 22, 24, 26, 27];
- Four studies used particular types of infant formula [6, 7, 23, 33];
- Three studies used multiple types of interventions (alone or in combination) [5, 32, 35];
- Three studies used acupuncture [2, 19, 25];
- Three studies used chiropractic treatment [8, 13, 34];
- Two studies changed the maternal diet [14, 18];
- Two studies used natural remedies [4, 10];
- One study used glucose [3];
- Two studies used parental counselling [20];
- One study used a homeopathic remedy [31].

1.4.2 Adverse events from an intervention

The majority of intervention studies reported that there were no side effects (15/31) from the intervention under investigation, or did not report whether patients experienced any side effects (12/31).

Four studies reported side effects associated with interventions. One study investigated adverse events in infants receiving Gali-col Baby, a homeopathic remedy, and showed that 9 of the 11 participants had at least two adverse event symptoms [31].

Three studies investigating formulas reported side effects; in one study a soy based formula was associated with adverse events in 50% of participants [6] while a second study investigated a range of formulas belonging to the Novalac line (Anti-Colic, Anti-Regurgitation, Anti-Diarrhoea, Anti-Constipation) and reported that 3.9% of infants suffered an adverse event, most frequently affecting the digestive tract (1.4%), including diarrhoea and constipation.[33] In a third study, a probiotic enriched formula reportedly caused gastrointestinal side effects in 44% of infants and 15% experienced feeding-related side effects.[12]

1.4.3 Comparator

Of the 26 RCTs with comparator groups, nine trials compared their interventions with placebo [3, 9-11, 16, 17, 22, 25, 27]; eight compared interventions to standard care [2, 7, 12, 14, 15, 18-20]; seven compared their interventions to an alternative intervention [4, 6, 8, 21, 23, 24, 26] and two used no comparator intervention [5, 13].

1.4.4 Adverse events from the comparator treatment

Three studies reported side effects associated with comparator treatments.[6, 12, 22] One study investigated adverse events in 77 infants randomised to a comparator group who received a partially hydrolysed cow's milk protein, low lactose formula. 44 participants (58%) had at least one adverse event [6].

A second study investigated adverse events in 24 infants randomised to a comparator group who received a control formula (not enriched with probiotics as per the intervention) and found that 67% of the comparator group experienced GI side effects including constipation, vomiting, colitis, regurgitation and flatulence [12].

A third study investigated adverse events in 25 infants randomised to a placebo comparator group. Compared to the one infant in the probiotic intervention group who developed rhinitis, four infants in the placebo group experienced an adverse event including eczema, fever, otalgy and gastroesophageal reflux [22].

1.4.5 Length of treatment

The length of treatment varied across the included studies, but overall ranged from one to four weeks.

Full details of the interventions and comparators of the included studies are reported in Table 1.4.

1.4.6 Cost of illness studies

Two of the cost of illness studies reported on hospital care for infants with functional constipation [28, 29] in the United States based upon retrospective analysis of a database covering 20% of all admissions and ED attendances. One study [28] reported 50,934 ED attendances for infants with constipation at a cost of $2470 per attendance – although the cost was based upon all attendances for adults and children. The second study [29] reported 499 hospital admissions for infants with constipation in 2010 at a cost of $17,518 per admission but again this cost was for children and adults.

The third cost of illness study [30] also reported an analysis of a large databse of hospital admissions, but for a range of FGIDs including constipation and abdominal pain. The rate of discharge for infants aged under 12 months was 0.8 per 10,000 discharges for constipation, 1.0 per 10,000 discharges for abdominal pain and 0.1 per 10,000 discharges for dyspepsia. Costs per discharge were provided but covered all patient under 18 years of age. Details of the cost of illness studies are reported in Table 1.5.

Table 1.4: Systematic review: details of interventions and comparators

Study ID	Intervention	Treatment dosing and frequency	Adverse events from treatment	Comparator(s)	Comparator dosing and frequency	Adverse events from comparator	Length of treatment
Akcam 2006 [3]	30% glucose solution	1ml drop – frequency unclear	None	Placebo - distilled water	1ml drop - unclear how often	None	NR - at least 8 days
Alves 2012 [4]	Mentha piperita	1 drop per kg body weight daily	None	Simethicone	Liquid drops - 2.5 mg per kg body weight daily	None	7 days for each treatment with a washout period of 3 days in between
Arikan 2008 [5]	1) massage, 2) sucrose solution, 3) herbal tea and 4) hydrolysed formula	1) Parents were advised to administer massage twice a day for 25 minutes duration during symptoms of colic, 2) 2 ml of 12% solution twice a day at 5 pm and 8 pm, 3) fennel tea was administered at a dose of 35 ml (maximum dose of 150 ml) three times a day, 4) hydrolysed formula (dose not reported)	NR	Control (no intervention)	NA	NR	1 week
Aviner 2010 [31]	Gali-col Baby (homeopathic remedy)	The manufacturer's recommended dose is "up to 5 drops which might be repeated once in 15 minutes or	All 11 patients had an ALTE. 9/11 (81.8%) infants who received Gali-col	NA	NA	NA	NA

Study ID	Intervention	Treatment dosing and frequency	Adverse events from treatment	Comparator(s)	Comparator dosing and frequency	Adverse events from comparator	Length of treatment
		according to the physician or pharmacist instructions." The amount of Gali-col Baby administered was recorded for 8 patients. For 3 patients, it was much greater than the manufacturer's recommended dose, 4 other infants received the drug several times a day, and 1 patient received a single recommended dose.	Baby showed at least 2 symptoms of an ALTE *(this may be misleading because only patients with an ALTE were included in this study) Six patients were hospitalised for 1 day, four were hospitalised for 2 days, and 1 was hospitalised for 3 day*				
Berseth 2009 [6]	Soy-based formula (Soy; Enfamil, ProSobee, LIPIL)	NA	41 (50%) experienced at least 1 adverse event	Partially hydrolysed cow's milk protein, low-lactose formula	NA	44 (58%) experienced at least 1 adverse event: (P = 0.34)	28 days
Bongers 2007 [7]	A new infant formula (NF; Nutrilon Omneo, Nutricia Nederland BV, Zoetermeer, the Netherlands) which contains modified vegetable oil with a high proportion (41%) of palmitic acid at the sn-2 position, a mixture of prebiotic oligosaccharides, partially hydrolysed whey protein and a reduced lactose content	NA	No serious adverse effects	Standard formula	NA	No serious adverse effects	Two - 3 week treatment periods
Browning	Spinal manipulative therapy	Treatment was given	None	Occipito-sacral	Treatment	None	2 weeks

Study ID	Intervention	Treatment dosing and frequency	Adverse events from treatment	Comparator(s)	Comparator dosing and frequency	Adverse events from comparator	Length of treatment
2008 [8]		2 -3 times per week, for 2 weeks, or less if the symptoms resolved		decompression	was given 2 - 3 times per week, for 2 weeks, or less if the symptoms resolved		
Chau 2015 [9]	Probiotic L reuteri DSM 17938 (10^8 cfu)	5 drops orally, once daily	None	Placebo - the same excipient ingredients but without the live bacteria	5 drops orally, once daily	None	21 days
Ciftci 2007 [32]	Treatments used by parents included: Taking the infant to a calm and dark room; holding the infant in their arms; rocking the infant; positioning the infant; giving a massage to the infant; warming the infant; having the infant listen to music; giving the infant fennel tea; giving the infant anise; giving the infant simethicone (metsil); taking the infant to the hospital; giving the infant a sweet drink; giving the infant lemon water; stimulating the rectum; giving the infant olive oil; Using suppositories	NA	NR	NA	NA	NR	NA
Cirgin 2006 [10]	Dr. Brown's Natural Flow baby bottle	NA	NR	Placebo baby bottle	NA	NR	14 days
Coccorullo 2010 [11]	Probiotic L reuteri (DSM 17938) (10^8 cfu)	5 drops, once daily	None	Placebo	Not explicitly stated	None	8 weeks

Study ID	Intervention	Treatment dosing and frequency	Adverse events from treatment	Comparator(s)	Comparator dosing and frequency	Adverse events from comparator	Length of treatment
Dupont 2010 [12]	α-lactalbumin-enriched and probiotic-supplemented infant formula (Lactobacillus rhamnosus, Bifidobacterium infantis)	NA	44% experienced GI-side effects; 15% experienced feeding related side effects ('feeding-related' GI side effects were: vomiting (one infant), colitis (one infant)	Control formula (not enriched in α-lactalbumin, with a higher quantity of proteins and lactose, and neither probiotics nor starch)	NA	67% experienced GI-side effects; 85% experienced feeding related side effects ('feeding related' GI side effects were: constipation (five), vomiting (four), colitis (one), regurgitations (three) and flatulence (one infant)	1 month
Hayden 2006 [13]	Cranial osteopathic manipulation	Once a week	NR	No treatment	Once a week (all infants were brought to the osteopathic clinic)	NR	4 weeks
Hill 2005 [14]	Low-allergen maternal elimination diet (mothers excluded all foods containing dairy products, soy, wheat, eggs, peanuts, tree nuts, and fish from their diet. Their diet included a rice milk drink, meats, vegetables, fruits, and cereals (corn and rice). A calcium supplement (1.2 g/day) was prescribed. Mothers were supplied with a rice-based drink in powder form (500 mL/day), as well	NA	NR	Control diet that included these foods (Mothers received 7 days of rations of a soy and cow's milk powder mixture to make 500 mL of a milk drink per day (equivalent to 200 mL of soy milk and 300 mL of cow's milk). Mothers were	NA	NR	1 week

Study ID	Intervention	Treatment dosing and frequency	Adverse events from treatment	Comparator(s)	Comparator dosing and frequency	Adverse events from comparator	Length of treatment
	as a daily supply of fresh rice bread)			asked to eat 1 serving of peanuts, 1 serving of wheat, and 1 chocolate muesli bar per day. Mothers were encouraged to maintain their usual intake of vegetables, meats, rice, and other cereals)			
Infante Pina 2008 [33]	A range of formulas belonging to the Novalac line (Anti-Colic, Anti-Regurgitation, Anti-Diarrhoea, Anti-Constipation)	NR	3.9% suffered an adverse event. Most frequent affected the digestive tract (1.4%), including diarrhoea and constipation, and respiratory (0.7%) (e.g. bronchitis, bronchiolitis). Ten infants (0.5%) required hospital admission for septicaemia (n=1), dehydration (n=2), hernia (n=1) and	NR	NR	NR	Unclear – (patients were included into the study over a period of two weeks. And "patients were visited on two occasions: at the time of inclusion and after four weeks"

Study ID	Intervention	Treatment dosing and frequency	Adverse events from treatment	Comparator(s)	Comparator dosing and frequency	Adverse events from comparator	Length of treatment
			bronchitis or bronchiolitis (n=2)				
Keefe 2006 [15]	"REST Routine for Infant Irritability" - an individualised intervention programme	4 week programme	NR	"Standard well-child care"	4 week programme	NR	4 weeks treatment over am 8 week study period
Kianifar 2014 [16]	Protexom Restore; a mixture of seven probiotic strains (Lactobacillus casei, L. rhamnosus, S. thermophiles, Bifidobacterium breve, L. acidophilus, B. infantis, L. bulgaricus) plus fructooligosacharide	Parents advised to mix treatment or placebo sachet with breast milk daily for a period of 30 days	None	Placebo - matched for size, volume, shape and manufactured by the same company	Same as treatment - daily for 30 days	None	30 days
Landgren 2010 [2]	Acupuncture	Structured programme with six visits to the clinic, including acupuncture	NR	Control group	Structured programme with six visits to the clinic, without acupuncture	NR	Six weeks
Mi 2015 [17]	L. reuteri DSM 17938	daily	None	Placebo	daily	None	28 days
Miller 2012 [34]	Chiropractic treatment	Varied	NR	NA	NA	NA	Varied
Moravej 2010 [18]	Mothers of infants in the case group were asked to avoid cow and goat milk as well as dairy products for 2 weeks and were prescribed calcium supplements, and instructed to take a calcium-rich diet.	NA	NR	No change in the mother's diet (regular diet)	NA	NR	2 weeks

Study ID	Intervention	Treatment dosing and frequency	Adverse events from treatment	Comparator(s)	Comparator dosing and frequency	Adverse events from comparator	Length of treatment
Oshikoya 2009 [35]	353 infants were treated using self-medication: Herbal medicines (183/51.8%); Nospamin (125/35.4%); Gripe water (106/30%); Bonababe (19/5.4%); Piccan (7/2%); Kidcare (4/1.1%); Teething powder (4/1.1%); Gbomoro (3/0.8%); Paracetamol (3/0.8%); Ascorbic acid (3/0.8%); Ampicillin/cloxacillin (3/0.8%) 120 (31.8%) used chiropractic intervention (e.g. massage) 133 (35.2%) used psychosocial interventions 157 mothers sought hospital-based intervention - 59.3% of infants were prescribed medicines (Nospamin: 49.5%; Gripe water: 43%; Piccan: 12.9%; Erythromycin: 10.8%; Abidec: 9.7%); 24.8% of mothers received counselling	NA	NA	NA	NA	NA	NA
Reinthal 2008 [19]	Children were breastfed prior to treatment. Light needling (minimal	Light needling session every two weeks	NR	Received same procedure by the parents and	Every two weeks	NR	2 weeks (4 treatments total)

Study ID	Intervention	Treatment dosing and frequency	Adverse events from treatment	Comparator(s)	Comparator dosing and frequency	Adverse events from comparator	Length of treatment
	acupuncture) by penetrating the skin with a 0.2mm sterile disposable needle at acupuncture site LI4, located between the thumb and forefinger, deep enough to reach the dorsal interosseous muscle, on both left and right hands. The needle was briefly rotated for a few seconds (less than 5), left in place for another period of second and then removed			caring by the investigator except for light needling			
Salisbury 2012 [20]	Therapy sessions in which a behavioural paediatrician and mental health clinician worked together to assess potential causes of infant crying and to address emotional and psychological needs of parents. Clinicians worked with patients to develop and individualised family treatment plan which families took home	Therapy at baseline, 2- and 6-week follow up	NR	Standard care from own healthcare provider	Standard care- clinic appointments at times individualised to families	NR	10 weeks
Savino 2015 [21]	L. reuteri DSM 17938 + vitamin D3	10^8 cfu + 400 UI	NR	vitamin D3	400 UI daily	NR	12 weeks
Savino 2010 [22]	A suspension of freeze-dried lactobacillus reuteri in a mixture of sunflower oil and medium-chain triglyceride oil supplied in a 5-mL dark bottle fitted with a dropper cap.	5 drops, once a day, 30 minutes before the feed in the morning	Rhinitis (n=1) (deemed unrelated to study product).	Placebo - identical in appearance and taste but without the live bacteria.	5 drops, once a day, 30 minutes before the feed in the morning	Eczema (n=1), fever (n=1), otalgy (n=1), gastroesophageal reflux (n =1).	21 days

Study ID	Intervention	Treatment dosing and frequency	Adverse events from treatment	Comparator(s)	Comparator dosing and frequency	Adverse events from comparator	Length of treatment
Savino 2006 [23]	New formula: formula contains partially hydrolysed whey proteins, a mixture of OS 0.8 g/100 ml, comprising 90% galacto-OS and 10% fructo OS low lactose level, modified vegetable oil with 41% of the palmitic acid in the b-position and starch.	The feeding volume was based on a feeding ad libitum procedure. Feeding frequency was decided by parents	NR	Standard formula + simethicone	simethicone (6 mg/kg twice a day)	NR	14 days
Savino 2007 [24]	Probiotic L reuteri (American Type Culture Collection strain 55730)	10^8 cfu in 5 drops of a commercially available oil suspension, 30 minutes after feeding, once per day	None	simethicone	60 mg/day in 15 drops twice per day of a commercially available solution, after feeding	None	28 days
Skjeie 2013 [25]	Acupuncture - The GP made a mark, 3 mm in diameter, at the point ST36 bilaterally on all children, to hide the insertion mark. In the intervention group, an ethylene-oxidised sterile Seirin acupuncture-needle (0.20 X15mm) was inserted at the acupuncture point ST36. The point was needled bilaterally to approximately 12 mm depth. The two needles were left inserted without manipulation for 30 seconds. The needles were withdrawn and the insertion area was was covered with	The same procedure was performed on days 4 and 5.	No serious adverse events	An identical procedure, except for the needle insertions	The same procedure was performed on days 4 and 5.	No serious adverse events	5 days

Study ID	Intervention	Treatment dosing and frequency	Adverse events from treatment	Comparator(s)	Comparator dosing and frequency	Adverse events from comparator	Length of treatment
	an adhesive dressing.						
Sung 2014 [26]	L reuteri DSM 17938 (0.2×10^8 cfu per drop) in an oil suspension	Five drops orally given once daily	None	Maltodextrin in the same oil suspension with the same appearance, colour and taste as the treatment, identically packaged and stored.	NR	None	One month
Szajewska 2013 [27]	L reuteri DSM 17938, administered orally, or placebo.	10^8 cfu. 5 drops, 1 time daily	None	Identical formulation in all respects except that the live probiotic bacteria were excluded	5 drops, 1 time daily	None	21 days
Key: cfu – colony forming units; NR: Not reported; NA: Not Applicable; GP: General Practitioner							

Table 1.5: Cost of illness studies: details of evidence and results

Study ID	Method of estimating COI	Components included	Evidence sources	Currency and year	Results	Limitations
Park 2015 [30]	Measurement of hospitalisations from the Kids Inpatient Sample Database (KIDS) covering 44 US states with calculation of mean cost per stay	Hospitalisations	Admissions database and hospital charges	2009 US$	The rate of discharge for those under 12 months was 0.8 per 10,000 discharges for constipation, 1.0 per 10,000 discharges for abdominal pain and 0.1 per 10,000 discharges for dyspepsia. Average cost per hospitalization for FGID increased from $6115 (1997) to $18058 (2009); Costs for patients diagnosed with abdominal pain increased (on average) from $3558 to $13331; Length of hospital stay increased from 1.7 (1997) to 2.0 (2009) days; Costs for IBS increased from $5278 (1997) to $18853 (2009); Costs for abdominal migraine increased from $4876 (1997) to $15139 (2009); Costs for dyspepsia increased from $12674 to $35898 (2009); Costs for fecal incontinence increased from $6609 to $13252 (2009); Costs for constipation increased from $3693 to $11873. The costs for all hosptializations of paediatric FGIDs increased significantly from 1997 to 2009 .	Costs are for all children under 18
Sethi 2014 [29]	Measurement of inpatient stays from national inpatient sample (NIS) database (approx 20% sample of USA inpatient stays) with calculation of mean cost per stay	Inpatient stays	Admissions database and hospital charges	2010 US$	Mean costs per stay were $17,518 in 2010 but this was for all patients (children and adults). Total admissions for children under 12 months from the NIS database was 499 in 2010	Provides only a 20% sample and costs are for children and adults.
Sommers 2014 [28]	Measurement of ED visits from Nationwide Emergency Department Sample (NEDS) database (approx 20% sample of USA ED Visits) with calculation of mean cost per visit	ED visits	ED database and hospital charges	2011 US$	Mean costs per ED visit were $2,470 in 2011 but this was for all patients (children and adults). Total ED visits in 2011 from the NEDS database was 50,934 for children under 12 months	Provides only a 20% sample and costs are for children and adults.

Key: COI – cost of ilness; ED – emergency department; FGID - Functional gastrointestinal disorders.

1.5 RISK OF BIAS ASSESSMENT

The risk of bias (quality) of the 26 included RCTs was generally unclear (Table 1.6). Five trials had a high risk of bias [13, 19-21, 24]; six trials had an unclear risk of bias [5, 6, 11, 12, 15, 18]; seven trials had a low/unclear risk of bias [2, 4, 8, 14, 16, 17, 25]; eight trials had a low risk of bias [3, 7, 9, 10, 22, 23, 26, 27].

The quality of the 5 eligible observational studies was generally poor. Further details of the quality assessment for the observational studies are reported in Table 1.7.

The quality of the cost of illness studies was generally good being based upon database analysis and providing reasonable samples of the entire population. However, the studies were focussed on just one aspect of the cost of illness and the costs applied were not specific to infants under 12 months. The risk of bias assessment of the three COI studies is reported in Table 1.8.

1.6 CONCLUSIONS

The systematic review identified a range of treatments that have been or are used for infant FGID from countries across all continents. It also identified three studies from the USA that estimated an aspect of the COI of FGID. However, the detail contained in all identified studies was insufficient to generate a unified COI calculation for a single country. In particular, there was no evidence found on the scale of use of different treatments and interventions for infant FGID and colic outside of the use of hospital care in the USA, predominantly for constipation.

The information identified in the systematic review, whilst not directly estimating a COI of infant FGID in any particular country, provides useful background in constructing a de novo calculation.

Table 1.6: Systematic review: Risk of bias assessment of RCTs

Study ID	Was the allocation sequence adequately generated?	Was allocation adequately concealed?	Was knowledge of the allocated interventions adequately prevented during the study?	Were incomplete outcome data adequately addressed?	Are reports of the study free of suggestion of selective outcome reporting?	Was the study apparently free of other problems that could put it at a high risk of bias?	Overall risk of bias
Akcam 2006 [3]	Yes	Yes	Yes	No	Unclear	Yes	Low
Alves 2012 [4]	Yes	Unclear	Yes	Yes	Unclear	Unclear	Low/Unclear
Arikan 2008 [5]	Unclear	Unclear	No	Yes	Unclear	Unclear	Unclear
Berseth 2009 [6]	Unclear	Unclear	Unclear	Yes	Unclear	Yes	Unclear
Bongers 2007 [7]	Yes	Yes	Yes	Unclear	Unclear	Unclear	Low
Browning 2008 [8]	Yes	Unclear	Yes	No	Unclear	Unclear	Low/Unclear
Chau 2015 [9]	Yes	Yes	Yes	No	Unclear	Yes	Low
Cirgin 2006 [10]	Yes	Yes	Yes	No	Unclear	Yes	Low
Coccorullo 2010 [11]	Yes	Unclear	Unclear	No	Unclear	Unclear	Unclear
Dupont 2010 [12]	Unclear	Unclear	Unclear	No	Unclear	Yes	Unclear
Hayden 2006 [13]	Yes	Unclear	No	No	Unclear	Unclear	High
Hill 2005 [14]	Yes	Unclear	Yes	Yes	Unclear	Yes	Low/Unclear
Keefe 2006 [15]	Yes	Unclear	Unclear	Yes	Unclear	Yes	Unclear
Kianifar 2014 [16]	Yes	Unclear	Yes	Yes	Yes	Yes	Low/Unclear
Landgren 2010 [2]	Yes	Unclear	Yes	Yes	Yes	Yes	Low/Unclear
Mi 2015 [17]	Yes	Unclear	Yes	Yes	Unclear	Yes	Low/Unclear
Moravej 2010 [18]	Unclear	Unclear	Yes	No	Unclear	Unclear	Unclear
Reinthal 2008 [19]	No	Unclear	Unclear	NA	Yes	Yes	High
Salisbury 2012 [20]	Unclear	Unclear	No	Unclear	Yes	No	High
Savino 2015 [21]	Yes	No	Unclear	Yes	Yes	Yes	High
Savino 2010 [22]	Yes	Yes	Yes	No	Yes	Yes	Low
Savino 2006 [23]	Yes	Yes	Yes	No	Unclear	Yes	Low
Savino 2007 [24]	Yes	No	No	No	Yes	Yes	High
Skjeie 2013 [25]	Unclear	Yes	Yes	No	Unclear	Yes	Low/Unclear
Sung 2014 [26]	Yes	Yes	Yes	No	Yes	Yes	Low
Szajewska 2013 [27]	Yes	Yes	Yes	Yes	Yes	Yes	Low

Table 1.7: Systematic review: Risk of bias assessment of observational studies

Cohort study

	Is there sufficient description of the groups and the distribution of prognostic factors?	Is the group(s) assembled at a similar point in their disease progression?	Is the intervention / treatment reliably ascertained?	Were the groups comparable on all important confounding factors?	Was there adequate adjustment for the effects of these confounding variables?	Was a dose-response relationship between intervention and outcome demonstrated?	Was outcome assessment blind to exposure status?	Was follow up long enough for the outcomes to occur?	What proportion of the cohort was followed up?	Were drop-out rates and reasons for drop-out similar across intervention and unexposed groups?
Miller 2012 [34]	Yes	No	No	No	Yes	Not Applicable	No	Not Applicable	Not Applicable	No
Overall quality: Poor Precludes any association of changes seen with treatment as all the effects observed may be a consequence of effect upon the mothers reporting rather than direct effects on the infant. Subject to sampling bias, limited to one teaching clinic.										

Case series

	Is the study based on a representative sample selected from a relevant population?	Are the criteria for inclusion explicit?	Did all individuals enter the survey at a similar point in their disease progression?	Was follow-up long enough for important events to occur?	Were outcomes assessed using objective criteria or was blinding used?	If comparisons of sub-series are being made, was there sufficient description of the series and the distribution of prognostic factors?
Aviner 2010 [31]	Yes	Yes	Yes	NA (retrospective)	Yes	NA

Cross sectional

	Representativeness of the sample	Sample size: a) Justified satisfactory. * b) Not justified	Non-respondents:	Ascertainment of the exposure (risk factor)	Comparability: The subjects in different outcome groups are comparable based on the study design or analysis. Confounding factors are controlled.	Assessment of the outcom	Statistical test of the outcome.
Ciftci 2007 [32]	Truly representative of the average in the target population	Satisfactory	No description of the characteristics of non-responders	Non-validated measurement tool, but the tool is available or described	Only one group	Self-report	Statistical analysis described
Infante Pina 2008 [33]	Non-random sample	Not justified	Only one group	No description of measurement tool	Only one group	Investigator assessed	Statistical analysis described
Oshikoya 2009 [35]	Truly representative of the average in the target population	Not justified	Only one group	No description of validation tool	Only one group	Investigator assessed	Statistical analysis described

Table 1.8: Systematic review: Quality assessment of COI studies

Study ID	Was the COI method clearly described?	Were the quality of the data used assessed and described?	Were data sources and dates clearly reported?	Were data gaps described?	Were data extrapolations reasonable?	Were reasonable methods employed to avoid double counting?	Were the calculations of cost clearly described?	Were the methods used to handle uncertainty appropriate?	Have the researchers offered assessments of the limitations of the study approach?	Was the COI method clearly described?
Park 2015[30]	Yes	No	Yes	No	NA	Unclear	Unclear	Unclear	Yes	Yes
Sethi 2014[29]	Yes	Yes	Yes	Yes - only primary diagnosis recorded	Yes	NR	Yes	No uncertainty analysis undertaken	Yes	Yes
Sommers 2015[28]	Yes	Yes	Yes	Yes - only primary diagnosis recorded	Yes	NR	Yes	No uncertainty analysis undertaken	Yes	Yes

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APPENDIX A

Search Strategies for the Systematic Review

A.1: Source: MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R) 1946 to Present.

Interface: Ovid SP
Coverage: 1946 to present. Updated daily.
Search date: 14/01/16
Retrieved records: 2793
Search strategy:

Database: Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R) <1946 to Present>
Search Strategy:
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1 "cost of illness"/ (19777)
2 (costing adj3 (illness$ or disease$ or sickness$)).ti,ab,kf. (39)
3 (burden adj3 (illness$ or disease$ or sickness$)).ti,ab,kf. (18484)
4 (burden adj3 (family or families or human$1 or mother$ or father$ or parent$ or caregiver$ or care-giver$)).ti,ab,kf. (5253)
5 ((economic or human$) adj3 consequence$1).ti,ab,kf. (4627)
6 "costs and cost analysis"/ or cost-benefit analysis/ (105504)
7 exp health care costs/ (50444)
8 (cost or costs or economic evaluation or pharmacoeconomic).ti,ab,kf. (367790)
9 (resource$1 adj4 use$1).ti,ab,kf. (20035)
10 (resource$1 adj4 usage).ti,ab,kf. (402)
11 (resource$1 adj4 utili$).ti,ab,kf. (10141)
12 (visit or visits or hospitalization$1 or hospitalisation$1 or admission$1 or admitted or emergency room or rescue).ti,ab,kf. (495389)
13 quality-adjusted life years/ or "quality of life"/ (137895)
14 (quality adjusted life or qol).ti,ab,kf. (30636)
15 (qaly$ or qald$ or qale$ or qtime$).ti,ab,kf. (6312)
16 (sf36 or sf 36 or sf thirtysix or sf thirty six).ti,ab,kf. (15336)
17 (sf6 or sf 6 or short form or shortform or sf six or sfsix).ti,ab,kf. (21906)
18 (sf12 or sf 12 or sf twelve or sftwelve).ti,ab,kf. (2821)
19 (sf16 or sf 16 or sf sixteen or sfsixteen).ti,ab,kf. (19)
20 (sf20 or sf 20 or sf twenty or sftwenty).ti,ab,kf. (310)
21 (euroqol or eq5d or eq 5d).ti,ab,kf. (5304)
22 (hql or hqol or hrqol or hrql or hr ql).ti,ab,kf. (12031)
23 (hye or hyes).ti,ab,kf. (57)
24 health$1 year$1 equivalent$1.ti,ab,kf. (40)
25 (hui or hui1 or hui2 or hui3).ti,ab,kf. (1051)
26 disutili$.ti,ab,kf. (273)
27 (quality adj3 (wellbeing or well being)).ti,ab,kf. (1606)
28 qwb.ti,ab,kf. (185)
29 (willingness adj3 pay).ti,ab,kf. (2954)
30 standard gamble$.ti,ab,kf. (712)
31 (time trade off$1 or time tradeoff$1 or tto or timetradeoff).ti,ab,kf. (1349)
32 ((valu$ or measur$) adj3 (health or outcome$1 or effect$1 or change$1 or state$1)).ti,ab,kf. (305820)

33 (preference$ adj3 (patient$1 or public or valu$ or measur$)).ti,ab,kf. (13395)
34 ((quality adj3 life) or qol).ti,ab,kf. (180949)
35 (index adj3 wellbeing).ti,ab,kf. (90)
36 (multiattribute$ health or multi attribute$ health).ti,ab,kf. (54)
37 (multiattribute$ theor$ or multi attribute$ theor$ or multiattribute$ analys$ or multi attribute$ analys$).ti,ab,kf. (10)
38 (multiattribute$ utilit$ or multi attribute$ utilit$).ti,ab,kf. (214)
39 (utilit$ adj3 (valu$ or measur$ or health or life or estimat$ or elicit$ or disease)).ti,ab,kf. (7231)
40 (euro qual or euroqual).ti,ab,kf. (15)
41 (visual analog$ or vas).ti,ab,kf. (52444)
42 (prom or proms or patient reported outcome$1 or pro or pros).ti,ab,kf. (139404)
43 functional assessment.ti,ab,kf. (6663)
44 (symptom$1 adj4 (score$1 or scale$ or instrument$1 or measur$)).ti,ab,kf. (42712)
45 exp patient satisfaction/ (67136)
46 (satisfaction or dissatisf$ or unsatisf$).ti,ab,kf. (115925)
47 (anxiety or depression or anxious or depressed).ti,ab,kf. (373073)
48 exp emotions/ (184194)
49 exp fatigue/ or absenteeism/ or presenteeism/ (30147)
50 stress,psychological/ (93810)
51 (gastrointestinal rating scale or GSRS or (gastrointestinal quality adj3 index) or GIQLI or (severity adj2 dyspepsia assessment) or SODA).ti,ab,kf. (3661)
52 ((parent$ or family or families or mother$ or father$ or caregiver$ or care-giver$) adj5 (concern$1 or perception$1 or view$1 or worry or worrie$1)).ti,ab,kf. or exp parents/px (48279)
53 or/1-52 (2181547)
54 (colic/ or exp diarrhea/ or colonic diseases, functional/ or exp abdominal pain/) and (exp infant/ or child, preschool/) (18890)
55 diarrhea, infantile/ (6791)
56 gastrointestinal diseases/ and pain/ and (exp infant/ or child, preschool/) (52)
57 (constipation/ or vomiting/) and (exp infant/ or child, preschool/) (5457)
58 ((infantile or infant$1 or baby or babies or neonat$ or newborn$1 or new born or toddler$1 or child or children or pediatric or paediatric) adj5 (colic or constipation or constipated or regurgitat$ or spitting or spit)).ti,ab,kf. (2580)
59 ((infantile or infant$1 or baby or babies or neonat$ or newborn$1 or new born or toddler$1 or child or children or pediatric or paediatric) adj5 (colicky or defecat$ or stool$1 or bowel movement$1)).ti,ab,kf. (2979)
60 ((fgid or fgids) and (infantile or infant$1 or neonat$ or baby or babies or newborn$1 or new born or toddler$1 or child or children or pediatric or paediatric)).ti,ab,kf. (111)
61 (crying adj5 (infantile or infant$1 or neonat$ or baby or babies or newborn$1 or new born or toddler$1 or child or children or pediatric or paediatric)).ti,ab,kf. (1101)
62 (gastrointestinal adj5 (infantile or infant$1 or neonat$ or baby or babies or newborn$1 or new born or toddler$1 or child or children or pediatric or paediatric)).ti,ab,kf. (4306)
63 ((dyschezia or colonic inertia or diarrhea or diarrhoea or cramp$ or reflux or functional abdominal pain or bowel symptom$1 or irritable bowel or IBS) adj5 (infantile or infant$1 or neonat$ or baby or babies or newborn$1 or new born or toddler$1 or child or children or pediatric or paediatric)).ti,ab,kf. (15466)
64 or/54-63 (39733)

65 53 and 64 (6472)
66 exp animals/ not humans/ (4171020)
67 (news or comment or editorial or letter or case reports).pt. or case report.ti. (3216568)
68 65 not (66 or 67) (5990)
69 limit 68 to (english language and yr="2005 -Current") (2812)
70 remove duplicates from 69 (2793)

A.2: Source: Embase

Interface: Ovid SP
Coverage: 1974-13/01/2016
Search date: 14/01/16
Retrieved records: 6500
Search strategy:

Database: Embase <1974 to 2016 January 13>
Search Strategy:
---
1 "cost of illness"/ (15923)
2 (costing adj3 (illness$ or disease$ or sickness$)).ti,ab,kw. (60)
3 (burden adj3 (illness$ or disease$ or sickness$)).ti,ab,kw. (27543)
4 (burden adj3 (family or families or human$1 or mother$ or father$ or parent$ or caregiver$ or care-giver$)).ti,ab,kw. (7788)
5 ((economic or human$) adj3 consequence$1).ti,ab,kw. (5927)
6 exp "health care cost"/ (227557)
7 "cost benefit analysis"/ (70174)
8 (cost or costs or economic evaluation or pharmacoeconomic).ti,ab,kw. (492815)
9 (resource$1 adj4 use$1).ti,ab,kw. (27684)
10 (resource$1 adj4 usage).ti,ab,kw. (600)
11 (resource$1 adj4 utili$).ti,ab,kw. (16726)
12 (visit or visits or hospitalization$1 or hospitalisation$1 or admission$1 or admitted or emergency room or rescue).ti,ab,kw. (759153)
13 quality-adjusted life year/ or "quality of life"/ or gastrointestinal quality of life index/ (316485)
14 (quality adjusted life or qol).ti,ab,kw. (53815)
15 (qaly$ or qald$ or qale$ or qtime$).ti,ab,kw. (11705)
16 (sf36 or sf 36 or sf thirtysix or sf thirty six).ti,ab,kw. (24797)
17 (sf6 or sf 6 or short form or shortform or sf six or sfsix).ti,ab,kw. (28593)
18 (sf12 or sf 12 or sf twelve or sftwelve).ti,ab,kw. (4810)
19 (sf16 or sf 16 or sf sixteen or sfsixteen).ti,ab,kw. (35)
20 (sf20 or sf 20 or sf twenty or sftwenty).ti,ab,kw. (298)
21 (euroqol or eq5d or eq 5d).ti,ab,kw. (9656)
22 (hql or hqol or hrqol or hrql or hr ql).ti,ab,kw. (18786)
23 (hye or hyes).ti,ab,kw. (102)
24 health$1 year$1 equivalent$1.ti,ab,kw. (42)
25 (hui or hui1 or hui2 or hui3).ti,ab,kw. (1520)
26 disutili$.ti,ab,kw. (500)
27 (quality adj3 (wellbeing or well being)).ti,ab,kw. (2241)

28 qwb.ti,ab,kw. (218)
29 (willingness adj3 pay).ti,ab,kw. (4665)
30 standard gamble$.ti,ab,kw. (887)
31 (time trade off$1 or time tradeoff$1 or tto or timetradeoff).ti,ab,kw. (1892)
32 ((valu$ or measur$) adj3 (health or outcome$1 or effect$1 or change$1 or state$1)).ti,ab,kw. (381531)
33 (preference$ adj3 (patient$1 or public or valu$ or measur$)).ti,ab,kw. (19215)
34 ((quality adj3 life) or qol).ti,ab,kw. (283686)
35 (index adj3 wellbeing).ti,ab,kw. (137)
36 (multiattribute$ health or multi attribute$ health).ti,ab,kw. (67)
37 (multiattribute$ theor$ or multi attribute$ theor$ or multiattribute$ analys$ or multi attribute$ analys$).ti,ab,kw. (19)
38 (multiattribute$ utilit$ or multi attribute$ utilit$).ti,ab,kw. (277)
39 (utilit$ adj3 (valu$ or measur$ or health or life or estimat$ or elicit$ or disease)).ti,ab,kw. (11011)
40 (euro qual or euroqual).ti,ab,kw. (24)
41 (visual analog$ or vas).ti,ab,kw. (76768)
42 (prom or proms or patient reported outcome$1 or pro or pros).ti,ab,kw. (203085)
43 functional assessment.ti,ab,kw. (10049)
44 (symptom$1 adj4 (score$1 or scale$ or instrument$1 or measur$)).ti,ab,kw. (64027)
45 patient preference/ or patient satisfaction/ (105494)
46 (satisfaction or dissatisf$ or unsatisf$).ti,ab,kw. (157169)
47 (anxiety or depression or anxious or depressed).ti,ab,kw. (505966)
48 exp emotion/ (420006)
49 fatigue/ or exhaustion/ or lassitude/ (138163)
50 absenteeism/ or job performance/ or productivity/ (54173)
51 caregiver burden/ or emotional stress/ or mental stress/ or maternal stress/ or parental stress/ (84316)
52 (gastrointestinal rating scale or GSRS or (gastrointestinal quality adj3 index) or GIQLI or (severity adj2 dyspepsia assessment) or SODA).ti,ab,kw. (4773)
53 ((parent$ or family or families or mother$ or father$ or caregiver$ or care-giver$) adj5 (concern$1 or perception$1 or view$1 or worry or worrie$1)).ti,ab,kw. (21366)
54 or/1-53 (3222665)
55 infantile colic/ or newborn vomiting/ or infantile diarrhea/ (3950)
56 (colic/ or diarrhea/ or chronic diarrhea/ or colon disease/ or intestine function disorder/ or exp abdominal pain/ or irritable colon/ or defecation disorder/) and (exp infant/ or preschool child/) (22242)
57 (gastrointestinal pain/ or gastrointestinal symptom/) and (exp infant/ or preschool child/) (2097)
58 (exp constipation/ or vomiting/) and (exp infant/ or preschool child/) (14916)
59 ((infantile or infant$1 or baby or babies or neonat$ or newborn$1 or new born or toddler$1 or child or children or pediatric or paediatric) adj5 (colic or constipation or constipated or regurgitat$ or spitting or spit)).ti,ab,kw. (3546)
60 ((infantile or infant$1 or baby or babies or neonat$ or newborn$1 or new born or toddler$1 or child or children or pediatric or paediatric) adj5 (colicky or defecat$ or stool$1 or bowel movement$1)).ti,ab,kw. (3761)
61 ((fgid or fgids) and (infantile or infant$1 or neonat$ or baby or babies or newborn$1 or new born or toddler$1 or child or children or pediatric or paediatric)).ti,ab,kw. (222)

62 (crying adj5 (infantile or infant$1 or neonat$ or baby or babies or newborn$1 or new born or toddler$1 or child or children or pediatric or paediatric)).ti,ab,kw. (1426)
63 (gastrointestinal adj5 (infantile or infant$1 or neonat$ or baby or babies or newborn$1 or new born or toddler$1 or child or children or pediatric or paediatric)).ti,ab,kw. (5608)
64 ((dyschezia or colonic inertia or diarrhea or diarrhoea or cramp$ or reflux or functional abdominal pain or bowel symptom$1 or irritable bowel or IBS) adj5 (infantile or infant$1 or neonat$ or baby or babies or newborn$1 or new born or toddler$1 or child or children or pediatric or paediatric)).ti,ab,kw. (17369)
65 or/55-64 (58135)
66 54 and 65 (11408)
67 (editorial or letter or note).pt. (2039212)
68 case report/ or case report.ti. (2087284)
69 (animal/ or animal experiment/ or animal model/ or animal tissue/ or nonhuman/) not exp human/ (5260862)
70 66 not (67 or 68 or 69) (9940)
71 limit 70 to (english language and yr="2005 -Current") (6500)

A.3: Source: PubMed

Interface: http://www.ncbi.nlm.nih.gov/pubmed/
Coverage: 1946-current. Updated daily
Search date: 15/01/16
Retrieved records: 1395
Search strategy:

Note – PubMed muddles the lines in the search history, and therefore the order of the search lines is altered from the original MEDLINE strategy and is not especially logical.

#87 Search (#83 NOT #84) Filters: Publication date from 2005/01/01 to 2016/12/31; English 1395
#86 Search (#83 NOT #84) Filters: Publication date from 2005/01/01 to 2016/12/31 1442
#85 Search (#83 NOT #84) 1569
#84 Search MEDLINE[sb] 22893753
#83 Search (#80 NOT (#81 OR #82)) 15594
#82 Search animals[mh] NOT humans[mh:noexp] 4167646
#81 Search news[pt] OR editorial[pt] OR letter[pt] OR comment[pt] OR case reports[pt] OR case report[ti] 3223352
#80 Search (#79 AND #62) 17287
#79 Search (#63 OR #64 OR #65 OR #66 OR #67 OR #68 OR #69 OR #70 OR #71 OR #72 OR #73 OR #74 OR #75 OR #76 OR #77 OR #78) 70185
#78 Search (infantile[ot] OR infant[ot] OR infants[ot] OR baby[ot] OR babies[ot] OR neonat*[ot] OR newborn*[ot] OR new born[ot] OR toddler*[ot] OR child[ot] OR children[ot] OR pediatric[ot] OR paediatric[ot]) AND (dyschezia[ot] OR colonic inertia[ot] OR diarrhea[ot] OR diarrhea[ot] OR cramp*[ot] OR reflux[ot] OR functional abdominal pain[ot] OR bowel symptom*[ot] OR irritable bowel[ot] OR IBS[ot]) 2364
#77 Search (infantile[tiab] OR infant[tiab] OR infants[tiab] OR baby[tiab] OR babies[tiab] OR neonat*[tiab] OR newborn*[tiab] OR new born[tiab] OR toddler*[tiab] OR child[tiab] OR

children[tiab] OR pediatric[tiab] OR paediatric[tiab]) AND (dyschezia[tiab] OR colonic inertia[tiab] OR diarrhea[tiab] OR diarrhea[tiab] OR cramp*[tiab] OR reflux[tiab] OR functional abdominal pain[tiab] OR bowel symptom*[tiab] OR irritable bowel[tiab] OR IBS[tiab]) 26271

#76 Search (infantile[ot] OR infant[ot] OR infants[ot] OR baby[ot] OR babies[ot] OR neonat*[ot] OR newborn*[ot] OR new born[ot] OR toddler*[ot] OR child[ot] OR children[ot] OR pediatric[ot] OR paediatric[ot]) AND gastrointestinal[ot] 807

#75 Search (infantile[tiab] OR infant[tiab] OR infants[tiab] OR baby[tiab] OR babies[tiab] OR neonat*[tiab] OR newborn*[tiab] OR new born[tiab] OR toddler*[tiab] OR child[tiab] OR children[tiab] OR pediatric[tiab] OR paediatric[tiab]) AND gastrointestinal[tiab] 17631

#74 Search (infantile[ot] OR infant[ot] OR infants[ot] OR baby[ot] OR babies[ot] OR neonat*[ot] OR newborn*[ot] OR new born[ot] OR toddler*[ot] OR child[ot] OR children[ot] OR pediatric[ot] OR paediatric[ot]) AND crying[ot] 59

#73 Search (infantile[tiab] OR infant[tiab] OR infants[tiab] OR baby[tiab] OR babies[tiab] OR neonat*[tiab] OR newborn*[tiab] OR new born[tiab] OR toddler*[tiab] OR child[tiab] OR children[tiab] OR pediatric[tiab] OR paediatric[tiab]) AND crying[tiab] 2477

#72 Search (infantile[ot] OR infant[ot] OR infants[ot] OR baby[ot] OR babies[ot] OR neonat*[ot] OR newborn*[ot] OR new born[ot] OR toddler*[ot] OR child[ot] OR children[ot] OR pediatric[ot] OR paediatric[ot]) AND (fgid[ot] OR fgids[ot]) 2

#71 Search (infantile[tiab] OR infant[tiab] OR infants[tiab] OR baby[tiab] OR babies[tiab] OR neonat*[tiab] OR newborn*[tiab] OR new born[tiab] OR toddler*[tiab] OR child[tiab] OR children[tiab] OR pediatric[tiab] OR paediatric[tiab]) AND (fgid[tiab] OR fgids[tiab]) 115

#70 Search (infantile[ot] OR infant[ot] OR infants[ot] OR baby[ot] OR babies[ot] OR neonat*[ot] OR newborn*[ot] OR new born[ot] OR toddler*[ot] OR child[ot] OR children[ot] OR pediatric[ot] OR paediatric[ot]) AND (colicky[ot] OR defecat*[ot] OR stool*[ot] OR bowel movement*[ot]) 53

#69 Search (infantile[tiab] OR infant[tiab] OR infants[tiab] OR baby[tiab] OR babies[tiab] OR neonat*[tiab] OR newborn*[tiab] OR new born[tiab] OR toddler*[tiab] OR child[tiab] OR children[tiab] OR pediatric[tiab] OR paediatric[tiab]) AND (colicky[tiab] OR defecat*[tiab] OR stool*[tiab] OR bowel movement*[tiab]) 11169

#68 Search (infantile[ot] OR infant[ot] OR infants[ot] OR baby[ot] OR babies[ot] OR neonat*[ot] OR newborn*[ot] OR new born[ot] OR toddler*[ot] OR child[ot] OR children[ot] OR pediatric[ot] OR paediatric[ot]) AND (colic[ot] OR constipation[ot] OR constipated[ot] OR regurgitat*[ot] OR spitting[ot] OR spit[ot]) 244

#67 Search (infantile[tiab] OR infant[tiab] OR infants[tiab] OR baby[tiab] OR babies[tiab] OR neonat*[tiab] OR newborn*[tiab] OR new born[tiab] OR toddler*[tiab] OR child[tiab] OR children[tiab] OR pediatric[tiab] OR paediatric[tiab]) AND (colic[tiab] OR constipation[tiab] OR constipated[tiab] OR regurgitat*[tiab] OR spitting[tiab] OR spit[tiab]) 7520

#66 Search (Constipation[mh:noexp] OR vomiting[mh:noexp]) AND (infant[mh] OR child, preschool[mh:noexp]) 5459

#65 Search gastrointestinal diseases[mh:noexp] AND pain[mh:noexp] AND (infant[mh] OR child, preschool[mh:noexp]) 52

#64 Search diarrhea, infantile[mh:noexp] 6788

#63 Search (colic[mh:noexp] OR diarrhea[mh] OR colonic diseases, functional[mh:noexp] OR abdominal pain[mh]) AND (infant[mh] OR child, preschool[mh:noexp]) 18868

#62 Search (#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33

OR #34 OR #35 OR #36 OR #37 OR #38 OR #39 OR #40 OR #41 OR #42 OR #43 OR #44 OR #45 OR #46 OR #47 OR #48 OR #49 OR #50 OR #51 OR #52 OR #53 OR #54 OR #55 OR #56 OR #57 OR #58 OR #59 OR #60 OR #61) 3966477

#61 Search euroqual[tiab] OR euro qual[tiab] OR euroqual[ot] OR euro qual[ot] 16

#60 Search ((parent*[tiab] OR family[tiab] OR families[tiab] OR mother*[tiab] OR father*[tiab] OR caregiver*[tiab] OR care-giver*[tiab]) AND (concern*[tiab] OR perception*[tiab] OR view*[tiab] OR worry[tiab] OR worrie*[tiab])) OR "Parents/psychology"[Mesh] 97038

#59 Search (parent*[ot] OR family[ot] OR families[ot] OR mother*[ot] OR father*[ot] OR caregiver*[ot] OR care-giver*[ot]) AND (concern*[ot] OR perception*[ot] OR view*[ot] OR worry[ot] OR worrie*[ot]) 522

#58 Search symptom*[ot] AND (score*[ot] OR scale*[ot] OR instrument*[ot] OR measur*[ot]) 746

#57 Search satisfaction[tiab] OR dissatisf*[tiab] OR unsatisf*[tiab] OR satisfaction[ot] OR dissatisf*[ot] OR unsatisf*[ot] 119170

#56 Search anxiety[tiab] OR depression[tiab] OR anxious[tiab] OR depressed[tiab] OR anxiety[ot] OR depression[ot] OR anxious[ot] OR depressed[ot] 381561

#55 Search emotions[mh] 184091

#54 Search stress,psychological[mh] 99836

#53 Search fatigue[mh] OR absenteeism[mh:noexp] OR presenteeism[mh:noexp] 30106

#52 Search (gastrointestinal[tiab] AND rating scale[tiab]) OR (gastrointestinal[ot] AND rating scale[ot]) 603

#51 Search GSRS[tiab] OR GIQLI[tiab] OR SODA[tiab] OR GSRS[ot] OR GIQLI[ot] OR SODA[ot] 3609

#50 Search gastrointestinal[tiab] AND quality[tiab] AND index[tiab] 834

#49 Search severity[tiab] AND dyspepsia[tiab] AND assessment[tiab] 118

#48 Search utilit*[tiab] AND (valu*[tiab] OR measur*[tiab] OR health[tiab] OR life[tiab] OR estimat*[tiab] OR elicit*[tiab] OR disease[tiab]) 78309

#47 Search utilit*[ot] AND (valu*[ot] OR measur*[ot] OR health[ot] OR life[ot] OR estimat*[ot] OR elicit*[ot] OR disease[ot]) 289

#46 Search visual analog*[tiab] OR vas[tiab] OR visual analog*[ot] OR vas[ot] 53203

#45 Search prom[ot] OR proms[ot] OR patient reported outcome*[ot] OR pro[ot] OR pros[ot] OR prom[tiab] OR proms[tiab] OR patient reported outcome*[tiab] OR pro[tiab] OR pros[tiab] 143056

#44 Search functional assessment[tiab] OR functional assessment[ot] 6822

#43 Search symptom*[tiab] AND (score*[tiab] OR scale*[tiab] OR instrument*[tiab] OR measur*[tiab]) 238078

#42 Search patient satisfaction[mh] 67067

#41 Search (valu*[tiab] OR measur*[tiab]) AND (health[tiab] OR outcome*[tiab] OR effect*[tiab] OR change*[tiab] OR state*[tiab]) 2131060

#40 Search (valu*[ot] OR measur*[ot]) AND (health[ot] OR outcome*[ot] OR effect*[ot] OR change*[ot] OR state*[ot]) 7042

#39 Search preference*[tiab] AND (patient[tiab] OR patients[tiab] OR public[tiab] OR valu*[tiab] OR measur*[tiab]) 47688

#38 Search preference*[ot] AND (patient[ot] OR patients[ot] OR public[ot] OR valu*[ot] OR measur*[ot]) 814

#37 Search (quality[tiab] AND life[tiab]) OR qol[tiab] 204509

#36 Search (quality[ot] AND life[ot]) OR qol[ot] 9470
#35 Search (index[tiab] AND wellbeing[tiab]) OR (index[ot] AND wellbeing[ot]) 503
#34 Search multiattribute*[tiab] OR multi attribute*[tiab] OR multiattribute*[ot] OR multi attribute*[ot] 603
#33 Search healthy years equivalent[tiab] OR healthy years equivalent[ot] 23
#32 Search hui[tiab] OR hui1[tiab] OR hui2[tiab] OR hui3[tiab] OR hui[ot] OR hui1[ot] OR hui2[ot] OR hui3[ot] 1064
#31 Search disutili*[tiab] OR disutili*[ot] 282
#30 Search quality[tiab] AND (wellbeing[tiab] OR well being[tiab]) 14021
#29 Search quality[ot] AND (wellbeing[ot] OR well being[ot]) 157
#28 Search qwb[tiab] OR qwb[ot] 186
#27 Search (willingness[ot] AND pay[ot]) OR (willingness[tiab] AND pay[tiab]) 3312
#26 Search standard gamble[tiab] OR standard gamble[ot] 715
#25 Search time trade off*[ot] OR time tradeoff*[ot] OR tto[ot] OR timetradeoff[ot] OR time trade off*[tiab] OR time tradeoff*[tiab] OR tto[tiab] OR timetradeoff[tiab] 1385
#24 Search visit[tiab] OR visits[tiab] OR hospitalization*[tiab] OR hospitalisation*[tiab] OR admission*[tiab] OR admitted[tiab] OR emergency room[tiab] OR rescue[tiab] 505212
#23 Search visit[ot] OR visits[ot] OR hospitalization*[ot] OR hospitalisation*[ot] OR admission*[ot] OR admitted[ot] OR emergency room[ot] OR rescue[ot] 3817
#22 Search quality-adjusted life years[mh:noexp] or quality of life[mh:noexp] 137823
#21 Search quality adjusted life[tiab] OR qol[tiab] OR quality adjusted life[ot] OR qol[ot] 31622
#20 Search qaly*[tiab] OR qald*[tiab] OR qale*[tiab] OR qtime*[tiab] OR qaly*[ot] OR qald*[ot] OR qale*[ot] OR qtime*[ot] 6516
#19 Search sf36[ot] OR sf 36[ot] OR sf36[tiab] or sf 36[tiab] 15719
#18 Search sf6[tiab] OR sf 6[tiab] OR short form[tiab] OR shortform[tiab] OR sf six[tiab] OR sfsix[tiab] 22568
#17 Search hye[tiab] OR hyes[tiab] OR hye[ot] OR hyes[ot] 57
#16 Search hql[tiab] OR hqol[tiab] OR hrqol[tiab] OR hrql[tiab] OR hr ql[tiab] OR hql[ot] OR hqol[ot] OR hrqol[ot] OR hrql[ot] OR hr ql[ot] 12433
#15 Search euroqol[tiab] OR eq5d[tiab] OR eq 5d[tiab] OR euroqol[ot] OR eq5d[ot] OR eq 5d[ot] 5548
#14 Search sf16[tiab] OR sfsixteen[tiab] OR sf16[ot] OR sfsixteen[ot] OR sf20[tiab] OR sftwenty[tiab] OR sf20[ot] OR sftwenty[ot] 31
#13 Search sf12[tiab] OR sftwelve[tiab] OR sf12[ot] OR sftwelve[ot] 217
#12 Search sf6[ot] OR sf 6[ot] OR short form[ot] OR shortform[ot] OR sf six[ot] OR sfsix[ot] 242
#11 Search resource use[tiab] OR resource usage[tiab] OR resource utili*[tiab] OR resource use[ot] OR resource usage[ot] OR resource utili*[ot] 11538
#10 Search cost[ot] OR costs[ot] OR economic evaluation[ot] OR pharmacoeconomic[ot] 7838
#9 Search cost[tiab] OR costs[tiab] OR economic evaluation[tiab] OR pharmacoeconomic[tiab] 377282
#8 Search "costs and cost analysis"[mh:noexp] OR cost-benefit analysis[mh:noexp] OR health care costs[mh] 142701
#7 Search (economic[ot] OR human*[ot]) AND consequence*[ot] 14
#6 Search (economic[tiab] OR human*[tiab]) AND consequence*[tiab] 52990

#5 Search burden[ot] AND (family[ot] OR families[ot] OR human*[ot] OR mother*[ot] OR father*[ot] OR parent*[ot] OR caregiver*[ot] OR care-giver*[ot]) 441
#4 Search burden[tiab] AND (family[tiab] OR families[tiab] OR human*[tiab] OR mother*[tiab] OR father*[tiab] OR parent*[tiab] OR caregiver*[tiab] OR care-giver*[tiab]) 27962
#3 Search (costing[ot] OR burden[ot]) AND (illness*[ot] OR disease*[ot] OR sickness*[ot]) 596
#2 Search (costing[tiab] OR burden[tiab]) AND (illness*[tiab] OR disease*[tiab] OR sickness*[tiab]) 53782
#1 Search cost of illness[mh:noexp] 19779

A.4: Source: PsycINFO

Interface: Ovid SP
Coverage: 1806-January Week 2 2016
Search date: 15/01/16
Retrieved records: 746
Search strategy:

1 exp "costs and cost analysis"/ (21310)
2 Health Care Economics/ or Pharmacoeconomics/ (810)
3 (costing adj3 (illness$ or disease$ or sickness$)).ti,ab,id. (5)
4 (burden adj3 (illness$ or disease$ or sickness$)).ti,ab,id. (3340)
5 (burden adj3 (family or families or human$1 or mother$ or father$ or parent$ or caregiver$ or care-giver$)).ti,ab,id. (4180)
6 ((economic or human$) adj3 consequence$1).ti,ab,id. (1447)
7 (cost or costs or economic evaluation or pharmacoeconomic).ti,ab,id. (72698)
8 (resource$1 adj4 use$1).ti,ab,id. (7968)
9 (resource$1 adj4 usage).ti,ab,id. (152)
10 (resource$1 adj4 utili$).ti,ab,id. (2629)
11 (visit or visits or hospitalization$1 or hospitalisation$1 or admission$1 or admitted or emergency room or rescue).ti,ab,id. (95253)
12 "quality of life"/ (30977)
13 (quality adjusted life or qol).ti,ab,id. (7917)
14 (qaly$ or qald$ or qale$ or qtime$).ti,ab,id. (803)
15 (sf36 or sf 36 or sf thirtysix or sf thirty six).ti,ab,id. (3552)
16 (sf6 or sf 6 or short form or shortform or sf six or sfsix).ti,ab,id. (9357)
17 (sf12 or sf 12 or sf twelve or sftwelve).ti,ab,id. (809)
18 (sf16 or sf 16 or sf sixteen or sfsixteen).ti,ab,id. (0)
19 (sf20 or sf 20 or sf twenty or sftwenty).ti,ab,id. (42)
20 (euroqol or eq5d or eq 5d).ti,ab,id. (1292)
21 (hql or hqol or hrqol or hrql or hr ql).ti,ab,id. (3836)
22 (hye or hyes).ti,ab,id. (13)
23 health$1 year$1 equivalent$1.ti,ab,id. (5)
24 (hui or hui1 or hui2 or hui3).ti,ab,id. (438)
25 disutili$.ti,ab,id. (158)
26 (quality adj3 (wellbeing or well being)).ti,ab,id. (1293)
27 qwb.ti,ab,id. (91)

28 (willingness adj3 pay).ti,ab,id. (1320)
29 standard gamble$.ti,ab,id. (188)
30 (time trade off$1 or time tradeoff$1 or tto or timetradeoff).ti,ab,id. (311)
31 ((valu$ or measur$) adj3 (health or outcome$1 or effect$1 or change$1 or state$1)).ti,ab,id. (77177)
32 (preference$ adj3 (patient$1 or public or valu$ or measur$)).ti,ab,id. (6173)
33 ((quality adj3 life) or qol).ti,ab,id. (51129)
34 (index adj3 wellbeing).ti,ab,id. (114)
35 (multiattribute$ health or multi attribute$ health).ti,ab,id. (14)
36 (multiattribute$ theor$ or multi attribute$ theor$ or multiattribute$ analys$ or multi attribute$ analys$).ti,ab,id. (17)
37 (multiattribute$ utilit$ or multi attribute$ utilit$).ti,ab,id. (235)
38 (utilit$ adj3 (valu$ or measur$ or health or life or estimat$ or elicit$ or disease)).ti,ab,id. (3270)
39 (euro qual or euroqual).ti,ab,id. (4)
40 (visual analog$ or vas).ti,ab,id. (6171)
41 (prom or proms or patient reported outcome$1 or pro or pros).ti,ab,id. (14435)
42 functional assessment.ti,ab,id. (2267)
43 (symptom$1 adj4 (score$1 or scale$ or instrument$1 or measur$)).ti,ab,id. (20641)
44 (satisfaction or dissatisf$ or unsatisf$).ti,ab,id. (98236)
45 (anxiety or depression or anxious or depressed).ti,ab,id. (313389)
46 exp Emotions/ (253774)
47 fatigue/ (7014)
48 employee absenteeism/ (1964)
49 exp job performance/ (17969)
50 psychological stress/ (7972)
51 (gastrointestinal rating scale or GSRS or (gastrointestinal quality adj3 index) or GIQLI or (severity adj2 dyspepsia assessment) or SODA).ti,ab,id. (656)
52 ((parent$ or family or families or mother$ or father$ or caregiver$ or care-giver$) adj5 (concern$1 or perception$1 or view$1 or worry or worrie$1)).ti,ab,id. (27094)
53 Caregiver Burden/ (4856)
54 or/1-53 (862938)
55 infant vocalization/ (992)
56 ((infantile or infant$1 or baby or babies or neonat$ or newborn$1 or new born or toddler$1 or child or children or pediatric or paediatric).id. or (pediatrics/ or exp infant development/)) and (colon disorders/ or gastrointestinal disorders/ or constipation/ or diarrhea/ or irritable bowel syndRome/ or crying/) (1008)
57 ((infantile or infant$1 or baby or babies or neonat$ or newborn$1 or new born or toddler$1 or child or children or pediatric or paediatric) and (colic or constipation or constipated or regurgitat$ or spitting or spit)).ti,ab,id. (540)
58 ((infantile or infant$1 or baby or babies or neonat$ or newborn$1 or new born or toddler$1 or child or children or pediatric or paediatric) and (colicky or defecat$ or stool$1 or bowel movement$1)).ti,ab,id. (322)
59 ((fgid or fgids) and (infantile or infant$1 or neonat$ or baby or babies or newborn$1 or new born or toddler$1 or child or children or pediatric or paediatric)).ti,ab,id. (16)
60 (crying and (infantile or infant$1 or neonat$ or baby or babies or newborn$1 or new born or toddler$1 or child or children or pediatric or paediatric)).ti,ab,id. (1789)

61 (gastrointestinal and (infantile or infant$1 or neonat$ or baby or babies or newborn$1 or new born or toddler$1 or child or children or pediatric or paediatric)).ti,ab,id. (664)
62 ((dyschezia or colonic inertia or diarrhea or diarrhoea or cramp$ or reflux or functional abdominal pain or bowel symptom$1 or irritable bowel or IBS) and (infantile or infant$1 or neonat$ or baby or babies or newborn$1 or new born or toddler$1 or child or children or pediatric or paediatric)).ti,ab,id. (749)
63 or/55-62 (4627)
64 54 and 63 (1338)
65 limit 64 to (english language and yr="2005 -Current") (745)
66 remove duplicates from 65 (746)

A.5: Source: NHS Economic Evaluation Database (NHS EED)

Interface: Cochrane Library – Wiley
Coverage: Issue 2 of 4 April 2015
Search date: 17/01/16 and 03/02/16
Retrieved records: 25 (22 and 3)

Search Name:
Date Run: 17/01/16 18:13:19.750
Description:

ID Search Hits
#1 [mh ^colic] or [mh diarrhea] or [mh ^"colonic diseases, functional"] or [mh "abdominal pain"] or [mh ^constipation] or [mh ^vomiting] 7012
#2 [mh infant] or [mh ^"child, preschool"] 13527
#3 #1 and #2 238
#4 [mh ^"diarrhea, infantile"] 454
#5 [mh ^"gastrointestinal diseases"] and [mh ^pain] 53
#6 #5 and #2 0
#7 (infantile or infant? or baby or babies or neonat* or newborn? or "new born" or toddler? or child or children or pediatric or paediatric) near/5 (colic or constipation or constipated or regurgitat* or spitting or spit) 491
#8 (infantile or infant? or baby or babies or neonat* or newborn? or "new born" or toddler? or child or children or pediatric or paediatric) near/5 (colicky or defecat* or stool? or bowel next movement?) 198
#9 (FGID or FGIDS) and (infantile or infant? or baby or babies or neonat* or newborn? or "new born" or toddler? or child or children or pediatric or paediatric) 13
#10 (infantile or infant? or baby or babies or neonat* or newborn? or "new born" or toddler? or child or children or pediatric or paediatric) near/5 crying 268
#11 (infantile or infant? or baby or babies or neonat* or newborn? or "new born" or toddler? or child or children or pediatric or paediatric) near/5 gastrointestinal 443
#12 (dyschezia or "colonic inertia" or diarrhea or diarrhoea or cramp? or reflux or "functional abdominal pain" or bowel next symptom? or "irritable bowel" or IBS) near/5 (infantile or infant? or baby or babies or neonat* or newborn? or "new born" or toddler? or child or children or pediatric or paediatric) 2014
#13 #12 or #11 or #10 or #9 or #8 or #7 or #6 or #5 or #4 or #3 3163
#14 #13 Publication Year from 2005 to 2016, in Economic Evaluations 22

#15 #13 Publication Year from 2005 to 2016, in Technology Assessments 10
#16 #13 Publication Year from 2005 to 2016, in Other Reviews 94

Search rerun 03/02/16 after it was noted that the ? wildcard was not performing correctly in Cochrane interface. Searched again using the * truncation option in place of the ? – combined with the original search results using NOT to find only “new” records

ID Search Hits
#1 [mh ^colic] or [mh diarrhea] or [mh ^"colonic diseases, functional"] or [mh "abdominal pain"] or [mh ^constipation] or [mh ^vomiting] 7331
#2 [mh infant] or [mh ^"child, preschool"] 14352
#3 #1 and #2 258
#4 [mh ^"diarrhea, infantile"] 461
#5 [mh ^"gastrointestinal diseases"] and [mh ^pain] 55
#6 #5 and #2 0
#7 (infantile or infant? or baby or babies or neonat* or newborn? or "new born" or toddler? or child or children or pediatric or paediatric) near/5 (colic or constipation or constipated or regurgitat* or spitting or spit) 501
#8 (infantile or infant? or baby or babies or neonat* or newborn? or "new born" or toddler? or child or children or pediatric or paediatric) near/5 (colicky or defecat* or stool? or bowel next movement?) 204
#9 (FGID or FGIDS) and (infantile or infant? or baby or babies or neonat* or newborn? or "new born" or toddler? or child or children or pediatric or paediatric) 14
#10 (infantile or infant? or baby or babies or neonat* or newborn? or "new born" or toddler? or child or children or pediatric or paediatric) near/5 crying 274
#11 (infantile or infant? or baby or babies or neonat* or newborn? or "new born" or toddler? or child or children or pediatric or paediatric) near/5 gastrointestinal 451
#12 (dyschezia or "colonic inertia" or diarrhea or diarrhoea or cramp? or reflux or "functional abdominal pain" or bowel next symptom? or "irritable bowel" or IBS) near/5 (infantile or infant? or baby or babies or neonat* or newborn? or "new born" or toddler? or child or children or pediatric or paediatric) 2051
#13 #12 or #11 or #10 or #9 or #8 or #7 or #6 or #4 or #3 3231
#14 [mh ^colic] or [mh diarrhea] or [mh ^"colonic diseases, functional"] or [mh "abdominal pain"] or [mh ^constipation] or [mh ^vomiting] 7331
#15 [mh infant] or [mh ^"child, preschool"] 14352
#16 #14 and #15 258
#17 [mh ^"diarrhea, infantile"] 461
#18 [mh ^"gastrointestinal diseases"] and [mh ^pain] 55
#19 #17 and #18 0
#20 (infantile or infant* or baby or babies or neonat* or newborn* or new next born* or toddler* or child or children or pediatric or paediatric) near/5 (colic or constipation or constipated or regurgitat* or spitting or spit) 541
#21 (infantile or infant* or baby or babies or neonat* or newborn* or new next born* or toddler* or child or children or pediatric or paediatric) near/5 (colicky or defecat* or stool* or bowel next movement*) 384
#22 (FGID or FGIDS) and (infantile or infant* or baby or babies or neonat* or newborn* or new next born* or toddler* or child or children or pediatric or paediatric) 14

#23 (infantile or infant* or baby or babies or neonat* or newborn* or new next born* or toddler* or child or children or pediatric or paediatric) near/5 crying 412
#24 (infantile or infant* or baby or babies or neonat* or newborn* or new next born* or toddler* or child or children or pediatric or paediatric) near/5 gastrointestinal 628
#25 (dyschezia or "colonic inertia" or diarrhea or diarrhoea or cramp* or reflux or "functional abdominal pain" or bowel next symptom* or "irritable bowel" or IBS) near/5 (infantile or infant* or baby or babies or neonat* or newborn* or new next born* or toddler* or child or children or pediatric or paediatric) 2224
#26 #16 or #17 or #19 or #20 or #21 or #22 or #23 or #24 or #25 3727
#27 #13 Publication Year from 2005 to 2016, in Economic Evaluations 22
#28 #26 Publication Year from 2005 to 2016, in Economic Evaluations 25
#29 #28 not #27 3

A.6: Source: Health Technology Assessment Database (HTA Database)
Interface: Cochrane Library – Wiley
Coverage: Issue 4 of 4 October 2015
Search date: 17/01/16 and 03/02/16
Retrieved records: 11 (10 and 1)
Search strategy:

Search Name:
Date Run: 17/01/16 18:13:19.750
Description:

ID Search Hits
#1 [mh ^colic] or [mh diarrhea] or [mh ^"colonic diseases, functional"] or [mh "abdominal pain"] or [mh ^constipation] or [mh ^vomiting] 7012
#2 [mh infant] or [mh ^"child, preschool"] 13527
#3 #1 and #2 238
#4 [mh ^"diarrhea, infantile"] 454
#5 [mh ^"gastrointestinal diseases"] and [mh ^pain] 53
#6 #5 and #2 0
#7 (infantile or infant? or baby or babies or neonat* or newborn? or "new born" or toddler? or child or children or pediatric or paediatric) near/5 (colic or constipation or constipated or regurgitat* or spitting or spit) 491
#8 (infantile or infant? or baby or babies or neonat* or newborn? or "new born" or toddler? or child or children or pediatric or paediatric) near/5 (colicky or defecat* or stool? or bowel next movement?) 198
#9 (FGID or FGIDS) and (infantile or infant? or baby or babies or neonat* or newborn? or "new born" or toddler? or child or children or pediatric or paediatric) 13
#10 (infantile or infant? or baby or babies or neonat* or newborn? or "new born" or toddler? or child or children or pediatric or paediatric) near/5 crying 268
#11 (infantile or infant? or baby or babies or neonat* or newborn? or "new born" or toddler? or child or children or pediatric or paediatric) near/5 gastrointestinal 443
#12 (dyschezia or "colonic inertia" or diarrhea or diarrhoea or cramp? or reflux or "functional abdominal pain" or bowel next symptom? or "irritable bowel" or IBS) near/5

(infantile or infant? or baby or babies or neonat* or newborn? or "new born" or toddler? or child or children or pediatric or paediatric) 2014
#13 #12 or #11 or #10 or #9 or #8 or #7 or #6 or #4 or #3 3163
#14 #13 Publication Year from 2005 to 2016, in Economic Evaluations 22
#15 #13 Publication Year from 2005 to 2016, in Technology Assessments 10
#16 #13 Publication Year from 2005 to 2016, in Other Reviews 94

Search rerun 03/02/16 after it was noted that the ? wildcard was not performing correctly in Cochrane interface. Searched again using the * truncation option in place of the ? – combined with the original search results using NOT to find only “new” records

ID Search Hits
#1 [mh ^colic] or [mh diarrhea] or [mh ^"colonic diseases, functional"] or [mh "abdominal pain"] or [mh ^constipation] or [mh ^vomiting] 7331
#2 [mh infant] or [mh ^"child, preschool"] 14352
#3 #1 and #2 258
#4 [mh ^"diarrhea, infantile"] 461
#5 [mh ^"gastrointestinal diseases"] and [mh ^pain] 55
#6 #5 and #2 0
#7 (infantile or infant? or baby or babies or neonat* or newborn? or "new born" or toddler? or child or children or pediatric or paediatric) near/5 (colic or constipation or constipated or regurgitat* or spitting or spit) 501
#8 (infantile or infant? or baby or babies or neonat* or newborn? or "new born" or toddler? or child or children or pediatric or paediatric) near/5 (colicky or defecat* or stool? or bowel next movement?) 204
#9 (FGID or FGIDS) and (infantile or infant? or baby or babies or neonat* or newborn? or "new born" or toddler? or child or children or pediatric or paediatric) 14
#10 (infantile or infant? or baby or babies or neonat* or newborn? or "new born" or toddler? or child or children or pediatric or paediatric) near/5 crying 274
#11 (infantile or infant? or baby or babies or neonat* or newborn? or "new born" or toddler? or child or children or pediatric or paediatric) near/5 gastrointestinal 451
#12 (dyschezia or "colonic inertia" or diarrhea or diarrhoea or cramp? or reflux or "functional abdominal pain" or bowel next symptom? or "irritable bowel" or IBS) near/5 (infantile or infant? or baby or babies or neonat* or newborn? or "new born" or toddler? or child or children or pediatric or paediatric) 2051
#13 #12 or #11 or #10 or #9 or #8 or #7 or #6 or #4 or #3 3231
#14 [mh ^colic] or [mh diarrhea] or [mh ^"colonic diseases, functional"] or [mh "abdominal pain"] or [mh ^constipation] or [mh ^vomiting] 7331
#15 [mh infant] or [mh ^"child, preschool"] 14352
#16 #14 and #15 258
#17 [mh ^"diarrhea, infantile"] 461
#18 [mh ^"gastrointestinal diseases"] and [mh ^pain] 55
#19 #17 and #18 0
#20 (infantile or infant* or baby or babies or neonat* or newborn* or new next born* or toddler* or child or children or pediatric or paediatric) near/5 (colic or constipation or constipated or regurgitat* or spitting or spit) 541

#21 (infantile or infant* or baby or babies or neonat* or newborn* or new next born* or toddler* or child or children or pediatric or paediatric) near/5 (colicky or defecat* or stool* or bowel next movement*) 384
#22 (FGID or FGIDS) and (infantile or infant* or baby or babies or neonat* or newborn* or new next born* or toddler* or child or children or pediatric or paediatric) 14
#23 (infantile or infant* or baby or babies or neonat* or newborn* or new next born* or toddler* or child or children or pediatric or paediatric) near/5 crying 412
#24 (infantile or infant* or baby or babies or neonat* or newborn* or new next born* or toddler* or child or children or pediatric or paediatric) near/5 gastrointestinal 628
#25 (dyschezia or "colonic inertia" or diarrhea or diarrhoea or cramp* or reflux or "functional abdominal pain" or bowel next symptom* or "irritable bowel" or IBS) near/5 (infantile or infant* or baby or babies or neonat* or newborn* or new next born* or toddler* or child or children or pediatric or paediatric) 2224
#26 #16 or #17 or #19 or #20 or #21 or #22 or #23 or #24 or #25 3727
#27 #13 Publication Year from 2005 to 2016, in Technology Assessments 10
#28 #26 Publication Year from 2005 to 2016, in Technology Assessments 11
#29 #28 not #27 1

A.7: Source: Database of Abstracts of Reviews of Effects (DARE)

Interface: Cochrane Library – Wiley
Coverage: Issue 2 of 4 April 2015
Search date: 17/01/16 and 03/03/16
Retrieved records: 109 (94 and 15)
Search strategy:

ID Search Hits
#1 [mh ^colic] or [mh diarrhea] or [mh ^"colonic diseases, functional"] or [mh "abdominal pain"] or [mh ^constipation] or [mh ^vomiting] 7012
#2 [mh infant] or [mh ^"child, preschool"] 13527
#3 #1 and #2 238
#4 [mh ^"diarrhea, infantile"] 454
#5 [mh ^"gastrointestinal diseases"] and [mh ^pain] 53
#6 #5 and #2 0
#7 (infantile or infant? or baby or babies or neonat* or newborn? or "new born" or toddler? or child or children or pediatric or paediatric) near/5 (colic or constipation or constipated or regurgitat* or spitting or spit) 491
#8 (infantile or infant? or baby or babies or neonat* or newborn? or "new born" or toddler? or child or children or pediatric or paediatric) near/5 (colicky or defecat* or stool? or bowel next movement?) 198
#9 (FGID or FGIDS) and (infantile or infant? or baby or babies or neonat* or newborn? or "new born" or toddler? or child or children or pediatric or paediatric) 13
#10 (infantile or infant? or baby or babies or neonat* or newborn? or "new born" or toddler? or child or children or pediatric or paediatric) near/5 crying 268
#11 (infantile or infant? or baby or babies or neonat* or newborn? or "new born" or toddler? or child or children or pediatric or paediatric) near/5 gastrointestinal 443
#12 (dyschezia or "colonic inertia" or diarrhea or diarrhoea or cramp? or reflux or "functional abdominal pain" or bowel next symptom? or "irritable bowel" or IBS) near/5

(infantile or infant? or baby or babies or neonat* or newborn? or "new born" or toddler? or child or children or pediatric or paediatric) 2014
#13 #12 or #11 or #10 or #9 or #8 or #7 or #6 or #4 or #3 3163
#14 #13 Publication Year from 2005 to 2016, in Economic Evaluations 22
#15 #13 Publication Year from 2005 to 2016, in Technology Assessments 10
#16 #13 Publication Year from 2005 to 2016, in Other Reviews 94

Search rerun 03/02/16 after it was noted that the ? wildcard was not performing correctly in Cochrane interface. Searched again using the * truncation option in place of the ? – combined with the original search results using NOT to find only “new” records

ID Search Hits
#1 [mh ^colic] or [mh diarrhea] or [mh ^"colonic diseases, functional"] or [mh "abdominal pain"] or [mh ^constipation] or [mh ^vomiting] 7331
#2 [mh infant] or [mh ^"child, preschool"] 14352
#3 #1 and #2 258
#4 [mh ^"diarrhea, infantile"] 461
#5 [mh ^"gastrointestinal diseases"] and [mh ^pain] 55
#6 #5 and #2 0
#7 (infantile or infant? or baby or babies or neonat* or newborn? or "new born" or toddler? or child or children or pediatric or paediatric) near/5 (colic or constipation or constipated or regurgitat* or spitting or spit) 501
#8 (infantile or infant? or baby or babies or neonat* or newborn? or "new born" or toddler? or child or children or pediatric or paediatric) near/5 (colicky or defecat* or stool? or bowel next movement?) 204
#9 (FGID or FGIDS) and (infantile or infant? or baby or babies or neonat* or newborn? or "new born" or toddler? or child or children or pediatric or paediatric) 14
#10 (infantile or infant? or baby or babies or neonat* or newborn? or "new born" or toddler? or child or children or pediatric or paediatric) near/5 crying 274
#11 (infantile or infant? or baby or babies or neonat* or newborn? or "new born" or toddler? or child or children or pediatric or paediatric) near/5 gastrointestinal 451
#12 (dyschezia or "colonic inertia" or diarrhea or diarrhoea or cramp? or reflux or "functional abdominal pain" or bowel next symptom? or "irritable bowel" or IBS) near/5 (infantile or infant? or baby or babies or neonat* or newborn? or "new born" or toddler? or child or children or pediatric or paediatric) 2051
#13 #12 or #11 or #10 or #9 or #8 or #7 or #6 or #4 or #3 3231
#14 [mh ^colic] or [mh diarrhea] or [mh ^"colonic diseases, functional"] or [mh "abdominal pain"] or [mh ^constipation] or [mh ^vomiting] 7331
#15 [mh infant] or [mh ^"child, preschool"] 14352
#16 #14 and #15 258
#17 [mh ^"diarrhea, infantile"] 461
#18 [mh ^"gastrointestinal diseases"] and [mh ^pain] 55
#19 #17 and #18 0
#20 (infantile or infant* or baby or babies or neonat* or newborn* or new next born* or toddler* or child or children or pediatric or paediatric) near/5 (colic or constipation or constipated or regurgitat* or spitting or spit) 541

#21 (infantile or infant* or baby or babies or neonat* or newborn* or new next born* or toddler* or child or children or pediatric or paediatric) near/5 (colicky or defecat* or stool* or bowel next movement*) 384
#22 (FGID or FGIDS) and (infantile or infant* or baby or babies or neonat* or newborn* or new next born* or toddler* or child or children or pediatric or paediatric) 14
#23 (infantile or infant* or baby or babies or neonat* or newborn* or new next born* or toddler* or child or children or pediatric or paediatric) near/5 crying 412
#24 (infantile or infant* or baby or babies or neonat* or newborn* or new next born* or toddler* or child or children or pediatric or paediatric) near/5 gastrointestinal 628
#25 (dyschezia or "colonic inertia" or diarrhea or diarrhoea or cramp* or reflux or "functional abdominal pain" or bowel next symptom* or "irritable bowel" or IBS) near/5 (infantile or infant* or baby or babies or neonat* or newborn* or new next born* or toddler* or child or children or pediatric or paediatric) 2224
#26 #16 or #17 or #19 or #20 or #21 or #22 or #23 or #24 or #25 3727
#27 #13 Publication Year from 2005 to 2016, in Other Reviews 94
#28 #26 Publication Year from 2005 to 2016, in Other Reviews 109
#29 #28 not #27 15

A.8: Source: NEXIS UK
Interface: LexisNexis
Coverage: No information provided. Last update 19/01/16
Search date: 20/01/16
Retrieved records: 528
Search strategy:

Search of this database intended to identify commercial/market reports on over the counter sales of interventions

All searches had the following limits applied: Search Market Insight, 01/01/2005 – 20/01/16. Search All Countries, All Industries, All 20 sources.

Each search string searched separately and the full text downloaded as a Word document.

(infantile OR infant* OR baby OR babies OR neonat? OR newborn* OR “new born” OR toddler* OR child OR children OR pediatric OR paediatric) W/5 (colic OR constipation OR constipated OR regurgitat? OR spitting OR spit) 62 results

(infantile OR infant* OR baby OR babies OR neonat? OR newborn* OR “new born” OR toddler* OR child OR children OR pediatric OR paediatric) W/5 (colicky OR defecat? OR stool* OR “bowel movement*”) 42 results

(infantile OR infant* OR baby OR babies OR neonat? OR newborn* OR “new born” OR toddler* OR child OR children OR pediatric OR paediatric) and (fgid or fgids) 0 results

(infantile OR infant* OR baby OR babies OR neonat? OR newborn* OR “new born” OR toddler* OR child OR children OR pediatric OR paediatric) W/5 (crying OR cry). Due to the excessive volume of irrelevant results returned by this search line, these terms were

additionally limited to the following industries: Food, Health Care, Marketing & Advertising, Pharmaceuticals, Retail & Wholesale Trade. 27 results.

(infantile OR infant* OR baby OR babies OR neonat? OR newborn* OR “new born” OR toddler* OR child OR children OR pediatric OR paediatric) W/5 gastrointestinal 146 results

(infantile OR infant* OR baby OR babies OR neonat? OR newborn* OR “new born” OR toddler* OR child OR children OR pediatric OR paediatric) W/5 (dyschezia OR “colonic inertia” OR diarrhea OR diarrhoea OR cramp? OR reflux OR “functional abdominal pain” OR “bowel symptom*” OR “irritable bowel” OR IBS) Due to the excessive volume of irrelevant results returned by this search line, these terms were additionally limited to the following industries: Food, Health Care, Marketing & Advertising, Pharmaceuticals, Retail & Wholesale Trade. 251 results.

A.9: Source: CEA Registry

Interface:https://research.tufts-nemc.org/cear4/SearchingtheCEARegistry/SearchtheCEARegistry.aspx
Coverage: No information provided.
Search date: 20/01/16
Retrieved records: 0
Search strategy:

Database only supports searching single terms – following used 1 at a time
No export options available. Information specialist added potentially relevant records ONLY to EndNote by hand. Duplicate records not added.

Colic 3 records/0 potentially relevant
Colicky 0 records
Constipation 5 records/0 potentially relevant
Constipated 1 record/0 potentially relevant
Regurgitation 5 records/0 potentially relevant
Regurgitate 0 records
Regurgitates 0 records
Spitting 0 records
Spits 0 records [NB spit could not be used as a search term as it retrieved over 900 records, all of the first 5 pages were irrelevant suggesting it is overly sensitive]
Defecation 0 records
Defecate 0 records
Defecated 0 records
Stool 3 records/0 potentially relevant
Stooling 0 records
Stools 0 records
Bowel 29 records/0 potentially relevant
IBS 14 records/0 potentially relevant
FGID 0 records
FGIDS 0 records
Cry 11 records/0 potentially relevant

Crying 0 records
Gastrointestinal 65 records/0 potentially relevant
Dyschezia 0 records
Colon 78 records/0 potentially relevant
Colonic 11 records/0 potentially relevant
Diarrhea 9 records/0 potentially relevant
Diarrhea 7 records/0 potentially relevant
Cramp 2 records/ 0 potentially relevant
Cramps 0 records
Cramping 0 records
Reflux 27 records/0 potentially relevant

A.10: Source: NHS Evidence Search

Interface: http://www.evidence.nhs.uk/
Coverage: No information provided.
Search date: 20/01/16
Retrieved records: 16
Search strategy:

Note: NHS Evidence is not intended for systematic or structured searches and it does not have the functionality to support this. The search was translated pragmatically in order to allow it to be used in NHS Evidence, prioritizing the most specific search terms.

(infantile OR infant* OR baby OR babies OR neonat* OR newborn* OR "new born*" OR toddler* OR child OR children OR pediatric OR paediatric) AND (fgid or fgids or "functional gastrointestinal disorder*") 22 records.

(infantile OR infant* OR baby OR babies OR neonat* OR newborn* OR “new born*” OR toddler* OR child OR children OR pediatric OR paediatric) AND (colic OR colicky) In order to manage the search volumes the results were filtered by publication type: primary research, systematic reviews, ongoing research and health technology assessment. 120 records.

(infantile OR infant* OR baby OR babies OR neonat* OR newborn* OR “new born*” OR toddler* OR child OR children OR pediatric OR paediatric) AND (“excessive crying” OR “inconsolable crying”) In order to manage the search volumes the results were filtered by publication type: primary research, systematic reviews, ongoing research and health technology assessment. 16 records.

(infantile OR infant* OR baby OR babies OR neonat* OR newborn* OR new born* OR toddler* OR child OR children OR pediatric OR paediatric) AND (regurgitat* OR spit OR spitting) In order to manage the search volumes the results were filtered by publication type: primary research, systematic reviews, ongoing research and health technology assessment. 147 records.

All records rapidly assessed by information specialist – 38 potentially relevant records cut and pasted into Word document. 16 of these had not been previously identified by other search resources and so were added to EndNote.

A.11: Source: REPEC
Interface: IDEAS https://ideas.repec.org
Coverage: No information provided.
Search date: 20/01/16
Retrieved records: 1
Search strategy:

Each search line run individually

(infantile | infant* | baby | babies | neonat* | newborn* | "new born" | “new borns” | toddler* | child | children | pediatric | paediatric) + (colic | colicky) 1 record

(infantile | infant* | baby | babies | neonat* | newborn* | "new born" | “new borns” | toddler* | child | children | pediatric | paediatric) + (regurgitat* | spit | spitting) 0 records

fgid | fgids 0 records

(infantile | infant* | baby | babies | neonat* | newborn* | "new born" | “new borns” | toddler* | child | children | pediatric | paediatric) + (cry OR crying) 24 records

(infantile | infant* | baby | babies | neonat* | newborn* | "new born" | “new borns” | toddler* | child | children | pediatric | paediatric) + (constipation | constipated) 4 records

(infantile | infant* | baby | babies | neonat* | newborn* | "new born" | “new borns” | toddler* | child | children | pediatric | paediatric) + (defecat* | stool* | “bowel movement” | "bowel movements" | gastrointestinal) 22 records

(infantile | infant* | baby | babies | neonat* | newborn* | "new born" | “new borns” | toddler* | child | children | pediatric | paediatric) + (dyschezia | “colonic inertia” | diarrhea | diarrhoea | cramp* | reflux | “functional abdominal pain”) 129 records

(infantile | infant* | baby | babies | neonat* | newborn* | "new born" | “new borns” | toddler* | child | children | pediatric | paediatric) + ("bowel symptom" | "bowel symptoms" | IBS | "irritable bowel") 1 record

All results rapidly assessed in REPEC by the information specialist for relevance. Only records not previously identified by database searches were added to EndNote. 1 potentially relevant, non duplicate record remained after this process.

A.12: Source: OAISTER
Interface: Worldcat http://oaister.worldcat.org/
Coverage: No information provided.
Search date: 21/01/16
Retrieved records:240
Search strategy:

Note: OAISTER is not intended for systematic or structured searches and it does not have the functionality to support this. The search was translated pragmatically in order to allow it to be used in this resource, prioritizing the most specific search terms.

Each search line run individually and the following limits applied: Non juvenile, English language only, 2005-2016

'kw:(infantile OR infant* OR baby OR babies OR neonat* OR newborn* OR “new born” OR “new borns” OR toddler* OR child OR children OR pediatric OR paediatric) AND (colic OR colicky)' 104 records

‘kw(infantile OR infant* OR baby OR babies OR neonat* OR newborn* OR “new born” OR “new borns” OR toddler* OR child OR children OR pediatric OR paediatric) AND (fgid or fgids or "functional gastrointestinal disorder" OR “functional gastrointestinal disorders”)’ 47 records

‘kw(infantile OR infant* OR baby OR babies OR neonat* OR newborn* OR “new born” OR “new borns” OR toddler* OR child OR children OR pediatric OR paediatric) AND (inconsolab* OR excessiv*) AND (cry OR crying)’ 21 records

‘kw(infantile OR infant* OR baby OR babies OR neonat* OR newborn* OR “new born” OR “new borns” OR toddler* OR child OR children OR pediatric OR paediatric) AND (regurgitat* OR spit OR spitting) 68

A.13: Source: International Society For Pharmacoeconomics and Outcomes Research (ISPOR) conference

Search date: 18/12/15
Retrieved records: 0
Search strategy:

Latin America Conference (every 2 years) – 2013 and 2015 – both indexed in Embase – no handsearching required

Annual European Congress – 2013, 2014, 2015 – all three indexed in Embase – no handsearching required

Annual International Meeting – 2013, 2014, 2015 - all three indexed in Embase – no handsearching required

Asia Pacific Conference (every 2 years) – 2014 – not indexed – handsearched

ISPOR 6TH Asia-Pacific Conference 6-9 September 2014. Beijing, China. Abstract book scanned by eye by an information specialist at http://www.ispor.org/conferences/beijing0914/ISPOR-6th-Asia-Pacific-Conference-Research-Abstracts.pdf [Accessed 18th December 2015]. 0 potentially relevant records identified.

The ISPOR Scientific Presentation Database [https://www.ispor.org/RESEARCH_STUDY_DIGEST/research_index.asp] was also browsed on 18/12/13 for presentations catagorised as the disease group:
a) GI Disorders (8 results returned - no potentially relevant records identified);
b) Health – Children (10 results returned - no potentially relevant records identified);
c) Multiple Diseases. (125 results returned – no potentially relevant records identified)

A.14: Source: European Society for Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) conference

Search date: 03/02/16
Retrieved records: 18
Search strategy:

2013, 2014, 2015 annual meeting abstracts not indexed in Embase and so were handsearched.

As the terms for the population that must be used to search the abstracts using the “Control F” function (such as FGID, constipation, diarrhoea) are too imprecise in the context of this confernece to be used efficeintly, and the list of necessary search terms to capture the costs concept was prohibitively long, it was decided to scan the abstract book by eye to identify any potentially relevant studies. The decision to select an abstract was made by the information specialist – to minimise the risk of missing potentially relevant studies, selection was over inclusive if there was any doubt on the relevance of the abstract.

ESPGHAN Annual Meeting May 6-9 2015; Amsterdam Abstract book searched online at http://espghan.org/uploads/media/ESPGHAN_A4_Abstract_2015_v2.pdf
[Accessed 3rd February 2016].
5 abstracts selected

ESPGHAN Annual Meeting June 9-12 2014; Jerusalem Abstract book searched online at http://journals.lww.com/jpgn/Documents/ESPGHAN%202014%20Abstracts%20-%20Complete%20abstracts.pdf
[Accessed 3rd February 2016].
5 abstracts selected

ESPGHAN Annual Meeting May 8-11 2013; London Abstract book searched online at http://journals.lww.com/jpgn/Documents/ESPGHAN%20Abstracts%202013.pdf
[Accessed 3rd February 2016].
8 abstracts selected

A.15: Source: North American Society for Pediatric Gastroenterology, Hepatology and Nutrition (NASPGHAN) conference

Search date: 18/12/15
Retrieved records: 5
Search strategy:

2013, 2014, 2015 annual meeting abstracts not indexed in Embase and so were handsearched.

As the terms for the population that must be used to search the abstracts using the "Control F" function (such as FGID, constipation, diarrhoea) are too imprecise in the context of this confernece to be used efficeintly, and the list of necessary search terms to capture the costs concept was prohibitively long, it was decided to scan the abstract book by eye to identify any potentially relevant studies. The decision to select an abstract was made by the information specialist – to minimise the risk of missing potentially relevant studies, selection was over inclusive if there was any doubt on the relevance of the abstract.

NASPGHAN Annual Meeting October 8-11 2015; Washington, DC. Abstract book searched online at http://journals.lww.com/jpgn/Documents/Abstracts%20from%202015%20NASPGHAN%20Meeting%20in%20Washington,%20DC.pdf [Accessed 18th December 2015].
1 abstract selected

NASPGHAN Annual Meeting October 23-26 2014; Atlanta, GA. Abstract book searched online at http://journals.lww.com/jpgn/Documents/NASPGHAN%202014%20abstracts.pdf
[Accessed 18th December 2015].
1 abstract selected

NASPGHAN Annual Meeting October 10-12 2013; Chicago, IL. Abstract book searched online at http://journals.lww.com/jpgn/Documents/NASPGHAN2013_Abstract_Book%20-%20revised%20Sept%2018,%202013.pdf Accessed 18th December 2015].

3 abstracts selected

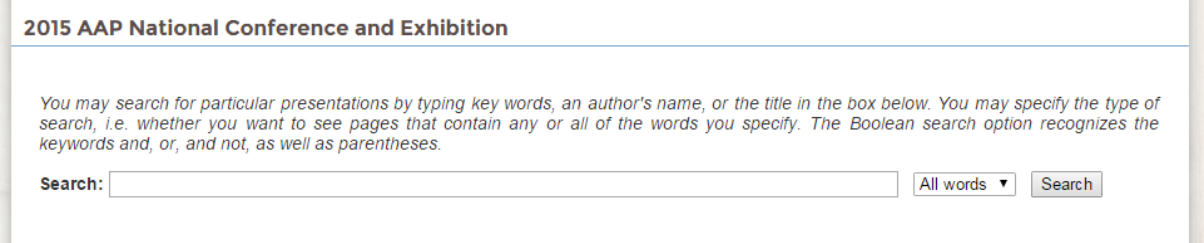
A.16: Source: World Congress of Pediatric Gastroenterology, Hepatology and Nutrition.
Search date: 18/12/15
Retrieved records: 0
Search strategy:

Last conference held 2012, next in October 2016 so outside scope of search. Not handsearched.

A.17: Source: American Academy of Pediatrics National Conference
Search date: 03/02/16
Retrieved records: 1
Search strategy:

AAP National Conference October 24-27 2015; Washington, DC. Abstracts searchable online at: https://aap.confex.com/aap/2015/webprogrampress/start.html
Accessed 3rd February 2015

Online database of abstracts –



Boolean search does not seem to be performing correctly – all search terms used one at a time:

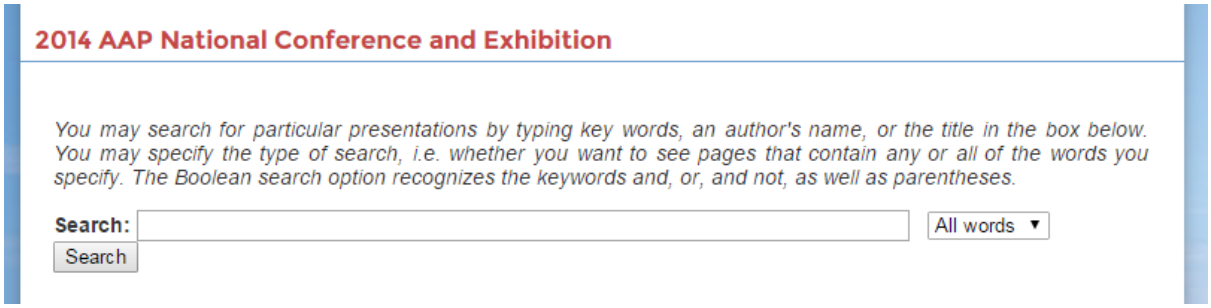
colic
colicky
cry
cries
crying
constipation
constipated
constipating
reflux
GERD
GORD
regurgitation
gastrointestinal

gastro-intestinal
fgid
fgids

0 potentially relevant abstracts identified.

AAP National Conference October 11-14 2014; San Diego. Abstracts searchable online at: https://aap.confex.com/aap/2014/webprogrampress/start.html Accessed 3rd February 2015

Online database of abstracts –



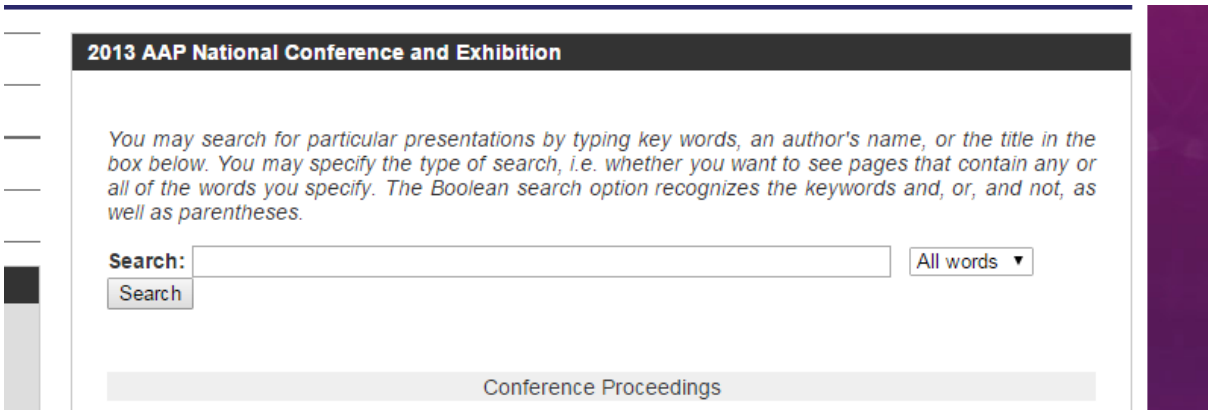
Boolean search does not seem to be performing correctly – all search terms used one at a time:

colic
colicky
cry
cries
crying
constipation
constipated
constipating
reflux
GERD
GORD
regurgitation
regurgitate
gastrointestinal
gastro-intestinal
fgid
fgids

1 potentially relevant abstract identified

AAP National Conference October 26-29 2013; Orlando Abstracts searchable online at: https://aap.confex.com/aap/2013/webprogram/start.html Accessed 3rd February 2015

Online database of abstracts –



Boolean search does not seem to be performing correctly – all search terms used one at a time:

colic
colicky
cry
cries
crying
constipation
constipated
constipating
reflux
GERD
GORD
regurgitation
regurgitate
gastrointestinal
gastro-intestinal
fgid
fgids

0 potentially relevant abstracts identified.

APPENDIX B

Excluded Studies

Table B.1: Unobtainable records (1)

Record	Exclusion reason
Tikochinski Y, Kukliansky I. Examination of the effect of BornFree ActiveFlow baby bottles on infant colic. Gastroenterol Nurs. 2013;36(2):123-7.	Record unobtainable

Table B.2: Excluded records (125) with reasons for exclusion

Record	Exclusion reason
Ansari H, Ansari Z, Hutson JM, Southwell BR. Potentially avoidable hospitalisation for constipation in Victoria, Australia in 2010-11. BMC Gastroenterol. 2014;14:125.	Ineligible patient population
Ansari H, Ansari Z, Lim T, Hutson JM, Southwell BR. Factors relating to hospitalisation and economic burden of paediatric constipation in the state of Victoria, Australia, 2002-2009. J Paediatr Child Health. 2014;50(12):993-9.	Ineligible patient population
Arumugam J, Sivandam S, Vijayalakshmi AM. The evaluation and management of an incessantly crying infant. SLJCH. 2012;41(4):192-98.	Literature review
Asipu D, Jaffray B. Treatment of severe childhood constipation with restorative proctocolectomy. Arch Dis Child. 2010;95(11):867-70.	Ineligible patient population
Bae SH, Son JS, Lee R. Effect of fluid intake on the outcome of constipation in children: PEG 4000 versus lactulose. Pediatr Int. 2010;52(4):594-7.	Ineligible patient population
Barr RG, Rajabali F, Aragon M, Colbourne M, Brant R. Education about crying in normal infants is associated with a reduction in pediatric emergency room visits for crying complaints. J Dev Behav Pediatr. 2015;36(4):252-7.	Ineligible patient population
Bishop J, Furman M, Thomson M. Omeprazole for gastroesophageal reflux disease in the first 2 years of life: a dose-finding study with dual-channel pH monitoring. J Pediatr Gastroenterol Nutr. 2007;45(1):50-5.	Ineligible population (babies with gastroesophageal reflux)
Bu LN, Chang MH, Ni YH, Chen HL, Cheng CC. Lactobacillus casei rhamnosus Lcr35 in children with chronic constipation. Pediatr Int. 2007;49(4):485-90.	Ineligible patient population
Burgers R, Bonanno E, Madarena E, Graziano F, Pensabene L, Gardner W, et al. The care of constipated children in primary care in different countries. Acta Paediatr. 2012;101(6):677-80.	Ineligible study design
Calado CS, Pereira AG, Santos VN, Castro MJ, Maio JF. What brings newborns to the emergency department?: a 1-year study. Pediatr Emerg Care. 2009;25(4):244-8.	Prevalence study
Chao HC, Vandenplas Y. Effect of cereal-thickened formula and upright positioning on regurgitation, gastric emptying, and weight gain in infants with regurgitation. Nutrition. 2007;23(1):23-8.	Ineligible population (babies with gastroesophageal reflux)
Chellani H, Dabas A, Arya S. Gastro-esophageal reflux: spitting and possetting in a neonate. Indian J Pediatr. 2015;82(1):39-43.	Literature review
Chen SL, Cai SR, Deng L, Zhang XH, Luo TD, Peng JJ, et al. Efficacy and complications of polyethylene glycols for treatment of constipation in children: a meta-analysis (Provisional abstract). DARE. 2014; (2): e65. Available from: http://onlinelibrary.wiley.com/o/cochrane/cldare/articles/DARE-12014063218/frame.html	Literature review
Chitkara DK, Talley NJ, Weaver AL, Katusic SK, De Schepper H, Rucker MJ, et al. Incidence of presentation of common functional gastrointestinal disorders in children from birth to 5 years: a cohort study. Clin Gastroenterol Hepatol. 2007;5(2):186-91.	Prevalence study
Chu H, Zhong L, Li H, Zhang X, Zhang J, Hou X. Epidemiology characteristics of constipation for general population, pediatric population, and elderly	Literature review

Record	Exclusion reason
population in china. Gastroenterol Res Pract. 2014;2014:532734.	
Chumpitazi CE, Henkel EB, Valdez KL, Chumpitazi BP. Soap Suds Enema are Efficacious and Safe for Treating Fecal Impaction in Children with Abdominal Pain. J Pediatr Gastroenterol Nutr. 2015	Ineligible patient population
Coccorullo P, Quitadamo P, Martinelli M, Staiano A. Novel and alternative therapies for childhood constipation. J Pediatr Gastroenterol Nutr. 2009;48(SUPPL. 2):S104-S06.	Literature review
Cohen Engler A, Hadash A, Shehadeh N, Pillar G. Breastfeeding may improve nocturnal sleep and reduce infantile colic: potential role of breast milk melatonin. Eur J Pediatr. 2012;171(4):729-32.	Ineligible patient population
Collaco JM, Aherrera AD, Au Yeung KJ, Lefton-Greif MA, Hoch J, Skinner ML. Interdisciplinary pediatric aerodigestive care and reduction in health care costs and burden. JAMA Otolaryngol Head Neck Surg. 2015;141(2):101-5.	Ineligible patient population
Cook F, Bayer J, Le HND, Mensah F, Cann W, Hiscock H. Baby Business: a randomised controlled trial of a universal parenting program that aims to prevent early infant sleep and cry problems and associated parental depression. BMC Pediatr. 2012;12:13.	Ineligible patient population
Crotteau CA, Wright ST. What is the best treatment for infants with colic? J Fam Pract. 2006;55(7):634-36.	Literature review
Dattoli E, Tandoi F, Agosti M, Luini C, Meneghin F, Dilillo D, et al. Functional gastrointestinal disorders in infants and neonatal period: Which correlation? [Conference Abstract]. Dig Liver Dis. 2012;44:S264.	Conference abstract
Dehghani SM, Askarian M, Kaffashan HA. Oral domperidone has no additional effect on chronic functional constipation in children: a randomized clinical trial. Indian J Gastroenterol. 2014;33(2):125-30.	Ineligible patient population
Dehghani SM, Erjaee A, Imanieh MH, Haghighat M. Efficacy of the standard quadruple therapy versus triple therapies containing proton pump inhibitor plus amoxicillin and clarithromycin or amoxicillin-clavulanic acid and metronidazole for helicobacter pylori eradication in children. Dig Dis Sci. 2009;54(8):1720-24.	Ineligible patient population
Del Buono R, Wenzl TG, Ball G, Keady S, Thomson M. Effect of Gaviscon Infant on gastro-oesophageal reflux in infants assessed by combined intraluminal impedance/pH. Arch Dis Child. 2005;90(5):460-3.	Ineligible population (babies with gastroesophageal reflux)
Devitt P, Thornley E, Hinks M. An evaluation of an inter-disciplinary constipation clinic for childhood constipation. J Res Nurs. 2007;12(5):539-47.	Ineligible study design
Di Mauro A, Riezzo G, Civardi E, Intini C, Corvaglia L, Ballardini E, et al. Act and not react: Prophylactic use of probiotic in colic, regurgitation and functional constipation, clinical and socio-economic impact. Dig Liver Dis. 2013;45:e302.	Conference abstract
Diamanti A, Bracci F, Reale A, Crisogianni M, Pisani M, Castro M. Incidence, clinical presentation, and management of constipation in a pediatric ED. Am J Emerg Med. 2010;28(2):189-94.	Prevalence study
Ditty A, Garg A, Leggett C, Turner S. Are proton pump inhibitors over-prescribed in infants? J Pharm Pract Res. 2014;44(4):220-23.	Ineligible population (babies with gastroesophageal reflux)
Dupont C, Leluyer B, Maamri N, Morali A, Joye J-P, Fiorini J-M, et al. Double-blind randomized evaluation of clinical and biological tolerance of polyethylene glycol 4000 versus lactulose in constipated children. J Pediatr Gastroenterol Nutr. 2005;41(5):625-33.	Ineligible patient population
Dziechciarz P, Horvath A, Szajewska H. Polyethylene glycol 4000 for treatment of functional constipation in children. J Pediatr Gastroenterol Nutr. 2015;60(1):65-8.	Ineligible patient population
Elitsur Y. The diagnostic yield of upper endoscopy procedures in children- is it cost effective? Curr Gastroenterol Rep. 2014;16(5):385.	Ineligible study design
European School of Osteopathy. Cranial Osteopathy in Infantile Colic. In: UK Clinical Trials Gateway [internet]. 2013. Available from https://ukctg.nihr.ac.uk/trials/trial-details/trial-details?trialNumber=NCT01942928. Identifier: NCT01942928	Ineligible study design
Falconer J. Gastro-oesophageal reflux and gastrooesophageal reflux disease in infants and children. J Fam Health Care. 2010;20(5):175-7; quiz 78.	Ineligible study design

Record	Exclusion reason
Fazil M. Prevalence and risk factors for infantile colic in District Mansehra. J Ayub Med Coll Abbottabad. 2011;23(2):115-7.	Prevalence study
Gomes PB, Duarte MA, Melo Mdo C. Comparison of the effectiveness of polyethylene glycol 4000 without electrolytes and magnesium hydroxide in the treatment of chronic functional constipation in children. J Pediatr. 2011;87(1):24-8.	Ineligible patient population
Hays LJ. Impact upon emotional availability: Infant GERD and infant massage therapy. Diss Abstr Int (B). 2015;75(9-B(E)):No Pagination Specified.	Ineligible patient population
Hegar B, Rantos R, Firmansyah A, De Schepper J, Vandenplas Y. Natural evolution of infantile regurgitation versus the efficacy of thickened formula. J Pediatr Gastroenterol Nutr. 2008;47(1):26-30.	Ineligible population (babies with gastroesophageal reflux)
Howard CR, Lanphear N, Lanphear BP, Eberly S, Lawrence RA. Parental responses to infant crying and colic: the effect on breastfeeding duration. Breastfeed Med. 2006;1(3):146-55.	Ineligible outcomes
Hua S, Peters RL, Allen KJ, Dharmage SC, Tang ML, Wake M, et al. Medical intervention in parent-reported infant gastro-oesophageal reflux: A population-based study. J Paediatr Child Health. 2014(Nov 11):[Epub ahead of print].	Ineligible patient population
Hussain M, Batool F, Masood-Us-Syed SS. Association of various factors with infantile colic. Pak Paed J. 2013;37(4):217-21.	Ineligible outcomes
Hussain S, Kierkus J, Hu P, Hoffman D, Lekich R, Sloan S, et al. Safety and efficacy of delayed release rabeprazole in 1- to 11-month-old infants with symptomatic GERD. J Pediatr Gastroenterol Nutr. 2014;58(2):226-36.	Ineligible population (babies with gastroesophageal reflux)
Iacono G, Merolla R, D'Amico D, Bonci E, Cavataio F, Di Prima L, et al. Gastrointestinal symptoms in infancy: a population-based prospective study. Dig Liver Dis. 2005;37(6):432-8.	Prevalence study
Iacovou M, Ralston RA, Muir J, Walker KZ, Truby H. Dietary management of infantile colic: a systematic review. Matern Child Health J. 2012;16(6):1319-31.	Literature review
Indrio F, Di Mauro A, Riezzo G, Cavallo L, Francavilla R. Infantile colic, regurgitation, and constipation: an early traumatic insult in the development of functional gastrointestinal disorders in children? Eur J Pediatr. 2015;174(6):841-2.	Ineligible patient population
Indrio F, Di Mauro A, Riezzo G, Civardi E, Intini C, Corvaglia L, et al. Prophylactic use of a probiotic in the prevention of colic, regurgitation, and functional constipation: a randomized clinical trial. JAMA Pediatr. 2014;168(3):228-33.	Ineligible population (babies with gastroesophageal reflux)
Indrio F, Di Mauro A, Riezzo G, Panza R, Cavallo L, Francavilla R. Prevention of functional gastrointestinal disorders in neonates: Clinical and socioeconomic impact. Benef Microbes. 2015;6(2):195-98.	Literature review
Indrio F, Riezzo G, Raimondi F, Bisceglia M, Cavallo L, Francavilla R. The effects of probiotics on feeding tolerance, bowel habits, and gastrointestinal motility in preterm newborns. J Pediatr. 2008;152(6):801-6.	Ineligible patient population
Indrio F, Riezzo G, Raimondi F, Cavallo L, Francavilla R. Regurgitation in healthy and non healthy infants. Ital J Pediatr. 2009;35(1):39.	Literature review
Indrio F. Randomised controlled trial: Study concludes L. reuteri not effective for infant colic, but findings may be limited by participants' heterogeneity. Evid Based Med. 2014;19(6):215.	Ineligible study design
Jadcherla SR, Slaughter JL, Stenger MR, Klebanoff M, Kelleher K, Gardner W. Practice Variance, Prevalence, and Economic Burden of Premature Infants Diagnosed With GERD. Hosp Pediatr. 2013;3(4):335-41.	Ineligible patient population
Johnson JD, Cocker K, Chang E. Infantile Colic: Recognition and Treatment. Am Fam Physician. 2015;92(7):577-82.	Literature review
Jordan B, Heine RG, Meehan M, Catto-Smith AG, Lubitz L. Effect of antireflux medication, placebo and infant mental health intervention on persistent crying: a randomized clinical trial. J Paediatr Child Health. 2006;42(1-2):49-58.	Ineligible population (babies with gastroesophageal reflux)

Record	Exclusion reason
Jordan GJ. Elimination communication as colic therapy. Med Hypotheses. 2014;83(3):282-5.	Ineligible study design
Khan ZA, Ahmad S, Sheikh MY. Gastro esophageal reflux: an over investigated entity in neonates and infants. JPMA J Pak Med Assoc. 2010;60(12):984-6.	Ineligible population (babies with gastroesophageal reflux)
Khoshoo V, Dhume P. Clinical response to 2 dosing regimens of lansoprazole in infants with gastroesophageal reflux. J Pediatr Gastroenterol Nutr. 2008;46(3):352-4.	Ineligible population (babies with gastroesophageal reflux)
Kirby CN, Segal AY, Hinds R, Jones KM, Piterman L. Infant gastro-oesophageal reflux disease (GORD): Australian GP attitudes and practices. J Paediatr Child Health. 2016;52(1):47-53.	Ineligible patient population
Koivusalo AI, Pakarinen MP, Wikstrom A, Rintala RJ. Assessment and treatment of gastroesophageal reflux in healthy infants with apneic episodes: a retrospective analysis of 87 consecutive patients. Clin Pediatr. 2011;50(12):1096-102.	Ineligible population (babies with gastroesophageal reflux)
Kokke FT, Scholtens PA, Alles MS, Decates TS, Fiselier TJ, Tolboom JJ, et al. A dietary fiber mixture versus lactulose in the treatment of childhood constipation: a double-blind randomized controlled trial. J Pediatr Gastroenterol Nutr. 2008;47(5):592-7.	Ineligible patient population
Koppen IJN, Lammers LA, Benninga MA, Tabbers MM. Management of Functional Constipation in Children: Therapy in Practice. Paediatr Drugs. 2015;17(5):349-60.	Ineligible study design
Korterink JJ, Ockeloen L, Benninga MA, Tabbers MM, Hilbink M, Deckers-Kocken JM. Probiotics for childhood functional gastrointestinal disorders: a systematic review and meta-analysis. Acta Paediatr. 2014;103(4):365-72.	Literature review
Kramer EA, den Hertog-Kuijl JH, van den Broek LM, van Leengoed E, Bulk AM, Kneepkens CM, et al. Defecation patterns in infants: a prospective cohort study. Arch Dis Child. 2015;100(6):533-6.	Ineligible study design: prevalence study
Kuizenga-Wessel S, Benninga MA, Tabbers MM. Reporting outcome measures of functional constipation in children from 0 to 4 years of age. J Pediatr Gastroenterol Nutr. 2015;60(4):446-56.	Literature review
Kurowski J, Kaur S, Katsogridakis Y, Wershil BK, Bass LM. Educational Module Improves Emergency Department Evaluation for Suspected Constipation. J Pediatr. 2015;167(3):706-10.e1.	Ineligible patient population
Landgren K, Hallstrom I. Parents' experience of living with a baby with infantile colic--a phenomenological hermeneutic study. Scand J Caring Sci. 2011;25(2):317-24.	Ineligible outcomes
Landgren K. Acupuncture in Practice: Investigating Acupuncturists' Approach to Treating Infantile Colic. Evid Based Complement Alternat Med. 2013. :Article ID 456712.	Ineligible outcomes
Landgren K, Tiberg I, Hallstrom I. Standardized minimal acupuncture, individualized acupuncture, and no acupuncture for infantile colic: study protocol for a multicenter randomized controlled trial - ACU-COL. BMC Altern Med. 2015;15:325.	Ineligible study design
Levitt MA, Pena A. Minimally invasive treatment of fecal incontinence and constipation in children. Minerva Chir. 2010;65(2):223-34.	Ineligible patient population
Liem O, Harman J, Benninga M, Kelleher K, Mousa H, Di Lorenzo C. Health utilization and cost impact of childhood constipation in the United States. J Pediatr. 2009;154(2):258-62.	Ineligible patient population
Litmanovitz I, Bar-Yoseph F, Lifshitz Y, Davidson K, Eliakim A, Regev RH, et al. Reduced crying in term infants fed high beta-palmitate formula: a double-blind randomized clinical trial. BMC Pediatr. 2014;14:152.	Ineligible patient population
Loening-Baucke V, Pashankar DS. A randomized, prospective, comparison study of polyethylene glycol 3350 without electrolytes and milk of magnesia for children with constipation and fecal incontinence. Pediatrics. 2006;118(2):528-35.	Ineligible patient population
Loots C, Kritas S, van Wijk M, McCall L, Peeters L, Lewindon P, et al. Body	Ineligible

Record	Exclusion reason
positioning and medical therapy for infantile gastroesophageal reflux symptoms. J Pediatr Gastroenterol Nutr. 2014;59(2):237-43.	population (babies with gastroesophageal reflux)
Martigne L, Delaage PH, Thomas-Delecourt F, Bonnelye G, Barthelemy P, Gottrand F. Prevalence and management of gastroesophageal reflux disease in children and adolescents: a nationwide cross-sectional observational study. Eur J Pediatr. 2012;171(12):1767-73.	Paediatric population
Maxted AE, Dickstein S, Miller-Loncar C, High P, Spritz B, Liu J, et al. Infant colic and maternal depression. Infant Ment Health J. 2005;26(1):56-68.	Ineligible outcomes
Miller J. Cry babies: A framework for chiropractic care. Clin Chiropr. 2007;10(3):139-46.	Ineligible study design
Miller J, Caprini Croci S. Cry baby, why baby? Beyond colic: Is it time to widen our views? J Clin Chiropr Pediatr. 2005;6:419-23.	Literature review
Miller JE. Costs of Routine Care for Infant Colic in the UK and Costs of Chiropractic Manual Therapy as a Management Strategy Alongside a RCT for this Condition. J Clin Chiropr Pediatr. 2013;14(1):1063-69.	Ineligible study design
Miyazawa R, Tomomasa T, Kaneko H, Arakawa H, Morikawa A. Effect of formula thickened with reduced concentration of locust bean gum on gastroesophageal reflux. Acta Paediatr. 2007;96(6):910-4.	Ineligible population (babies with gastroesophageal reflux)
Mugie SM, Di Lorenzo C, Benninga MA. Constipation in childhood. Nat Rev Gastroenterol Hepatol. 2011;8(9):502-11.	Literature review
Mugie SM, Korczowski B, Bodi P, Green A, Kerstens R, Ausma J, et al. Prucalopride is no more effective than placebo for children with functional constipation. Gastroenterology. 2014;147(6):1285-95.e1.	Ineligible patient population
Nel ED. Gastro-oesophageal reflux in infants and children. S Afr Fam Pract. 2013;54(5):414-17.	Literature review
Neu M, Schmiege SJ, Pan Z, Fehringer K, Workman R, Marcheggianni-Howard C, et al. Interactions during feeding with mothers and their infants with symptoms of gastroesophageal reflux. J Altern Complement Med. 2014;20(6):493-9.	Ineligible outcomes
Ngoenmak T, Treepongkaruna S, Buddharaksa Y, Khositseth A. Effects of Domperidone on QT Interval in Children with Gastroesophageal Reflux Disease. Pediatr neonatol. 2016;57(1):60-4.	Ineligible population (babies with gastroesophageal reflux)
Noviello C, Romano M, Zangari A, Papparella A, Martino A, Cobellis G. Management of severe constipation in children. Minerva Pediatr. 2013;65(2):193-8.	Ineligible patient population
Omari T, Davidson G, Bondarov P, Naucler E, Nilsson C, Lundborg P. Pharmacokinetics and acid-suppressive effects of esomeprazole in infants 1-24 months old with symptoms of gastroesophageal reflux disease. J Pediatr Gastroenterol Nutr. 2007;45(5):530-7.	Ineligible population (babies with gastroesophageal reflux)
Omari TI, Benninga MA, Sansom L, Butler RN, Dent J, Davidson GP. Effect of baclofen on esophagogastric motility and gastroesophageal reflux in children with gastroesophageal reflux disease: A randomized controlled trial. J Pediatr. 2006;149(4):468-74.e2.	Ineligible patient population
Osatakul S, Puetpaiboon A. Use of Rome II versus Rome III criteria for diagnosis of functional constipation in young children. Pediatr Int. 2014;56(1):83-8.	Prevalence study
Ostrom KM, Jacobs JR, Merritt RJ, Murray RD. Decreased regurgitation with a soy formula containing added soy fiber. Clin Pediatr (Phila). 2006;45(1):29-36.	Ineligible population (babies with gastroesophageal reflux)
Papadopoulou F, Tsampoulas C, Siomou E, Tzovara J, Siamopoulou A, Efremidis SC. Cyclic contrast-enhanced harmonic voiding urosonography for the evaluation of reflux. Can we keep the cost of the examination low? Eur Radiol. 2006;16(11):2521-6.	Ineligible patient population

Record	Exclusion reason
Phatak UP, Pashankar DS. Role of polyethylene glycol in childhood constipation. Clin Pediatr. 2014;53(10):927-32.	Ineligible study design
Quitadamo P, Miele E, Alongi A, Brunese FP, Di Cosimo ME, Ferrara D, et al. Italian survey on general pediatricians' approach to children with gastroesophageal reflux symptoms. Eur J Pediatr. 2015;174(1):91-6.	Ineligible population (babies with gastroesophageal reflux)
Rafati MR, Karami H, Salehifar E, Karimzadeh A. Clinical efficacy and safety of polyethylene glycol 3350 versus liquid paraffin in the treatment of pediatric functional constipation. DARU J Pharma Sci. 2011;19(2):154-58.	Ineligible patient population
Ratanamongkol P, Lertmaharit S, Jongpiputvanich S. Polyethylene glycol 4000 without electrolytes versus milk of magnesia for the treatment of Functional constipation in infants and young children: A randomized controlled trial. Asian Biomed. 2009;3(4):391-99.	Ineligible patient population
Reinthal M, Lund I, Lundeberg T. Acupuncture in baby colic. Accu Rel Ther. 2013;1(2-3):31-34.	Ineligible study design
Rodriguez LA, Flores A, Doody DP. Evaluation and Management of Intractable Constipation in Children. Semin Colon Rectal Surg. 2006;17(1):29-37.	Literature review
Rouster AS, Karpinski AC, Silver D, Monagas J, Hyman PE. Functional Gastrointestinal Disorders Dominate Pediatric Gastroenterology Outpatient Practice. J Pediatr Gastroenterol Nutr. 2016;62(6):847-51.	Prevalence study
Sacco O, Mattioli G, Girosi D, Battistini E, Jasonni V, Rossi GA. Gastroesophageal reflux and its clinical manifestation at gastroenteric and respiratory levels in childhood: physiology, signs and symptoms, diagnosis and treatment. Expert Rev Respir Med. 2007;1(3):391-401.	Literature review
Salvatore S, Hauser B, Salvatoni A, Vandenplas Y. Oral ranitidine and duration of gastric pH >4.0 in infants with persisting reflux symptoms. Acta Paediatr. 2006;95(2):176-81.	Ineligible population (babies with gastroesophageal reflux)
Saps M, Youssef N, Miranda A, Nurko S, Hyman P, Cocjin J, et al. Multicenter, randomized, placebo-controlled trial of amitriptyline in children with functional gastrointestinal disorders. Gastroenterology. 2009;137(4):1261-9.	Ineligible patient population
Semeniuk J, Kaczmarski M. Gastroesophageal reflux in children and adolescents. clinical aspects with special respect to food hypersensitivity. Adv Med Sci. 2006;51:327-35.	Ineligible patient population
Shanmuganathan S. Compliance by Australasian Paediatricians with the 2009 Naspghan-Espghan Guideline for the Diagnosis and Management of Gastro-Oesophageal Reflux in Children. Gastro Open Access. 2015;3(119):1-8.	Ineligible patient population
Steutel NF, Benninga MA, Langendam MW, de Kruijff I, Tabbers MM. Reporting outcome measures in trials of infant colic. J Pediatr Gastroenterol Nutr. 2014;59(3):341-6.	Literature review
Sullivan JS, Sundaram SS. Gastroesophageal reflux. Pediatr Rev. 2012;33(6):243-53.	Literature review
Sung V, Hiscock H, Tang M, Mensah FK, Heine RG, Stock A, et al. Probiotics to improve outcomes of colic in the community: protocol for the Baby Biotics randomised controlled trial. BMC Pediatr. 2012;12:135.	Ineligible study design
Suskind DL, Thompson DM, Gulati M, Huddleston P, Liu DC, Baroody FM. Improved infant swallowing after gastroesophageal reflux disease treatment: a function of improved laryngeal sensation? Laryngoscope. 2006;116(8):1397-403.	Ineligible population (babies with gastroesophageal reflux)
Tappin D, Nawaz S, McKay C, MacLaren L, Griffiths P, Mohammed TA. Development of an early nurse led intervention to treat children referred to secondary paediatric care with constipation with or without soiling. BMC Pediatr. 2013;13:193.	Ineligible patient population
Terblanche A. Gastro-oesphageal reflux disease in infants. S Afr Pharm J. 2010;78(7):24-26.	Literature review
Turco R, Miele E, Russo M, Mastroianni R, Lavorgna A, Paludetto R, et al. Early-life factors associated with pediatric functional constipation. J Pediatr Gastroenterol Nutr. 2014;58(3):307-12.	Prevalence study
Ummarino D, Miele E, Martinelli M, Scarpato E, Crocetto F, Sciorio E, et al.	Ineligible patient

Record	Exclusion reason
Effect of magnesium alginate plus simethicone on gastroesophageal reflux in infants. J Pediatr Gastroenterol Nutr. 2015;60(2):230-5.	population
Urganci N, Akyildiz B, Polat TB. A comparative study: the efficacy of liquid paraffin and lactulose in management of chronic functional constipation. Pediatr Int. 2005;47(1):15-9.	Ineligible patient population
Ustundag G, Kuloglu Z, Kirbas N, Kansu A. Can partially hydrolyzed guar gum be an alternative to lactulose in treatment of childhood constipation? Turk J Gastroenterol. 2010;21(4):360-4.	Ineligible patient population
Utokpat P, Chongsrisawat V. Management of functional gastrointestinal disorders in infants: A survey of pediatricians' perspective [Conference Abstract]. Neurogastroenterol Motil. 2014;26:78.	Conference abstract
van Sleuwen BE, L'Hoir MP, Engelberts AC, Busschers WB, Westers P, Blom MA, et al. Comparison of behavior modification with and without swaddling as interventions for excessive crying. J Pediatr. 2006;149(4):512-7.	Ineligible outcomes
van Tilburg MAL, Hyman PE, Walker L, Rouster A, Palsson OS, Kim SM, et al. Prevalence of functional gastrointestinal disorders in infants and toddlers. J Pediatr. 2015;166(3):684-9.	Paediatric population
van Wering HM, Tabbers MM, Benninga MA. Are constipation drugs effective and safe to be used in children? A review of the literature. Expert Opin Drug Saf. 2012;11(1):71-82.	Literature review
Varni JW, Bendo CB, Nurko S, Shulman RJ, Self MM, Franciosi JP, et al. Health-related quality of life in pediatric patients with functional and organic gastrointestinal diseases. J Pediatr. 2015;166(1):85-90.	Ineligible patient population
Vivatvakin B, Mahayosnond A, Theamboonlers A, Steenhout PG, Conus NJ. Effect of a whey-predominant starter formula containing LCPUFAs and oligosaccharides (FOS/GOS) on gastrointestinal comfort in infants. Asia Pac J Clin Nutr. 2010;19(4):473-80.	Ineligible patient population
Vlieger AM, Blink M, Tromp E, Benninga MA. Use of complementary and alternative medicine by pediatric patients with functional and organic gastrointestinal diseases: Results from a multicenter survey. Pediatrics. 2008;122(2):e446-e51.	Ineligible patient population
Vlieger AM, Benninga MA. Complementary therapies for pediatric functional gastrointestinal disorders. J Pediatr Gastroenterol Nutr. 2008;47(5):707-09.	Ineligible study design
Xinias I, Mouane N, Le Luyer B, Spiroglou K, Demertzidou V, Hauser B, et al. Cornstarch thickened formula reduces oesophageal acid exposure time in infants. Dig Liver Dis. 2005;37(1):23-7.	Ineligible population (babies with gastroesophageal reflux)
Xu M, Wang J, Wang N, Sun F, Wang L, Liu XH. The Efficacy and Safety of the Probiotic Bacterium Lactobacillus reuteri DSM 17938 for Infantile Colic: A Meta-Analysis of Randomized Controlled Trials. PLOS ONE. 2015;10(10):e0141445.	Literature review
Yang CH, Punati J. Practice patterns of pediatricians and trainees for the management of functional constipation compared with 2006 NASPGHAN guidelines. J Pediatr Gastroenterol Nutr. 2015;60(3):308-11.	Ineligible patient population
Yang M, Chen P-Y, Gong S-T, Lyman B, Geng L-L, Liu L-Y, et al. Cost-effectiveness analysis of an enteral nutrition protocol for children with common gastrointestinal diseases in China: good start but still a long way to go. JPEN J Parenter Enteral Nutr. 2014;38(2 Suppl):72S-6S.	Ineligible patient population
Young RJ, Beerman LE, Vanderhoof JA. Increasing oral fluids in chronic constipation in children. Gastroenterol Nurs. 1998;21(4):156-61.	Pre 2005 study
Zohalinezhad ME, Imanieh MH, Samani SM, Mohagheghzadeh A, Dehghani SM, Haghighat M, et al. Effects of Quince syrup on clinical symptoms of children with symptomatic gastroesophageal reflux disease: A double-blind randomized controlled clinical trial. Complement Ther Clin Pract. 2015;21(4):268-76.	Paediatric population