Quantifying Racial/Ethnic Disparities in Kidney Graft Failure Rates Using US Registry Data with Federated Learning Algorithms

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Background

Kidney transplantation is a vital renal replacement therapy for patients with end-stage renal disease (ESRD). Disparities exist in access to and outcomes of kidney transplants for different racial and ethnic groups. Non-Hispanic Black (NHB) patients are less likely to receive kidney transplants and experience longer waiting times compared to Non-Hispanic White (NHW) patients.[1–4]. Moreover, when NHB patients do undergo transplants, their graft survival rates are lower than those of NHW patients[3,5–7].

There is a critical need to understand and assess if the disparities are associated with site of care. A conventional way to understand this racial/ethnic disparity is to compare graft failure rates for NHB and NHW patients, statistically adjusting for patient-level characteristics, such as various demographic and clinical factors. However, such an analysis would not reflect the possible contribution of the site of care. Counterfactual modeling can be used to study the potential association between the site of care and racial/ethnic disparity with multi-site data[8]. For example, a study by Asch, et al. (2020)[9] explored racial/ethnic disparities for patients hospitalized with COVID-19 infection. In this study, a generalized linear mixed model (GLMM) in modeling the patient-level and hospital-level characteristics simultaneously, was fit on *centralized* multi-site data to characterize the restricted mean survival time (RMST) with adjustments for other characteristics.

However, in large-scale multi-stakeholder international initiatives like the Observational Health Data Sciences and Informatics (OHDSI), a challenge arises due to the distributed nature of individual-level data within various centers across multiple countries. This decentralization prevents the sharing of data across different centers, creating a barrier to fitting the GLMM using pooled data from all the sites.

This abstract introduces a federated learning algorithm framework called dGEM-t2e-disparity, (decentralized algorithm with time-to-event outcomes for GLMM for disparity quantification). We aim to address three major challenges: barrier in sharing patient-level data, assessment of site-of-care-associated disparities, and consideration of time-to-event outcome. In particular, the framework consists of two modules. The first module, dGEM-t2e, fits GLMM given the decentralized multi-site data adjusting for patient-level characteristics (e.g., age, gender, race, etc). This first module is a *few-shot* algorithm that requires only aggregated data without sharing the patient-level data, which is a significant feature beneficial to the collaborative international studies. The second (disparity) module utilizes the estimated effects from Module 1 to calculate counterfactual restricted mean survival time and assess site-associated racial/ethnic disparities.

Methods

We used the counterfactual model to simulate the outcome for a patient from a certain transplant center as if the patient had been admitted to another center. The NHW and NHB patients went to the same transplant centers in general, but in different distributions. We simulated the outcomes under the assumption that Black patients received their care in transplant centers in the same distribution as White patients received their care, thereby teasing apart the racial/ethnic disparity associated with the site of care. The hypothesis is that the counterfactual graft failure rates would be lower than the observed graft failure rates for the Black patients if site-of-care-associated racial/ethnic disparities exist for Black patients receiving kidney transplants. To answer the question, we proposed a federated learning algorithm called dGEM-t2e-disparity.

The main steps of the dGEM-t2e-disparity for the counterfactual model are:

1. Federated convert the time-to-event outcomes into GLMM-format.
2. Fit decentralized algorithm for the GLMM to obtain the hospital-specific effects.
3. At each collaborative site, calculate the counterfactual mean survival time for each NHB patient by assigning a new hospital for each NHB patient.
4. Obtain the overall counterfactual survival time for NHB patients. We then estimated the difference between the observed mean survival time and the counterfactual mean survival time (prolonged survival time).

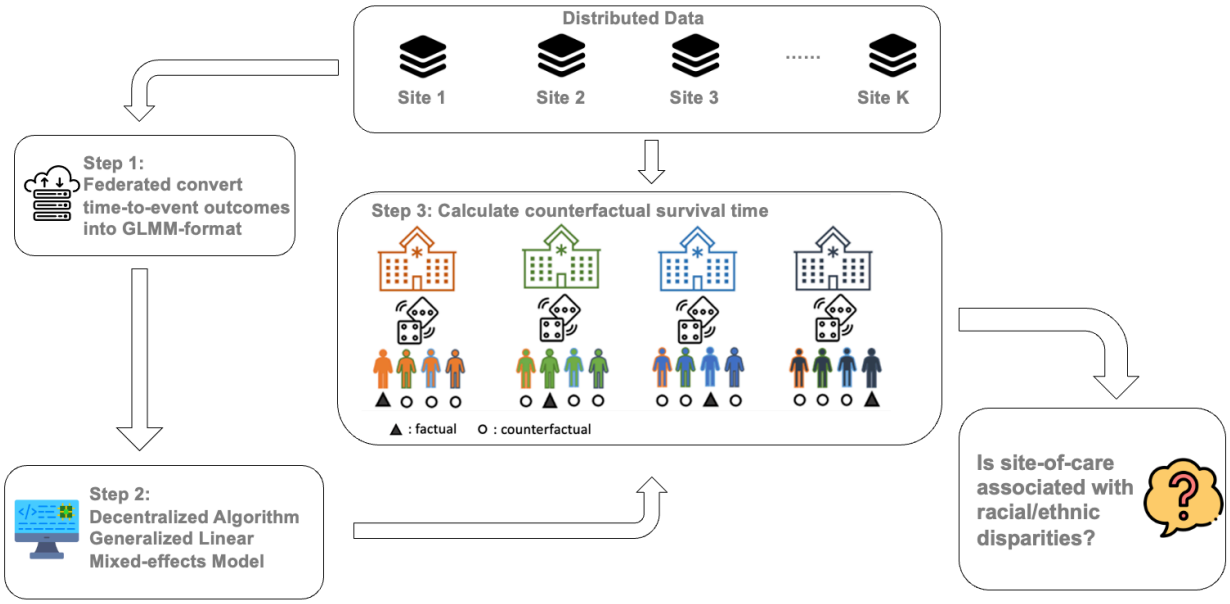

Figure 1. Schematic illustration of the dGEM-t2e-disparity. The Step 1 is to federated convert the time-to-event outcomes into GLMM-format. The Step 2 is to fit the GLMM in a distributed manner. The Step 3 is to obtain the counterfactual survival time and the last step is to compare the counterfactual survival time with the observed survival time.

Results

We first assessed the performance of the dGEM algorithm. In this process, we created a simulated centralized dataset, applied the dGEM algorithm and the GLMM algorithm to the pooled data. The results from the GLMM algorithm can be seen as the gold standard results. However, the GLMM can not be implemented in the decentralized dataset. As shown in the **Figure 2**, the outcomes obtained from the

dGEM algorithm exhibited an identical level of performance when compared to the GLMM algorithm.

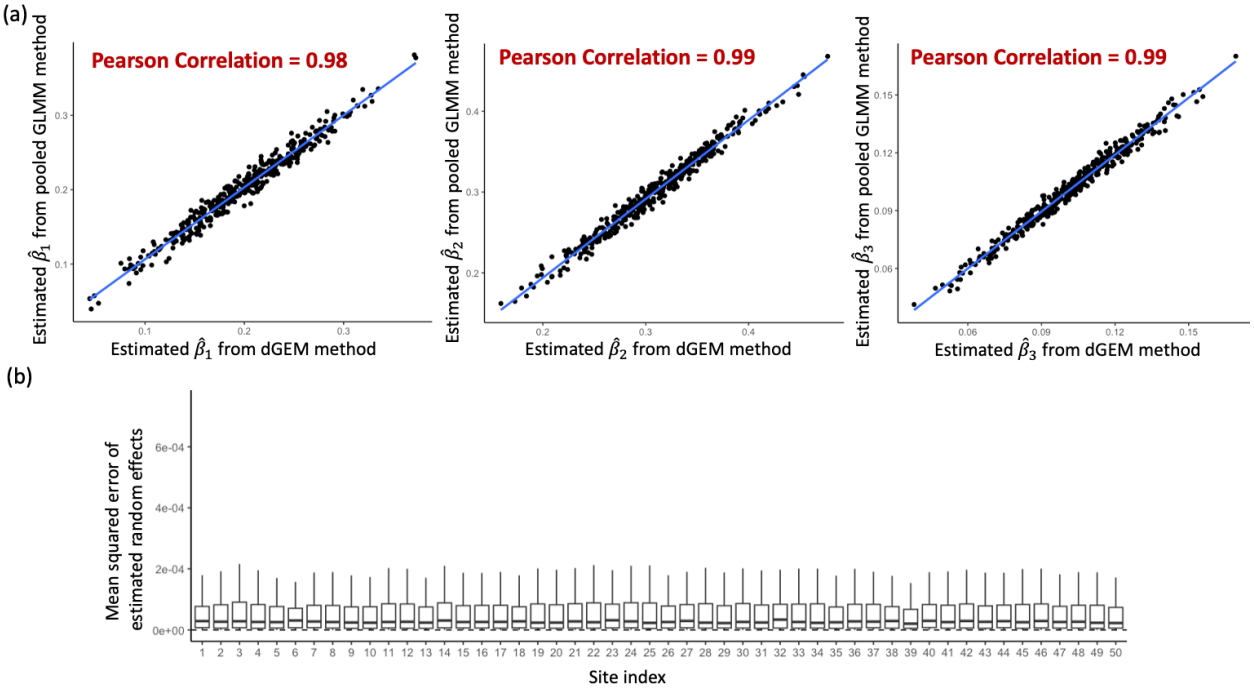

Figure 2. The performance of the dGEM algorithm.

We analyzed a dataset that included 39,043 adult kidney transplant recipients from 73 transplant centers who underwent transplantation between January 1, 2009, and December 31, 2018. Of these patients, 16,688 were Non-Hispanic Black (NHB) (42.7%), and 22,355 were Non-Hispanic White (NHW) (57.3%).

As shown in **Figure 3**, the percentages of the admitted NHB and NHW patients varied across these centers. The centers with the highest proportion of Non-Hispanic Black patients (Quintile 5) had a percentage of >72.0%, while those with the lowest proportion of Non-Hispanic Black patients (Quintile 1) had a percentage of <14.0%, indicating that NHB and NHW patients are distributed differently across centers. This distribution of patients across centers underscores the need to investigate the potential impact of site of care on disparities in kidney transplant outcomes for different racial/ethnic groups.

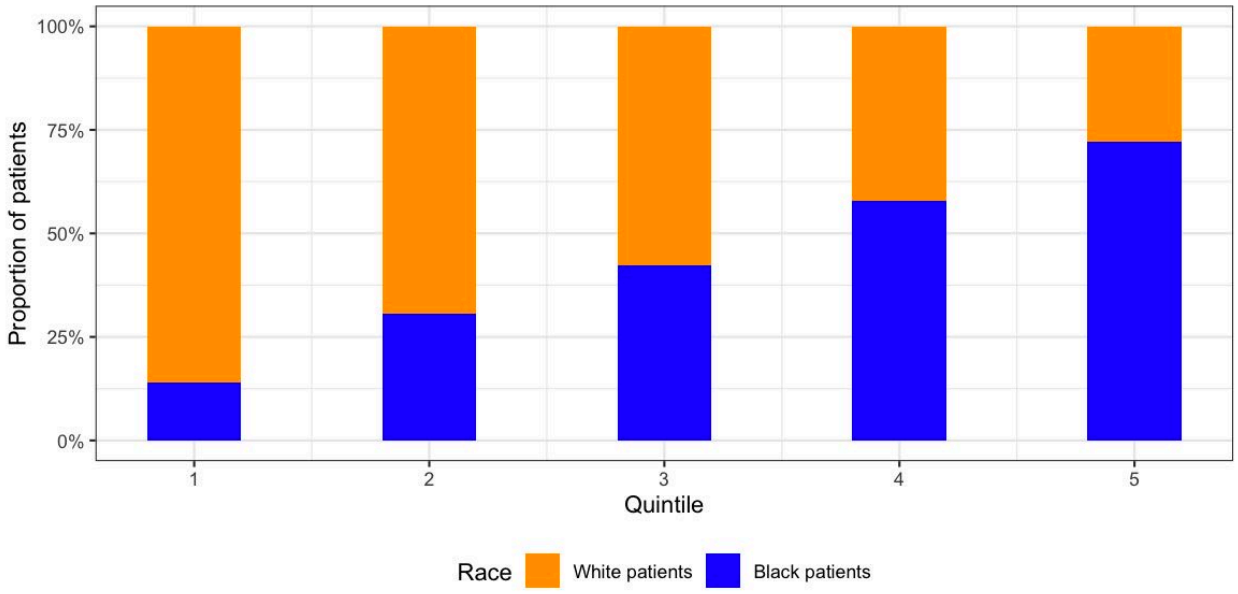

Figure 3. The proportion of the NHB and NHW patients across five quintiles of 73 centers. NHB: Non-Hispanic Black; NHW: Non-Hispanic White.

As shown in **Figure 4**, the dGEM-t2e-disparity analysis revealed that NHB patients experienced a prolonged lifetime of 0.05 days over a 120-day period. However, when the total time was restricted to 240 days, the extended lifespan for black patients increased to 0.13 days. Furthermore, if we assume an observation period of one year, NHB patients demonstrated a prolonged lifetime of 0.24 days.

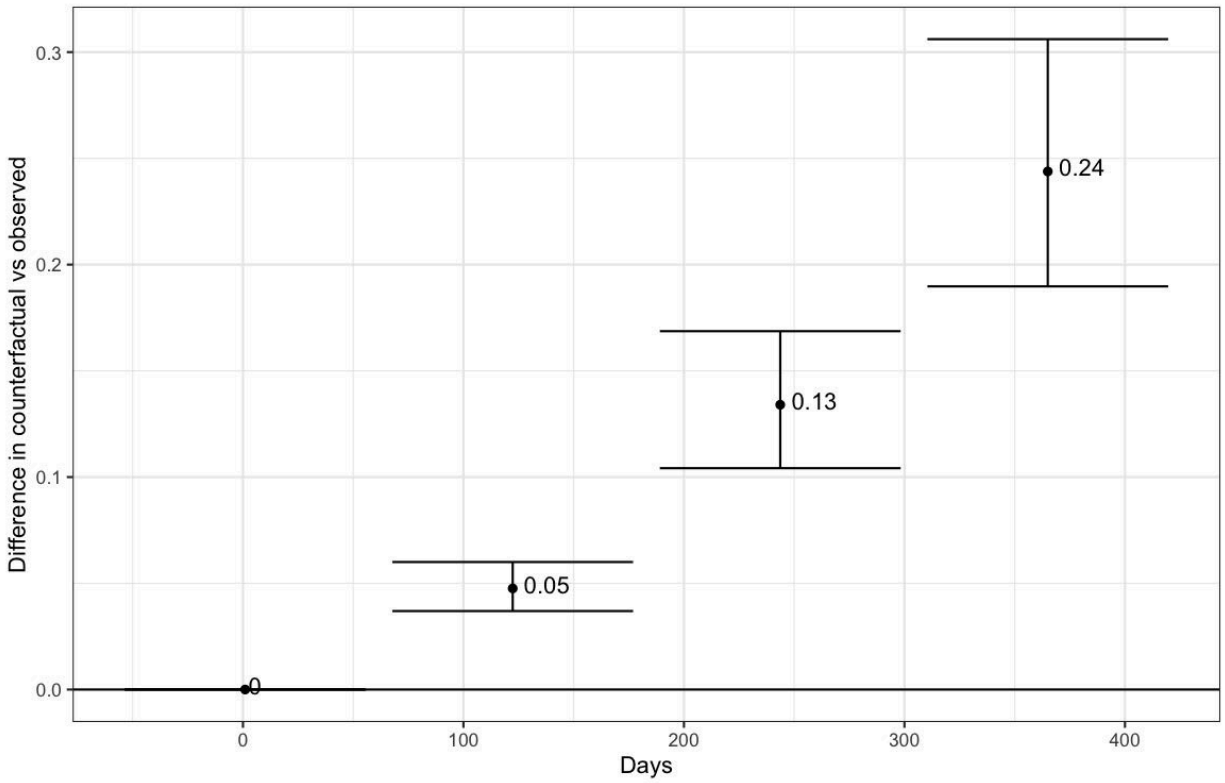

Figure 4. The difference in the counterfactual mean survival time vs observed mean survival time with the restricted time points 120 days, 240 days, and 365 days. The number indicates the value of the difference. The error bars indicate the 95% confidence interval after the bootstrap of the variance estimation.

Conclusion

We proposed the dGEM-t2e-disparity algorithm to answer whether the site-of-care is associated with the racial/ethnic disparities. This algorithm can incorporate the time-to-events outcomes by converting into the count outcomes. We believe that dGEM-t2e-disparity is a significant contribution to this new generation of distributed research networks. We found that racial/ethnic disparities associated with site-of-care in the 73 centers for the kidney transplant. We are planning to apply our algorithm to the OHDSI framework to quantify disparities such as race/ethnicity or gender.

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