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Original Research Article

Measuring the effect of the COVID-19 pandemic on solid organ transplantation

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A R T I C L E I N F O

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A B S T R A C T

Background: The COVID-19 pandemic has uniquely affected the United States. We hypothesize that transplantation would be uniquely affected.

Methods: In this population-based cohort study, adult transplantation data were examined as time series data. Autoregressive-integrated-moving-average models of transplantation rates were developed using data from 1990 to 2019 to forecast the 2020 expected rates in a theoretical scenario if the pandemic did not occur to generate observed-to-expected (O/E) ratios.

Results: 32,594 transplants were expected in 2020, and only 30,566 occurred (O/E 0.94, CI 0.88–0.99). 58,152 waitlist registrations were expected and 50,241 occurred (O/E 0.86, CI 0.80–0.94). O/E ratios of transplants were kidney 0.92 (0.86–0.98), liver 0.96 (0.89–1.04), heart 1.05 (0.91–1.23), and lung 0.92 (0.82–1.04). O/E ratios of registrations were kidney 0.84 (0.77–0.93), liver 0.95 (0.86–1.06), heart 0.99 (0.85–1.18), and lung 0.80 (0.70–0.94).

Conclusions: The COVID-19 pandemic was associated with a significant deficit in transplantation. The impact was strongest in kidney transplantation and waitlist registration.

1. Introduction

The United States spends twice as much as other high-income countries on medical care[1] however, it was uniquely affected by the COVID-19 pandemic as it has just four percent of the world's population but a fifth of its confirmed cases and deaths.[2] Understanding this phenomenon requires exploring multiple facets of the healthcare system. Hospitals and facilities are rewarded by running close to capacity and do not receive incentives to invest in spare beds, hold a stockpile of supplies, or form contingency plans that make them inadequately prepared for a pandemic. The Pandemic Playbook,[3] which was drafted by the National Security Council under the Obama Biden administration, was never set into action during the pandemic.[4,5] The bulk of resources directed towards the healthcare system during the pandemic were directed towards inpatient care, despite only a fraction of individuals affected by the virus would require hospital care, while insufficient funds were directed towards preventing transmission in the community.[6] The personal protective equipment supply chains – many of which are based in the Hubei province – were directly affected by the pandemic, leaving many expecting assistance from national stockpile which was consumed at an unstainable rate. At the peak of the pandemic, four out of five frontline nurses did not have enough personal protective equipment.[7] Diagnostic tests were only widely available two months after the first COVID-19 infection detected in Washington state, providing a head start for the virus to disperse undetected. Lastly, the contingency plan in the face of an overrun healthcare system was to reenlist retired personnel, graduate medical and nursing students early, and relocate inexperienced personnel to areas of high acuity such emergency departments and intensive care units. While the valiant and courageous efforts of these healthcare workers will never be forgotten, having called upon them emphasizes the degree of duress that the SARS-CoV-2 virus inflicted on the United States.

Solid organ transplantation is a resource-intensive field that requires the highest level of care. A recent report estimated that the average

; ARIMA, autoregressive integrated moving averagemodel; CI, confidence intervals; O/E, observed to expected ratio.

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billed charges between 30 days before and 180 days after transplantation for each organ were as follows: kidney (USD $442,500), liver ($878,400), heart ($1,664,800), and lung ($929,600 to $1,295,900).[8] Additionally, transplantation recipients are much higher risk than the general population in terms of the pandemic. Recipients are at higher risk of developing critical illness from the virus,[9–11] graft dysfunction and rejection,[12,13] and overall have a grim prognosis once infected.[10,14,15] The virus is so devastating among recipients that the mortality of kidney transplant recipients who become infected is higher than the waitlist mortality of those who become infected while on renal replacement therapy.[16] We hypothesized that organ transplantation was uniquely affected during 2020 given the stress imposed on the healthcare system and vulnerability of immunosuppressed recipients to this virus.

2. Methods

This observational cohort study was based on a prospectively collected dataset of solid organ transplantations in the United States. The purpose of this study was to measure the variation between observed and expected rates of transplantation during the COVID-19 pandemic. To model the expected rates, data from 1990 to 2019 were utilized to forecast the expected number of transplants, donors, and waitlist registrations, if the 2020 pandemic did not occur. Granted proper confidence intervals, the theoretical difference between observed and expected rates may be attributed to the effects of the pandemic on the healthcare system.

2.1. Study data

The Organ Procurement and Transplantation Network provided the publicly available Standard Transplant Analysis Research files, which consist of prospectively collected data on all solid organ transplantations in the United States beginning in 1987. The Organ Procurement and Transplantation Network provided us with data on the condition that it would not be shared. We signed a written agreement accepting this condition; however, these data are available to investigators for purposes approved by this network. Individuals included in these files consent to their data being collected and made publicly available for research purposes. This study was approved by the Institutional Review Board of the University of Colorado.

2.2. Selection criteria

The study included adult (≥18 years) recipients, donors, and candidates for kidney, liver, heart, or lung transplantation in the United States between January 1, 1990 and December 31, 2020. Intestinal or pancreatic transplantations were not examined in the present study. Furthermore, individuals considered or who underwent repeat or multiple organ transplantations were excluded from the analysis.

2.3. Study endpoints

The main outcomes were observed to expected (O/E) ratios, which were calculated by the quotient between the number of actual events (i.e. transplants, donors, and waitlist registrations) during 2020 divided by the expected number of events obtained from forecasting models. Year- or month-level ratios were generated depending on the period examined. These ratios are reported with 95% confidence intervals.

2.4. Statistical analysis

Calculating the expected rates of transplantation, donation, and registration was not straightforward because the time series exhibited trends, seasonality, and changes over time. An autoregressive integrated moving average (ARIMA) model was fit to account for these features.

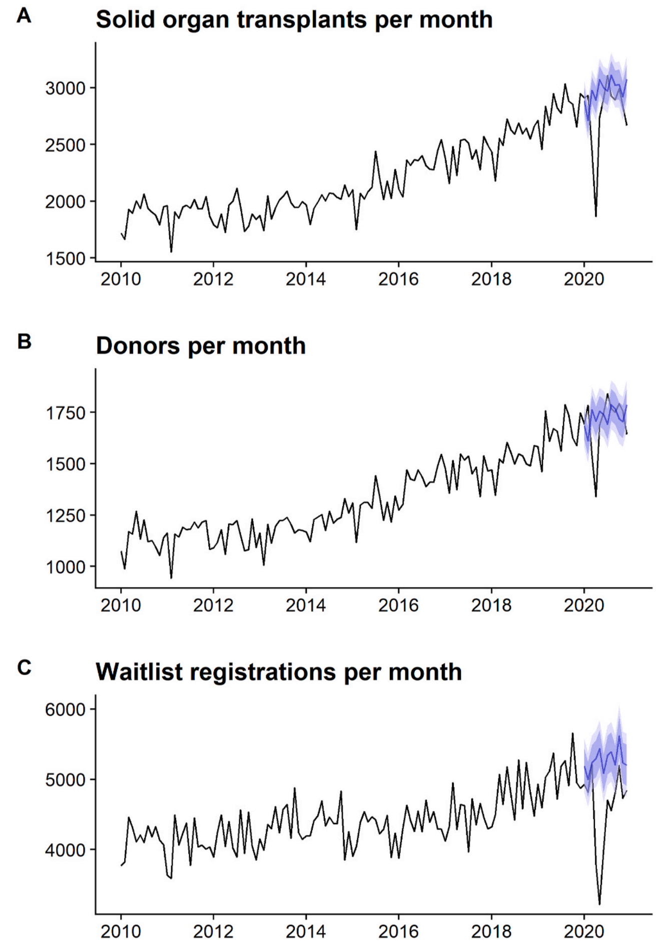

Fig. 1. Forecasts of organ transplants, donors, and waitlist registrations during the COVID-19 pandemic. Time series data of transplants, donors, and waitlist registration by month in the United States from January 1, 1990 to December 31, 2020 represented by the black line. Overlying forecast of expected organ transplants is represented by a blue line with 95% confidence intervals. Model parameters: [A] ARIMA (0,1,1) (2,0,0) with drift, [B] ARIMA (0,1,1) (2,0,0) with drift, and [C] ARIMA (2,1,2) (1,0,0) with drift. Abbreviations: CI, confidence intervals. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

Where conventional regression models estimate the outcome variable based on independent variables, ARIMA models estimate the outcome variable based on past values of the same variable. An ARIMA model takes the form of ARIMA (p,d,q) (P,D,Q). p and q represent the number of non-seasonal autoregressive and moving average terms, respectively. d represents the order of non-seasonal differencing. P, D, and Q represent analogues in the seasonal part of the model.

In brief, the number of predicted events (i.e. transplants, donors, and waitlist registrations) in each month is a function of the parameters denoted by p, q, P, and Q. p refers to the number of prior intervals for which the model considers events. q refers to the number of prior intervals for which the model considers measurement errors (i.e. the magnitude of the difference between the predicted and observed number of events). P and Q are analogues of p and q, but these refer to the seasonal components of the model. The autoregressive (p, P) and moving average (q, Q) components of the model directly update predictions about events by incorporating information on prior events. The model parameters were optimized using the Hyndman-Khandakar algorithm,[17] which selects the values of p and q by minimizing Akaike's information criterion and the maximum likelihood estimation. Hence, by the time the model switched from fitting mode (January 1990 through December 2019) to forecasting mode (January 2020 through December 2020), the

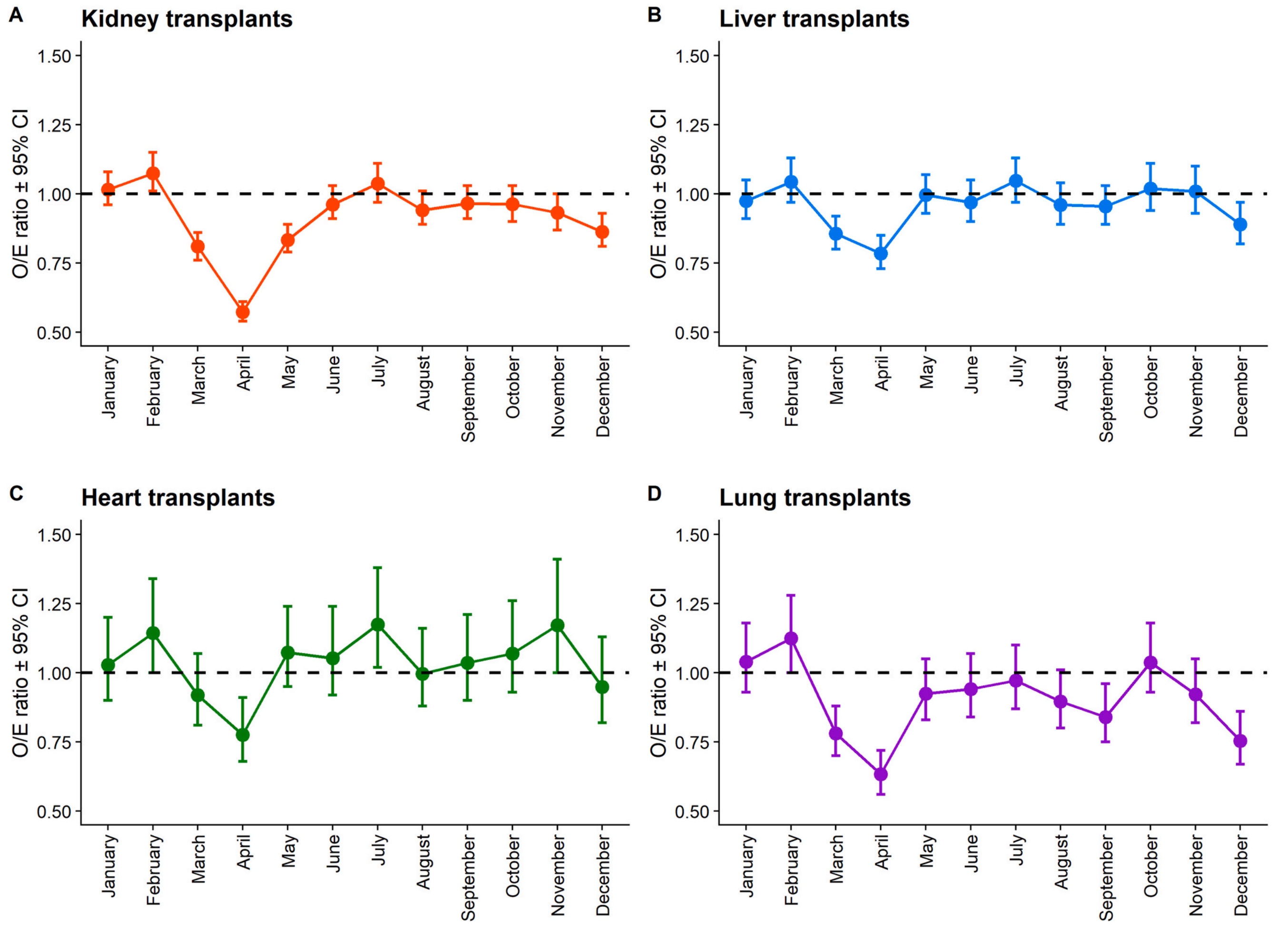

Fig. 2. Observed to expected ratio plots for organ transplantation during 2020 by organ. Expected number of transplants obtained from autoregressive integrated moving average forecasts for each organ by month based on data from 1990 to 2019. Abbreviations: CI, confidence intervals; O/E, observed to expected.

equation considers every fluctuation in transplantation rates that occurred since January 1990. This would include any signal attributable to other pandemics (such as SARS in 2003 or H1N1 in 2009), changes to allocation systems, and any other events that may affect transplantation. Analyses were performed using R version 3.5.3[18] with the forecast package.[19,20]

3. Results

3.1. Transplantation

A total of 32,594 solid organ transplants were expected in 2020, of which only 30,566 happened. This yields an O/E ratio of 0.94 (95% CI 0.88–1.99). The months with the lowest O/E ratios for number of transplants were March 0.82 (95% CI 0.78–0.88), April 0.65 (95% CI 0.61–0.69), and December 0.87 (95% CI 0.81–0.93) (Fig. 1A).

The observed number of kidney transplants fell below expected with an O/E ratio of 0.91 (0.86–0.98) for the year (Fig. 2). The months of March, April, May, and December fell below the 95% confidence interval of expected with ratios of 0.81, 0.57, 0.87, and 0.86, respectively. The yearly O/E ratios for liver 0.96 (95% CI 0.89–1.04), heart 1.03 (95% CI 0.90–1.21), and lung 0.91 (95% CI 0.81–1.03) did not fall below expected. However, each organ had statistically significant drops in transplantation during several months of the year (Fig. 2).

4. Donation

A total of 20,718 individuals were expected to donate in 2020, of which only 20,344 were available. This yields an O/E ratio of 0.98 (95% CI 0.92–1.05). The months with the lowest O/E ratios for donors were March 0.87 (95% CI 0.82–0.93), April 0.79 (95% CI 0.74–0.84), and December 0.92 (95% CI 0.86–0.99) (Fig. 1B). The months with the lowest O/E ratios for living donors were March 0.88 (95% CI 0.82–0.94), April 0.80 (95% CI 0.75–0.87), and December 0.91 (95% CI 0.85–0.99). The months with the lowest O/E ratios for deceased donors were March 0.87 (95% CI 0.82–0.93), April 0.77 (95% CI 0.72–0.82), and December 0.92 (95% CI 0.87–0.99) (Fig. 3).

4.1. Waitlist registration

A total of 63,217 candidates were expected to be registered in 2020, of which only 54,800 were registered. This yields an O/E ratio of 0.87 (95% CI 0.80–0.94). The months with the lowest O/E ratios for registrations were April 0.72 (95% CI 0.66–0.77), May 0.59 (95% CI 0.55–0.64), and June 0.79 (95% CI 0.73–0.86) (Fig. 1C).

The observed number of registrations for kidney transplantation fell below the expected value with an O/E ratio of 0.84 (95% CI 0.77–0.93) for the year (Fig. 4). The ratios for kidney registrations had a statistically significant decrease from April – with nadir in May – through September.

The observed number of registrations for liver and heart transplantation were within the expected confidence intervals with O/E

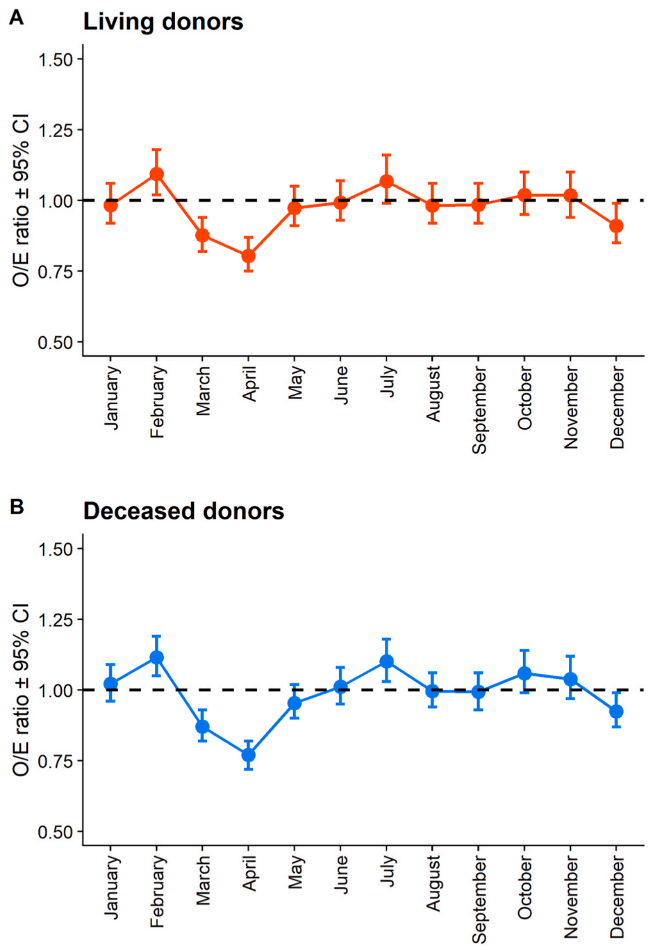

Fig. 3. Observed to expected ratio plots for donors during 2020 by donor type. Expected number of donors obtained from autoregressive integrated moving average forecasts for each organ by month based on data from 1990 to 2019. Abbreviations: CI, confidence intervals; O/E, observed to expected.

ratios of 0.95 (95% CI 0.86–1.06) and 0.99 (95% CI 0.85–1.18), respectively. The number of heart registrations was above expected for December 1.20 (95% CI 1.02–1.48).

The observed number of registrations for lung transplantation fell below expected with an O/E ratio of 0.80 (95% CI 0.70–0.94) for the year, which was the lowest among all waitlists. The ratios had a statistically significant drop for each month of the year except January 0.97 (95% CI 0.85–1.13), July 0.93 (95% CI 0.82–1.09), and October 0.98 (95% CI 0.85–1.14) despite wide confidence intervals in comparison with other organ waitlists (Fig. 4).

5. Discussion

These findings illustrate that the COVID-19 pandemic was associated with a significant decrease in solid organ transplantation, organ donation, and waitlist registration. There was an overall six percent decrease in the number of organ transplants and a fourteen percent decrease in the number of waitlist registrations. The months of April, May, and December fell the furthest below the expected forecast for 2020. To put things into perspective – during April alone – close to one thousand transplants that were expected to happen, did not occur.

Kidney transplantation appears to be the most affected organ during the pandemic, perhaps because these procedures can be postponed while patients continue renal replacement therapy without a significant short-term increase in mortality.[21,22] Despite month-level decreased O/E ratios for liver, heart, and lung transplantation during March, April, and December, the year O/E ratios were not below expected. This may reflect the lifesaving nature of these procedures.[23]

Two interesting findings were noted in waitlist registration. First, there was a relative delay between the drop in the ratio of transplantation that occurred in March and the drop in the ratio of registration that occurred in April. These data do not provide insight into the reasons for this delay. It is possible that this lag is explained by a natural delay between transplant evaluation and listing; meaning that patients who were being evaluated in February (prior to the critical months of the pandemic) were still listed in March. Second, registrations for hearts appear to pick up in the fourth quarter, which may reflect the buildup of patients with end-stage heart failure who postponed transplantation during the pandemic. It is unclear to what extent this increasing number of candidates will modify the urgency of heart transplants, waitlist mortality, and post-transplantation outcomes in the following months.

There have been several reports describing concerns and signals of decreasing volume of transplantation emerging from Spain,[24] Netherlands,[25] France,[26] and the United Kingdom.[27] A prior study from the United States described an increase in the observed number of waitlist registrations and deaths over the first months of the pandemic.[28] The present study is unique because it used an objective method to quantify the deficit of transplants, donors, and waitlist registrations, while also providing confidence intervals to distinguish whether these deficits are significantly different from noise signals. This modeling strategy allows the adjustment of major changes to the allocation policy that have taken place at different intervals for each organ, such as the implementation of the MELD and PELD scores in 2002,[29] the lung allocation score in 2005,[30] the kidney allocation system in 2014,[31,32] and the heart allocation policy in 2018.[33] In addition, this study provides a national picture in the field of transplantation during the first year of the pandemic.

6. Limitations

Given the observational nature of this study, the difference between observed and expected events is associated with the pandemic and not necessarily caused by it. Measuring the isolated effect of this pandemic on transplantation is complicated given that transplantation patterns vary over time and appear to be sensitive to events that occur regularly. This modeling approach adjusts for some of these issues; however, it cannot account for factors other than the past values utilized to train the model. These findings are valid only under the assumption that forecasting models accurately represent the expected transplantation setting. The pandemic had a dynamic geographic and chronological distribution among states, and this study was only performed at a national level with no adjustment for these patterns. This study did not examine the effects of the pandemic on repeat or multiple organ transplantation. Waitlist mortality rates were not available for analysis in the present study. Lastly, national databases may suffer from variability in data entry; however, the events examined in this study are concise and interpreted universally across practices.

7. Conclusions

The COVID-19 pandemic was associated with a significant deficit in solid organ transplantation, donation, and waitlist registrations in the United States in 2020. The impact was strongest in kidney transplantation and waitlist registration. While the pandemic persisted through 2020, the transplant system adapted remarkably well with a record number of transplantations performed.

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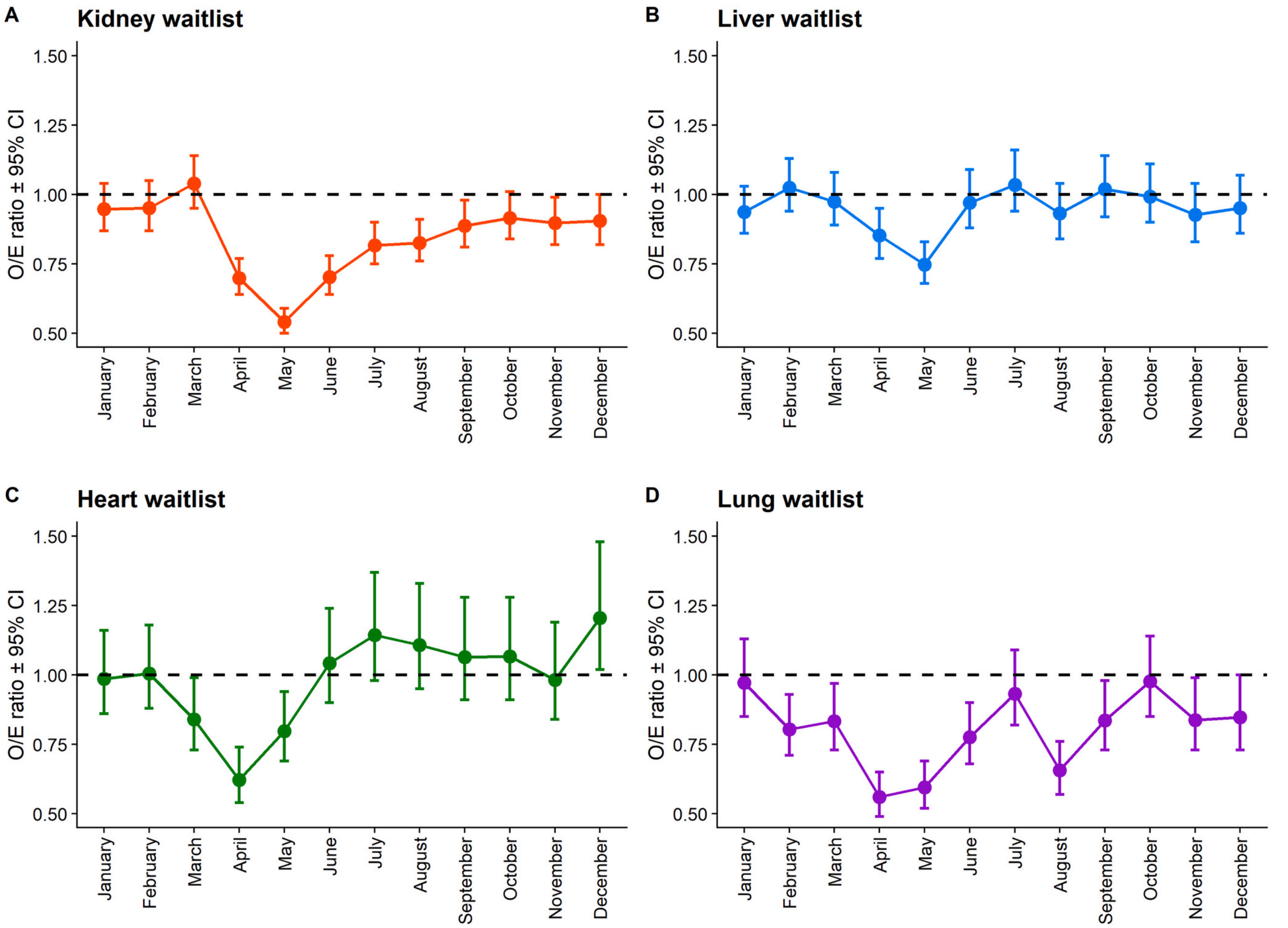

Fig. 4. Observed to expected ratio plots for waitlist registration during 2020 by organ. Expected number of donors obtained from autoregressive integrated moving average forecasts for each organ by month based on data from 1990 to 2019. Abbreviations: CI, confidence intervals; O/E, observed to expected.

view or policies of the Department of Health and Human Services, no does mention of trade names, commercial products, or organizations imply endorsement by the U.S. Government.

Conflicts of interest

None.

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None.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.amjsurg.2021.12.036.

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