

**Title: Healthcare Utilization in Obese Caregiver Living Donors**

**NCT04341896**

**Date: December 16, 2024**

**Study Protocol and Statistical Analysis Plan (with Results)**

## PROTOCOL

**Study population.** 25,352 donors from 278 centers will be studied. Contact information for donors was provided by the Scientific Registry of Transplant Recipients (SRTR) and is verified using Lexis Nexis Accurint. We anticipate that approximately 20% (n=5,070) of this cohort will have served as the primary caregiver for their recipient. Characteristics of the overall cohort and the subset of caregiver donors are in Table 1. Moreover, the subset of caregivers > 50 years is greater than the whole cohort, further highlighting the need for aging research in this population.

Table 1. Characteristics of obese living donors

	1R01DK113980 (Overall cohort) (n=25,232)	Subset of caregiver donors (n=5,070)
Age in years, median (IQR)	41 (33-49)	46 (39-53)
Age 50+ years, %	23.8	38.6
Female, %	58.4	65.0
Minority race/ethnicity, %	18.5	17.0

**Donor questionnaire.** All participants are contacted through a centralized phone bank maintained by the parent R01's PI at UAB and are administered a survey by phone, mail, or email. The following data are collected and maintained using a robust, redundant, secure, web-based computer entry system (REDCap): demographics (gender, date of birth, race/ethnicity); socioeconomic (education, employment, marital status); family history of comorbid disease; follow-up (frequency of doctor visits pre and post-donation); comorbidities pre and post-donation (smoking, cardiovascular disease, diabetes, etc.), current hypertension, diabetes, or chronic kidney disease/end-stage renal disease, and mental health quality of life. Patients are contacted for follow-up surveys annually. Furthermore, we will leverage the infrastructure of the parent R01 to collect new primary data specific to caregivers. Among those who were the primary caregivers for their recipients, we will administer additional questions derived from the Bakas Caregiver Outcomes Scale and National Alliance for Caregiving quantitative interviews, to describe their physical and mental health at time of donation, including self-reported caregiver burden and benefit pre and post-donation, the economic impact of caregiving, and the caregiving role in the context of donation.

**Medical records abstraction.** During completion of the questionnaire, donors are asked to provide signed waivers for medical records requests from their primary and other care providers. Pre-donation medical records are obtained from the transplant center. Post-donation medical records are obtained from the transplant center, as available, and from the participants' medical providers over time.

**Aim 1: To assess emergency department utilization associated with caregiving among a cohort of living kidney donors who were obese at the time of donation.** We will leverage an existing multi-center R01 study of a national cohort of obese living kidney donors, to quantify the association between a donor reporting that they served as the primary caregiver for the transplant recipient and ED utilization using generalized estimating equations. We will adjust for baseline characteristics and will explore the presence of effect modification and interaction between caregiving status and donor age, race/ethnicity, and rurality.

**Study population.** The study population will consist of living donors with obesity identified by the parent R01, categorized by whether or not they served as the primary caregiver for their transplant recipient. Donors will be stratified by relationship to the recipient (parent, child, spouse/life partner, other caregiver) and sex to allow us to explore sex as a biological variable. We estimate that approximately 20% (n=5,070) were the caregiver for their recipient, of whom 40% were  $\geq 50$  years old (3%  $> 65$  years), and 17% were minorities.

**Definition of caregiver.** Donors are asked whether they served as the primary caregiver (i.e., the main individual who provided unpaid caregiving activities pre and post-donation) for their transplant recipient.

**Definition of outcome of interest.** As part of the parent R01, healthcare utilization data are obtained from the questionnaire and include whether donors have utilized the ED since donation. Donors are asked to report not only whether they used the ED as well as the frequency of use.

**Aim 2: To assess hospitalization associated with caregiving among a cohort of living kidney donors who were obese at the time of donation.** We will use the same cohort from Aim 1 to quantify the association between a donor reporting that they served as the primary caregiver for their transplant recipient and hospitalization using generalized estimating equations.

**Study population.** The same study population identified in Aim 1 will be used.

**Definition of outcome of interest.** The parent R01 also captures data on whether the donor has been hospitalized since donation and the number of times the donor has been hospitalized.

## STATISTICAL DESIGN AND POWER

**Aim 1. Power calculation.** Goren et al. demonstrated a significant difference in ED utilization by caregiver status (7.2% for caregivers vs. 4.0% for non-caregivers).<sup>39</sup> Assuming a two-tailed test and a proportion of 4% experiencing ED use in the non-caregiver group, we will have 99% power to detect a relative risk of 1.8 for ED utilization among caregivers vs. non-caregivers. This is likely an underestimate, given that individuals with obesity have a greater use of hospital services,<sup>33,34</sup> and incidence is likely to be higher in our cohort.

**Aim 1. Statistical analyses.** We will explore post-donation ED use by caregiver status, using generalized estimating equations (GEE) accounting for repeated measurements, to estimate whether odds of ED use differ by caregiver status. We will use Poisson regression to explore count of ED visits among those who report having used these services by caregiver status, adjusting for baseline characteristics, including demographic, socioeconomic, and health status at donation. We will explore the presence of effect modification and interaction between caregiving status and donor age, race/ethnicity, and rurality. As a sub-aim, we will explore whether utilization differs by self-reported physical, mental, and financial burden among caregiver donors.

**Aim 2. Power calculation.** Goren et al. demonstrated a significant difference in the proportion of Alzheimer's caregivers experiencing hospitalization (8.1% for caregivers vs. 5.1% for non-caregivers).<sup>39</sup> Assuming a two-tailed test and a proportion of 5% experiencing hospitalization in the non-caregiver group, we will have 99% power to detect a relative risk of 1.6 for hospitalization among caregivers vs. non-caregivers. This is likely an underestimate, given that this study was performed in Japan, and hospital admissions for many preventable diseases are higher in the United States than in other countries.<sup>40</sup>

**Aim 2. Statistical analyses.** We will explore odds of post-donation hospitalization by caregiver status, first using generalized estimating equations to account for repeated measurements, then using Poisson regression to explore the counts of hospitalization among those who report having used these services. As in Aim 1, we will explore the presence of effect modification and interaction by stratification and interaction terms between caregiving status and donor age, ethnicity, and rurality, in addition to exploring the role of self-reported burden in hospitalization among the subset of caregiver donors.

## RESULTS

Among 784 donors (median 10.4yrs post-donation), 148 (18.9%) identified as caregivers. Caregiver donors were older (62.6 vs. 57.9yrs,  $p < 0.001$ ), more often female (69.6% vs. 58.3%,  $p=0.01$ ), the recipient's spouse (50.0% vs. 7.9%) or parent (16.2% vs. 4.6%,  $p < 0.001$ ), and retired (38.4% vs. 24.9%,  $p=0.004$ ), with no racial differences. Among those identifying as the caregiver and responding to the question about hospitalization ( $n=138$ ), 71 (51.5%) reported having been admitted to the hospital since donation, compared to 237 (40.3%) among non-caregivers. Among those identifying as the caregiver and responding to the question about emergency room utilization since donation ( $n=144$ ), 77 (53.5%) reported having been admitted to the hospital since donation, compared to 305 (49.4%) among non-caregivers.