

# Evaluation of Comparative Effectiveness: A Model for Generating Hypothesis and Determining Sample Size

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## Objectives

- Although payers are asking for comparative effectiveness data, risk of conducting these studies is significant.
- One possible intermediate step is to leverage a validated instrument, the Treatment Satisfaction Questionnaire for Medication Version 1.4 (TSQM), to identify domains for separation and calculate sample size required for superiority in a comparative study.

## Methods

- We used data from iGuard.org, a consumer medication monitoring service totaling over 1 million members, whereby patients are randomly invited to complete the TSQM on an on-going basis.
- TSQM is a 14-item reliable and valid instrument providing scores on four scales—effectiveness, side effects, convenience and global satisfaction.
- For this study, we analyzed all responses from patients using lisinopril and metoprolol, two drugs used to treat high blood pressure.
- For sample size evaluation, adjusted means (LsMean) and standard deviations (SD) were generated for each treatment using an analysis of covariance model controlling for: patient age; gender; self-reported severity of disease; and use of other hypertensive, diabetes and heart failure medications.
- Analysis were conducted using SAS Version 9 and nQuery Advisor Version 7.

## Results

- 625 patients, 363 (58.1%) on lisinopril and 262 (41.9%) on metoprolol completed the TSQM between March and November 2008.
- TSQM domains had good internal consistency with Cronbach's alpha values over 0.85.
- There were significant differences between the two treatments on age, self-reported severity, use of diabetes medications and heart failure medications (Table 1).
- Figure 1 shows the adjusted mean (LsMean) and 95% confidence intervals (CI) for lisinopril and metoprolol for each of the TSQM domains.
- Given the observed difference in means and the standard deviation (SD) of the TSQM scores, Figure 2 describes the sample size required for a comparative effectiveness study to detect a statistically significant difference at a two-sided alpha of 0.05 with 80% power.

Table 1. Patient Baseline Characteristics

Patient Characteristics	Lisinopril N (%)	Metoprolol N (%)	P-value
N	363	262	<0.0001
Gender			
Female	227 (62.5%)	156 (59.5%)	0.4486
Male	136 (37.5%)	106 (40.5%)	
Self-reported severity			
Mild	141 (43.7%)	77 (31.6%)	0.0044
Moderate	155 (47.9%)	132 (54.1%)	
Severe	27 (8.4%)	35 (14.3%)	
Diabetes medications	89 (24.5%)	35 (13.4%)	0.0006
Heart Failure medications	45 (12.4%)	58 (22.1%)	0.0012
Other antihypertensive medications	213 (58.7%)	162 (61.8%)	0.4270

Figure 1. Least Square Means by Treatment

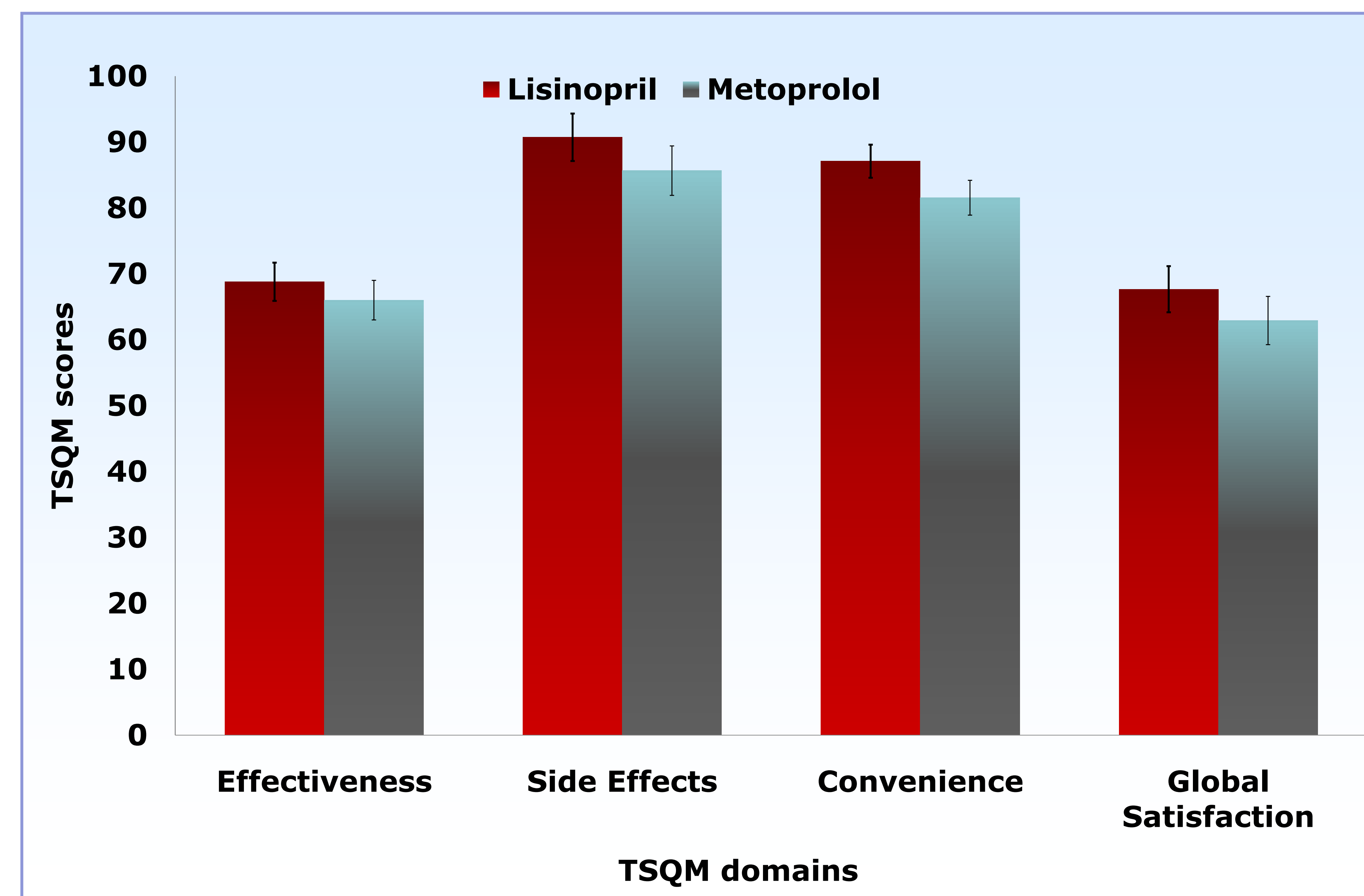
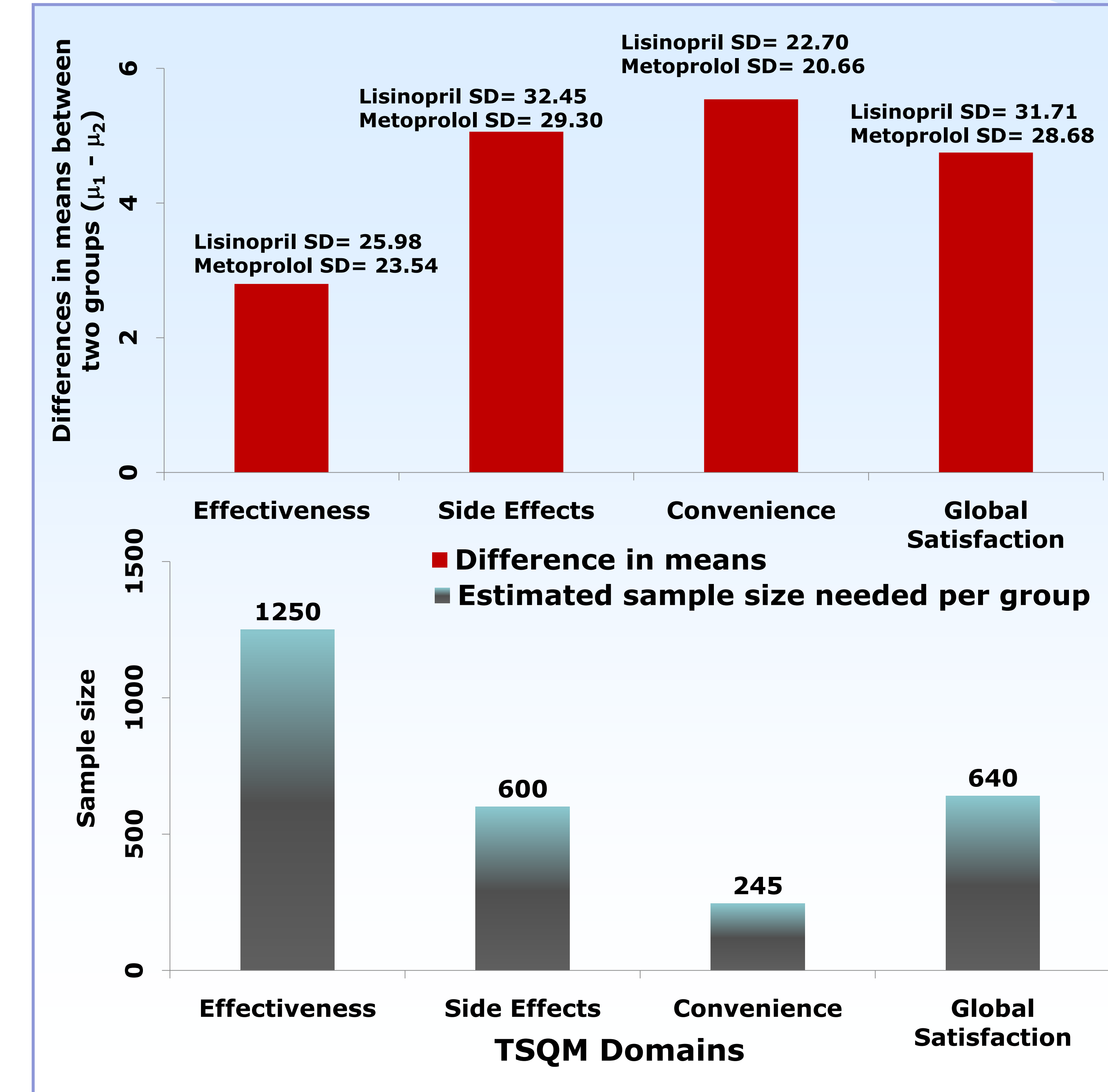


Figure 2. Sample Size Determination



## Conclusions

- In comparing treatment satisfaction between lisinopril and metoprolol among all four domains of the TSQM, detecting statistically significant differences in the Effectiveness requires the greatest sample size, while detecting differences in the Convenience domain requires the least sample size.
- This study demonstrates a quick and inexpensive model for obtaining feedback on comparative effectiveness study designs.
- By conducting a patient-reported feasibility survey prior to fielding a prospective comparative effectiveness study, researchers can increase their chances of a successful study.