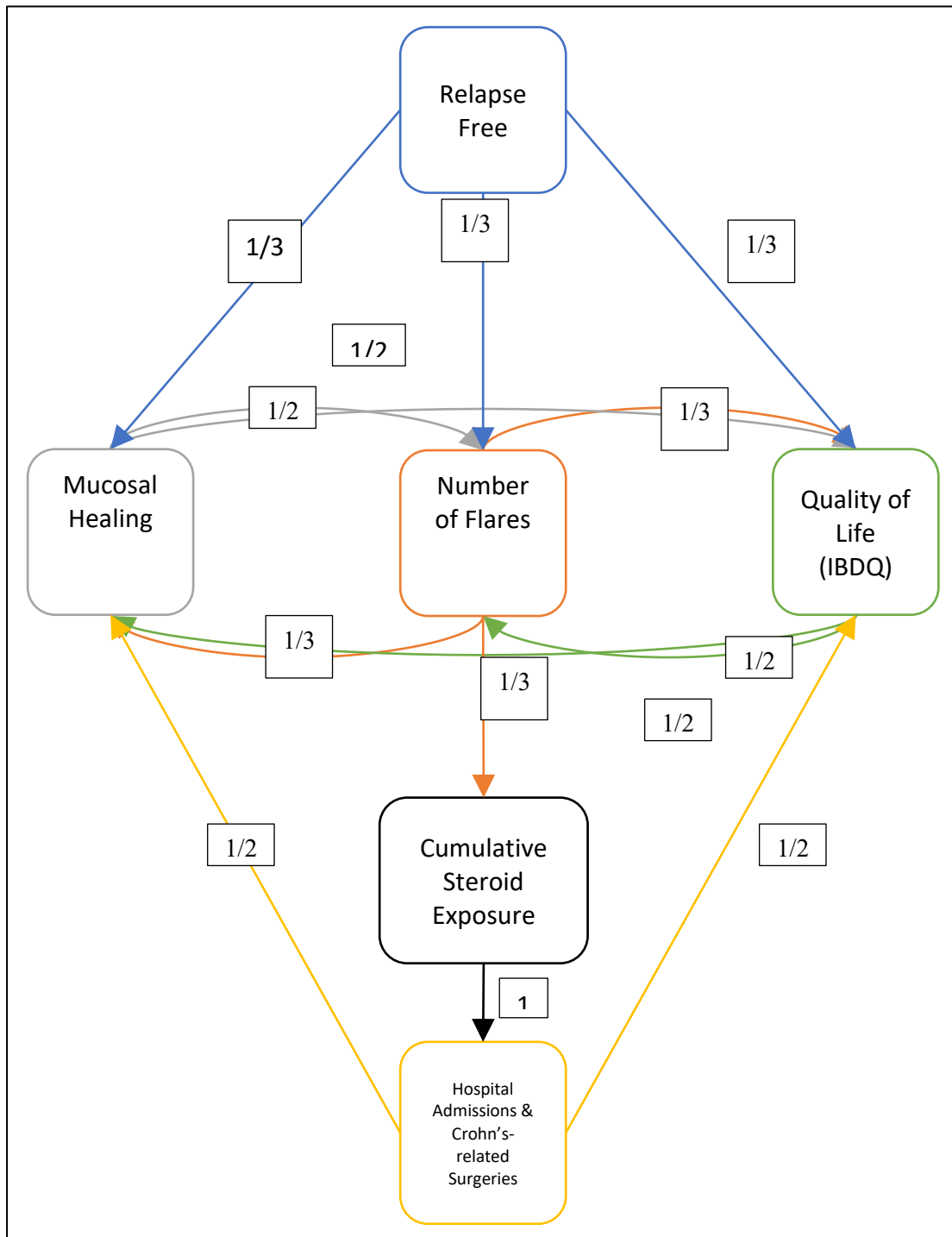**Supplementary Material**

Supplementary Figure 1 – Statistical approach for the PROFILE trial.

The methodology will combine together gate-keeping and Holm-Bonferroni methods in formal hypothesis testing, with the above diagram defining how the significance levels will be transitioned assuming an initial configuration of 5% at the primary endpoint (relapse-free remission) and 0% on all other tests. All the secondary endpoints are continuous variables and will be analysed using a linear regression framework adjusting for baseline covariates.