Multistage design options for phamacogenetic studies

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The practice of individualized medicine for therapy or prevention could be informed by studies of genetic modifiers of treatment effects. This special case of gene-environment interaction studies offers several unique opportunities by exploiting random assignment of treatments. Two basic approaches are possible, one based on genetic studies added on to a pre-existing randomized controlled trial, the other based on targeted intervention studies added on to a pre-existing genetic cohort study. I will focus in particular on multistage sampling designs that exploit the prior information from the parent study to improve the statistical efficiency of the study of genetic modifiers of treatment effects. In particular, I will discuss different contexts in which either design might be used -- a study of a single candidate gene, an entire pathway, or a genome-wide association scan. I I will also discuss the relevance of the concept of Mendelian randomization and the potential utility of formal.pathway modeling as bases for causal inference about the role of intermediate biomarkers