


# Aortic valve replacement among patients with Alzheimer's disease and related dementias

Brent K. Hollenbeck MD  | Rodney L. Dunn MS | Devraj Sukul MD |  
Parth K. Modi MD | Brahmajee K. Nallamothe MD | Ananda Sen PhD |  
Julie P. Bynum MD

Departments of Urology, Medicine, and Biostatistics, University of Michigan, Ann Arbor, Michigan, USA

## Correspondence

Brent K. Hollenbeck, MD, MS, Dow Division for Health Services Research, Department of Urology, University of Michigan, 2800 Plymouth Road, Bldg. 16, Ann Arbor, MI 48109-2800, USA. Email: bhollen@med.umich.edu

## Funding information

This work was supported by research funding from the NIA (R01 AG-048071) to BKH and JPB

## Abstract

**Background:** Transcatheter aortic valve replacement (TAVR) has made palliation from aortic stenosis more broadly available to populations previously thought to be too high risk for surgery, such as those with Alzheimer's disease and related dementias (ADRD); however, its safety and effectiveness in this context are uncertain.

**Methods:** We performed a retrospective cohort study of national Medicare beneficiaries, aged 66 and older with Parts A and B, between 2010 and 2016. Patients undergoing AVR were identified, and follow-up was available through 2017. Multivariable regression was used to measure the independent association between having a diagnosis of ADRD at the time of AVR, stratified by TAVR and surgery, and outcomes (mortality and Medicare institutional days at 1 year after AVR).

**Results:** The average rate of increase in AVR per year was 17.5 cases per 100,000 ADRD and 8.4 per 100,000 non-ADRD beneficiaries, largely driven by more rapid adoption of TAVR. Adjusted mortality following AVR declined significantly between those treated in 2010 and 2016, from 13.5% (95% CI 10.2%–17.7%) to 6.3% (95% CI 5.2%–7.6%) and from 13.7% (95% CI 12.7%–14.7%) to 6.3% (95% CI 5.8%–6.9%) in those with and without ADRD, respectively. The sharpest decline was noted for patients undergoing TAVR between 2011 and 2016, with adjusted mortality declining from 19.9% (95% CI 11.2%–32.8%) to 5.2% (95% CI 4.1%–6.5%) and from 12.2% (95% CI 9.3%–15.8%) to 5.0% (95% CI 4.4%–5.6%) in patients with and without ADRD, respectively. Similar declines were evident for Medicare institutional days in the year after AVR in both patient groups.

**Conclusions:** Rates of AVR in those with ADRD increased during the past decade largely driven by the diffusion of TAVR. The use of TAVR in this vulnerable population did not come at the expense of increasing Medicare institutional days or mortality at 1-year.

## KEYWORDS

Alzheimer's disease, aortic valve replacement, outcomes, TAVR

## INTRODUCTION

Innovations in procedural and peri-procedural care (e.g., minimally invasive technology, enhanced recovery pathways) have resulted in procedures that reduce illness and hospitalizations, making them more broadly available. As a means of improving survival and palliation from the symptoms of severe aortic stenosis, such as shortness of breath, chest pain, or syncope, transcatheter aortic valve replacement (TAVR) was initially adopted among patients who were deemed too high risk for open surgical valve replacement.<sup>1,2</sup> In this very-high-risk population, TAVR reduced mortality and hospitalizations while simultaneously enhancing functional status and quality of life.<sup>3</sup> More recent studies have supported broadening eligibility for TAVR to include patients who are suitable for surgical aortic valve replacement (SAVR).<sup>4-9</sup> Since the introduction of TAVR in 2011, rates of aortic valve replacement (AVR) have more than doubled largely due to diffusion of TAVR.<sup>10</sup> Given enthusiasm for its safety and effectiveness across a wide range of patients, some worry that it may be used in contexts where its palliative effects, and potential for extending life,<sup>11</sup> are less clear.

People with Alzheimer's disease and related dementias (ADRD) are challenging in this context because the risks and benefits of surgery include not only operative risk but also the risks associated with anesthesia and postoperative delirium that may not be mitigated by less invasive procedures, such as TAVR. Additionally, elective surgery, such as AVR in most circumstances, has a narrower margin of benefit in those with ADRD in whom life expectancy, and quality of life is influenced by the underlying dementia itself. One must decide between intervening—and its risks related to anesthesia, surgery, and hospitalization—versus medical management—and its implications for symptoms related to progressive heart failure and associated consequences. Balancing these risks and consequences depends heavily on the procedure itself. On the one hand, use of new technologies, such as TAVR, in those with ADRD improves access to palliative relief from a significant illness. On the other hand, procedures in patients with ADRD can worsen cognitive decline, as evidenced by the high incidence of postoperative delirium in this population,<sup>12-17</sup> or result in high rates of complications, both of which may hasten decline or amplify the underlying dementia.

As the prevalence of ADRD is expected to grow to 13 million people by 2050,<sup>18</sup> patients with the disease will increasingly interact with healthcare systems and face decisions about treatment for competing illnesses. Dissemination of new technologies has the potential to spur utilization in these patients, in whom the calculus for the

### Key Points

- TAVR diffusion occurred more rapidly in those with ADRD.
- TAVR diffusion was associated with significant declines in 1-year mortality and Medicare institutional care days in those with and without ADRD.

### Why Does this Paper Matter?

TAVR diffusion in the ADRD population did not come at the expense of adverse outcomes.

risks and benefits is less certain. This national study uses national Medicare data to assess the uptake of AVR in the era of TAVR, its safety (30-day mortality, complications, and readmissions) and effectiveness (1-year rates of Medicare institutional days and mortality) in those with and without a diagnosis of ADRD.

## METHODS

### Data and study population

A 20% national sample of Medicare claims was used to perform a retrospective cohort study of fee-for-service beneficiaries between January 1, 2010, and December 31, 2016. Patients undergoing AVR were identified using Healthcare Common Procedure Coding System codes in the Carrier file (see Table S1). Follow-up was available through December 31, 2017. We chose to study AVR because it is a relatively common procedure in older persons. Further, the study period coincided with the rapid diffusion of TAVR, a less invasive alternative to SAVR, that greatly increased the population eligible for treatment, including those with ADRD. To identify patients with ADRD, an established and validated method, similar to that used by the Chronic Conditions Warehouse, was implemented (diagnosis codes available in Tables S2 and S3).<sup>19</sup> A study evaluating the performance of this algorithm indicates good specificity but lack of sensitivity to the earliest stage of the disease (i.e., those with minimal symptoms).<sup>19</sup>

The study included patients age 66 years or older to permit risk adjustment using a 1-year look back. Only those with continuous enrollment in both Medicare Parts A and B from 1 year before through 1 year after the procedure were included. Patients participating in

Medicare Advantage plans were excluded due to the absence of complete claims.

## Outcomes

For all outcomes, the patient was the unit of analysis. Primary outcomes of the study were assessed at 1 year following AVR and included mortality (explicitly available in the Medicare Beneficiary Summary File) and the number of Medicare institutional days post discharge. Because of the relatively high underlying mortality rate in the ADRD population and the palliative nature of AVR, and TAVR in particular, mortality was modeled as a binary outcome. The latter measure was inclusive of days spent in an acute care hospital (i.e., either as an inpatient or observation stay) or skilled nursing facility. Secondary outcomes, including complications, readmission, and mortality, were measured at 30-days post discharge to determine safety and feasibility of AVR in those with and without ADRD. Complications were enumerated using the Agency for Healthcare Research and Quality's patient safety indicators.<sup>20</sup>

## Analysis

For each year of study, we compared patient characteristics between those with and without ADRD using the Wilcoxon Rank-sum Test and Fisher's Exact Test for continuous and binary data, respectively. Next, we estimated rates of AVR annually among these two populations both overall and by procedure type (i.e., SAVR vs. TAVR and urgent vs. elective). In all cases, the numerator was characterized by the number of eligible patients undergoing the procedure. The denominator was represented by the entitlement eligible Medicare population that did and did not have the procedure, regardless of the presence or absence of aortic stenosis. Logistic regression models were used to adjust the rates for patient age, gender, and race.

To examine the independent effect of ADRD, multi-variable logistic regression (binary outcomes, such as mortality) and linear (continuous outcomes, such as Medicare institutional days) models were fit separately for all primary and secondary outcomes. All models were adjusted for patient age, race, gender, comorbidity as measured by hierarchical condition categories (HCCs), procedure urgency (i.e., elective vs. nonelective as noted in MedPAR), hospital days in the year prior to surgery, having a nursing home stay within 90 days of the procedure, and a zip code-level measure of socioeconomic class.<sup>21</sup>

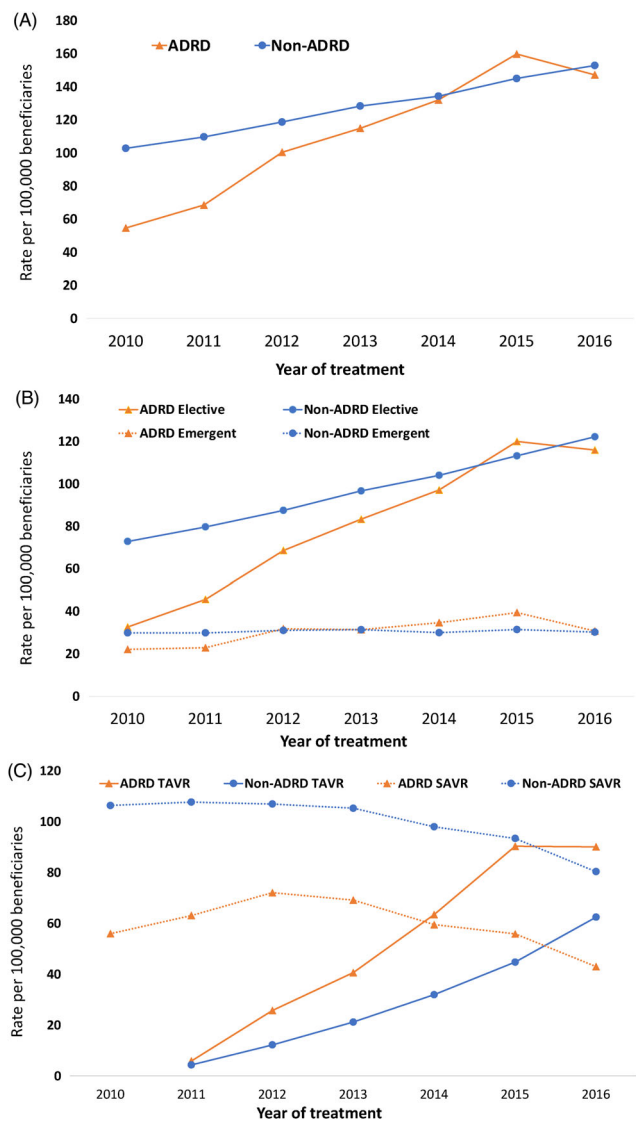
All analyses were carried out using computerized software (SAS 9.4, Cary, NC). All tests were two-sided, and the probability of type 1 error was set at 0.05. The study protocol was judged to be exempt by the institutional review board.

## RESULTS

Adjusted rates of AVR increased from 99.6 per 100,000 (95% CI 97.0–102.2) in 2010 to 152.0 per 100,000 in 2016 (95% CI 148.7–155.2). As illustrated in Figure 1A, rates increased more rapidly over this period among those with ADRD (between rate  $p$ -value <0.001). The increase in the rate of AVR in patients with and without ADRD was primarily due to the introduction of TAVR (Figure 1B). For instance, in those with ADRD, adjusted rates of SAVR decreased from 49.1 per 100,000 (95% CI 43.5–55.4) in 2010 to 36.8 per 100,000 in 2016 (95% CI 32.9–41.2), while adjusted rates of TAVR increased from 0 in 2010 to 107.8 per 100,000 (95% CI 100.4–115.7) in 2016 ( $p$ -value for trend <0.001). Importantly, the adoption of TAVR in those with ADRD was significantly faster than in patients without ADRD (between rate  $p$ -value <0.001). As illustrated in Figure 1C, the growth in use of AVR in both patient groups occurred in an elective context.

Table S4 compares patient characteristics according to the presence of ADRD for those undergoing AVR over time. Generally, patients with ADRD were older, had higher levels of comorbidity, spent more days in an acute care hospital in the preceding 12-month period, and were more likely to have a nursing home stay within 90 days of the index procedure. Interestingly, those with ADRD were more likely to undergo a nonelective procedure in 2010 (40.0% [95% confidence interval {CI} 34.1%–46.1%] vs. 29.2% [95% CI 27.9%–30.4%]), though this difference ebbed over time and was not statistically different by 2016 (21.5% [95% CI 19.1%–24.0%] vs. 20.2% [95% CI 19.3%–21.1%]).

During the study period, unadjusted mortality at 1 year following AVR was 17.9% (95% CI 16.9–19.0) and 12.2% (95% CI 11.9–12.5) for those with and without ADRD, respectively. Unadjusted mortality declined between 2010 and 2016 particularly among those undergoing TAVR (ADRD: from 37.5% (95% CI 21.8%–53.2%) to 10.6% (95% CI 8.5%–12.8%), non-ADRD: from 23.5% (95% CI 18.3%–28.6%) to 8.5% (95% CI 7.6%–9.4%), see Figure S1). After adjusting for patient differences, mortality at 1 year following AVR by either TAVR or SAVR declined significantly from 13.5% (95% CI 10.2%–17.7%) to 6.3% (95% CI 5.2%–7.6%) and from 13.7% (95% CI 12.7%–14.7%) to 6.3% (95% CI 5.8%–6.9%) in those with and without ADRD, respectively. As illustrated in

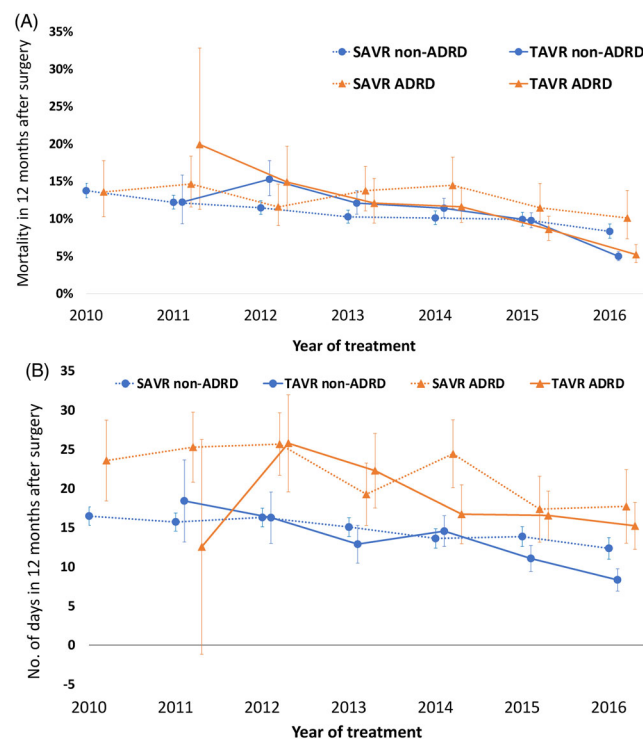


**FIGURE 1** Rates of aortic valve replacement (AVR) adjusted for age, race, and gender. (A) Overall in those with and without Alzheimer’s disease and related dementias (ADRD). The average rate of change per year was 17.5 cases per 100,000 ADRD beneficiaries and 8.4 per 100,000 non-ADRD,  $p < 0.001$  for test between slopes. (B) Rates in those with and without ADRD according to approach (transcatheter aortic valve replacement [TAVR] vs. surgical aortic valve replacement [SAVR]). Rates of SAVR declined in both populations over time ( $p < 0.01$  for trend over time in those with and without ADRD), while that for TAVR increased ( $p < 0.01$  for trend over time in those with and without ADRD). The average annual growth rate was 17.0 per 100,000 ADRD beneficiaries and 10.3 per 100,000 non-ADRD,  $p < 0.001$  for test between slopes. (C) Rates in those with and without ADRD according to whether the procedure was classified as nonelective. Rates of nonelective surgery were flat in those without ADRD ( $p = 0.31$  for trend over time) but increased slightly in patients with ADRD (from 21.9 [95% CI 18.1–26.4] to 30.9 [95% CI 27.2–35.0] per 100,000 beneficiaries). Conversely, rates of elective AVR increased dramatically over time in both populations ( $p < 0.001$  for trend over time in those with and without ADRD)

Figure 2A, the sharpest decline was noted for patients undergoing TAVR, with mortality declining from 19.9% (95% CI 11.2%–32.8%) to 5.2% (95% CI 4.1%–6.5%) and 12.2% (95% CI 9.3%–15.8%) to 5.0% (95% CI 4.4%–5.6%) between 2011 and 2016, in patients with and without ADRD, respectively.

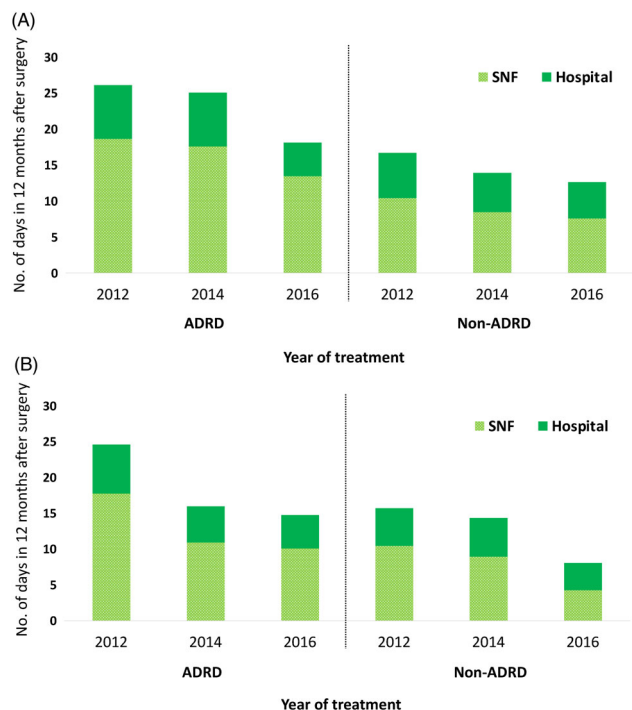
Decreasing trends in the number of Medicare institutional days in the year following valve replacement for TAVR and SAVR (Figure 2B) were also evident in both patient populations (Figure 2B). Among patients undergoing TAVR without ADRD, days spent in an institution decreased from 18.4 (95% CI 13.2–23.7) to 8.3 (95% CI 6.9–9.7) days between 2011 and 2016. In those with ADRD, the rate initially increased between 2011 and 2012, from 12.5 (95% CI -1.2–26.3) to 25.8 (19.6–32.0) days, but then declined to 15.2 (95% CI 12.2–18.2) days for those treated in 2016. As illustrated in Figure 3, trends in Medicare institutional days after TAVR were largely due to declines in days spent in a skilled nursing facility in both populations.

Among secondary outcomes assessing safety of AVR within 30 days post discharge, patients with ADRD had a similar risk of complications, readmission, and mortality compared with those without ADRD (Table 1). In



**FIGURE 2** Rates of mortality (A) and Medicare institutional days (B) in the 1 year after aortic valve replacement (AVR), adjusted for age, race, gender, socioeconomic class, hospital days in 1-year prior to surgery, nursing home days in 90-days prior to surgery, and comorbidities





**FIGURE 3** Among patients undergoing (A) surgical aortic valve replacement (SAVR) and (B) transcatheter aortic valve replacement (TAVR), the number of days spent in a hospital (inclusive of observation stays) and skilled nursing facility (SNF) in the 1-year period after the procedure among those with and without ADRD, adjusted for age, race, gender, socioeconomic class, hospital days in 1-year prior to surgery, nursing home days in 90-days prior to surgery, and comorbidities (NB. data shown for even years). (A) In those with Alzheimer's disease and related dementias (ADRD), hospital and SNF days following SAVR decreased by an average of 0.46 (95% CI 0.22–0.70) and 0.91 (95% CI 0.11–1.72) days per year, respectively. Declines were also evident in those without ADRD (average decrease of 0.24 [95% CI 0.18–0.31] and 0.43 [95% CI 0.21–0.64] days, respectively). (B) In those with ADRD, hospital and SNF days following TAVR decreased by an average of 0.56 (95% CI 0.22–0.90) and 1.36 (95% CI 0.21–2.52) days per year, respectively. Declines were also evident in those without ADRD (average decrease of 0.46 [95% CI 0.30–0.62] and 1.55 [95% CI 0.99–2.10] days, respectively)

patients with ADRD, the risk of complications, readmission, and mortality within 30 days post discharge decreased over time by 58.1% (95% CI 53.7%–62.5%), 37.9% (95% CI 34.5%–41.3%), and 50.2% (95% CI 48.5%–51.8%), respectively. Among patients without ADRD, the risk of complications, readmission, and mortality within 30 days post discharge decreased over time by 50.0% (95% CI 48.8%–51.2%), 38.4% (95% CI 37.5–39.3), and 51.2% (95% CI 50.6%–51.7%), respectively.

## DISCUSSION

Rates of AVR increased significantly between 2010 and 2016, largely due to the rapid dissemination of elective TAVR. Diffusion of TAVR among patients with ADRD outpaced that in those without ADRD such that by 2016, rates of AVR were similar in the two populations. Importantly, growing use of AVR did not compromise safety, as evidenced by decreasing risk of complications, readmissions, and mortality within 30 days post discharge in both the vulnerable ADRD population and those without ADRD. Importantly, TAVR diffusion was associated with significant declines in 1-year mortality and institutional care days. Among those treated with TAVR in 2016, 1-year risk-adjusted mortality rates were 5.2% and 5.0% for those with and without ADRD, respectively.

The development and dissemination of new technology is a major determinant of growth in Medicare spending,<sup>22–24</sup> of which surgical procedures are one important sector.<sup>25</sup> Some new procedures, such as catheter ablation of atrial fibrillation,<sup>26</sup> are aimed at replacing pharmacologic therapy. Others fill a void, treating conditions for which there was no prior therapy (e.g., vertebroplasty and kyphoplasty<sup>27,28</sup>). However, most are designed to replace an established procedure, aimed at achieving comparable effectiveness while lowering the morbidity to patients (e.g., endovascular abdominal aortic aneurysm

**TABLE 1** Secondary outcomes (complications, readmissions, and mortality) assessed 30 days post discharge, adjusted for age, race, gender, year, socioeconomic class, hospital days in 1-year prior to surgery, nursing home days in 90-days prior to surgery, and comorbidities

Outcome	Non-ADRD			ADRD		
	Total	SAVR	TAVR	Total	SAVR	TAVR
Complication % (95% CI)	38.4 (37.9–38.9)	42.5 (41.9–43.1)	27.2 (26.2–28.3)	38.1 (36.6–39.6)	45.7 (43.6–47.8)	26.1 (24.3–28.0)
Readmission, % (95% CI)	16.4 (16.0–16.8)	17.4 (16.9–17.8)	13.6 (12.9–14.3)	17.6 (16.6–18.7)	18.1 (16.7–19.6)	15.9 (14.5–17.4)
Mortality, % (95% CI)	4.8 (4.5–5.0)	5.4 (5.1–5.6)	3.1 (2.8–3.5)	4.7 (4.2–5.2)	5.8 (5.0–6.6)	3.0 (2.5–3.5)

Abbreviations: ADRD, Alzheimer's disease and related dementias; CI, confidence interval; SAVR, surgical aortic valve replacement; TAVR, transcatheter aortic valve replacement.

repair,<sup>29,30</sup> laparoscopic colectomy<sup>31,32</sup>). In some instances, such as with newer treatment technologies for prostate cancer, diffusion can occur prior to evidence development and in populations that stand little to benefit.<sup>33,34</sup> TAVR has transformed AVR over the past decade, accounting for nearly half all procedures.<sup>35</sup> Aimed at palliating symptoms and improving survival, TAVR provides treatment for a debilitating disease for those who would be at too high risk for SAVR due to competing health risks. Indeed, beyond those at prohibitive risk for surgery, TAVR has been shown to be noninferior to SAVR for those with low and moderate risk for surgery, suggesting the importance of patient preference and clinical factors, such as the presence of ADRD, when selecting treatment approach.

People with ADRD are emblematic of a population with significant competing health risks, with mortality from the disease approaching 20% at 1 year after diagnosis among enrollees in fee-for-service Medicare.<sup>36</sup> With few effective treatments either to prevent the disease or slow its progression, clinicians are limited to managing established disease and avoiding further negative outcomes at a cost of \$200 billion per year.<sup>37</sup> This extraordinary cost arises in part because ADRD complicates the management of comorbid conditions, especially in the hospital setting.<sup>38–41</sup> Postoperative management among those with ADRD is particularly prone to complications and worsening cognition, due to the high incidence of delirium and the use of anesthetics.<sup>14,42–44</sup> This study offers unique insight into the implementation of a new technology, TAVR, in a population in whom the net benefits are unclear. On the one hand, the dissemination of TAVR in ADRD could afford this vulnerable population the benefits of palliation from the symptoms of aortic stenosis that yield improvements in functional status and quality of life. On the other hand, increasing use of these procedures could result in deteriorating cognition, thereby accelerating a downward spiral and result in unacceptable rates of mortality and loss of independence. Importantly, this study demonstrated that the real-world implementation of TAVR in the ADRD population was both safe and effective at reducing hospital use as evidenced by the reassuring 30-day and 1-year outcomes. Future studies are warranted to determine the impact on quality of life and cognitive function in this population, particularly given concerns of possible subclinical brain infarcts with TAVR insertion.<sup>45,46</sup>

Our findings that the real-world implementation of AVR in those with ADRD is safe and effective must be interpreted in the context of two limitations. First, both ADRD and aortic stenosis have a wide range of severity, which we are unable to completely account for in Medicare claims. We address this by adjusting for hospitalization days in the preceding 12 months and the use of a nursing home stay within 90 days of the procedure.

Further, we perform comprehensive risk adjustment using the Centers for Medicare and Medicaid HCCs. Indeed, we observed that measured comorbidity during dissemination remained relatively stable between 2012 and 2016 in those with (mean HCC score 2.68 vs. 2.73, respectively) and without (mean HCC score 2.14 vs. 2.21, respectively) ADRD. Second, we fully appreciate that indications for TAVR have broadened over the period study from inoperable aortic stenosis<sup>1,2</sup> to those with less severe disease.<sup>4–6</sup> Evolving indications for treatment with TAVR toward less severe aortic stenosis over time (which likely further enriches the SAVR population with the most robust patients) coupled with increasing physician experience with the procedure itself likely contribute to noted improvements in both primary and secondary outcomes. To some extent, these issues are addressed by our modeling framework that incorporates a fixed effect for year of treatment and our robust approach to risk adjustment. However, as the intent of the study focused on outcomes of implementation within diverse populations (i.e., those with and without ADRD), we view this as a potential strength as it represents real-world outcomes.

## CONCLUSIONS

This study demonstrates that rates of AVR have increased dramatically among those with ADRD during the past decade and are largely driven by the diffusion of TAVR. By 2016, rates of AVR were similar for those with and without ADRD. Importantly, broader implementation of AVR in patients with ADRD did not come at the expense of increasing Medicare institutional days or mortality at 1-year after the procedure.

## ACKNOWLEDGMENTS

This represents original work and all authors have contributed significantly, as detailed below.

## CONFLICT OF INTEREST

Grant funding for this work was provided to Drs. Hollenbeck and Bynum from the NIA, as noted on the title page. No other authors have additional financial conflicts with respect to this work. No authors have personal conflicts with respect to this work.

## AUTHOR CONTRIBUTIONS

Drs. Brent K. Hollenbeck, Julie P. Bynum, and Ananda Sen are responsible for the concept and design of the study. Drs. Brent K. Hollenbeck and Julie P. Bynum and Mr. Rodney L. Dunn are responsible for data acquisition. All authors participated in the analysis and interpretation of the data and in manuscript preparation.

## SPONSOR'S ROLE

The sponsor played no role in the study beyond providing financial support. The views expressed in this article are those of the authors and do not necessarily reflect the position or policy of the US government.

## ORCID

Brent K. Hollenbeck  <https://orcid.org/0000-0003-4840-1260>

## REFERENCES

- Makkar RR, Fontana GP, Jilalawi H, et al. Transcatheter aortic-valve replacement for inoperable severe aortic stenosis. *N Engl J Med.* 2012;366(18):1696-1704.
- Leon MB, Smith CR, Mack M, et al. Transcatheter aortic-valve implantation for aortic stenosis in patients who cannot undergo surgery. *N Engl J Med.* 2010;363(17):1597-1607.
- Kim CA, Rasania SP, Afilalo J, Popma JJ, Lipsitz LA, Kim DH. Functional status and quality of life after transcatheter aortic valve replacement: a systematic review. *Ann Intern Med.* 2014;160(4):243-254.
- Smith CR, Leon MB, Mack MJ, et al. Transcatheter versus surgical aortic-valve replacement in high-risk patients. *N Engl J Med.* 2011;364(23):2187-2198.
- Leon MB, Smith CR, Mack MJ, et al. Transcatheter or surgical aortic-valve replacement in intermediate-risk patients. *N Engl J Med.* 2016;374(17):1609-1620.
- Popma JJ, Deeb GM, Yakubov SJ, et al. Transcatheter aortic-valve replacement with a self-expanding valve in low-risk patients. *N Engl J Med.* 2019;380(18):1706-1715.
- Adams DH, Popma JJ, Reardon MJ, et al. Transcatheter aortic-valve replacement with a self-expanding prosthesis. *N Engl J Med.* 2014;370(19):1790-1798.
- Reardon MJ, Van Mieghem NM, Popma JJ, et al. Surgical or transcatheter aortic-valve replacement in intermediate-risk patients. *N Engl J Med.* 2017;376(14):1321-1331.
- Mack MJ, Leon MB, Thourani VH, et al. Transcatheter aortic-valve replacement with a balloon-expandable valve in low-risk patients. *N Engl J Med.* 2019;380(18):1695-1705.
- Sedrakyan A, Dhruva SS, Sun T, Mao J, Gaudino MFL, Redberg RF. Trends in use of transcatheter aortic valve replacement by age. *JAMA.* 2018;320(6):598-600.
- Braunwald E. Aortic stenosis: then and now. *Circulation.* 2018;137(20):2099-2100.
- Seitz DP, Gill SS, Bell CM, et al. Postoperative medical complications associated with anesthesia in older adults with dementia. *J Am Geriatr Soc.* 2014;62(11):2102-2109.
- Silverstein JH. Influence of anesthetics on Alzheimer's disease: biophysical, animal model, and clinical reports. *J Alzheimers Dis.* 2014;40(4):839-848.
- Avidan MS, Evers AS. Review of clinical evidence for persistent cognitive decline or incident dementia attributable to surgery or general anesthesia. *J Alzheimers Dis.* 2011;24(2):201-216.
- Lee HB, Oldham MA, Sieber FE, Oh ES. Impact of delirium after hip fracture surgery on one-year mortality in patients with or without dementia: a case of effect modification. *Am J Geriatr Psychiatry.* 2017;25(3):308-315.
- Lundstrom M, Stenvall M, Olofsson B. Symptom profile of postoperative delirium in patients with and without dementia. *J Geriatr Psychiatry Neurol.* 2012;25(3):162-169.
- Cortese GP, Burger C. Neuroinflammatory challenges compromise neuronal function in the aging brain: postoperative cognitive delirium and Alzheimer's disease. *Behav Brain Res.* 2017;322(Pt B):269-279.
- Hebert L, Scherr P, Bienias JL, Bennett DA, Evans DA. Alzheimer disease in the US population: prevalence Estimates using the 2000 census. *Arch Neurol.* 2003;60(8):1119-1122.
- Taylor DH Jr, Ostbye T, Langa KM, Weir D, Plassman BL. The accuracy of Medicare claims as an epidemiological tool: the case of dementia revisited. *J Alzheimers Dis.* 2009;17(4):807-815.
- Agency for Healthcare Research and Quality. Patient Safety Indicators Overview. Published 2020. Accessed April 1, 2020. [https://www.qualityindicators.ahrq.gov/modules/psi\\_overview.aspx](https://www.qualityindicators.ahrq.gov/modules/psi_overview.aspx)
- Diez Roux AV, Merkin SS, Arnett D, et al. Neighborhood of residence and incidence of coronary heart disease. *N Engl J Med.* 2001;345(2):99-106.
- Maxwell S, Zuckerman S, Berenson RA. Use of physicians' services under Medicare's resource-based payments. *N Engl J Med.* 2007;356(18):1853-1861.
- Fuchs VR. *The Health Economy.* Cambridge, MA: Harvard University Press; 1986.
- Newhouse JP. Medical care costs: how much welfare loss? *J Econ Perspect.* 1992;6(3):3-21.
- Kaye DR, Luckenbaugh AN, Oerline M, et al. Understanding the costs associated with surgical care delivery in the Medicare population. *Ann Surg.* 2020;271(1):23-28.
- Terasawa T, Balk EM, Chung M, et al. Systematic review: comparative effectiveness of radiofrequency catheter ablation for atrial fibrillation. *Ann Intern Med.* 2009;151(3):191-202.
- Buchbinder R, Osborne RH, Ebeling PR, et al. A randomized trial of vertebroplasty for painful osteoporotic vertebral fractures. *N Engl J Med.* 2009;361(6):557-568.
- Kallmes DF, Comstock BA, Heagerty PJ, et al. A randomized trial of vertebroplasty for osteoporotic spinal fractures.[Erratum appears in N Engl J Med. 2012 Mar 8;366(10):970]. *N Engl J Med.* 2009;361(6):569-579.
- Jackson RS, Chang DC, Freischlag JA. Comparison of long-term survival after open vs endovascular repair of intact abdominal aortic aneurysm among Medicare beneficiaries. *JAMA.* 2012;307(15):1621-1628.
- United Kingdom EVAR Trial Investigators, Greenhalgh RM, Brown LC, et al. Endovascular versus open repair of abdominal aortic aneurysm. *N Engl J Med.* 2010;362(20):1863-1871.
- Fleshman J, Sargent DJ, Green E, et al. Laparoscopic colectomy for cancer is not inferior to open surgery based on 5-year data from the COST Study Group trial. *Ann Surg.* 2007;246(4):655-662.
- Delaney CP, Kiran RP, Senagore AJ, Brady K, Fazio VW. Case-matched comparison of clinical and financial outcome after laparoscopic or open colorectal surgery. *Ann Surg.* 2003;238(1):67-72.
- Jacobs BL, Zhang Y, Schroeck FR, et al. Use of advanced treatment technologies among men at low risk of dying from prostate cancer. *JAMA.* 2013;309(24):2587-2595.
- Hollenbeck BK, Kaufman SR, Yan P, et al. Urologist practice affiliation and intensity modulated radiation therapy for prostate cancer in the elderly. *Eur Urol.* 2018;73(4):491-498.

35. Culler SD, Cohen DJ, Brown PP, et al. Trends in aortic valve replacement procedures between 2009 and 2015: has transcatheter aortic valve replacement made a difference? *Ann Thorac Surg*. 2018;105(4):1137-1143.
36. Koller D, Hua T, Bynum JP. Treatment patterns with antidementia drugs in the United States: medicare cohort study. *J Am Geriatr Soc*. 2016;64(8):1540-1548.
37. Hurd MD, Martorell P, Langa KM. Monetary costs of dementia in the United States. *N Engl J Med*. 2013;369(5):489-490.
38. Beydoun MA, Gamaldo AA, Beydoun HA, Shaked D, Zonderman AB, Eid SM. Trends, predictors, and outcomes of healthcare resources used in patients hospitalized with Alzheimer's disease with at least one procedure: the nationwide inpatient sample. *J Alzheimers Dis*. 2017;57(3):813-824.
39. Rao A, Suliman A, Vuik S, Aylin P, Darzi A. Outcomes of dementia: systematic review and meta-analysis of hospital administrative database studies. *Arch Gerontol Geriatr*. 2016;66:198-204.
40. Briggs R, Dyer A, Nabeel S, et al. Dementia in the acute hospital: the prevalence and clinical outcomes of acutely unwell patients with dementia. *QJM*. 2017;110(1):33-37.
41. Reynish EL, Hapca SM, De Souza N, Cvorov V, Donnan PT, Guthrie B. Epidemiology and outcomes of people with dementia, delirium, and unspecified cognitive impairment in the general hospital: prospective cohort study of 10,014 admissions. *BMC Med*. 2017;15(1):140.
42. Jansen E, Peltola M, Puolakka T, Eskelinen A, Lehto MU. Surgical outcomes of hip and knee arthroplasties for primary osteoarthritis in patients with Alzheimer's disease: a nationwide registry-based case-controlled study. *Bone Joint J*. 2015;97-B(5):654-661.
43. Partridge JS, Harari D, Martin FC, Dhesei JK. The impact of pre-operative comprehensive geriatric assessment on postoperative outcomes in older patients undergoing scheduled surgery: a systematic review. *Anaesthesia*. 2014;69(Suppl 1):8-16.
44. Hu CJ, Liao CC, Chang CC, Wu CH, Chen TL. Postoperative adverse outcomes in surgical patients with dementia: a retrospective cohort study. *World J Surg*. 2012;36(9):2051-2058.
45. Khan MM, Herrmann N, Gallagher D, et al. Cognitive outcomes after transcatheter aortic valve implantation: a metaanalysis. *J Am Geriatr Soc*. 2018;66(2):254-262.
46. Ghanem A, Dorner J, Schulze-Hagen L, et al. Subacute subclinical brain infarctions after transcatheter aortic valve implantation negatively impact cognitive function in long-term follow-up. *PLoS ONE*. 2017;12(1):e0168852.

## SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

**Table S1.** Healthcare Common Procedure Coding System (HCPCS) codes to identify TAVR and SAVR in the Carrier file.

**Table S2.** Dementia and cognitive impairment (ICD-9 codes).

**Table S3.** Dementia and cognitive impairment (ICD-10 codes).

**Table S4.** Characteristics of patients undergoing AVR in those with and without ADRD.

**Figure S1.** Unadjusted mortality in patients with and without Alzheimer's disease and related dementias (ADRD) undergoing transcatheter aortic valve replacement (TAVR) and surgical aortic valve replacement (SAVR).

**How to cite this article:** Hollenbeck BK, Dunn RL, Sukul D, et al. Aortic valve replacement among patients with Alzheimer's disease and related dementias. *J Am Geriatr Soc*. 2021;69(12):3468-3475. doi:10.1111/jgs.17432