**Non-Inferiority Design**

a randomized control trial should show that a new treatment/experimental therapy (T) is superior to the placebo or no treatment at all

placebo-controlled trials are not appropriate or ethical when effective treatments have already been identified

need to demonstrate that T is as good as and not inferior to active control C, the best available treatment, but it’s impossible to prove treatment equality

non-inferiority margin = acceptable threshold that T can be inferior to C and still be considered as clinically important

use one-sided hypothesis test with

**Non-Inferiority Design for Positive Outcomes**

Risk Difference

Do not reject H0 Reject H0

T is inferior to C 0 T is superior to C

T is neither superior nor inferior to C

T is within the acceptable margin

H0: T is inferior to C

HA: T is not inferior to C

if lower bound is greater than , do not reject H0 and conclude inferiority

if lower bound is less than , reject H0 and conclude non-inferiority

Relative Risk/Risk Ratio

H0: T is inferior to C

HA: T is not inferior to C

if lower bound is greater than , do not reject H0 and conclude inferiority

if lower bound is less than , reject H0 and conclude non-inferiority

**Non-Inferiority Design for Negative Outcomes**

Risk Difference

Reject H0 Do not reject H0

T is superior to C 0 T is inferior to C

T is neither superior nor inferior to C

T is within the acceptable margin

H0: T is inferior to C

HA: T is not inferior to C

if upper bound is greater than , do not reject H0 and conclude inferiority

if upper bound is less than , reject H0 and conclude non-inferiority

Relative Risk/Risk Ratio

H0: T is inferior to C

HA: T is not inferior to C

if upper bound is greater than , do not reject H0 and conclude inferiority

if upper bound is less than , reject H0 and conclude non-inferiority

for a negative outcome, it takes a larger sample to prove non-inferiority using than

for a positive outcome, it takes a larger sample to prove non-inferiority using than

**Choosing Non-Inferiority Margin**

Step 1: Define M1

effect of active control relative to placebo

e.g. value of

the smallest, most conservative estimate of benefit of C against P

, otherwise there is no evidence that C is superior to P

Step 2: Define M2

non-inferiority margin

the largest clinically acceptable difference/degree of inferiority of the test treatment compared to the active control

