Systematic review and meta-analysis: the effects of fermented milk with *Bifidobacterium lactis* CNCM I-2494 and lactic acid bacteria on gastro-intestinal discomfort in the general adult population.

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Background

Digestive symptoms are very common in the general adult population. It has been suggested that probiotics might alleviate digestive symptoms and improve gastrointestinal (GI) discomfort. Not all probiotics exhibit the same metabolic activities or physiological effects on the host and therefore systematic reviews and meta-analyses on probiotics should only be performed on well-defined probiotic strains or strain combinations.

Aim

This systematic review and meta-analysis aimed to evaluate the effectiveness of a specific probiotic fermented milk (PFM) that contains *Bifidobacterium lactis* CNCM I-2494 and lactic acid bacteria, on GI discomfort in the general population.

Methods

Six relevant biomedical and multidisciplinary science databases were searched up to February 2015. Grey literature was identified via OAISTER, OpenGrey and NTIS. Unpublished studies were identified from clinical trial registries and conference proceedings.

Eligible studies were prospective double-blind randomised controlled trials comparing PFM with a control dairy product for at least four weeks; recruiting individuals aged 18 and over, from the general population with minimal GI discomfort at study entry and assessing the effectiveness of PFM on GI discomfort or comfort.

Two reviewers conducted the screening and data extraction/quality assessment processes. Meta-analyses using random-effects models, with individual subject data were undertaken.

Two outcome measures for GI discomfort were considered: i) a dichotomous responder score to capture an overall assessment of GI discomfort; ii) a scaled continuous score to capture a composite score of digestive symptoms.

Dichotomous data were reported as Odds Ratio (OR) and continuous data as standard mean difference (SMD), both with 95% confidence intervals (CI) (PROSPERO registration number: CRD42015016660).

The search strategy identified 12,439 documents. Three trials with a total of 598 subjects (female: 96.5%; age range: 18-59 years) were eligible.

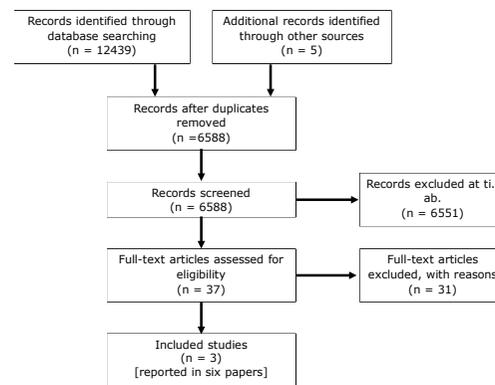Fig 1: PRISMA diagram showing study selection process

Table 1: Characteristics of included studies

Author	Donazzolo 2007	Guyonnet 2009	Marteau 2013
Country	France; single centre	Germany; single centre	France; single centre
Study design	Double blind, controlled, parallel-group RCT	Double blind, controlled, parallel-group RCT	Double blind, controlled, parallel-group RCT
Subjects randomised	60 (M:35%; F:65%)	202 (F:100%)	336 (F:100%)
Intervention period	4 weeks	4 weeks	4 weeks
Population group	Healthy adults with low stool frequency	Adult females without a diagnosis of any digestive disease	Adult females without a diagnosis of any digestive disease
Intervention (n)	Fermented milk containing *B. lactis* CNCM I-2494 and lactic acid bacteria (n=30)	Fermented milk containing *B. lactis* CNCM I-2494 and lactic acid bacteria (n=102)	Fermented milk containing *B. lactis* CNCM I-2494 and lactic acid bacteria (n=168)
Control (n)	Non-fermented dairy product without probiotics (n=30)	Non-fermented dairy product without probiotics (n=100)	Non-fermented dairy product without probiotics (n=168)

RCT= Randomised Controlled Trials; M= Male; F=Female

Results

The consumption of PFM was associated with a significant improvement of GI discomfort (responder rate) over the control product (OR = 1.48; 95% CI 1.07, 2.05) (Fig 2) with a NNT of 10.2 (95% CI 5.6, 55.9). PFM was also superior to the control for the reduction of digestive symptoms measured by a composite score (SMD = -0.21 95% CI -0.37, -0.05) (Fig 3). Sensitivity analyses produced similar results, and the heterogeneity of the studies was minimal.

Fig 2: Meta-analysis of studies assessing the effect of a PFM on overall gastrointestinal discomfort/well-being in the general population.
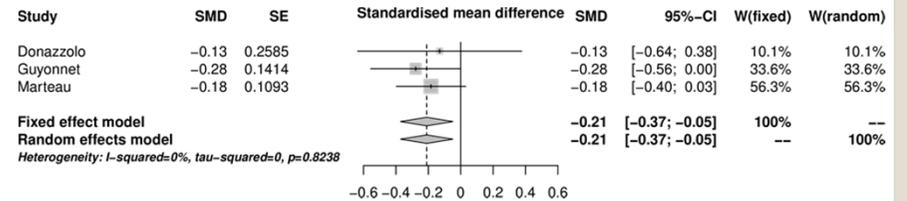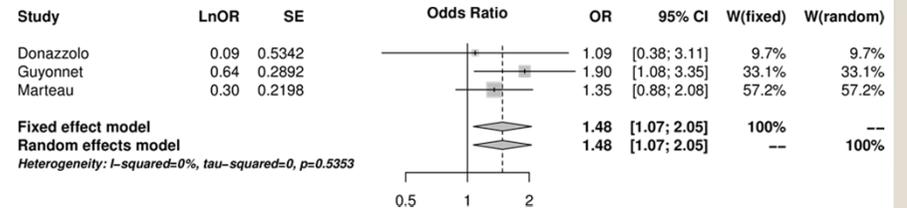

Fig 3: Meta-analysis of studies assessing the effect of a PFM on composite score of digestive symptoms in the general population.

Additional analyses showed that: i) There are many more subjects who responded than deteriorated each week, and the percentage of subjects reporting a deterioration of their GI well-being is generally lower in the PFM group vs. control group; ii) The analysis of the change from baseline for composite symptom score in the subgroup of subjects with bloating as the predominant baseline symptom, showed that the evidence in favour of an improvement is stronger in this subgroup vs. the overall population.

Conclusion

This meta-analysis shows that the consumption of this PFM containing *Bifidobacterium lactis* CNCM I-2494 and lactic acid bacteria is associated with a consistent and clinically significant improvement of outcomes related to GI discomfort in the general population. Future studies should investigate the profile of individuals most likely to respond.

References: 1) Guyonnet et al., Br J Nutr 2009, 102:1654-62; 2) Marteau et al., Neurogastroenterol Motil 2013, 25:331-e252; 3) Donazzolo et al., unpublished study report, 2007.