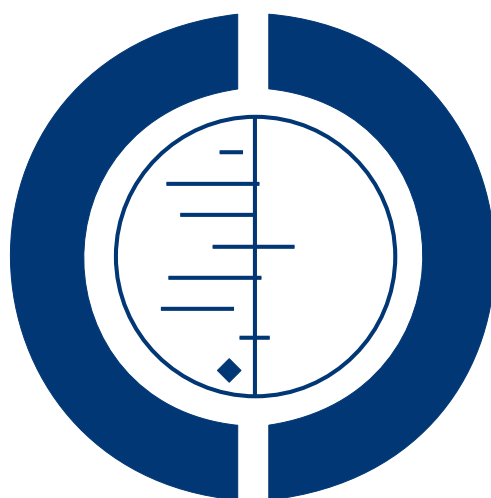


Transpyloric versus gastric tube feeding for preterm infants (Review)

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[Intervention Review]

Transpyloric versus gastric tube feeding for preterm infants

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ABSTRACT

Background

Enteral feeding tubes for preterm infants may be placed in the stomach (gastric tube feeding) or in the upper small bowel (transpyloric tube feeding). There are potential advantages and disadvantages to both routes.

Objectives

To determine the effect of feeding via the transpyloric route versus feeding via the gastric route on feeding tolerance, growth and development and adverse consequences in preterm infants who require enteral tube feeding.

Search strategy

The standard search strategy of the Cochrane Neonatal Review Group was used. This included electronic searches of MEDLINE and EMBASE (up to March 2007) and of The Cochrane Controlled Trials Register in The Cochrane Library (Issue 1, 2007), and searches of the references in previous reviews including cross references.

Selection criteria

Randomised or quasi-randomised controlled trials comparing transpyloric with gastric tube feeding in preterm infants.

Data collection and analysis

Data were extracted using the standard methods of the Cochrane Neonatal Review Group, with separate evaluation of trial quality and data extraction by each author and synthesis of data using relative risk (RR) and weighted mean difference (WMD).

Main results

Data from nine trials were available. No evidence of an effect on short term growth rates was found: weight: WMD -0.7 g/week (95% confidence interval (CI) -25.2, 23.8); crown heel length: WMD -0.7 mm/week (95% CI -2.4, 1.0); head circumference: WMD 0.6 mm/week (95% CI -0.9, 2.1). Longer term growth was reported in one study. There were not any statistically significant differences between the groups in the mean body weight or occipitofrontal head circumference at three months or at six months corrected age. None of the included studies provided data on neurodevelopmental outcomes. Transpyloric feeding was associated with a greater incidence of gastro-intestinal disturbance (RR 1.45, 95% CI 1.05, 2.09). There was some evidence that feeding via the transpyloric route increased mortality (RR 2.46, 95% CI 1.36, 4.46). However, the outcomes of the study that contributed most to this finding were likely to have been affected by selective allocation of the less mature and sicker infants to transpyloric feeding. No statistically significant differences in the incidence of other adverse events, including necrotising enterocolitis, intestinal perforation, and aspiration pneumonia was found.

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Authors' conclusions

No evidence of any beneficial effect of transpyloric feeding in preterm infants was found. However, evidence of adverse effects was noted. Feeding via the transpyloric route cannot be recommended for preterm infants.

PLAIN LANGUAGE SUMMARY

Transpyloric versus gastric tube feeding for preterm infants

Preterm infants often have poor co-ordination of sucking and swallowing and this can delay the establishment of safe oral feeding. Enteral feeds may be delivered through a catheter passed via the nose or the mouth into the stomach or upper small bowel. The review of trials found that babies receiving transpyloric tube feeding had more adverse effects, without any evidence of any increased benefit over gastric tube feeding.

BACKGROUND

Preterm infants often have poor co-ordination of sucking and swallowing and this can delay the establishment of safe oral feeding. Enteral feeds may be delivered through a catheter passed via the nose or the mouth into the stomach or upper small bowel.

In preterm infants the gastro-oesophageal valve is more lax and gastric peristalsis and emptying is less effective than in term infants (Berseeth 1989). Placement of the enteral feeding tube in the duodenum or jejunum (transpyloric route) ensures delivery of enteral feeds to the main sites of nutrient absorption, and has the theoretical advantage of decreasing the potential for oesophageal reflux and aspiration of milk into the lungs. However, feeding by the transpyloric route has potential problems. The gastric phase of the digestion is by-passed and secretion of upper intestinal hormones and growth factors may be impaired (Milner 1981). There is also a risk that potentially pathogenic organisms, which would have been removed in the acidic environment of the stomach, may be delivered to upper small bowel (Dellagrammaticas '83). These factors might contribute to an increased risk of necrotising enterocolitis in infants fed via the transpyloric route, as suggested by observational studies (Vazquez 1980; Vinocur 1990). Additionally, transpyloric feeding tubes are difficult to position and, unlike gastric tubes, the position of the transpyloric catheter must be confirmed with imaging. Following placement, the transpyloric tube may still migrate back to the stomach. Serious adverse events, including cases of intestinal perforation and of pyloric stenosis, have also been reported (Boros 1974; Raine 1982).

OBJECTIVES

To determine the effect of feeding via the transpyloric route versus feeding via the gastric route on feeding tolerance, growth and development and adverse consequences (death, gastro-intestinal disturbance including necrotising enterocolitis, aspiration pneumonia, chronic lung disease, pyloric stenosis) in preterm infants who require tube feeding.

METHODS

Criteria for considering studies for this review

Types of studies

Controlled trials utilizing either random or quasi-random patient allocation.

Types of participants

Preterm infants (less than 37 week's gestation) who require enteral tube feeding, cared for in a hospital setting.

Types of interventions

Trials comparing transpyloric versus gastric tube feeding with catheters passed via the nose or mouth. Trials of gastrostomy, duodenostomy, or jejunostomy feeding were not included. Trials in

which parenteral nutritional support was available during the period of advancement of enteral feeds were acceptable, provided that the groups received similar treatment other than the route of enteral feeding.

Types of outcome measures

Primary outcomes: Growth and development

1. Short term (prior to discharge from hospital) growth parameters: Weight gain, linear growth, head growth, skinfold thickness
2. Longer term (following discharge from hospital) growth parameters: Weight gain, linear growth, head growth, skinfold thickness
3. Neurodevelopmental outcomes during infancy and beyond using validated assessment tools: Neurological evaluations, developmental scores, and classifications of disability, including auditory and visual disability

Secondary outcomes:

1. Time, from birth, to establish full oral feeds, independently of parenteral fluids or nutrition or of enteral tube feeding
2. Time, from birth, to establish full enteral tube feeds, independently of parenteral fluids or nutrition
3. Adverse events:
 - a. Death before discharge from hospital
 - b. Gastrointestinal disturbance such as diarrhoea or feeding intolerance that results in cessation of enteral feeding
 - c. Necrotising enterocolitis
 - d. Aspiration pneumonia/pneumonitis: Clinical and/or radiological evidence of lower respiratory tract compromise that has been attributed to covert or evident aspiration of gastric contents
 - e. Chronic lung disease: defined as an additional oxygen requirement at 36 weeks corrected gestation.
 - f. Intestinal perforation
 - g. Pyloric stenosis requiring surgical intervention

There were no pre-planned subgroup analyses.

Search methods for identification of studies

The standard search strategy of the Cochrane Neonatal Review Group was used. This included electronic searches of the Cochrane Central Register of Controlled Trials (CENTRAL, The Cochrane Library, Issue 1, 2007), MEDLINE (1966 - March 2007), EMBASE (1980 - March 2007). The search strategy used the following text words and MeSH terms: [Infant-Newborn/, OR infan*, OR neonat*, OR prematur*, OR preterm], AND [Infant-Nutrition/, OR Feeding-Methods/, OR Intubation, Gastrointestinal/, OR gastric, OR transpyloric, OR nasoduodenal, OR nasojejunal. We limited the searches with the relevant filter for controlled trials. No language restriction was applied. References in studies identified as potentially relevant, and in previous reviews were examined.

Data collection and analysis

1. The studies identified by the above search strategy were screened (title and abstract) by the first review author. The full text of the report of each study identified as of potential relevance was re-screened by both review authors. These independent assessments followed pre-specified guidelines for inclusion. The decision to include or exclude a specific study was made by consensus of the two review authors.
2. The criteria and standard methods of the Cochrane Neonatal Review Group were used to assess the methodological quality of the included trials. Quality of the trials included was evaluated in terms of allocation concealment, blinding of parents or caregivers and assessors to intervention, and completeness of assessment in all randomised individuals. Additional information was requested from the authors of each trial to clarify methodology and results as necessary.
3. A data collection form was used to aid extraction of relevant information and data from each included study. Each review author extracted the data separately, compared data, and resolved differences by consensus.
4. The standard method of the Neonatal Review Group was used to synthesize the data. Heterogeneity between trial results was examined using the I^2 test for dichotomous outcomes and ANOVA for continuous outcomes. Effects were expressed as relative risk and 95% confidence interval and risk difference and 95% confidence interval for categorical data, weighted mean difference and 95% confidence interval for continuous data, fixed effect model for meta-analysis.

RESULTS

Description of studies

See: [Characteristics of included studies](#); [Characteristics of excluded studies](#).

Nine studies were included (Drew 1979; Laing 1986; Macdonald 1992; Pereira 1981; Pyati 1976; Roy 1977; Van Caillie 1975; Wells 1975; Whitfield 1982). These are described in the table, Characteristics of Included Studies. All of the included studies were undertaken in the 1970's or early 1980's. Most recruited very low birth weight infants (birth weight of less than 1500 g). However, only infants grown appropriately for gestational age were eligible for inclusion in most of the trials. In some trials infants who required respiratory or ventilatory support were not eligible for inclusion. Feeding by the allocated route was usually started in the first few days after birth when enteral feeds were commenced. Most feeding tubes used were made of silastic, polyvinyl, or polypropylene. The transpyloric tubes were placed in the second or third part of duodenum or the jejunum with the assistance of positioning of

the infant and peristalsis. In all of the trials the position of the tube was confirmed radiologically. All trials reported nutrient (usually energy) intake and short term growth as the primary outcomes. In most reports, data on adverse events (including death, necrotising enterocolitis, intestinal perforation, and aspiration pneumonia) were available.

Ten reports were excluded following inspection of the full report (Agarwal 1980; Avery 1977; Boros 1974; Celestin 1978; Cheek 1973; Chen 1974; Price 1978; Uauy 1975; Valman 1973; Wolfsdorf 1975) (see table, Characteristics of Excluded Studies).

Risk of bias in included studies

All of the trials were small, and none presented a power or sample size calculation. In the majority of the studies, allocation was not concealed; therefore, the assignment of infants to one or other feeding route could be predicted. This may have allowed bias in allocation of infants that could have affected the outcomes independently of the intervention. This may be of particular importance with regard to the largest of the included studies (Laing 1986), as discussed below. In the majority of studies, the intervention was not blind to the caregivers.

A further methodological issue that is important when considering the validity of the data in this review is the lack of complete follow up in the included trials. This is relevant mainly to the growth data. For adverse events, it proved possible to assemble a more complete data set from the majority of the published reports. In some of the studies infants who were allocated to the transpyloric feeding tube route, but in whom the tube could not be placed successfully, were excluded from the analysis of outcomes. This was a major problem in the largest study where only 16 of the 45 infants allocated to nasoduodenal feeding completed the study (Laing 1986).

Effects of interventions

TRANSPYLORIC VERSUS GASTRIC TUBE FEEDING FOR PRETERM INFANTS: GROWTH (COMPARISON 01):

Growth and development:

All of the included trials reported short term (prior to discharge from hospital) growth outcomes, but only three studies presented the data in a form that could be used in a meta-analysis (Laing 1986; Roy 1977; Van Caillie 1975). One study provided data on longer term (following discharge from hospital) growth (Whitfield 1982). None of the included studies provided data on neurodevelopmental outcomes during infancy or beyond.

a. Short term (prior to hospital discharge) weight gain (Outcome 01.01- 01.02):

Five trials reported no statistically significant differences in the rate of weight gain (Drew 1979; Laing 1986; Macdonald 1992; Pereira 1981; Roy 1977). Two trials found statistically significantly higher

rates of weight gain in the group allocated to transpyloric feeding (Van Caillie 1975; Wells 1975). Pyati 1976 reported that there was not a statistically significant difference in the mean weight of the groups at the end of the three weeks study period. Three studies provided data in a form that could be used in a meta-analysis (Macdonald 1992; Roy 1977; Van Caillie 1975). The combined data from these studies did not reveal a statistically significant difference; weighted mean difference: -0.7 g/week (95% confidence interval -25.2, 23.8).

Whitfield 1982 reported that the overall weight velocity from birth until reaching a weight of 1.5 kg, was statistically significantly higher in the gastric tube feeding group. As data were reported as grams/kilogram/day, these were not included in the meta-analysis.

b. Short term linear growth:

(i) Crown heel length (Outcome 01.03): In five of the included studies the investigators reported that they did not find any statistically significant difference in the rate of short term increase in crown heel length (Drew 1979; Laing 1986; Macdonald 1992; Pereira 1981; Roy 1977). Only three studies provided data in a form that could be used in a meta-analysis (Laing 1986; Macdonald 1992; Roy 1977). The combined data from these studies did not reveal a statistically significant difference in the rate of short term increase in crown heel length; weighted mean difference: -0.7 mm/week (95% confidence interval -2.4, 1.0).

(ii) Crown rump length (Outcome 01.04): Laing 1986 did not find any statistically significant difference in the rate of short term increase in crown rump length; mean difference: 1.0 mm/week (95% confidence interval -2.1, 4.1).

c. Short term head growth (Outcome 01.05): In five of the included studies the investigators reported that they did not find any statistically significant difference in the rate of short term increase in occipitofrontal head circumference (Drew 1979; Laing 1986; Macdonald 1992; Pereira 1981; Roy 1977). Only two reports provided data in a form that could be used in a meta-analysis (Laing 1986; Macdonald 1992). The combined data from these studies did not demonstrate a statistically significant difference in the rate of short term increase in head circumference; weighted mean difference: 0.6 mm/week (95% confidence interval -0.9, 2.1).

d. Short term change skinfold thickness (Outcome 01.06):

This was reported in one study (Roy 1977). The investigators did not find a statistically significant difference in the rate of gain of subscapular skinfold thickness in the infants fed via the nasogastric compared with the transpyloric route; mean difference: -0.2 mm/week (95% confidence interval -1.2, 0.8).

e. Longer term growth: Growth following hospital discharge was reported in only one of the included studies (Whitfield 1982). At the expected date of delivery, body weight and occipito-frontal head circumference were significantly less in the nasojejunal as compared to the nasogastric group; mean difference -0.3 kg (95% CI -0.6, -0.03), and -1.0 cm (95% CI -1.7, -0.3), respectively. At three months after the expected date of delivery, there were

no statistically significant differences between the groups in body weight; mean difference 0.2 kg (95% CI -0.2, 0.6) or occipito-frontal head circumference; mean difference 1.0 cm (95% CI -6.9, 8.9). Similarly at six months after the expected date of delivery, there were no statistically significant differences between the groups in body weight; mean difference 0.3 kg (95% CI -0.3, 0.9) or occipito-frontal head circumference; mean difference 3.0 cm (95% CI -6.5, 12.5). However, there was considerable loss to follow-up, mainly in the transpyloric feeding group where 12 of the recruited 28 infants were not assessed at 6 months post-expected date of delivery.

Secondary outcomes:

1. Time to establish full oral feeds.

This outcome was not reported by any of the included studies.

2. Time to establish full enteral tube feeds.

This outcome was reported by [Macdonald 1992](#) and by [Pereira 1981](#). These investigators did not find any statistically significant difference in the length of time required to achieve full enteral feeding. However, the data were presented without standard deviations and could not be used in a meta-analysis.

TRANSPYLORIC VERSUS GASTRIC TUBE FEEDING FOR PRETERM INFANTS: ADVERSE EVENTS (COMPARISON 02):

Seven of the included trials reported data on adverse events including death, necrotising enterocolitis, gastrointestinal disturbance, aspiration pneumonia, and intestinal perforation. Adverse events were often reported as withdrawal criteria, rather than as pre-defined outcome measures. Although there was often incomplete follow-up of recruited infants with regard to growth data, in the majority of the reports we have been able to determine the incidence of adverse events for the complete or near complete cohort.

a. Death before discharge from hospital (**Outcome 02.01**): Six trials reported this outcome ([Drew 1979](#); [Laing 1986](#); [Macdonald 1992](#); [Van Caillie 1975](#); [Wells 1975](#); [Whitfield 1982](#)). Only [Laing 1986](#), the largest trial, found that nasojejunal feeding was associated with a statistically significantly higher mortality rate: Relative risk: 2.7 (95% confidence interval 1.2, 6.0); risk difference: 0.3 (95% confidence interval 0.1, 0.5). The other trials did not find any statistically significant difference in mortality. The data from the six trials were combined in a meta-analysis. There was a statistically significantly higher rate of death in the infants who were fed via the transpyloric route: Relative risk: 2.5 (95% confidence interval 1.4, 4.5); risk difference: 0.16 (95% confidence interval 0.07, 0.26).

In a sensitivity analysis (**Outcome 02.02**), [Laing 1986](#) was excluded because of the differences in the baseline characteristics of the feeding groups. When only the remaining five studies were included in the meta-analysis, the increase in mortality in the transpyloric group was not quite statistically significant: Relative risk: 2.2 (95% confidence interval 0.9, 5.4); risk difference: 0.1 (95% confidence interval 0.00, 0.2).

b. Gastrointestinal disturbance such as diarrhoea or feeding intolerance (**Outcome 02.03**): Seven trials reported this outcome ([Drew 1979](#); [Laing 1986](#); [Macdonald 1992](#); [Pereira 1981](#); [Roy 1977](#); [Van Caillie 1975](#); [Whitfield 1982](#)). None of the individual trials found any statistically significant difference in the incidence of gastrointestinal disturbance. However a meta-analysis of the studies demonstrated a statistically significantly increased risk of gastrointestinal disturbance in the infants fed via the transpyloric route: Relative risk: 1.5 (95% confidence interval 1.1, 2.1); risk difference: 0.1 (95% confidence interval 0.02, 0.17).

In a sensitivity analysis (**Outcome 02.04**), removing [Laing 1986](#), there remained a statistically significant difference in the incidence of gastrointestinal disturbance: Relative risk: 1.4 (95% confidence interval 1.02, 2.0); risk difference: 0.1 (95% confidence interval 0.01, 0.21).

c. Necrotising enterocolitis (**Outcome 02.05**): Seven trials ([Drew 1979](#); [Laing 1986](#); [Macdonald 1992](#); [Pereira 1981](#); [Van Caillie 1975](#); [Wells 1975](#); [Whitfield 1982](#)) reported this outcome. None of the individual trials, nor a meta-analysis of the studies, found any statistically significant difference in the incidence of necrotising enterocolitis: Relative risk: 0.6 (95% confidence interval 0.3, 1.5); risk difference: -0.03 (95% confidence interval -0.09, 0.03).

In a sensitivity analysis (**Outcome 02.06**), [Laing 1986](#), there was not any statistically significant difference in the incidence of necrotising enterocolitis: Relative risk: 0.9 (95% confidence interval 0.3, 2.6); risk difference: -0.01 (95% confidence interval -0.08, 0.06).

d. Aspiration pneumonia/pneumonitis (**Outcome 02.07**): Four trials ([Drew 1979](#); [Macdonald 1992](#); [Pereira 1981](#); [Pyati 1976](#); [Van Caillie 1975](#)) reported this outcome. None of the individual trials, nor a meta-analysis of the studies, found any statistically significant difference in the incidence of aspiration pneumonia/pneumonitis. Meta-analysis: Relative risk: 1.35 (95% confidence interval 0.44, 4.14); risk difference: 0.02 (95% confidence interval -0.06, 0.1).

e. Chronic lung disease: This outcome was not reported in any of the trials

f. Intestinal perforation (**Outcome 02.08**): Four trials ([Pereira 1981](#); [Roy 1977](#); [Van Caillie 1975](#); [Whitfield 1982](#)) reported this outcome. Of the 129 infants studied, there was only one reported case of intestinal perforation. None of the individual trials, nor a meta-analysis of the studies, found any statistically significant difference in the incidence of aspiration pneumonia: Meta-analysis: Relative risk: 2.3 (95% confidence interval 0.1, 50.1); risk difference: 0.01 (95% confidence interval -0.05, 0.08).

g. Pyloric stenosis: This outcome was not reported in any of the trials

DISCUSSION

We did not find any evidence of benefit for the transpyloric compared with the gastric route for preterm infants who need enteral tube feeding. We did find some evidence that transpyloric feeding is associated with increased mortality. However, many of the studies included in the review had a variety of methodological weaknesses, and this finding should be interpreted with caution. In particular, the outcomes for Laing 1986 may have been affected by preferential allocation of some of the less mature or sicker infants to the transpyloric feeding route. When this study was excluded from the meta-analysis the increase in mortality in the transpyloric group was not quite statistically significant.

The incidence of gastrointestinal disturbance that results in cessation of enteral feeding was found to be statistically significantly higher in infants fed via the transpyloric route in a meta-analysis of the studies that reported these outcomes. This finding remained when Laing 1986 was removed in a sensitivity analysis. It should be noted that “gastrointestinal disturbance” included a variety of clinical problems such as abdominal distention, gastric bleeding, bilious vomiting, and diarrhoea. We did not detect any statistically significant differences in the incidences of necrotising enterocolitis or intestinal perforation between the feeding groups. Additionally, although it may be pragmatic to compare continuous transpyloric feeding with intermittent or bolus gastric feeding, as was the case in seven of the included studies, it should be noted that this covariable may also have affected the outcomes. The Cochrane review that compared continuous nasogastric tube feeding versus intermittent bolus feeding for very low birth weight preterm infants did not find any evidence of an effect on the incidence of necrotising enterocolitis. However, the review authors concluded that the clinical benefits and risks of continuous versus intermittent nasogastric tube feeding could not be reliably discerned from the available data from randomised trials (Premji 2002).

We did not find any evidence that feeding via the transpyloric route versus the gastric route results in higher rates of growth in preterm infants who require tube feeding. However, in many of the trials the growth data from infants who developed complications during the study period, or in whom enteral tube placement was unsuccessful, were not reported. In the largest included trial only 41 of the 80 infants who entered the study were included in the growth data analysis (Laing 1986). In Drew 1979, of the 66 infants allocated to a feeding route, there were outcome data for only 44

infants. Given these levels of loss to follow up, the findings should be treated with caution. For example, it may be that the repeated failed attempts to position the transpyloric tube introduces a delay in starting or establishing nutritional input. Since it is plausible that such delay may affect growth, the findings may have been different in a true intention-to-treat analysis.

A clinically plausible putative benefit of transpyloric tube feeding is a reduced risk of aspiration pneumonia. This review did not find any evidence that this is the case. The narrow 95% confidence intervals, estimating the effect to lie between a 5% reduction in risk and a 10% increase in risk, suggest that a modest effect on aspiration pneumonia has not been missed.

Finally, although the majority of the trials recruited infants of birth weight less than 1500 g, in seven of the trials intra-uterine growth restricted infants were excluded. This sub-population may be at increased risk of adverse events that may be related to the enteral feeding regime, such as necrotising enterocolitis (McDonnell 1994). The exclusion of these infants is another factor that limits the applicability of the findings of this review.

AUTHORS' CONCLUSIONS

Implications for practice

The available data suggest that the transpyloric route should not be used for preterm infants who require enteral tube feeding.

Implications for research

Even if the concerns regarding an effect on mortality are discounted, the lack of evidence of an effect on growth and the finding of an increased risk of gastrointestinal disturbance suggest that a randomised controlled trial of transpyloric versus gastric tube feeding in preterm infants is not a priority.

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Vinocur 1990

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McGuire W, McEwan P. Transpyloric versus gastric tube feeding for preterm infants. *Cochrane Database of Systematic Reviews* 2002, Issue 3. [DOI: 10.1002/14651858.CD003487]

* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

Characteristics of included studies [ordered by study ID]

Drew 1979

Methods	Blinding of randomisation: No (alternate) Blinding of intervention: No Complete follow-up: No Blinding of outcome measurement: No
Participants	66 appropriate for gestational age infants of birth weight less than 1500 g. Infants who were receiving assisted ventilation were not included. University of Melbourne, Australia, 1974- 1977.
Interventions	Nasojejunal (N= 32) versus nasogastric feeding (N=34) until achieving an enteral intake of 200 ml/kg/day.
Outcomes	Gain in weight, length and head circumference prior to hospital discharge, calorie intake, and adverse events (including death, necrotising enterocolitis, intestinal perforation, and aspiration pneumonia).
Notes	Nasojejunal group: - 11 infants withdrawn after allocation; one required assisted ventilation, 10 because of failure to pass the feeding tube Nasogastric group: - 11 infants withdrawn after allocation; five required assisted ventilation, four died within 24 hours, two had "insufficient data to compute".

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	No	C - Inadequate

Laing 1986

Methods	Blinding of randomisation: No (alternate) Blinding of intervention: No Complete follow-up: No Blinding of outcome measurement: No
Participants	100 infants allocated, of whom 80 were included. These were infants of birth weight less than 1500 g (and appropriate for gestational age-between the 10th and the 90th centile for birth weight). University of Edinburgh, 1982-1984.
Interventions	Continuous nasoduodenal (N= 45) versus intermittent nasogastric tube feeding (N=35) for seven weeks.
Outcomes	Weight and length gain, and head growth prior to hospital discharge, and adverse events (including death, necrotising enterocolitis, intestinal perforation, and aspiration pneumonia).

Laing 1986 (Continued)

Notes	<p>There were statistically significant differences in the baseline characteristics of the two cohorts that may have affected clinical outcomes. The group of infants who were allocated to nasoduodenal feeding were of statistically significantly lower gestational age, and had statistically significantly lower Apgar scores at 1 minute and at 5 minutes. It seems unlikely that these differences were due to chance. We consider that because of the lack of allocation concealment it is likely that some of the less mature and sicker infants were allocated preferentially to nasoduodenal feeding.</p> <p>Growth data were reported only for infants who had successfully tolerated the allocated feeding route: 16 of the 45 infants allocated to the nasoduodenal route, and 25 of the 35 infants allocated to the nasogastric route.</p> <p>In this review, the data on adverse events on all 80 infants included have been extracted from the report.</p>
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Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	No	C - Inadequate

Macdonald 1992

Methods	<p>Blinding of randomisation: Yes Blinding of intervention: No Complete follow-up: No Blinding of outcome measurement: No</p>
Participants	43 infants of birth weight less than 1400 g. Infants who were to be fed with expressed human breast milk were excluded from the trial.
Interventions	Continuous nasoduodenal tube feeding (N= 15) versus bolus nasogastric (N= 15) or continuous nasogastric (N=13) tube feeding until a weight of 1600 g was attained.
Outcomes	Gain in weight, head circumference, and length in surviving infants until 36 week's gestation, calorie intake, time to achieve enteral feeding, plasma albumin, transferrin, urea, and alkaline phosphatase levels, and adverse events (including necrotising enterocolitis, intestinal perforation, and aspiration pneumonia)
Notes	<p>The data from the bolus nasogastric and continuous nasogastric feeding groups have been combined in this review.</p> <p>The number of infants who died in each group is reported, although this does not appear to have been a primary outcome measure in the study. Growth data are reported only for those infants who survived to the end of the study period.</p> <p>Transpyloric group: 15 infants allocated</p> <ul style="list-style-type: none"> - 10 infants completed study - growth data available - 3 infants died before milk feeding established - no growth data available - 1 infant transferred to another hospital - no growth data available - 1 infant failure to position tube - no growth data available <p>Nasogastric group: 28 infants (13 in the continuous NG feed group, 15 in the bolus NG feed group)</p> <ul style="list-style-type: none"> - 24 "completed study" - growth data available - 3 infants died before milk feeding established - no growth data available

Macdonald 1992 (Continued)

	- 1 infant transferred to another hospital - no growth data available
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Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Yes	A - Adequate

Pereira 1981

Methods	Blinding of randomisation: Can't tell Blinding of intervention: No Complete follow-up: Can't tell Blinding of outcome measurement: No
Participants	53 infants of birth weight less than 1700 g or of gestational age less than 33 completed weeks.
Interventions	Continuous nasojejunal (N=26) versus intermittent nasogastric tube feeding (N=27) until breast feeding was established.
Outcomes	Weight gain and head growth prior to hospital discharge, calorie intake, and adverse events (including death, necrotising enterocolitis, intestinal perforation, and aspiration pneumonia).
Notes	There were not any standard deviations reported with the growth velocity data.

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Unclear	B - Unclear

Pyati 1976

Methods	Blinding of randomisation: Can't tell Blinding of intervention: No Complete follow-up: Can't tell Blinding of outcome measurement: No
Participants	19 infants of birth weight less than 1500 g. All participants were of birth weight 'appropriate for gestational age'.
Interventions	Continuous nasojejunal (N=8) versus nasogastric feeding (N=11) with standard-calorie formula milk started within 30 hours after birth and continued until 3 weeks after birth.
Outcomes	Calorie intake and weight gain until 3 weeks after birth.
Notes	There were limited numerical data reported. We have not been able to contact the investigators to obtain any unpublished data.

Pyati 1976 (Continued)

<i>Risk of bias</i>		
Item	Authors' judgement	Description
Allocation concealment?	Unclear	D - Not used

Roy 1977

Methods	Blinding of randomisation: Can't tell Blinding of intervention: No Complete follow-up: No Blinding of outcome measurement: No
Participants	21 infants of birth weight less than 1500 g, and appropriate for gestational age. Infants who required assisted ventilation or phototherapy were excluded.
Interventions	Continuous nasojejunal (N=12) versus intermittent nasogastric tube feeding (N=9) for 7 days.
Outcomes	Gain in weight, length and skinfold thickness prior to hospital discharge, and stool frequency.
Notes	3 infants in the nasojejunal tube feeding group who developed complications were withdrawn, and not included in the growth comparison. One infant was withdrawn because of persistent displacement of the tube back to the stomach. A second infant developed "transitory but extensive abdominal distention". Since it is unclear whether this complication resulted in cessation of enteral feeding, we have not classified this as an adverse event. The third infant developed peritonitis following duodenal perforation (confirmed at laparotomy).

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Unclear	B - Unclear

Van Caillie 1975

Methods	Blinding of randomisation: No (alternate) Blinding of intervention: No Complete follow-up: Yes Blinding of outcome measurement: No
Participants	11 preterm infants of birthweight less than 1300 g. University of Texas, USA. Early 1970's.
Interventions	Allocated alternately to continuous nasoduodenal (N=6) versus continuous nasogastric tube feeding (N=5) for 40 days.

Van Caillie 1975 (Continued)

Outcomes	Weight gain prior to hospital discharge, calorie intake, adverse events (including death, necrotising enterocolitis, intestinal perforation, and aspiration pneumonia).	
Notes	The report gives outcome data on all infants who entered the study. However, one of the infants who had been allocated to nasoduodenal feeding died at aged 30 hours. This infant was included in the analysis of adverse outcomes, but not included in the calculations of short term growth parameters presented by the investigators.	
Risk of bias		
Item	Authors' judgement	Description
Allocation concealment?	No	C - Inadequate

Wells 1975

Methods	Blinding of randomisation: No (alternate) Blinding of intervention: No Complete follow-up: No Blinding of outcome measurement: No	
Participants	22 infants of birth weight less than 1500 g and of gestational age less than 32 completed weeks.	
Interventions	Continuous nasojejunal (N=11) versus intermittent nasogastric tube feeding (N=11) for 21 days.	
Outcomes	Weight gain for the 21 days study period, calorie intake, and adverse events (death, necrotising enterocolitis)	
Notes	Three of the infants who had been allocated to the nasogastric feeding group were switched during the study to nasojejunal feeding because of concern about the level of calorie intake. These infants were not included in the analysis of growth rates. There were insufficient data for one other infant, who had been allocated to nasojejunal feeding, to be included in the analysis of growth outcomes presented in the report.	
Risk of bias		
Item	Authors' judgement	Description
Allocation concealment?	No	C - Inadequate

Whitfield 1982

Methods	Blinding of randomisation: No (alternate months) Blinding of intervention: No Complete follow-up: No Blinding of outcome measurement: No	
Participants	44 appropriate for gestational age preterm infants of birth weight 1000 - 1500 g.	
Interventions	Continuous nasojejunal (N=28) versus intermittent nasogastric tube feeding (N=16) until attaining a weight of 1500 g.	
Outcomes	Weight gain and head growth until six months old, and adverse events (death, necrotising enterocolitis, intestinal perforation).	
Notes	<p>Short term weight gain data are presented for only those infants with birth weight less than 1.4 kg - i.e. these data are not presented for infants of birth weight 1.4 - 1.5 kg</p> <ul style="list-style-type: none"> - Transpyloric group: 20 infants - NG group: 10 infants <p>2. Longer term growth data: presented for infants for whom a weight at the expected data of delilvery was available:</p> <p>At EDD:</p> <ul style="list-style-type: none"> - Transpyloric group: 21 infants available for follow up (4 infants had died, 2 infants had been transferred to another hospital, 1 infant had been "withdrawn" because of "intractable abdominal distension", and the reason for the non-availability of the unaccounted for infant is unclear from the report). - NG group: 15 infants available for follow up (1 infant had been transferred to another hospital) <p>At EDD +3 months - further loss to follow up occurred, leaving:</p> <ul style="list-style-type: none"> - Transpyloric group: 18 infants available for evaluation - NG group: 15 infants available for evaluation <p>At EDD + 6 months - further loss to follow up occurred, leaving:</p> <ul style="list-style-type: none"> - Transpyloric group: 16 infants available for evaluation - NG group: 15 infants available for evaluation 	
<i>Risk of bias</i>		
Item	Authors' judgement	Description
Allocation concealment?	No	C - Inadequate

Characteristics of excluded studies [ordered by study ID]

Agarwal 1980	Although not apparent from the title, this is not a report of either a randomised or quasi-randomised trial.
Avery 1977	Although not apparent from the title, this is not a report of either a randomised or quasi-randomised trial.
Boros 1974	Although not apparent from the title, this is not a report of either a randomised or quasi-randomised trial.

(Continued)

Celestin 1978	Although not apparent from the title, this is not a report of either a randomised or quasi-randomised trial.
Cheek 1973	Although not apparent from the title, this is not a report of either a randomised or quasi-randomised trial.
Chen 1974	Although not apparent from the title, this is not a report of either a randomised or quasi-randomised trial.
Price 1978	Although not apparent from the title, this is not a report of either a randomised or quasi-randomised trial.
Uauy 1975	Reported as an abstract only, this is described as a “controlled study”, but is unlikely to represent a report of a randomised or quasi-randomised trial.
Valman 1973	Although not apparent from the title, this is not a report of either a randomised or quasi-randomised trial.
Wolfsdorf 1975	Although not apparent from the title or abstract, this is not a report of a randomised or quasi-randomised trial.

DATA AND ANALYSES

Comparison 1. Transpyloric versus gastric tube feeding for preterm infants: Growth

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Change in weight (g/week)	3	63	Mean Difference (IV, Fixed, 95% CI)	-0.69 [-25.17, 23.79]
2 Change in weight (g/kg/week)	1	30	Mean Difference (IV, Fixed, 95% CI)	-18.0 [-28.15, -7.85]
3 Change in crown heel length (mm/week)	3	93	Mean Difference (IV, Fixed, 95% CI)	-0.67 [-2.36, 1.02]
4 Change in crown rump length (mm/week)	1	41	Mean Difference (IV, Fixed, 95% CI)	1.0 [-2.11, 4.11]
5 Change in occipito-frontal head circumference (mm/week)	2	75	Mean Difference (IV, Fixed, 95% CI)	0.56 [-0.95, 2.08]
6 Change in subscapular skinfold thickness (mm/week)	1	18	Mean Difference (IV, Fixed, 95% CI)	-0.20 [-1.18, 0.78]

Comparison 2. Transpyloric versus gastric tube feeding for preterm infants: Adverse events

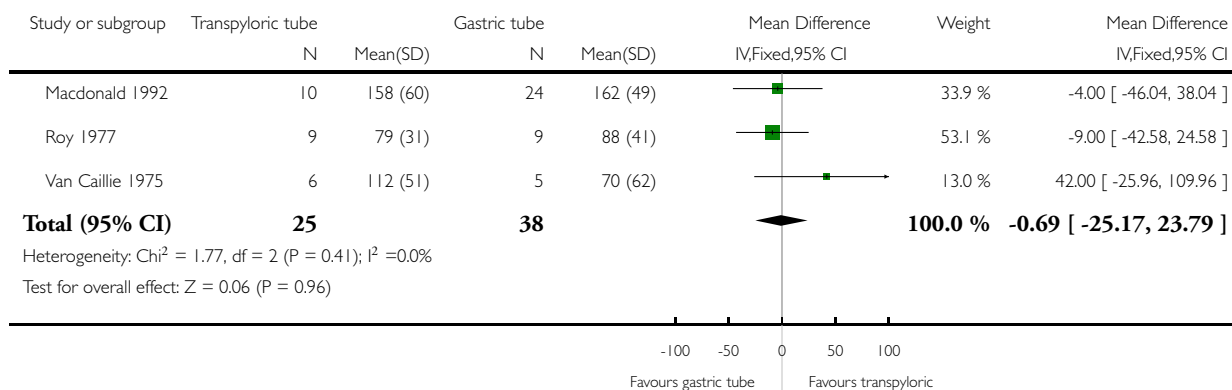
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Death prior to hospital discharge	6	245	Risk Ratio (M-H, Fixed, 95% CI)	2.46 [1.36, 4.46]
2 Death prior to hospital discharge (excluding Laing 1986)	5	165	Risk Ratio (M-H, Fixed, 95% CI)	2.19 [0.89, 5.35]
3 Gastrointestinal disturbance (including diarrhoea) prior to hospital discharge	7	297	Risk Ratio (M-H, Fixed, 95% CI)	1.48 [1.05, 2.09]
4 Gastrointestinal disturbance (including diarrhoea) prior to hospital discharge (excluding Laing 1986)	6	217	Risk Ratio (M-H, Fixed, 95% CI)	1.43 [1.02, 2.01]
5 Necrotising enterocolitis prior to hospital discharge	7	298	Risk Ratio (M-H, Fixed, 95% CI)	0.63 [0.26, 1.53]
6 Necrotising enterocolitis prior to hospital discharge (excluding Laing 1986)	6	218	Risk Ratio (M-H, Fixed, 95% CI)	0.91 [0.32, 2.58]
7 Aspiration pneumonia prior to hospital discharge	5	171	Risk Ratio (M-H, Fixed, 95% CI)	1.35 [0.44, 4.14]
8 Intestinal perforation prior to hospital discharge	4	129	Risk Ratio (M-H, Fixed, 95% CI)	2.31 [0.10, 50.85]

Analysis 1.1. Comparison 1 Transpyloric versus gastric tube feeding for preterm infants: Growth, Outcome 1 Change in weight (g/week).

Review: Transpyloric versus gastric tube feeding for preterm infants

Comparison: 1 Transpyloric versus gastric tube feeding for preterm infants: Growth

Outcome: 1 Change in weight (g/week)

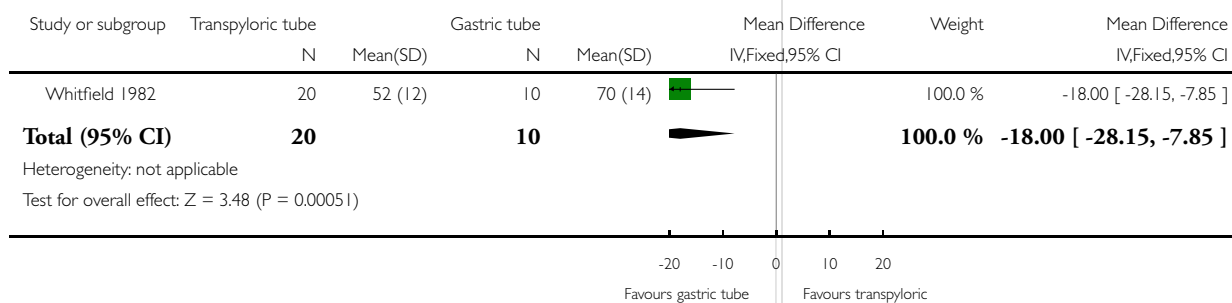


Analysis 1.2. Comparison 1 Transpyloric versus gastric tube feeding for preterm infants: Growth, Outcome 2 Change in weight (g/kg/week).

Review: Transpyloric versus gastric tube feeding for preterm infants

Comparison: 1 Transpyloric versus gastric tube feeding for preterm infants: Growth

Outcome: 2 Change in weight (g/kg/week)

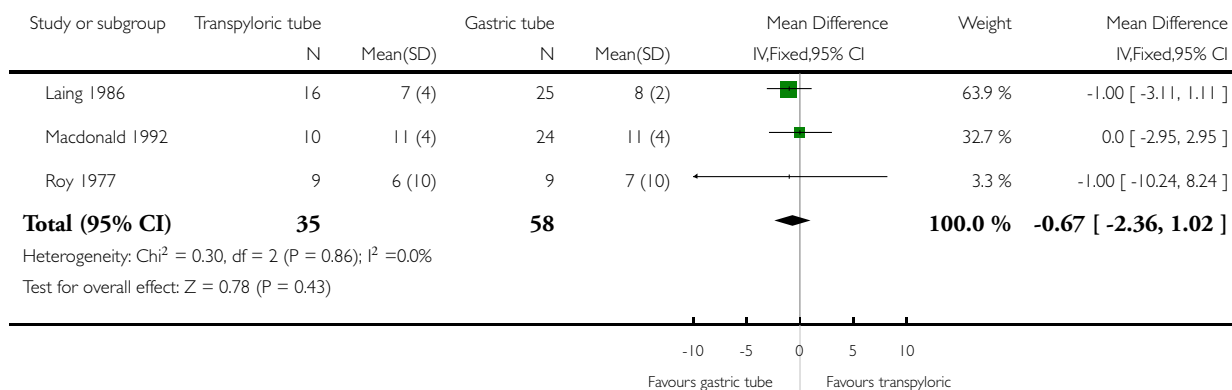


Analysis 1.3. Comparison 1 Transpyloric versus gastric tube feeding for preterm infants: Growth, Outcome 3 Change in crown heel length (mm/week).

Review: Transpyloric versus gastric tube feeding for preterm infants

Comparison: 1 Transpyloric versus gastric tube feeding for preterm infants: Growth

Outcome: 3 Change in crown heel length (mm/week)

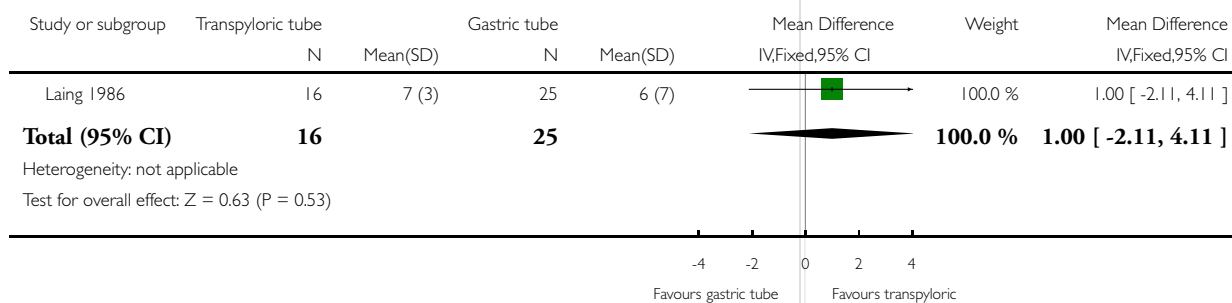


Analysis 1.4. Comparison 1 Transpyloric versus gastric tube feeding for preterm infants: Growth, Outcome 4 Change in crown rump length (mm/week).

Review: Transpyloric versus gastric tube feeding for preterm infants

Comparison: 1 Transpyloric versus gastric tube feeding for preterm infants: Growth

Outcome: 4 Change in crown rump length (mm/week)

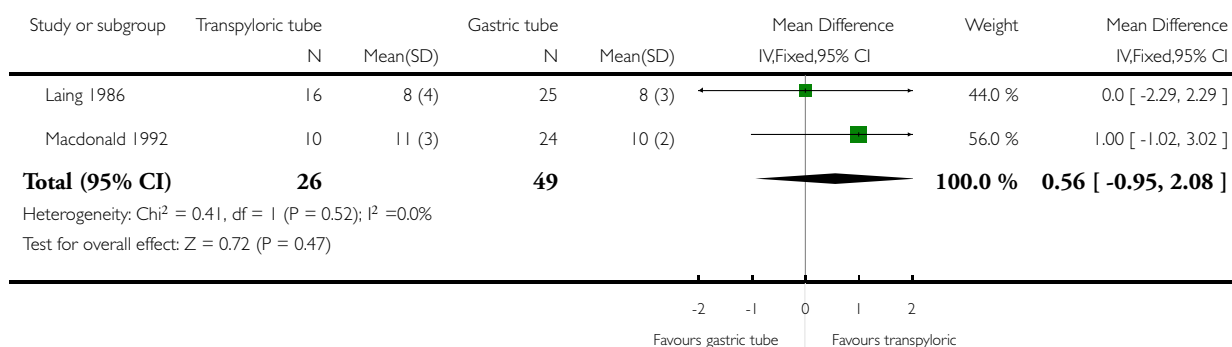


Analysis 1.5. Comparison 1 Transpyloric versus gastric tube feeding for preterm infants: Growth, Outcome 5 Change in occipito-frontal head circumference (mm/week).

Review: Transpyloric versus gastric tube feeding for preterm infants

Comparison: 1 Transpyloric versus gastric tube feeding for preterm infants: Growth

Outcome: 5 Change in occipito-frontal head circumference (mm/week)

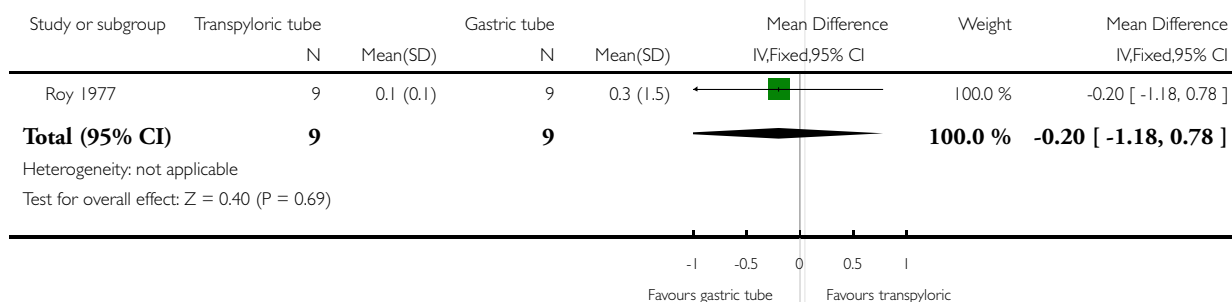


Analysis 1.6. Comparison 1 Transpyloric versus gastric tube feeding for preterm infants: Growth, Outcome 6 Change in subscapular skinfold thickness (mm/week).

Review: Transpyloric versus gastric tube feeding for preterm infants

Comparison: 1 Transpyloric versus gastric tube feeding for preterm infants: Growth

Outcome: 6 Change in subscapular skinfold thickness (mm/week)

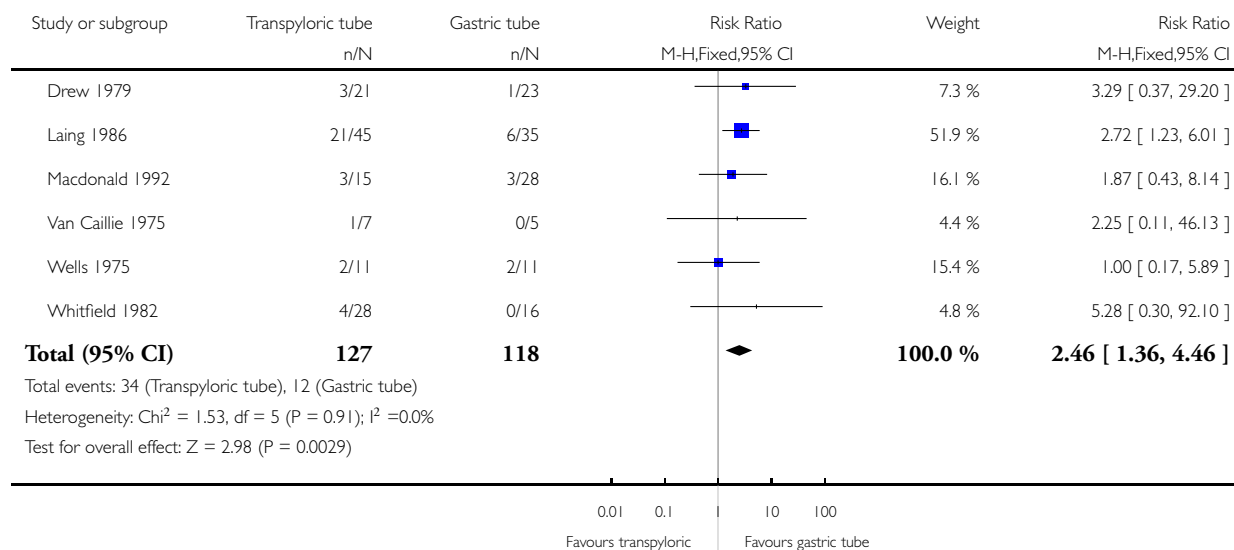


Analysis 2.1. Comparison 2 Transpyloric versus gastric tube feeding for preterm infants: Adverse events, Outcome 1 Death prior to hospital discharge.

Review: Transpyloric versus gastric tube feeding for preterm infants

Comparison: 2 Transpyloric versus gastric tube feeding for preterm infants: Adverse events

Outcome: 1 Death prior to hospital discharge

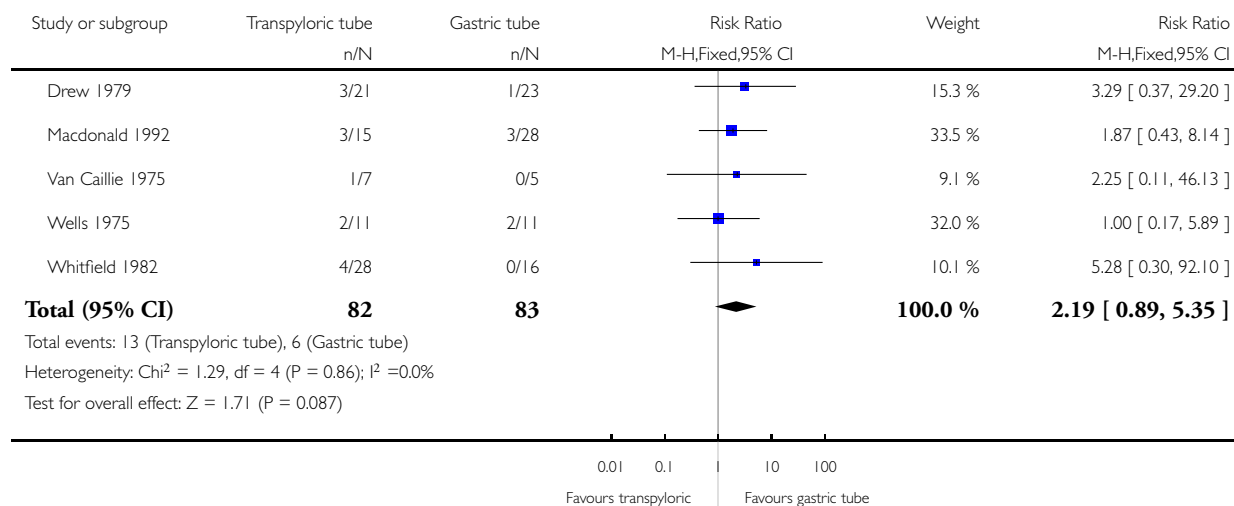


Analysis 2.2. Comparison 2 Transpyloric versus gastric tube feeding for preterm infants: Adverse events, Outcome 2 Death prior to hospital discharge (excluding Laing 1986).

Review: Transpyloric versus gastric tube feeding for preterm infants

Comparison: 2 Transpyloric versus gastric tube feeding for preterm infants: Adverse events

Outcome: 2 Death prior to hospital discharge (excluding Laing 1986)

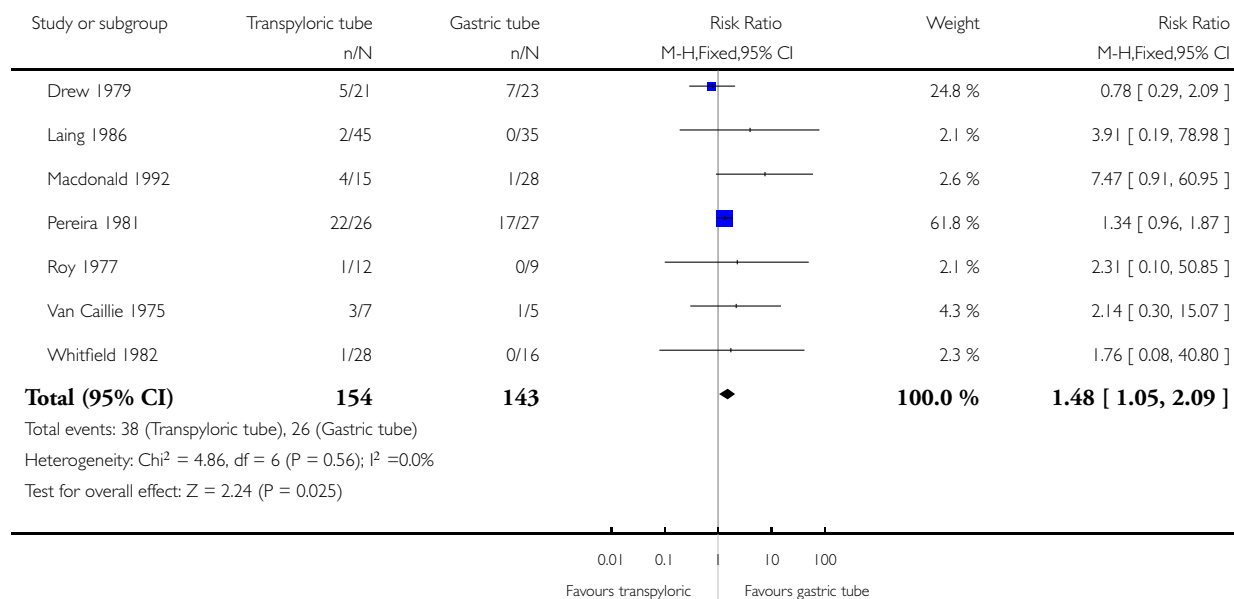


Analysis 2.3. Comparison 2 Transpyloric versus gastric tube feeding for preterm infants: Adverse events, Outcome 3 Gastrointestinal disturbance (including diarrhoea) prior to hospital discharge.

Review: Transpyloric versus gastric tube feeding for preterm infants

Comparison: 2 Transpyloric versus gastric tube feeding for preterm infants: Adverse events

Outcome: 3 Gastrointestinal disturbance (including diarrhoea) prior to hospital discharge

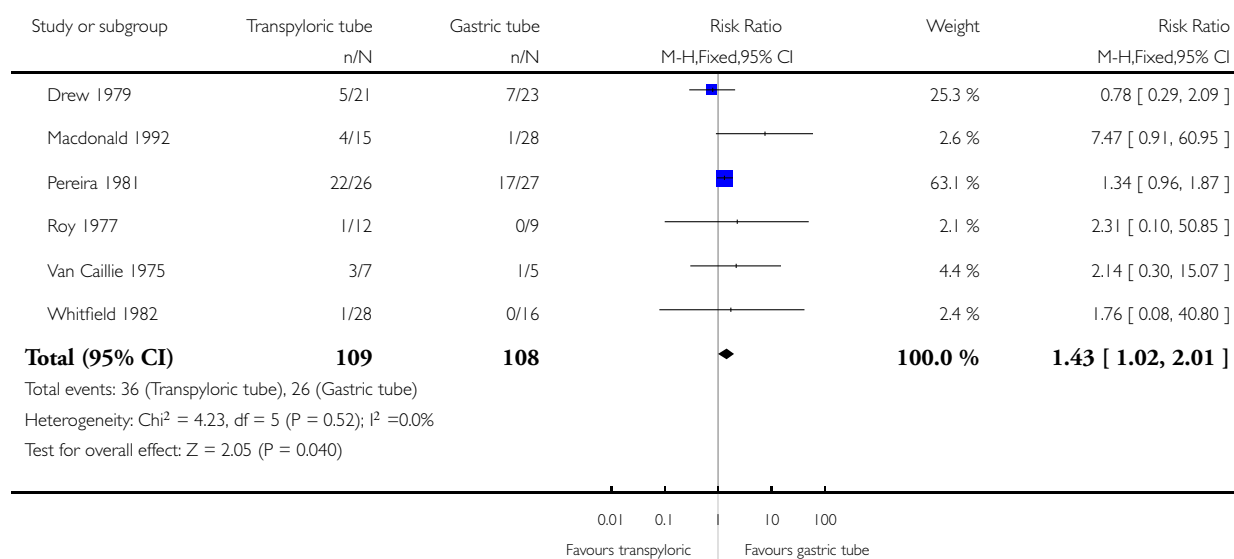


Analysis 2.4. Comparison 2 Transpyloric versus gastric tube feeding for preterm infants: Adverse events, Outcome 4 Gastrointestinal disturbance (including diarrhoea) prior to hospital discharge (excluding Laing 1986).

Review: Transpyloric versus gastric tube feeding for preterm infants

Comparison: 2 Transpyloric versus gastric tube feeding for preterm infants: Adverse events

Outcome: 4 Gastrointestinal disturbance (including diarrhoea) prior to hospital discharge (excluding Laing 1986)

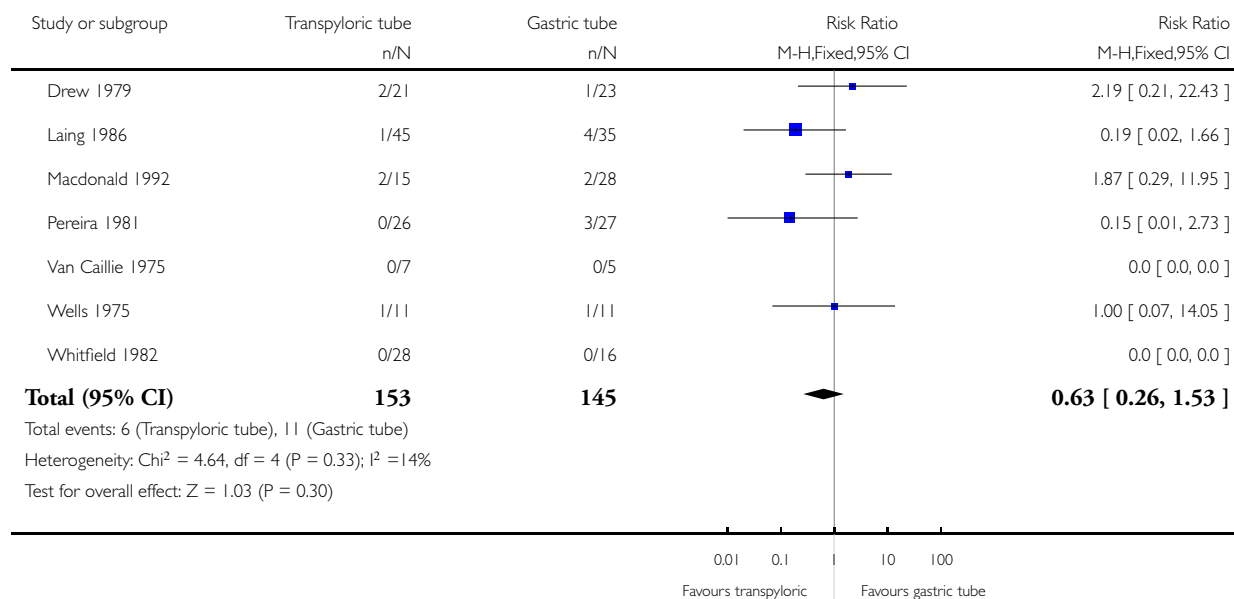


Analysis 2.5. Comparison 2 Transpyloric versus gastric tube feeding for preterm infants: Adverse events, Outcome 5 Necrotising enterocolitis prior to hospital discharge.

Review: Transpyloric versus gastric tube feeding for preterm infants

Comparison: 2 Transpyloric versus gastric tube feeding for preterm infants: Adverse events

Outcome: 5 Necrotising enterocolitis prior to hospital discharge

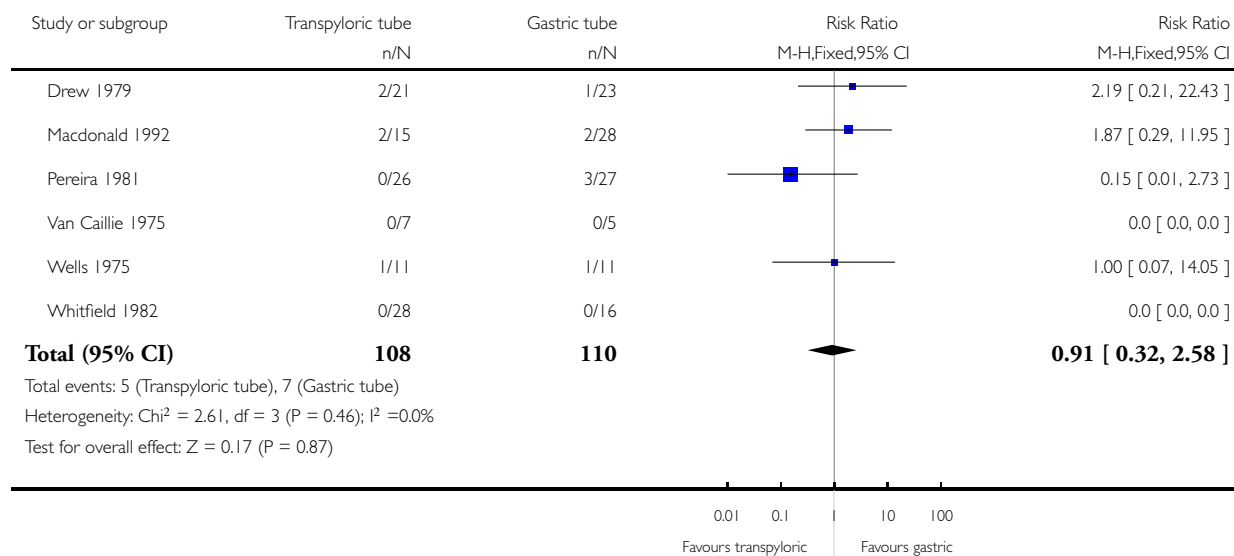


Analysis 2.6. Comparison 2 Transpyloric versus gastric tube feeding for preterm infants: Adverse events, Outcome 6 Necrotising enterocolitis prior to hospital discharge (excluding Laing 1986).

Review: Transpyloric versus gastric tube feeding for preterm infants

Comparison: 2 Transpyloric versus gastric tube feeding for preterm infants: Adverse events

Outcome: 6 Necrotising enterocolitis prior to hospital discharge (excluding Laing 1986)

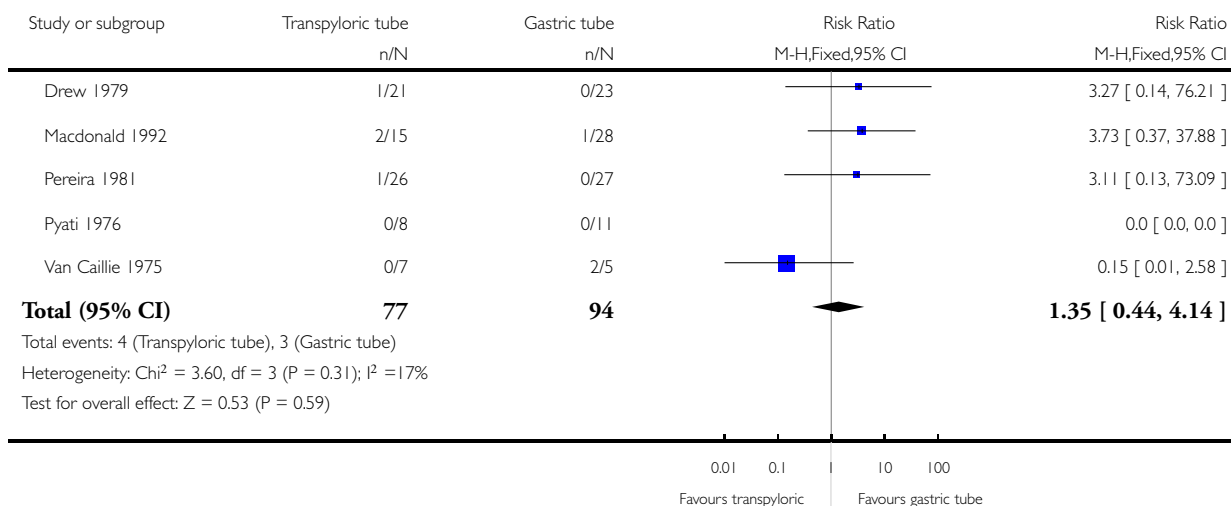


Analysis 2.7. Comparison 2 Transpyloric versus gastric tube feeding for preterm infants: Adverse events, Outcome 7 Aspiration pneumonia prior to hospital discharge.

Review: Transpyloric versus gastric tube feeding for preterm infants

Comparison: 2 Transpyloric versus gastric tube feeding for preterm infants: Adverse events

Outcome: 7 Aspiration pneumonia prior to hospital discharge

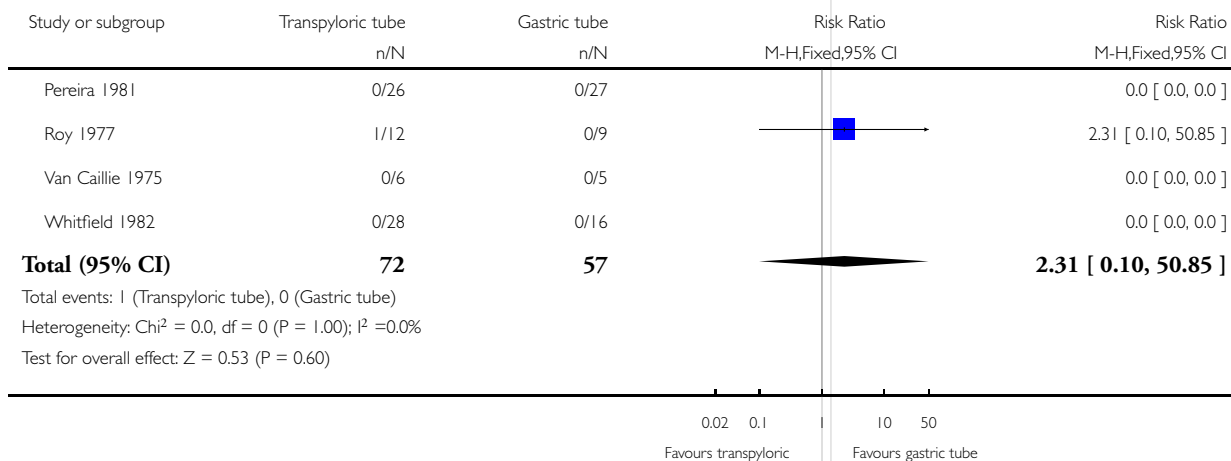


Analysis 2.8. Comparison 2 Transpyloric versus gastric tube feeding for preterm infants: Adverse events, Outcome 8 Intestinal perforation prior to hospital discharge.

Review: Transpyloric versus gastric tube feeding for preterm infants

Comparison: 2 Transpyloric versus gastric tube feeding for preterm infants: Adverse events

Outcome: 8 Intestinal perforation prior to hospital discharge



WHAT'S NEW

Last assessed as up-to-date: 19 March 2007.

11 June 2008	Amended	Converted to new review format.
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HISTORY

Protocol first published: Issue 1, 2002

Review first published: Issue 3, 2002

20 March 2007	New search has been performed	<p>This review updates “Transpyloric versus gastric tube feeding for preterm infants”, published in the Cochrane Database of Systematic Reviews, The Cochrane Library, Issue 3, 2002 (McGuire 2002).</p> <p>Our electronic search was updated in March 2007. No new trials were identified in this updated search.</p> <p>We re-classified one study that was reported as an abstract only from “excluded” to “included”, as it is clear that this trial was randomised. Inclusion of this small trial did not change any of the conclusions of the review.</p>
20 March 2007	New citation required but conclusions have not changed	Substantive amendment

CONTRIBUTIONS OF AUTHORS

Peter McEwan and William McGuire developed the protocol, undertook the electronic and hand searches, screened the title and abstract of all

studies identified, and the full text of potentially relevant reports.

Each review author independently assessed the methodological quality of the included trials, extracted the relevant information and data, and completed the final review.

DECLARATIONS OF INTEREST

None

SOURCES OF SUPPORT

Internal sources

- Tayside Institute of Child Health, Ninewells Hospital and Medical School, Dundee, UK.

External sources

- No sources of support supplied

INDEX TERMS

Medical Subject Headings (MeSH)

*Infant, Premature; Enteral Nutrition [*methods]; Infant, Newborn; Pylorus; Randomized Controlled Trials as Topic

MeSH check words

Humans