## ESTIMATION AFTER THE GROUP SEQUENTIAL DESIGN OF A PHASE 2 BIOMARKER STUDY

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The national Early Detection Research Network (EDRN) has as its mission to discover and validate biomarkers for early detection of cancer, risk prediction, and prognosis. Since the majority of initial biomarker discoveries will not lead to useful clinical tests, the objective of a Phase 2 biomarker validation study is to confirm the initial findings and estimate performance characteristics (sensitivity, specificity, and ROC curve) for designing subsequent Phase 3 studies. The scarcity of high quality specimens and the cost of conducting validation studies require a group sequential design of phase 2 studies, with early termination if the marker is performing poorly. A unique feature of such studies is that unbiased and efficient parameter estimation for biomarkers selected for further study is of primary interest.

We propose a group sequential method in which estimation is conditional on the completion of the Phase 2 study. We propose a conditional UMVUE estimator that is the expectation of the estimate based on the final stage data conditional on the full data and completion of the study. This estimator is superior to the traditional unconditional UMVUE estimator. Our results also have implications for estimation following phase 2 therapeutic studies.