Table 66: Clinical evidence profile: Comparison 2.1. High dose PERT versus low dose PERT in children

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	High dose PERT	Low dose PERT	Relative (95% CI)	Absolute	Quality	Importance
Faecal fat excretion (FFE) (follow-up 14 days; measured with: g/kg/day; Better indicated by lower values)												
1 (Brady 1991)[1]	randomised trials[2]	serious[3]	no serious inconsistency	very serious[4,a]	not calculable[5]	Other[6]	9	-		MD 0.141 lower (0.253 to 0.029 lower)	VERY LOW	CRITICAL
Faecal fat excretion (FFE) (follow-up 14 days; measured with: % of intake , or consumed fat that is excreted; Better indicated by lower values)												
1 (Brady 1991)[1]	randomised trials[2]	serious[3]	no serious inconsistency	very serious[4]	not calculable[5]	Other[6]	9 Mean±SEM[5] 8.7±2.2 *versus* 13±3.06	-		-	VERY LOW	CRITICAL
Faecal fat excretion (FFE) (follow-up 9 days; measured with: g/day; Better indicated by lower values)												
2 (Brady 1991[1], Beker 1994[3])	randomised trials[2]	serious[7]	no serious inconsistency	very serious[4,a]	Not calculable[5]	none	30	-		MD 5 lower (8.877 to 1.123 lower)	VERY LOW	CRITICAL
Faecal fat excretion (FFE) (follow-up 4 weeks; measured with: g/day; Better indicated by lower values)												
1	randomised trials[2]	serious[9]	no serious inconsistency	very serious[4,a]	serious[10]	none[11]	12 Mean±SD[9]	-		ns	VERY LOW	CRITICAL

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	High dose PERT	Low dose PERT	Relative (95% CI)	Absolute	Quality	Importance
(Mitchell 1982)[8]							8.7±4.1 *versus*. 11.5±6.9					
Fat absorption (CFA) (follow-up 4 weeks; measured with: % of intake or consumed fat that is absorbed; Better indicated by higher values)												
1 (Mitchel 1982)[8]	randomised trials[2]	serious[9]	no serious inconsistency	very serious[4]	very serious[12]	none[11]	12 Mean±SEM[11] 89.5±4.2 *versus*. 85.4±11.26		-	-	VERY LOW	CRITICAL
Fat absorption (CFA) (follow-up 9 days; measured with: % of intake; Better indicated by higher values)												
1 (Beker 1984)[3]	randomised trials[2]	serious[13]	no serious inconsistency	very serious[4]	very serious[12]	none[14]	21 Mean±SEM[11] 91.2±1.6 *versus*. 86.2±3.2		-		VERY LOW	CRITICAL
Stool frequency (follow-up 4 weeks; measured with: bowel movements/ day, self-report; Better indicated by lower values)												
1 (Mitchel 1982)[8]	randomised trials[2]	serious[9]	no serious inconsistency	very serious[4]	no serious imprecision	none[11]	12			MD 0.1 lower (0.189 lower to 0.011 higher)	VERY LOW	CRITICAL
Abdominal pain (follow-up 4 weeks; assessed with: self-report; Better indicated by lower values)												
1 (Mitchell 1982)[8]	randomised trials[2]	serious[9]	no serious inconsistency	very serious[4]	Not calculable[15]	none[11]	12		-	The study reports that there were no differences between the groups[15]	VERY LOW	CRITICAL
							-	-				

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	High dose PERT	Low dose PERT	Relative (95% CI)	Absolute	Quality	Importance
Adverse events (constipation, elevation in serum uric acid levels) (follow-up 9 days; assessed with: self-report; Better indicated by lower values)												
1 (Beker 1994)[3]	randomised trials[2]	serious[1] [3]	no serious inconsistency	very serious[4]	Not calculable[15]	none[14]	0/21 (0%)	0/21 (0%)	-	No episodes were observed[15]	VERY LOW	CRITICAL

Abbreviations: CFA: coefficient of fat absorption; CI: confidence interval; FFE: faecal fat excretion; g: grams; kg: kilogrammes; MD: mean difference; ns: not significant; PERT: pancreatic endocrine enzyme therapy; SEM: standard error of measurement
a. The method of measuring fat excreted is inaccurate, as it does not take into account fat intake. The evidence could not be downgraded further for indirectness.
1 Cross-over trial
2 Treatment details: high-dose 12 (8 to 18) & low-dose 3 (2 to 5) capsules per meal. Constituent enzymes per capsule: 7.020u of lipase. Daily fat intake (g) 94±6 in both groups.
3 Treatment details: high-dose: 1500u lipase per kg/body for meals & 750u lipase per kg/body for snacks. Low-dose: 500u lipase per kg/body for meals & 250u lipase per kg/body for snacks. Daily fat intake (g): 100g in both groups.
4 The quality of the evidence was downgraded by 2 as these doses are not used in current practice. Low-dose is in fact very low dose, and high-dose is just low-dose
5 Imprecision could not be calculated, as SD was not available for the control group
6 Reporting bias not detected, although funding not reported. Evidence downgraded by 1 due to small sample (n=9)
7 The quality of the evidence was downgraded by 1 due to unclear randomization and concealment in both studies.
8 Treatment details: high-dose 22 capsules/day & low-dose 11 capsules/ day Pancrease®. Constituent enzymes per capsule 4,000 USNF lipase units; 25,000 USNF protease units; 20,000 amylase units.
9 The quality of the evidence was downgraded by 1 due to unclear randomization and concealment. It is unclear if blinding was done, but given the outcome this may not have an impact.
10 The quality of the evidence was downgraded by 1 as the results are poorly reported: authors do not report p-value and MD cannot be calculated
11 Reporting bias not detected, although Pancrealipase capsules were provided by Ethnor Pty Ltd.
12 The quality of the evidence was downgraded by 2 due to the quality of the statistical analysis. Means are provided instead of medians, although it is not normally distributed, therefore differences cannot be calculated as it is not appropriate.
13 The quality of the evidence was downgraded by 1 because it is an open-label study.
14 Reporting bias not detected, although the study is partly funded by a grant from Johnson Pharmaceutical.
15 Imprecision cannot be calculated.