



# KidneyNews

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## Business Shifts Likely to Shape Future of Nephrology

By Bridget M. Kuehn



The merger between pharmacy giant CVS and health insurer Aetna is among the latest shake-ups in the healthcare industry that are likely to have ripple effects on nephrologists and patients with kidney diseases. The merger was finalized on November 28, 2018.

For nephrologist Bruce Culleton, MD, vice president of CVS Health, the CVS-Aetna merger offers the prospect of a new care delivery model that better meets patients' needs.

"We believe this type of consolidation encourages the development of business models that are more patient-centric and more holistic than the current paradigm, which is focused on in-center dialysis care," Culleton said. "Future models will support chronic kidney disease identification and care, dialysis options education with an emphasis on access to transplantation and home dialysis, and innovation to deliver improved outcomes at lower overall healthcare costs."

Other experts in nephrology are cautiously optimistic that the merger could lead to new models of care and possibly better care for chronic diseases like hypertension that lead to kidney disease. But they also acknowledge that it is difficult to predict how this unusual merger might affect competition, costs, and quality. Most research to date on consolidation in healthcare has focused on mergers between care providers like hospitals or dialysis providers, which have mixed effects on care quality, access, and cost.

"The economics are less clear about what [the CVS-Aetna merger] will do to things like prices and potentially quality of care, compared to what sort of economic theory predicts about mergers and consolidations among the same types of organizations like among dialysis providers," said nephrologist Kevin Erickson, MD, MS, assistant professor of medicine at Baylor College of Medicine in Houston.

### Seismic shifts

The Aetna-CVS merger will bring together a large national insurance company with a powerhouse in the pharmacy and retail clinic space. The goal, according to a statement from CVS Health President and Chief Executive Officer Larry J. Mello, is to create a better experience for healthcare consumers by merging Aetna's data and analytics with CVS frontline care.

It's also a move to protect CVS's mail order and pharmacy business lines, noted Janis Orlowski, MD, chief health care officer of the Association of American Medical Colleges. She explained that pharmaceutical manufac-

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## Debate Rages on About Role of Obesity in Transplant Outcomes

By Bridget M. Kuehn

Obesity should not disqualify patients from kidney transplants, suggested one study presented at Kidney Week 2018, while two other studies provided conflicting information on whether pretransplant weight loss may be beneficial.

The prevalence of obesity in both adult and child prospective kidney transplant recipients has increased, mirroring a trend in the general population.

Observational studies have found that higher body mass index (BMI) is associated with an increased risk of delayed graft function, noted Krista Lentine, MD, professor of inter-

nal medicine at Saint Louis University School of Medicine, and colleagues, "but [higher BMI] is often *not* associated with inferior long-term allograft or patient survival in these studies." There are, however, increased risks of performing transplantation on patients who are obese compared to normal weight patients, including more surgical site complications, and there is some evidence of increased cardiovascular complications, noted Lentine, who has published a review on the topic.

"The debate regarding the impact of obesity on out-

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## Role of Obesity

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comes before and after kidney transplantation, and implications for transplant candidacy, have been waging for decades,” Lentine said. “Part of the uncertainty and difficulty resolving the debate relates to limitations of a BMI, which is a measure of overall body size, and not specific for adiposity, as well as the limitations of available data.”

The studies presented at Kidney Week are likely to add fuel to the debate, though they are unlikely to resolve it.

“Registry analyses can be very useful for hypothesis generation, but are also potentially limited by selection bias and uncontrolled confounding due to the nature of the available data,” Lentine said.

### Cutoff conundrum

It’s common for transplant centers to consider BMI in assessing prospective kidney transplant recipients and opt against transplant for patients with BMIs above a set threshold.

“The impact of recipient obesity on long-term outcomes for kidney transplantation is not clear,” said Bhavna Chopra, MD, a nephrologist in the renal transplant program at Allegheny General Hospital in Pittsburgh.

To further assess the effects of BMI on transplant outcomes, Bhavna and her colleagues used United Network of Organ Sharing data to identify all cases between 2006 and 2016 where each of a deceased donor’s kidneys were transplanted into a different recipient. They looked at 39,334 paired kidney recipients who shared a donor to assess the effects of BMI on outcomes. Recipients with BMIs between 18 and 25 had significantly lower risks of death-censored graft failure and graft failure compared with patients whose BMIs were above 35, but risk of death was similar between the groups. Recipients with BMIs between 25 and 30 had a lower risk of death-censored graft failure than individuals with BMIs 35 and up, but the two groups had similar rates of graft failure and death.

Bhavna suggested that the non-inferior outcomes among patients with BMIs above 35 may reflect careful pretransplant selection in this subgroup for those most likely to have a successful outcome. Or it could reflect a survival advantage similar to that seen in patients who are obese and on dialysis, she noted. Lentine agreed that patient selection could have an impact on the outcome of an observational study.

“[Patients with obesity] who are selected for listing and ultimate transplantation are inherently healthier than the full population of [patients with obesity] with kidney failure,” she said.

Based on the data, Bhavna suggested kidney transplantation BMI cutoffs between 35 and 40 are “arbitrary and unfounded.”

“Potential kidney transplant recipients should not be excluded from UNOS transplantation solely on the basis of obesity; however, transplant patients [with obesity] should have careful optimization prior to surgery to minimize perioperative morbidity and reduce the likelihood of additional graft injury.”

However, Lentine argued for considering both transplant center and patient-level factors in decision-making.

“I believe that obesity is prognostically important and potentially modifiable, but that it is also difficult to prescribe

a one-size-fits-all threshold for candidacy across transplant programs,” she said. She explained that not all centers have the expertise to manage patients with obesity during and after transplant or may have lower tolerance for surgical risks or for the potential elevated costs.

She argued for considering the potential risks and benefits of transplant for patients with obesity and engaging patients in shared decision-making.

“At a minimum, we advocate for lifestyle alterations such as healthy diet and appropriate exercise,” she said. However, she noted transplant programs may have limited interactions with waiting list patients; so primary nephrologists may need to take a larger role. However, she noted there are few data to guide such interventions, and patients and physicians may have limited resources to pursue them.



**[P]ursuing and maintaining healthy body composition based on guidelines for nutrition in renal failure are important priorities for kidney transplant candidates and recipients.**

### Pediatric perils

The data on the impact of obesity on pediatric outcomes have also been mixed. So, Heather Wasik, MD, a pediatric transplant fellow at Johns Hopkins University in Baltimore, and her colleagues conducted a retrospective cohort study using data from the Scientific Registry of Transplant Recipients, a US database of all donors, waitlist candidates, and recipients. They looked at recipients between 2 and 17 years of age to see if BMI categories were associated with outcomes.

They found that pediatric kidney transplant recipients classified as obese had the highest incidence of all cause graft failure at 37% at 10 years as compared with individuals who were normal or overweight at 34%, and those who were underweight at 32%.

“Based on these results, further study is warranted to evaluate whether weight-loss before or after kidney transplantation can result in improved graft survival in pediatric kidney transplant recipients,” Wasik noted.

Lentine cautioned that “observational registry studies

have not identified beneficial outcomes among ESRD patients who lost weight before transplantation; however, it is critical to recognize that association studies cannot distinguish intentional from unintentional weight loss as a result of illness and comorbidity, and offer little guidance on potential benefits of purposeful weight reduction.”

“Prospective evaluations of the impact of intentional risk modification efforts are urgently needed, including dietary changes, monitored exercise programs, and bariatric surgery in obese patients,” Lentine said.

### Weight loss worry

Growing evidence that substantial weight loss is associated with a higher risk of mortality in patients with CKD and ESRD led Meera Harhay, MD, associate professor of medicine at Drexel University and her colleagues to find out whether weight loss may also be risky during the pre-transplant period.

Harhay said there are many reasons patients may lose weight prior to transplant. Some may be intentionally losing weight to get below a hospital’s BMI cutoff for transplant at the request of their physicians. Others may lose weight because of fluid removal during dialysis or because they have progressive sarcopenia and frailty.

“Each of these etiologies have links to potentially adverse outcomes,” Harhay said. “Things like excess cardiovascular risk in our volume overloaded patients, excess inflammation in the frailty phenotype, and even malnutrition for patients who take on aggressive weight loss strategies in the setting of end state kidney disease.”

To better understand how such circumstances may affect transplant outcomes, Harhay and her colleagues used United Network of Organ Sharing’s national registry of adult deceased donor kidney transplants between 2005 and 2014. They found a steep increase in the risk of death among recipients who lost 10% or more of their body weight prior to transplant. When they adjusted for potential confounders like waiting time and dialysis vintage, they found those who lost 10% or more of their weight pretransplant had a 14% greater risk of dying posttransplant.

“Kidney transplant recipients with substantial pretransplant weight loss may benefit from closer surveillance post-transplant,” Harhay said.

One limitation of the study is that it cannot disentangle intentional and unintentional weight loss, and obviously those etiologies are very different. But the increased mortality risk extended across BMI categories, Harhay noted.

“Obese and morbidly obese recipients who lost 10% of their body weight between listing and transplantation showed the same association of higher mortality risk, adjusted for all those factors, as did the underweight, normal weight that came onto the list and lost weight,” she said.

Lentine emphasized the limitations of the available data to resolve these questions.

“I strongly advocate for ongoing research, including investigation of more accurate measures of body composition beyond BMI, and prospective studies, including prospective evaluations of intentional weight loss in patients who are obese,” Lentine said. “For now, pending more evidence, I believe that pursuing and maintaining healthy body composition based on guidelines for nutrition in renal failure are important priorities for kidney transplant candidates and recipients.” ■



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