POLE mutation Meta-Analysis

Derek Chiu, Aline Talhouk

June 26, 2015

An intro is needed..

What are we doing? What are meta-analyses? What is their purpose? What are the publications we considered? How did we go about selecting the papers? A brief description of the cohorts what they have in common how they are different, a reference to the excel spreadsheet, and you should attach a copy when you forward to Jessica and Melissa

# Hazard Ratios Extraction

All of the hazard ratios were extracted from available publications or were computed from available data. Where possible, hazard ratios from multivariable models that include POLE mutation status and other predictors were used.

- In the PORTEC cohort, multivariable analysis included age, tumor type, grade, LVSI, depth of myometrial invasion, and treatment as covariates.

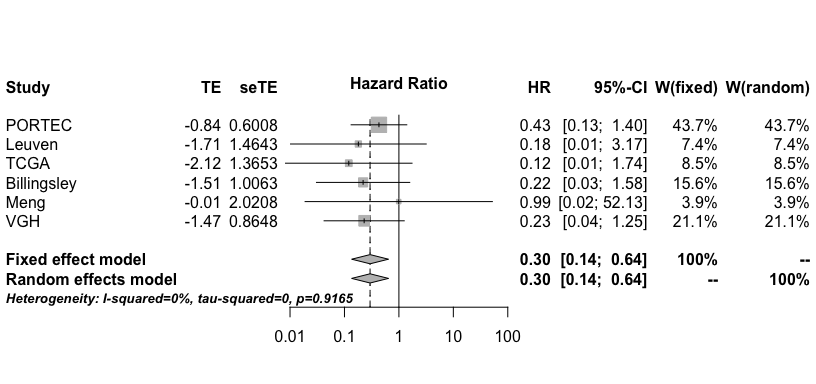
- Billingsley et. al conducted multivariable analysis using age (>= 60), stage (I/II vs. III/IV), grade (1 vs. 2), grade (1 vs. 3), LVSI, deep myometrial invastion (>= 50%), any kind of adjuvant therapy, and BMI (>= 30) as covariates. Since POLE mutation was not significant at 10% level in univariable analysis for progression-free survival, it was not included in the multivariable model. Therefore, the hazard ratio we use in the meta-analysis is from the univariable model with only POLE.

- Hazard ratios from Meng et. al were calculated from clinical data provided to us. Covariates included were age at surgery, whether they had any chemotherapy or radiation therapy, and stage.

TCGA? VGH? Leuven and Basel/Zurich?

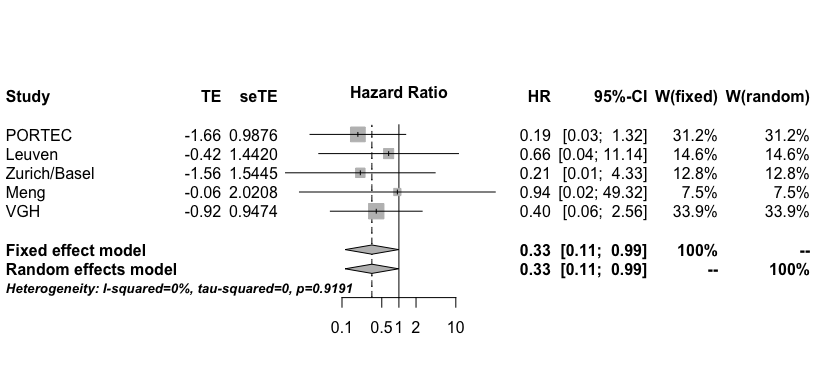
## Recurrence-Free Survival

There are 6 studies used for recurrence-free survival hazard ratios: PORTEC, Leuven, TCGA, Billingsley, Meng, VGH.



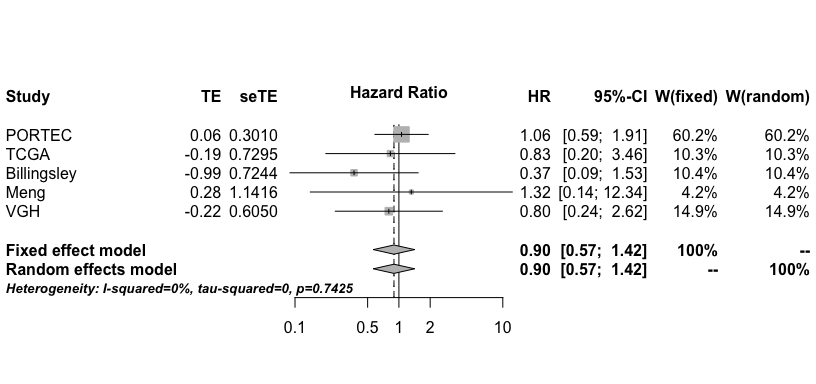
From the forest plot, we see that the overall hazard reatio is 0.295269, and is significant at the 5% level.

## Disease-Specific Survival



From the forest plot, we see that overall hazard ratio is 0.3348975, and is *barely* significant at 5% level.

## Overall Survival



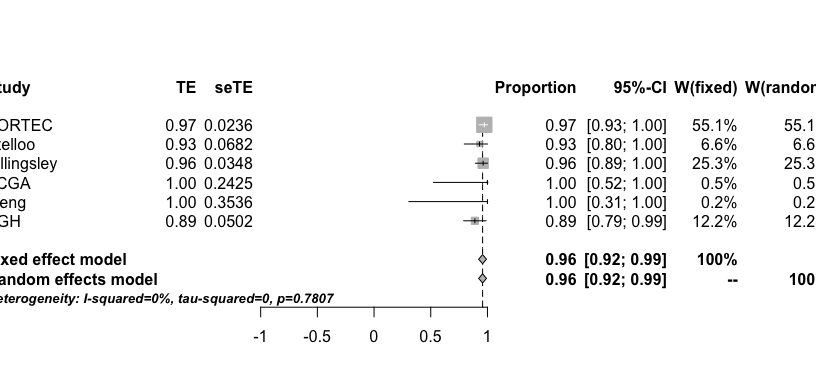
From the forest plot, we see that the overall hazard ratio is 0.8963225, but is not significant at 5% level.

In general, the reassuring take-home message is that for all 3 survival outcomes, POLE mutation has a protective effect.

# Five-Year Survival Rate

Stelloo et. al did not report hazard ratios in their paper, but did report 5-year survival rates. We decided to perform a meta-analysis on 5-year survival rates based on this measure. The problem is that the other papers did not report these rates, but they did have Kaplan-Meier curves including up to five years. To extract the survival rates, we printed our the curves, and estimated the rates by finding where the curve intersects with the five year follow-up time point.

To obtain standard errors for these survival rates, we used the equation for the stanadard deviation of a sample proportion.



Five-year survival is quite high for POLE mutations at 0.9571712.