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# Effects of fibre-supplemented enteral feeds on bowel function of non-critically ill tube-fed adults: a meta-analysis of randomised controlled trials

Valerie Xin Pei Tay*, Nur Asyikin Mohamed Noor and Lee Boo Tan

*Department of Dietetics, Singapore General Hospital, Outram Road Singapore 169608, Singapore*

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## Abstract

Diarrhoea is common in enterally fed patients and can impact their nutritional and overall outcomes. This meta-analysis evaluates the potential benefits of fibre-supplemented (FS) feeds on incidence of diarrhoea and stool frequency in non-critically ill tube-fed adults. Databases including PubMed, Embase and CINAHL with full text were searched for randomised controlled trials (RCT) with adults on exclusive tube feeding, published until August 2022. The Cochrane Collaboration's tool was used for quality assessment. Studies with published results on incidence of diarrhoea and stool frequency were analysed using RevMan 5. Thirteen RCT with 847 non-critically ill patients between 20 and 90 years old without diarrhoea at the onset of enteral feeding were included. Study duration ranged from 3 to 35 d. Nine papers investigated the incidence of diarrhoea where intervention group was given FS and control was given non-fibre-supplemented (NFS) enteral feeds. Those receiving FS feeds were significantly less likely to experience diarrhoea as compared with those using NFS feeds (OR 0·44; 95 % CI 0·20, 0·95; $P = 0·04$; I2 = 71 %). Combined analysis showed no differences in stool frequency in those receiving NFS feeds (SMD 0·32; 95 % CI −0·53, 1·16; $P = 0·47$; I2 = 90 %). Results should be interpreted with caution due to considerable heterogeneity between study population, assessment tool for diarrhoea, potential conflict of interest and short duration of studies. This meta-analysis shows that FS feeds can reduce the incidence of diarrhoea in non-critically ill adults; however, the effects of stool frequency remain debatable.

**Key words: Dietary fibre: Enteral feeding: Bowel function: Adults**

Enteral tube feeding is indicated when an individual with a functioning gastrointestinal tract is unable to consume sufficient nutrition orally to meet their metabolic needs. It aims to maintain or prevent deterioration of nutrition status for all ages. The duration of enteral tube feeding can be as short as a few days to years depending on the individual's co-morbidities and contra-indications with oral feeding.

One of the most common considerations for enteral tube feeding is dysphagia, a condition associated with an increased risk of aspiration pneumonia, dehydration and malnutrition[1]. Dysphagia is attributed to a variety of diseases including stroke and cognitive impairment but can also result from functional decline, even in the absence of disease[2]. In Singapore, almost 40 % of residents in long-term care homes were receiving enteral tube feeding due to dysphagia[3]. Studies from different countries including the USA, Germany, Taiwan, Japan and Israel found the prevalence of enteral feeding in non-acute long-term care facilities ranging from 29 % up to 34 %[4–8]. The prevalence is expected to be higher in acute settings[7].

Some individuals receiving enteral nutrition reported symptoms, including abdominal distension, diarrhoea, vomiting and reflux[9]. The incidence of diarrhoea ranged from 2 % to 95 %[10]. The wide-ranging incidence rate was attributed to the heterogeneity of the population and the lack of a standardised definition of diarrhoea internationally. Diarrhoea is related to the alterations in fluid and electrolyte balance in the intestine which is driven by either one or all of the following processes: osmosis, active secretion, exudation and altered motility. This can lead to an increase in stool frequency, stool mass and liquidity[11]. The feeding formula type including its temperature, osmolality, fat content, energetic density and delivery of feeding such as the feeding rate, location, and preparation were thought to be responsible for post-feeding diarrhoea. However, there are other risks for diarrhoea unrelated to feeding formula and preparation during enteral tube feedings such as malabsorption syndromes, infection, gastrointestinal complications or concomitant drug use[12–17]. Direct links between enteral feeding and diarrhoea were not supported by research evidence and remained controversial[18]. Diarrhoea can lead to feeding disruptions and complications such as electrolyte imbalance, dehydration and increased vulnerability to wound infection, making it one of the most crucial issues to avert[19].

**Abbreviations:** FS, fibre-supplemented; NFS, non-fibre-supplemented; RCT, randomised controlled trials.

* **Corresponding author:** Valerie Tay Xin Pei, email valerie.tay.x.p@sgh.com.sg

Polymeric feeds have been used as the first choice for individuals receiving enteral tube feeding due to their complete nutritional profile and mostly intact nutrients, suitable for those with a functioning gut. Its formula consists of whole protein as the nitrogen source, partially hydrolysed starch, long-chain TAG, minerals, vitamins, and trace elements and sometimes enriched with fibre[20]. Dietary fibre consists of non-digestible carbohydrates and lignin that are intrinsic and intact in plants with influences on bowel health through stool bulking, stool weight and colonic fermentation[21]. They can be grouped according to their physical properties such as solubility, fermentability and viscosity or their physiological effects. For this review, dietary fibre is classified by its solubility: insoluble (such as cellulose, lignin and some hemicelluloses, and wheat bran) and soluble fibres (such as pectin, guar gums, mucilage, inulin, psyllium, β-glucans and wheat dextrin)[22].

Dietary fibre undergoes bacterial fermentation in the distal colon which increases the water-holding capacity of stools[23]. Although insoluble fibres have relatively low water-holding capacity, they undergo partial fermentation in the colon and retain water, thus contributing to stool bulking. Conversely, soluble fibres are almost completely fermented in the colon and despite high water-holding capacity have little effect on transit time[24]. However, recent investigations suggested that soluble fibres can increase colonic transit time[25]. The water-holding properties of soluble fibres may potentially improve the consistency of liquid stools, thus reducing both constipation and diarrhoea.

Nutrition guidelines from selected countries proposed that the addition of fibre into enteral feeds reduces diarrhoea in certain population groups[26]. However, due to a lack of evidence around the efficacy of fibre-supplemented (FS) enteral feeds on diarrhoea, recommendations on fibre and its benefits on bowel health remained controversial.

Two recent systematic reviews concluded that the inclusion of soluble fibre in enteral feeds is safe and may be beneficial in reducing the incidence of diarrhoea in haemodynamically stable critically ill patients[27,28]. However, gastrointestinal symptoms particularly diarrhoea is frequently observed in patients admitted into the intensive care unit[29,30]. Thus, the beneficial impact of fibre-containing enteral feeds on reducing the incidence of diarrhoea in critically ill patients may not be extrapolated to non-critically ill adults. This present paper aims to investigate whether the use of FS enteral feeds can reduce the incidence of diarrhoea and stool frequency in non-critically ill adults on exclusive enteral tube feeding.

## Materials and methods

The authors employed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) protocol to write this systematic review. The systematic review protocol had been registered via open-access repository (Open Science Framework) and can be accessed at https://doi.org/10·17605/OSF.IO/UBHW4.

### Literature search

Literature published until August 2022 that described the effects of FS enteral feeds on the incidence of diarrhoea was systematically identified by searching PubMed, Embase and CINAHL with full text. The search strategies for these databases were defined by terms related to: 'enteral nutrition' (enteral feed*, tube feed*, artificial nutrition, artificial feed*, nutrition support, tube feeding formula, enteral pump), ' dietary fibre' (prebiotic, 'fructo oligosaccharides', FOS, psyllium, oligofructose, inulin, 'inulin types', oat*, polysaccharides, lignin, 'soy polysaccharides', fructan*, 'non-starch polysaccharides', 'resistant starch*', cellulose, pectin, 'Arabic gum', 'pea fibre', guar, 'acacia gum') and 'diarrhoea' ('stool frequency', 'stool consistency', 'bowel habit*', 'bowel movement*', 'stool chart'). Additionally, references used in primary and secondary research studies were hand-searched for additional articles that were not accessible through electronic databases. The authors also sought assistance from the librarian to locate articles without full text.

### Study selection

Two reviewers (VXPT and NAMN) independently assessed potentially relevant articles for eligibility. The articles were first selected based on eligibility by titles, followed by the abstract and finally the full-text papers. Disagreements were resolved through discussion and the third author (LBT). Inclusion criteria for this review were (1) adults (aged 18 years and above) with any health conditions or nutritional status, (2) primary research of randomised controlled trials (RCT) and (3) exclusive enteral feeding. Exclusion criteria included studies that were (1) non-human studies, (2) not an original research article, (3) patients admitted to the intensive care unit or known to be critically ill, (4) not fed via an enteral tube, (5) did not report on diarrhoea or other secondary outcomes of concern as study outcome or (6) stated intervention was specifically used to treat existing diarrhoea conditions. This review was limited to articles that were published in peer-reviewed academic journals or dissertations with full-text available. The inclusion and exclusion criteria applied for this systematic review are summarised using the Population, Intervention, Comparison, and Outcome (PICO) framework (Table 1).

### Data extraction and outcome measures

All reviewers (VXPT, NAMN and LBT) extracted the data independently from the included studies by using a standard template which included population descriptions (location, inclusion and exclusion criteria), methodology (aim, design, study duration and sample size), risk of bias assessment, participants (number of randomised, withdrawals and exclusions, and characteristics including age and duration on exclusive enteral feeding), interventions (enteral tube feed used, and fibre dosage and type) and outcomes (diarrhoea incidence and stool frequency).

### Critical appraisal and quality assessment

Two reviewers (VXPT and NAMN) independently assessed the methodological quality of the included studies using the



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**Table 1.** Inclusion and exclusion criteria summarised using the PICO framework

| | Inclusion criteria | Exclusion criteria |
|---|---|---|
| Population | • Adults (aged 18 years and above) with any health conditions or nutritional status on exclusive enteral tube feeding | • Non-human studies or studies involving neonates, children or youths<br>• Patients admitted to the intensive care unit or known to be critically ill<br>• Not exclusively fed via an enteral tube |
| Intervention | • Exclusively using fibre-containing enteral feeds | • Enteral feeds used in both intervention and control groups include or exclude fibre |
| Comparison | • Exclusively using non-fibre containing enteral feeds | |
| Outcome | • Diarrhoea incidence<br>• Stool frequency | • Did not report on diarrhoea or other secondary outcomes of concern as the study outcome<br>• Stated intervention was specifically used to treat existing diarrhoea conditions |

PICO, Population, Intervention, Comparison, and Outcome.

2008 Cochrane Collaboration's tool for assessing the risk of bias; disputes were resolved by discussion with a third author (LBT). The Cochrane Collaboration tool assesses the following in the included studies: selection, performance, detection, attrition and reporting biases[31]. After this, authors concluded the overall risk of bias within or across trials to summarise assessments across categories in the tool for each outcome within each trial.

### *Statistical analysis*

Statistical analyses were carried out using the Mantel–Haenszel method via the RevMan 5.3 software developed by Cochrane[32]. Results were presented in OR and standard mean difference (SMD) for incidence of diarrhoea and stool frequency, respectively, with 95 % CI. Due to the use of different measurement tools for stool frequency, SMD was used to standardise the results of the studies. An OR < 1 indicates that FS feeds are associated with a lower incidence of diarrhoea. An SMD > 0 indicates the degree to which FS feeds reduce stool frequency compared with non-fibre-supplemented (NFS) feeds. Random-effects model was used to calculate outcomes of interest to account for potential confounding factors. Forest plots were used to illustrate the effects of FS on the incidence of diarrhoea and stool frequency. The $I^2$ statistical test and $\chi^2$ test were used to evaluate statistical heterogeneity. An $I^2$ value of more than 50 % indicated substantial heterogeneity. Subgroup analyses were performed when statistically significant heterogeneity of the data is present to further investigate the effects between feeds containing mixed fibres and feeds containing soluble fibres only on study outcomes. A $P$-value < 0·05 was considered statistically significant.

## Results

The literature search identified 646 records. Sixteen records were identified through hand-searching from the bibliography. A total of forty-four studies were retrieved after excluding titles and abstracts that were not relevant to the research question and not meeting the inclusion criteria. A flow diagram describing the selection of studies is shown in Fig. 1. After assessing full-text papers by inclusion and exclusion criteria, thirteen RCT were included in this review.

The characteristics of included studies are presented in Table 2.

Thirteen RCT with 847 participants between 20 and 90 years old without diarrhoea at the onset of enteral feeding were included. Out of the 432 participants, 51 % were male. Ten studies were conducted on hospitalised elderly, of which two were admitted into general medical wards[33,34], two were in general surgery wards[35,36], one in the geriatric ward[37] and others non-specified[38–42]. The remaining studies were conducted on older adults in long-term care settings ($n$ 3)[43–45]. Duration of the study ranged from 3 to 35 d.

Nine out of thirteen papers investigated the incidence of diarrhoea where the intervention group was given FS feeds and the control group was given NFS feeds for enteral tube feeding[33–35,39–43,45]. Most studies that investigated FS feeds used soy polysaccharides as part of their formulation ($n$ 7)[33,35,39–41,43,44], followed by inulin ($n$ 6)[36–41]. Six studies used FS feeds in the intervention group[33,36,38,41,43,44], while fibre was added to the feeds separately in the remaining studies. Two studies did not specify if the control feeds contained any fibre[37,44]. The actual daily fibre intake was not explicitly reported in two studies[42,44].

There was variability in the definition of diarrhoea among studies, considering partly or all of the stool properties: volume, consistency and frequency. Diarrhoea definitions were based on diarrhoea score, number of liquid stools per d and/or volume, number of loose or watery stools, with a scale based on consistency and frequency, and use of stool charts, such as the Bristol or King's stool chart.

Those receiving FS feeds were significantly less likely to experience diarrhoea as compared with those using NFS feeds (Fig. 2(a); OR 0·44; 95 % CI 0·20, 0·95; $P = 0·04$; $\chi^2 = 27·63$, $P < 0·05$, $I^2 = 71$ %). Further subgroup analyses comparing the incidence of diarrhoea between feeds containing both insoluble and soluble fibre and feeds containing soluble fibre only showed no differences between them (Fig. 2(b); $P = 0·36$). This suggests that the incidence of diarrhoea is not modified based on the type of fibre used in enteral feeds. However, a smaller number of studies and participants contributed data to the group receiving mixed fibre feeds than soluble fibre only feeds meaning the analysis may not be able to detect subgroup differences. Moreover, there is substantial unexplained heterogeneity between studies within each of these subgroups (feeds containing both insoluble and soluble fibre: $I^2 = 57$ %; feeds containing soluble fibre only: $I^2 = 81$ %).

After excluding a small RCT that strongly favoured the treatment group[43], results for the incidence of diarrhoea became non-significant (Fig. 3; OR 0·57; 95 % CI 0·31, 1·05;

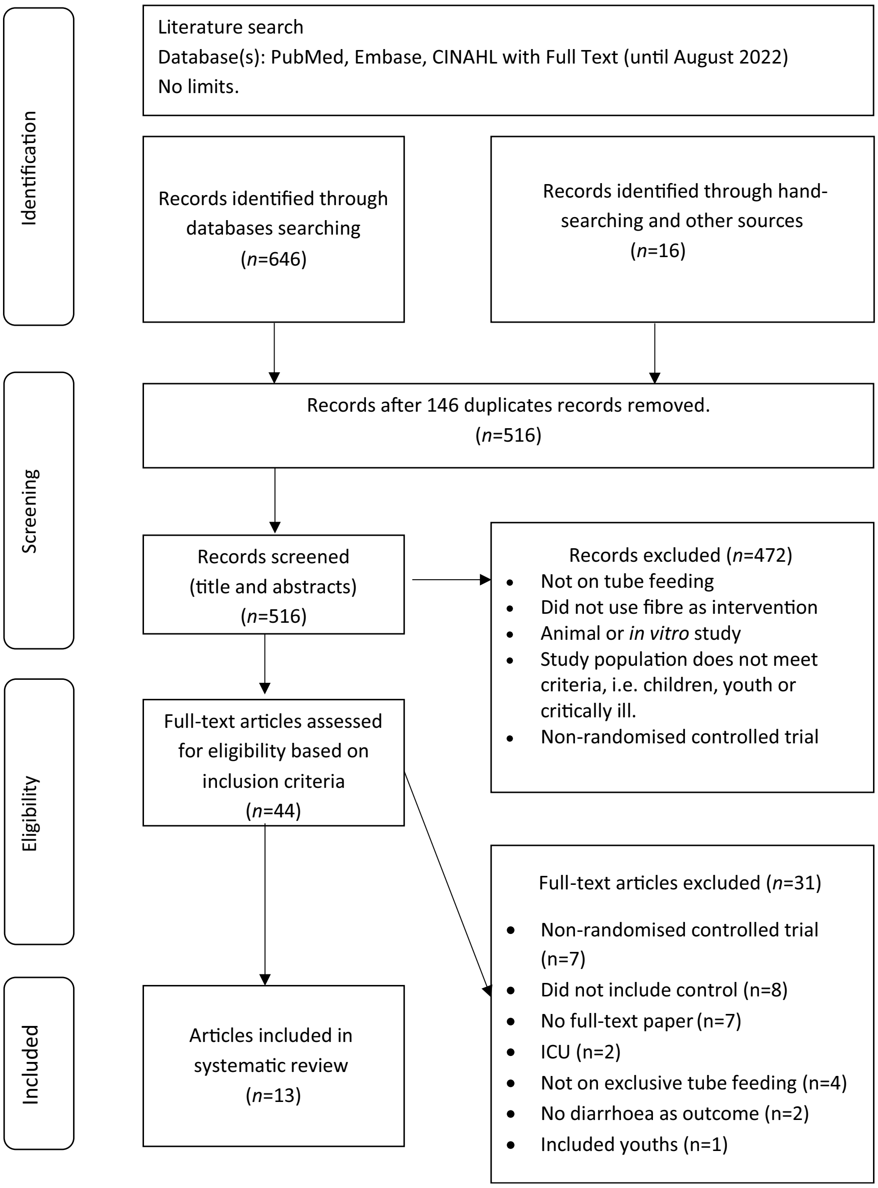


**Fig. 1.** PRISMA flow diagram.

$P = 0{\cdot}07$; $\chi^2 = 14{\cdot}59$, $P < 0{\cdot}04$, $I^2 = 52\,\%$). The statistical heterogeneity was also reduced from 71 % to 52 %. This finding may be attributed to the study population receiving long-term enteral feeding – all participants were on exclusive enteral tube feeding for at least 1 month before study enrolment. This study addressed the effects of one fibre-containing enteral feed and fibre-free enteral feed on bowel function and laxative use in chronic care patients, the majority of whom were comatose and have a high incidence of constipation and subsequent laxative use. Although there were no significant differences in stool frequency found in the control (fibre-free) and treatment (fibre-containing) groups, there were significantly more laxatives used in the control group. The use of laxatives may have resulted in subsequent diarrhoea and affected the results.

Combined analysis from five out of thirteen RCT showed no differences in stool frequency for those receiving NFS feeds (Fig. 4(a); SMD 0·32; 95 % CI −0·53, 1·16; $P = 0{\cdot}47$; $\chi^2 = 29{\cdot}27$, $P < 0{\cdot}05$, $I^2 = 90\,\%$). Further subgroup analyses found that those receiving feeds containing both insoluble and soluble fibre experienced significantly lower stool frequency compared with those receiving feeds containing soluble fibres only (Fig. 4(b); $P < 0{\cdot}05$). However, there were far fewer participants included in the group receiving feeds containing soluble fibre only (two studies; thirty-eight participants) compared with the group receiving feeds containing both insoluble and soluble fibre (three studies; 118 participants).

The risk of bias assessment for the included studies is shown in Fig. 5(a) and (b). There were mixed results across the different domains. Most of the studies were rated unclear concerning bias arising from the selection process (> 70 %); however, studies were rated to have a low risk of bias for reporting of results (85 %) and attrition bias (100 %). More than half of the studies

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**Table 2.** Characteristics of included studies

| Author, year | Location | Study design, blinding | Study population | Sample size, N | Duration of feeding | Control | Intervention | Fibre content | Tools |
|---|---|---|---|---|---|---|---|---|---|
| Lertpipopmetha *et al.*, 2018[34] | Thailand | RCT, double-blinded | Patients from General Medical wards | 83 (intention-to-treat analysis) | Median: psyllium group – 5 d<br>Control group – 5 d | Blendera (Fibre-free) | Blendera added with Mucilin | Mucilin SF (5 g per sachet) consisted of 3·5 g of ispaghula husk (10·5 g fibre per litre). | King's stool chart |
| Tabei et al, 2018[45] | Japan | RCT, blinding NS | Patients from medical centres | 27 | 14 d | Liquid enteral nutrition (EN) diet, K-LEC (Fibre free) | Viscosity-regulating pectin solution, REF-P1 | REF-P1 contained 1·4 g fibre (pectin) per bag | Bristol stool chart |
| Zhao *et al.*, 2017[42] | China | RCT, blinding NS | Hospitalised patients who underwent gastrectomy | 120 | 7 d | EN emulsion from Sino-Swed Pharmaceutical Corp. Ltd, Beijing, China (fibre-free) | EN + Shen Jia (Beijing Tiantian Yikang Biological Technology Corp. Ltd, Beijing, China)<br>EN + Shen Jia + combination of live Bifidobacterium and lactobacillus (Inner Mongolia Shuangqi Pharmaceutical Corp. Ltd, Beijing, China) | NS | King's stool chart |
| Jackobsen *et al.*, 2017[41] | Germany and Denmark | RCT, double-blind | Hospitalised patients | 51 | 7–8 d | Nutrison Protein Plus (fibre-free) | Nutrison Protein Plus + Multi Fibre | MF6 Multi Fibre provided 22·5 g soluble and insoluble fibre per 1500 ml formula (1·5 g fibre per 100 ml)<br>Type of fibre used: NS | Bristol stool chart |
| De luis *et al.*, 2009[40] | Spain | RCT, double-blinded | Hospitalised patients | 72 | At least 10 d | Isoenergetic, isonitrogenous EN (fibre-free) | EN supplemented with arginine and fibre | The formula provides 0·9 g fibre per 100 ml.<br>Dietary fibre: (oligofructose, inulin, soy polysaccharide, resistant starch, Arabic gum, cellulose). | No use of stool chart; defined diarrhoea as > 5 liquid stools over 24 h or an estimated volume > 2000 ml/d |
| Shimoni *et al.*, 2007[33] | Israel | RCT, double-blinded | Patients from General Internal Medicine wards | 148 | Minimum 5 d. Total duration: NS | Osmolite (Fibre-free) | Jevity (Contains fibre) | 13·2 g/l of soya fibre Per 1000 kcal provides | Diarrhoea is defined as 2 liquid stools or (≥ 3 more semi-solid or liquid stools over 24 h) |
| Vandewoude *et al.*, 2005[37] | Belgium | RCT, blinding NS | Patients from the Department of Geriatrics | 172 | Mean: Intervention: 27·5 ± 4·3 d<br>Control: 27·9 ± 4·0 d | Standard EN (description of feeds: NS) | Standard EN supplemented with fibre | 30 g of fibre with 33 % insoluble (cellulose and hemicellulose A) and 67 % soluble (pectin, hemicellulose B, inulin) fibre | Validated tool for recording stools frequency, volume (small < 1/2 cup, large > 1/2 cup), and consistency (solid-formed, soft-pasty, or liquid-watery).<br>A visual scale to define the consistency of the stools was provided. |

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**Table 2.** (*Continued*)

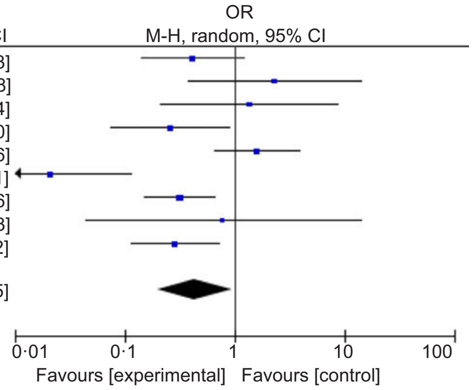
| Author, year | Location | Study design, blinding | Study population | Sample size, N | Duration of feeding | Control | Intervention | Fibre content | Tools |
|---|---|---|---|---|---|---|---|---|---|
| De luis *et al.*, 2002[39] | Spain | RCT, double-blinded | Hospitalised patients | 47 | 22 ± 12 d | Isoenergetic, isonitrogenous EN (fibre-free) | EN supplemented with arginine and fibre | The formula provides 0·9 g fibre per 100 ml. Dietary fibre: (oligofructose, inulin, soy polysaccharide, resistant starch, Arabic gum, cellulose). | No use of stool chart; defined diarrhoea as > 5 liquid stools over 24 h or an estimated volume > 2000 ml/d |
| Khalil *et al.*, 1998[36] | Singapore | RCT, single-blinded | Patients from the Neurology or General Surgery wards | 16 | 10 d | Isocal liquid (fibre-free) | Ultracal liquid (Contains fibre) | 1·44 g of dietary fibre 44 % soya (insoluble) and 56 % oat fibre (soluble) | Diarrhoea is defined as having both (a) reduced stool consistency (pasty, semi watery or watery) and (b) increased stool frequency (≥ 3 more times/d) |
| Grant *et al.*, 1994[44] | USA | RCT, blinding NS | Veteran patients | 7 | 49 d | NS | Jevity (contains fibre) | NS | NS |
| Zarling *et al.*, 1994[38] | USA | Randomised, crossover trial, blinding NS | Hospitalised patients undergoing rehabilitation | 10 | 10-d treatment arms and a crossover design with a 3-d washout period between the two study arms | Isocal HN (Fibre free) | Ultracal (Contains fibre) | 14·4 g/l of fibre (pea fibre, Arabic gum, fructo-oligosaccharide, inulin) | Symptomatic tolerance was recorded, and intestinal transit time was calculated from the time elapsed between the initial appearance of each of the faecal dye markers. Also during each treatment arm, gastric emptying, gastroesophageal reflux and pulmonary aspiration were assessed by radioscintigraphic measurement |
| De Kruif, 1993[35] | The Netherlands | RCT, double-blinded | Patients from surgical wards | 60 | Minimum 1 week. Total duration: NS | Osmolite (Fibre-free) | Osmolite supplemented with soy polysaccharide | 10 g of soluble fibre (soy polysaccharides) | Diarrhoea score (DS) is calculated by the addition of stool consistency (1 = formed, 3 = loose, 5 = liquid) at every bowel evacuation in 3 consecutive 8-h periods. Diarrhoea is defined as moderate (DS between 6 and 15 points for at least 2 d), severe (DS ≥ 15 points or more on any of the 5 observation days), not present (DS between 0–6 points for at least 4 d and between 6–15 points for not more than 1 d). |
| Shankardass *et al.*, 1990[43] | Canada | RCT, double-blinded, crossover trial | Long-term enterally fed patients | 28 | Crossover study with two consecutive 6-week periods. Each 6-week period consisted of a 2-week adaptation period, followed by a 4-week study period (fibre-free) | Ensure (fibre-free) | Enrich (contains fibre) | Contains 12·8 g of dietary fibre per 1000 kcal (soy polysaccharides) | Daily faecal wet weight and stool frequency |

RCT, randomised controlled trial; NS, not stated; EN, enteral nutrition.

(a)

| Study or subgroup | Fibre-containing Events | Fibre-containing Total | Non-fibre-containing Events | Non-fibre-containing Total | Weight | OR M-H, random, 95% CI |
|---|---|---|---|---|---|---|
| de Kruif et al 1993 | 8 | 30 | 14 | 30 | 13·0% | 0·42 [0·14, 1·23] |
| de Luis et al 2002 | 4 | 23 | 2 | 24 | 8·9% | 2·32 [0·38, 14·08] |
| de Luis et al 2002 | 3 | 38 | 2 | 34 | 8·7% | 1·37 [0·22, 8·74] |
| Jackobsen et al 2017 | 5 | 26 | 12 | 25 | 11·9% | 0·26 [0·07, 0·90] |
| Lettpipometha et al 2018 | 18 | 42 | 13 | 41 | 14·1% | 1·62 [0·66, 3·96] |
| Shankardass et al 1990 | 6 | 28 | 26 | 28 | 9·5% | 0·02 [0·00, 0·11] |
| Shimoni et al 2007 | 15 | 78 | 30 | 70 | 15·0% | 0·32 [0·15, 0·66] |
| Tabei et al 2018 | 1 | 15 | 1 | 12 | 5·1% | 0·79 [0·04, 14·03] |
| Zhao et al 2017 | 12 | 40 | 24 | 40 | 13·9% | 0·29 [0·11, 0·72] |
| Total (95% CI) | | 320 | | 304 | 100·0% | 0·44 [0·20, 0·95] |
| Total events | 72 | | 124 | | | |

Heterogeneity: $Tau^2 = 0·90$; $Chi^2 = 27·63$, df = 8 (P = 0·0006); $I^2 = 71\%$
Test for overall effect: Z = 2·10 (P = 0·04)




(b)

| Study or subgroup | Fibre-containing Events | Fibre-containing Total | Non-fibre-containing Events | Non-fibre-containing Total | Weight | OR M-H, random, 95% CI |
|---|---|---|---|---|---|---|
| 1·1·1 Feeds containing both soluble and Insoluble fibre | | | | | | |
| de Luis et al 2002 | 4 | 23 | 2 | 24 | 10·7% | 2·32 [0·38, 14·08] |
| de Luis et al 2009 | 3 | 38 | 2 | 34 | 10·5% | 1·37 [0·22, 8·74] |
| Jackobsen et al 2017 | 5 | 26 | 12 | 25 | 13·8% | 0·26 [0·07, 0·90] |
| Subtotal (95% CI) | | 87 | | 83 | 35·0% | 0·82 [0·20, 3·39] |
| Total events | 12 | | 16 | | | |
| Heterogeneity: $Tau^2 = 0·90$; $Chi^2 = 4·62$, df = 2 (P = 0·10); $I^2 = 57\%$ | | | | | | |
| Test for overall effect: Z = 0·28 (P = 0·78) | | | | | | |
| 1·1·2 Feeds containing soluble fibre only | | | | | | |
| de kruif et al 1993 | 8 | 30 | 14 | 30 | 14·8% | 0·42 [0·14, 1·23] |
| Lertpipometha et al 2018 | 18 | 42 | 13 | 41 | 15·8% | 1·62 [0·66, 3·96] |
| Shankardass et al 1990 | 6 | 28 | 26 | 28 | 11·3% | 0·02 [0·00, 0·11] |
| Shimoni et al 2007 | 15 | 78 | 30 | 70 | 16·7% | 0·32 [0·15, 0·66] |
| Tabei et al 2018 | 1 | 15 | 1 | 12 | 6·5% | 0·79 [0·04, 14·03] |
| Subtotal (95% CI) | | 193 | | 181 | 65·0% | 0·34 [0·10, 1·16] |
| Total events | 48 | | 84 | | | |
| Heterogeneity: $Tau^2 = 1·47$; $Chi^2 = 21·48$, df = 4 (P = 0·0003); $I^2 = 81\%$ | | | | | | |
| Test for overall effect: Z = 1·72 (P = 0·08) | | | | | | |
| Total (95% CI) | | 280 | | 264 | 100·0% | 0·47 [0·19, 1·15] |
| Total events | 72 | | 124 | | | |

Heterogeneity: $Tau^2 = 1·14$; $Chi^2 = 26·69$, df = 7 (P = 0·0004); $I^2 = 74\%$
Test for overall effect: Z = 1·65 (P = 0·10)
Test for subgroup differences: $Chi^2 = 0·85$, df = 1 (P = 0·36), $I^2 = 0\%$

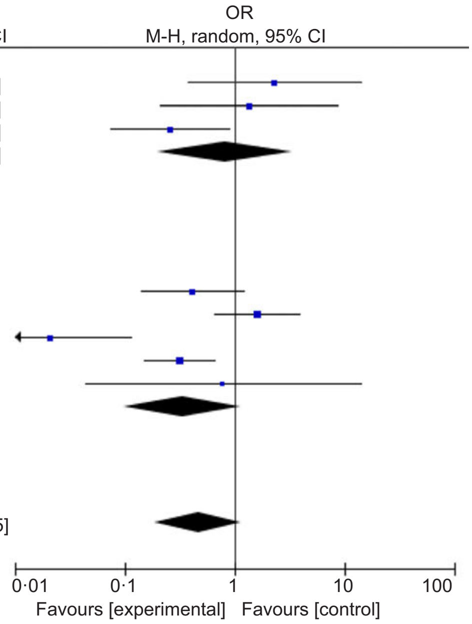



**Fig. 2.** (a) Incidence of diarrhoea between FS feeds and NFS feeds. (b) Subgroup analyses comparing the incidence of diarrhoea between feeds containing both soluble and insoluble fibre and feeds containing soluble fibre only. FS, fibre-supplemented; NFS, non-fibre- supplemented.

| Study or subgroup | Fibre-containing Events | Fibre-containing Total | Non-fibre-containing Events | Non-fibre-containing Total | Weight | OR M-H, random, 95% CI |
|---|---|---|---|---|---|---|
| de Kruif et al 1993 | 8 | 30 | 14 | 30 | 14·6% | 0·42 [0·14, 1·23] |
| de Luis et al 2002 | 4 | 23 | 2 | 24 | 8·1% | 2·32 [0·38, 14·08] |
| de Luis et al 2009 | 3 | 38 | 2 | 34 | 7·8% | 1·37 [0·22, 8·74] |
| Jackobsen et al 2017 | 5 | 26 | 12 | 25 | 12·7% | 0·26 [0·07, 0·90] |
| Lertpipometha et al 2018 | 18 | 42 | 13 | 41 | 17·0% | 1·62 [0·66, 3·96] |
| Shimoni et al 2007 | 15 | 78 | 30 | 70 | 19·3% | 0·32 [0·15, 0·66] |
| Tabei et al 2018 | 1 | 15 | 1 | 12 | 3·9% | 0·79 [0·04, 14·03] |
| Zhao et al 2017 | 12 | 40 | 24 | 40 | 16·6% | 0·29 [0·11, 0·72] |
| Total (95% CI) | | 292 | | 276 | 100·0% | 0·57 [0·31, 1·05] |
| Total events | 66 | | 98 | | | |

Heterogeneity: $Tau^2 = 0·37$; $Chi^2 = 14·59$, df = 7 (P = 0·04); $I^2 = 52\%$
Test for overall effect: Z = 1·79 (P = 0·07)

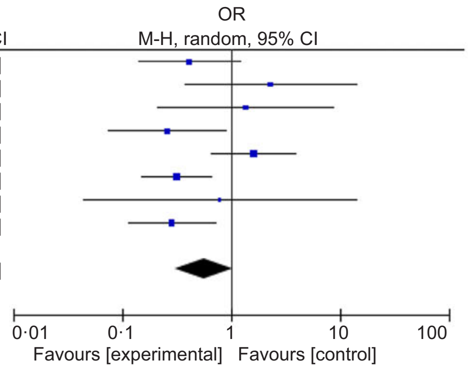



**Fig. 3.** Incidence of diarrhoea between FS feeds and NFS feeds after excluding Shankardass *et al.* 1990. FS, fibre-supplemented; NFS, non-fibre- supplemented.

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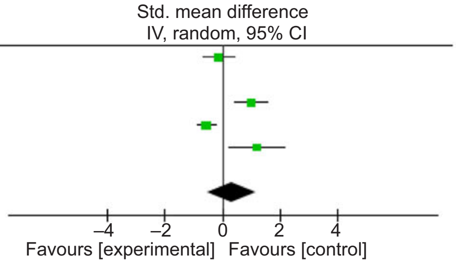
(a)

| Study or subgroup | Fibre-containing Mean | SD | Total | Non-fibre-containing Mean | SD | Total | Weight | Std. mean difference IV, random, 95% CI |
|---|---|---|---|---|---|---|---|---|
| Jackobsen et al 2017 | 1·62 | 1·49 | 26 | 1·88 | 2·06 | 25 | 25·7% | −0·14 [−0·69, 0·41] |
| Khalil et al 1998 | 0·56 | 0 | 8 | 0·2 | 0 | 8 | | Not estimable |
| Shankardass et al 1990 | 1·5 | 0·1 | 28 | 1·4 | 0·1 | 28 | 25·7% | 0·99 [0·43, 1·54] |
| Vandewoude et al 2005 | 0·59 | 0·37 | 70 | 0·9 | 0·67 | 85 | 27·7% | −0·56 [−0·88, −0·23] |
| Zarling et al 1994 | 0·9 | 0·4 | 10 | 0·5 | 0·2 | 10 | 20·9% | 1·21 [0·24, 2·18] |
| Total (95% CI) | | | 134 | | | 148 | 100·0% | 0·32 [−0·53, 1·16] |

Heterogeneity: $Tau^2 = 0·65$; $Chi^2 = 29·27$, df = 3 (P < 0·00001); $I^2 = 90\%$
Test for overall effect: Z = 0·73 (P = 0·47)




(b)

| Study or subgroup | Fibre-containing Mean | SD | Total | Non-fibre-containing Mean | SD | Total | Weight | Std· mean difference IV, random, 95% CI |
|---|---|---|---|---|---|---|---|---|
| 1·2·1 Feeds containing both soluble and insoluble fibre | | | | | | | | |
| Jackobsen et al 2017 | 1·62 | 1·49 | 26 | 1·88 | 2·06 | 25 | 25·7% | −0·14 [−0·69, 0·41] |
| Khalil et al 1998 | 0·56 | 0 | 8 | 0·2 | 0 | 8 | | Not estimable |
| Vandewoude et al 2005 | 0·59 | 0·37 | 70 | 0·9 | 0·67 | 85 | 27·7% | −0·56 [−0·88, −0·23] |
| Subtotal (95% CI) | | | 104 | | | 118 | 53·4% | −0·41 [−0·80, −0·03] |
| Heterogeneity: $Tau^2 = 0·03$; $Chi^2 = 1·61$ , df = 1 (P = 0·20); $I^2 = 38\%$ | | | | | | | | |
| Test for overall effect: Z = 2·09 (P = 0·04) | | | | | | | | |
| 1·2·2 Feeds containing soluble fibre only | | | | | | | | |
| Shankardass et al 1990 | 1·5 | 0·1 | 28 | 1·4 | 0·1 | 28 | 25·7% | 0·99 [0·43, 1·54] |
| Zarling et al 1994 | 0·9 | 0·4 | 10 | 0·5 | 0·2 | 10 | 20·9% | 1·21 [0·24, 2·18] |
| Subtotal (95% CI) | | | 38 | | | 38 | 46·6% | 1·04 [0·56, 1·53] |
| Heterogeneity: $Tau^2 = 0·00$; $Chi^2 = 0·16$, df = 1 (P = 0·69); $I^2 = 0\%$ | | | | | | | | |
| Test for overall effect: Z = 4·23 (P < 0·0001) | | | | | | | | |
| Total (95% CI) | | | 142 | | | 156 | 100·0% | 0·32 [−0·53, 1·16] |

Heterogeneity: $Tau^2 = 0·65$; $Chi^2 = 29·27$, df = 3 (P < 0 00001); $I^2 = 90\%$
Test for overall effect: Z = 0·73 (P = 0·47)
Test for subgroup differences: $Chi^2 = 21·24$, df = 1 (P < 0·00001), $I^2 = 95·3\%$

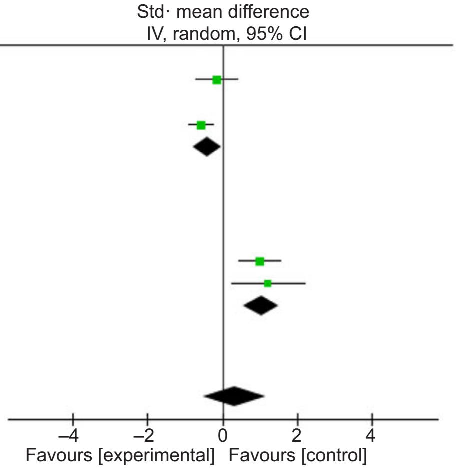



**Fig. 4.** (a) Mean differences in stool frequency between FS feeds and NFS feeds. (b) Subgroup analyses comparing stool frequency between feeds containing both soluble and insoluble fibre and feeds containing soluble fibre only. FS, fibre-supplemented; NFS, non-fibre- supplemented.

were rated to have a low risk of detection bias and performance bias. One study was rated high risk in performance bias[36], and one other study was rated high risk in other bias (assessment)[34]. Two studies were rated to have a low risk of bias across all domains with their clear reported methodology[35,41].

## Discussion

This meta-analysis presented the effects of FS feeds on the incidence of diarrhoea and stool frequency in non-critically ill adults on exclusive enteral feeding. Overall, results showed that there was a significant reduction of participants experiencing diarrhoea in the group with FS feeds compared with NFS feeds (OR 0·44, 95 % CI 0·20, 0·95, $P = 0·04$), but no differences were found in regard to stool frequency. There were no differences in the incidence of diarrhoea when feeds containing both insoluble and soluble fibre and feeds containing soluble fibre only were compared, but the former was found to have a lower stool frequency.

Several systematic reviews had demonstrated the positive effects of exclusive enteral nutrition using FS feeds on the incidence of diarrhoea and stool frequency in hospitalised patients. One of these is a systematic review[46] investigating the incidence of diarrhoea between healthy volunteers or patients more than 1-year-old of any nutritional status and based in any setting on enteral tube feeding as the main source of nutrition using FS feeds compared with NFS feeds. It was found that the incidence of diarrhoea was significantly reduced as a result of fibre administration in the intervention group (OR 0·68; 95 % CI 0·48, 0·96; $P = 0·03$). Subgroup analyses revealed a significant reduction in the incidence of diarrhoea in the non-critically ill hospitalised patients (OR 0·42, 95 % CI 0·25, 0·72; $P = 0·001$). A subsequent systematic review[47] investigated the effect of FS feeds on diarrhea, especially in adults regardless of nutritional status, both critically ill and non-critically ill, and found a protective effect of fibre in reducing the incidence of diarrhoea (OR 0·47, 95 % CI 0·29, 0·77; $P = 0·02$). However, further subgroup analyses revealed a similar effect of FS feeds on the incidence of diarrhoea in non-critically ill patients (OR 0·31, 95 % CI 019, 0·51; $P < 0·01$) but not in the critically ill patients (OR 0·89, 95 % CI 0·41, 1·92; $P = 0·07$)[47]. More recently, a systematic review[48] investigated the incidence of diarrhoea in patients who underwent gastrointestinal surgery. The authors found that when comparing FS feeds and NFS feeds, there was a significantly lower incidence of diarrhoea in adults on FS feeds ($\chi 2 = 7·3$; $P = 0·007$). However, similar to our paper, the quantity of supplementary fibre used varied greatly, and furthermore, fibre was taken enterally in different forms (pill, mixture, powder or fibre-containing feed)[48].

Based on the results of our meta-analysis, there was a significant reduction of diarrhoea incidence in the group with FS feeds compared with NFS feeds (OR 0·44; 95 % CI 0·20, 0·95; $P = 0·04$). Consistent with the results from previous

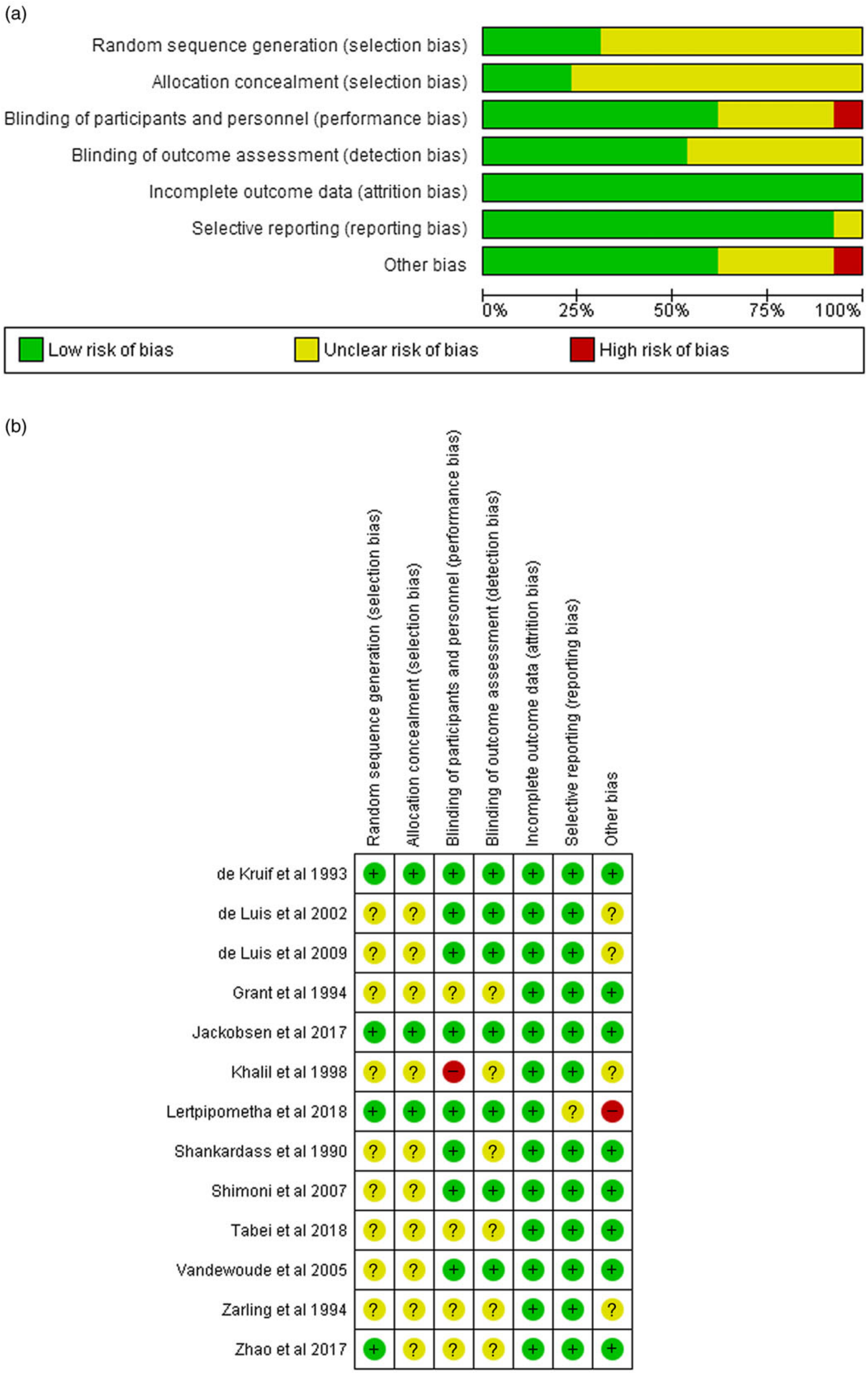



**Fig. 5.** (a) Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies. (b) Risk of bias summary: review authors' judgements about each risk of bias item for each included study.



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meta-analyses, this suggests that the use of FS feeds presents benefits in the reduction of diarrhoea in non-critically ill adults.

The main components of fibre used in the studies with feeds containing both insoluble and soluble fibre were non-starch polysaccharides, inulin and fructo-oligosaccharides, resistant starch, cellulose and lignin. Whereas, feeds containing soluble fibre comprised of soy polysaccharides, psyllium and pectin. Our paper found no difference in the incidence of diarrhoea between feeds containing both insoluble and soluble fibre and feeds containing soluble fibre only (OR 0·82, 95 % CI 0·20, 3·39 *v.* OR 0·34, 95 % CI 0·10, 1·16; $P = 0{\cdot}36$). This is inconsistent with another study that found a higher incidence of diarrhoea within the group on soluble fibre only feeds (35 %) compared with feeds containing both insoluble and soluble fibre (10 %)[49]. High heterogeneity remains between trials suggesting that the effects on diarrhoea may be confounded by other factors such as the addition of arginine and probiotics. One study included in our paper administered probiotics on top of fibre in the intervention group[42] which may provide gut health benefits and influence the incidence of diarrhoea[50]. The use of a mixture of insoluble and soluble fibre may be effective for the prevention of enteral tube feeding-induced diarrhoea in non-critically ill patients or those requiring long-term enteral nutrition.

Our paper found no difference between those receiving FS feeds and NFS feeds on stool frequency. In contrast, a systematic review[46] previously found that the use of FS feeds compared with NFS feeds significantly increased bowel frequency (test of overall effect, 0·27 (S.E. 0·08) times/d, $P = 0{\cdot}001$; $I^2 = 0\,\%$, $P = 0{\cdot}68$). After excluding non-RCT and limiting the analysis to adults only, the effect of FS feeds in increasing bowel frequency remained significant [test of overall effect, 0·25 (S.E. 0·10) times/d, $P = 0{\cdot}009$; $I^2 = 0{\cdot}00$, $P = 0{\cdot}52$][46]. This is consistent with our subgroup analysis with an increased stool frequency in the group receiving feeds containing soluble fibre only compared with those receiving feeds containing both insoluble and soluble fibres. Results are to be interpreted with caution given the limited data contributed by both groups.

Most studies included in the present paper investigated soluble FS feeds containing soy polysaccharides as a main component of fibre. There were contradicting results from previous studies investigating the effects of soy polysaccharides on stool frequency[51,52]. The second commonly used soluble fibre studied in the present paper, inulin, was previously found to increase stool frequency[53]. Another soluble fibre such as psyllium is also shown to help solidify loose stools which may help to reduce stool frequency[54]. Like soy polysaccharides, there was mixed evidence found regarding the effects on stool frequency for pectin[55,56]. The varying effect observed may be related to the different characteristics of dietary fibre. Dietary fibres are categorised into non-starch polysaccharides, resistant starch, and resistant oligosaccharides or grouped based on their physicochemical characteristics such as fermentation, solubility and viscosity[57,58]. These characteristics influence the therapeutic effects of dietary fibres after ingestion[59].

Insoluble fibre has been shown to increase stool mass with the help of particle formation and absorption of water, while the fermentability of some soluble fibres by the gut bacteria and production of SCFA may help normalise stool form and reduce diarrhoea[22]. The location at which fermentation occurs in the gastrointestinal tract is partly dependent on the degree of solubility. Fibres of higher solubility such as short-chain fructooligosaccharides and pectin are fermented by bacteria in the proximal colon, whereas fibres of lower solubility, such as cellulose, are not fermented or partially fermented in the distal colon where transit time is slower[60]. As a result, the concentration of SCFA varies throughout the length of the gastrointestinal tract, with the highest concentrations in the proximal colon and diminishing concentrations in the distal colon, the region of the gastrointestinal tract with the greatest density of microbes[61]. About 90 % of these SCFA are rapidly absorbed by the colon, stimulating water and Na absorption[62]. Thus, increased soluble fibre intake can stimulate colonic reabsorption of water and Na and minimise loose, watery stools. Most soluble non-starch polysaccharides, especially high-molecular-weight structures such as guar gum, certain pectins, b-glucans (or oat fibres), and psyllium, can form a gel structure in the intestinal tract that can delay absorption, possibly help to manage diarrhoea and promote bowel regularity[58], similarly shown in a previous study[63]. It was purported that soluble fibre is useful for creating favourable bowel movement by improving symptoms of small intestinal mucosal atrophy and normalising the intestinal flora[51]. This is important as antibiotics-induced diarrhoea is one of the primary causes of diarrhoea, especially in patients with acute illnesses which resulted from alterations of the gut microbiota[64].

### *Limitations*

As seen in the risk of bias assessment, there was a high risk of selection bias across all studies due to the lack of transparency in their allocation concealment and randomisation processes. There was a risk of human error as most data collection relied on subjective reporting which increases the risk of interpersonal error. All RCT involved a short duration and small sample size which may be underpowered and could result in sampling bias. As our paper included studies with other substances such as arginine and probiotics in addition to fibre, this may potentially affect diarrhoea incidence. There was widespread interstudy variation in the quantification of diarrhoea such as the use of different assessment tools (e.g. Bristol stool chart and King's stool chart) to assess key outcome measures including diarrhoea and frequency of stool output. There was also no consistent definition used across studies to define diarrhoea. Although most studies excluded participants with pre-existing medical conditions that predispose them to increased risk of diarrhoea (e.g. inflammatory bowel diseases or gut infection) and/or developed diarrhoea at the onset of the study[34–38,41–43,45], two studies specified that antibiotics were prescribed as a prophylaxis pre-surgery for their participants[39,40], and two studies did not explicitly specify[33,44]. Two papers did not state the specific type and quantity of fibre necessary for preventing diarrhoea[42,44].

Although our systematic review used a robust search methodology to include studies of interest, we had restricted access to journal databases and only included three databases. Additionally, only RCT published in English were included. As there were limited studies included in our paper, a publication



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bias analysis using the funnel plot was not able to produce a valid result and hence omitted. All studies included specified that the control feeds used were non-fibre containing except one[44]; however, due to limited data available from the article, it was not analysed.

Future studies would benefit from the use of consistent definitions of diarrhoea and the use of clinically relevant and objective markers of gastrointestinal function. The use of a standard methodology to assess diarrhoea outcomes across studies will allow for a more thorough evaluation of different types and quantities of fibres in different patient groups and healthcare settings and allow a more robust comparison between trials.

## Conclusion

This systematic review has shown that the use of FS feeds can reduce the incidence of diarrhoea in non-critically ill adults on exclusive enteral tube feeding. However, results should be interpreted with caution due to considerable heterogeneity between the study population, assessment tool for diarrhoea, a potential conflict of interest and the short duration of studies. Further well-designed RCT are needed to prove the efficacy of FS feeds used in enteral tube feeding.

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All authors contributed to the literature search, study selection, data extraction, critical appraisal of the evidence and analysis for this systematic review. VXPT and NANM drafted the initial manuscript. LBT provided feedback on the initial manuscript. All authors have read and approved the final draft.

The authors have no conflicts of interest to declare relevant to this article's content.

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