Predictive Modeling

Lecture IV

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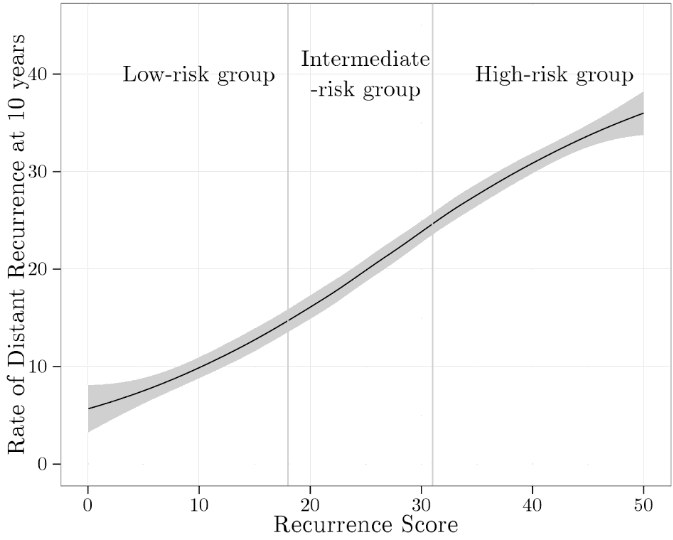
Case Studies

Oncotype DX


Low-risk group
Intermediate
-risk group
High-risk group
Rate of Distant Recurrence at 10 years
0
10
20
30
40
0
10
20
30
40
50
Recurrence Score

Development Process Studies

1. Assay development
   - High dimensional RT-PCR assay
   - Literature review to identify candidate genes
   - Measure gene expression of about 250 genes
   - Demonstrate acceptible measurements in FFPE breast cancer biopsy specimens
2. Signature Development
   - Multiple studies to test associations between recurrence and genes
   - Number of genes whittled down to 16 plus 5 reference genes
   - Model estimated to combine genes into a recurrence score

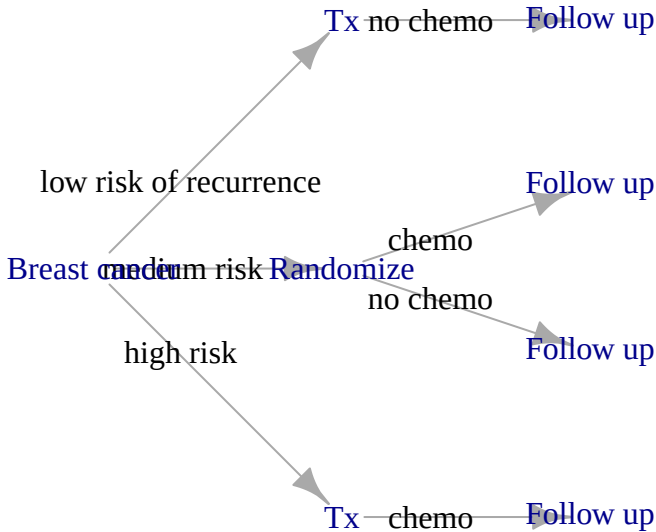
Development Process continued

3. Assay refinement
   - New assay developed to measure only the 21 genes
   - Validated and commercialized
4. Clinical validation
   - Independent study used to validate performance of score
   - Began entering clinical practice for prognosis

Continued further

5. Decision impact
   - Sought to answer: Can it be used to guide treatment?
   - Low risk patients may not need chemotherapy
   - Relation to other clinical factors (ER status, node status, stage)
6. Clinical trial (TAILORx)
   - Low risk group received hormonal therapy alone;
   - High risk group received hormonal therapy plus chemotherapy;
   - Mid-range Recurrence Score were randomized to receive hormonal therapy with or without chemotherapy.
   - Does the use of Oncotype DX have a positive impact for patients?

TailorX Trial



Results

- In September 2015, results were reported from an analysis of the women in the lowest-risk group. The findings showed that at 5 years, rates of distant relapse-free survival were 99.3%, of invasive disease-free survival were 93.8%, and of overall survival were 98.0%. These results provide prospective evidence that the gene expression test identifies women with a low risk of recurrence who can be spared chemotherapy.
- Results for women in the intermediate-risk group were published in the New England Journal of Medicine in 2018. The findings showed that adjuvant hormone therapy alone worked as well as hormone therapy and chemotherapy together. After 9 years of follow-up, the rates of invasive disease-free survival were 83.3% for hormone therapy alone and 84.3% for hormone therapy and chemotherapy, and for overall survival, the rates were 93.9% and 93.8%, respectively.

Conclusion

- What is the predictive model going to be used for?
- Provide valid estimates of performance
- Clearly describe what you did so that others can replicate it
- Does the use of the model have benefit for patients?
- Dishonest estimates of error may get you a publication, but will never get you a useful biomarker signature.

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