Math 288 - Statistics Seminar

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Early detection of ovarian cancer using each woman as their own control via a longitudinal change-point model.

Abstract:

Over 75% of ovarian cancers are detected in late stage disease with poor prognosis while if detected in early stage prognosis is often excellent. Despite therapeutic advances the mortality rate has not changed over the past 50 years. This makes early detection an appealing approach to investigate for its potential to reduce ovarian cancer mortality.

Screening trials starting in 1985 tested serum CA125 annually, a newly discovered blood test for monitoring ovarian cancer therapy. Women with CA125 exceeding a threshold were referred to transvaginal ultrasound and additional CA125 tests. This multi-modal approach attained an acceptable positive predictive value (PPV) however greater sensitivity for early stage disease remained a significant concern. Statistical analysis of longitudinal CA125 values from these trials indicated that most cases had exponentially rising CA125 from a baseline while most non-cases had relatively flat CA125 profiles. The challenge for the statistician was to devise a screening approach that leveraged the information in longitudinal CA125 values to increase sensitivity while maintaining the same PPV. Statistical modeling of these data led to a calculation of the risk of having a change-point given age and one or more serial CA125 values, essentially using each woman as her own control. The basis for the risk calculation was a hierarchical longitudinal change-point mixture model. This risk estimate incorporating longitudinal information is a surrogate for the risk of having undetected ovarian cancer which is the optimal information on which screening decisions should be based.

In 1996, the first of five screening trials implemented this risk calculation in general population post-menopausal women and in women at increased genetic risk. Trials in the general population measured CA125 annually and the algorithm referred women with intermediate risks to an additional CA125 test in 3 months, and women with elevated risks to an immediate ultrasound. All published trials implementing the risk of ovarian cancer algorithm showed an increase in early stage detection. No other ovarian cancer screening trials in the general or high risk populations have achieved this result.

Statisticians were also crucial in the design and analyses of these screening trials. The largest trial had ovarian cancer mortality as the endpoint and showed a mortality difference (p ≤ 0.05) with a 28% reduction in the second half. This reduction was seen in the 80% of cases where the first CA125 test preceded the change-point (incident cases) enabling such cases to be their own control. However, further follow-up is needed for definitive conclusions. (Jacobs Menon et. al. The Lancet 2015).

Host: Lily Xu

Monday, March 13, 2017
3:00 PM
AP&M 6402