Sample Size Calculation

This analysis calculates sample sizes required for a randomized controlled trial evaluating the effect of pomegranate on mortality, sonographically measured carotid plaque size, and blood pressure.

1. Mortality

General assumption: The analysis assumes that the recruited population has a medium cardiovascular risk (i.e., risk of dying from cardiovascular diseases over 10 years equals to 20%) (Reference: Conroy RM et al. Eur Heart J 2003; 24: 987).

Assumptions	**Sample Size**
• RCT lasting 1 year (i.e., 2% mortality in placebo group) • 10% relative risk reduction in active group • Power 80%, two-sided alpha 0.05 • 2 samples (e.g., RCT)	74’144 participants per group
• RCT lasting 1 year (i.e., 2% mortality in placebo group) • 10% relative risk reduction in active group • Power 90%, two-sided alpha 0.05 • 2 samples (e.g., RCT)	98’920 participants per group
• RCT lasting 1 year (i.e., 2% mortality in placebo group) • 20% relative risk reduction in active group • Power 80%, two-sided alpha 0.05 • 2 samples (e.g., RCT)	17’838 participants per group
• RCT lasting 1 year (i.e., 2% mortality in placebo group) • 20% relative risk reduction in active group • Power 90%, two-sided alpha 0.05 • 2 samples (e.g., RCT)	23’712 participants per group
• RCT lasting 1 year (i.e., 2% mortality in placebo group) • 30% relative risk reduction in active group • Power 80%, two-sided alpha 0.05 • 2 samples (e.g., RCT)	7’616 participants per group
• RCT lasting 1 year (i.e., 2% mortality in placebo group) • 30% relative risk reduction in active group • Power 90%, two-sided alpha 0.05 • 2 samples (e.g., RCT)	10’084 participants per group
• RCT lasting 1 year (i.e., 2% mortality in placebo group) • 40% relative risk reduction in active group • Power 80%, two-sided alpha 0.05 • 2 samples (e.g., RCT)	4’107 participants per group
• RCT lasting 1 year (i.e., 2% mortality in placebo group) • 40% relative risk reduction in active group • Power 90%, two-sided alpha 0.05 • 2 samples (e.g., RCT)	5’415 participants per group
• RCT lasting 1 year (i.e., 2% mortality in placebo group) • 50% relative risk reduction in active group • Power 80%, two-sided alpha 0.05 • 2 samples (e.g., RCT)	2’515 participants per group
• RCT lasting 1 year (i.e., 2% mortality in placebo group) • 50% relative risk reduction in active group • Power 90%, two-sided alpha 0.05 • 2 samples (e.g., RCT)	3’300 participants per group

• RCT lasting 2 years (i.e., 4% mortality in placebo group) • 10% relative risk reduction in active group • Power 80%, two-sided alpha 0.05 • 2 samples (e.g., RCT)	36'363 participants per group
• RCT lasting 2 years (i.e., 4% mortality in placebo group) • 10% relative risk reduction in active group • Power 90%, two-sided alpha 0.05 • 2 samples (e.g., RCT)	48'511 participants per group

2. Carotid plaque size

General assumption: Middle-aged to elderly population with carotid artery stenosis (i.e., 3D ultrasound assessed plaque volume 700 ± 400 mm^3) (Reference: Ainsworth CD et al. Stroke 2005; 36: 1904).

Assumptions	**Sample Size**
• 10% reduction of plaque volume in active group • Power 80%, two-sided alpha 0.05 • 2 samples (e.g., RCT)	513 participants per group
• 10% reduction of plaque volume in active group • Power 90%, two-sided alpha 0.05 • 2 samples (e.g., RCT)	687 participants per group
• 20% reduction of plaque volume in active group • Power 80%, two-sided alpha 0.05 • 2 samples (e.g., RCT)	129 participants per group
• 20% reduction of plaque volume in active group • Power 90%, two-sided alpha 0.05 • 2 samples (e.g., RCT)	172 participants per group
• 30% reduction of plaque volume in active group • Power 80%, two-sided alpha 0.05 • 2 samples (e.g., RCT)	57 participants per group
• 30% reduction of plaque volume in active group • Power 90%, two-sided alpha 0.05 • 2 samples (e.g., RCT)	77 participants per group
• 40% reduction of plaque volume in active group • Power 80%, two-sided alpha 0.05 • 2 samples (e.g., RCT)	33 participants per group
• 40% reduction of plaque volume in active group • Power 90%, two-sided alpha 0.05 • 2 samples (e.g., RCT)	43 participants per group
• 50% reduction of plaque volume in active group • Power 80%, two-sided alpha 0.05 • 2 samples (e.g., RCT)	21 participants per group
• 50% reduction of plaque volume in active group • Power 90%, two-sided alpha 0.05 • 2 samples (e.g., RCT)	28 participants per group

3. Blood pressure

General assumption: Blood pressure in a middle-aged population with medium cardiovascular risk (i.e., systolic blood pressure 144 ± 24 mmHg and diastolic blood pressure 75 ± 10 mmHg) (Reference: Schoenenberger AW et al. Int J Cardiol 2013; 167: 168).

Assumptions	**Sample Size**
• 5% reduction of systolic BP in active group • Power 80%, two-sided alpha 0.05 • 2 samples (e.g., RCT)	175 participants per group
• 5% reduction of systolic BP volume in active group • Power 90%, two-sided alpha 0.05 • 2 samples (e.g., RCT)	234 participants per group
• 10% reduction of systolic BP in active group • Power 80%, two-sided alpha 0.05 • 2 samples (e.g., RCT)	44 participants per group
• 10% reduction of systolic BP volume in active group • Power 90%, two-sided alpha 0.05 • 2 samples (e.g., RCT)	59 participants per group
• 15% reduction of systolic BP in active group • Power 80%, two-sided alpha 0.05 • 2 samples (e.g., RCT)	20 participants per group
• 15% reduction of systolic BP volume in active group • Power 90%, two-sided alpha 0.05 • 2 samples (e.g., RCT)	26 participants per group
• 20% reduction of systolic BP in active group • Power 80%, two-sided alpha 0.05 • 2 samples (e.g., RCT)	11 participants per group
• 20% reduction of systolic BP volume in active group • Power 90%, two-sided alpha 0.05 • 2 samples (e.g., RCT)	15 participants per group
• 5% reduction of diastolic BP in active group • Power 80%, two-sided alpha 0.05 • 2 samples (e.g., RCT)	112 participants per group
• 5% reduction of diastolic BP volume in active group • Power 90%, two-sided alpha 0.05 • 2 samples (e.g., RCT)	150 participants per group
• 10% reduction of diastolic BP in active group • Power 80%, two-sided alpha 0.05 • 2 samples (e.g., RCT)	28 participants per group
• 10% reduction of diastolic BP volume in active group • Power 90%, two-sided alpha 0.05 • 2 samples (e.g., RCT)	38 participants per group
• 15% reduction of diastolic BP in active group • Power 80%, two-sided alpha 0.05 • 2 samples (e.g., RCT)	13 participants per group
• 15% reduction of diastolic BP volume in active group • Power 90%, two-sided alpha 0.05 • 2 samples (e.g., RCT)	17 participants per group
• 20% reduction of diastolic BP in active group • Power 80%, two-sided alpha 0.05 • 2 samples (e.g., RCT)	7 participants per group

• 20% reduction of diastolic BP volume in active group • Power 90%, two-sided alpha 0.05 • 2 samples (e.g., RCT)	10 participants per group