

Appendix 4: Trial sequential analysis of cumulative meta-analysis of effect of exercise interventions v no exercise control for pain relief and physical function. Required information size of participants is calculated based on exercise intervention effect compared with no intervention based on risk of type I error of 5% and power of 90%. With these presumptions, cumulated Z curve crosses trial sequential monitoring boundaries (inner sloping lines) in 2002 implying that at that point in time there was firm evidence for beneficial effect of exercise intervention compared with no intervention

