4.5.2 Children with diarrhoea

The effectiveness of homeopathy for the treatment of children with diarrhoea was assessed in four systematic reviews as summarised in Table 9 and Table 10. In total, the systematic reviews included four Level II studies that were all conducted by the same research group (Table 9).

Table 9   Matrix indicating the studies that were included in the systematic reviews of diarrhoea

		Study ID			
		Jacobs (2006) [Level II]	Jacobs (1997/2000)[a] [Level II]	Jacobs (1994) [Level II]	Jacobs (1993) [Level II]
Systematic review	NCC-WCH (2009) [Level I]	✓	✓	✓	✓
	Altunc et al (2007) [Level I]		✓	✓	✓
	Cucherat et al (2000) [Level I]			✓	
	Linde and Melchart (1998) [Level I]		✓	✓	✓

[a] Jacobs (1997) and Jacobs (2000) were the same study. The study was referred to as Jacobs (1997) in Linde and Melchart (1998) and Jacobs (2000) in NCC-WCH (2009) and Altunc et al (2007).

The National Collaborating Centre for Women's and Children's Health (2009) (hereafter referred to as NCC-WCH, 2009; AMSTAR score of 5/10) performed a systematic review of alternative or complementary therapies in the treatment of gastroenteritis. The results of this review formed the basis of a NICE clinical practice guideline on diarrhoea and vomiting caused by gastroenteritis. One review and one good-quality Level II study were included. Jacobs (2006) was a Level II study that investigated the effect of homeopathic combination therapy tablets in children aged between 5 months and 6 years who had acute diarrhoea. The study found no significant difference between homeopathy and placebo for the duration of diarrhoea, mean rate of unformed stool passage per day, or total number of unformed stools during follow-up. NCC-WCH (2009) also considered the results of a review[1] and meta-analysis (Jacobs et al, 2003) that included the Level II studies by Jacobs (1993), Jacobs (1994) and Jacobs (2000). Overall, NCC-WCH (2009) concluded "the clinical trials assessing homeopathy had significant methodological limitations. Moreover, there was a lack of consistency in the evidence. Therefore, no recommendation was made for the use of homeopathy".

The systematic review by Altunc et al (2007) (AMSTAR score of 6/10) assessed the evidence of any type of therapeutic or preventive intervention testing homeopathy for childhood and adolescent ailments. Three Level II studies (each assigned a Jadad score of 5 by Altunc et al) were identified for the treatment of children with diarrhoea (Jacobs, 2000; Jacobs, 1994; Jacobs, 1993). All three Level II studies were similar in design and tested individualised homeopathy in acute childhood diarrhoea. Two Level II studies (Jacobs, 2000; Jacobs, 1994) reported significant effects in favour of homeopathy

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[1] This review was excluded for the purposes of the current overview as the included studies were not identified by systematic means.

for the duration of diarrhoea and the number of unformed stools. The third Level II study (Jacobs, 1993) found no significant differences between homeopathy and placebo for either of these outcomes. Altunc et al (2007) concluded that "the evidence from rigorous clinical trials of any type of therapeutic or preventive intervention testing homeopathy for childhood and adolescence ailments is not convincing enough for recommendations in any condition".

Cucherat et al (2000) (AMSTAR score 10/11) aimed to answer the question of "whether there is any evidence from randomised controlled trials that homeopathy is efficacious for the treatment of disease in humans". One Level II study (Jacobs, 1994) was identified for the childhood diarrhoea indication. Similar to the other systematic reviews, Cucherat et al (2000) also reported that there was a significant effect of homeopathy (p=0.048) in the duration of diarrhoea. The quality of Jacobs (1994) was not formally assessed by Cucherat et al (2000); however, a general comment was made about all of the included studies that "the strength of this evidence is low because of the low methodological quality of the trials". Cucherat et al (2000) also noted that the studies of high methodological quality were more likely to provide negative results for homeopathy compared to the lower quality studies. Overall, the authors concluded that "it is clear that the strength of available evidence is insufficient to conclude that homeopathy is clinically effective".

In addition, Cucherat et al (2000) conducted several meta-analyses with different combinations of studies (based on attributes such as blinding, attrition and type of homeopathic preparation). However, the authors acknowledge that "the meta-analysis method used does not allow any conclusion on what homeopathic treatment is effective in which diagnosis or against which symptoms". For that reason, the results of the meta-analyses will not be discussed in detail in the remainder of this report.

Linde and Melchart (1998) (AMSTAR score of 8/11) examined the state of clinical efficacy research on individualised homeopathy and identified three Level II studies (Jacobs, 1993; Jacobs, 1994; Jacobs, 1997) for the childhood diarrhoea indication. Consistent with all of the above systematic reviews, Linde and Melchart (1998) reported a significant effect of homeopathy in all of the primary outcomes measured in Jacobs (1994). The authors of the systematic review also noted that there were "positive trends, but no significant inter-group differences" between homeopathy and placebo in Jacobs (1993). Jacobs (1997), reported elsewhere as Jacobs (2000), was a Level II study that tested the effect of individualised homeopathy in children with diarrhoea. The study found no significant difference between the homeopathy and placebo groups.

A meta-analysis of all included studies for all clinical conditions (not specific to children with diarrhoea) conducted by Linde and Melchart (1998) found an overall trend in favour of homeopathy (RR 1.62; 95% CI 1.17, 2.23). However, the pooled rate ratio of the "methodologically best" studies (which included Jacobs, 1994) was clearly smaller and no longer statistically significant (RR 1.12; 95% CI 0.87, 1.44). The pooled findings are unlikely to be of value due to the highly heterogeneous group of studies and conditions that were included in the meta-analyses. As such, the results of the meta-analyses conducted by Linde and Melchart (1998) will not be discussed in detail in the remainder of this report. Overall, Linde and Melchart (1998) concluded that any evidence suggesting that homeopathy has an effect over placebo is "not convincing because of methodological shortcomings and inconsistencies".

Reviewer comments

The current evidence base for homeopathy for the treatment of children with diarrhoea is limited by the fact that all of the identified studies were carried out by the same research group.

Evidence statement

Four systematic reviews of poor to good quality identified four randomised controlled trials (medium to good quality; total of 544 participants, range: 34-292), all conducted by the same research group, that compared homeopathy with placebo for the treatment of children with diarrhoea.

The one medium-sized, good-quality trial (292 participants) did not detect a difference between combined homeopathy and placebo in the treatment of children with diarrhoea.

The studies of individualised homeopathy are of insufficient quality and/or size to warrant further consideration of their findings. LOC: Low - moderate.

Based on the body of evidence evaluated in this review combined homeopathy is not more effective than placebo for the treatment of children with diarrhoea and there is no reliable evidence that individualised homeopathy is more effective than placebo for the treatment of children with diarrhoea.

Table 10 Evidence summary table: the effectiveness of homeopathy for the treatment of children with diarrhoea

Study ID Level of evidence[a] Quality[b]	Included study Level of evidence[a] Quality[c] Sample size	Patient population	Intervention	Comparator	Outcome	Results as reported in the systematic review	Systematic review interpretation
NCC-WCH (2009) [Level I] AMSTAR: 5/10 SR of CAM for childhood diarrhoea	Jacobs (2006) [Level II] SIGN EL 1+[d] N=292	Children aged between 5 months and 6 years who had acute diarrhoea (defined as the passage of three or more unformed stools in the previous 24 hours) that was confirmed visually by study staff	Homeopathic combination therapy tablets (Arsenicum album, Calcarea carbonica, chamomilla, podophyllum and *sulphur* – in a liquid homeopathic dilution in the 30C potency)	Placebo	Duration of diarrhoea	No significant difference	"The Guidelines Development Group considered that the clinical trials assessing homeopathy had significant methodological limitations. Moreover, there was a lack of consistency in the evidence. Therefore, no recommendation was made for the use of homeopathy."
					Mean rate of unformed stool passage per day during follow up	No significant difference	
					Total number of unformed stools during follow up	No significant difference	
Altunc et al (2007) [Level I] AMSTAR: 6/10 SR of homeopathy for multiple conditions	Jacobs (2000)[e] [Level II] Jadad score 5[f] N=126	Children with diarrhoea • Intervention: mean age 1.7 years • Control: mean age 1.4 years • 67.5% male • Concomitant treatment: oral rehydration therapy, normal feeding; standard antiparasitic medication at end of intervention if needed	19 different remedies in 30C potency, one dose after every unformed stool for 5 days; 5 most common: *Podophyllum, sulphur, Arsenicum album, Calcarea carbonica, Chamomilla*	Placebo	Number of days with diarrhoea	Significant effect in favour of homeopathy (p=0.04)	"The evidence from rigorous clinical trials of any type of therapeutic or preventive intervention testing homeopathy for childhood and adolescence ailments is not convincing enough for recommendations in any condition." (Note: this conclusion refers to all clinical conditions and is
					Number of daily stools	Significant effect in favour of homeopathy (p=0.02)	

Study ID Level of evidence[a] Quality[b]	Included study Level of evidence[a] Quality[c] Sample size	Patient population	Intervention	Comparator	Outcome	Results as reported in the systematic review	Systematic review interpretation
	Jacobs (1994) [Level II] Jadad score 5[f] N=92	Children with diarrhoea • Intervention: mean age 1.6 yr • Control: mean age 1.5 yr • Concomitant treatment: oral rehydration therapy, normal feeding; standard antiparasitic medication at the end of intervention if needed; 11 children were given antidiarrheal medication by their parents (6 in placebo group; 5 in homeopathy group)	18 different remedies in 30C potency, one dose after every unformed stool for 5 days: *Podophyllum, Chamomilla, Arsenicum album, Calcarea carbonica, sulphur, Mercurius vivus, Pulsatilla, phosphorus, China, Gambogia, Aethusia, aloe, belladonna, Bryonia, Colchicum, Croton tiglium, Dulcamara, Nux vomica*	Placebo	Number of days with diarrhoea	Significant effect in favour of homeopathy (p=0.048)	not specific to childhood diarrhoea)
					Number of daily stools	Significant effect in favour of homeopathy difference (p<0.05)	
					Adverse events	No adverse events	
	Jacobs (1993) [Level II] Jadad score 5[f] N=34	Children aged between 6 months to 5 years with diarrhoea • Concomitant treatment: oral rehydration therapy, normal feeding; standard antiparasitic medication at the end of intervention if needed	Various remedies in 30C potency (no details reported), 2 pills daily for 3 days or until improvement	Placebo	Number of days with diarrhoea	No significant difference	
					Number of daily stools	No significant difference	
Cucherat et al (2000) [Level I] AMSTAR: 10/11 SR of homeopathy for multiple	Jacobs (1994) [Level II] Quality not specified N=92 (81 evaluated)	Children with acute childhood diarrhoea	Individualised homeopathy	Placebo	Number of days with diarrhoea	Significant difference in favour of homeopathy (p=0.048)	"It is clear that the strength of available evidence is insufficient to conclude that homeopathy is clinically effective." (Note: this conclusion refers to all clinical conditions and is

Study ID Level of evidence[a] Quality[b]	Included study Level of evidence[a] Quality[c] Sample size	Patient population	Intervention	Comparator	Outcome	Results as reported in the systematic review	Systematic review interpretation
conditions							not specific to childhood diarrhoea)
Linde and Melchart (1998) [Level I] AMSTAR: 8/11 SR of homeopathy for multiple conditions	Jacobs (1997)[e] [Level II] Quality not specified N=126	Children with diarrhoea	Fully individualised, computer-assisted (RADAR) choice of remedy, taken as C30 after each unformed stool	Placebo	Number of days with diarrhoea	No significant difference	Conclusion of the systematic review: A meta-analysis found an overall trend in favour of homeopathy. 1. The rate ratio was 1.62 (95% CI 1.17 to 2.23) and the odds ratio was 2.62 2. The pooled rate ratio of the methodologically best studies was clearly smaller and not statistically significant (1.12, 95% CI 0.87, 1.44). This meta-analysis included Jacobs (1994). 3. The rate ratio of the six studies published in MEDLINE-listed journals was not significantly different from placebo (1.22, 95% CI 0.94, 1.56). This meta-analysis included Jacobs (1994) (Note: results of meta-analysis refer to all clinical conditions and are not specific to diarrhoea)
	Jacobs (1994) [Level II] Quality: 5,5[g] N=92	Children with diarrhoea	Fully individualised, computer-assisted (RADAR) choice of remedy, taken as C30 after each unformed stool	Placebo	Number of days with diarrhoea	Significant difference between groups (p<0.05) • Intervention: 3.0 days • Control: 3.8 days	
					Days to first formed stool	"Homeopathy significantly better" (p-value not reported)	
					Diarrhoea score	"Homeopathy significantly better" (p-value not reported)	
	Jacobs (1993) [Level II] Quality: 3,3[g] N=34	Children with diarrhoea	Fully individualised computer-assisted (RADAR) choice of remedy, taken as C30 twice daily for 3 days	Placebo	Number of days with diarrhoea	Positive trends, but no significant inter-group differences (p=0.28) • Intervention: 2.4 days	

Study ID Level of evidence[a] Quality[b]	Included study Level of evidence[a] Quality[c] Sample size	Patient population	Intervention	Comparator	Outcome	Results as reported in the systematic review	Systematic review interpretation
						• Control: 3.0 days	

Abbreviations: AMSTAR, Assessment of Multiple Systematic Reviews; C, centesimal; CAM, complementary and alternative medicines; EL, Evidence level; SIGN, Scottish Intercollegiate Guidelines Network; SR, systematic review.

[a] Level of evidence as assessed by the evidence reviewer.

[b] Study quality as assessed by the evidence reviewer using the AMSTAR measurement toolkit.

[c] Study quality as reported in the systematic review.

[d] SIGN evidence level assesses the quality of the evidence based on study design and risk of bias. The range of possible scores is 4 (low) to 1++ (high). Studies with a level of evidence '–' should not be used as a basis for making a recommendation due to high risk of bias.

[e] Jacobs (1997) and Jacobs (2000) were the same study. The study was referred to as Jacobs (1997) in Linde and Melchart (1998) and Jacobs (2000) in NCC-WCH (2009) and Altunc et al (2007).

[f] The Jadad scale assesses the quality of published clinical trials based methods relevant to random assignment, double blinding and the flow of patients. The range of possible scores is zero (bad quality) to 5 (good quality).

[g] Quality was assessed using (i) Jadad score, out of five; (ii) internal validity score, out of six.