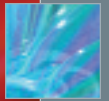
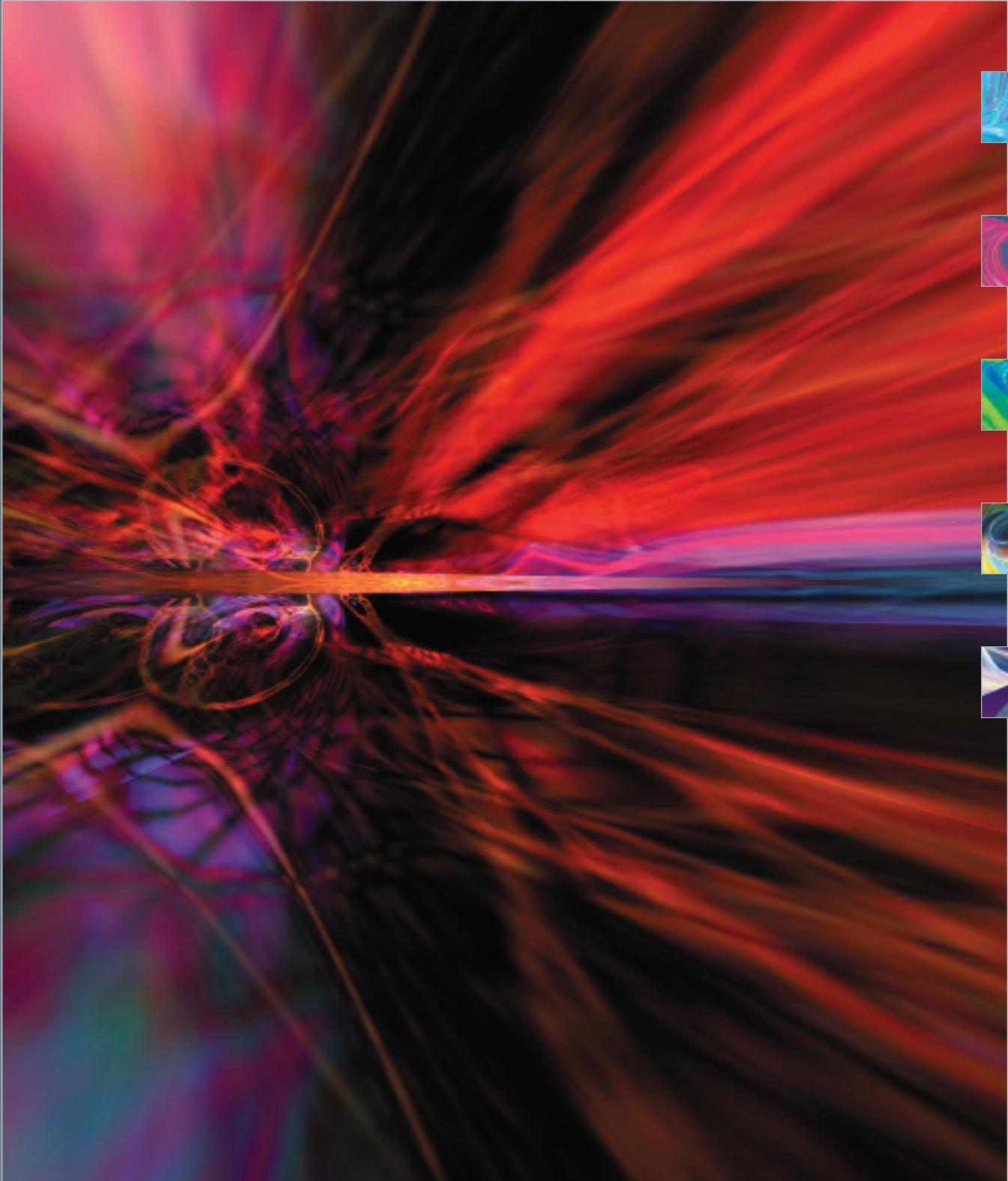
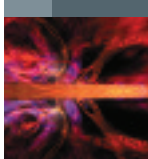
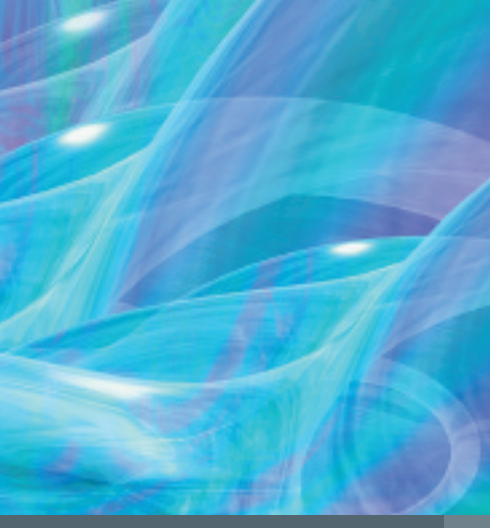


*Chronic Disease and Medical Innovation in an Aging Nation*

# The Silver Book<sup>®</sup>: **Thrombosis**







# Introduction

Introduction 

Cost of Thrombosis 

Innovative Medical Research 

Conclusion 

References 

Americans are living longer than ever before, but the added years of life are not often enjoyed in excellent health. Eighty percent of Americans age 65 and older have at least one chronic health condition that often leads to extensive hospital stays and medical visits, lost independence, and disabilities. Age-related diseases also impose a huge burden on our nations' health care system and the U.S. economy itself. With the leading edge of the Baby Boomers now entering the Medicare rolls, policymakers are urgently searching for ways to curb health care spending.

In order to promote national policies that will look to investing in innovation rather than short-sighted cost-cutting, the Alliance for Aging Research publishes *The Silver Book®: Chronic Disease and Medical Innovation in an Aging Nation*. *The Silver Book* is an almanac of compelling statistics that spotlight this mounting burden of chronic diseases, as well as the promise of innovation in mitigating that burden. While much of this information is buried in dense reports and diverse technical studies, *The Silver Book* extracts the key findings and provides essential information in a single, easy-to-use, and well-referenced resource.

First launched in 2006, *The Silver Book* and subsequent volumes have become a trusted resource for policymakers and thought leaders. This newest volume includes data on atrial fibrillation (AF), stroke\*, and venous thromboembolism (VTE)—three common *causes of* and *results of* thrombosis. While there are numerous different types of thrombosis, these three were chosen for this volume because they all disproportionately impact older Americans (**note that information pertaining specifically to the older population is in silver type**), and because the available data illustrates the burden of thrombosis and makes a compelling case for innovation. All sources are cited for easy integration into presentations and work, and for easy access to the original source. All data are also available on-line at [www.silverbook.org](http://www.silverbook.org); a site that is easily searchable and regularly updated. >

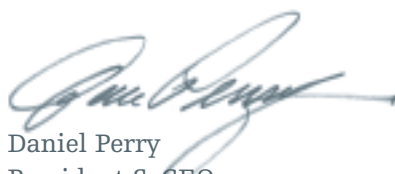
\*When possible stroke statistics are specific to ischemic stroke; however, data that does not specify stroke type are included.



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Each year around 75,000 Americans are diagnosed with AF, 900,000 experience a VTE event, and 800,000 have a stroke. Some 2 million Americans die from thrombosis or its consequences. The burden for those who survive is enormous and the cost of care a major expense for individuals and the nation. Stroke alone costs around \$73.7 billion annually. Fortunately research advances are offering significant hope. A number of investigative anticoagulants have the potential to reduce strokes in AF patients while also reducing the risk of bleeds; clot-dissolving agents are proving to lessen the effects of strokes; and the same drugs in the pipeline for AF could prevent VTE after major orthopedic surgery.

Advances in thrombosis continue to offer breakthroughs, making it critical that we ensure support and incentives for future research, and that innovation remain the bedrock of good public policy. By bringing this resource to those shaping public health policy, the Alliance for Aging Research aims to enrich the national debate on health care and on chronic diseases of aging.

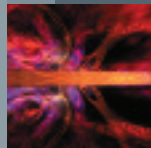
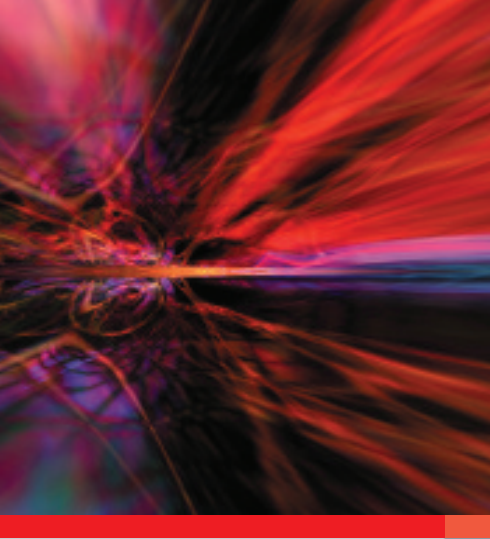


Daniel Perry  
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**Advancing Science. Enhancing Lives.**

[www.silverbook.org/thrombosis](http://www.silverbook.org/thrombosis)  
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*Chronic Disease and Medical Innovation in an Aging Nation*

# The Silver Book<sup>®</sup>: Thrombosis

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*The Human and Economic Burden*

## Cost of Thrombosis

■ Each year, close to 1.8 million Americans are diagnosed with atrial fibrillation, have a stroke, or experience a venous thromboembolism event. These diseases can all be *caused by* or be the *result of* thrombosis—the formation of a blood clot in a blood vessel. While these are not the only forms of thrombosis, they are some of the most common and they all tend to strike later in life.

■ An estimated 600,000 people die from these diseases each year and those that survive often face continued illness and disability—not to mention the extensive office and ER visits, hospital stays, and outpatient appointments. Stroke survivors are a good example with a significant risk of one-sided paralysis, difficulty speaking, depression, trouble with activities of daily living, and eventually nursing home admissions.

■ Those that survive also face staggering health care bills. Medicare alone is estimated to pay \$15.7 billion a year to treat newly diagnosed atrial fibrillation patients. For those that develop venous thromboembolism after orthopedic surgery, the bills are as much as \$13,000 higher than those who don't. And stroke alone saddles the nation with \$73.7 billion in direct and indirect costs each year.

Advancing age is a significant risk factor for all of these diseases. They not only become more common with age, but are also more difficult and costly to manage in the elderly due to comorbid conditions and the increased risk of drug interactions and serious complications.

We are fortunate to be at a time where new treatments to prevent and treat thrombosis and its consequences are being discovered at a promising pace. However, without significant advances, the associated costs will continue to rise as our nation ages and a growing number of Americans face these diseases. For instance, while there are an increasing number of anticoagulants that help prevent stroke in atrial fibrillation patients, these drugs still carry a high risk of bleeding which is poorly understood in a lot of ways—including how age plays a role. Unless research advances, in this and other areas of thrombosis, are well financed and rewarded, the personal and public costs of these diseases will continue to become an increasing burden on the nation.

## Prevalence and Incidence of Thrombosis

### Atrial Fibrillation

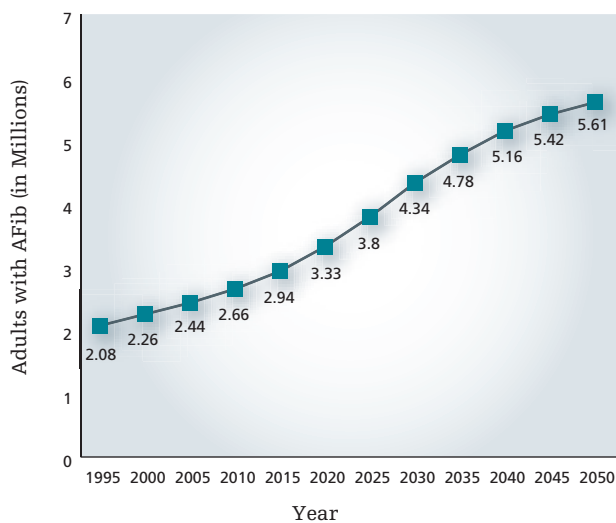
- An estimated 2.66 million Americans currently have atrial fibrillation.

Go et al. 2001, *Prevalence of Diagnosed Atrial Fibrillation in Adults*

- As much as 1% of the U.S. population is estimated to have atrial fibrillation.

Fuster et al. 2006, *ACC/AHA/ESC 2006 Guidelines for the Management of Patients with Atrial Fibrillation*

- Atrial Fibrillation is Increasingly Prevalent in the United States



Go et al. 2001, *Prevalence of Diagnosed Atrial Fibrillation in Adults*

- The lifetime risk of developing atrial fibrillation is around 1 in 4 for both men and women age 40 and older.

Lloyd-Jones et al. 2004, *Lifetime Risk for Development of Atrial Fibrillation*

### Venous Thromboembolism (VTE)

- More than 900,000 incident or recurrent, fatal and nonfatal, venous thromboembolism events occur each year.

Heit et al. 2005, *Estimated Annual Number of Incident and Recurrent, Non-Fatal and Fatal VTE Events*

- Around 200,000 of the venous thromboembolism events each year are new cases.

Heit 2002, *Venous Thromboembolism Epidemiology*

- Venous thromboembolism occurs for the first time in around 100 per 100,000 people each year.

White 2003, *The Epidemiology of Venous Thromboembolism*

- Around 60% of all venous thromboembolism cases are in hospitalized patients and nursing home residents.

Heit et al. 2002, *Relative Impact of Risk Factors for Deep Vein Thrombosis and Pulmonary Embolism*

### Stroke

- An estimated 7,000,000 Americans age 20 and older have had a stroke.

Roger et al. 2011, *Heart Disease and Stroke Statistics—2011 Update*

- Every year, around 795,000 Americans have a stroke—around 610,000 are first time strokes and 185,000 are recurrent attacks.

Roger et al. 2011, *Heart Disease and Stroke Statistics—2011 Update*

- Every 40 seconds, on average, someone in the U.S. has a stroke.

Roger et al. 2011, *Heart Disease and Stroke Statistics—2011 Update*

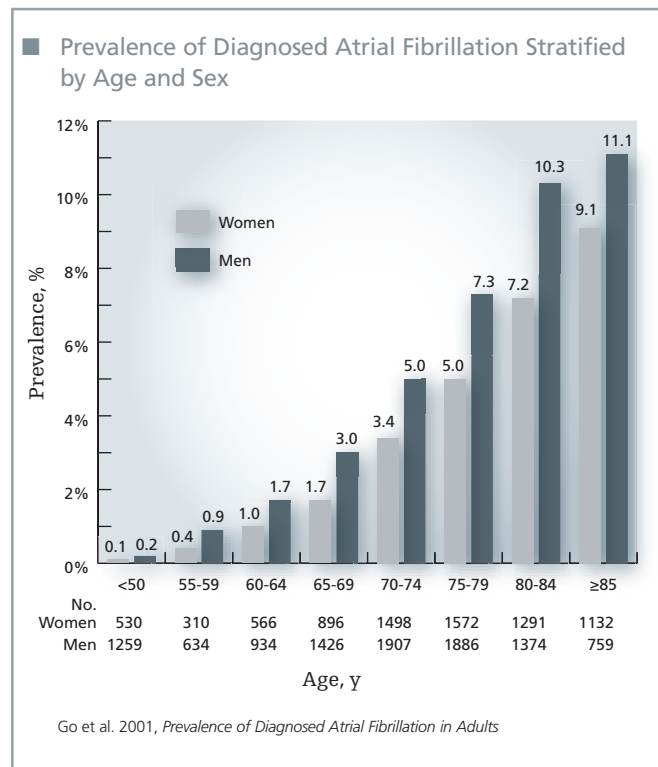
- Around 87% of all strokes are ischemic.

NHLBI 2006, *Incidence and Prevalence*

## Age—A Major Risk Factor

### Atrial Fibrillation

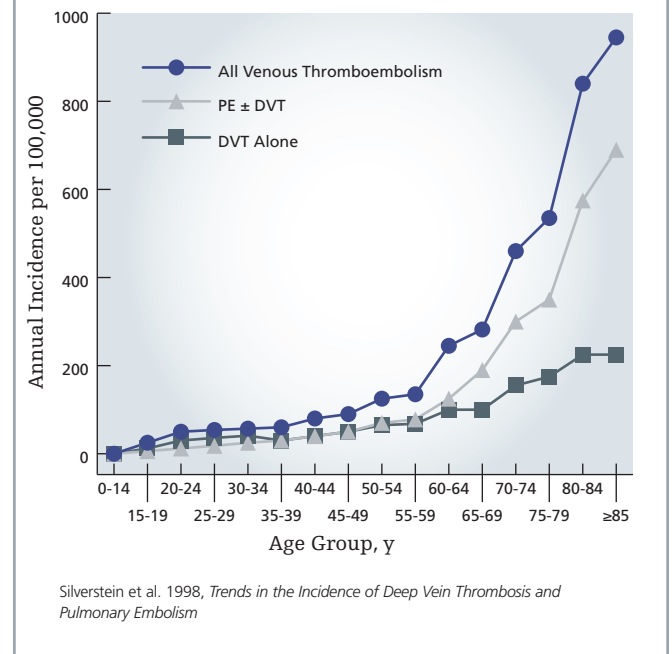
- The median age of people with atrial fibrillation is about 75 years.  
*Go et al. 2001, Prevalence of Diagnosed Atrial Fibrillation in Adults*
- Atrial fibrillation prevalence doubles with each decade of age—reaching close to 9% by age 80.  
*Go et al. 2001, Prevalence of Diagnosed Atrial Fibrillation in Adults*
- Atrial fibrillation affects around 1 in 25 Americans age 60 and older, increasing to close to 1 in 10 adults by age 80.  
*Go et al. 2001, Prevalence of Diagnosed Atrial Fibrillation in Adults*
- Around 82% of Americans with atrial fibrillation are age 65 and older. Around 37% are age 80 and older.  
*Go et al. 2001, Prevalence of Diagnosed Atrial Fibrillation in Adults*
- At age 80, the remaining lifetime risk of atrial fibrillation is around 22%.  
*Lloyd-Jones et al. 2004, Lifetime Risk for Development of Atrial Fibrillation*



### Venous Thromboembolism (VTE)

- Incidence of venous thromboembolism increases significantly with age—from less than 5 cases per 100,000 people ages 15 and younger, to around 500 cases per 100,000 people ages 80 and older.  
*White 2003, The Epidemiology of Venous Thromboembolism*

- Annual incidence of all thromboembolism, deep vein thrombosis (DVT) alone, and pulmonary embolism (PE) with or without deep vein thrombosis (PE ± DVT) among residents of Olmsted County, Minnesota, from 1966 to 1990, by age







## Stroke

- Stroke prevalence increases with age—the rate at ages 85 to 94 is 3.5 times higher than at ages 65 to 74.

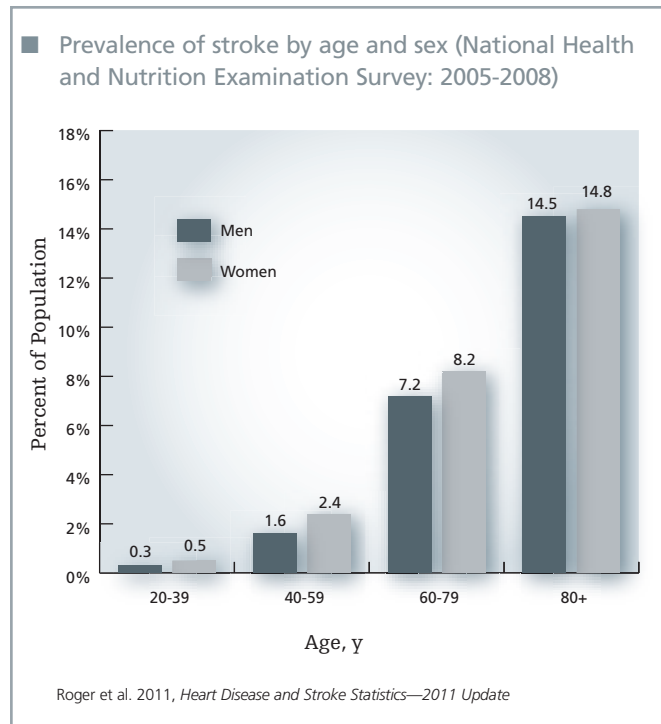
NHLBI 2006, *Incidence and Prevalence, 2006 Chart Book on Cardiovascular & Lung Diseases*

- In 2002, the mean age at death from stroke was 79.6 years.

CDC 2005, *Disparities in Deaths from Stroke Among Persons Aged <75 Years*

- Thirty-day mortality rates after stroke increase with age—from 9% in Medicare beneficiaries ages 65 to 74, to 13.1% in beneficiaries ages 74 to 84, to 23% in beneficiaries 85 and older.

Casper et al. 2008, *Atlas of Stroke Hospitalizations Among Medicare Beneficiaries*



## The Burden of Thrombosis

### The Human Burden

#### Atrial Fibrillation

- Atrial fibrillation is a contributory cause of death for around 93,000 Americans each year.

Roger et al. 2011, *Heart Disease and Stroke Statistics—2011 Update*

- Around 84% of all deaths with atrial fibrillation as a contributory cause are in individuals age 75 and older.

CDC 2003, *Atrial Fibrillation as a Contributing Cause of Death and Medicare Hospitalization*

- Atrial fibrillation is associated with an approximate doubling of mortality risk.

Fuster et al. 2006, *ACC/AHA/ESC 2006 Guidelines for the Management of Patients with Atrial Fibrillation*

- Of Medicare beneficiaries who receive an atrial fibrillation diagnosis, 1 in 4 will die within a year.

Piccini et al. 2010, *Incidence of Atrial Fibrillation and Associated Mortality Among Medicare Beneficiaries*

- Within the first 4 months of diagnosis of atrial fibrillation, the most common cause of cardiovascular deaths are coronary artery disease (22%), heart failure (14%), and ischemic stroke (10%). After 4 months of diagnosis, coronary artery disease is responsible for 15% of deaths, heart failure is responsible for 16%, and stroke is responsible for 7%.

Miyasaka et al. 2007, *Mortality Trends in Patients Diagnosed with First Atrial Fibrillation*



- Heart failure was listed as the primary diagnosis for 11.8% of patients hospitalized with atrial fibrillation (AF). Coronary heart disease was listed for 9.9% of AF patients, and stroke was listed for 4.9%.

CDC 2003, *Atrial Fibrillation as a Contributing Cause of Death and Medicare Hospitalization*

- A study of Medicare beneficiaries found that those with atrial fibrillation (AF) were significantly more likely to experience heart failure than their non-AF counterparts (36.7% versus 10.4%).

Lee et al. 2008, *Direct Treatment Cost of Atrial Fibrillation in the Elderly American Population*

- The risk of ischemic stroke in nonvalvular atrial fibrillation patients is 2 to 7 times (200% to 700%) greater than in those without the disease.

Fuster et al. 2006, *ACC/AHA/ESC 2006 Guidelines for the Management of Patients with Atrial Fibrillation*

- Atrial fibrillation is responsible for at least 15% to 20% of all ischemic strokes.

Go 2005, *The Epidemiology of Atrial Fibrillation in Elderly Persons*

- Atrial fibrillation accounts for between 75,000 and 100,000 strokes per year.

Wolf et al. 1991, *Atrial Fibrillation as an Independent Risk Factor for Stroke*

- Atrial fibrillation (AF) increases the risk of severe and recurrent ischemic stroke. Patients not treated with anticoagulants have a 2.1-fold increase in risk of recurrent stroke and 2.4-fold increase in risk of recurrent severe stroke.

Penado et al. 2003, *Atrial Fibrillation as a Risk Factor for Stroke Recurrence*

- The risk of stroke attributable to atrial fibrillation increases from 1.5% for those ages 50 to 59 to 23.5% for those ages 80 to 89.

Wolf et al. 1998, *Impact of Atrial Fibrillation on Mortality, Stroke, and Medical Costs*

- Close to half of all atrial fibrillation associated strokes occur in patients age 75 and older.

Fuster et al. 2006, *ACC/AHA/ESC 2006 Guidelines for the Management of Patients with Atrial Fibrillation*

- In 2001, atrial fibrillation was the cause of around:

- 350,000 hospitalizations
- 5 million office visits
- 276,000 emergency department visits
- 234,000 out-patient visits

Coyne et al. 2006, *Assessing the Direct Costs of Treating Nonvalvular Atrial Fibrillation in the United States*

- A study of Medicare beneficiaries found that during the year following an atrial fibrillation (AF) diagnosis:

- 28% of AF patients (versus 7% of non-AF patients) had 3 or more hospital admissions
- 14% of AF patients (versus 3% of non-AF patients) had 3 or more emergency room visits
- 72% of AF patients (versus 61% of non-AF patients) had 3 or more outpatient visits

Lee et al. 2008, *Direct Treatment Cost of Atrial Fibrillation in the Elderly American Population*

- Individuals with atrial fibrillation (AF) are 4 times more likely to visit the hospital 3 or more times in the year following an AF diagnosis—compared to those without the disease.

Lee et al. 2008, *Direct Treatment Cost of Atrial Fibrillation in the Elderly American Population*

- In the year following initial hospitalization for atrial fibrillation (AF), 12.5% of chronic AF patients were readmitted for AF—17.6% of readmissions occurred within 1 month. Among newly-diagnosed patients, 10.1% were readmitted—22.7% of readmissions occurred within 1 month.

Kim et al. 2009, *Incidence and Temporal Pattern of Hospital Readmissions for Patients with Atrial Fibrillation*

- Around 1/3 of atrial fibrillation patients have elevated levels of depression and anxiety.

Thrall et al. 2007, *Depression, Anxiety, and Quality of Life in Patients with Atrial Fibrillation*

### Venous Thromboembolism (VTE)

- Venous thromboembolism causes an estimated 300,000 deaths each year.

Heit et al. 2005, *Estimated Annual Number of Incident and Recurrent, Non-Fatal and Fatal VTE Events*

- About 1 in 8 patients who develop venous thromboembolism in the hospital will die as a result.

Anderson et al. 1991, *A Population-Based Perspective of the Hospital Incidence and Case-Fatality Rates of DVT and PE*



- The number of in-hospital deaths that are caused by venous thromboembolism is more than five times the number of deaths caused by all hospital-acquired infections.

House of Commons Health Committee 2005, *The Prevention of Venous Thromboembolism in Hospitalised Patients*

- More than 59% of the 300,000 people who die from venous thromboembolism in the U.S. each year have undetected pulmonary embolism.

Heit et al. 2005, *Estimated Annual Number of Incident and Recurrent, Non-Fatal and Fatal VTE Events*

- More than 50% of all cases of venous thromboembolism in the community can be attributed to institutionalization.

Heit et al. 2002, *Relative Impact of Risk Factors for Deep Vein Thrombosis and Pulmonary Embolism*

- Around one-third of patients with symptomatic venous thromboembolism manifest pulmonary embolism. Two-thirds manifest deep vein thrombosis alone. Death occurs within 1 month of diagnosis in approximately 6% of deep vein thrombosis cases and 12% of pulmonary embolism cases.

White 2003, *The Epidemiology of Venous Thromboembolism*

- Of the more than 200,000 new cases of venous thromboembolism (VTE) that occur each year, 30% die within 30 days, 20% suffer a sudden death from pulmonary embolism, and around 30% of survivors develop recurrent VTE within 10 years.

Heit 2002, *Venous Thromboembolism Epidemiology*

- An estimated 250,000 patients are hospitalized each year with venous thromboembolism.

Goldhaber 1998, *Pulmonary Embolism*

- The mean length of stay for patients hospitalized after major orthopedic surgery was more than twice as long for patients with venous thromboembolism (VTE)—as compared to those without VTE. VTE patients were also often admitted to intensive care—17.2% of patients with deep vein thrombosis and 36.2% of those with pulmonary embolism.

Ollendorf et al. 2002, *Cost of Venous Thromboembolism Following Major Orthopedic Surgery in Hospitalized Patients*

- The mean length of stay in the intensive care unit for patients hospitalized after major orthopedic surgery was roughly ten times longer for patients who developed venous thromboembolism.

Ollendorf et al. 2002, *Cost of Venous Thromboembolism Following Major Orthopedic Surgery in Hospitalized Patients*

- Hip and knee replacement surgeries significantly raise the risk of venous thromboembolism—without prophylaxis around half develop deep vein thrombosis and 1% to 2% develop pulmonary embolism.

Haake & Berkman 1989, *Venous Thromboembolic Disease after Hip Surgery*

### Stroke

- Stroke is the third most common cause of death in the United States, when considered separately from other cerebrovascular diseases.

Roger et al. 2011, *Heart Disease and Stroke Statistics—2011 Update*

- One in every 18 deaths in the United States is caused by stroke.

Roger et al. 2011, *Heart Disease and Stroke Statistics—2011 Update*

- Stroke is a contributory cause of death for around 230,000 people each year.

Roger et al. 2011, *Heart Disease and Stroke Statistics—2011 Update*

- The mean age at death from stroke was 79.6 in 2002.

CDC 2005, *Disparities in Deaths from Stroke Among Persons Aged <75 Years*

- Within 30 days of ischemic stroke, 8.1% of people age 65 and older were dead.

El-Saed et al. 2006, *Geographic Variations in Stroke Incidence and Mortality Among Older Populations*

- Every 4 minutes, on average, someone dies of a stroke.

Roger et al. 2011, *Heart Disease and Stroke Statistics—2011 Update*

- Stroke is a leading cause of serious long-term disability in the United States.

CDC 2001, *Prevalence of Disabilities and Associated Health Conditions Among Adults*



- Ischemic stroke survivors who were 65 years and older had the following disabilities 6 months after their stroke:
  - 50% had some one-sided paralysis
  - 30% needed help walking
  - 26% needed help with activities of daily living
  - 19% had trouble speaking or understanding speech
  - 35% had symptoms of depression
  - 26% were admitted to nursing homes

Kelly-Hayes et al. 2003, *The Influence of Gender and Age on Disability Following Ischemic Stroke*

- Of those who survived a stroke, 30% received outpatient rehabilitation.

CDC 2007, *Outpatient Rehabilitation Among Stroke Survivors*

- Of those that survive a stroke, only 10% recover completely.

Rosenberg & Popelka 2000, *Post-Stroke Rehabilitation*

- After a stroke, 15% to 30% of survivors are permanently disabled and 20% require institutional care at 3 months after the stroke.

Asplund et al. 1998, *From the Twentieth to the Twenty-First Century*

- In 2004, stroke hospitalizations totaled 726,000.

Fang et al. 2007, *Declining U.S. Stroke Hospitalization Since 1997*

- The mean length of stay for patients hospitalized for stroke ranges from 4.6 to 12.4 days.

Demaerschalk et al. 2010, *U.S. Cost Burden of Ischemic Stroke*

- Stroke was listed as the first-diagnoses for 3,764,000 ambulatory care visits in 2007.

Schappert & Rechsteiner 2010, *Ambulatory Medical Care Utilization Estimates for 2007*

- In one year alone (1990), stroke led to more than 100,000 nursing home admissions with a mean length of stay of 432 days.

Taylor et al. 1996, *Lifetime Cost of Stroke in the United States*

## The Economic Burden

### Atrial Fibrillation

- In 2001, the estimated treatment costs of atrial fibrillation were \$6.65 billion per year—this included hospitalization costs, in- and out-patient care, and medications. This did not include costs of stroke prevention treatments, inpatient drug costs, inpatient physician fees, or indirect costs.

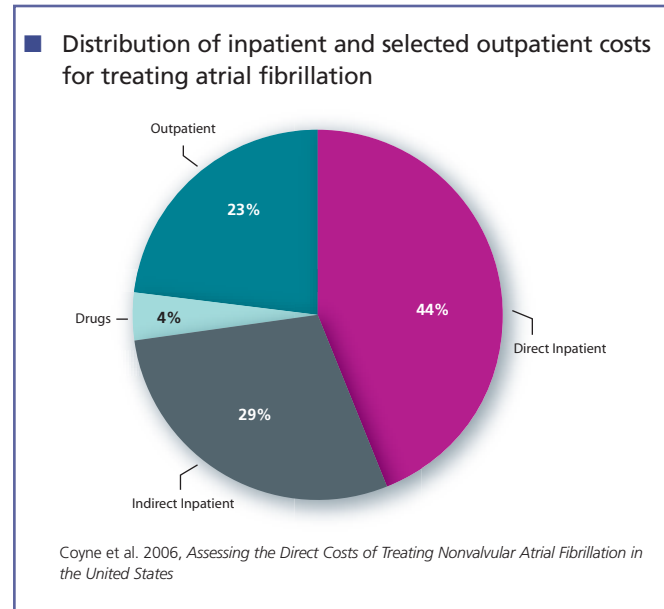
Coyne et al. 2006, *Assessing the Direct Costs of Treating Nonvalvular Atrial Fibrillation in the United States*

- The estimated costs for hospitalization of atrial fibrillation (AF) patients in 2001 were \$2.93 billion for patients with AF as their primary discharge diagnosis.

Coyne et al. 2006, *Assessing the Direct Costs of Treating Nonvalvular Atrial Fibrillation in the United States*

- The direct medical costs for ambulatory and outpatient treatment of atrial fibrillation patients in 2001 was an estimated \$1.76 billion. Office visits accounted for 66% of those costs, emergency department visits for 17%, and hospital outpatient department visits for 16%.

Coyne et al. 2006, *Assessing the Direct Costs of Treating Nonvalvular Atrial Fibrillation in the United States*



- Around 73% of total U.S. atrial fibrillation costs are for inpatient expenses.

Coyne et al., 2006, *Assessing the Direct Costs of Treating Nonvalvular Atrial Fibrillation in the United States*



- Medicare alone is estimated to pay \$15.7 billion per year to treat newly diagnosed atrial fibrillation patients.

Lee et al. 2008, *Direct Treatment Costs of Atrial Fibrillation in the Elderly American Population* AND Sullivan et al. 2009, *Medicare and Atrial Fibrillation*

- Atrial fibrillation (AF) is a major economic burden for society with the biggest cost driver being hospitalizations—accounting for 52% of costs. Drugs for AF account for 23% of costs, consultations at 9%, further investigations at 8%, loss of work at 6%, and paramedical procedures at 2%.

Le Heuzey et al. 2004, *Cost of Care Distribution in Atrial Fibrillation Patients*

- The annual cost of treating privately insured patients for atrial fibrillation (AF) is \$12,350 per patient—approximately 5 times greater than treating patients without AF.

Wu et al. 2005, *Economic Burden and Co-Morbidities of Atrial Fibrillation in a Privately Insured Population*

### Venous Thromboembolism (VTE)

- The mean total cost for inpatient care of patients who develop in-hospital venous thromboembolism (VTE) after orthopedic surgery is almost double compared to those who don't develop VTE—\$17,114 for deep vein thrombosis only, \$18,521 for pulmonary embolism, and \$9,345 for no VTE.

Ollendorf et al. 2002, *Cost of Venous Thromboembolism Following Major Orthopedic Surgery in Hospitalized Patients*

- The difference in inpatient care costs between patients who developed venous thromboembolism after orthopedic surgery and those who didn't, was highest among those who underwent hip-fracture repair. Costs were \$10,000 to \$13,000 higher.

Ollendorf et al. 2002, *Cost of Venous Thromboembolism Following Major Orthopedic Surgery in Hospitalized Patients*

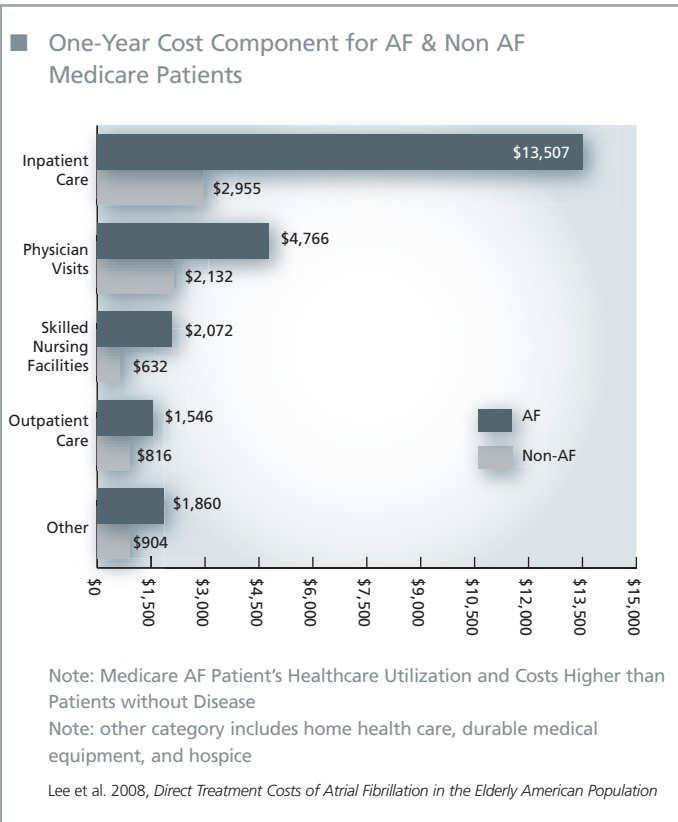
### Stroke

- The annual direct and indirect costs of stroke are between \$40.9 billion and \$73.7 billion.

Roger et al. 2011, *Heart Disease and Stroke Statistics—2011 Update* AND Lloyd-Jones et al. 2010, *Heart Disease and Stroke Statistics—2010 Update*

- Of the \$73.7 billion cost of stroke in 2010—\$21 billion was for hospital costs, \$17.1 billion for nursing home costs, \$3.8 billion for physicians and other professionals, \$1.3 billion for medical durables, \$5 billion for home health care, and \$25.5 billion in lost productivity.

Lloyd-Jones et al. 2010, *Heart Disease and Stroke Statistics—2010 Update*



- The incremental treatment costs associated with stroke in the year following diagnosis of atrial fibrillation are an estimated \$7,907 per Medicare patient.

Lee et al. 2008, *Direct Treatment Costs of Atrial Fibrillation in the Elderly American Population*

- A study of Medicare beneficiaries with atrial fibrillation found that total medical costs for treating these patients during a 15-month follow-up period were an average of \$24,000 per patient—63% of these costs were related to readmission.

Sullivan et al. 2010, *Health Services Utilization and Medical Costs Among Medicare Atrial Fibrillation Patients*

- The annual cost of stroke in Medicare patients with atrial fibrillation is estimated at \$8 billion.

Caro 2004, *An Economic Model of Stroke in Atrial Fibrillation*

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- The mean lifetime cost of ischemic stroke is an estimated \$140,048.

Taylor et al. 1996, *Lifetime Cost of Stroke in the U.S.*

- The estimated cost of stroke for the first 30 days after the event is \$20,346 for severe ischemic strokes and \$13,019 for mild ones.

Leibson et al. 1996, *Utilization of Acute Care Services in the Year Before and After First Stroke*

- The mean hospitalization costs for patients admitted for stroke range from \$8,000 to \$23,000 (in 2008 dollars).

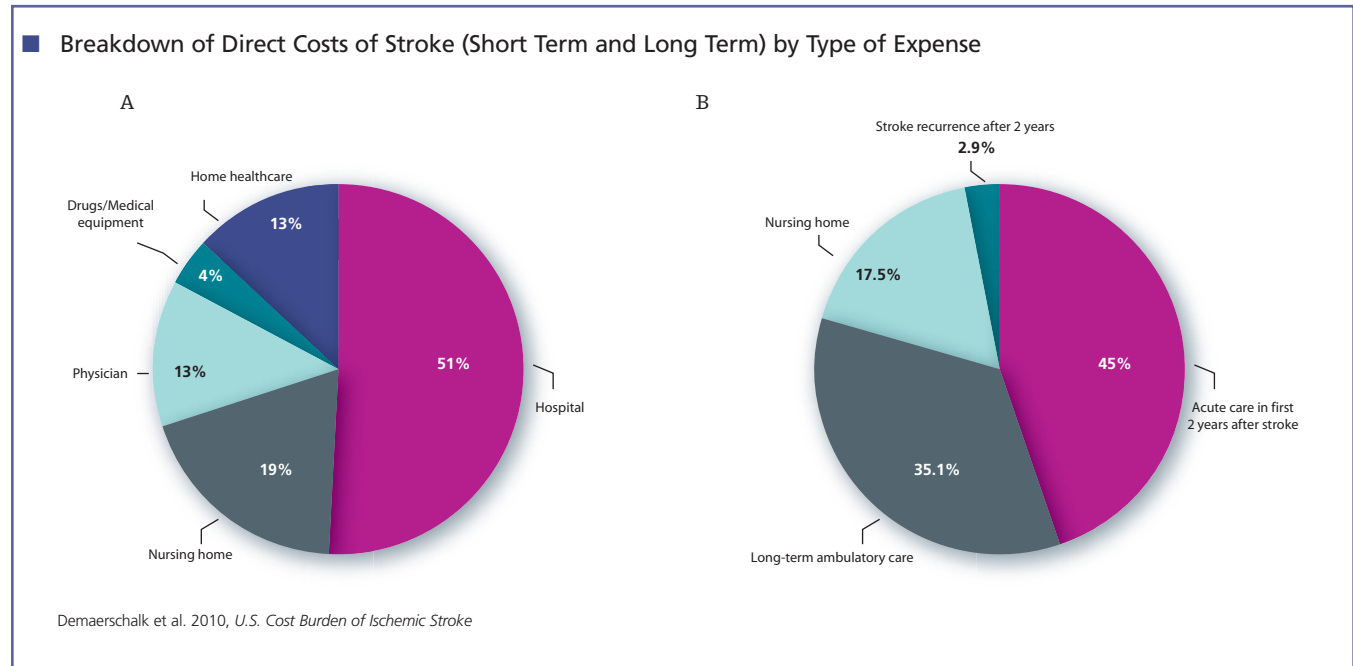
Demaerschalk et al. 2010, *U.S. Cost Burden of Ischemic Stroke*

- In 2006, \$3.9 billion was paid to Medicare beneficiaries discharged from short-stay hospitals for stroke.

Lloyd-Jones et al. 2010, *Heart Disease and Stroke Statistics—2010 Update*

- Stroke in Medicare patients with atrial fibrillation who were not treated with anticoagulants, cost Medicare \$4.8 billion each year in direct costs. Those who had strokes despite prophylactic treatment cost an additional \$3.1 billion.

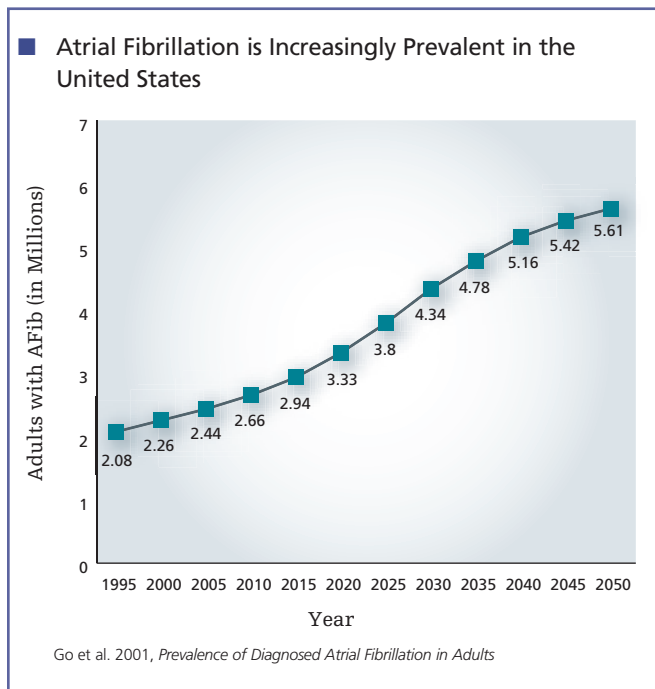
Caro 2004, *An Economic Model of Stroke in Atrial Fibrillation*



## The Future Cost

- By 2050, the prevalence of atrial fibrillation will have more than doubled since 2001—growing to an estimated 5.6 million to 12.1 million Americans.

Go et al. 2001, *Prevalence of Diagnosed Atrial Fibrillation in Adults* AND Miyasaka et al. 2006, *Secular Trends in Incidence of Atrial Fibrillation in Olmsted County, Minnesota*



- If current incidence estimates are applied to Census Bureau projections, by 2050 the number of Americans with atrial fibrillation could exceed 12 million. If increases in incidence continue, that number could be as high as 15 million.

Miyasaka et al. 2006, *Secular Trends in Incidence of Atrial Fibrillation in Olmsted County, Minnesota*

- By 2050, it is estimated that 88% of Americans with atrial fibrillation will be age 65 and older.

Go et al. 2001, *Prevalence of Diagnosed Atrial Fibrillation in Adults*

- By 2050, it is estimated that more than 50% of Americans with atrial fibrillation will be age 80 and older.

Go et al. 2001, *Prevalence of Diagnosed Atrial Fibrillation in Adults*

- The incidence of VTE is predicted to more than double by 2050—from 0.95 million in 2006 to 1.82 million in 2050.

Deitelzweig et al. 2010, *Prevalence of Clinical Venous Thromboembolism in the USA*

- By 2030, the prevalence of stroke is projected to increase approximately 25%. This means there will be an additional 4 million Americans with stroke (compared to 2010).

Heidenreich et al. 2011, *Forecasting the Future of Cardiovascular Disease in the United States*

- If current trends in mortality continue, the United States will see a doubling in deaths from ischemic stroke between 2003 and 2033.

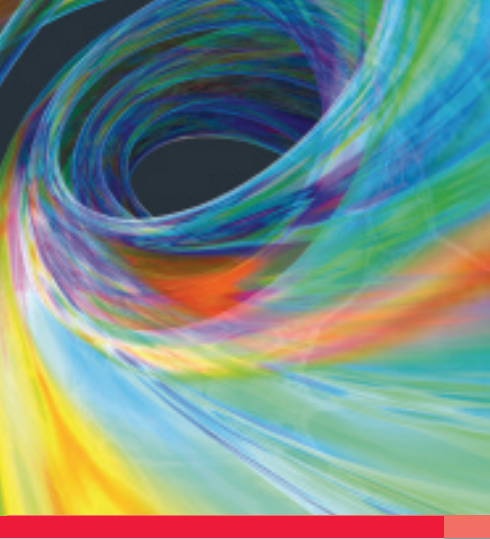
Elkins & Johnston 2003, *Thirty-Year Projections for Deaths from Ischemic Stroke in the United States*

- Total direct and indirect costs of stroke in the U.S. are projected to reach \$140 billion by 2030. This represents a 238% change in direct costs compared to 2010, and a 73% change in indirect costs.

Heidenreich et al. 2011, *Forecasting the Future of Cardiovascular Disease in the U.S.*

- The projected total cost of ischemic stroke from 2005 to 2050 (in 2005 dollars) is around \$2.2 trillion.

Brown et al. 2006, *Projected Costs of Ischemic Stroke in the U.S.*



*Investing in Science*

## Innovative Medical Research

■ **A**s our older population continues to grow, the extreme strain of chronic diseases on our society will only worsen. The good news is that advances from innovation in medical research are transforming the standard of care when it comes to prevention and treatment of thrombosis, and offering tremendous advances that allow people to live longer, healthier lives.

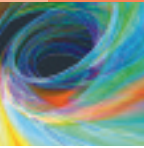
■ Cardiovascular medicine is experiencing tremendous breakthroughs with the emergence of novel anticoagulants that may very well replace warfarin and aspirin as the “gold standards” of stroke prevention in atrial fibrillation. Clinical trials of these direct thrombin inhibitors are yielding promising results that suggest better and easier stroke prevention is on the horizon. Efforts to identify atrial fibrillation patients at an early stage—and to predict stroke risk with better accuracy—will also need the same attention if we’re going to see the most optimal use of these new anticoagulants.

These emerging antithrombotics are also promising to change the standard of care in prevention of venous thromboembolism in patients at high risk post hip and knee replacement surgery. They promise improved prevention of clotting with a reduced risk of bleeds.

In the world of stroke prevention and treatment, substances are being explored that offer both neuro-protective and neuro-repair effects. New medicines are being tested that help slow nerve cell degeneration caused by oxygen deprivation. Stem cells are also being used to try to replace brain cells damaged by stroke. New imaging techniques such as high-definition MRI and intravascular sonogram should also lead to more accurate diagnosis and better understanding of stroke mechanisms.

Medical advances that prevent thrombosis and reduce its impact often far outweigh the initial financial investments. As we enter a critical time in health care for older Americans, we must be sure to consider both the financial and human impact that innovation can have. Short-sighted efforts to reduce spending too often target the initial expenses of innovation while ignoring the remarkable returns on investment.





## The Human Value

- In one year, 58,283 of the 1.265 million Medicare beneficiaries with atrial fibrillation that did not receive prophylaxis suffered a stroke. For those who did receive anti-coagulants, 38,468 suffered strokes.

Caro 2004, *An Economic Model of Stroke in Atrial Fibrillation*

- Meta-analysis of a number of randomized controlled trials found that aspirin use in atrial fibrillation patients reduced stroke risk by an average 22%.

Hart et al. 1999, *Antithrombotic Therapy to Prevent Stroke in Patients with Atrial Fibrillation*

- Meta-analysis of randomized trials found that adjusted-dose warfarin reduced stroke risk in atrial fibrillation patients by 60%. Antiplatelet agents reduced risk by 20%.

Hart et al. 2007, *Meta-Analysis*

- A recently approved direct thrombin inhibitor was found to reduce the risk of stroke/peripheral embolic events in atrial fibrillation patients by 34%, and the risk of hemorrhagic stroke by 74%—compared with warfarin.

Connolly et al. 2009, *Dabigatran Versus Warfarin in Patients with Atrial Fibrillation*

- The use of practice guidelines in atrial fibrillation patients saw a decrease in rate of hospitalization from 74% to 38%.

Zimetbaum et al. 2003, *Impact of a Practice Guideline for Patients with Atrial Fibrillation on Medical Resource Utilization and Costs*

- Atrial fibrillation patients who underwent catheter ablation had a reduced risk of stroke and death—2.2% of those who had ablation experienced stroke versus 4.7% on medications alone, and 6% died from stroke versus 23.5% of those on medications alone.

Day et al. 2010, *Atrial Fibrillation Ablation Significantly Reduces Long-Term Mortality and Strokes in a Large Patient Population*

- Using simple bedside measures, identification of individuals at risk for developing atrial fibrillation is feasible. Selecting high-risk individuals for inclusion in atrial fibrillation prevention trials may also enhance prevention strategies.

Schnabel et al. 2009, *Development of a Risk Score for Atrial Fibrillation*

- A study of the effectiveness of treating ischemic stroke victims with rt-PA within 3 hours of symptom onset found an estimated impact on long-term health outcomes of 564 quality-adjusted life-years saved per 1,000 patients over 30 years.

Fagan et al. 1998, *Cost-Effectiveness of Tissue Plasminogen Activator for Acute Ischemic Stroke*

- Lowering of blood pressure is associated with a 30% to 40% reduction in stroke risk.

Furie et al. 2010, *Guidelines for the Prevention of Stroke in Patients with Stroke or Transient Ischemic Attack*

- Treatment of high blood pressure with antihypertensive drugs is associated with a significant reduction in risk of recurrent stroke.

Rashid et al. 2003, *Blood Pressure Reduction and Secondary Prevention of Stroke and Other Vascular Events*

- The PROactive trial to manage glucose in diabetics with a history of cardiovascular disease, stroke, or other vascular risk factors found that treatment with pioglitazone was associated with a 47% relative risk reduction in recurrent stroke.

Wilcox et al. 2007, *Effects of Pioglitazone in Patients with Type 2 Diabetes with or without Previous Stroke*

- Studies of patients with myocardial infarction found that warfarin reduced stroke risk compared to placebo by 40% to 55%.

ASPECT Group 1994, *Effect of Long-Term Oral Anticoagulant Treatment on Mortality and Cardiovascular Morbidity After Myocardial Infarction* AND van Es et al. 2002, *Aspirin and Coumadin After Acute Coronary Syndromes*

- Aspirin reduces stroke rate by 20% in patients with myocardial infarction.

Hurlen et al. 2002, *Warfarin, Aspirin, or Both After Myocardial Infarction*

- Anti-platelet therapy after a stroke or TIA reduces the risk of nonfatal ischemic strokes by 28% and fatal strokes by 16%.

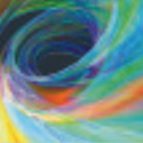
Antithrombotic Trialists' Collaboration 2002, *Collaborative Meta-Analysis of Randomised Trials of Antiplatelet Therapy for Prevention of Death, Myocardial Infarction, and Stroke in High Risk Patients*

- An investigational direct thrombin inhibitor reduced relative risk of venous thromboembolism after total hip replacement surgery by 65.7%—compared to a currently available treatment.

Fuji et al. 2010, *Efficacy and Safety of Edoxaban Versus Enoxaparin for the Prevention of Venous Thromboembolism Following Total Hip Arthroplasty*

- An oral pharmacologic agent has been demonstrated to be at least as effective as an injectable anticoagulant in the prevention of venous thrombosis following hip replacement.

Eriksson et al. 2007, *Dabigatran Etxilate Versus Enoxaparin for Prevention of Venous Thromboembolism After Total Hip Replacement*



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## The Economic Value

- The use of practice guidelines in atrial fibrillation (AF) patients significantly decreased hospitalization and resource utilization—with an average decrease in 30-day total direct health care costs of around \$1,400 per patient.

Zimetbaum et al. 2003, *Impact of a Practice Guideline for Patients with Atrial Fibrillation on Medical Resource Utilization and Costs*

- Warfarin use in Medicare patients with nonvalvular atrial fibrillation was independently associated with lower medical costs averaging \$9,836 per patient, per year.

Mercaldi et al. 2011, *Cost Efficiency of Anticoagulation with Warfarin to Prevent Stroke in Medicare Beneficiaries with Nonvalvular Atrial Fibrillation*

- In patients with nonvalvular atrial fibrillation (AF) and one additional stroke risk factor, warfarin therapy cost \$8,000 per quality-adjusted life-year (QALY) saved.

Gage et al. 1995, *Cost-Effectiveness of Warfarin and Aspirin for Prophylaxis of Stroke in Patients with Nonvalvular Atrial Fibrillation*

- The per-patient annual cost of treating stroke in atrial fibrillation patients was found to be \$1,485 in a well-controlled anti-coagulation clinic, \$3,710 for those receiving warfarin in routine medical care, and \$3,778 for those not receiving any anti-coagulant.

Caro 2004, *An Economic Model of Stroke in Atrial Fibrillation*

- The total annual benefit to society from t-PA use in the United States is around \$363 million—\$60 million in direct cost savings to society plus an additional 7,510 QALYs. This means that t-PA saves \$6,074 and adds 0.75 QALY per use.

Johnston 2010, *The Economic Case for New Stroke Thrombolytics*

- A study of the effectiveness of treating ischemic stroke victims with rt-PA within 3 hours of symptom onset showed a decrease in rehabilitation costs of \$1.4 million and nursing home costs of \$4.8 million, per 1,000 eligible rt-PA-treated patients.

Fagan et al. 1998, *Cost-Effectiveness of Tissue Plasminogen Activator for Acute Ischemic Stroke*

## The Future Value

- If half of all atrial fibrillation patients receiving suboptimal or no anticoagulation instead received optimal anticoagulation, 28,000 strokes could be prevented each year at a savings of around \$2.5 billion in direct costs.

Caro 2004, *An Economic Model of Stroke in Atrial Fibrillation*

- If 50% of individuals with atrial fibrillation who do not receive prophylaxis were optimally anti-coagulated, 19,380 emboli would be prevented and \$1.1 billion would be saved each year.

Caro 2004, *An Economic Model of Stroke in Atrial Fibrillation*

- If 50% of atrial fibrillation patients who currently receive warfarin in routine medical care were optimally anticoagulated, 9,852 emboli would be prevented and \$1.3 billion would be saved each year.

Caro 2004, *An Economic Model of Stroke in Atrial Fibrillation*

- If half of atrial fibrillation patients who currently receive warfarin in a routine care setting had their anti-coagulation optimized, around 9,000 strokes and more than 29,000 bleeds would be prevented.

Caro 2004, *An Economic Model of Stroke in Atrial Fibrillation*

- A \$600 net savings is associate with each ischemic stroke patient treated with t-PA. In 2005, only 2% of all ischemic stroke patients received t-PA. If that percentage was increased to 4% the realized cost savings would be approximately \$15 million. If increased to 20%, the savings would be around \$74 million.

Demaerschalk & Yip 2005, *Economic Benefit of Increasing Utilization of Intravenous Tissue Plasminogen Activator for Acute Ichemic Stroke in the U.S.*



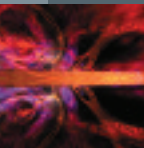
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## Conclusion

- *The Silver Book®: Thrombosis* volume underscores the growing burden of thrombosis in America and makes a strong case for innovation that could lessen the impact of diseases like atrial fibrillation, venous thromboembolism, and stroke. We at the Alliance for Aging Research fully expect this volume to join *The Silver Book* collection as an invaluable tool that encourages advocacy and policies that support investments in medical research and innovation. Without significant breakthroughs and changes to standards of care, the number of Americans with atrial fibrillation alone could reach more than 12 million by 2050. This would add an intolerable burden to individuals, families, and a nation already struggling to stay afloat as we face an unprecedented surge of age-related chronic diseases.
- Sound public policy should strive for cost containment strategies that assure high quality health care that is patient-centered, values-driven, knowledge-intensive, innovation-rich, and prevention-oriented. We must ensure long-range plans for supporting research and medical innovation that reduces the burdens imposed by thrombosis. Historically, investments that produce new medical innovations often pay for themselves through decreased medical expenses and increased human productivity. Medical innovation is essential if we want to attempt to contain the health care costs of an aging nation. Research and discovery—properly applied to health care and prevention—are essential to avoiding an unacceptably high toll due to thrombosis.

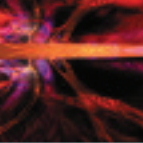
# References

- Anderson, FA, HB Wheeler, RJ Goldberg, DW Hosmer, NA Patwardhan, B Jovanovic, A Forcier, and JE Dalen. 1991. A Population-Based Perspective of the Hospital Incidence and Case-Fatality Rates of Deep Vein Thrombosis and Pulmonary Embolism: The Worcester DVT Study. *Arch Intern Med* 151(5):933-8.
- Antithrombotic Trialists' Collaboration. 2002. Collaborative Meta-Analysis of Randomised Trials of Antiplatelet Therapy for Prevention of Death, Myocardial Infarction, and Stroke in High Risk Patients. *BMJ* 324(7329):71-86.
- ASPECT (Anticoagulants in the Secondary Prevention of Events in Coronary Thrombosis) Group. 1994. Effect of Long-Term Oral Anticoagulant Treatment on Mortality and Cardiovascular Morbidity After Myocardial Infarction. *Lancet* 343(8896):499-503.
- Asplund, K, B Stegmayr, and M Peltonen. 1998. From the Twentieth to the Twenty-First Century: A public health perspective on stroke. In: Ginsberg MD, B Julien, eds. *Cerebrovascular Disease Pathophysiology, Diagnosis, and Management*. Malden, MA: Blackwell Science.
- Brown, DL, B Boden-Albala, KM Langa, LD Lisabeth, M Fair, MA Smith, RL Sacco, and LB Morgenstern. 2006. Projected Costs of Ischemic Stroke in the United States. *Neurology* 67(8):1390-5.
- Caro, JJ. 2004. An Economic Model of Stroke in Atrial Fibrillation: The cost of sub-optimal oral anticoagulation. *Am J Managed Care* 10(14):S451-61.
- Casper, ML, IA Nwaise, JB Croft, and DS Nilasena. 2008. *Atlas of Stroke Hospitalizations Among Medicare Beneficiaries*. Atlanta: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention.
- Centers for Disease Control and Prevention. 2007. Outpatient Rehabilitation Among Stroke Survivors: 21 states and the District of Columbia. *MMWR Morb Mortal Wkly Rep* 56:504-7.
- Centers for Disease Control and Prevention. 2005. Disparities in Deaths from Stroke Among Persons Aged <75 Years: United States, 2002. *MMWR Morb Mortal Wkly Rep* 54:477-81.
- Centers for Disease Control and Prevention. 2003. Atrial Fibrillation as a Contributing Cause of Death and Medicare Hospitalization: United States 1999. *MMWR Morb Mortal Wkly Rep* 52(7):128-131.
- Centers for Disease Control and Prevention. 2001. Prevalence of Disabilities and Associated Health Conditions Among Adults: United States, 1999. *MMWR Morb Mortal Wkly Rep* 50:120-5.
- Connolly, SJ, MD Ezekowitz, S Yusuf, J Eikelboom, J Oldgren, A Parekh, J Pogue, PA Reilly, E Themeles, J Varrone, S Wang, M Alings, D Xavier, J Zhu, R Diaz, BS Lewis, H Darius, H-C Deiner, CD Joyner, L Wallentin; and the RE-LY Steering Committee and Investigators. 2009. Dabigatran Versus Warfarin in Patients with Atrial Fibrillation. *NEJM* 361(12):1139-51.
- Coyne, KS, C Paramore, S Grandy, M Mercader, M Reynolds, and P Zimetbaum. 2006. Assessing the Direct Costs of Treating Nonvalvular Atrial Fibrillation in the United States. *Value in Health* 9(5):348-56.
- Day, JD, BG Crandall, JS Osborn, JP Weiss, DL Lappe, T Bair, H May, JL Anderson, B Muhlestein, J Nelson, and TJ Bunch. 2010. Atrial Fibrillation Ablation Significantly Reduces Long-Term Mortality and Strokes in a Large Patient Population. *Heart Rhythm Society 2010 Scientific Sessions* AB40-2.
- Deitelzweig, S, BH Johnson, J Lin, and KL Schulman. 2010. Prevalence of Venous Thromboembolism in the USA: Current trends and future projections. *Hematol* DOI: 10.1002/ajh.21917.
- Demaerschalk, BM, H-M Hwang, and G Leung. 2010. U.S. Cost Burden of Ischemic Stroke: A systematic literature review. *Am J Manag Care* 16(7):525-33.
- Demaerschalk, BM and TR Yip. 2005. Economic Benefit of Increasing Utilization of Intravenous Tissue Plasminogen Activator for Acute Ischemic Stroke in the United States. *Stroke* 36(11):2500-3.
- Elkins, JS and SC Johnston. 2003. Thirty-Year Projections for Deaths from Ischemic Stroke in the United States. *Stroke* 34(9):2109-12.
- El-Saed, A, LH Kuller, AB Newman, O Lopez, J Costantino, K McTigue, M Cushman, and R Kronmal. 2006. Geographic Variations in Stroke Incidence and Mortality Among Older Populations in Four U.S. Communities. *Stroke* 37(8):1975-9.
- Eriksson, BI, OE Dahl, N Rosencher, AA Kurth, CN van Dijk, SP Frostick, MH Prins, R Nettiarchchi, S Hantel, J Schnee, and HR Buller; for the RE-NOVATE Study Group. 2007. Dabigatran Etxilate Versus Enoxaparin for Prevention of Venous Thromboembolism After Total Hip Replacement: A randomised, double-blind, non-inferiority trial. *The Lancet* 370(9591):949-56.
- Fagan, SC, LB Morgenstern, A Petitta, RE Ward, BC Tilley, JR Marler, SR Levine, JP Broderick, TG Kwiatkowski, M Frankel, TG Brott, and MD Walker; for the NINDS rt-PA Stroke Study Group. 1998. Cost-Effectiveness of Tissue Plasminogen Activator for Acute Ischemic Stroke. *Neurology* 50(4):883-890.
- Fang, J, MH Alderman, NL Keenan, and JB Croft. 2007. Declining U.S. Stroke Hospitalization Since 1997: National Hospital Discharge Survey, 1998-2004. *Neuroepidemiology* 29(3-4):243-9.
- Fuji, T et al. December 4 – 7, 2010. *Efficacy and Safety of Edoxaban Versus Enoxaparin for the Prevention of Venous Thromboembolism Following Total Hip Arthroplasty: STARS J-V Trial*. Orlando, Florida.
- Furie, KL, SE Kasner, RJ Adams, GW Albers, RL Bush, SC Fagan, JL Halperin, SC Johnston, I Katzan, WN Kernan, PH Mitchell, B Ovbiagele, YY Palesch, RL Sacco, LH Schwamm, S Wassertheil-Smoller, TN Turan, D Wentworth; on behalf of the American Heart Association Stroke Council, Council on Cardiovascular Nursing, Council on Clinical Cardiology, and Interdisciplinary Council on Quality of Care and Outcomes Research. 2010. Guidelines for the Prevention of Stroke in Patients with Stroke or Transient Ischemic Attack: A guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke* 37(2):577-617.



- Fuster, V, LE Rydén, DS Cannom, HJ Crijns, AB Curtis, KA Ellenbogen, JL Halperin, J-Y Le Heuzey, GN Kay, JE Lowe, SB Olsson, EN Prystowsky, JL Tamargo, S Wann, SC Smith, AK Jacobs, CD Adams, JL Anderson, EM Antman, SA Hunt, R Nishimura, JP Ornato, RL Page, B Riegel, SG Priori, J-J Blanc, A Budaj, AJ Camm, V Dean, JW Deckers, C Despres, K Dickstein, J Lekakis, K McGregor, M Metra, J Morais, A Osterspey, and JL Zamarano. 2006. ACC/AHA/ESC 2006 Guidelines for the Management of Patients with Atrial Fibrillation: A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the European Society of Cardiology Committee for Practice Guidelines (Writing Committee to Revise the 2001 Guidelines for the Management of Patients with Atrial Fibrillation). *J Am Coll Cardiol* 48:e149-246.
- Gage, BF, AB Cardinali, GW Albers, and DK Owens. 1995. Cost-Effectiveness of Warfarin and Aspirin for Prophylaxis of Stroke in Patients with Nonvalvular Atrial Fibrillation. *JAMA* 274(23):1839-45.
- Go, AS. 2005. The Epidemiology of Atrial Fibrillation in Elderly Persons: The tip of the iceberg. *Am J Geriatr Cardiol* 14(2):56-61.
- Go, AS, EM Hylek, KA Phillips, Y Chang, LE Henault, JV Selby, and DE Singer. 2001. Prevalence of Diagnosed Atrial Fibrillation in Adults: National implications for rhythm management and stroke prevention—the AnTicoagulation and Risk Factors In Atrial Fibrillation (ATRIA) Study. *JAMA* 285(18):2370-5.
- Goldhaber, SZ. 1998. Pulmonary Embolism. *NEJM* 339(2):93-104.
- Haake, DA and SA Berkman. 1989. Venous Thromboembolic Disease after Hip Surgery: Risk factors, prophylaxis, and diagnosis. *Clin Orthop Relat Res* 242:212-31.
- Hart, RG, LA Pearce, and MI Aguilar. 2007. Meta-Analysis: Antithrombotic Therapy to Prevent Stroke in Patients Who Have Nonvalvular Atrial Fibrillation. *Ann Intern Med* 146(12):857-67.
- Hart, RG, O Benavente, R McBride, and LA Pearce. 1999. Antithrombotic Therapy to Prevent Stroke in Patients with Atrial Fibrillation. *Ann Intern Med* 131(7):492-501.
- Heidenreich, PA, JG Trogdon, OA Khavjou, J Butler, K Dracup, MD Ezekowitz, EA Finkelstein, Y Hong, SC Johnston, A Khera, DM Lloyd-Jones, SA Nelson, G Nichol, De Orenstein, PWF Wilson, YJ Woo; on behalf of the American Heart Association Advocacy Coordinating Committee et al. 2011. Forecasting the Future of Cardiovascular Disease in the United States: A policy statement from the American Heart Association. *Circ* published online DOI: 10.1161/CIR.0b013e31820a55f5.
- Heit, JA, AT Cohen, and FA Anderson Jr.; for the VTE Impact Assessment Group. 2005. Estimated Annual Number of Incident and Recurrent, Non-Fatal and Fatal Venous Thromboembolism (VTE) Events in the U.S. *Blood* 106(11): abstract #910:267a.
- Heit, JA. 2002. Venous Thromboembolism Epidemiology: Implications for prevention and management. *Semin Thromb Hemost* 28(Supp 2):3-13.
- Heit, JA, WM O'Fallon, TM Petterson, CM Lohse, MD Silverstein, DN Mohr, and LJ Melton. 2002. Relative Impact of Risk Factors for Deep Vein Thrombosis and Pulmonary Embolism: A population-based study. *Arch Intern Med* 161(11):1245-8.
- House of Commons Health Committee. 2005. *The Prevention of Venous Thromboembolism in Hospitalised Patients: Second Report of Session 2004-05*. London: House of Commons.
- Hurlen, M, M Abdelnoor, P Smith, J Erikssen, and H Arnesen. 2002. Warfarin, Aspirin, or Both After Myocardial Infarction. *NEJM* 347(13):969-74.
- Johnston, SC. 2010. The Economic Case for New Stroke Thrombolytics. *Stroke* 41(10):559-62.
- Kelly-Hayes M, A Beiser, CS Kase, A Scaramucci, RB D'Agostino, and PA Wolf. 2002. The Influence of Gender and Age on Disability Following Ischemic Stroke: The Framingham Study. *J Stroke Cerebrovasc Dis* 12(3):119-26.
- Kim, MH, J Lin, M Hussein, and D Battleman. 2009. Incidence and Temporal Pattern of Hospital Readmissions for Patients with Atrial Fibrillation. *Curr Med Res Opin* 25(5):1215-20.
- Le Heuzey, J-Y, O Paziand, O Piot, SM Ait, X Copie, T Lavergne, and L Guize. 2004. Cost of Care Distribution in Atrial Fibrillation Patients: The COCAF study. *Am Heart J* 147(1):121-6.
- Lee, WC, GA Lamas, S Balu, J Spalding, Q Wang, and CL Pashos. 2008. Direct Treatment Cost of Atrial Fibrillation in the Elderly American Population: A Medicare perspective. *J Med Econ* 11(2):281-98.
- Leibson, CL, T Hu, RD Brown, SL Hass, WM O'Fallon, and JP Whisnaut. 1996. Utilization of Acute Care Services in the Year Before and After First Stroke: A population-based study. *Neurology* 46:861-9.
- Lloyd-Jones, DM, RJ Adams, TM Brown, M Carnethon, S Dai, G De Simone, TB Ferguson, E Ford, K Furie, C Gillespie, AS Go, K Greenlund, N Haase, S Hailpern, PM Ho, V Howard, B Kissela, S Kittner, D Lackland, L Lisabeth, A Marelli, MM McDermott, J Meigs, D Mozaffarian, M Mussolino, G Nichol, VL Roger, W Rosamond, R Sacco, P Sorlie, R Stafford, T Thom, S Wasserthiel-Smoller, ND Wong, and J Wylie-Rosett; on behalf of the American Heart Association Statistics Committee and Stroke Subcommittee. 2010. Heart Disease and Stroke Statistics—2010 Update: A report from the American Heart Association. *Circ* 121(7):e46-215.
- Lloyd-Jones, DM, TJ Wang, EP Leip, MG Larson, D Levy, RS Vasan, RB D'Agostino, JM Massaro, A Beiser, PA Wolf, and EJ Benjamin. 2004. Lifetime Risk for Development of Atrial Fibrillation: The Framingham Heart Study. *Circ* 110(9):1042-6.
- Mercaldi, CJ, M Ciaramentaro, B Hahn, G Chalissery, MW Reynolds, SD Sander, GP Samsa, and DB Matchar. 2011. Cost Efficiency of Anticoagulation with Warfarin to Prevent Stroke in Medicare Beneficiaries with Nonvalvular Atrial Fibrillation. *Stroke* 42(1):112-8.
- Miyasaka, Y, ME Barnes, KR Bailey, SS Cha, BJ Gersh, JB Seward, and TSM Tsang. 2007. Mortality Trends in Patients Diagnosed with First Atrial Fibrillation: A 21-year community-based study. *J Am Coll Cardiol* 49(9):986-92.





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- 
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- 
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Miyasaka, Y, ME Barnes, BJ Gersh, SS Cha, KR Bailey, WP Abhayaratna, JB Seward, and TSM Tsang. 2006. Secular Trends in Incidence of Atrial Fibrillation in Olmsted County, Minnesota, 1980 to 2000, and Implications on the Projections for Future Prevalence. *Circ* 114(2):119-25.

National Heart, Lung, and Blood Institute. *Incidence and Prevalence: 2006 chart book on cardiovascular and lung diseases*. 2006. Bethesda, MD: NIH, National Heart, Lung, and Blood Institute.

Ollendorf, DA, M Vera-Llonch, and G Oster. 2002. Cost of Venous Thromboembolism Following Major Orthopedic Surgery in Hospitalized Patients. *Am J Health-Sys Pharm* 59(18):1750-4.

Penado, S, M Cano, O Acha, JL Hernández, and JA Riancho. 2003. Atrial Fibrillation as a Risk Factor for Stroke Recurrence. *Am J Med* 114(3):206-10.

Piccini, JP, BG Hammill, MF Sinner, PN Jensen, AF Hernandez, SR Heckbert, E Benjamin, and LH Curtis. 2010. Incidence of Atrial Fibrillation and Associated Mortality Among Medicare Beneficiaries from 1993 to 2007. *Circ* 122:A19718.

Rashid, P, J Leonardi-Bee, and P Bath. 2003. Blood Pressure Reduction and Secondary Prevention of Stroke and Other Vascular Events. *Stroke* 34(11):2741-8.

Roger, VL, AS Go, DM Lloyd-Jones, RJ Adams, JD Berry, TM Brown, MR Carnethon, S Dai, G de Simone, ES Ford, CS Fox, HJ Fullerton, C Gillespie, KJ Greenlund, SM Hailpern, JA Heit, P Ho, VJ Howard, BM Kissela, SJ Kittner, DT Lackland, JH Lichtman, LD Lisabeth, DM Makuc, GM Marcus, A Marelli, DB Matchar, MM McDermott, JB Meigs, CS Moy, D Mozaffarian, ME Mussolino, G Nichol, NP Paynter, WD Rosamond, PD Sorlie, RS Stafford, TN Turan, MB Turner, ND Wong, J Wylie-Rosett; on behalf of the American Heart Association Statistics Committee and the Stroke Statistics Committee. 2011. Heart Disease and Stroke Statistics—2011 Update. *Circ* published online DOI: 10.1161/CIR.0b013e3182009701.

Rosenberg, CH and GM Popelka. 2000. Post-Stroke Rehabilitation: A review of the guidelines for patient management. *Geriatrics* 55(9):75-81.

Schappert, SM and EA Rechsteiner. 2010. Ambulatory Medical Care Utilization Estimates for 2007. *Natl Health Stat Rep*. Hyattsville, MD: National Center for Health Statistics.

Schnabel, RB, LM Sullivan, D Levy, MJ Pencina, JM Massaro, RB D’Agostino, C Newton-Cheh, JF Yamamoto, JW Magnani, TM Tadros, WB Kannel, TJ Wang, PT Ellinor, PA Wolf, RS Vasan, and EJ Benjamin. 2009. Development of a Risk Score for Atrial Fibrillation (Framingham Heart Study): A community-based cohort study. *The Lancet* 373(9665):739-45.

Silverstein, MD, JA Heit, DN Mohr, TM Petterson, WM O’Fallon, and LJ Melton III. 1998. Trends in the Incidence of Deep Vein Thrombosis and Pulmonary Embolism: A 25-year population based study. *Arch Int Med* 158(6):585-93.

Sullivan, E, S Braithwaite, K Dietz, and C Hickey. 2010. *Health Services Utilization and Medical Costs Among Medicare Atrial Fibrillation Patients*. Washington, D.C.: Avalere Health.

Sullivan, E, E Eisenhart, A Herr, C Hickey, F Hussain, P Mills, and S Sadownik. 2009. *Medicare and Atrial Fibrillation: Consequences in cost and care*. Washington, D.C.: Avalere Health.

Taylor, TN, PH Davis, JC Torner, J Holmes, JW Meyer, and MF Jacobson. 1996. Lifetime Cost of Stroke in the United States. *Stroke* 27(9):1459-66.

Thrall, G, GYH Lip, D Carroll, and D Lane. 2007. Depression, Anxiety, and Quality of Life in Patients with Atrial Fibrillation. *CHEST* 132(4):1259-64.

Van Es, RF, J Jonker, FW Verheugt, JW Deckers, and DE Grobbee; for the Antithrombotics in the Secondary Prevention of Events in Coronary Thrombosis-2 (ASPECT-2) Research Group. 2002. Aspirin and Coumadin After Acute Coronary Syndromes (the ASPECT-2 Study): A randomized controlled trial. *Lancet* 360(9327):109-13.

White, RH 2003. The Epidemiology of Venous Thromboembolism. *Circ* 107(23 Supp1):14-8.

Wilcox, RG, M-G Bousser, DJ Betteridge, G Schernthaner, V Pirags, S Kupfer, and J Dormandy. 2007. Effects of Pioglitazone in Patients with Type 2 Diabetes with or without Previous Stroke: Results from PROactive (PROspective pioglitAzone Clinical Trial in macro Vascular Events 04). *Stroke* 38(3):865-73.

Wolf, PA, JB Mitchell, CS Baker, WB Kannel, and RB D’Agostino. 1998. Impact of Atrial Fibrillation on Mortality, Stroke, and Medical Costs. *Arch Intern Med* 158(3):229-34.

Wolf, PA, RD Abbott, and WB Kannel. 1991. Atrial Fibrillation as an Independent Risk Factor for Stroke: The Framingham Study. *Stroke* 22(8):983-8.

Wu, EQ, HG Birnbaum, M Mareva, E Tuttle, AR Castor, W Jackman, and J Ruskin. 2005. Economic Burden and Co-Morbidities of Atrial Fibrillation in a Privately Insured Population. *Curr Med Res Opin* 21(10):1693-9.

Zimetbaum, P, MR Reynolds, KKL Ho, T Gaziano, MJ McDonald, S McClennan, R Berezin, ME Josephson, and DJ Cohen. 2003. Impact of a Practice Guideline for Patients with Atrial Fibrillation on Medical Resource Utilization and Costs. *Am J Cardiol* 92(6):677-81.

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### **Acknowledgements:**

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The Alliance extends its thanks to the following experts for reviewing *The Silver Book®: Thrombosis*:

- **Bart M. Demaerschalk**, MD, MSc, FRCP(C),  
Director, Cerebrovascular Diseases Center,  
Mayo Clinic
- **Valentin Fuster**, MD, Director, Cardiovascular  
Institute, The Mount Sinai Medical Center
- **Steven A. Lubitz**, MD, MPH, Fellow,  
Cardiac Arrhythmia Service, Massachusetts  
General Hospital
- **Wayne D. Rosamond**, PhD, Professor,  
Department of Epidemiology, UNC Gillings  
School of Public Health

This volume of *The Silver Book®* is supported by

