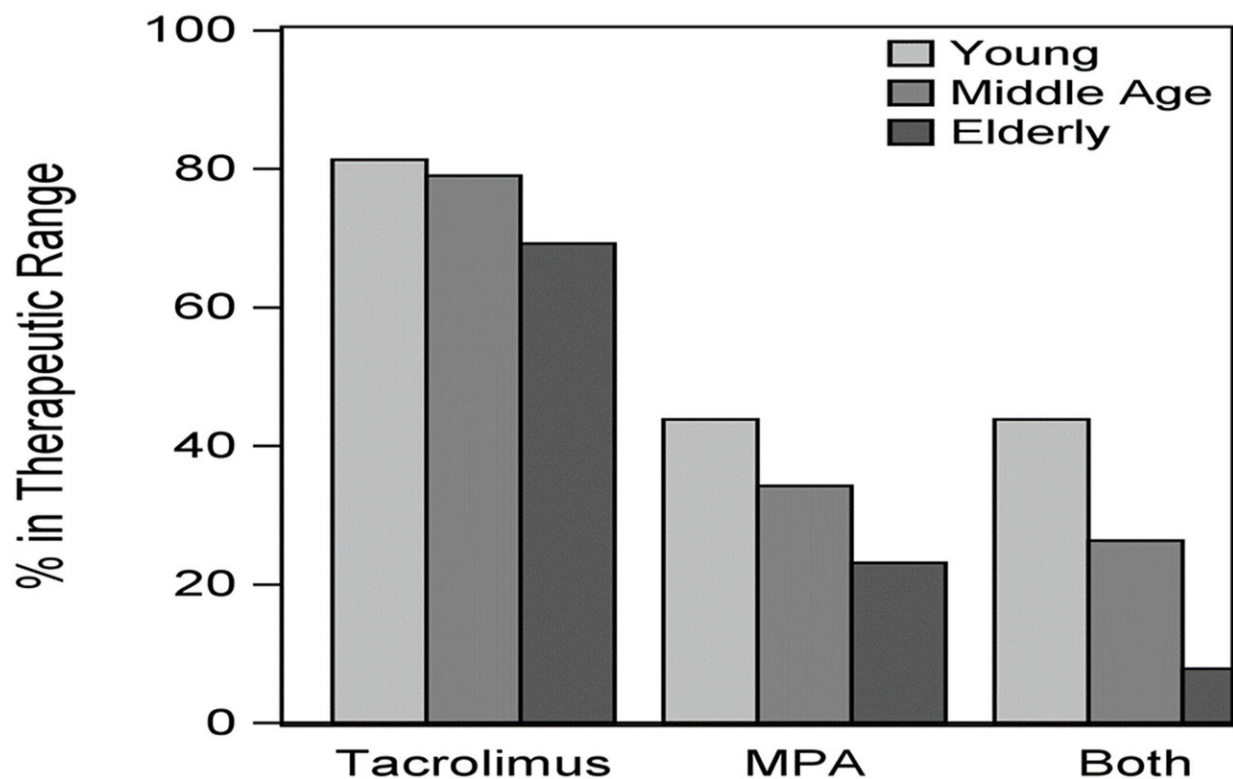


Study: Older kidney transplant patients metabolize immunosuppressive drugs slower than younger people

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Relationship of stable KTR by age group that achieved TAC or MPA therapeutic AUC_{0-12h} target range. The bar graphs depict the percent of recipients by age group within the therapeutic AUC_{0-12h} target for MPA or TAC. This is nonsignificant for each immunosuppressive. When combining the patients that achieved both TAC and MPA target AUC_{0-12h} labeled "Both" in above graph for each age group, an age-related decline in achieving the target range was noted in the elderly ($p = 0.036$). AUC_{0-12h}, area under the concentration-time curve 0–12

h; KTR, kidney transplant recipient; MPA, mycophenolic acid; TAC, tacrolimus. Credit: *Clinical and Translational Science* (2023). DOI: 10.1111/cts.13495

At one time, individuals over age 65 typically did not qualify for a kidney transplant. Now, due to advances in medicine and longer life expectancies, these patients represent approximately 15% of all kidney transplants, according to researchers at the University at Buffalo. Meanwhile, transplants that were performed in younger patients decades ago last longer, and these recipients are now aging.

Therefore, age-related issues can arise in some older [transplant](#) recipients that affect their long-term care and dosing of their essential immunosuppressive medicines.

A [clinical study](#) led by Kathleen Tornatore, PharmD, professor of pharmacy practice at UB's School of Pharmacy and Pharmaceutical Sciences, suggests that older [kidney transplant](#) patients do not metabolize the immunosuppressive drugs as well as their younger counterparts.

Their [preliminary findings](#) were reported in the article, "Age associations with tacrolimus and mycophenolic acid pharmacokinetics in stable Black and white [kidney](#) transplant recipients: Implications for [health inequities](#)," which was published earlier this year in *Clinical and Translational Science*.

The National Institutes of Health awarded a \$3.27 million grant in 2018 to support the five-year study, "Age and Race Influences on Immunosuppression after Renal Transplant," which enabled Tornatore's Immunosuppressive Pharmacology Research Program to further investigate this important area.

The published report provided a secondary analysis that supported the research objective of the 2018 NIH grant, which is focused on closing the knowledge gap regarding the pharmacology of immunosuppressive drugs and the impact of age and race in kidney transplant patients.

This preliminary study examined 67 Black and white renal transplant recipients between the ages of 25 and 70 who were clinically stable. They were divided into three age groups: young (20–40), middle aged (41–60) and elderly (61 and older).

Tornatore and her team observed that the participants over age 60 metabolized the [immunosuppressive drugs](#) tacrolimus and mycophenolic acid more slowly after a kidney transplant than young and middle-aged participants. This means that at commonly used dosages these medicines remained in their bodies longer and resulted in greater overall drug exposure. This contributed to an increase in adverse drug effects, including tremors.

Tornatore noted that [health care providers](#) may need to make adjustments to the immunosuppressive dosing regimen based upon the recipient's age to achieve a safe, therapeutic exposure over the survival time of the kidney transplant. This may minimize adverse drug effects. Investigation into immune responses over a range of ages is another important objective of this study.

"With an increased survival rate of kidney recipients, this research has immediate relevance," said Tornatore, whose clinical research program has had an ongoing collaboration with the Division of Nephrology at the Erie County Medical Center (ECMC) for more than 20 years. "A person can receive a kidney transplant at age 29 that continues to function well into their 60s. While that's a very positive advance, their bodies also change through the years. We wanted to better understand what was happening with older recipients, their immunosuppressive medicines and

their kidney transplants."

Brian Murray, MD, interim chair of the Department of Medicine at UB's Jacobs School of Medicine and Biomedical Sciences, served as the clinical nephrology co-investigator on the study. The other researchers were Kristopher Attwood, Ph.D., MA, assistant professor of oncology at Roswell Park Comprehensive Cancer Center, and Rocco C. Venuto, MD, professor of medicine and a former chief of the Division of Nephrology at the Jacobs School, who passed away in 2019 during the study.

Murray noted that physicians now assess patients as candidates for transplants not so much by their chronological age as by their biological and functional age.

"You can have a 75-year-old who is healthier than a 56-year-old," he said. "We have to look at factors such as cardiovascular health and whether or not the patient has had cancer or is harboring cancer."

As a result, only about 30% of individuals with end-stage kidney disease are healthy enough to qualify for transplant surgery, and secondly, the longevity benefits of transplant over dialysis start to diminish with age.

"When you get to the late 70s and 80s, depending on a patient's overall health, a transplant may not be beneficial," he said. "This determination must be made on a case-by-case basis. However, there is no hard stop on age. This is why studies such as this one, focusing on how to best monitor and treat older transplant recipients, is so important."

The COVID-19 pandemic caused an 18-month pause in the trial, which Tornatore noted is a long time in the life of a research grant. Nevertheless, enrollment has now increased at ECMC, and interest in participating is steadily progressing.

"We are hoping to reach enrollment of 100 additional kidney transplant recipients over the next year," Tornatore said, "and continue to investigate this vital issue."

More information: Kathleen M. Tornatore et al, Age associations with tacrolimus and mycophenolic acid pharmacokinetics in stable Black and white kidney transplant recipients: Implications for health inequities, *Clinical and Translational Science* (2023). [DOI: 10.1111/cts.13495](https://doi.org/10.1111/cts.13495)

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