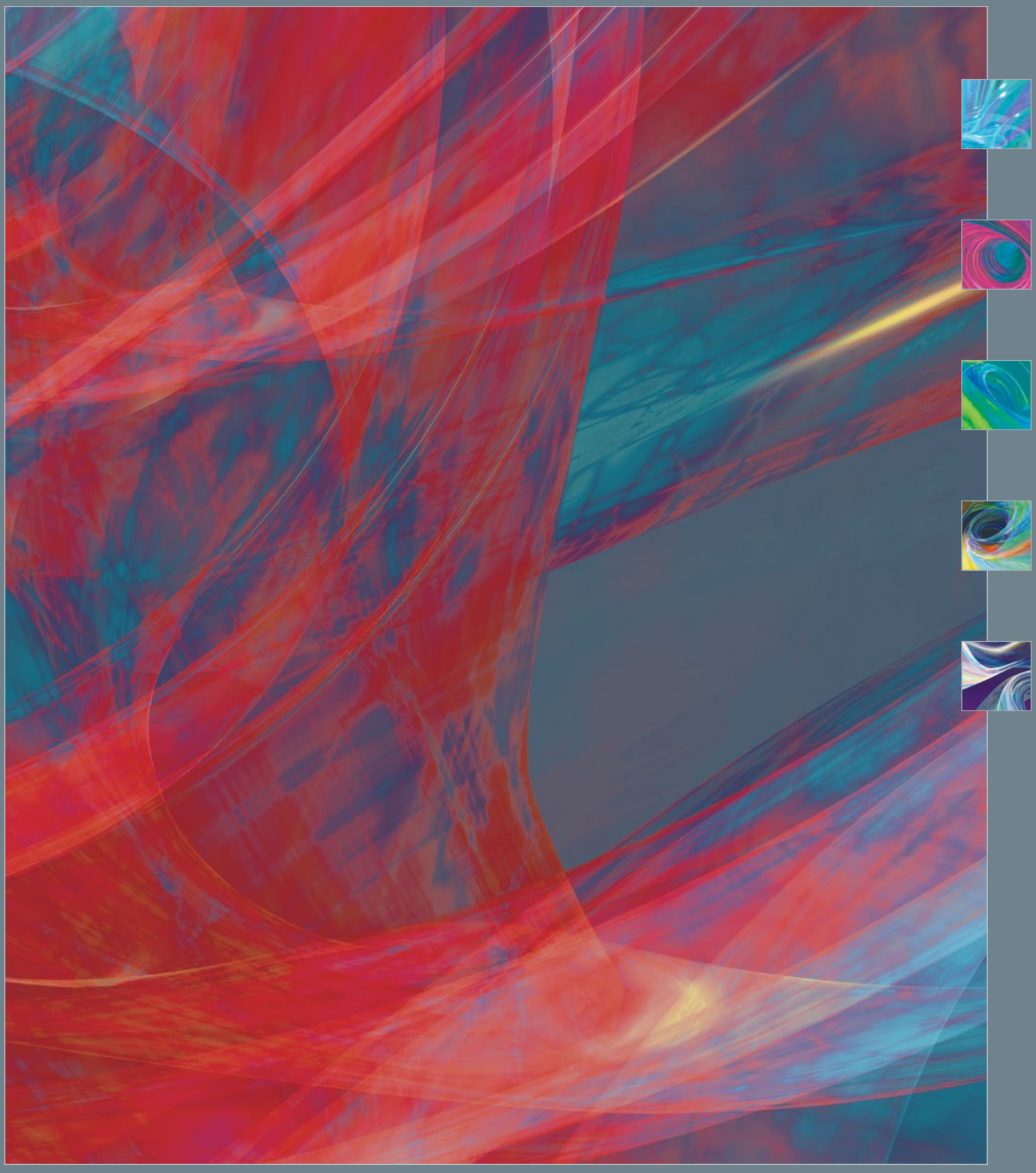
Alliance FOR AGING RESEARCH

Chronic Disease and Medical Innovation in an Aging Nation

The Silver Book®: Valve Disease



www.silverbook.org/valvedisease

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Introduction

The United States is a graying nation. The number of people ages 65 and older in the U.S. is projected to almost double by 2050 — from 43 million to 83.7 million. At that point, 20 percent of our population will be 65 years or older. With these shifting demographics come far-reaching and wide-ranging implications for our society, not the least of which is the potentially crippling effect of chronic and costly diseases that become more prevalent with age.

Chronic diseases and conditions impact 85 percent of Americans — many of whom spend their later years at medical visits, in extensive hospital stays, and dealing with disabilities and lost independence. Age-related diseases also impose a huge burden on our health care system and economy — costing our nation $1.7 trillion a year.

Heart valve disease is a leading type of cardiovascular disease that becomes more common with age, and imposes a significant burden on patients and their families. It involves damage to one or more of the heart's valves, interrupting blood flow and causing serious complications — including death. Every year, more than 25,000 people in the U.S. die from heart valve disease.

If diagnosed in time, heart valve disease can usually be successfully treated in patients of all ages. Advances in detection, valve repair and replacement through less-invasive procedures, and prevention of post-operative complications are all leading to better outcomes and survival in heart valve disease patients.

This latest addition to *The Silver Book*® series focuses the conversation on the burden of heart valve disease, as well as the value of continued investments in research that are leading to improvements in treatment and care. The Alliance for Aging Research publishes *The Silver Book*®: *Chronic Disease and Medical Innovation in an Aging Nation* to promote national policies for investments in research and innovation, which will ultimately bend the cost curve on chronic diseases of aging.

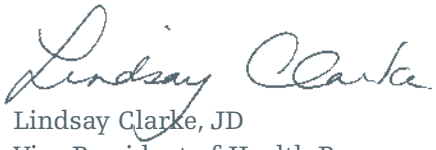
First launched in 2006, *The Silver Book* has become a trusted resource for policymakers, thought leaders, academics, and health advocates across the nation who are looking for the latest data on chronic diseases of aging and innovation in the field. *The Silver Book* is an almanac of compelling statistics and key findings extracted from dense reports and technical studies and provides essential information in a single, easy-to-use, and well-referenced resource. Previous volumes have included data

continued >

on cardiovascular disease (including stroke, thrombosis, aortic stenosis, and atrial fibrillation), cancer, diabetes, health care-associated infections, infectious diseases, neurological diseases (including Alzheimer's disease and Parkinson's disease), osteoporosis, persistent pain, and vision loss.

All of the data from this volume are available on-line at **www.silverbook.org/valvedisease,** and join the more than 3,000 facts and figures from hundreds of sources and experts. All facts are cited and provide easy access to the original source. Note that information pertaining specifically to the older population is in **silver type**.

Most importantly, the data from this volume of *The Silver Book* help illustrate why it's critical that research and innovation continue to pave the way for breakthroughs in heart valve disease.



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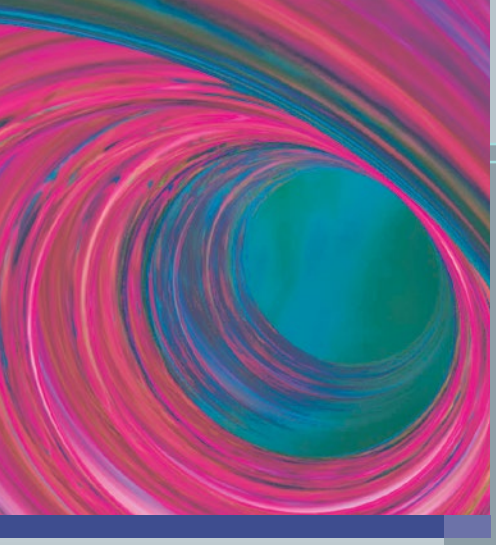


Cost of Valve Disease

A widely respected and cited study from Dr. Vuyisile Nkomo and colleagues estimates that in 2000 there were approximately five million Americans with heart valve disease. Based on current population estimates and other leading studies, that number is now somewhere between 8.7 million and 11.6 million. Even those numbers could be low since screening studies have revealed undiagnosed heart valve disease in as much as half of the population ages 65 and older.

Heart valve disease can affect any one of the heart's four valves, but the most common and deadly types impact the aortic and mitral valves. Repair or replacement of a valve is usually successful in patients of all ages — often extending lifespan and dramatically improving quality of life. But for patients who do not get treatment, or are managed with medicine only, the outcomes are quite different. In severe symptomatic aortic stenosis, those who do not undergo valve replacement have survival rates as low as 50 percent at two years, and 20 percent at five years after the onset of symptoms.

While valve disease can develop from congenital abnormalities and damage from certain types of infection, chest radiation, and other assaults on the heart that can occur at a younger age, heart valve disease is predominately a disease of older age. The risk of heart valve disease increases from less than 1 percent between the ages of 18 and 44, to 13.2 percent after age 75.

Heart valve disease takes its toll on the patient with increased hospitalization, loss of independence, and increased medical expenses. Currently, valve disease costs the U.S. $23.5 billion each year in direct healthcare expenditures alone. This burden is not going to abate anytime soon as significant heart valve disease will skyrocket with the aging of our population.

Prevalence & Incidence

- Published studies estimate that approximately 5 million people in the U.S. have heart valve disease. However, it may be as high as 8.7 to 11.6 million.

  Alliance for Aging Research generated statistics, based on year 2000 percentage prevalence estimates by Nkomo et al. 2006, *Burden of Valvular Heart Disease* AND Bach et al. 2007, *Prevalence, Referral Patterns, Testing, & Surgery in AVD* AND U.S. Census 2016, *American Fact Finder*

- Approximately 2.5% of the U.S. population is estimated to have heart valve disease:
  - 1.7% has mitral regurgitation
  - 0.1% has mitral stenosis
  - 0.5% has aortic regurgitation
  - 0.4% has aortic stenosis

  Nkomo et al. 2006, *Burden of Valvular Heart Disease*

- Prevalence estimates for heart valve disease are likely low. A U.K. population screening found previously undetected heart valve disease in 1 in 2 adults ages 65+.

  D'Arcy et al. 2016, *Large-Scale Community Echocardiographic Screening Reveals a Major Burden of Undiagnosed Valvular Heart Disease in Older People*

Aortic Valve Disease

- In 2016, an estimated 2.9 to 5.8 million adults in the U.S. had aortic valve disease.

  Alliance for Aging Research generated statistics, *based on 2000 percentage prevalence estimates by Nkomo et al. 2006, Burden of Valvular Heart Disease* AND Bach et al. 2007, *Prevalence, Referral Patterns, Testing, & Surgery in AVD* AND U.S. Census 2016, *American Fact Finder*

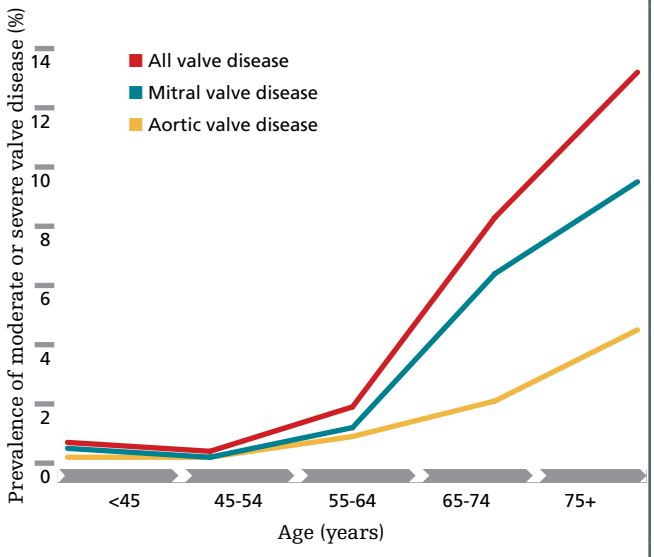
Mitral Valve Disease

- In 2016, an estimated 5.8 million adults in the U.S. had mitral valve disease — 5.49 million had mitral regurgitation and 323,127 had mitral stenosis.

  Alliance for Aging Research generated statistics, *based on year 2000 percentage prevalence estimates by Nkomo et al. 2006, Burden of Valvular Heart Disease* AND U.S. Census 2016, *American Fact Finder*

Age — A Major Risk Factor

Prevalence of Heart Valve Disease by Age

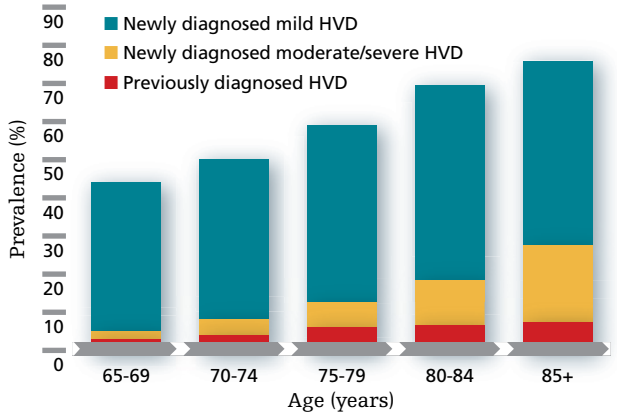


Nkomo et al. 2006, *Burden of Valvular Heart Disease.*

- Between the ages of 18 and 44, less than 1% of the U.S. population has heart valve disease. This increases to 8.5% between ages 65 and 74, and 13.2% after age 75.

  Nkomo et al. 2006. Burden of Valvular Heart Disease

Population Prevalence of Heart Valve Disease in U.K. According to Age



D'Arcy et al. 2016, *Large-Scale Community Echocardiographic Screening Reveals a Major Burden of Undiagnosed Valvular Heart Disease in Older People*

- **Facts in silver type deal specifically with older Americans.**

Aortic Valve Disease

- Moderate or severe aortic valve disease is present in 4.2% to 10.7% of the population ages 65 and older.

Nkomo et al. 2006, *Burden of Valvular Heart Disease* AND Bach et al. 2007, *Prevalence, Referral Patterns, Testing, & Surgery in AVD*

Mitral Valve Disease

- Mitral valve disease is present in 5.1% of the population ages 65 and older.

Nkomo et al. 2006, *Burden of Valvular Heart Disease*

Burden of Valve Disease

Human Burden

- Mortality and Any-Mention Mortality for Heart Valve Disease in 2014*

	2014 Mortality	2014 Any-Mention Mortality**
All Heart Valve Disease	25,114	51,005
Aortic Valve Disorders	17,136	34,408
Mitral Valve Disorders	2,344	5,366
Pulmonary Valve Disorders	15	50
Tricuspid Valve Disorders	24	105

*Based on ICD-10 Data
**Any-mention mortality means the condition was a contributing cause of death

Benjamin et al. 2017, *Heart Disease & Stroke Statistics-2017 Update*

- Hospital Discharges from Heart Valve Disease in 2010*

	2010 Hospital Discharges
All Heart Valve Disease	85,000
Aortic Stenosis	55,000
Mitral Valve Disorders	22,000

*Based on NHDS/NHCS data

Benjamin et al. 2017, *Heart Disease & Stroke Statistics-2017 Update*

Aortic Valve Disease

- Patients with severe symptomatic aortic stenosis (sSAS) who do not undergo valve replacement have survival rates as low as 50% at two years and 20% at five years after the onset of symptoms.

Otto 2000, *Timing of Aortic Valve Surgery*

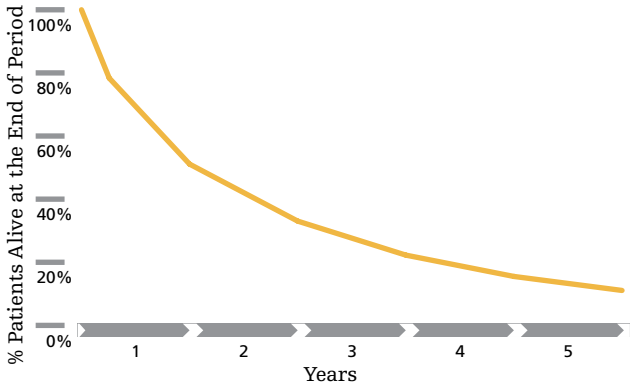
- Medicare patients with sSAS who do not undergo treatment have an average lifespan of 1.8 years.

Clark et al. 2012, *Five-Year Clinical and Economic Outcomes Among Patients with Medically Managed SAS*

- Waiting for treatment for sSAS can be deadly, with 1-month mortality at 3.7% and 6-month mortality at 11.6% (measured from the time intervention was recommended).

Malaisrie et al. 2014, *Mortality While Waiting for AVR*

- Survival Rates Over 5 Years for Patients with Medically Managed Severe Aortic Stenosis



Clark et al. 2012, *Five-Year Clinical and Economic Outcomes Among Patients with Medically Managed SAS*

- Medicare sSAS patients who do not undergo treatment have an average of 1.9 hospital admissions per year and prolonged lengths of stay — 11.5 hospital days per patient-year.

Clark et al. 2012, *Five-Year Clinical and Economic Outcomes Among Patients with Medically Managed SAS*

- Five-Year Health Care Resource Use in Medically Managed SAS Patients

Resource	Resource Use
Acute inpatient hospitalization	100%
Hospitalizations	4.4 (mean)
Hospital days	26.7 (mean)
Long-term care hospital	3.4%
Inpatient rehab facility	9.5%
Skilled nursing facility	52%
Skilled nursing days	25.5 (mean)
Hospice care	27.6%
Home health care	57.4%
Outpatient hospital care	84.2%
Physician services	100%
Durable medical equipment use	70.9%
Dialysis services	5.7%

Clark et al. 2012, *Five-Year Clinical and Economic Outcomes Among Patients with Medically Managed SAS*

- High risk aortic stenosis patients in one study experienced higher rates of myocardial infarction compared to non-high-risk patients (4.8% versus 2.0%) and higher rates of strokes (7.5% versus 6.6%).

Clark et al. 2012, *Clinical and Economic Outcomes After Surgical Aortic Valve Replacement in Medicare Patients*

Mitral Valve Disease

- Patients diagnosed with severe mitral regurgitation who do not undergo surgery have mortality rates of 20% after 1-year and 50% after 5-years.

Goel et al. 2014, *Prevalence and Outcomes of Unoperated Patients with Severe Symptomatic Mitral Regurgitation and Heart Failure*

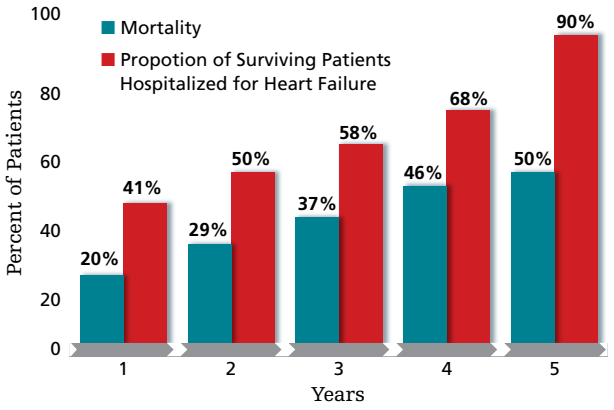
- Only 1 in 40 patients with moderate or severe mitral regurgitation undergoes surgical treatment.

Moore et al. 2016, *The Direct Health-Care Burden of Valvular Heart Disease*

- The proportion of surviving mitral regurgitation patients hospitalized for heart failure increases from 41% in the first year to 90% by 5 years.

Goel et al. 2014, *Prevalence and Outcomes of Unoperated Patients with Severe Symptomatic Mitral Regurgitation and Heart Failure*

- Mortality and rates of hospitalization for heart failure in unoperated patients with severe mitral regurgitation



Goel et al. 2014, *Prevalence and Outcomes of Unoperated Patients with Severe Symptomatic Mitral Regurgitation and Heart Failure*

- Mitral regurgitation patients who did not undergo surgery saw an increased use of medical therapies from 12% to 47% over 4.5 years.

Goel et al. 2014, *Prevalence and Outcomes of Unoperated Patients with Severe Symptomatic Mitral Regurgitation and Heart Failure*

- Pulmonary hypertension is a complication in at least 23% of patients with significant mitral regurgitation due to flail leaflet, and approximately doubles the risk of death and heart failure after diagnosis.

Barbieri et al. 2011, *Prognostic and Therapeutic Implications of Pulmonary Hypertension Complicating Degenerative Mitral Regurgitation Due to Flail Leaflet*

Economic Burden

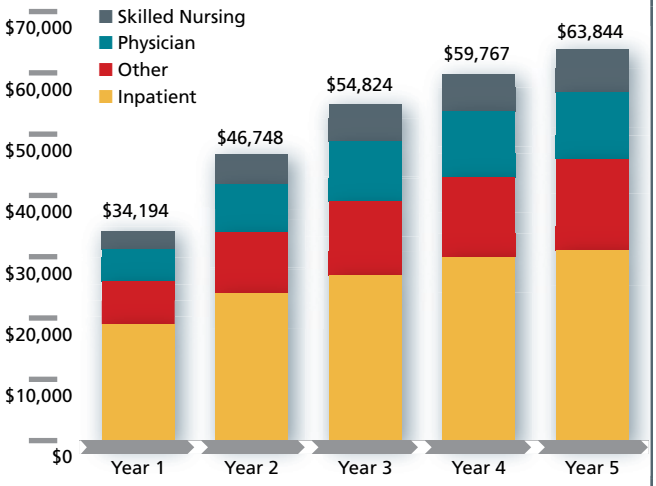
- Heart valve disease costs the U.S. $23.4 billion each year in direct health care expenditures.

Moore et al. 2016, *The Direct Healthcare Burden of Valvular Heart Disease*

- The annual total incremental per patient health care expenditures for heart valve disease patients ranged from $1,755 in 1996 to $12,789 in 2011.

Moore et al. 2016, *The Direct Healthcare Burden of Valvular Heart Disease*

Aortic Valve Disease



Clark et al. 2012, *Five-Year Clinical and Economic Outcomes Among Patients with Medically Managed Severe Aortic Stenosis*

- Symptomatic aortic valve disease costs the U.S. at least $5.6 billion in direct health care expenditures each year.

  Moore et al. 2016, *The Direct Healthcare Burden of Valvular Heart Disease*

- Asymptomatic aortic valve disease costs the U.S. at least $4.6 billion in direct health care expenditures each year.

  Moore et al. 2016, *The Direct Healthcare Burden of Valvular Heart Disease*

- SAS patients who do not undergo treatment have limited lifespans and cost Medicare as much as $1.3 billion each year due to rehospitalization, prolonged stays, admissions to skilled nursing facilities, and use of hospice care.

  Clark et al. 2012, *Five-Year Clinical and Economic Outcomes Among Patients with Medically Managed SAS*

Mitral Valve Disease

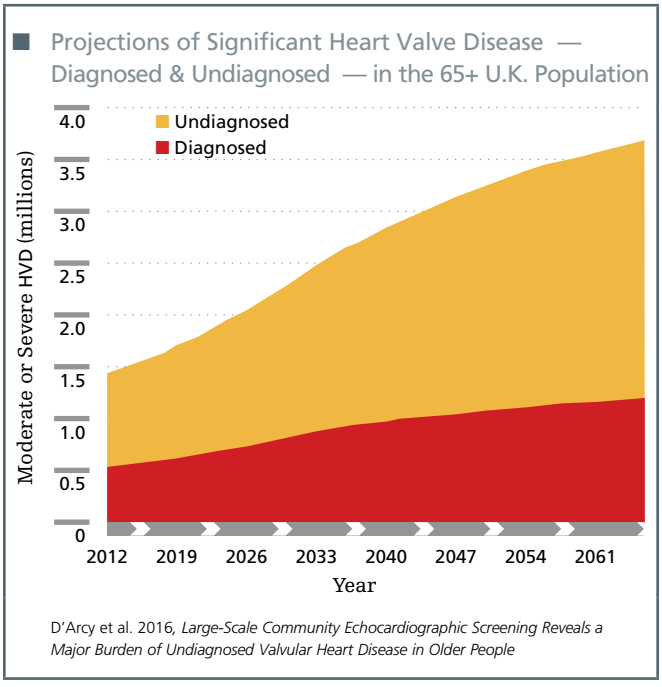
- Symptomatic mitral valve disease costs the U.S. at least $7.6 billion in direct healthcare expenditures each year.

  Moore et al. 2016, *The Direct Healthcare Burden of Valvular Heart Disease*

- Asymptomatic mitral valve disease costs the U.S. at least $5.6 billion in direct healthcare expenditures each year.

  Moore et al. 2016, *The Direct Healthcare Burden of Valvular Heart Disease*

Future Burden



D'Arcy et al. 2016, *Large-Scale Community Echocardiographic Screening Reveals a Major Burden of Undiagnosed Valvular Heart Disease in Older People*

- The number of elderly patients with sSAS in North America is expected to increase from 540,000 patients in 2012 to 800,000 in 2025 and 1.4 million in 2050.

  Osnabrugge et al. 2013, *Aortic Stenosis in the Elderly*

Investing in Science

Innovative Medical Research

In recent years, the heart valve disease field has experienced tremendous advances in improving survival, recovery, and quality of life for patients. We are fortunate to be living in a time where ground-breaking technologies, such as minimally invasive treatments for valve repair and replacement, are increasingly available and accessible. For example, transcatheter aortic valve replacement, or TAVR, and mitral valve repair and replacement — and increasingly personalized treatments — are giving hope to patients at previously prohibitive surgical risk, and drastically reducing recovery times and complications.

Advances like these have also created a positive space around heart valve repair and replacement procedures, allowing patients to feel more confident when choosing to go through treatment. Patient satisfaction rates among aortic and mitral valve disease surgery patients are at an all-time high, with 96 percent of patients reporting "full satisfaction" post-procedure.

Medical advances that help detect and treat heart valve disease in a timely manner far outweigh the initial financial investments in research. The national debate on the cost and value of health care is more pressing than ever, and it's imperative that we consider both the financial and human impact that innovation can have on an often-life-threatening disease. Limited efforts to reduce spending too often target the initial expenses of innovation while ignoring the remarkable returns on investment that will continue to impact the older population in the years to come.

Human Value

- Among treated heart valve disease patients, 96% express "full satisfaction" and 78% are "very satisfied" with their treatment.

  BRS. 2016, *Report of Findings from Opinion Research Among HVD Patients*

Aortic Valve Disease

- In 2010, ~67,500 surgical aortic valve replacements (SAVR) were performed in the U.S.

  Clark et al. 2012, *Clinical and Economic Outcomes After SAVR in Medicare Patients*

- Patients with SAS ages 80+ who underwent SAVR have 1-year, 2-year, and 5-year survival rates of 87%, 78%, and 68% respectively — compared with 52%, 40%, and 22% for those patients who did not have surgery.

  Varadarajan et al. 2006, *Survival in Elderly Patients with SAS is Dramatically Improved by AVR*

- At 1-year, sSAS patients with intermediate surgical mortality risk who underwent transcatheter aortic valve replacement (TAVR), had all-cause mortality rates of 7.4% (compared to 13% for SAVR), disabling stroke rates of 2.3% (compared to 5.9% for SAVR), and rehospitalization rates of 11.4% (compared to 15.1% for SAVR).

  Thourani et al. 2016, *TAVR versus SAVR in Intermediate-Risk Patients*

- From approval in 2011 through 2015, >54,000 TAVRs were performed in 418 centers in 48 states.

  Grover et al. 2017, *2016 Annual Report of The STS/ACC Transcatheter Valve Therapy Registry*

- A study of sSAS patients who received TAVR found 30-day mortality of 2.2% for those who were at high risk of surgical mortality/inoperable, and 1.1% for those at intermediate surgical mortality risk.

  Kodali et al. 2016, *Early Clinical and Echocardiographic Outcomes after SAPIEN 3 TAVR in Inoperable, High-Risk and Intermediate-Risk Patients with AS*

- Symptomatic SAS patients who underwent TAVR experienced quality of life (QoL) improvements from 5.3 baseline (10-point scale with 10=best imaginable health state) to 6.7 at one year and 7.4 at four years.

  Kovac 2016, *Four-Year Experience with the CoreValve Transcatheter Heart Valve*

- TAVR and SAVR in intermediate-risk SAS patients were associated with significant improvements in disease specific status (38%) and in generic health status (31%).

  Baron et al. 2017, *Health Status Benefits of Transcatheter vs Surgical Aortic Valve Replacement in Patients with SAS at Intermediate Surgical Risk*

Mitral Valve Disease

- The volume of mitral valve surgical procedures increased approximately 8.3% from 2010 to 2013.

  Stuntz 2016, *Mitral Valve Disease in the United States*

- Survival rates for mitral valve repair patients 65-75 years of age at 1-year and 5-years are 93.6% and 83.3% respectively.

  Vassileva et al. 2013, *Long-Term Survival of Patients Undergoing Mitral Valve Repair and Replacement*

- The 1-year and 5-year survival estimates for patients 65-75 years old undergoing mitral valve replacement are 85.9% and 70.7%.

  Vassileva et al. 2013, *Long-Term Survival of Patients Undergoing Mitral Valve Repair and Replacement*

- The rate of hospitalization from heart failure before and after transcatheter mitral valve repair (TMVR) decreases 73% (per patient year) in patients at prohibitive surgical risk.

  Lim et al. 2014., *Improved Functional Status and Quality of Life in Prohibitive Surgical Risk Patients with Degenerative Mitral Regurgitation After Transcatheter Mitral Valve Repair*

Economic Value

Aortic Valve Disease

- A study of 4,617 patients who underwent aortic valve replacement found significant gains in life expectancy and quality of life — over a period of 20 years there were 43,166 net life-years gained at a net value of $11.2 billion (~$14.2 billion in 2017 dollars).

  Wu et al. 2007, *The Value of Aortic Valve Replacement in Elderly Patients* AND Bureau of Labor Statistics, *CPI Inflation Calculator*

- The cost-effectiveness ratio for SAVR — compared to no surgery — was estimated at $13,528 per quality-adjusted life year (QALY) (~$17,226 in 2017 dollars).

  Wu et al. 2007, *Cost-Effectiveness of AVR in the Elderly* AND Bureau of Labor Statistics, *CPI Inflation Calculator*

- Patients with sSAS considered to be at high surgical risk who underwent TAVR, experienced lifetime incremental cost-effectiveness ratios of $55,090 per QALY gained and $43,114 per life-year (LY) gained.

  Reynolds 2016, *Cost-Effectiveness of TAVR with a Self-Expanding Prosthesis Versus SAVR*

Conclusion

The Silver Book®: Valve Disease shares the latest data on the staggering human and economic burden of valve disease in America, and verifies that innovation is the key to lessening that burden on the nation's older population. However, while new data is continuing to develop on the value of advances in the field, there is still a lack of economic projections that address the future burden of valve disease and that consider the value of new innovations. As less-invasive treatment options are considered for use earlier in the disease course, research on heart valve disease screening and detection options should broaden. Additionally, research is needed to better understand the risk factors, incidence, and treatment access barriers for heart valve disease in minority populations.

As always, any new data will be included in *The Silver Book* on-line at **www.silverbook.org/valvedisease.** We hope that this new edition on valve disease joins the existing *Silver Book* publications as an invaluable tool that encourages advocacy and policies that support investments in medical research and innovation.

Lastly, we must not ignore how long-term plans for research will reduce both the human and economic burdens that have been imposed by heart valve disease in the past. Time and time again, investments that yield novel medical innovations have paid for themselves many times over through reduced medical expenditures and increased patient outcomes. Heart valve disease research will not be the exception and is vital to enhancing the quality of life for older generations now, and in the years to come.

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