5-2022

The Use of a Mobile Application and Text Messaging Platform to Improve Adherence to Medications in Solid Organ Transplant Patients

Lindsay M. Bruce
University of Nebraska Medical Center

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Lindsay Bruce, PharmD; MPH Candidate 2022 (Public Health Administration and Policy)

Committee Information

Committee Chair: Hongmei Wang, PhD

Member 2: Jianghu Dong, PhD

Member 3: Donald Klepser, PhD, MBA

Abstract

Poor adherence to medication regimens is responsible for 30-70% of all medication-related hospital admission in the United States and can be calculated to cost approximately $100 billion per year (Burra et al., 2011). The purpose of this pre-post cohort analysis is to measure the impact of using a mobile phone application and text messaging service on the medication possession ratio (MPR), a measure of adherence, among solid organ transplant patients who fill at Nebraska Medicine Outpatient Pharmacy. These interventions make it more convenient for patients to request refills, for pharmacy staff to send push notifications, and automatic refill and/or pickup reminders to be generated. Higher medication adherence rates to immunosuppressive agents, along with all other medications, promote better long-term outcomes such as: longevity of transplanted organ and prevention of adverse events. I hypothesize a positive association between the use of a mobile phone application and/or text messaging service and the MPR. 59 patients were identified in pharmacy software, McKesson, that had voluntarily used the mobile phone application and/or text messaging service prior to 6/12/2020. Each patient's MPR was manually derived for one year before intervention (6/12/2019-6/11/2020) and

one year after intervention (6/12/2020-6/12/2021). MPR is the sum of the days' supply for all fills of a given drug in a particular time period, divided by the number of days in the time period (1 year). The sample characteristics were examined and reported in terms of type of transplant, sex, race, and age. Then t-tests were conducted to examine if MPR is associated with age, sex, race, or type of transplant at baseline, one-year pre-intervention, and one-year post-intervention. Then, a multiple linear regression was run to examine if there were significant change in patient MPR over the two years after controlling age, sex, race, and type of transplant in the model. The results of the two-tailed, paired t-test comparing the average MPR in year 2020-2021 to that of year 2019-2020 returned a p-value of 0.31, indicating no statistically significant differences between these two years. This result does not support our hypothesis that the use of a mobile phone application and/or text messaging service will increase the MPR of solid organ transplant patients. In conclusion, analyzing the effect of the same intervention on a larger patient population with a lower baseline MPR, such as diabetic patients, would be more powerful using the same pre-post study design.

Introduction

Specific Aims or Problem Statement:

The specific aims of this project are to analyze if the implementation of text messaging and/or mobile phone application is increasing the MPR in solid organ transplant recipients that fill their immunosuppressant medications at the Nebraska Medicine Outpatient Pharmacy. The analysis of this project will be used to present information to the Transplant Pharmacists at Nebraska Medicine to show the interventions that our pharmacy can provide on increasing medication adherence to immunosuppressant regimens. Patient safety and positive patient outcomes are at the forefront of this project and healthcare in general. Medication adherence

promotes graft function, prevents graft rejection, prevents hospital admissions and decreases financial burden on the healthcare industry as a whole.

Significance:

Adherence is a crucial component of transplant patients' therapeutic regimen. According to Adherence to Long-Term Therapies: Evidence for Action, adherence "refers to the extent to which a person's behavior—taking medication, following a diet, and or executing lifestyle changes, corresponds with the agreed recommendations from a health care provider (Sabate, 2003)." Immunosuppression nonadherence carries a risk of graft rejection and potential graft loss. Poor adherence to medication regimens is responsible for 30-70% of all medication-related hospital admission in the United States and can be calculated to cost approximately $100 billion per year (Burra et al., 2011).

More than 165,000 apps designed for smartphones are related to health, and 1 in 5 people have downloaded a mobile health app (Perez-Jover et. al, 2019). Among those subsets of downloaded mobile health apps, many help patients manage their chronic disease states and their medication management. For example, reminding users to take medications and providing tools on how to be adherent. Other than medication administration reminders, these apps can provide refill reminders, doses can be logged, data logs that can be accessed by patients or uploaded to care providers, and readily available medication information.

Background and Literature Review

Background on Mobile Phone Application:

Patients could voluntarily opt-in to the text message service prior to 6/12/2020, however, after this date patients were pre-enrolled and a link with directions was sent via text message on how to download the mobile application if a cell phone number was uploaded in McKesson

pharmacy software. Patients can download the mobile application in the following ways: (1) text "APP" to 54053, (2) search "Nebraska Medicine Pharmacy" in the iPhone App Store or Google Play Store, (3) using the website https://nebraskamed.medrefill/nmweb[nebraskamed.medrefill.com, patients can enter their cell phone number in the "get a text to download our mobile app" section, and (4) by scanning the QR Code on print materials at Point-of-Sale. Setting up an account on the mobile application allows the patient to fully manage their text message preferences. Additionally, patients can see all their prescriptions in one place and refill them by scanning their prescription or choosing from the list provided in the application. Reminders can be set to both refill medications and take medications. The mobile application and web portals allow patients to manage prescriptions on behalf of their family members. Downloading the mobile application gives patient access to print an expense report of their full prescription history at their convenience.

Real time text messages to patients are critical to maintain adherence. All of the text messages will include contact information for the pharmacy if they have any additional questions and/or concerns. If a patient chooses to sign up to receive text messages, they will be notified during the following points in the prescription process: (1) when their prescription is due to be refilled (patients have the ability to reply back and request their refill to be processed), (2) when their prescription is ready (including the copayment amount due), (3) when their prescription has been shipped to them (including the tracking number), (4) a reminder that their prescription is at the pharmacy waiting to be picked up, (5) a reminder when their prescription has not yet been picked up and will soon be returned to sock. In addition to the automated messages, pharmacy staff has the ability to send push text messages in specific circumstances to make it easier to communicate with patients. Some examples of messages include: (1) fill on arrival—medication

delay (we are ordering the medication and will notify the patient when it is ready for pick up the following business day), (2) prior authorization needed (the medication requires additional insurance review/approval), (3) insurance issue (insurance on file expired, need new insurance information to process prescription), (4) prescriber denial (prescriber denied refill request; patient needs to contact provider), (5) prescription clarification (prescriber clarification needed on prescription), (6) refill too soon (prescription is too soon to fill), (7) contact Specialty Pharmacy (please contact Specialty Pharmacy at (402) 559-2484 to schedule your next refill), (8) more information needed for medication assistance application, and (9) payment information on file needs updated.

Literature Review:

In *Mobile Health Medication Adherence and Blood Pressure Control in Renal Transplant Recipients*, this study assessed a prototype mobile health medication and blood pressure self-management system for kidney transplant patients with uncontrolled hypertension (McGillicuddy et. al, 2013). This study used an electronic medication tray on a mobile phone application and received push notifications to remind them to take their various medications at the varying times of the day. Participation and retention rates were 75% and 91%, respectively (McGillicuddy et. al, 2013). The problems with the study were the small sample size (20 patients) and short time frame (3 months) and did not have any statistical measures of the effect on medication adherence. My capstone project will provide a larger sample size, a longer time frame, and using statistical measures to quantify using a mobile phone application and/or text messaging service on medication adherence in solid organ transplant patients.

In *Assessing Medication Adherence in Solid-Organ Transplant Recipients*, this cross-sectional, single-center, retrospective cohort study evaluated 225 lung, kidney, and liver

transplant recipients' adherence to immunosuppressant mediation based on dosages and dispensing records using MPR and gaps in prescription refills (>30-day lapse between expected depletion of supply and next refill) in assessing adherence for 2 years (Chun-Wei Su, 2013). Overall, MPR was 95.4%, 95.9%, and 92.7% in lung, kidney, and liver recipients' (Chun-Wei Su, 2013). Only 7.1% of patients had a MPR lower than 80%, which was the cutoff for nonadherence (Chun-Wei Su, 2013). Statistical analyses were not performed for factors of nonadherence due to the small percentage of nonadherent patients. The problem with this study was no statistical analysis was completed on population characteristics: age, gender, race, and type of transplant. My capstone project with include statistical analysis of population characteristics: age, gender, race, and type of transplant at baseline and 1-year post-intervention in the form of average MPR, paired t-test, and multiple linear regression.

Data & Methods

A group of 82 patients that were voluntarily enrolled in the mobile phone application/text messaging service before 6/12/2020 were identified via a report within the pharmacy software, McKesson. Further analysis excluded two patients that were recently deceased, five pediatric patients (< 19-years-old), and two bone marrow transplant patients. Pediatric patients were excluded because a parent or guardian must still be involved in their healthcare which could contribute to their medication adherence. Another 14 patients were excluded during initial data analysis due to insufficient data due to switching pharmacies due to personal preference or insurance requirements. With the above exclusions, the final study population included 59 patients. I built a custom Microsoft Excel report to include, medical record number, gender, race, age, and type of transplant (lung, liver, heart, kidney, or combination). Next, I used Microsoft Excel to enter each patient's average individual MPR for immunosuppressant therapy (from

McKesson patient profile data that was manually extracted) one year prior to text messaging or mobile phone application intervention (6/12/2019-6/11/2020) and comparing that to their average MPR 1 year post intervention (6/12/2020-6/11/2021). In this way, each patient acts as their own comparator.

The MPR is the sum of the days' supply for all fills of a given drug in a particular time period, divided by the number of days in the time period (1 year). 2020 was a leap year, which was accounted for in my calculations, by using 366 days as my denominator in the MPR calculation (instead of 365 in a normal year). In a patient that is perfectly adherent to medication therapy, the MPR would equal 100% or 1:1. MPR may be skewed if the patient is obtaining medications earlier than needed which will make the ratio greater than 100%; in this study, the cap was at 100% so it doesn't skew other calculations such as further analysis based on demographic information or transplant type.

The sample characteristics were examined and reported in terms of type of transplant, sex, race, and age. Then t-tests were conducted to examine if MPR is associated with age, sex, race, or type of transplant at baseline. Paired t-tests were conducted to examine differences in MPR in the whole study sample and stratified samples by age, sex, race, and type of transplant pre- and post- the intervention. In the end, a multiple linear regression was run to examine if there were significant change in patient MPR over the two years after controlling age, sex, race, and type of transplant in the model.

Results (See Appendix for Data Tables)

As shown in Table 1, my study population consisted primarily of kidney transplants (80%), male gender (63%), white race (59%), and a close split of 40-59 year-olds (42%) and 60-79 year-

olds (44%). Heart and combination transplants comprised each 7% of the study population. While lung and liver transplants accounted for each 3% of the study population.

Table 2 shows group differences in MPR for 2019-2020 at baseline. The results showed that lung and combination transplant patients had a higher level of MPR compared to patients with other types of transplants (0.96 vs. 0.87, p=0.003) at baseline. Ages 20-59 had a higher level of MPR compared to patients ages 60-0.99 (0.85 vs. 0.91, p=0.03) at baseline. There were no statistically significant differences between patients with kidney transplants and patients with other solid organ transplant types (0.87 vs.0.91, p=0.28), female patients and male patients (0.90 vs. 0.87, p=0.47), and white and other races (0.89 vs. 0.86, p=0.31).

Table 3 shows the study population by average MPR in 2019-2020 and 2020-2021, difference in MPR in two years, and p-value for the paired t-tests comparing the difference in MPR for the whole sample and by different groups over time. The average MPR for all 59 study participants were 0.88 in year 2019-2020 and 0.86 in year 2020-2021. The results of the two-tailed, paired t-test comparing the average MPR in year 2020-2021 to that of year 2019-2020 returned a p-value of 0.31, indicating no statistically significant differences between these two years. This result does not support our hypothesis that the use of a mobile phone application and/or text messaging service will increase the MPR of solid organ transplant patients. Pre-post comparison was also conducted for different groups by transplant type, age, sex, and race. There were no statistically significant differences in MPR between the two years for any of the groups tested. For lung and combination transplant patients the average MPR was 0.96 in 2019-2020 and 0.88 in 2020-2021, the differences were not statistically significant (change= -0.08, p=0.24). Patient with other types of transplants showed an average MPR of 0.87 for 2019-2020 and 0.86 for 2020-2021, the differences were not statistically significant (change= -0.01, p=0.56). Patients

of the white race had an average MPR of 0.89 in 2019-2020 and 0.89 and 2020-2021, however, the differences were not statistically significant (change=0, p=0.68). Patients of other races had an average MPR of 0.86 for 2019-2020 and 0.83 for 2020-2021, however, the differences were not statistically significant (change= -0.03, p=0.34). For female patients, the average MPR was 0.90 for 2019-2020 and 0.87 for 2020-2021, the differences were not statistically significant (change= -0.03, p=0.21). For male patients, the average MPR was 0.87 for 2019-2020 and 0.86 for 2020-2021, the differences were not statistically significant (change= -0.01, p=0.73). For patients aged 60-99 years-old, the average MPR was 0.91 in year 2019-2020 and 0.93 in year 2020-2021, however, the differences were not statistically significant (change=0.02, p=0.53). 20-59 years-old patients the average MPR was 0.85 in year 2019-2020 and 0.81 in 2020-2021, however, the differences were not statistically significant (change= -0.04, p=0.14).

The results of linear regression analysis are to test the year differences after controlling age, sex, race, and types of transplant are shown in Table 4. The outcome variable is the level of MPR for all participants. Type of transplant was categorized in two groups: other transplants vs. lung & combination (reference group). Race was categorized in two groups: other vs. white (reference group). Sex was categorized in two groups: male and female (reference group). Age was categorized in two groups: age 20-59 (reference group) vs. 60-99 years-old. No statistically significant association was found between year and MPR (coefficient= -0.02, p=0.52) after controlling for transplant type, race, sex, and age. The result does not support our hypothesis that the use of a mobile phone application and/or text messaging service will increase the MPR of solid organ transplant patients. There was a statistically significant difference for the age covariable (coefficient=0.091, p=0.0009). The average MPR for patients aged 60-99 years was 0.091 higher compared to patients aged 20-59 years after controlling for other variables in the

model. There was no statistically significant association and type of transplant (lung and combination vs. other transplants) (coefficient=0.05, p=0.16), race (coefficient= -0.05, p-value=0.10), or sex (coefficient= -0.02, p-value=0.51) over the two years.

Discussion

The results of this study did not support my hypothesis of an overall positive association between the use of a mobile phone application and/or text messaging service and the MPR. This could be due to the following limitations of MPR: MPR does not accurately measure medication adherence to the extent that the patient is actually taking the medication as directed, it does assess whether the patient has access to the drug to take as directed by the physician. In a patient that is perfectly adherent to medication therapy, the MPR would equal 100% or 1. However, a threshold of ≥0.80 is conventionally used to indicate optimal adherence (Tang et. al, 2017). In this study, the average MPR in both years and for all categories was ≥0.80. It could be argued that transplant patients should have a higher baseline MPR than other patients due to the continued education they receive from medical providers about the importance of medication adherence to immunosuppressant medications and the survival of their graft. Additionally, it would have been interesting to analyze as an additional covariable how much time has passed since transplantation for each patient. Theoretically, a patient may be more adherent to medication therapy immediately after transplantation due to more frequent office visits and lab draws for immunosuppressant levels for dose adjustments. This study was also conducted in the midst of the COVID-19 pandemic, and the effect this had is unknown, but should be acknowledged. In conclusion, analyzing the effect of the same intervention on a larger patient population with a lower baseline MPR, such as diabetic patients, would be more powerful using the same pre-post study design.

Group differences at baseline MPR indicated a statistically significant finding in both lung & combo transplants when compared to other transplants and age 20-59 when compared to age 60-99. However, the sample size of lung & combo transplants was small at just 6 participants. In practice, lung and combination transplants are less frequently conducted, on average, compared to kidney transplants; for example, so a larger sample size of these specific transplant types would be hard to achieve when compared with other types of transplants. A multiple linear regression analysis results did find a statistical difference between patient MPR and age even after controlling for sex, race, year, and transplant types. Patients in 60-99 age group may have better adherence due to more extensive screening for medical clearance prior to transplant listing due to higher risk for surgery or closer post-transplant follow-up, potentially better health literacy and health habits, and more family/home health worker involvement in older adults post-transplant.

The strengths of this study included: length of study (2 years) and using statistical measures to quantify medication adherence (MPR). When compared to *Mobile Health Medication Adherence and Blood Pressure Control in Renal Transplant Recipients* consisted of 20 patients, a 3-month time period, and no statistical measures to quantify medication adherence (McGillicuddy et. al, 2013). This prototype system studied by McGillicuddy et. al, of using push notifications on a mobile phone application to remind them to take their various medications at varying times of the day appeared to be safe, highly acceptable, and useful to patients and providers to promote medication adherence. When compared to *Assessing Medication Adherence in Solid-Organ Transplant Recipients*, the study population consisted of 225 patients, was 2 years in length, but did not do a quantitative analysis due to over 90% of patient population having an average MPR ≥ 0.80. My study limitations are a pre-post design, small sample size, and using Microsoft Excel for data analysis. Without a control group the true impact of these

interventions is not accurately captured by the pre-post comparison. The sample size of our study could still be too small to effectively detect the effect of the intervention on MPR of the patients studied. Finally, Microsoft Excel is difficult to use and less powerful when compared to SPSS for performing data analysis.

The results of this study continue to shed light on the complexity of medication adherence and the many factors that play into it. It is difficult to compare adherence rates of one patient to another without taking into account the various factors that may impact adherence such as: convenience (text messaging/mobile phone application), cost, environment, and health literacy to name a few. The best way to improve future studies on the impact of Nebraska Medicine Outpatient Pharmacy's Text Messaging/Mobile Phone Application is to increase patient enrollment by continuing to spread the word to not only patients with promotional materials, but also, enlist the help of other healthcare professionals (like Transplant Pharmacists) to promote the service and use this technology as a tool in their toolbelt to continue to improve medication adherence which my study ultimately did. In addition, a randomized controlled trial, conducting multiple regression to control for other factors of adherence (cost, socioeconomic status, and health literacy), and using SPSS statistical software for data analysis would be beneficial in future studies with a larger patient population to further assess the benefit of technology to promote medication adherence in solid organ transplant recipients.

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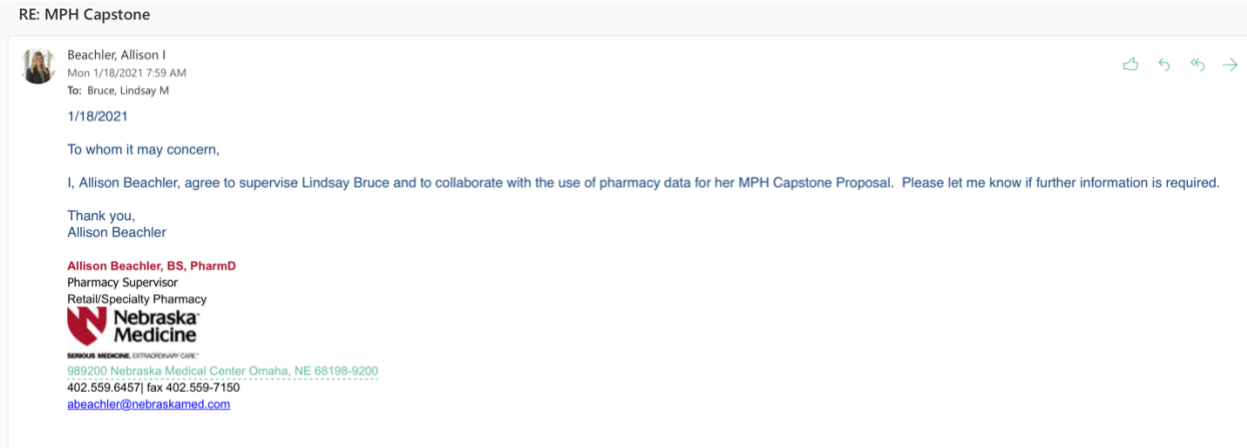
Application of Public Health Competencies:

1. MPHF3: Analyze quantitative and qualitative data using biostatistics, informatics, computer-based programming and software, as appropriate.
    i. My capstone incorporated the above foundational competency by analyzing data using the McKesson pharmacy software data to determine each patient's average MPR, paired t-test, and linear regression using Microsoft Excel before and after intervention of text messaging/mobile phone application.
2. HSRAMPH5: Examine information about health policy issues and problems, and evaluate alternative policy options for these issues.
    ii. My capstone incorporated the above concentration competency by drawing conclusions after analyzing the data on how to better utilize technology to improve medication adherence in solid organ transplant patients that fill their medications at the Nebraska Medicine Outpatient Pharmacy to get a larger patient population to study more accurately the impact this program is having by possibly doing a randomized controlled trial or calculating multiple regression analysis.
3. HSRAMPH1: Demonstrate the skills to analyze and resolve organizational issues through a multidisciplinary systems-based approach.
    iii. My capstone incorporated the above concentration competency by presenting information to the Transplant team pharmacists at Nebraska Medicine with the findings of my Capstone Project before the end of the Spring semester (before my presentation) to promote patients to use the Nebraska Medicine Outpatient Pharmacy for the filling of their

medications which includes a free mobile phone application/text messaging service. Additionally, in order to create the custom report within the pharmacy software, McKesson, to identify a specific subset of transplant patients that had downloaded the app and/or using the text messaging software and had voluntarily opted-in before 6/12/2020 I worked with a team with representatives from McKesson and IT, 340B Analysts, and Pharmacy Management at Nebraska Medicine. I tried to resolve the issue of medication nonadherence that increases healthcare expenditures to the organization, by showing a possible benefit of the new mobile phone application and/or text messaging service that the Nebraska Medicine Outpatient Pharmacy had recently implemented could increase medication adherence in a high-risk group of patients, solid organ transplant recipients.

Supervision and Facilities:

Allison Beachler—Pharmacist Lead at Nebraska Medicine Outpatient Pharmacy at Durham Outpatient Center; (402) 559-5215


RE: MPH Capstone

Beachler, Allison I
Mon 1/18/2021 7:59 AM
To: Bruce, Lindsay M

1/18/2021

To whom it may concern,

I, Allison Beachler, agree to supervise Lindsay Bruce and to collaborate with the use of pharmacy data for her MPH Capstone Proposal. Please let me know if further information is required.

Thank you,
Allison Beachler

Allison Beachler, BS, PharmD
Pharmacy Supervisor
Retail/Specialty Pharmacy
Nebraska Medicine
989200 Nebraska Medical Center Omaha, NE 68198-9200
402.559.6457| fax 402.559-7150
abeachler@nebraskamed.com

Human Subjects:

After consultation with UNMC IRB, my project is considered a Quality Improvement Project which does not require an application to the IRB, and I am allowed to publish my findings as well without approval.

Appendix

Table 1: Study Population Breakdown by Type of Transplant, Sex, Race, and Age for 59 Participants

Characteristics	N	Percent
Type of Transplant		
Heart	4	6.78
Lung	2	3.39
Liver	2	3.39
Kidney	47	79.66
Combination	2	6.78
Sex		
Female	22	37.29
Male	37	62.71
Race		
American Indian/Alaskan Native	3	5.08
Native Hawaiian or Other Pacific Islander	2	3.40
Black	13	22.03
Hispanic	5	8.48
Asian	1	1.69
White	35	59.32
Age		
20-39	7	11.86
40-59	25	42.38
60-79	26	44.07
80-99	1	1.69

Table 2: Group Differences at Baseline MPR (2019-2020)

Group	N	Average MPR	P-Value
Kidney Transplant	47	0.87	0.28
Other Solid Organ Transplant Types	12	0.91	
Lung & Combo Transplant	6	0.96	0.003
Other Transplant Types	53	0.87	
Female	22	0.90	0.47
Male	37	0.87	
White Race	35	0.89	0.31
Other Races	24	0.86	
Ages 20-59	32	0.85	0.03
Ages 60-99	27	0.91	

Table 3: Average MPR of the Study Participants and by Transplant Type, Race, Gender, Age Groups Over Two Years

	N	Average MPR in 2019-2020	Average MPR in 2020-2021	Difference in MPR	P-Value
Total Sample	59	0.88	0.86	-0.02	0.31
Type of Transplant					
Lung & Combo	6	0.96	0.88	-0.08	0.24
Other	53	0.87	0.86	-0.01	0.56
Race					
White	35	0.89	0.89	0	0.68
Other	24	0.86	0.83	-0.03	0.34
Sex					
Female	22	0.90	0.87	-0.03	0.21
Male	37	0.87	0.86	-0.01	0.73
Age					
20-59	32	0.85	0.81	-0.04	0.14
60-99	27	0.91	0.93	0.02	0.53

Table 4: Linear Regression of Average MPR for Years 2019-2020 & 2020-2021

Variable	Coefficient	P-Value
Type of Transplant (Lung & Combo vs. Other)	0.05	0.16
Race (White vs. Other)	-0.05	0.10
Sex (Female vs. Male)	-0.02	0.51
Age (20-59 vs. 60-99)	0.091	0.0009
Year (2019-2020 vs. 2020-2021)	-0.02	0.52