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Efficacy and tolerability of a low-residue diet for bowel preparation: systematic review and meta-analysis

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Abstract

Background Colorectal cancer (CRC) contributes significantly to cancer mortality worldwide. In an effort to reduce the risk of death, detection of polyps through colonoscopy is crucial. The success of the colonoscopy depends on the diet administered the day before the test. Our aim was to evaluate the efficacy, tolerability, and adverse effects of bowel preparation when using a low-residual diet (LRD) compared to a clear-liquid diet (CLD) the day before a scheduled colonoscopy.

Methods PubMed/Medline, Embase, the Cochrane Central Register of Controlled Trials (CENTRAL) and Scopus databases were searched. We included studies of patients undergoing a scheduled colonoscopy for CRC screening and surveillance or for diagnostic purposes that compared a LRD with a CLD the day before the colonoscopy. Efficacy, the primary outcome, was evaluated as the rate of adequate bowel preparation. Secondary outcomes were tolerability and adverse effects of bowel preparation.

Results Thirteen RCTs ($N=2587$) were included. Patients receiving a LRD compared to a CLD showed no difference in adequate bowel preparations (RR 1.02; 95% CI 0.99–1.05; $I^2=60\%$). However, the LRD improved patient tolerability (RR 1.17; 95% CI 1.12–1.23; $I^2=66\%$) and had fewer adverse effects (RR 0.89; 95% CI 0.84–0.94; $I^2=73\%$) compared to the CLD. Groups using a LRD with 4L of polyethylene glycol in a single dose or a LRD with < 2000 kcal < 32 g of fibres/day had better tolerability.

Conclusion Based on these findings, our recommendation is strong in favour of a LRD for bowel preparation of patients undergoing a scheduled colonoscopy. This diet could also be useful as a preoperative colonic preparation, but this requires further research.

Keyword Low-residue diet · Bowel preparation · Meta-analysis

Colorectal cancer contributes significantly to cancer mortality worldwide. In an effort to reduce the risk of death associated with CRC, detection of polyps with a scheduled colonoscopy is crucial [1]. The rate of polyps missed during endoscopy is 20 to 28%, although inadequate colon cleansing can increase that proportion and the risk of advanced lesions in the short term [2]. The success of colonoscopy in detecting polyps depends on the experience of the endoscopist, the quality of bowel cleansing, and patient's tolerability of different colonic preparation schedules [2, 3].

Adequate bowel cleansing is essential for the endoscopist to be able to perform a good exploration of the colonic mucosa in search of pre-malignant lesions [4]. On the other hand, the surveillance interval between an index screening endoscopy and the subsequent follow-up endoscopy will depend on the number and type of polyps detected in the first one, but it will also depend on the quality of the intestinal preparation of the index endoscopy [2]. When the cleansing of the colon is not optimal, small polyps may be missed and the endoscopic test should be repeated within a year of the index endoscopy [1].

Another fundamental aspect related to the success of colonoscopy in detecting pre-malignant lesions is patients' tolerability of intestinal preparation [4]. Preparation

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schedules that are better tolerated and have fewer adverse events tend to increase patient adherence and satisfaction to the preventive test [2]. Our aim was to evaluate the efficacy, tolerability, and adverse effects of bowel preparation when using a LRD compared to a CLD administered the day before a scheduled colonoscopy.

Methods

Inclusion criteria for the studies in this review.

Types of studies Randomized clinical trials were included.

Types of participants Adult patients undergoing a scheduled colonoscopy for CRC screening and surveillance or for diagnostic purposes.

Types of interventions LRD with CLD the day before a scheduled colonoscopy (See Table 1; Fig. 11).

Types of outcome measures The primary outcome (efficacy) was the rate of adequate bowel preparation which was studied using different validated scales (BBPS scale, Ottawa, Aronchick). Adequacy was defined as a colonoscopy with a score of BBPS (2 or 3 points in each colon segment), Aronchick (good or excellent), Ottawa (< 6 points total) (See Table 2). The secondary outcome was patients' tolerability and adverse effects to bowel preparation. Tolerability was assessed by the acceptability rate and the rate of patients who would choose the same preparation in the future. Adverse effects were assessed by the rate of events such as nausea, vomiting, and abdominal discomfort experienced by patients during bowel preparation.

Search methods for identifying studies

PubMed/Medline, Embase, Cochrane Central Register of Controlled Trials (CENTRAL), and Scopus databases were searched.

Search terms "low-residue diet and colonoscopy," "fibre-free diet and colonoscopy," and "diet liberalization and colonoscopy.

Data collection and analysis

Data collection and analysis was carried out in three steps. First, by using the above search strategy, documents that appeared to be potentially relevant were identified by two authors. Then, after reading the full texts, the authors independently assessed the eligibility of all identified trials using ad hoc eligibility based on the above inclusion criteria. The data extracted included the following elements: (a) Patient characteristics: age, sex, risk factors; (b) Total number of patients originally assigned to each intervention arm; (c) Low-Residue Diet administered the day before colonoscopy (intervention arm); (d) Clear-Liquid Diet administered the day before colonoscopy (control arm); (e) results: primary and secondary outcomes. Disagreement between the authors was discussed and an agreement was reached by consensus. Finally, the methodological quality of the selected trials was independently assessed by two authors. There is no need for IRB approval and written consent to this meta-analysis.

Bias assessment in the included studies

The Cochrane 'Risk of bias' tools [5] were used to assess the following domains: Random sequence generation,Allocation concealment; Blinding of participants and staff; Blinding of outcome assessment; Incomplete outcome data; Selective outcome reporting; Other sources of bias [6]. We consider subjective outcomes separately in our assessment of blinding and incomplete data. Studies were considered to have a high, low, or unclear risk of bias for each domain assessed. We judged the risk of bias amongst studies as follows: Low risk of bias (plausible bias that is unlikely to seriously alter outcomes) if all domains are at low risk of bias; Risk of unclear bias (plausible bias that raises doubts about the results) if

Table 1 Example of a low-residue diet (LRD) for the day before colonoscopy

	Breakfast	Snack	Lunch	Snack	Dinner
Carbohydrate	80 g of white bread or 3 slices of white toast	1 low-fat yogurt without fruits or cereals	White rice (130 g) or plain white pasta (200 g) or peeled potatoes baked, or boiled) (300 g)	1 low-fat yogurt without fruits or cereals	White rice (130 g) or plain white pasta (200 g) or peeled potatoes baked, or boiled) (300 g
Protein	Poultry (120 g) or ham (120 g)		Lean meat: poultry (160 g) or fish (200 g) or eggs (2 units)		Lean meat: poultry (160 g) or fish (200 g) or eggs (2 units)
Dairy products	1 glass (250 ml) skim milk (coffee allowed at will)				

The LFD provide up to 2000 kcal/day with a mean dietary fibre content < 10 g

Table 2 Validated bowel preparation scales

Scale	Colon segment to be rated	Description	Segment score	Minimum total score	Maximum total score	Adequacy
Aronchick score	Global quality of the preparation	1 (excellent): small volume of clear liquid or > 95% of the surface seen 2 (good): large volume of clear liquid covering 5–25% of the surface but > 90% seen 3 (fair): some semi-solid stool that could be suctioned or washed away but > 90% of surface seen 4 (poor): semi-solid stool that could not be suctioned or washed away and < 90% of surface seen 5 (inadequate): repeat preparation and colonoscopy needed	Not applicable	1	5	Good or excellent (1 or 2)
Ottawa score	Right colon Mid colon Rectosigmoid colon	For each segment: 0 (excellent): prior to suction/wash 1: between 0 and 2 2: suction liquid stool to see colonic wall adequately 3: wash + suction necessary 4: colonic wall not visualized	For each segment: Min: 0; Max: 4	0 (Perfectly clean colon)	14 (Solid stool in each colon segment and lots of fluid)	< 6 points
	Fluid quantity is a global value for the entire colon	2: large quantity of fluid 1: moderate quantity of fluid 0: small quantity of fluid	Min: 0; Max: 2			
BBPS	Right colon Transverse (including the hepatic and splenic flexures) Left colon (including the descending colon, sigmoid colon, and rectum)	For each segment: 0: unprepared colon segment with mucosa not seen because of solid stool that cannot be cleared 1: portion of mucosa of the colon segment seen, but other areas of the colon segment not well seen because of staining, residual stool, and/or opaque liquid 2: minor amount of residual staining, small fragments of stool, and/or opaque liquid, but mucosa of colon segment is seen well 3: entire mucosa of colon segment well seen	For each segment: Min: 0; Max: 3	0 (Unprepared colon)	9 (Perfectly clean colon with-out any residual liquid)	2 or 3 points in each colon segment (> 6 points)

one or more domains have an unclear risk of bias; High risk of bias (plausible bias that seriously undermines confidence in outcomes) if one or more domains have a high risk of bias. Biases in the included studies (Fig. 1).

Methodological quality of the studies

The quality of evidence assessment was carried out using the GRADE approach [5, 7, 8].

Statistical analysis

The Cochrane Collaboration review manager software (RevMan version 5.1) was used for data analysis. Data were analysed according to the intention to treat principle. Patients with final missing outcomes were assumed to be treatment failures. Dichotomous Variables Odd ratios (OR) and 95% confidence intervals (95% CI) were calculated based on a fixed-effect model. Heterogeneity amongst trial results was assessed by inspection of graphical presentations and by

calculating the chi-square test of heterogeneity (P value of 0.05 was regarded as statistically significant). We used the I^2 statistic to quantify the effect of heterogeneity [5].

Heterogeneity assessment

The decision to group the results of the individual studies depended on an assessment of clinical and methodological heterogeneity. If the studies were considered sufficiently homogeneous for data pooling, the statistical heterogeneity was assessed by visual inspection of the forest plots using the Chi ^{2} test. We also used the I^2 statistic, for which we based our interpretations on those suggested by Higgins et al. [5]: from 0 to 40%: may not be important; from 41 to 60%: may represent moderate heterogeneity; from 61 to 100%: considerable heterogeneity [6].

Publication bias

A funnel plot analysis was conducted to investigate publication bias (Fig. 2).

Results

Description of studies

We selected 19 potentially relevant published studies for full text review after title review and abstract selection (Fig. 3). Six studies were excluded: one of the studies was excluded because it compared a LRD administered during three previous days with a LRD administered during the day before endoscopy [9]. Another study was excluded because it assessed a pre-packaged LRD compared to a non-pre-packaged LRD [10]. Three studies were excluded because they were systematic reviews with meta-analyses [11–13]. One study was excluded because it was not randomized [14]. After full text review, there were 13 studies that met the inclusion criteria [6, 15–26].

Details of the studies included

The 13 included randomized clinical trials are summarized (See Table 3). All of them were performed in adult patients who underwent a scheduled colonoscopy for CRC screening and surveillance or for diagnostic purposes. Different purging agents (polyethylene glycol, sodium sulphate, sodium phosphate, bisacodyl), different schedules (split or single doses), and different timing between the last dose of the purging agent and the colonoscopy (timing > or < 5 h) were used. There were also variations in the type of LRD and the number of meals patients were allowed to have. There were differences between the studies with respect to the scales on which colonic cleansing and tolerability were assessed. Four studies reported the LRD caloric content and only two on the LRD fibre content.

Risk of bias of the studies included

Out of the 13 primary studies included in the meta-analysis, eleven studies had a low risk of bias [6, 15–20, 22, 23, 25, 26], and only two studies had a high risk of bias [21, 24]. The random sequence generation was not clear in three studies [17, 21, 23]. The allocation concealment was not clear in five studies [17, 23–26]. When blinding process was assessed, it was not clear in five studies [6, 15, 17, 19, 24]. Full follow-up was not clear in only one of the studies [6]. In two studies, the intention to treat analysis had a high risk of bias due to serious problems [21, 24], and in one study the intention to treat analysis was not clear [22]. Regarding early termination, no problems were detected in the studies. Finally, there were no other biases in the included studies.

Effects of interventions

Primary outcomes

Thirteen RCT studies were included ($N = 2587$). Patients who received a LRD compared to a CLD showed no differences in adequate bowel preparations (RR 1.02; 95% CI 0.99–1.05; $I^2 = 60\%$). For this result, different subgroups of patients were analysed.

One analysis evaluated the adequacy of the bowel preparation of a LRD compared to a CLD according to the volume of purgatives and form of administration. The group that used small volume in split-doses (< 4L of PEG or phosphate/sulphate or picosulphate salts) showed no difference in efficacy between the two diets (RR 0.97 95% CI 0.94–1.01; $I^2 = 0\%$) as did the group that used small volume in single dose (RR 0.98 95% CI 0.87–1.11; $I^2 = 44\%$). Heterogeneity in the results was low; therefore, there was no inconsistency. In turn, the group that used a high volume in split-doses (4L of PEG) did not show differences in efficacy between the two diets either (RR 1.07 95% CI 1.00–1.15) and the same was true for the group that used a high volume in a single dose (RR 1.13 95% CI 1.04–1.22; $I^2 = 91\%$). Heterogeneity in this last subgroup was important; therefore, there was inconsistency (Fig. 4).

Another analysis evaluated the efficacy of a LRD compared to CLD according to the timing between the last dose of purgative and colonoscopy. The subgroup using a timing of less than 5 h showed no difference in efficacy between the two diets (RR 1.01 95% CI 0.98–1.04; $I^2 = 25\%$). No important heterogeneity was detected. The group in which the timing of intestinal preparation was greater than 5 h, showed no difference in efficacy between the two diets (RR

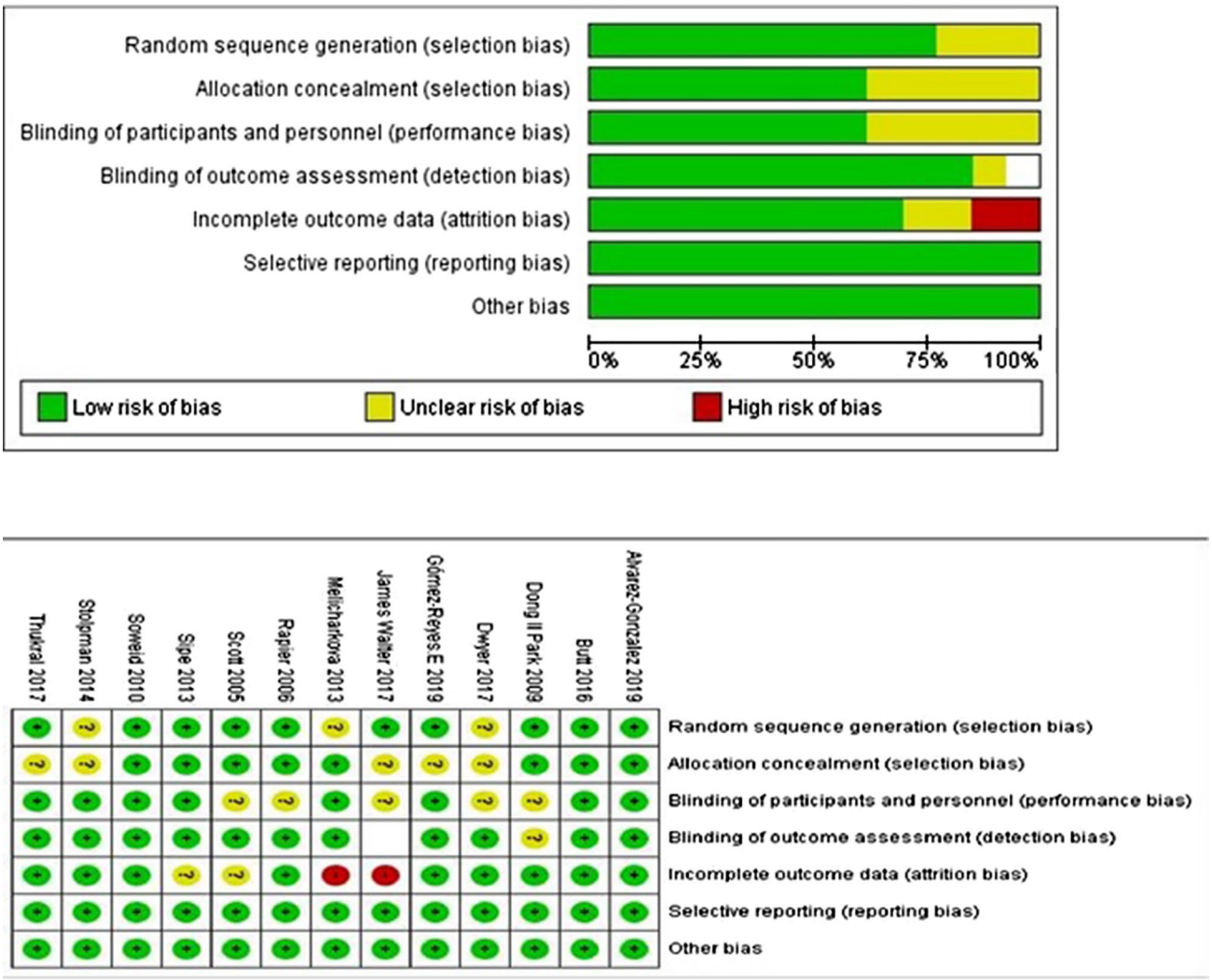

Fig. 1 Biases in the included studies

1.03 95% CI 0.97–1.09; $I^2 = 74\%$), but heterogeneity was detected. (Fig. 5).

Finally, one analysis evaluated the efficacy of a LRD compared to a CLD according to caloric and fibre content of a LRD. This analysis showed that studies reporting the caloric and fibre content of LRD (LRD < 2000 kcal < 32 g fibre/day) had the same bowel preparation efficacy between the two diets (RR 1.03 95% CI 0.98–1.07; $I^2 = 0\%$). There was no heterogeneity in the results. There was also no difference in efficacy in the subgroup that did not report the caloric and fibre content of the LRD (RR 1.01 95% CI 0.97–1.06: $I^2 = 69\%$). However, heterogeneity was detected in this last subgroup. (Fig. 6).

By using the GRADE approach, we determined that for the primary outcome the quality of evidence was downgraded to moderate due to inconsistency and there was no difference in efficacy of both diets regarding absolute results (17 more patients per 1000; 95% CI from 8 fewer patients to 42 more) (See Fig. 10).

Secondary outcomes

Thirteen RCT studies were included ($N = 2587$). The LRD compared to the CLD demonstrated better tolerability (RR 1.17; 95% CI 1.12–1.23; $I^2 = 66\%$). Multiple subgroup analyses were performed for this outcome.

One of these analyses assessed tolerability of a LRD compared to a CLD based on purgative volume and form of administration. The group that used a small volume (< 4L of PEG or phosphate/sulphate or picosulphate salts) in split-doses showed greater tolerability in favour of a LRD (RR 1.13 95% CI 1.07–1.20; $I^2 = 41\%$) as well as when a small volume was used in a single dose (RR 1.16 95% CI 1.02–1.32; $I^2 = 87\%$). This last subgroup showed

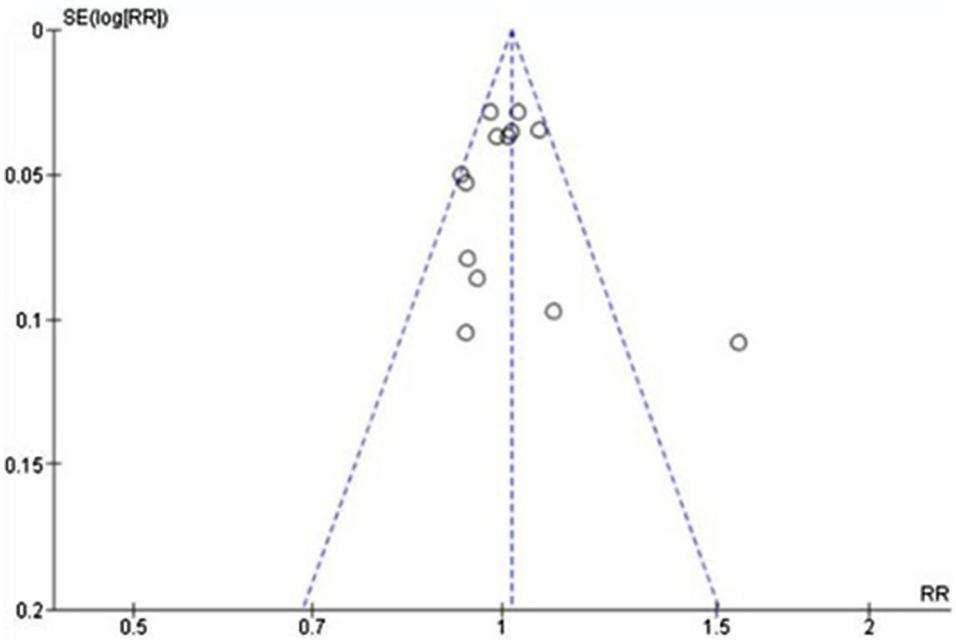

Fig. 2 Funnel plot analysis

inconsistency in the results. In turn, the group using a high volume (4L of PEG) in unsplit dose also showed greater tolerability in favour of LRD (RR 1.48; 95% CI 1.26–1.75; $I^2 = 33\%$). Heterogeneity in this case was not important. Therefore, there was no inconsistency. The subgroup using a high volume in split-doses included a single study and showed no difference in tolerability between LRD and CLD (RR 1.06; 95% CI 0.94–1.19). (Fig. 7).

Another subgroup analysis that evaluated tolerability of LRD compared to CLD based on LRD caloric and fibre reported content, showed that the LRD with < 2000 kcal < 32 g fibre/day had better tolerability (RR 1.20; 95% CI 1.09–1.32; $I^2 = 78\%$). Heterogeneity in the results was observed. There was also greater tolerability in favour of a LRD in the subgroup that did not report caloric and fibre content of the diet (RR 1.16 95% CI 1.10–1.23: $I^2 = 62\%$). There was detectable heterogeneity in this last subgroup. (Fig. 8).

The incidence of adverse effects was measured by assessing the rate of nausea, vomiting, and abdominal discomfort. Seven studies were included for this outcome (N-1552). Patients who followed a LRD compared to a CLD showed fewer adverse effects (RR 0.89; 95% CI 0.84–0.94; $I^2 = 73\%$). Heterogeneity in the results was detected. (Fig. 9).

By using the GRADE approach, we determined that for tolerability of the bowel preparation outcome, the quality of evidence was downgraded to moderate due to inconsistency. There was greater tolerability of a LRD compared to a CLD when observing the absolute results (106 more patients per 1000; 95% CI from 75 more patients to 144 more). (See Fig. 10).

Regarding adverse effects of bowel preparation, the quality of evidence was downgraded to moderate due to inconsistency. Lower frequency of adverse effects was observed for a LRD compared to a CLD when analysing the absolute results (81 fewer patients per 1000; 95% CI from 119 fewer patients to 44 fewer) (See Fig. 11).

Discussion

For many years, the diet administered the day before a colonoscopy has been limited to clear liquids assuming their benefit for adequate colonic cleansing. In the mid-1990s, different studies [27, 28] incorporated a soft diet the day before the endoscopic test instead of just liquids and noted that bowel cleansing was not affected [29]. One of the first studies to evaluate colon cleansing with a LRD the day before the colonoscopy was Scott et al. [6]. This study found no difference in bowel cleansing between the two diets. Rapier et al. [19] and Stolpman et al. [23] concluded that there was no difference between the two diets regarding the adequacy of colon cleansing and patient tolerability. The Park et al. [15] study controlled the caloric and fibre content of the LRD (1095 kcal and 32 g fibre per day) and although no difference was observed with respect to the colonic cleansing efficacy ($P = 0.063$), the reported tolerability was higher in the LRD group ($P = 0.036$). Multiple subsequent studies such as Melicharkova et al. [21], Sipe et al. [22], Butt et al. [16], Dwyer and Tan [17], Walter et al. [24], Thukral et al. [25] reported similar results. The Soweid et al. [20] study concluded that the quality of the colon preparation was better in the LRD group (81.4% vs. 52.0%, $P < 0.001$) as was the patients' tolerability of the preparation ($P < 0.001$).

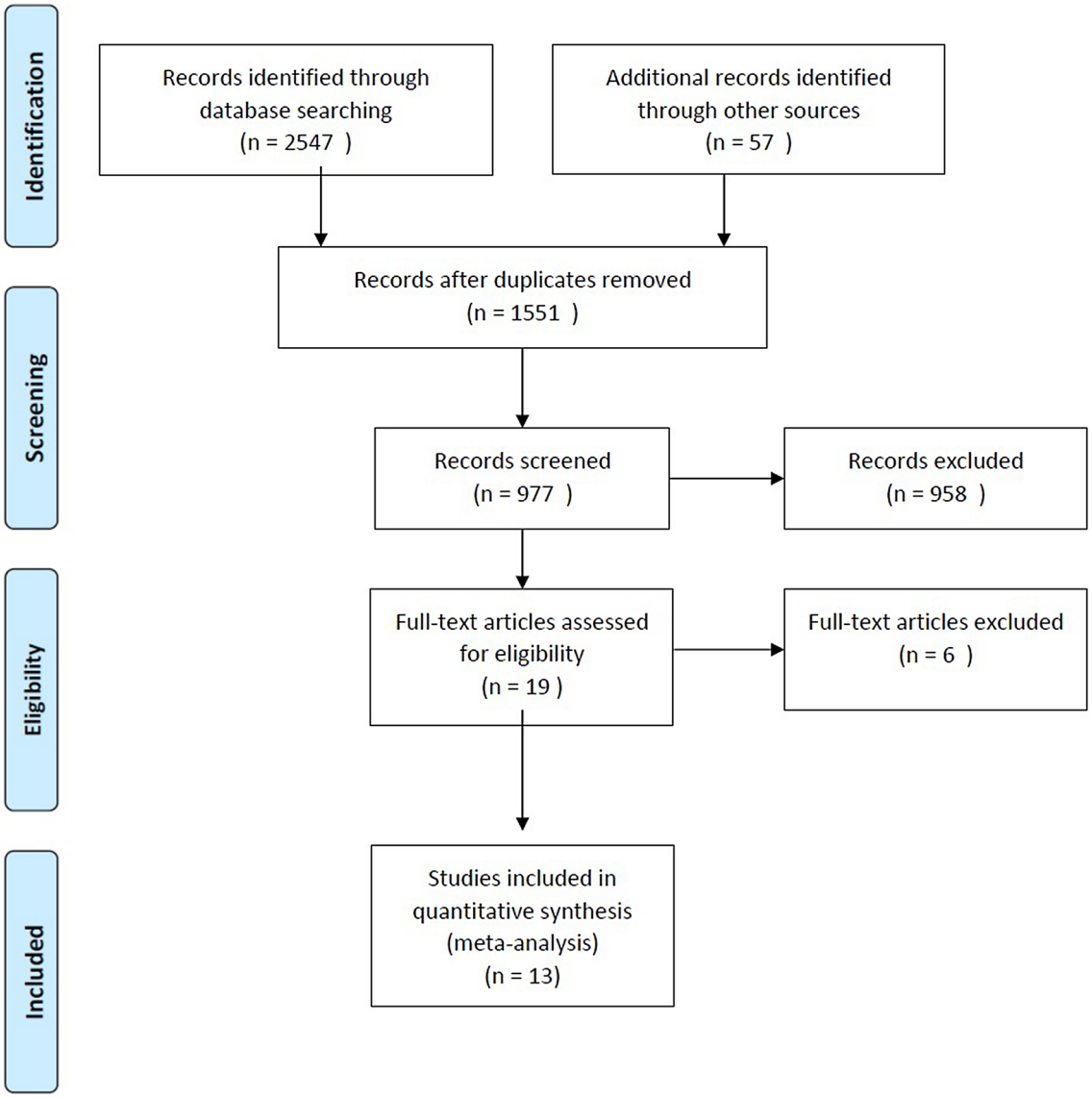

Fig. 3 Study identification flowchart

Recent studies controlled the number of calories and fibres in the LRD group on the assumption that it would improve efficacy and tolerability. For instance, Alvarez-Gonzalez et al. [18] evaluated a normocaloric LRD (2000 kcal/day) low in residues (< 10 g fibre/day) and showed that an adequate intestinal preparation was achieved in 95.7% of cases in the intervention arm ($P = 0.04$). In addition, participants reported less hunger ($P = 0.006$) and better tolerability ($P = 0.04$). Gómez-Reyes et al. [26] reported that efficacy of bowel preparation with a LRD was not superior to a CLD (70% vs. 73%, $P = 0.08$), although the LRD was better tolerated ($P = 0.07$).

The U.S. Multi-Society Task Force recommend a LRD for part or all of the day before colonoscopy (Weak recommendation, moderate-quality evidence). [30] However, the European Society of Gastrointestinal Endoscopy recommends LRD before colonoscopy with the same evidence (Strong recommendation, moderate-quality evidence) [31].

This meta-analysis demonstrated that when comparing a LRD to a CLD there was no difference in efficacy of bowel preparation for scheduled colonoscopy. Efficacy of both diets was not affected by different volumes of purgatives and forms of administration. Similarly, neither the timing between the last dose of purgative and colonoscopy nor the fibre content affected the efficacy of the diets.

However, compared to a CLD, a LRD demonstrated better tolerability of the bowel preparation used for scheduled

Table 3 Randomized clinical trials are summarized

Study	Type of Study	Participants	Control arm	Intervention arm	Type of LRD	Outcomes	Notes
Scott et al. [6]	RCT U. S	Adults, screening, and diagnostic colonoscopy	(n 100) CLD and intestinal preparation with 1 bottle of NaP (45 ml) administered the day before the test at 7 pm + 1 bottle of NaP (45 ml) administered 4hs before colonoscopy	(n 100) LRD and intestinal preparation with 1 bottle of NaP (45 ml) administered the day before the test at 7 pm + 1 bottle of NaP (45 ml) administered 4hs before colonoscopy	Administered at Breakfast and lunch time	Colonic cleansing evaluated with the Aronchick scale. Adverse effects and tolerability evaluated as a rate of discomfort	Last dose of purgative administered 4 h before colonoscopy It is not clear whether it excludes patients at risk of poor preparation It does not state the calories and fibre grams of the LRD
Rapier et al. [19]	RCT U. S	Adults, screening colonoscopy	(n 37) CLD and intestinal preparation with oral Mg citrate-bisacodyl and single dose suppositories administered the day before colonoscopy	(n 38) LRD and intestinal preparation with oral Mg citrate-bisacodyl administered the day before colonoscopy (n 39) LRD and intestinal preparation with PEG	Pre-packaged LRD administered at breakfast, lunch, and dinner time	Colonic cleansing evaluated with the Aronchick scale. Tolerability evaluated with visual analogue scale (tolerable or very tolerable and non-tolerable)	The last dose of the purgative exceeds 4–5 h to perform the endoscopy It does not state whether patients who are at risk of poor preparation are excluded It does not clarify the calories and fibre grams of the LRD
Park et al. [15]	RCT Korea	Adults, screening, and diagnostic colonoscopy	(n 106) CLD administered the day before and 4L of PEG administered at 6 am on the day of colonoscopy	(n 108) pre-packaged LRD administered the day before colonoscopy and 4L of PEG at 6am on the day of colonoscopy	Pre-packaged LRD administered at breakfast, lunch, and dinner time	Colonic cleansing rated with the Ottawa scale Adverse effects and Tolerance evaluated with visual analogue scale	It does not state the interval of the last PEG dose and colonoscopy It does not state whether patients who are at risk of poor preparation are excluded It does state the characteristics of LRD (1095 kcal/day; fibre 32 g)
Soweid et al. [20]	RCT Lebanon	Adults, screening, and diagnostic colonoscopy	(n 98) CLD and intestinal preparation with 4L of PEG administered the night before colonoscopy	(n 102) LRD and intestinal preparation with 4L of PEG administered the night before colonoscopy	Administered at breakfast, lunch, and dinner time	Colonic cleansing evaluated with the Ottawa scale Tolerability evaluated with visual analogue scale	It does not state the interval between the last dose of PEG and colonoscopy It does not state whether patients who are at risk of poor preparation are excluded It does not state Kcal or the grams of fibre in the LRD

Table 3 (continued)

Study	Type of Study	Participants	Control arm	Intervention arm	Type of LRD	Outcomes	Notes
Melicharkova et al. [21]	RCT Canada	Adults. Scheduled outpatient colonoscopy	(n 122) CLD with 10 mg bisacodyl and 2 sachets of sodium pico sulphate administered 8 h before the colonoscopy (single dose)	(n 126) LRD with 10 mg bisacodyl and 2 sachets of sodium Pico sulphate administered 8 h before the colonoscopy (single dose)	LRD administered only at breakfast time	Colonic cleansing evaluated with the Ottawa and Aronchick scale. Tolerability to the Preparation evaluated as acceptability with visual analogue scale	It exceeds the time of 4–5 h to perform the endoscopy It does not state whether it excludes patients who are at risk of poor preparation It does not state the calories and fibre grams of the LRD
Sipe et al. [22]	RCT U. S	Adults, screening, and surveillance colonoscopy	(n 114) CLD. Intestinal preparation was done with Split-dose OSS the night before and 4hs before the colonoscopy	(n 116) LRD Intestinal preparation was done with Split-dose OSS the night before and 4hs before the colonoscopy	LRD administered at breakfast and lunch time and as snacks	Colonic cleansing evaluated with the Boston scale Tolerability evaluated as patient satisfaction. Side effects measured with a visual analogue scale	It does not exceed the time of 4–5 h from the last dose of purgative to endoscopy (timing < 5hs) It is not stated whether patients who are at risk of poor preparation are excluded It indicates the calories (1000 kcal) but not the grams of fibre in the LRD
Stolpman et al. [23]	RCT U. S	Adults, screening, and surveillance colonoscopy	(n 101) CLD administered the previous day. Intestinal preparation was done with sodium sulphate in Split-doses the night before and 4 h before colonoscopy	(n 100) LRD administered the previous day. Intestinal preparation was done with sodium sulphate in Split-doses the night before and 4 h before colonoscopy	LRD administered at breakfast and lunch time	Colonic cleansing evaluated with the Boston scale Tolerability evaluated as acceptable/unacceptable preparation	It does not exceed the time of 4 h from the last dose of purgative to the endoscopy (timing < 5 h) It does not exclude patients who are at risk of poor preparation It does not indicate the calories or grams of fibre in the LRD

Table 3 (continued)

Study	Type of Study	Participants	Control arm	Intervention arm	Type of LRD	Outcomes	Notes
Butt et al. [16]	RCT Australia	Adults, scheduled screening, or diagnostic colonoscopy	(n 111) CLD and 2L of PEG. Split or single doses administered depending on the schedule of colonoscopy	(n 115): LRD and 2L of PEG. Split or single doses administered depending on the schedule of colonoscopy	LRD administered at breakfast, lunch, and dinner time	Colonic cleansing evaluated with the Harefield scale. Tolerability and acceptance were quantified using a visual analogue scale	It exceeds the time of 4–5 h from the last dose of purgative to endoscopy It does not exclude patients who are at risk of poor preparation It does not state the calories or the grams of fibre in the diet
Dwyer and Tan [17]	RCT Australia	Adults, outpatient colonoscopy	(n 125) CLD administered the day before and 1L of PEG at 6 pm + two sachets of SPMC (sodium Pico sulphate/magnesium citrate) at 7 pm the day before colonoscopy	(n 125) LRD administered the day before colonoscopy. Two sachets of Pico-Salax (picosulfate sodium, magnesium oxide, and citric acid) were administered in split-doses: one at 21 pm on the previous day and one 4 h before colonoscopy	LRD administered for 2 days before the test	Colonic cleansing evaluated with the Ottawa scale. Tolerability and adverse effects were quantified using an analogical scale visual	It does not state the interval between the last dose of purgative and the colonoscopy It does not specify LRD characteristics (Kcal-day; fibre g) It does not state whether it excludes patients at risk of poor preparation (severe constipation, etc.)
Walter et al. [24]	RCT U. S	Adults, scheduled screening, surveillance, and diagnostic colonoscopy	(n 72) CLD administered the previous day and preparation with of 2L PEG administered as a split-dose (the first litre at 5 pm the day before colonoscopy and the second litre 4 h before colonoscopy)	(n 68) LRD administered the previous day and preparation with of 2L PEG administered as a split-dose (the first litre at 5 pm the day before colonoscopy and the second litre 4 h before the colonoscopy)	LRD at breakfast and dinner time	Colonic cleansing evaluated with the Boston scale. Secondary outcomes included satisfaction and adverse effects	It considers the time of 4–5 h to perform the endoscopy. (timing < 5 h) It is not clear whether patients who are at risk of poor preparation are excluded It does not state whether it excludes calories or fibre grams from the low-residue diet

Table 3 (continued)

Study	Type of Study	Participants	Control arm	Intervention arm	Type of LRD	Outcomes	Notes
Thukral et al. [25]	RCT U. S	Adults, screening, and surveillance colonoscopy	(n 107) CLD administered the day before colonoscopy with a split-dose of Mg citrate (last dose of purgative administered 4 h before the test)	(n 108) LRD administered the day before colonoscopy with a split-dose of Mg citrate (last dose of purgative administered 4 h before the test)	LRD at breakfast and lunch time and as snacks	Colonic cleansing evaluated with the Boston scale Tolerability was evaluated with a visual analogue scale of satisfaction	It does not exceed the time of 4–5 h from the last dose of purgative to endoscopy. (timing < 5 h) It is not clear whether it excludes patients who are at risk of poor preparation It does not state the calories or grams of fibre in the LRD
Alvarez-Gonzalez et al. [18]	RCT Spain	Adults. Screening colonoscopy for CRC	(n 138) CLD administered the day before colonoscopy and 2L of PEG administered the previous afternoon and 2L administered 5 h before colonoscopy	(n 138) LRD administered for 4 days before colonoscopy and 2L of PEG on the previous afternoon and 2L administered 5 h before colonoscopy	LRD administered at breakfast and lunch time and both snacks	Colonic cleansing evaluated with the Boston scale Tolerability was evaluated with a visual analogue scale of satisfaction	It does not exceed the time of 4–5 h from the last dose of purgative to endoscopy Excludes patients who are at risk of poor preparation It states the calories (2000 kcal/day, < 10 g/day of fibre)
Gómez-Reyes et al. [26]	RCT Mexico	Adults. Screening colonoscopy	(n 105) CLD administered the day before colonoscopy and 4L of PEG from 4 pm ending at 8 pm	(n 100) LRD administered the day before colonoscopy and 4L of PEG from 4 pm ending at 8 pm	LRD administered at breakfast and lunch time and both snacks	Colonic cleansing evaluated with the Boston scale Tolerability was evaluated with a visual analogue scale according to the patients' symptoms caused by the preparation	It does not state the time of 4–5 h from the last dose of purgative to endoscopy It does not exclude patients at risk of poor preparation LRD had 1500 kcal but did not specify grams of dietary fibre

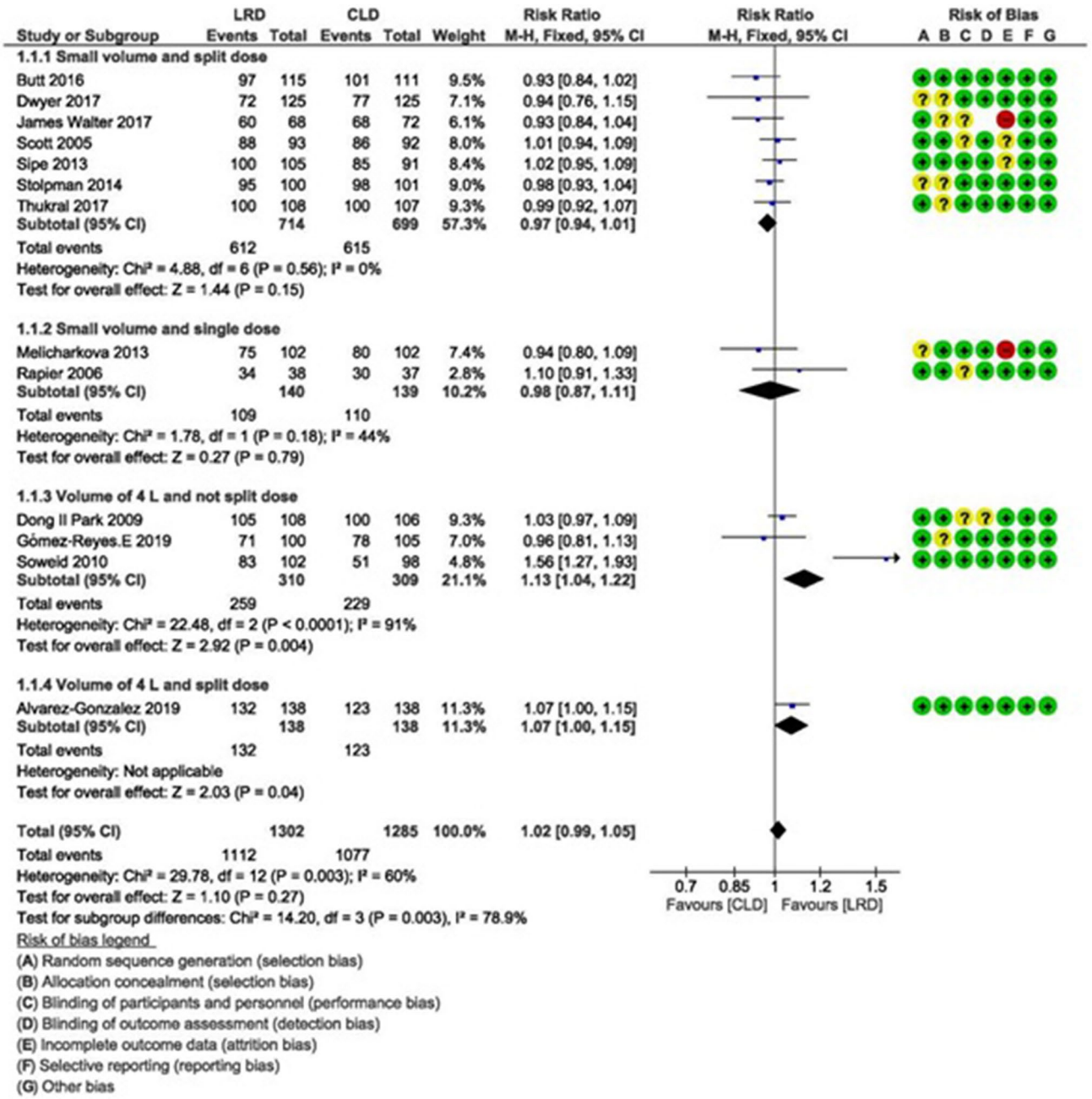

Fig. 4 Efficacy of bowel preparation and subgroup (according to volume of purgatives and form of administration)

colonoscopy. The subgroup analysis studying the volume of purgatives and form of administration demonstrated greater tolerability of a LRD compared to a CLD especially in the subgroup that used high volume purgatives (4L of PEG) in single doses.

Additionally, this study has shown that, compared to a CLD, the LRDs had better tolerability. However, the greatest tolerability was found in the LRD that reported fibre and caloric content (< 2000 kcal < 32 g fibre/day). Regarding adverse effects, when both diets were compared, a lower frequency was observed in a LRD.

According to these results, we believe this diet would be significantly beneficial for inpatients with comorbidities such as chronic kidney failure and hypertension who undergo a scheduled endoscopy, as they are usually given PEG instead of sulphates and phosphates. Since the volume of PEG administered is high (4L), the diet would increase tolerability to this regime. On the other hand, these findings highlight the importance of having a group of nutritionists

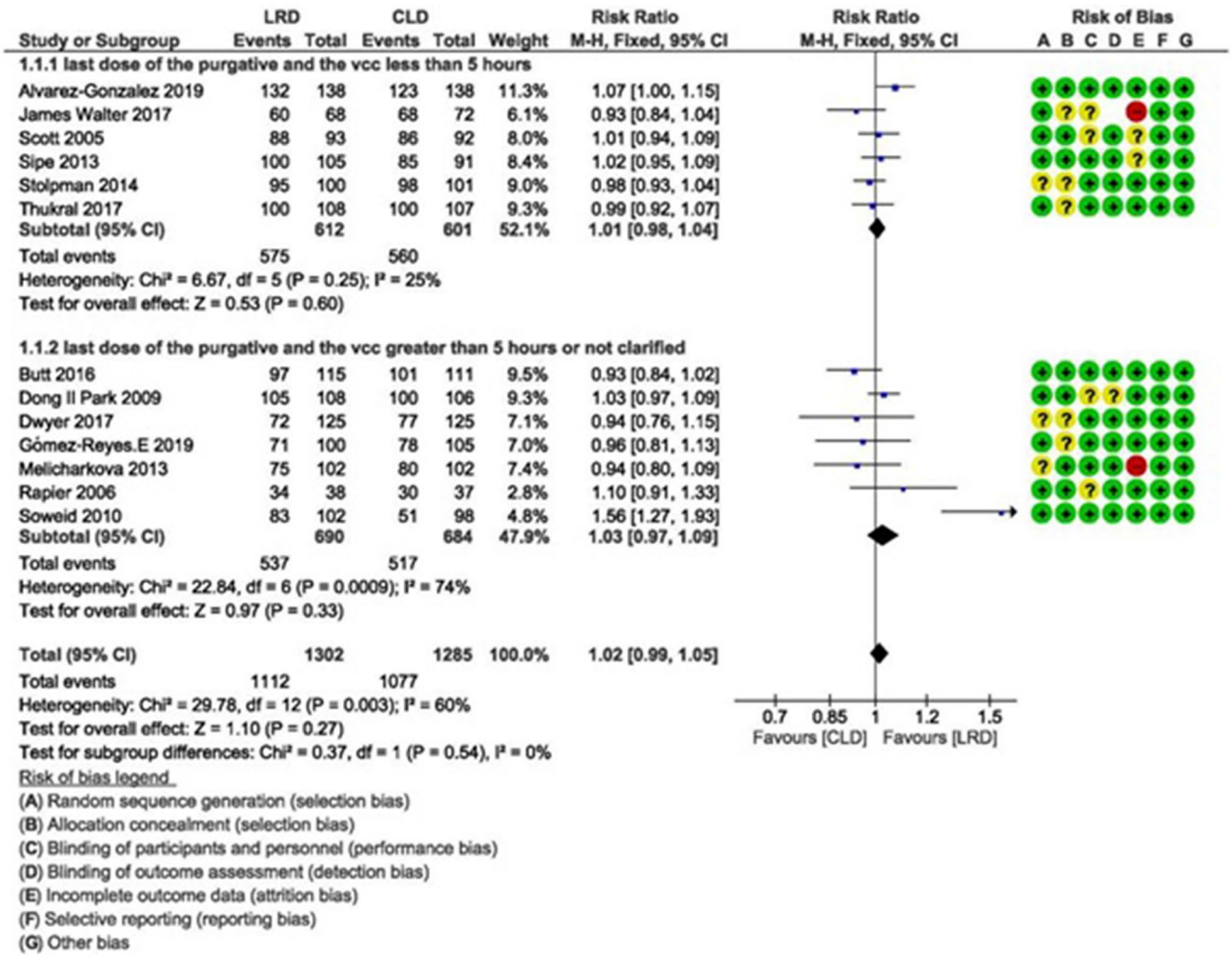

Fig. 5 Efficacy of bowel preparation and subgroup (according to timing between the last dose of purgative and colonoscopy)

contributing with the development of a specially designed diet for this purpose.

There were several strengths to the study; an extensive search of multiple databases was conducted without language restrictions and only randomized controlled trials were included. In addition, a thorough bias analysis was conducted in all included studies. Moreover, the different studies evaluated examined different types of bowel preparations (PEG, oral sodium solution, sodium phosphate, magnesium citrate), various dosage modes (single or split), different intervals between the last dose and colonoscopy (< 5 h vs > 5 h), and different characteristics of the LRD (amount of calories and grams of fibre known and not known). The most remarkable feature of this review was to have performed multiple subgroup analyses for each of the outcomes studied and used the GRADE approach to assess the certainty of the evidence, calculate absolute results based on the relative results, and make an estimate of the effect based on relative and absolute results.

However, there were also limitations; the LRDs, for instance, varied between studies. Park et al. [15] and Rapier et al. [19] used a pre-packaged LRD from different companies, whilst the other studies used a LRD plan specially designed by nutritionist or a study protocol. The number of meals allowed on the day before the colonoscopy differed between the studies. Soweid et al. [20] and Butt et al. [16] allowed a LRD at 3 meals the day before. Scott et al. [6], Stolpman et al. [23], and Walter et al. [24] allowed a LRD at breakfast and lunch. Melicharkova et al. [21] only used a LRD at breakfast the previous day. Sipe et al. [22], Thukral et al. [25], Alvarez-Gonzalez et al. [18], and Gomez-Reyes et al. (2019) used a LRD at breakfast, lunch, and snacks. The Dwyer and Tan [17] study administered a LRD two days before the colonoscopy. Another likely limitation was that in all studies except Alvarez-Gonzalez et al. [18], it was not clear whether patients at risk of poor bowel preparation due to severe constipation were excluded.

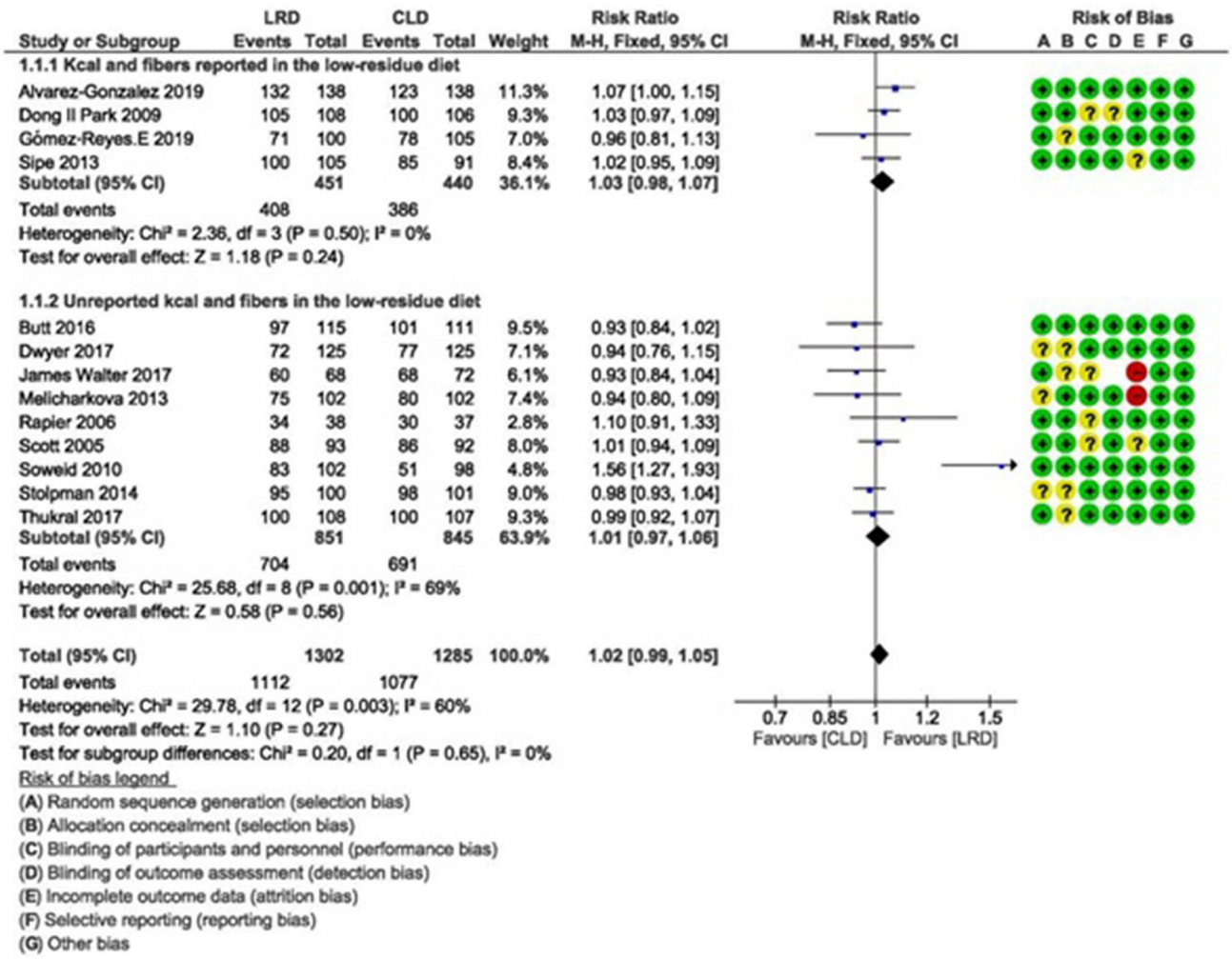

Fig. 6 Efficacy of bowel preparation and subgroup (according to caloric and fibre content of a LRD)

Conclusion

A successful colonoscopy depends on many factors, and bowel preparation is an especially important one. To achieve optimal colonic cleansing, the patient must adhere to a specific purgative regimen as well as a specific diet. By performing a GRADE analysis on our results, we observed that with moderate-quality evidence a LRD was as effective as a CLD. However, the LRD showed better tolerability and fewer adverse effects on bowel preparation. Certain patients would particularly benefit from greater tolerability, such as those who receive a LRD with a high volume of bowel preparation (4L PEG) in single doses or those who follow a LRD with a controlled amount of calories and fibre (< 2000 kcal and < 32 g of fibre / day). This can have significant implications for inpatients. This diet could also be useful as a preoperative colonic preparation, but this requires further research. Considering the aforementioned, our recommendation is strong in favour of a LRD for bowel preparation of patients undergoing a scheduled colonoscopy.

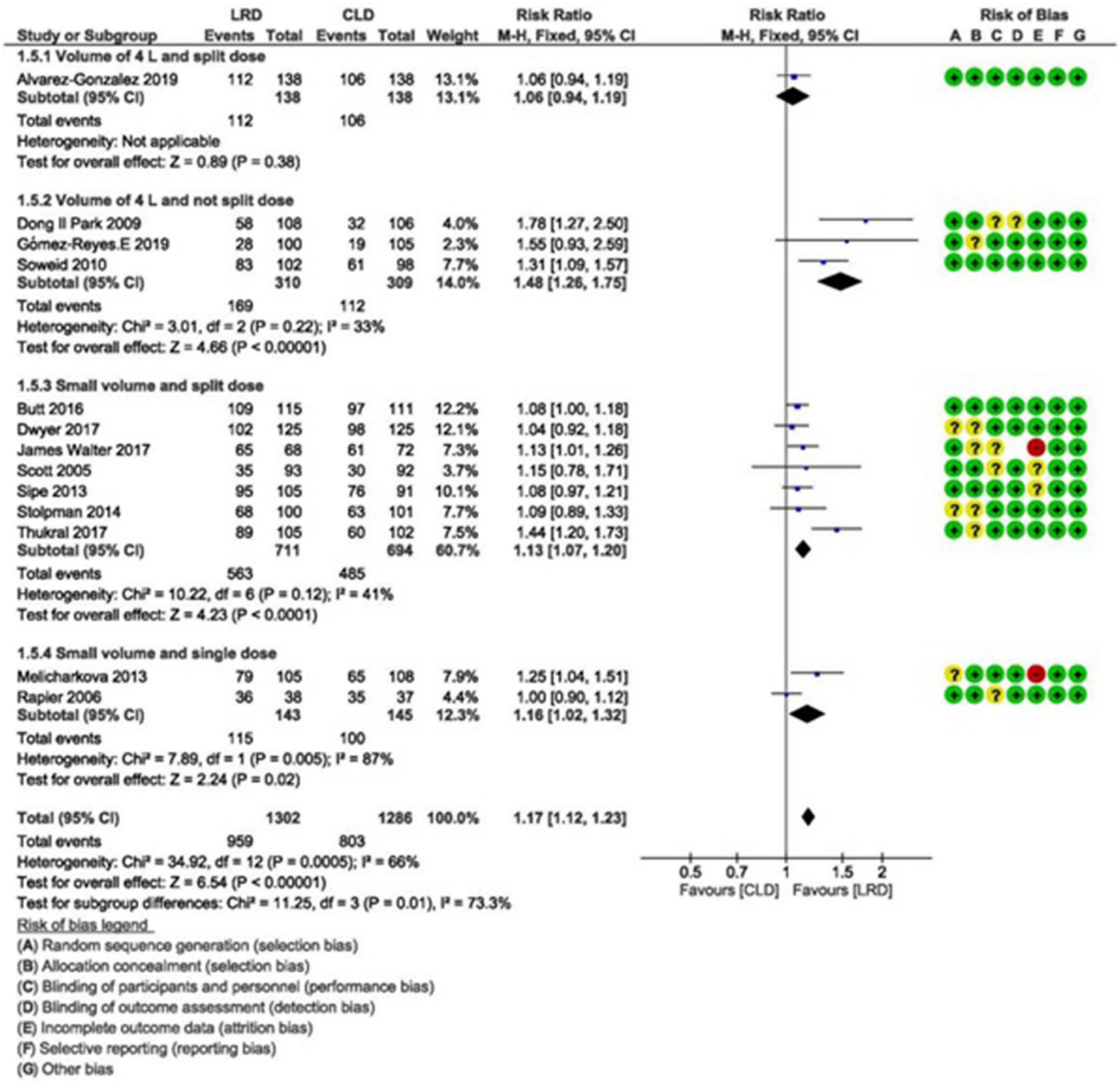

Fig. 7 Tolerance of bowel preparation and subgroup (according to volume of purgatives and form of administration)

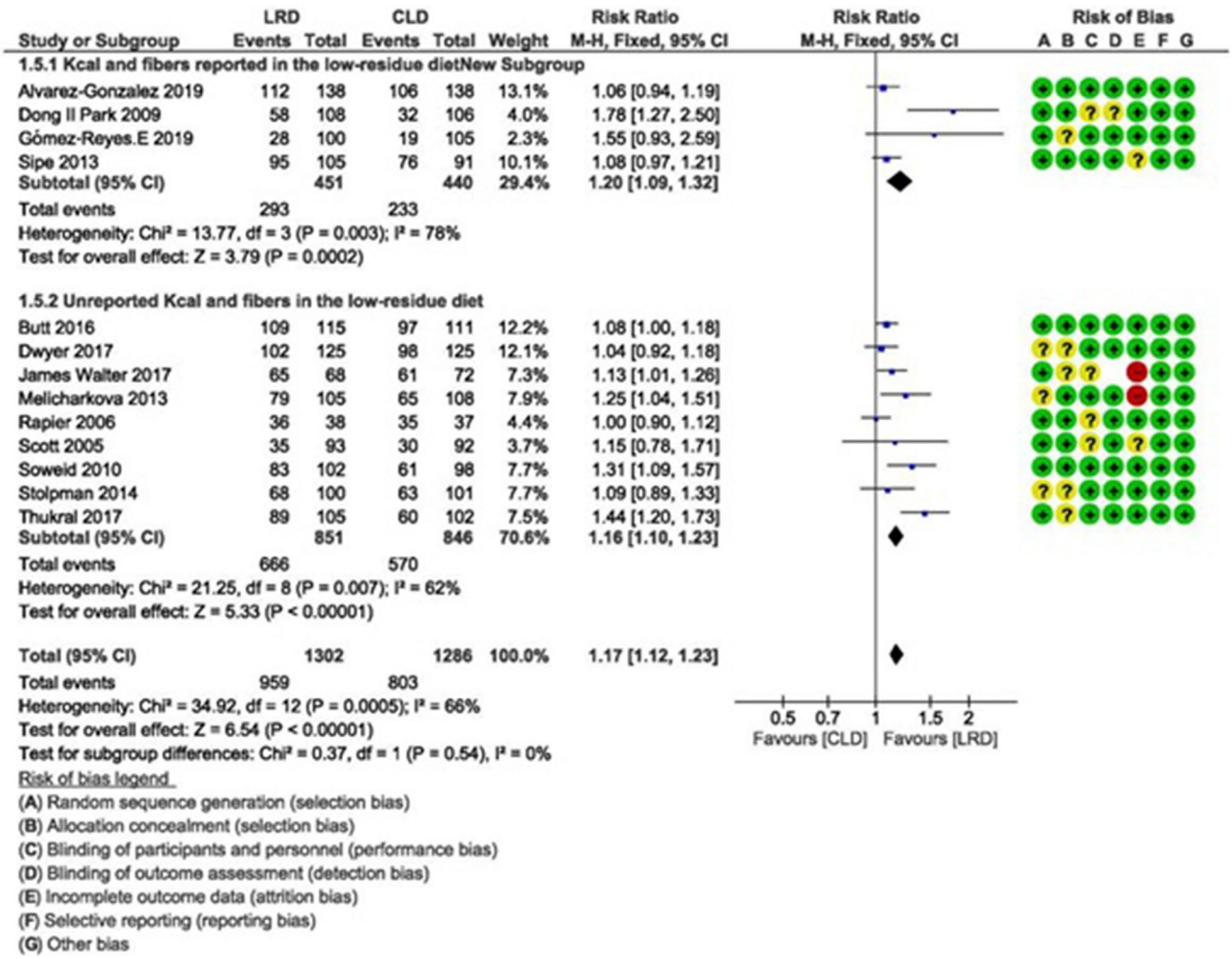

Fig. 8 Tolerance of bowel preparation and subgroup (according to caloric and fibre content of a LRD)

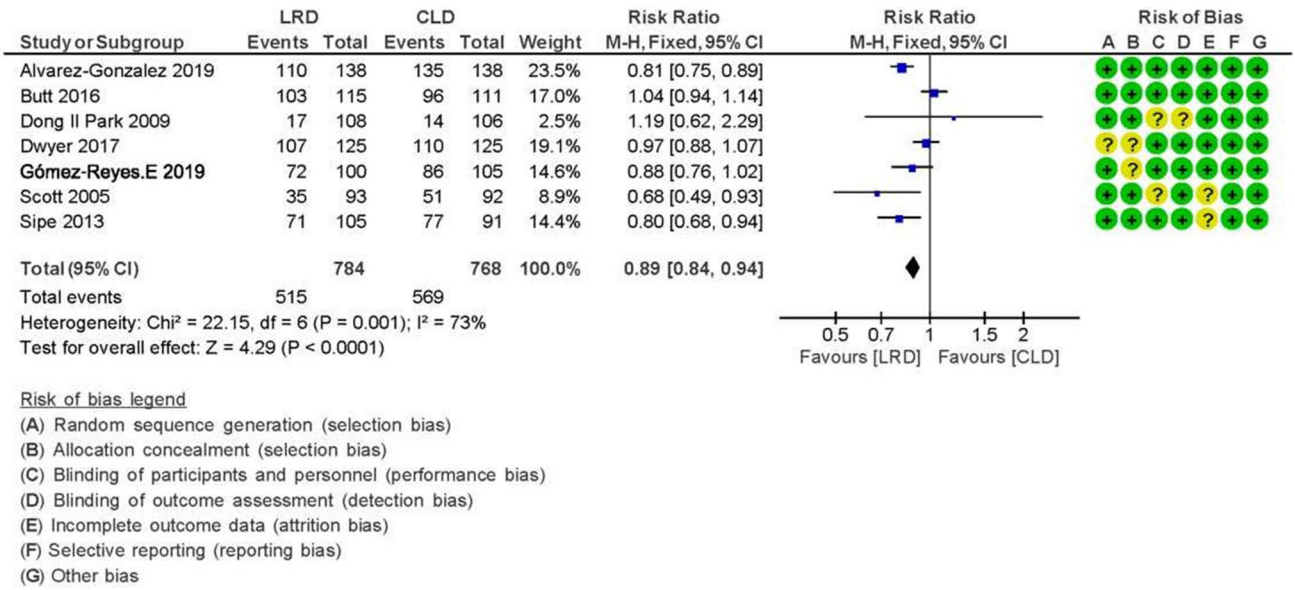

Fig. 9 Adverse effects

Certainty assessment							Summary of findings				
							Study event rates (%)			Anticipated absolute effects	
Participants (studies) Follow up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall certainty of evidence	With clear liquid diet (CLD) on the day before colonoscopy	With Low-residue diet (LRD)	Relative effect (95% CI)	Risk with clear liquid diet (CLD) on the day before colonoscopy	Risk difference with Low-residue diet (LRD)
Adequate Bowel Preparation											
2587 (13 RCTs)	not serious	serious [a]	not serious	not serious	none	⨁⨁⨁◯ MODERATE	1077/1285 (83.8%)	1112/1302 (85.4%)	**RR 1.02** (0.99 to 1.05)	838 per 1000	**17 more per 1000** (from 8 fewer to 42 more)
Tolerance											
2588 (13 RCTs)	not serious	serious [b]	not serious	not serious	none	⨁⨁⨁◯ MODERATE	803/1286 (62.4%)	959/1302 (73.7%)	**RR 1.17** (1.12 to 1.23)	624 per 1000	**106 more per 1000** (from 75 more to 144 more)
Adverse Effects											
1552 (7 RCTs)	not serious	serious [c]	not serious	not serious	none	⨁⨁⨁◯ MODERATE	569/768 (74.1%)	515/784 (65.7%)	**RR 0.89** (0.84 to 0.94)	741 per 1000	**81 fewer per 1000** (from 119 fewer to 44 fewer)

CI: Confidence interval; **RR:** Risk ratio

Explanations

a. I2 60%
b. I2 66%
c. I2 73%

Fig. 10 GRADE approach

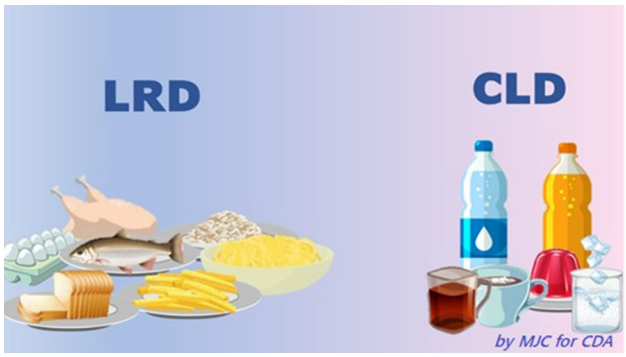

Fig. 11 Example of a LRD vs. CLD

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Declarations

Disclosures Cristian Ahumada, Lisandro Pereyra, Martín Galvarini, José Mella, Estanislao Gómez, Silvia C. Pedreira, Daniel G. Cimmino have no conflicts of interest or financial ties to disclose.

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