Appendix 4. Adverse events for manual therapies	
Authors	**Adverse Events**
Alcantara et al 2011(28)	No adverse events were reported although manual therapy is not risk-free
Carnes et al 2018(53)	Meta-analysis for the RCTs was possible for four studies, 3 of which were colic studies and one breastfeeding. There was an overall RR of 0.12 (95% CI 0.12 to 0.66); that is, those who had manual therapy had an 88% reduced risk of having an adverse event compared with those who did not have manual therapy.
Clar et al 2014(30)	Not reported
Dobson et al 2012(17)	Incidents reported by parents 1/6 (Miller 2010; N = 102). None were reported in the other studies.
Driehuis et al 2019(31)	1 observational study, 4 case reports, 1 control study, 3 retrospective case series. N=1823: 2 deaths, 1 temporary paralysis, 1 rib fracture
Ernst, E. 2009(32)	Not reported
Gleberson et al 2012(33)	No adverse effects were reported in any of the clinical trials reviewed.
Parnell Prevost et al 2019(34)	Adverse events were uncommonly reported. In one study an adverse event was reported in one patient in the control (non-treatment) group that reported increased crying
Perry et al 2011(52)	No adverse events were recorded.
Posadzki P, Ernst E. 2011(35)	Not reported
Posadzki et al 2013(36)	Not reported
Salehi et al 2017(37)	Not reported
Adverse events with simethicone	
Authors	**Adverse Events**
Biagioli et al(20)	One study (Sethi 1988) involving 26 infants reported no adverse effects. The other two studies provided no data on adverse effects.
Gordon et al(19)	Authors, Savino 2006, did not report data on adverse effects, but the lead author confirmed that these were assessed and recorded as part of the protocol, and that no infants experienced them.
Gutierrez-Castrellon et al 2017(50)	Not reported
Hall et al 2011(48)	Not reported
Adverse Events with probiotics	
Authors	**Adverse Events**
Anabrees et al 2013(38)	None of the included studies reported any adverse side effects of supplementation.
Batchelor et al 2015(39)	No adverse effects were reported, and probiotics were well tolerated.
Cruchet et al 2015(40)	Risk of developing bacteraemia from ingested lactobacilli probiotics is 1 per 1 million users. Risk of developing fungemia from S. boulardii is estimated at 1 per 5.6 million users. In countries where their use is widespread show low rates of systemic infection between 0.05 and 0.40 %.
Dryl et al 2018(41)	No adverse events were reported

Gutierrez-Castrellon et al 2017(50)	Not reported
Harb et al 2016(51)	Not reported
Lucassen 2015(2)	One RCT reported adverse effects using a questionnaire administered during the study, but none were recorded. The systematic review gave no further information on adverse effects.
Mugambi et al 2012(42)	No adverse events were reported
Ong et al 2019(18)	A meta-analysis of all six studies, and found no difference between the groups in relation to serious adverse effects (RR 1.02, 95% CI 0.14 to 7.21)
Perry et al 2011(52)	No adverse events were recorded.
Salvatore et al 2016(49)	Cimetropium bromide was reported to be more effective than placebo in reducing the duration of crying but lethargy, motion sickness and somnolence may occur. Dicyclomine was more effective than placebo in three trials, but dangerous side effects were described, such as respiratory symptoms, seizures, syncope, pulse rate fluctuations, muscular hypotonia, and even coma that contraindicate its use in infants.
Schreck Bird et al 2017(43)	Only one study reported adverse events. The only adverse event occurring in an infant given probiotic was rhinitis; the other adverse events occurred in infants given placebo and included 1 infant each with eczema, fever, otalgy, and gastroesophageal reflux. No adverse events occurred in the remaining studies.
Skorka et al 2017(21)	The available scientific data suggest that the administration of currently evaluated probiotic-supplemented formulae to healthy infants does not raise safety concerns with regard to growth and adverse effects.
Sung et al 2013(45)	None of the studies reported adverse effects of probiotic supplementation. Three trials did not include adverse effects as outcomes. The others concluded no adverse effects in gastrointestinal tolerance, growth, or infections.
Sung et al 2018(23)	Not reported
Urbanska, M., Szajewska, H.2014(46)	L. reuteri DSM 17938 was well tolerated, and no adverse events associated with its administration were reported in any of the included trials. One RCT in the colic group assessed growth parameters and found no difference between the probiotic and placebo groups.
Xu et al 2015(47)	Adverse events were reported in five RCTs. Savino et al. reported rhinitis in the L. reuteri group (n = 1) and eczema, fever, otalgy, and gastroesophageal reflux in the placebo group. Four studies reported no adverse events associated with the probiotic therapy or the placebo. No serious adverse events were observed in the six studies, and there were no differences in growth parameters between the two groups in the meta-analysis.
Adverse events with proton pump inhibitors	
Gieruszczak-Bialek et al 2015(21)	Both arms had adverse events, one RCT showed a significant difference between lansoprazole and the placebo for totality of serious adverse effects (10/81 vs 2/81, RR 5, 95% CI 1.3-20, number needed to harm 11, 95% CI 6 to 49)