



The University of Chicago
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Master's Seminar

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**Hazard of Recurrence in Lymph Node-Negative Breast Cancer:
Treatment Effects over Time by ER Status**

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ABSTRACT

Previous studies of disease recurrence after surgery in breast cancer patients have identified time-dependent patterns in the instantaneous risk (i.e. hazard) of recurrence, and that these patterns differ by disease characteristics such as tumor estrogen-receptor (ER) content. Benefits from post-surgical chemotherapy and hormonal therapy treatments have also been established. Using a cohort of 9,279 participants from five randomized trials, we examine and verify these observations using standard survival analysis techniques, such as Kaplan-Meier curves, nonparametric hazard estimates, and the Cox proportional hazards models. We further explore time-varying hazards according to ER and estimate time-varying treatment effects, using kernel-based smoothing estimation of the log hazard ratio with point-wise confidence bounds and simultaneous confidence bands over the time span.

Results validated the crossing of hazard functions for patients with ER-negative tumors relative to those with ER-positive tumor, with the former initially having higher failure hazard that in later follow-up is smaller than that for ER-positive tumors. Within both ER groups, the Cox regression model suggests significant reduction in risks for all treatment types, but the proportionality test fails to confirm the constant hazard ratio over time. Nonparametric estimates of log hazard ratio over time and their simultaneous confidence intervals suggest that all treatments reduce the risk significantly early in the follow up time, but that these effects diminish over time.