A Spatio-temporal Investigation of Breast Cancer Treatment Delay in Missouri

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Background

Treatment delay is defined as the number of days between date of diagnosis and the first treatment for the disease.

- Relationship between breast cancer survival and treatment delay has been established:
  - Greater time-to-surgery (TTS) is associated with lower overall and disease-specific breast cancer survival;
  - Young women with breast cancer with a longer treatment delay time (TDT) have significantly decreased survival time compared with those with a shorter TDT.
- Disparities in treatment delay exist:
  - Racial disparities in treatment delay exist among women <50 years old;
  - Treatment delay differs significantly between racial/ethnic groups and insurance type (public vs private).

Objective

To investigate if disparities exist in Missouri for breast cancer treatment delay by:

- Demographics (age, race, cancer stage);
- Over time (year of diagnosis); and/or
- Across space (county of residence at diagnosis).

Methods: Data Selection

Inclusion criteria for cases:

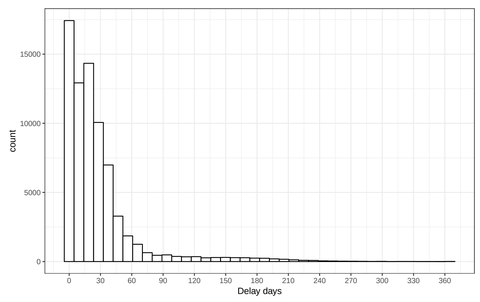
- Female;
- Diagnosed from 1997 through 2014;
- Known date of diagnosis, first treatment date, age, county of residence at diagnosis;
- Breast is the first primary tumor diagnosed.

There were 74,510 observations in our study. One problem we encountered: 16,011 (27.37%) cases had zero delayed days. The reasons are complicated.

Table 1: Data Layout

Delay	Stage	Age group	Race group	Year group	County
7	1	1	2	3	96
35	3	8	1	1	3
0	2	3	1	8	115
⋮	⋮	⋮	⋮	⋮	⋮

Figure 1: Treatment Delay Distribution (truncated at 365 days)



Methods: Models

A Bayesian Hurdle Poisson regression framework was used to model treatment delay. The first part is a Logistic regression to determine if the delay is zero. If it is not zero, a zero-truncated Poisson regression will be used:

The likelihood: Hurdle Poisson (HP) model:

$$\begin{aligned} L(y_i|p_i,\lambda_i) &= p_i \times 1_{[y_i=0]} + (1-p_i) \times \text{Poisson}(y_i|\lambda_i, y_i>0) \\ &= p_i \times 1_{[y_i=0]} + (1-p_i) \times \frac{\lambda_i^{y_i}}{(e_i^{\lambda}-1)y_i!} \times 1_{[y_i>0]} \end{aligned}$$

where

- y_i: delayed days for patient i;
- p_i: probability for patient i to have 0 delay;
- λ_i: parameter of Zero Truncated Poisson distribution for patient i;

Regression model:
Logistic regression for p_i:

$$\eta_i^{(0)} = \log(\frac{p_i}{1-p_i}) = \alpha^{(0)} + \beta_{r_i}^{(0)} + \omega_{s_i}^{(0)} + \theta_{a_i}^{(0)} + \xi_{c_i}^{(0)} + \gamma_{t_i}^{(0)} + \delta_{c_i t_i}^{(0)} + \epsilon_i^{(0)}$$

Poisson regression for λ_i:

$$\eta_i^{(1)} = \log(\lambda_i) = \alpha^{(1)} + \beta_{r_i}^{(1)} + \omega_{s_i}^{(1)} + \theta_{a_i}^{(1)} + \xi_{c_i}^{(1)} + \gamma_{t_i}^{(1)} + \delta_{c_i t_i}^{(1)} + \epsilon_i^{(1)},$$

- $\boldsymbol{\eta}^{(m)} = (\eta_1^{(m)}, ..., \eta_N^{(m)})'$ is the linear predictor: logit or log;
- $\alpha^{(m)}$ is the intercept;
- $\boldsymbol{\beta}^{(m)} = (\beta_1^{(m)}, \beta_2^{(m)})'$ is the race effect for whites and blacks;
- $\boldsymbol{\omega}^{(m)} = (\omega_1^{(m)}, ..., \omega_5^{(m)})'$ is the stage effect;
- $\boldsymbol{\theta}^{(m)} = (\theta_1^{(m)}, ..., \theta_{n_a}^{(m)})'$ is the age effect;
- $\boldsymbol{\xi}^{(m)} = (\xi_1^{(m)}, ..., \xi_K^{(m)})'$ is the spatial (county) effect;
- $\boldsymbol{\gamma}^{(m)} = (\gamma_1^{(m)}, ..., \gamma_T^{(m)})'$ is the temporal (year at diagnosis) effect;
- $\boldsymbol{\delta}^{(m)} = (\delta_{11}^{(m)}, ..., \delta_{K1}^{(m)}, ..., \delta_{1T}^{(m)}, ..., \delta_{KT}^{(m)})'$ is spatio-temporal interaction effect;
- $\boldsymbol{\epsilon}^{(m)} = (\epsilon_1^{(m)}, ..., \epsilon_N^{(m)})'$ is the patient-specific error term.

Priors:

- Normal distributions with mean zero and large variance were used for fixed effects $\alpha^{(m)}$, $\boldsymbol{\beta}^{(m)}$ and $\boldsymbol{\omega}^{(m)}$;
- $\boldsymbol{\theta}^{(m)} = (\theta_1^{(m)}, ..., \theta_{n_a}^{(m)})'$ is age effect;
- Intrinsic conditional autoregressive priors was used for spatial effect $\boldsymbol{\xi}^{(m)}$ to account for correlations among neighboring counties, for the temporal $\boldsymbol{\gamma}^{(m)}$ and the age $\boldsymbol{\theta}^{(m)}$ effect to account for nonlinearity and for the interaction effect $\boldsymbol{\delta}^{(m)}$ to account for correlations in space and time;

Hyper Priors:

- Penalized-complexity priors were used for remaining hyper parameters.

Results: Race and Stage Effects

Figure 2: Logistic Race

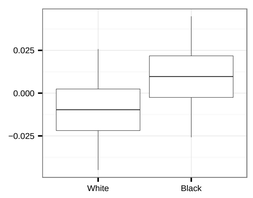


Figure 3: Poisson Race

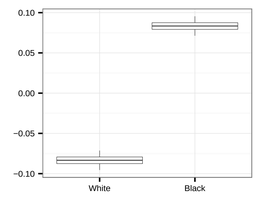


Figure 4: Logistic Stage

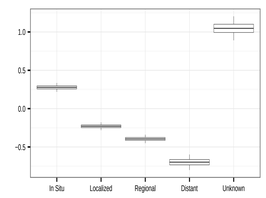
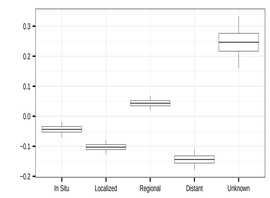


Figure 5: Poisson Stage



Results: Age and Temporal Effects

Figure 6: Logistic Age

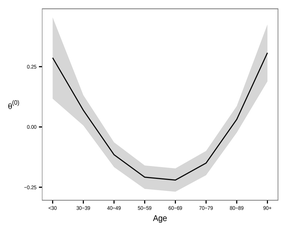


Figure 7: Poisson Age

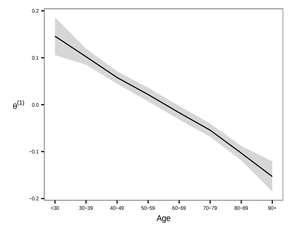


Figure 8: Logistic Year

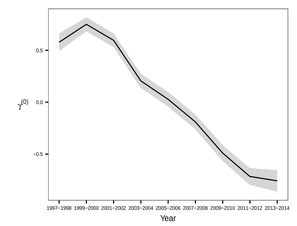
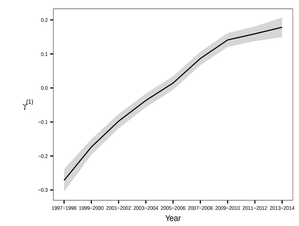


Figure 9: Poisson Year



Results: Spatial Main Effects

Figure 10: Logistic

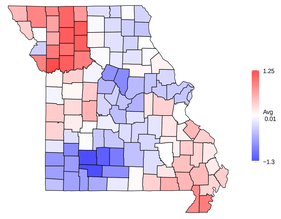
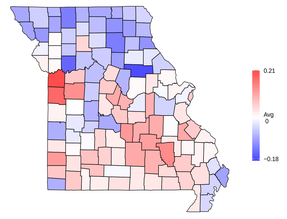


Figure 11: Poisson



Results: Space-time Interaction

Figure 12: Logistic

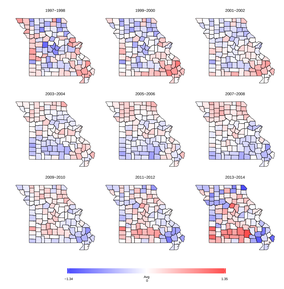
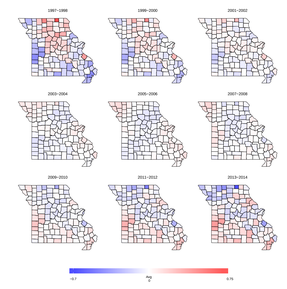


Figure 13: Poisson



Prediction: White, 60–69, Localized

Figure 14: Predicted Probability of Zero Delay

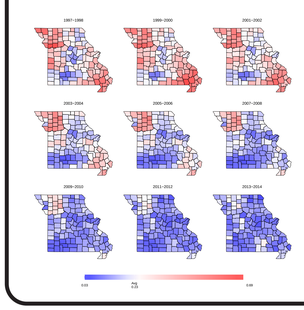
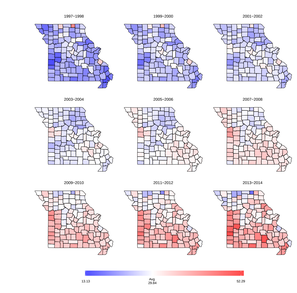


Figure 15: Predicted Delayed Days if Non-zero



Conclusion

- The probability of having a treatment delay of zero days decreased over time and had a "U" shape relationship with age.
- The mean days of non-zero delay increased over time and decreased with age.
- The spatial patterns changed over time for both quantities.
- Differences existed among race and cancer stages as well.

Discussion

- Reasons for zero treatment delay should be investigated.
- Definition of the date of first surgery has been changed over time. The accuracy of calculated delayed days should be evaluated.

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