

Supplementary information - Early stopping in clinical PET studies: how to reduce expense and exposure

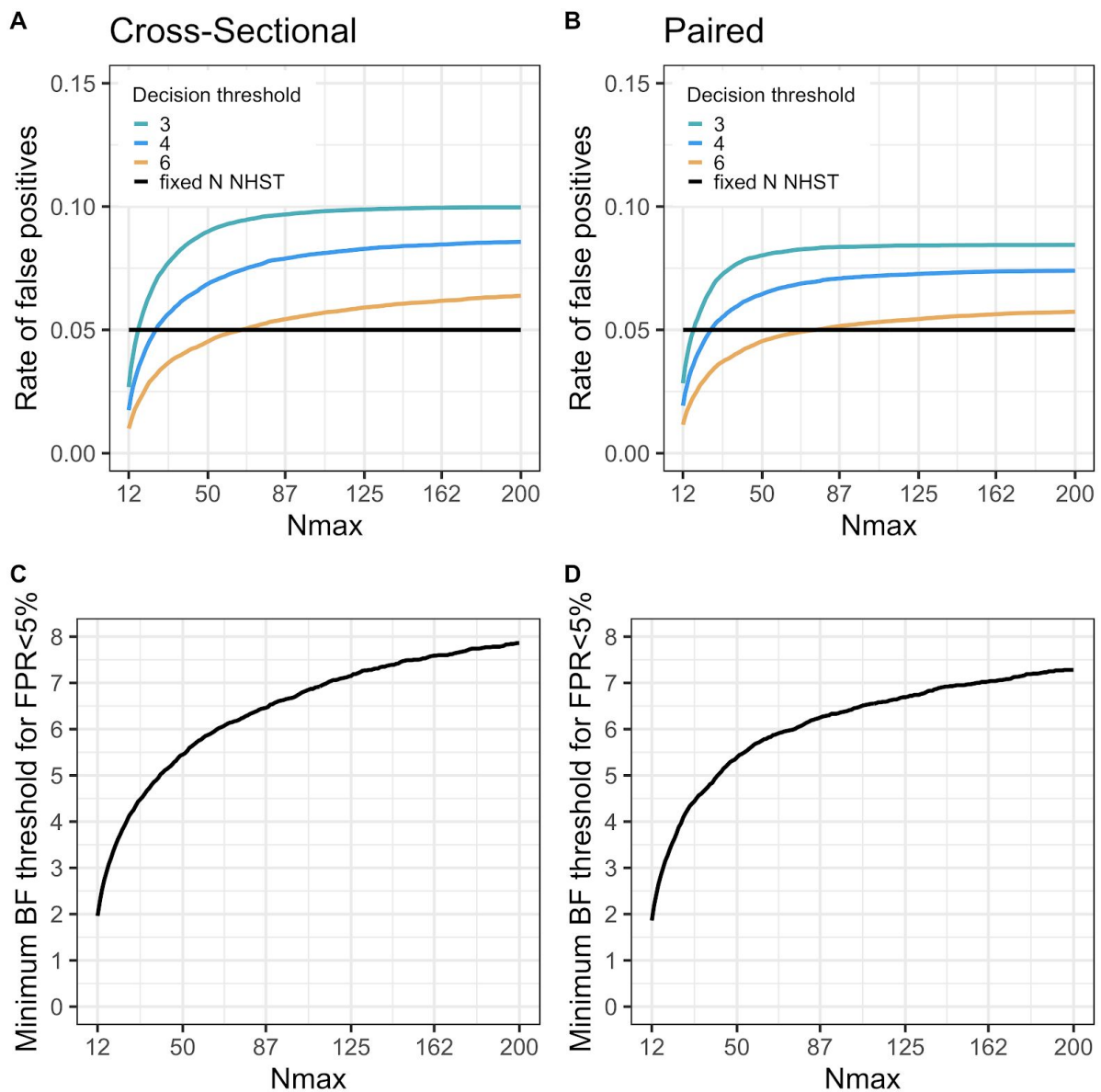


Figure S1. A and B) The rate of false positive stopping decisions increases but reaches an asymptote as the maximal number of subjects (N_{\max}) becomes higher. Three different BF decision thresholds are shown. C and D) The BF decision threshold can be adjusted to achieve a desired rate of false positives (here 5%) for different N_{\max} . For all figures: samples are drawn from two populations with the same mean value; testing starts at $N = 12/\text{group}$; and BF is checked after every additional comparison pair (1 set of patient-control scans or pre-post scans). Here stop decisions for H_0 are allowed and the tests are one-sided.

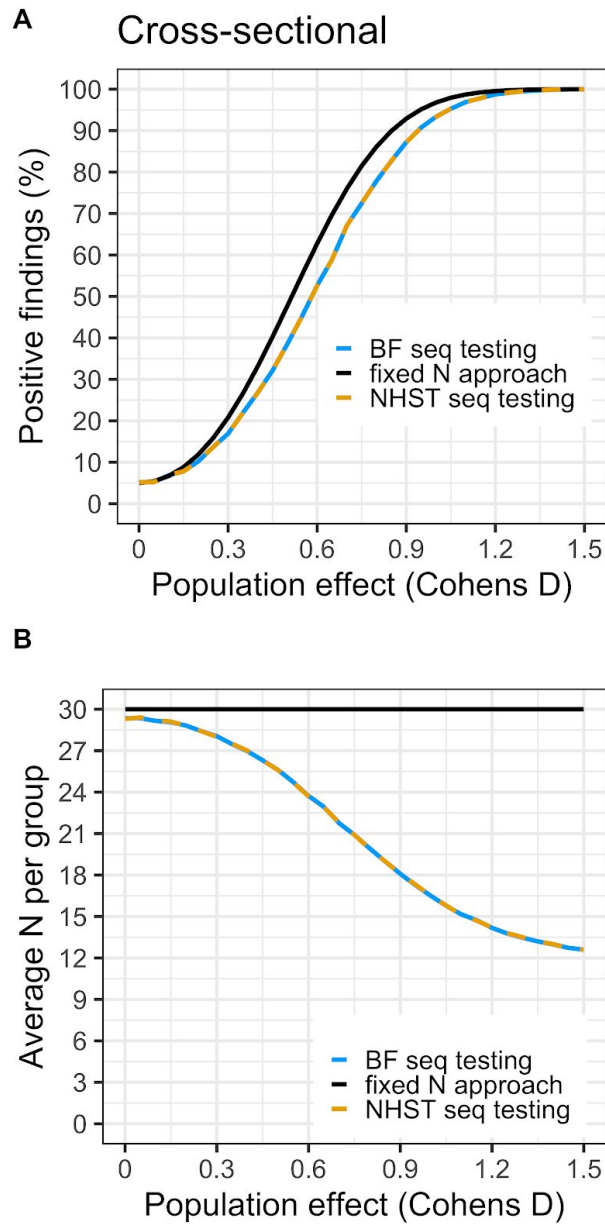


Figure S2. The sequential BF testning, using a zero-centered Cauchy to describe the alternative hypothesis, will produce the same results as a 5% family-wise error rate corrected sequential NHST procedure ($\alpha\text{-corrected} = 0.01$) when specifying the BF threshold to correspond to a 5% false positive rate ($BF = 4$).

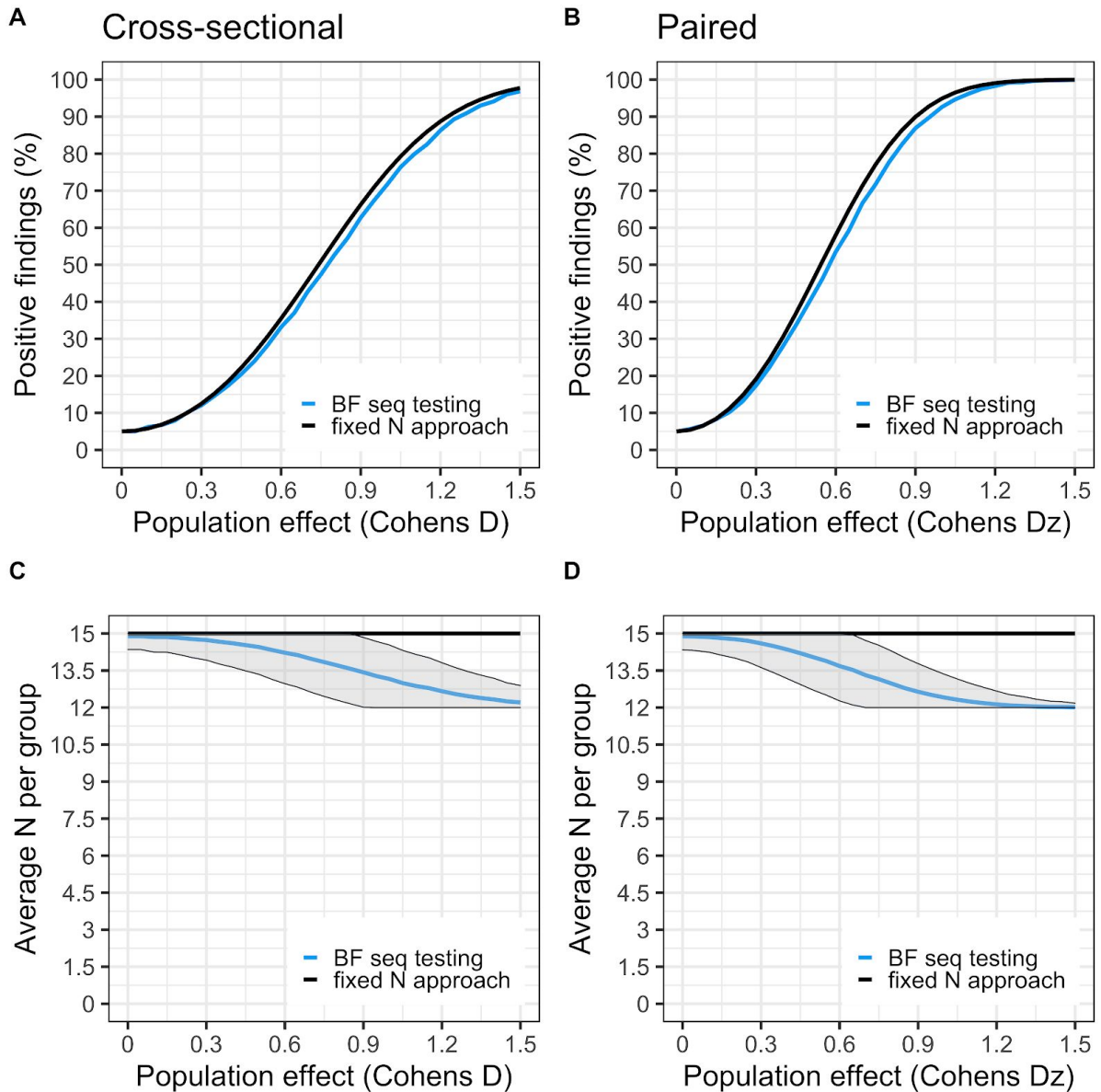


Figure S3. Settings for the simulation: $H1$ is a two-sided cauchy(0,0.707), ($N_{start} = 12$, $N_{max} = 15$, BF threshold = 2.4 and 2.5 for cross-sectional and paired respectively). Panel A and B shows true positive (or “power”) curves for BF sequential testing (blue) and a fixed N approach (black). The curves denote the rate of true positive findings at different population effects. For the fixed N approach, only one test is performed at $N=15$ per group. For the sequential testing, 8 subjects/group are first collected, then BF is checked after each added comparison pair until 15 subjects/group is reached, using a stopping threshold of 4. Panel C and D shows the average number of subjects needed to reach a stopping decision at different population effects. Fixed N is the black line (fixed at $N = 15$ /group); BF sequential testing is the blue line with shaded area denoting ± 1 SD.

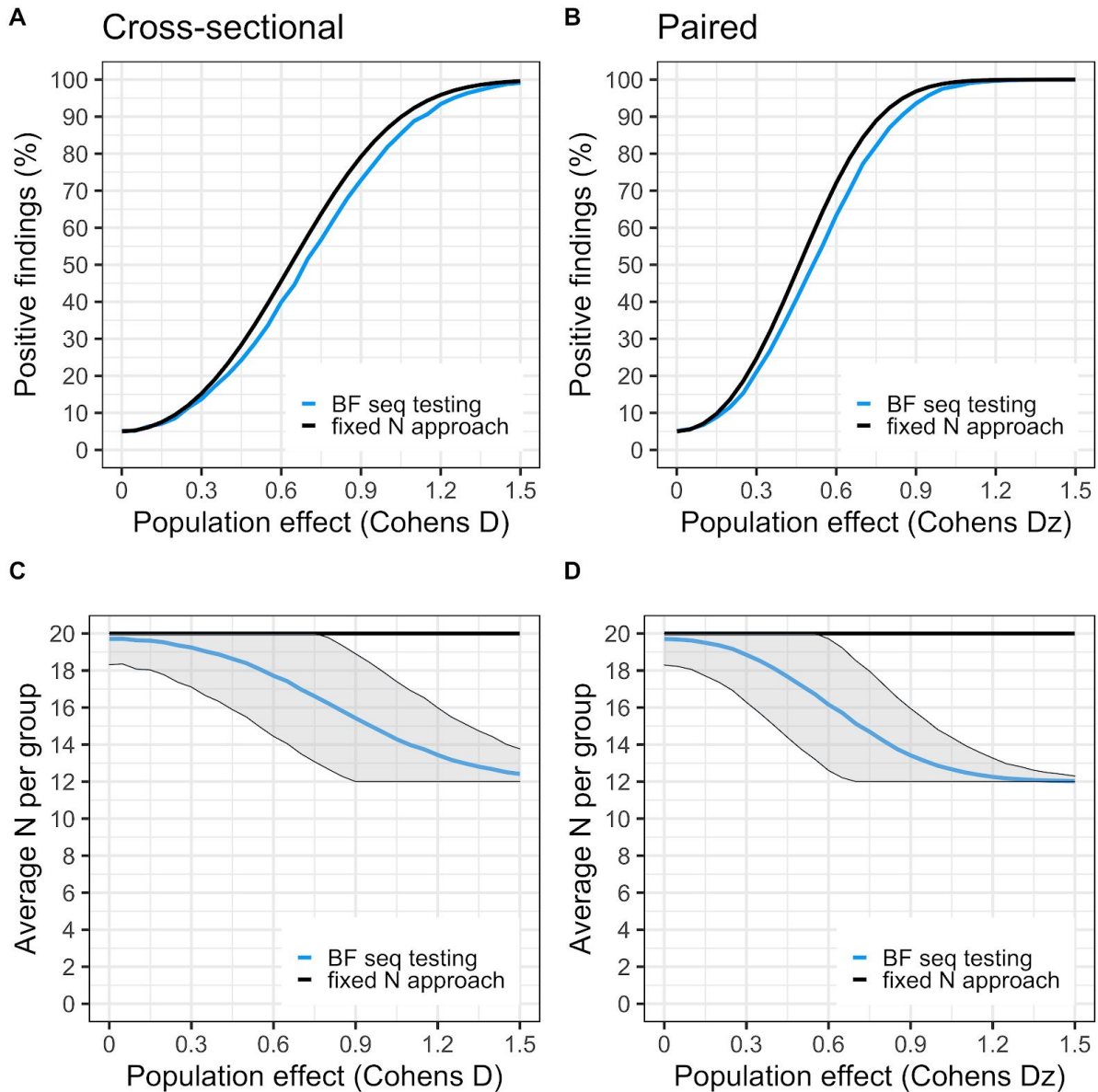


Figure S4. Settings for the simulation: $H1$ is a two-sided cauchy(0,0.707), ($N_{start} = 12$, $N_{max} = 20$, BF threshold = 3.1 and 3.3 for cross-sectional and paired respectively). Panel A and B shows true positive (or “power”) curves for BF sequential testing (blue) and a fixed N approach (black). The curves denote the rate of true positive findings at different population effects. For the fixed N approach, only one test is performed at $N=20$ per group. For the sequential testing, 12 subjects/group are first collected, then BF is checked after each added comparison pair until 20 subjects/group is reached, using a stopping threshold of 4. Panel C and D shows the average number of subjects needed to reach a stopping decision at different population effects. Fixed N is the black line (fixed at $N = 20$ /group); BF sequential testing is the blue line with shaded area denoting ± 1 SD.

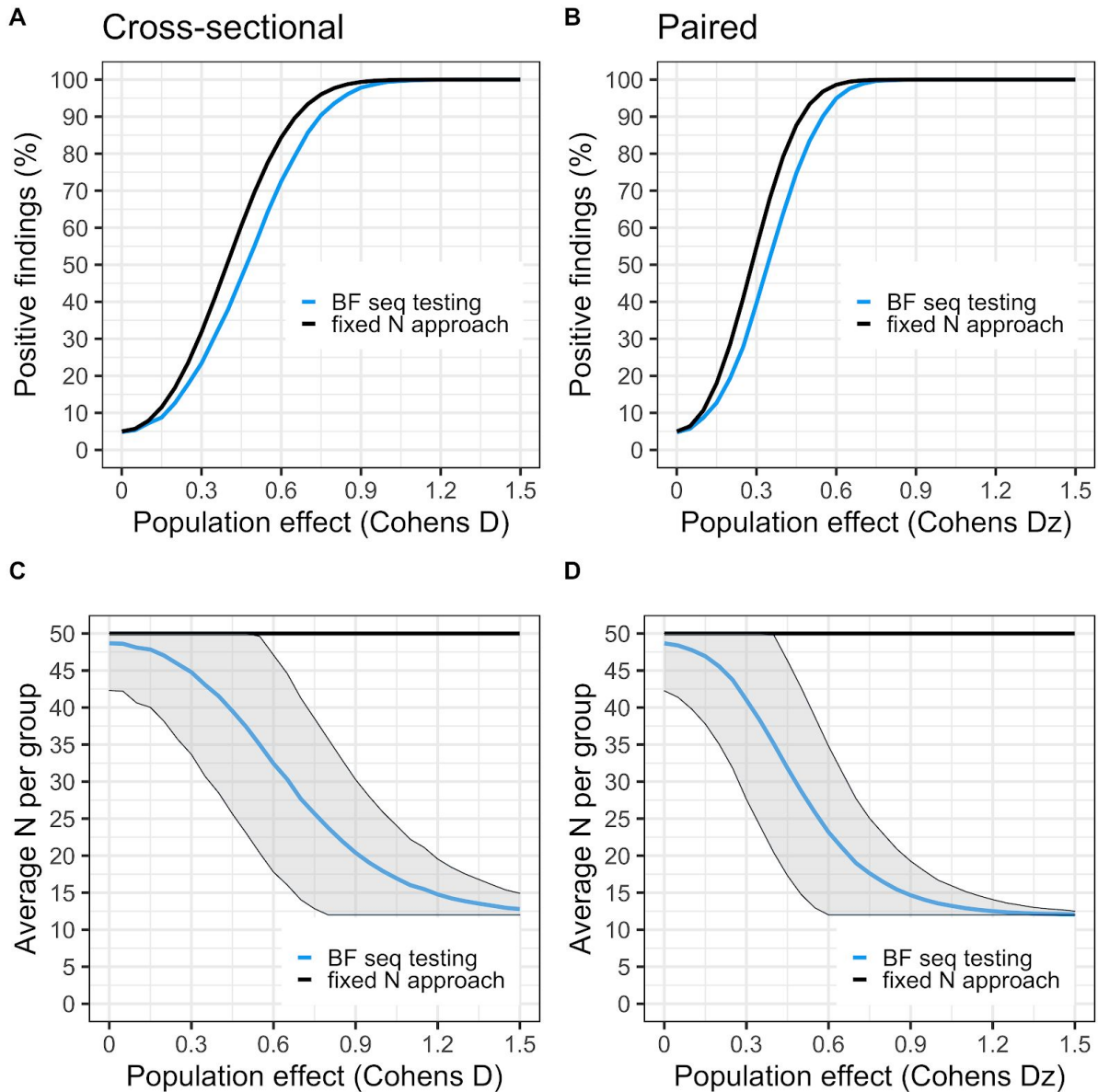


Figure S5. Settings for the simulation: $H1$ is a two-sided cauchy(0,0.707), ($N_{start} = 12$, $N_{max} = 50$, BF threshold = 5.2 and 5.4 for cross-sectional and paired respectively). Panel A and B shows true positive (or “power”) curves for BF sequential testing (blue) and a fixed N approach (black). The curves denote the rate of true positive findings at different population effects. For the fixed N approach, only one test is performed at $N=50$ per group. For the sequential testing, 12 subjects/group are first collected, then BF is checked after each added comparison pair until 50 subjects/group is reached, using a stopping threshold of 4. Panel C and D shows the average number of subjects needed to reach a stopping decision at different population effects. Fixed N is the black line (fixed at $N = 50$ /group); BF sequential testing is the blue line with shaded area denoting ± 1 SD.

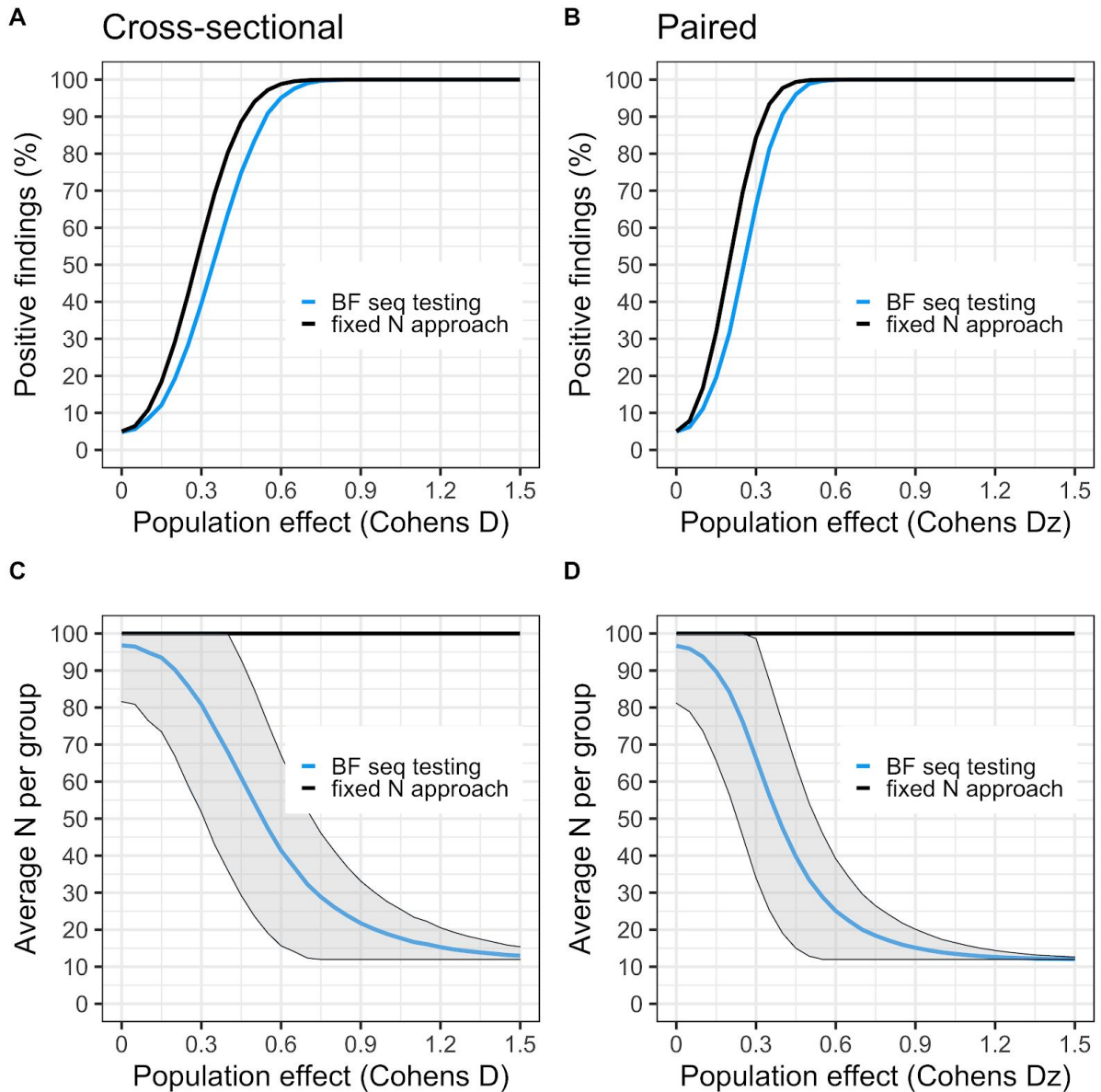


Figure S6. Settings for the simulation: $H1$ is a two-sided cauchy(0,0.707), ($N_{start} = 12$, $N_{max} = 100$, BF threshold = 6.6 and 6.7 for cross-sectional and paired respectively). Panel A and B shows true positive (or “power”) curves for BF sequential testing (blue) and fixed N approach (black). The curves denote the rate of true positive findings at different population effects. For the fixed N approach, only one test is performed at $N=100$ per group. For the sequential testing, 12 subjects/group are first collected, then BF is checked after each added comparison pair until 100 subjects/group is reached, using a stopping threshold of 4. Panel C and D shows the average number of subjects needed to reach a stopping decision at different population effects. Fixed N is the black line (fixed at $N = 100$ /group); BF sequential testing is the blue line with shaded area denoting ± 1 SD.

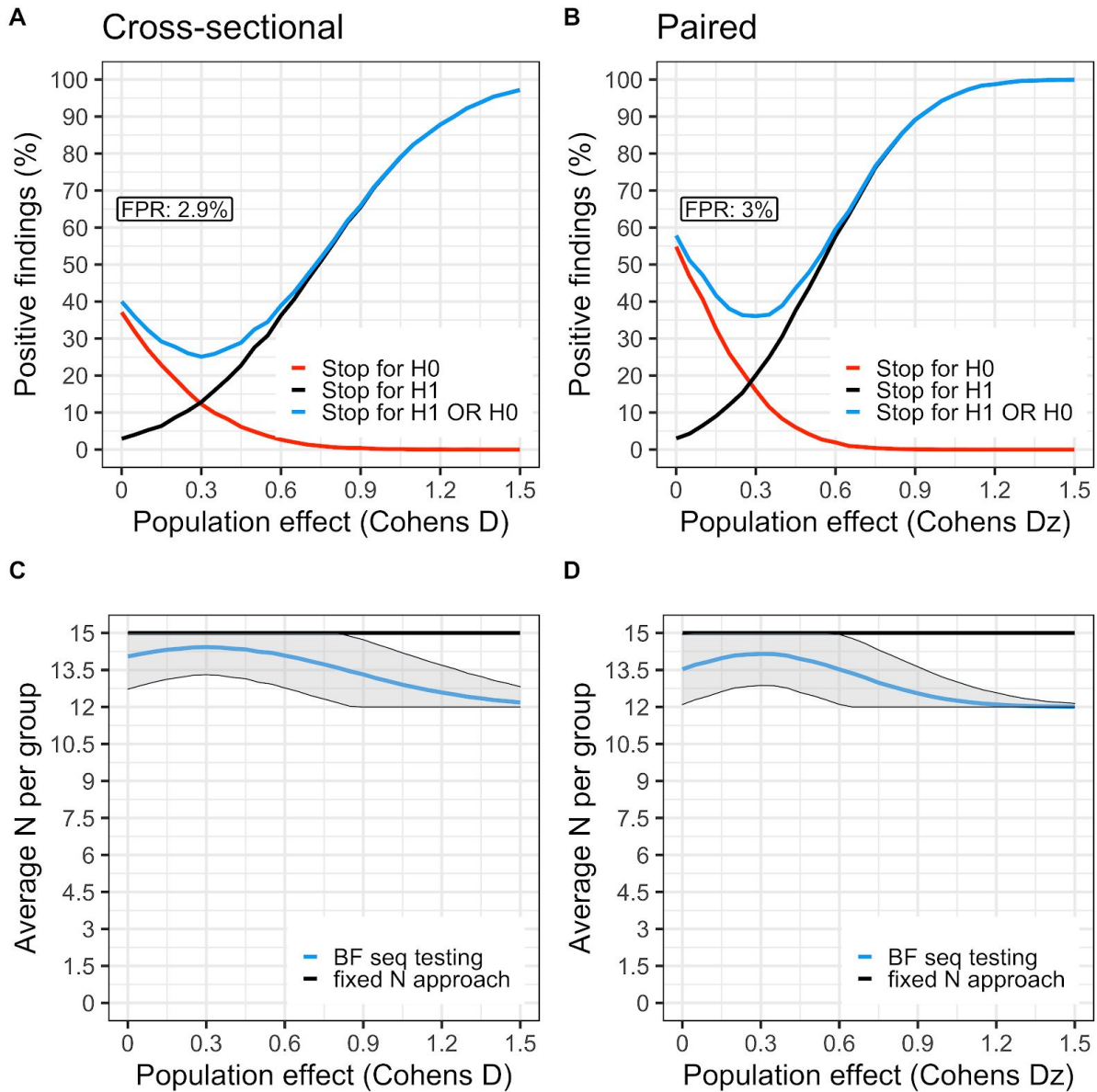


Figure S7. Settings for the simulation: $H1$ is a one sided cauchy($0, 0.707$), ($N_{start} = 12$, $N_{max} = 15$, BF threshold = 4). A and B) The black curve shows the proportion of studies that showed support for $H1$ ($BF > 4$) during data collection, at a range of population effects (starting at no effect, $D = 0$). The red curve is the proportion of studies showing support for $H0$ ($BF < 1/4$). The blue curve is the sum of the red and black curves. C and D) shows the average number of subjects needed to reach a stopping decision at different population effects. The flat black line represents N_{max} (15 subjects/group). BF sequential testing is the blue line with shaded area denoting ± 1 SD.

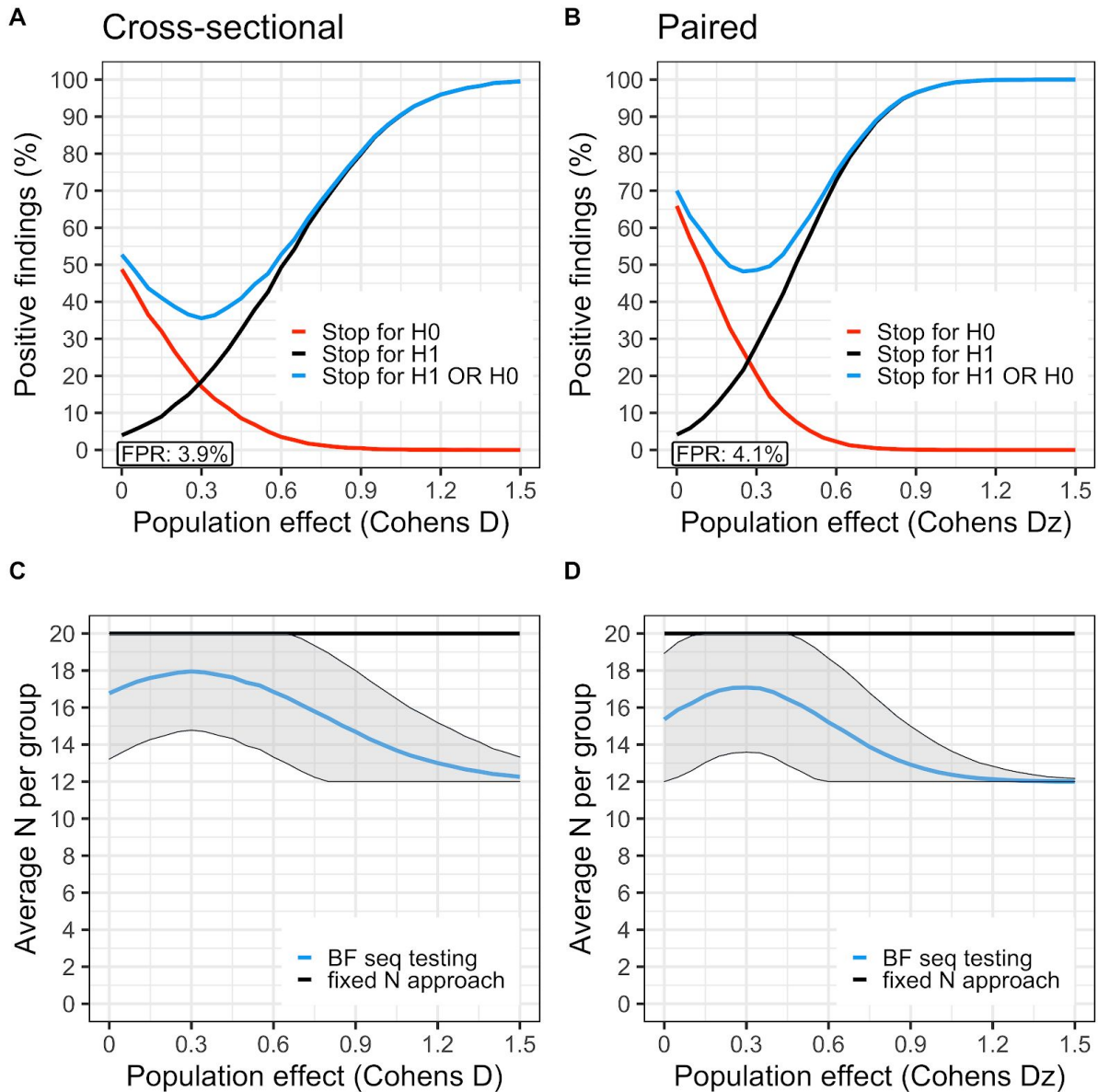


Figure S8. Settings for the simulation: $H1$ is a one sided cauchy(0,0.707), ($N_{start} = 12$, $N_{max} = 20$, BF threshold = 4). A and B) The black curve shows the proportion of studies that showed support for $H1$ ($BF > 4$) during data collection, at a range of population effects (starting at no effect, $D = 0$). The red curve is the proportion of studies showing support for $H0$ ($BF < 1/4$). The blue curve is the sum of the red and black curves. C and D) shows the average number of subjects needed to reach a stopping decision at different population effects. The flat black line represents N_{max} (20 subjects/group). BF sequential testing is the blue line with shaded area denoting ± 1 SD.

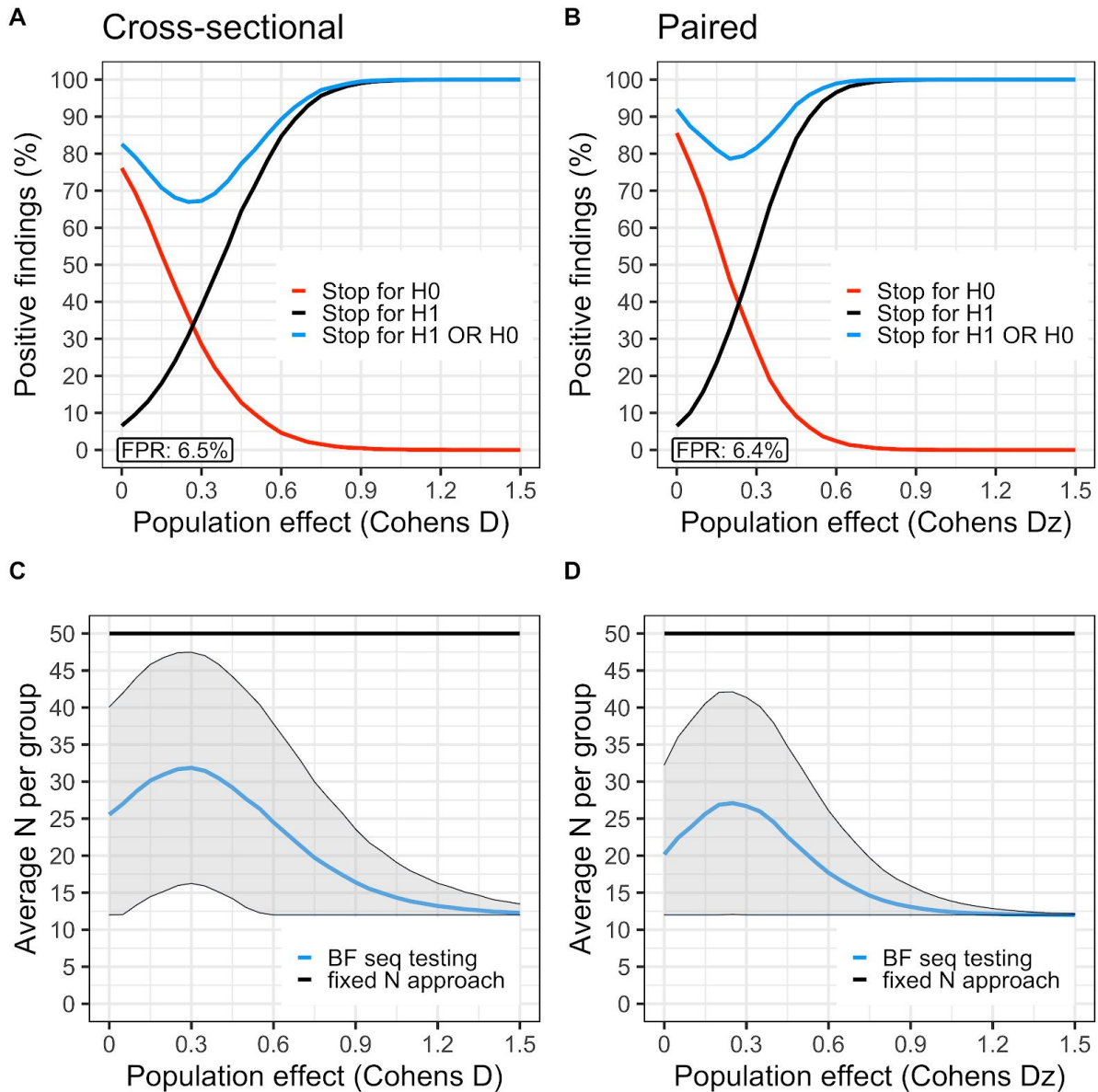


Figure S9. Settings for the simulation: $H1$ is a one sided cauchy(0,0.707), ($N_{start} = 12$, $N_{max} = 50$, BF threshold = 4). A and B) The black curve shows the proportion of studies that showed support for $H1$ ($BF > 4$) during data collection, at a range of population effects (starting at no effect, $D = 0$). The red curve is the proportion of studies showing support for $H0$ ($BF < 1/4$). The blue curve is the sum of the red and black curves. C and D) shows the average number of subjects needed to reach a stopping decision at different population effects. The flat black line represents N_{max} (50 subjects/group). BF sequential testing is the blue line with shaded area denoting ± 1 SD.

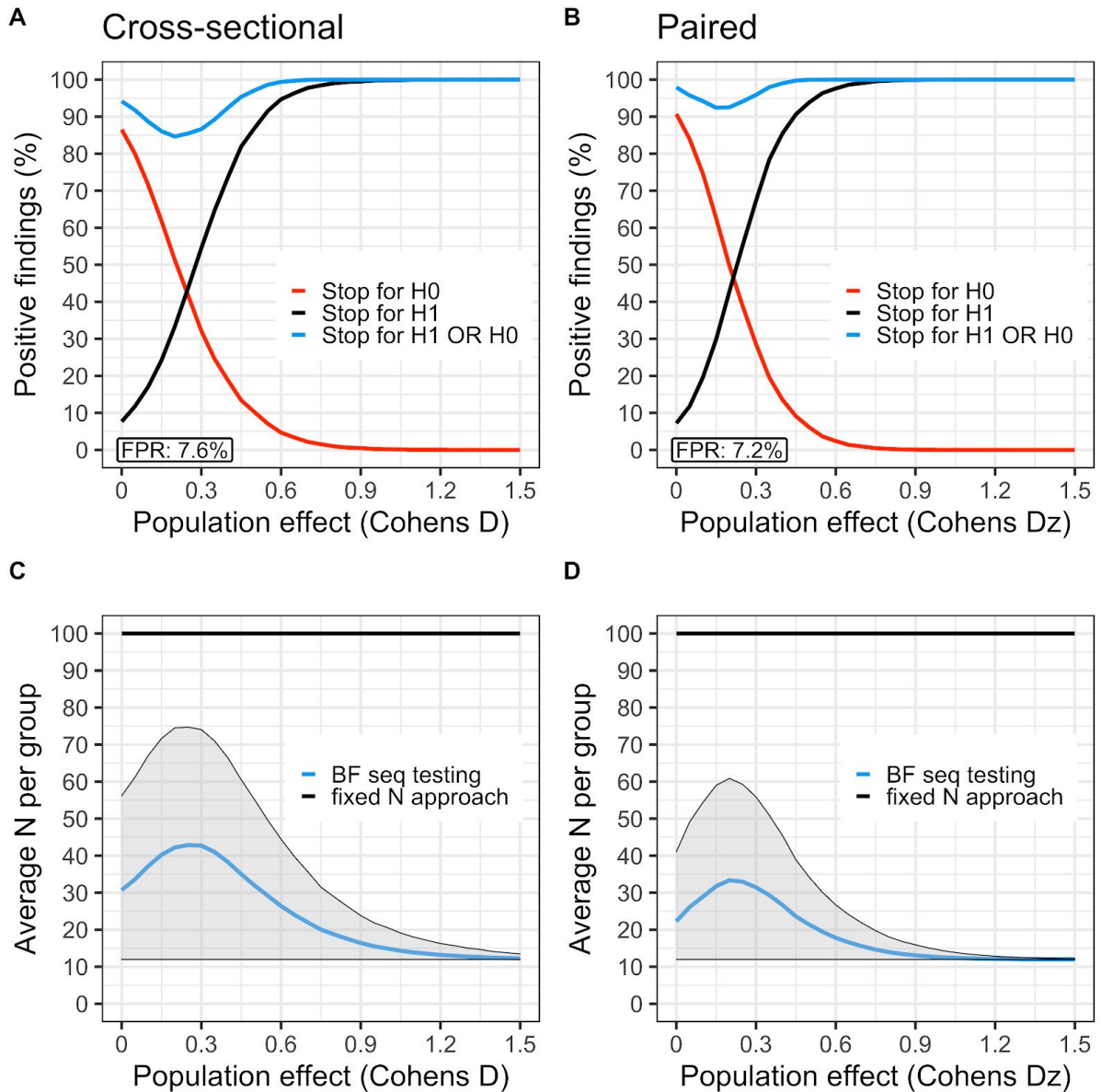


Figure S10. Settings for the simulation: $H1$ is a one sided cauchy($0, 0.707$), ($N_{start} = 12$, $N_{max} = 100$, $BF_{threshold} = 4$). A and B) The black curve shows the proportion of studies that showed support for $H1$ ($BF > 4$) during data collection, at a range of population effects (starting at no effect, $D = 0$). The red curve is the proportion of studies showing support for $H0$ ($BF < 1/4$). The blue curve is the sum of the red and black curves. C and D) shows the average number of subjects needed to reach a stopping decision at different population effects. The flat black line represents N_{max} (100 subjects/group). BF sequential testing is the blue line with shaded area denoting ± 1 SD.

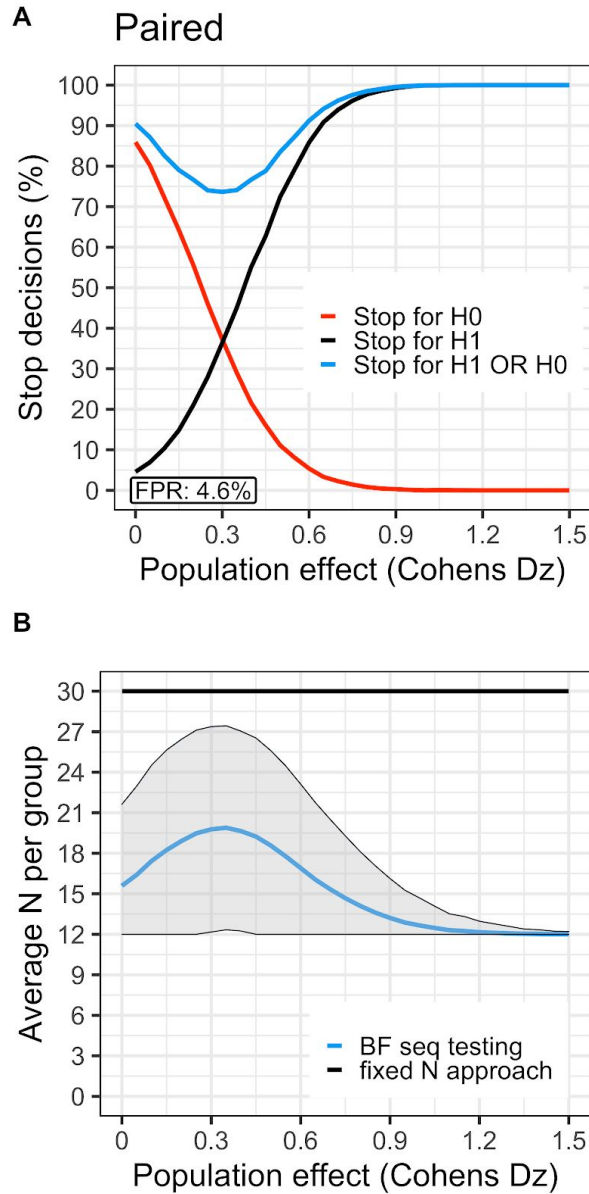


Figure S11. Settings for the simulation: $H1$ is a one sided cauchy(0,1), ($N_{start} = 8$, $N_{max} = 30$, BF threshold = 4). A) The black curve shows the proportion of studies that showed support for $H1$ ($BF > 4$) during data collection, at a range of population effects (starting at no effect, $D = 0$). The red curve is the proportion of studies showing support for $H0$ ($BF < 1/4$). The blue curve is the sum of the red and black curves. B) shows the average number of subjects needed to reach a stopping decision at different population effects. The flat black line represents N_{max} (30 subjects/group). BF sequential testing is the blue line with shaded area denoting ± 1 SD. The fact that a lower average sample size trades off against a higher risk of false negatives can be seen by comparing this figure to panel B and D in Figure 5 from the main text which have the same settings except for: 1) $H1 : \delta \sim \text{Cauchy}(0, 0.707)$ instead of $H1 : \delta \sim \text{Cauchy}(0, 1)$ and 2) testing starts at 12 subjects.

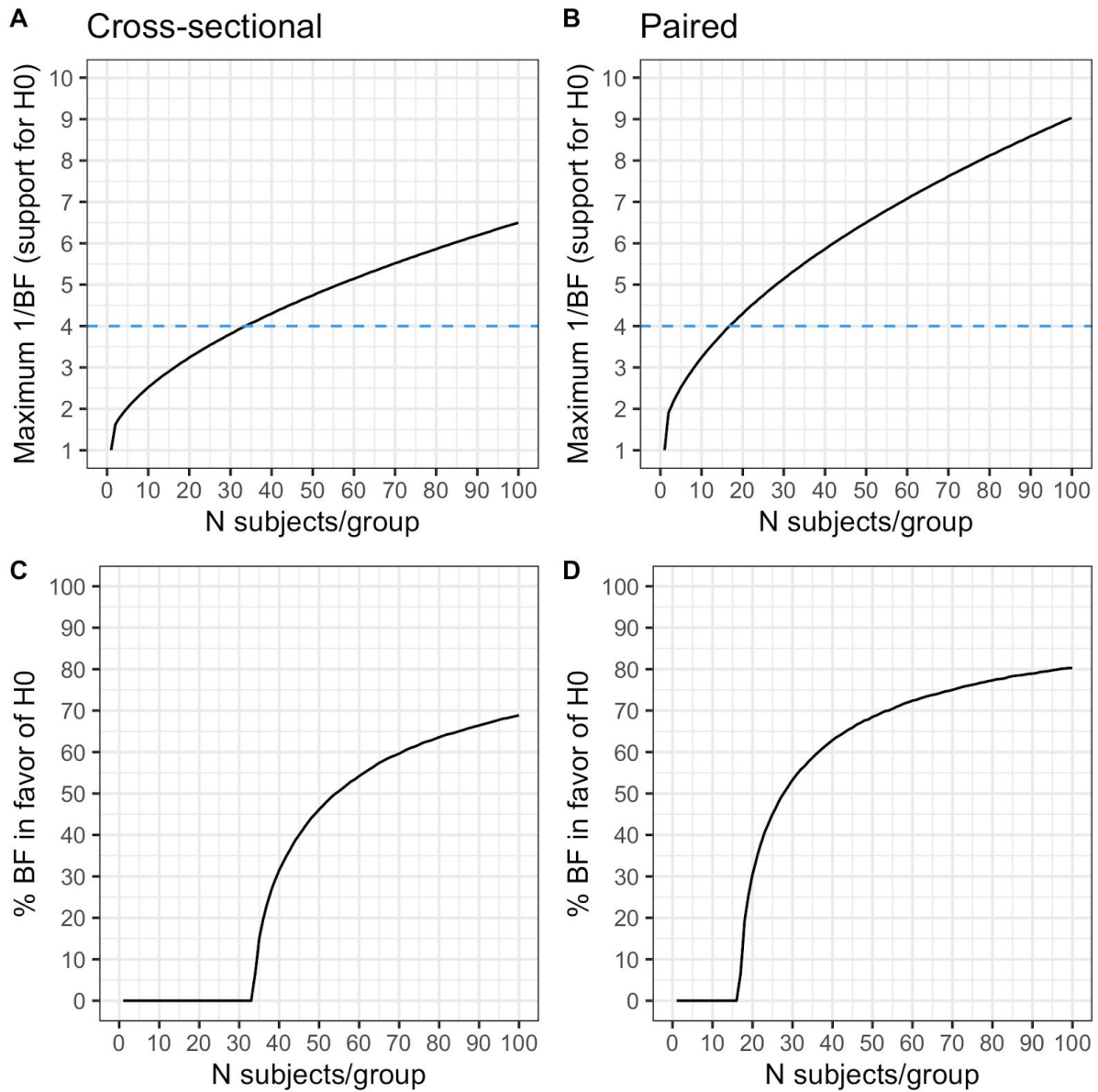


Figure S12. Maximum possible support ($1/BF$) in favor of H_0 compared to H_1 when using a two-tailed BF t-test. A-D) When using the settings described in the main article (H_1 is specified as a $\text{Cauchy}(0, 0.707)$, $N_{\text{start}} = 12$, threshold = 4) but a two-tailed test instead of a one-tailed test, it is not possible to obtain evidence in favor of H_0 at smaller N . E.g., in a cross-sectional design, at least 34 subjects/group are needed before the BF can reach a threshold of $1/4$. C-D) Percentage of BF showing support ($1/BF > 4$) for H_0 at different N . E.g., at 50 subjects/group, only 45% of BF will show support in favor of H_0 , when H_0 is true. Hence, in order to stop for H_0 when using commonly seen sample sizes in PET studies, we recommend to use a one-tailed BF t-test instead. This means that the researchers must make a prediction of the direction of the effect before initiating the study.

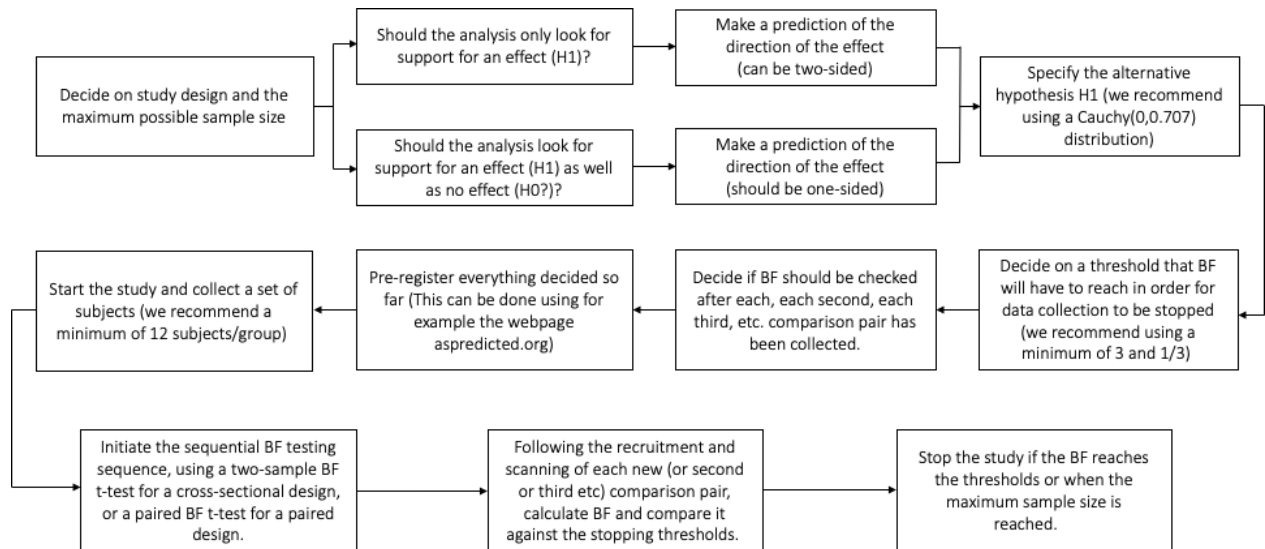


Figure S13. Recommended steps to follow in order to perform a clinical PET study using sequential BF testing, for a paired or cross-sectional design.