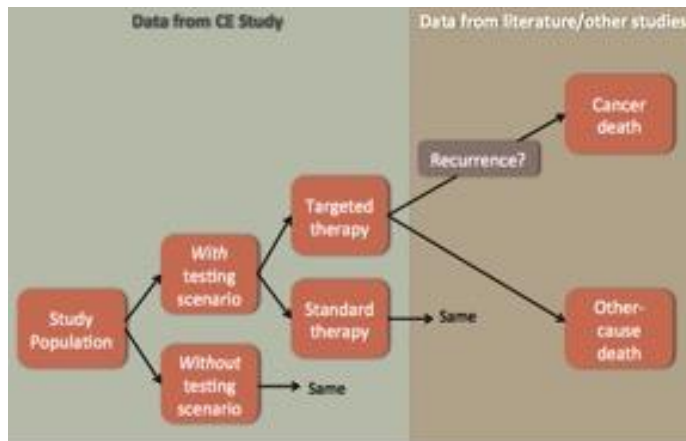# New public resource to model impact of cancer biomarkers

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Schematic of the Diagnostics Biomarker module. The virtual study population is subjected to two scenarios: all are tested for the diagnostic biomarker or none are tested. The resulting distribution of tailored versus standard therapy for each scenario is based on a comparative effectiveness (CE) study. CANTRANce uses additional data from the literature/other studies to project from the time of treatment to mortality.

Image provided by Dr. Ruth Etzioni.

Biomarkers assessed at the time of cancer diagnosis may help predict a patient's response to a specific treatment; such information can improve a patient's outcome and/or quality-of-life. Advances in genomic research over the past decade have produced a multitude of candidate "diagnostic biomarkers", which may disseminate into clinical practice long before survival data becomes available. In the interim, comparative effectiveness (CE) studies collect data on how a potentially diagnostic biomarker affects an intermediate endpoint, such as treatment recommendations. These studies often do not assess whether the biomarker reduces cancer mortality. One way to address this question is to conduct a complementary modeling study that translates changes in an intermediate endpoint into projected effects on mortality, quality-of-life, and costs. However, the resources needed to conduct such complementary modeling studies are not always readily available. Drs. Jeanette Birnbaum, Ruth Etzioni, and colleagues in the Public Health Sciences Division have developed a system of statistical simulation models for Cancer Translation of Comparative Effectiveness Research (CANTRANce), to project the mortality impact of interventions given their effects on intermediate endpoints. In a recent article in Medical Decision Making, the authors introduce the Diagnostic Biomarker module of CANTRANce and use it to evaluate a diagnostic breast cancer biomarker for mortality, quality-of-life, and costs.

CANTRANce uses an individual-level micro-simulation approach in which subjects transition through health states in continuous time. The Diagnostic Biomarker module of CANTRANce, presented in

the article, compares two scenarios: 1) all individuals receive a one-time testing intervention using the diagnostic biomarker and 2) no individuals receive testing. Based on primary or published data from a CE study, the model uses the distributions of the two possible treatments, tailored or standard, for each scenario. To then project mortality in each scenario, the model uses results of published prognostic studies; users can specify annual cost and utility weights to model cost and quality-of-life.

To validate the Diagnostic Biomarker module, the authors conducted two case studies. Each case study used data from CE studies testing an intervention of a gene recurrence score (RS) for breast cancer on treatment recommendations: adjuvant chemotherapy plus hormone therapy (tailored) vs. hormone therapy alone (standard).

The first case study compared CANTRANce's performance to that of a previously developed customized model by Reed and others. This case study used published CE data in which two medical oncologists made two treatment recommendations for node-negative, estrogen receptor (ER)-positive patients, with and without the patients' RS information. No individual-level data were available, but the Diagnostic Biomarker module can utilize summary statistics. Once all assumptions were matched, their model closely replicated the Reed model.

In the second case study the authors carried out a novel projection of the long-term impact of the RS using individual-level data from a previously published CE study of how RS information affected treatment recommendations in node-negative ER-positive women.

In both case studies the use of the RS decreased adjuvant chemotherapy (tailored treatment) among low-risk women and increased it among high-risk women. In addition, the models for both CE studies projected that testing with the RS increased life-years and quality-of-life at reasonable cost, but with substantial uncertainty. The models from the first case study projected greater benefit and costs than the second case study because of the different population risk distributions and the differences in the impact of the testing indicated by the two CE studies. According to the authors, "the interpretation and application of these projected outcomes should be considered in context of the original CE study population" and the quality of the input data.

"This work provides a flexible and fast tool for projecting the impact of a new biomarker for treatment targeting on disease outcomes and costs," says Dr. Etzioni. The novelty of CANTRANce "is the automation of the tool so that anyone with data on how a treatment-targeting biomarker affects treatment patterns can use the tool to project the downstream and long-term impacts of the marker.

This work is part of a larger suite of automated tools for projecting the long-term and downstream impacts of cancer interventions from studies that evaluate the impact of these interventions on short-term and intermediate outcomes." A user-friendly Windows application interface for CANTRANce, developed by Fred Hutch investigator Mark W. Mason, is downloadable to the public from http://www.fredhutch.org/en/labs/phs/projects/cantrance.html.

Citation:

Birnbaum JK, Ademuyiwa FO, Carlson JJ, Mallinger L, Mason MW, Etzioni R. 2015. Comparative effectiveness of biomarkers to target cancer treatment: modeling implications for survival and costs. *Med Decis Making*. doi: 10.1177/0272989x15601998.