

Appendix Table 6. Risk of Bias Assessment.

Study	Validity Domain				
	Randomization/ Allocation Concealment	Deviations from Intended Intervention (Evidence of large/differential cross-over for 1 treatment)	Bias from Missingness of Outcome Data (<10%; non- differential)	Bias in Outcome Measurement	Overall Assessment
CLOSURE	1	1+	1	2	2
PC Trial	1	1+	2	2+	2+
RESPECT	1	1+	2+	1+	2+
REDUCE	1	1	2	2	2
CLOSE	1	1+	1	2	2
DEFENSE	1	1+	1	2+	2+