Variation in the design of manual toothbrushes may lead to differences in their ability to remove plaque. This study compared a recently introduced manual brush to a currently marketed leader and flat trim control manual toothbrush. **Objective:** This randomized, single-blind, crossover study compared the safety and plaque removing efficacy of the Oral-B Advantage Plus (ADV), Oral-B Indicator (IND) and the Colgate 360 (COL) toothbrushes. **Method:** Qualified subjects with a mean whole mouth pre-brushing Rustogi Modified Navy Plaque Index score of ≥0.6 were randomly assigned to treatment sequence. After 1 min brushing, oral tissues were re-examined and plaque was reassessed. One examiner (NCS) evaluated all subjects at all time points. Changes in plaque scores from pre-treatment means within each treatment at each visit were analyzed using a paired t-test and between treatments using an analysis of variance. **Results:** All brushes significantly reduced mean plaque from pre to post brushing in all areas (p<0.001). ADV and IND removed significantly more plaque than COL whole mouth (0.552 ± 0.04, 0.527 ± 0.06 vs 0.456 ± 0.06, p=0.0001), marginal (0.745 ± 0.12, 0.683 ± 0.12 vs 0.547 ± 0.14, p=0.0001) and approximal areas (0.939 ± 0.07, 0.908 ± 0.09 vs 0.810 ± 0.13, p=0.0001). ADV and IND removed 21.9% and 15.6% more whole mouth plaque, 36.20% and 24.8% more marginal plaque, and 15.93% and 12.1% more approximal plaque respectively than Colgate 360. ADV also removed significantly more plaque than IND whole mouth, margin and approximal surfaces, p=0.0001. No evidence of oral hard and soft tissue trauma was found with any toothbrush. **Conclusion:** The results demonstrate that both Oral-B Advantage Plus and Oral-B Indicator were superior to Colgate 360 removing significantly more plaque from all areas.