

**Supplementary Table S1. Oxford Centre for Evidence-based Medicine – Levels of Evidence**

Level	
1a	Systematic review (with homogeneity) of RCTs
1b	Individual RCT (with narrow confidence interval)
1c	“All or none”
2a	Systematic review (with homogeneity) of cohort studies
2b	Individual cohort study (including low quality RCT)
2c	“Outcomes” research, ecological studies
3a	Systematic review (with homogeneity) of case-control studies
3b	Individual case-control study
4	Case-series (and poor-quality cohort and case-control studies)
5	Expert opinion without explicit critical appraisal, or based on physiology, bench research of “first principles”

RCT – randomized controlled trial

**Grades of recommendation**

Grade	
A	Consistent level 1 studies
B	Consistent level 2 or 3 studies or extrapolations from level 1 studies
C	Level 4 studies or extrapolations from level 2 or 3 studies
D	Level 5 evidence or troublingly inconsistent or inconclusive studies of any level