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Letter to the Editor

Importance of strain subgroup analysis in probiotic meta-analyses

I read with interest the meta-analysis by Sun & Buys[1] recently published in this journal that examined glucose and glycaemic factor-lowering effects of probiotics in patients with diabetes. The authors concluded that 'probiotics may be used as an important dietary supplement in reducing the glucose metabolic factors associated with diabetes'. However, there are several problems with this paper. They pooled the results of eleven trials and found a significant reduction for weighted mean differences in blood glucose (−0·52 mmol/l; 95 % CI −0·92, −0·11, $P = 0·01$) and a similar reduction in HbA1c. Although their conclusion is statistically valid, the ability of meta-analysis to statistically merge data from different studies may not reach a valid conclusion. Extrapolations based on the pooled outcome must be regarded with caution if the treatments differ. The efficacy of probiotics is known to be both species- and strain-specific and also dependent upon the disease examined[2,3]. Experts now agree that it is more appropriate to pool outcomes in those subgroups of probiotic types that are of the same strain and then to examine efficacy by individual subgroup[4,5]. Sun & Buys[1] did perform subgroup analyses, for the different outcomes (glucose, HbA1c, insulin resistance), and examined probiotics by dose, form and duration, but only separated out the probiotics by single *v.* multiple strains. They failed to examine the efficacy further by specific probiotic strain subgroup. When examining the data provided in their Table 2, the column label for probiotics is missing and is incorrectly labelled as 'controls', and thus caution is urged if readers use this table. Their analysis is limited by the lack of multiple studies using the same type of probiotic mix, as all seven studies using multi-strain mixtures of probiotics used different species and strains and all mixtures lacked a confirmatory trial. When a meta-analysis was performed for multi-strain probiotics for a different disease indication (*Helicobacter pylori* infections), the overall pooled relative risk showed significant improvement in *H. pylori* eradication, but significant differences in efficacy were found for different strains of probiotics[6] and two of the six strain mixtures were found to be ineffective. This may also hold true for different probiotic mixtures when trying to improve diabetes. For the single-strain probiotics, this meta-analysis reported that there were two types of probiotics (*Lactobacillus plantarum* and *L. salivarius*), but the strain type is only given for two of the lactobacilli. However, if the studies are pooled by genus and species (Fig. 1), no significant reduction in blood glucose is found in either the *L. plantarum* group or the *L. salivarius* group. The more valid conclusion for the studies in the Sun & Buys[1] paper when probiotics are grouped properly within similar subgroups is that no significant efficacy is shown for the control of diabetes, although certainly more studies are needed. Single-strain specificity has also been shown in several other meta-analyses of other diseases[7,8], and by carefully

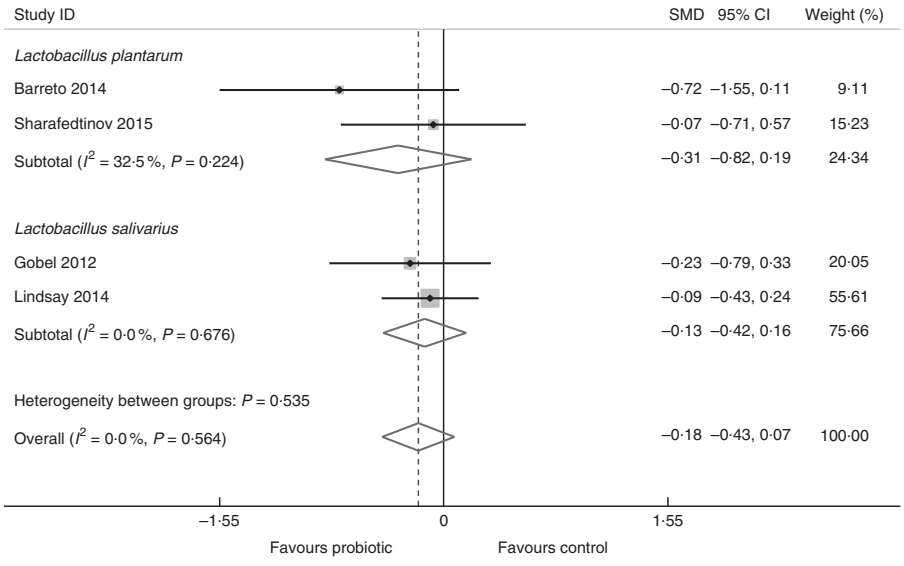

Fig. 1. Meta-analysis of standardised mean difference (SMD) in blood glucose levels in lactobacilli strains compared with controls by correct lactobacilli strain subgroups. Modified from Sun & Buys[1].

separating the different types of probiotic strains the ability to recommend which probiotic strain is effective for a specific disease can be useful in the clinical arena. However, not all probiotic strains are created equal and should not be treated as such.

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