Deloitte Access Economics

Off beat:

Atrial fibrillation and the cost of preventable strokes

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Contents

Charts

Tables

Figures

Glossary

AAD	anti-arrhythmic drug
AF	atrial fibrillation
BD	twice daily
CHF	congestive heart failure
ECG	electrocardiogram
GP	general practitioner
INR	international normalized ratio
NEMESIS	North East Melbourne Stroke Incidence Study
NSAIDS	non-steroidal anti-inflammatory drugs
NVAF	non-valvular atrial fibrillation
PBS	Pharmaceutical Benefits Scheme
RE-LY	Randomized Evaluation of Long-Term Coagulation Therapy
RR(R)	relative risk (reduction)
TIA	transient ischaemic attack
VKA	vitamin K antagonist

Executive Summary

Atrial fibrillation and the risk of stroke

Atrial fibrillation (AF) is the most common type of heart arrhythmia (rhythm disorder). People with AF have an irregular heartbeat which causes inefficient blood flow and through the formation of emboli (blood clots), may result in stroke. Most people with AF need medicines to prevent strokes. However, many are undiagnosed or receive no treatment at all despite initiatives to improve this. Ineffective or no stroke prevention treatment leads to even more strokes, poor outcomes for patients and is costly to the Australian health system. There is a clinical need for more efficacious stroke prevention medicines.

Stroke is one of the most serious consequences of AF and imposes substantial personal and economic costs. One in five Australians suffering a stroke will die within the first month and the impact on a stroke survivor's quality of life is considerable, often with reductions in mobility, conversation skills, memory, and perception. People suffering a stroke are likely to need the help of family, friends and other carers to perform everyday activities and will almost certainly require ongoing health care services.

Deloitte Access Economics estimates there to be 506,045 people aged 50 years and older in Australia with AF in 2011, a prevalence of 7.0% within this age group. This includes 456,511 people with non-valvular atrial fibrillation (NVAF), including 259,057 people at high stroke risk, 138,539 people with moderate stroke risk and 58,915 people at low stroke risk.

A proportion of Australians with AF are undiagnosed and thus not receiving treatment. Between 11% and 30% of Australians with AF are undiagnosed. Based on this, it is estimated that between 50,036 and 173,501 Australians have undiagnosed AF, with a best estimate of 101,209 Australians.

An estimated 61,981 strokes will occur among the Australian population in 2011 including 45,873 first-ever strokes. Nearly one-third of first-ever strokes among the Australian population (14,364 of 45,873 strokes) occur in people with AF and three-quarters of these (10,709 strokes) can be specifically attributed to patients' AF rather than other clinical factors.

The cost of strokes due to atrial fibrillation

Strokes are costly to manage and incur direct health care costs, community services and aged care costs. The average total direct cost of an AF-related ischaemic stroke is estimated to be $29,357 in the first year alone.

Total first-ever strokes occurring in Australia in 2011 are estimated to cost $1.4 billion in the first year and $2.4 billion over five years. First-ever strokes specifically due to AF in 2011 are estimated to cost $314.4 million in the first year and $562.7 million over five years.

The health care costs alone of strokes due to AF are expected to total $278.9 million in the first year. Almost 90% of this cost is attributed to inpatient treatment of the initial stroke and its complications (including recurrences) and inpatient/outpatient rehabilitation. Other key health care costs include general practitioner visits, medications and investigations.

These numbers underestimate the full cost of AF-related strokes each year, since patients may receive ongoing care beyond five years. Further, the five-year risk of recurrent stroke is around nine times greater following a previous stroke.

Total costs of stroke, including stroke in people with AF are presented in Table i.

Table i: Annual and five year costs of first-ever strokes (a), 2011

	Incidence in 2011	First year costs	Five year costs
	number	*$ million*	*$ million*
All first-ever strokes	45,873	1,420.6	2,363.9
First-ever strokes in people with AF	14,364	444.8	740.2
First-ever strokes in people with AF due to AF (i.e. ischaemic strokes)	10,709	314.4	562.7
First-ever strokes in people with NVAF at moderate-to-high stroke risk receiving no antithrombotic therapy	7,403	217.3	389.0

Notes: (a) Includes health care costs, costs of community services and costs related to aged care.
Source: Deloitte Access Economics calculations

Stroke prevention for people with atrial fibrillation in Australia

Treatment is essential to reduce the risk of stroke in people with AF. Commonly, on the PBS, warfarin is prescribed for high-risk patients, and either aspirin or warfarin is prescribed for moderate-risk patients. Australian guidelines are likely to change with the availability of new, more effective stroke prevention medicines.

International data suggest that around 1 in 5 cases of AF remain undiagnosed, and therefore untreated, and these people are at an elevated risk of developing stroke. In current practice, warfarin is commonly prescribed via the PBS to prevent strokes. However, patients must be monitored regularly to ensure their treatment is titrated to an optimum International Normalized Ratio (INR) to balance the risks of stroke and warfarin-related bleeding. In practice, patients achieve optimum control only 50-60% of the time and warfarin remains a major contributor to drug-related hospitalisations in Australia.

Warfarin places a considerable burden on patients and prescribers through:

- the need for frequent blood monitoring especially for patients living in rural or regional areas;
- fear of treatment-related bleeding, including difficult to treat and disabling stroke and major bleeds;
- requirements for patients to follow specific and consistent diets due to drug-food interactions; and
- interactions between warfarin and many common medicines.

For these reasons, even though warfarin has been available in Australia for over 50 years, it is only used by an estimated 40% of people diagnosed with non-valvular AF (NVAF) and at moderate-to-high stroke risk. Warfarin monitoring imposes a cost burden on society including costs of INR tests, patient out-of-pocket travel costs to/from clinics, productivity losses and health care costs of warfarin-related bleeds. The annual societal cost of

warfarin-related monitoring and bleeding is estimated to exceed $95.7 million. New antithrombotic treatments are emerging which have demonstrated greater stroke risk reduction than warfarin without an increased risk of major bleeding or the need for monitoring.

Available Australian data suggest that current clinical practice is suboptimal to minimise the risk of stroke for people with NVAF:

- Around 39% of high-risk patients and 42% of moderate-risk patients are undiagnosed and/or untreated for NVAF and should receive stroke prevention medicine;
- However, 10% of high-risk patients receive aspirin only.

Preventable strokes with greater diagnosis and better stroke prevention treatment

Better stroke prevention treatment and greater diagnosis in patients with AF can potentially prevent strokes and avert costs to patients and the Australian health care system as shown in Table ii.

Table ii: Incidence and cost of strokes (a) in people with NVAF at a moderate-to-high stroke risk, 2011

	Stroke numbers	First year stroke costs	Five year stroke costs
	number	*$ million*	*$ million*
First-ever strokes in people receiving no stroke prevention treatment (n = 127,999)	7,403	217.3	389.0
Preventable strokes using aspirin or warfarin	3,532	103.7	185.6

Notes: (a) Includes health care costs, costs of community services and costs related to aged care.
Source: Deloitte Access Economics calculations

Recommendations

Many people with AF are undiagnosed or receive no stroke prevention treatment at all, despite it being indicated. Ineffective or no stroke prevention treatment leads to even more strokes, poor outcomes for patients and is costly to the Australian health care system. In light of this, Deloitte Access Economics puts forward the following recommendations:

- raising awareness of the symptoms and effects of AF among older Australians;
- encouraging GPs to routinely check for heart arrhythmias in patients aged over 50 years;
- encouraging health care providers to optimise treatment practice by prescribing the most effective stroke prevention treatment; and
- making accessible new stroke prevention treatments with more favourable efficacy, safety and convenience on balance compared with warfarin.

This report was commissioned by Boehringer Ingelheim in the interests of improved stroke prevention among Australians with atrial fibrillation. The expert opinion of leaders in stroke prevention and cardiology was essential to the compilation of this timely report.

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1 Background

People with atrial fibrillation have an irregular heartbeat, which causes inefficient blood flow and, through the formation of blood clots, may result in ischaemic stroke. Valvular atrial fibrillation (rheumatic valve disease) is associated with an 18-fold increase in stroke risk and non-valvular atrial fibrillation is associated with a five-fold increase in stroke risk.

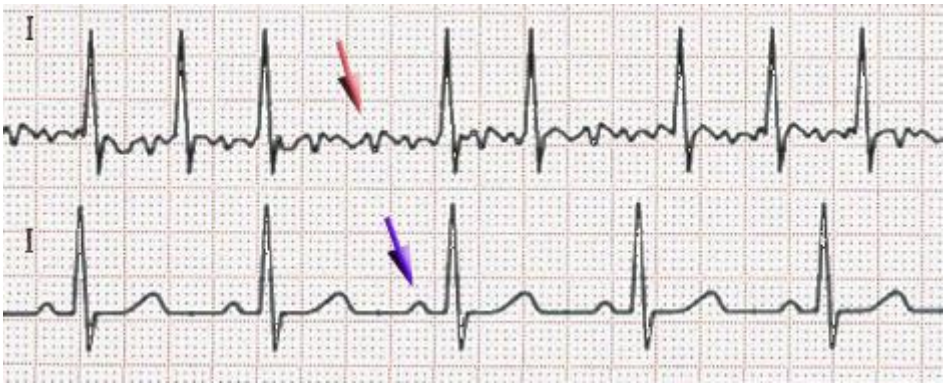
Most people with atrial fibrillation need medicines to prevent strokes as well as anti-arrhythmic drugs to maintain sinus rhythm. Greater anticoagulation through warfarin reduces the risk of blood clotting and ischaemic stroke but increases the risk of major bleeds. Patients on warfarin require frequent clinic visits for blood monitoring to modify doses. Warfarin interacts with many common medicines and foods. Aspirin is less effective than warfarin. There is therefore a clinical need for newer stroke prevention medicines which are more effective than warfarin and aspirin.

1.1 What is atrial fibrillation?

Atrial fibrillation (AF) is the most common cardiac heart arrhythmia (abnormal heart rhythm) and describes the fibrillation (quivering) of the heart muscles in the upper chambers of the heart (atria). AF is characterised by heart beats that do not occur at regular intervals, and variable intervals between two atrial activations.

The presence of AF is shown in Figure 1.1, where the electrocardiogram (ECG) reading for a person with AF (top reading) demonstrates greater variability in heart beats than for a person with a normal sinus rhythm (bottom reading). A distinct P wave (shown by the purple arrow on the bottom reading), which is normally present when there is a coordinated atrial contraction at the beginning of each heart beat, is not seen in a patient with AF.

Figure 1.1: ECG reading with AF compared to normal sinus rhythm



Source: Heuser (2005)

AF may develop from one or more cardiac and non-cardiac causes, including heart disease, hypertension, obesity, and excessive alcohol ingestion. Around 10% of AF is caused by rheumatic heart disease, primarily mitral valve disease (valvular AF). The other 90% of AF cases are categorised as non-valvular atrial fibrillation (NVAF).

AF may be further categorised as paroxysmal (recurrent episodes that self-terminate within one week), persistent (recurrent episodes lasting more than one week), or permanent (ongoing AF). AF is a chronic condition.

The irregular heart rhythms that characterise AF cause blood flow to be inefficient, which may in turn lead to clotting. This increases the risk of cardiovascular events such as chest pain (angina), congestive heart failure (CHF), transient ischaemic attack (TIA) and ischaemic stroke.

AF is considerably more prevalent among people aged over 50 years. The prevalence of AF in this age group is around 6%, compared with approximately 2% in the total population. As estimated in Chapter 2 of this report, around 400,000 people in Australia have diagnosed AF.

1.2 The risk of stroke in people with AF

A stroke is defined as the rapidly developing loss of brain function due to a disturbance in the blood supply to the brain. The two major types of stroke are:

- ischaemic stroke, when blood flow is interrupted to the brain e.g. when an embolus becomes lodged in a cranial artery;
- haemorrhagic stroke, when a blood vessel or artery in the brain bursts and there is a leakage of blood into the brain.

Haemorrhagic stroke is not generally associated with AF, unless hypertension is underlying both AF and haemorrhagic stroke, or if haemorrhage occurs due to bleeding as a consequence of therapy for AF.

AF associated with rheumatic valve disease (valvular AF) is associated with an approximately 18-fold increase in stroke risk (Wolf et al, 1978). NVAF increases the risk of stroke by approximately five times (Wolf et al, 1991). Specifically, AF causes blood to pool

and clot in the poorly contracting atria. A clot may eventually break away and travel through the blood stream where it becomes lodged in an artery. This may be an artery in the brain (an ischaemic stroke).

A stroke leads to the affected area of the brain being unable to function. This may result in a variety of debilitating effects on an individual's mobility, communication, quality of life and perception. These effects may be long lasting and can include:

- an inability to move one or more limbs on one side of the body;
- an inability to understand or formulate speech;
- an inability to see one side of the visual field;
- emotional problems and depression.

In the first instance, most people suffering a stroke will be admitted to a hospital stroke unit where treatment focuses on identifying the cause of the stroke and the appropriate treatment. Treatment for an ischaemic stroke is directed at breaking down the clot though thrombolysis, thrombectomy, antiplatelet therapy and/or anti-coagulation. Haemorrhagic strokes may be treated surgically.

Around one in five people will die within 28 days of a stroke (Thrift et al, 2000). Survivors are likely to suffer a decreased quality of life for many months, if not years, and will need rehabilitation and the help of family, friends and other carers to perform their everyday activities. They may also require ongoing health care support for many years.

The direct cost of treating a stroke is around $30,000 in the first year alone (see Chapter 3).

In people aged 50 years and older with NVAF, the risk of stroke is around five times higher in people of a similar age with a normal sinus rhythm (Wolf et al, 1991). The annual risk of stroke in people with untreated NVAF ranges from 1.9% to 18.2% depending on the number of other stroke risk factors present (Medi et al, 2010). In people with NVAF the strongest independent predictors of stroke are prior stroke or TIA (relative risk 1.9 to 3.7) and age (relative risk 1.4 per decade). Other independent risk factors include hypertension, diabetes, recent cardiac failure, and impaired left ventricular ejection fraction.

1.3 What can be done to prevent strokes in people with AF?

Current treatment for AF is targeted at: (1) maintaining the sinus rhythm using anti-arrhythmic drugs (AADs), and (2) preventing blood clotting using either antiplatelet therapy (aspirin) or oral anticoagulants.

Clinical studies have found warfarin to be clinically superior to no treatment and aspirin in preventing strokes in people with NVAF at a moderate-to-high risk of stroke (Medi et al, 2010).

Meta-analyses of these studies have reported:

- a 64% relative risk reduction for stroke with warfarin compared with no treatment (Hart et al, 2007);
- a 22% relative risk reduction for stroke with aspirin compared with no treatment, by reducing non-disabling non-cardioembolic strokes (van Walraven et al, 2002); and
- a 39% relative risk reduction for stroke with warfarin compared with aspirin (van Walraven et al, 2002).

Unfortunately, warfarin only operates effectively within a narrow therapeutic range, defined by an international normalized ratio (INR) range of 2-3. Greater anticoagulation reduces the risk of blood clotting and associated ischaemic stroke, but increases the risk of major bleeds, including haemorrhagic strokes. With warfarin there is a 70% increase in the risk of major bleeding relative to untreated patients (Hart et al, 2007). Patients require frequent clinic visits for regular blood monitoring to modify treatment doses where needed and balance their risks of stroke and treatment-related bleeding.

Because of these disadvantages, warfarin is generally recommended only for people at a moderate-to-high risk of stroke; with the stroke risk defined using one of several scoring algorithms, for example, the $CHADS_2$ system. Historically, clinical guidelines recommended the following stroke prevention treatments for AF (for example, Hankey, 2001 in Australia):

- no treatment or 75-300mg aspirin daily for people at a low stroke risk;
- warfarin (target INR 2-3) or 75-300mg aspirin daily for people at a moderate stroke risk;
- warfarin (target INR 2-3), if not contraindicated, for people at a high stroke risk.

Some clinical guidelines more broadly specify oral anticoagulation with a vitamin K antagonist (VKA), including warfarin, for moderate-to-high risk stroke patients.

Treatment guidelines (e.g. Canada, Europe and the US) are gradually beginning to recognise emerging pharmacological stroke prevention treatments (Cairns et al, 2010; Camm et al, 2010; Wann et al, 2011).

This report

The aim of this report is two-fold:

1. to quantify the extent of AF and the economic and patient burden of associated strokes in Australia; and
2. to assess how current clinical practice can be improved to reduce this burden.

The structure of this report is as follows:

- Chapter 2 estimates the prevalence of diagnosed and undiagnosed AF in Australia;
- Chapter 3 estimates the incidence and cost of strokes in people with AF in Australia;
- Chapter 4 discusses current stroke prevention treatment practice in Australia, including the proportion of patients currently untreated;
- Chapter 5 estimates the number and cost of strokes in Australia that could potentially be prevented through greater diagnosis and treatment of NVAF;
- Chapter 6 proposes some key recommendations to reduce the burden of stroke in Australia through better management of AF.

2 The prevalence of AF in Australia

The diagnosed prevalence of atrial fibrillation is estimated to be 4% of the Australian population aged greater than 30 years (Sturm et al, 2002). Prevalence rates increase with older age groups. It is estimated that 404,836 Australians aged 50 years and over have a diagnosis of atrial fibrillation in 2011. Of these, 10% (39,627 people) are estimated to have valvular atrial fibrillation and 90% (365,209 people) to have non-valvular atrial fibrillation. Within those with diagnosed non-valvular atrial fibrillation, an estimated 207,246 (57%) are at a high risk of stroke.

A proportion of Australians with AF are undiagnosed, and as such, not receiving treatment. The undiagnosed proportion of atrial fibrillation is estimated to be between 11% and 30%, from international studies. Based on this, it is estimated that 101,209 Australians have undiagnosed atrial fibrillation.

In total, it is estimated that 506,045 Australians have AF in 2011, including 404,836 diagnosed cases and 101,209 undiagnosed cases.

2.1 Australian prevalence studies of AF

International studies have found that around 6% of the general population aged 50 years and over have AF (Wolf et al, 1991). The number of Australian studies of AF prevalence is limited.

A systematic review of the literature undertaken for this study identified two previously published studies on the prevalence of AF in Australia:

- a Western Australia study of 1,770 community participants aged 60 years and over, which assessed relative mortality in people with and without AF (Lake et al, 1989); and
- a study of 16,148 participants aged 30 years and older attending general practices across Australia during 2000 which examined the prevalence of stroke risk factors including AF (Sturm et al, 2002).

The earlier study (Lake et al, 1989) conducted triennial surveys in the Busselton community in Western Australia from 1966 to 1981, with patient follow-up to 1983. Surveys included brief social and medical history, analysis of blood for serum cholesterol and ECG classification. The method for diagnosing AF was not stated.

The later study (Sturm et al, 2002), was conducted among 321 GPs in six Australian States and Territories, with each providing data on 50 consecutive patients aged 30 years and older. AF was defined as past history or current presentation of AF confirmed by an ECG reading.

For this study, AF prevalence rates are derived from the Sturm study due to its:

- recent data;
- larger sample size;
- coverage of a wider age range of participants;
- coverage of a larger area of Australia; and
- statement of how AF was diagnosed/defined in participants.

Sturm et al (2002) reported an overall AF prevalence rate of 4% in people aged 30 years and older (6% among 5,801 men, and 4% among 8,393 women). The study noted a very low prevalence of AF in people under 50 years of age. This is consistent with a low prevalence of AF internationally in people below 55 years of age (0-0.5%) (Phillips et al, 1990). Consequently, this study, which focuses on stroke prevention in people with AF, only focuses on people aged 50 years and older.

The AF prevalence rates reported by Sturm et al (2002) are presented in Table 2.1 and are considered the best representation of AF prevalence in the total Australian population.

Table 2.1: Prevalence rates for AF by age and sex

Age group	Males	Females
	%	*%*
50-59	2.0	1.0
60-69	6.0	2.5
70-79	14.0	8.0
80+	16.0	14.0

Source: Figure 3 of Sturm et al (2002)

Australian data on the relative proportions of valvular AF, where rheumatic heart disease is present and patients are at a high risk of stroke, and non-valvular AF (NVAF), where patients are at varying risks of stroke, are limited. A review of AF cases documented at Tasmania's major teaching hospital in 1997 revealed that 9.8% of AF patients had valvular AF (Ang et al, 1998). Therefore it is estimated that in Australia 90.2% of people with AF have NVAF. These proportions are applied to the AF prevalence rates derived from Sturm et al (2002) to disaggregate Australian AF prevalence estimates by valvular AF and NVAF.

When considering stroke prevention treatment for people with AF, it is important to consider their risk of stroke. People with valvular AF are considered to be at a high risk of stroke (Hankey, 2001).

The widely used $CHADS_2$ system is based on a total risk score, where the presence of congestive heart failure (CHF), hypertension, or diabetes, or age over 75 years, contribute one point each, and prior stroke or transient ischaemic attack (TIA) contributes two points. Low, moderate and high stroke risks are associated with $CHADS_2$ scores of zero, one and greater than one (or valvular AF), respectively.

Although no Australian-specific data were identified for NVAF, a UK study of 51,807 chronic AF patients without a history of heart valve problems estimated the proportions of low, moderate and high risk stroke patients (as measured by the $CHADS_2$ classification system) to be (Rietbrock et al, 2008):

- 12.9% of NVAF patients at low stroke risk ($CHADS_2 = 0$);
- 30.3% of NVAF patients at moderate stroke risk ($CHADS_2 = 1$); and
- 56.7% of NVAF patients at high stroke risk ($CHADS_2 > 1$).

Country-specific data from the Randomized Evaluation of Long-Term Anticoagulation Therapy (RE-LY) trial (Connolly et al, 2009) reports the proportion of high stroke risk patients among all moderate to high stroke risk patients to be 70% in Australia compared with 67% in the UK. Due to similar estimated distributions between Australia and the UK, the UK NVAF risk proportions have been applied in this report. Using this data, the estimated Australian prevalence rates of valvular AF and NVAF by stroke risk are presented in Table 2.2.

Prevalence rates for AF are higher for males than for females, particularly in people aged 60-79 years. People with AF are much more likely to have NVAF than valvular AF, and within NVAF patients are over twice as likely to have a high risk of stroke compared with a moderate risk of stroke. Because the prevalence rates for AF rise with age, with future demographic ageing of the population, the number of Australians with AF is expected to increase.

Table 2.2: Prevalence rates for valvular AF and NVAF by age and gender

Age group	Valvular AF	Non valvular AF				All AF
		Low stroke risk	Moderate stroke risk	High stroke risk	All NVAF	
	%	%	%	%	%	%
Males						
50-59	0.2	0.2	0.5	1.0	1.8	2.0
60-69	0.6	0.7	1.6	3.1	5.4	6.0
70-79	1.4	1.6	3.8	7.2	12.6	14.0
80+	1.6	1.9	4.4	8.2	14.4	16.0
Females						
50-59	0.1	0.1	0.3	0.5	0.9	1.0
60-69	0.2	0.3	0.7	1.3	2.3	2.5
70-79	0.8	0.9	2.2	4.1	7.2	8.0
80+	1.4	1.6	3.8	7.2	12.6	14.0
All people						
50-59	0.1	0.2	0.4	0.8	1.3	1.5
60-69	0.4	0.5	1.2	2.2	3.8	4.2
70-79	1.1	1.3	3.0	5.6	9.8	10.9
80+	1.4	1.7	4.0	7.6	13.3	14.8

Source: Deloitte Access Economics calculations using Ang et al (1998), Rietbrock et al (2008) and Sturm et al (2002).

2.2 How many Australians have diagnosed AF?

Prevalence rates for AF by gender/age group and stroke risk category in Section 2.1 were applied to age-gender population numbers from ABS population projections for 2011 (ABS 2011, series B) to estimate the numbers of Australians aged 50 years and over with AF in 2011 (Table 2.3).

Overall, it is estimated that 404,836 Australians aged 50 years and over have an AF diagnosis in 2011, of which 39,627 people have valvular AF and 365,209 have NVAF. Males comprise over half (58%) of all Australians aged over 50 years with AF. Importantly, most people with NVAF are considered to be at high risk of stroke. It is estimated that 207,246 (57%) of the 365,209 people with an NVAF diagnosis are at high risk of stroke in 2011. Prevalence numbers for all types of AF rise with age for both genders. Approximately three quarters of people with AF in 2011 are aged 70 years or over.

Table 2.3: People with diagnosed valvular AF and NVAF in Australia by age/gender, 2011

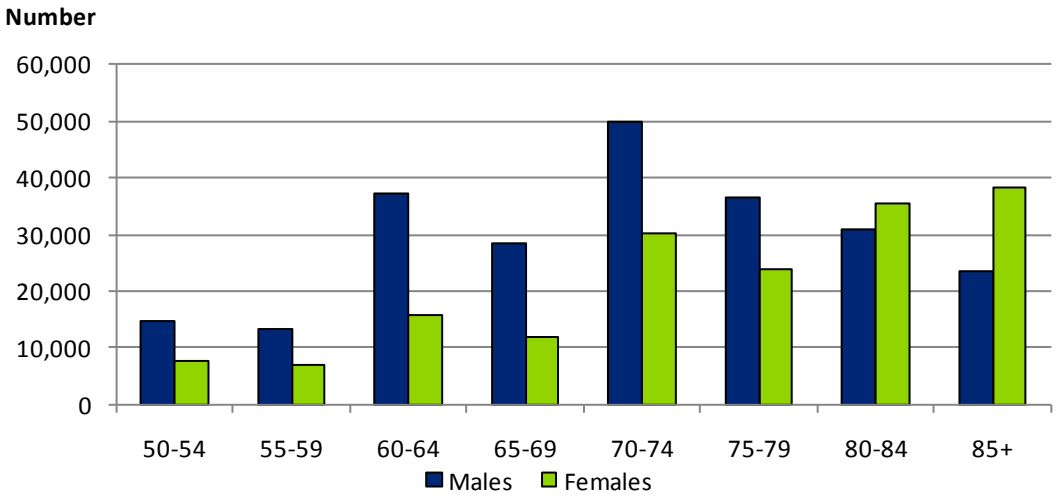
Age group	Valvular AF	Non valvular AF				All AF
		Low stroke risk	Moderate stroke risk	High stroke risk	All NVAF	
	number	*number*	*number*	*number*	*number*	*number*
Males						
50-54	1,443	1,717	4,037	7,549	13,303	14,746
55-59	1,308	1,556	3,659	6,842	12,056	13,365
60-64	3,638	4,327	10,174	19,025	33,526	37,164
65-69	2,783	3,311	7,785	14,557	25,653	28,436
70-74	4,873	5,797	13,631	25,488	44,915	49,789
75-79	3,587	4,266	10,032	18,759	33,058	36,645
80-84	3,035	3,610	8,488	15,871	27,969	31,003
85+	2,295	2,729	6,418	12,002	21,149	23,444
Total 50+	**22,963**	**27,312**	**64,223**	**120,093**	**211,628**	**234,591**
Females						
50-54	739	880	2,068	3,867	6,815	7,555
55-59	667	793	1,865	3,488	6,146	6,813
60-64	1,537	1,828	4,298	8,036	14,161	15,698
65-69	1,178	1,401	3,295	6,162	10,859	12,037
70-74	2,959	3,519	8,275	15,473	27,267	30,226
75-79	2,351	2,797	6,576	12,297	21,670	24,022
80-84	3,476	4,135	9,722	18,180	32,037	35,513
85+	3,757	4,469	10,508	19,649	34,625	38,382
Total 50+	**16,664**	**19,821**	**46,608**	**87,153**	**153,581**	**170,245**
All people						
50-54	2,183	2,596	6,105	11,416	20,118	22,301
55-59	1,975	2,349	5,524	10,329	18,202	20,177
60-64	5,174	6,154	14,472	27,061	47,687	52,861
65-69	3,962	4,712	11,080	20,719	36,512	40,473
70-74	7,832	9,316	21,905	40,961	72,182	80,015
75-79	5,938	7,063	16,608	31,057	54,728	60,666
80-84	6,511	7,744	18,210	34,051	60,006	66,516
85+	6,052	7,198	16,926	31,650	55,774	61,826
Total 50+	**39,627**	**47,132**	**110,831**	**207,246**	**365,209**	**404,836**

Source: Deloitte Access Economics calculations using ABS (2011), Ang et al (1998), Rietbrock et al (2008) and Sturm et al (2002).

The rising prevalence of diagnosed AF by age and gender is graphically depicted in Chart 2.1. The prevalence numbers for diagnosed AF generally rise by age group (older age groups have higher prevalence rates but lower general population numbers). For males,

diagnosed prevalence is highest for the 70 to 74 age group, and for females, prevalence is highest for the 85+ age group. The prevalence of AF in Australia will continue to rise, due to the demographic ageing of the population.

Chart 2.1: Diagnosed prevalence of AF by age and gender



Source: Deloitte Access Economics calculations using ABS (2011), Ang et al (1998), Rietbrock et al (2008) and Sturm et al (2002).

2.3 What proportion of AF is undiagnosed?

A systematic literature search identified no Australian studies reporting the proportion of AF that is undiagnosed. However, the findings of five relevant international studies are summarised below.

- Tveit et al (2008) tested 916 patients aged 75 years and over in Norway by ECG. It was reported that AF was previously undiagnosed in 10.9% of patients with AF (10/92).
- A study of 1,028 hypertensive patients in Spain (mean age 73 years) found 16.0% of patients with AF (16/106) were previously undiagnosed (Morillas et al, 2010).
- A US study of 294 health maintenance organisation beneficiaries found 19.0% of people with AF were undiagnosed (Mullenix et al, 2006).
- Sudlow et al (1997) found in a UK study of 1,530 patients aged 65 years and over that 76.0% of those with AF had AF recorded in past medical notes (71/93). This translates to an undiagnosed AF proportion of 24.0%.
- Another smaller UK study of 131 AF patients in St George's AF Clinic found 29.8% of these patients had AF diagnosed incidentally, and were thus previously undiagnosed (Savelieva and Camm, 2000).

The undiagnosed proportion of AF internationally is therefore estimated to be between 11% and 30%. Based on this, the proportion of AF in Australia that is undiagnosed is estimated to be 20% (midpoint), with the degree of uncertainty expected to range between 11% and 30%. It is therefore estimated that between 50,036 and 173,501 Australians have undiagnosed AF, with a best estimate of 101,209 Australians with undiagnosed AF. It is estimated that of these, 91,302 Australians have NVAF (Ang et al, 1998). Of these, 51,811

are estimated to be at high stroke risk, 27,708 at moderate stroke risk and 11,783 at low stroke risk, applying NVAF stroke risk distributions from UK data (Rietbrock et al, 2008).

2.4 Total prevalence of AF

Overall, it is estimated that 506,045 Australians have AF in Australia in 2011 including 101,209 undiagnosed and 404,836 diagnosed cases. Around 456,511 Australians are estimated to have NVAF (diagnosed and undiagnosed) including 259,057 at high stroke risk, 138,539 at moderate stroke risk and 58,915 at low stroke risk.

Table 2.4: Prevalence of AF in Australia, 2011

	Diagnosed	Undiagnosed	Total
	number	*number*	*number*
Valvular AF	**39,627**	**9,907**	**49,534**
NVAF	**365,209**	**91,302**	**456,511**
- High stroke risk	207,246	51,811	259,057
- Moderate stroke risk	110,831	27,708	138,539
- Low stroke risk	47,132	11,783	58,915
Total	**404,836**	**101,209**	**506,045**

Source: Deloitte Access Economics calculations (2011)

3 The impact of stroke in Australia

A stroke occurs when blood supply to the brain is blocked (ischaemic stroke) or when an intracranial blood vessel bursts (haemorrhagic stroke). AF can cause blood to pool and clot and therefore may increase the risk of ischaemic stroke.

It is estimated that 61,981 strokes will occur in Australia in 2011 including 45,873 first-ever strokes. It is estimated that 14,364 first-ever strokes will occur in people with AF in 2011. Of these strokes, around three quarters (10,709) will be specifically due to AF.

Strokes are costly to manage and incur direct health care costs, community services and aged care costs. Total first-ever strokes in Australia in 2011 are estimated to cost $1.4 billion in the first year and $2.4 billion over five years. First-ever strokes in people with AF are estimated to cost $444.8 million in the first year and $740.2 million over five years. First-ever strokes specifically due to AF are estimated to cost $314.4 million in the first year and $562.7 million over five years.

3.1 What is stroke?

A stroke is rapidly developing loss of brain function due to a disturbance in the blood supply to the brain. When blood cannot reach parts of the brain, oxygen supply to these areas is restricted and brain cells die. A loss of brain function and impairment of physical function may occur and may lead to death. The result of these processes is a stroke (Stroke NSW, 2011).

There are two types of stroke, described below:

- **Ischaemic stroke:** This type of stroke occurs when blood supply to the brain is blocked, for example by a blood clot. A blot clot may form somewhere in the body and travel through the blood stream to the brain (embolic), or blood vessels may narrow as a result of atheroma or small vessel disease. Ischaemic stroke is the most common type of stroke (AIHW, 2010).
- **Haemorrhagic stroke:** This type of stroke occurs when a blood vessel in the brain breaks or bursts and results in bleeding within the brain tissue (intracerebral haemorrhage) or in the space around the brain (subarachnoid haemorrhage).

A transient ischaemic attack (TIA) or 'mini-stroke' is a related condition which results in temporary stroke-like symptoms and is an important predictor of stroke. A TIA results from temporary blockage of blood vessels that reduce blood supply to the brain, and may last only a few minutes with symptoms disappearing within 24 hours (AIHW, 2010). Strokes and TIAs are sometimes collectively referred to as cerebrovascular events.

Consequences of stroke are serious and may include (Brain Foundation, 2011):

- weakness or lack of movement (paralysis) in legs and/or arms;
- pain;
- perceptual problems;
- sensory problems;
- cognitive problems;
- communication problems (i.e. trouble speaking, reading or writing);
- incontinence;
- depression;
- problems controlling feelings; and
- a significantly increased risk of death.

3.2 Extent of stroke in Australia

The most extensive Australian study of the incidence and cost of stroke is the North East Melbourne Stroke Incidence Study (NEMESIS). NEMESIS identified and assessed all suspected strokes occurring in a population of 133,816 residents (all ages) in suburbs north and east of Melbourne between 1996 and 1997. Multiple overlapping sources including daily admission lists, stroke unit lists of major public and private hospitals, and computerised discharge lists, were used to ascertain stroke cases. Standard clinical criteria for stroke and case fatality were used. A total of 381 strokes occurred during the study period.

Annual incidence rates for first-ever and recurrent strokes derived from NEMESIS data (Thrift et al, 2000, 2001) are presented by age and gender in Table 3.1. Incidence rates for stroke were found to increase substantially with age and were generally higher for males.

Table 3.1: Incidence rates for stroke

Age group	First-ever (ischaemic)	First-ever (all)	All strokes including recurrent (all)
	rate per 100,000	*rate per 100,000*	*rate per 100,000*
Males			
15-24	0	11	11
25-34	0	9	9
35-44	40	61	61
45-54	94	135	148
55-64	228	260	342
65-74	383	566	876
75-84	1,248	1,468	2,202
85+	2,389	3,344	4,459
Females			
15-24	0	0	0
25-34	25	49	49
35-44	10	29	29
45-54	64	77	77
55-64	107	168	260
65-74	396	507	634
75-84	832	1,178	1,756
85+	1,854	2,715	3,375

Source: Thrift et al (2000, 2001).

These incidence rates were applied to population projections (ABS, 2011, Series B) to estimate the number of strokes likely to occur in Australia in 2011 (Table 3.2) if stroke rates remain similar. It is estimated that 61,981 strokes will occur in Australia in 2011, of which 45,873 (74%) will be first-ever strokes. Within first-ever strokes, there are expected to be 33,374 ischaemic strokes, which is 73% of all first-ever strokes. Around three quarters of all first-ever strokes in 2011 are expected to occur in people aged 65 years and over, reflecting the increased risk of stroke with advanced age.

Table 3.2: Expected strokes in Australia in 2011

Age group	First-ever (ischaemic)	First-ever (all)	Recurrent (all)
	number	*number*	*number*
Males			
15-24	0	172	172
25-34	0	142	142
35-44	627	956	956
45-54	1,420	2,039	2,236
55-64	2,936	3,348	4,404
65-74	3,177	4,695	7,267
75-84	5,685	6,687	10,031
85+	3,501	4,900	6,534
Total 15+	17,346	22,940	31,742
Females			
15-24	0	0	0
25-34	388	761	761
35-44	159	460	460
45-54	986	1,186	1,186
55-64	1,401	2,199	3,404
65-74	3,403	4,357	5,448
75-84	4,609	6,525	9,727
85+	5,083	7,443	9,253
Total 15+	16,028	22,932	30,239
All people			
15-24	0	172	172
25-34	388	903	903
35-44	786	1,416	1,416
45-54	2,406	3,226	3,422
55-64	4,337	5,547	7,808
65-74	6,580	9,052	12,715
75-84	10,294	13,212	19,758
85+	8,583	12,343	15,786
Total 15+	33,374	45,873	61,981

Source: Deloitte Access Economics calculations using ABS (2011) and Thrift et al (2000, 2001).

3.3 Strokes in people with AF

To estimate the number of strokes in people with AF, the relative risk of stroke with AF was explored. An Australian study (Simons et al, 2009) following a cohort of 2,805 people aged 60 years and older in Dubbo, NSW, over 16 years between 1988 and 2004, estimated the relative risk of stroke with AF to be 3.06. This study did not report the relative risk by age group or for younger people also at a significant risk of AF (e.g. people aged 50-59 years).

The most widely quoted study for the relative risk of stroke with AF was undertaken by Wolf et al (1991), who examined the impact of NVAF on stroke incidence in 5,070 Framingham Heart Study participants in Massachusetts, US. This study analysed the relative risk of first-ever stroke in a community population, compared with other studies which examined hospitalised patients (Wolf et al, 1998; Yuan et al, 1998) and are therefore less reflective of the general population.

Relative risks for first-ever stroke with AF are presented by age group in Table 3.3. The relative risks for people aged 60 years and over are consistent with Australian data (Simons et al, 2009), and all relative risks reported by Wolf et al (1991) are therefore considered to be generalisable to the Australian population.

Table 3.3: Relative risk of first-ever stroke in people with AF

Age group	Relative risk
<50	1.0 (assumed)
50-59	4.0
60-69	2.6
70-79	3.3
80+	4.5

Source: Derived from Wolf et al (1991).

For each age/gender group, the annual rate of stroke for people without AF was estimated as follows:

Annual rate of stroke in people without AF = [annual rate of stroke in total population (including people with and without AF, Table 3.1)] ÷ [weighted relative risk of stroke in total population] × [population size].

For each age/gender group, the annual rate of stroke in people with AF was estimated as follows:

Annual rate of stroke in people with AF = annual rate of stroke in people without AF × relative risk of stroke with AF

These annual rates were then applied to AF population estimates (Table 2.3) to estimate the number of first-ever strokes in people with AF in 2011 (Table 3.4). It is estimated that 14,364 first-ever strokes will occur in people with AF in 2011.

This finding – that 14,634 of 45,873 first-ever strokes occur in people with AF – is consistent with the National Stroke Foundation (2009) audit finding that 31% of people admitted for stroke in 2008 had AF.

The number of strokes in people with AF is higher than the number of strokes *caused* by AF. AF specifically increases the risk of ischaemic stroke through blood clotting. Ischaemic strokes attributable to AF were estimated as:

Annual strokes due to AF = [Annual strokes in AF population] – [(AF prevalence) x (Incidence rate for strokes in non-AF population)]

Overall, it is estimated that 10,709 strokes will occur in people with AF due to their AF in 2011 (Table 3.4). These strokes constitute 75% of all strokes in people aged 50 years and older with AF, and would only include ischaemic strokes. The proportion of strokes due to AF generally increases with age.

Table 3.4 : Strokes in people with AF in 2011

Age group	All first-ever strokes	All first-ever strokes	First-ever strokes due specifically to AF
	rate per 100,000 AF population	*number*	*number*
Males			
50-54	520	96	72
55-64	698	441	292
65-74	1,363	1,333	895
75-84	3,609	3,051	2,259
85+	8,648	2,534	1,971
Total		7,455	5,489
Females			
50-54	302	29	21
55-64	485	136	91
65-74	1,377	728	493
75-84	3,303	2,458	1,846
85+	7,416	3,558	2,767
Total		6,909	5,219
Total		**14,364**	**10,709**

Source: Deloitte Access Economics calculations using ABS (2011), Thrift et al (2000, 2001) and Wolf et al (1991).

3.4 Costs of stroke

The most comprehensive data on the costs of strokes in Australia are from the NEMESIS study (Dewey et al, 2001, 2003; Cadilhac et al, 2009). The NEMESIS study measured stroke costs using an incidence-based, patient level costing approach, specifically direct health care costs, patient out-of-pocket expenses, and the costs of community services, aged care and informal care.

Cadilhac et al (2009) reported 2004 cost estimates using the NEMESIS data. These costs for the first year following a stroke are presented for a first-ever ischaemic or haemorrhagic stroke in Table 3.5, inflated to 2011 prices.[1]

For this study, per stroke costs for 'all strokes' were estimated by weighting ischaemic and haemorrhagic stroke costs by the estimated incidence shares of ischaemic (72.8%) and haemorrhagic strokes (28.2%) within total strokes from NEMESIS data (Thrift et al, 2000, 2001).

Average first year health care costs per stroke were estimated in 2011 prices to be $26,046 for an ischaemic stroke, $30,544 for an intracerebral haemorrhage and $27,271 for any strokes.

[1] Health care costs were inflated at the average health inflation rate in Australia, estimated to be 3.2% per annum (AIHW 2010a). Community services and aged care costs were adjusted to account for price changes between 2004 and 2011, estimated to be 3.0% per annum using change in the consumer price index between 2004 and 2011 (ABS, 2011a). Informal care costs were adjusted for wage growth of 3.9% per annum, estimated using change in the labour price index between 2004 and 2011 (ABS, 2011b).

Average total first year costs per stroke including informal care, health care, aged care and community services were $30,825 for an ischaemic stroke, $36,403 for an intracerebral haemorrhage and $32,345 for any strokes. Excluding informal care, these costs were estimated to be $29,357, $35,269 and $30,967, respectively.

Table 3.5: Costs per stroke in the first year for first-ever strokes ($), 2011 prices

Cost type	Ischaemic stroke	Intracerebral haemorrhage	All strokes (a)
	cost	*cost*	*cost*
Health care costs			
Pre-admission GP or ambulance	549	832	626
Acute hospitalisation	10,776	13,224	11,443
Inpatient rehabilitation	8,835	10,154	9,195
Medication	550	443	521
GP	209	92	178
Private allied health	133	130	132
Investigations (b)	276	157	243
Specialist medical care	218	143	198
Outpatient rehabilitation	838	1,242	948
Hospitalisation for recurrent strokes	999	573	883
Hospitalisation for stroke complications	1,798	601	1,472
Ambulance	145	62	122
Emergency department	41	15	34
Out-of-pocket costs	679	2,876	1,278
Total health care costs	**26,046**	**30,544**	**27,271**
Other costs			
Aged care	2,833	4,402	3,260
Community services	25	121	51
Respite care	376	101	301
Aged care assessment teams	77	101	84
Caregiver costs	1,469	1,135	1,378
Total other costs	**4,779**	**5,859**	**5,074**
Total health care and other costs	**30,825**	**36,403**	**32,345**
As above, excluding informal care	**29,357**	**35,269**	**30,967**

Notes: (a) 'All strokes' costs were calculated by weighting ischaemic stroke costs and intracerebral haemorrhage stroke costs by their incidence shares, derived from NEMESIS data. From NEMESIS, 72.8% of strokes were ischaemic (Thrift et al 2000, 2001). (b) Includes pathology, radiology and other diagnostic tests.

Source: Deloitte Access Economics calculations using AIHW (2010a), ABS (2011a, 2011b), Cadilhac et al (2009) and Thrift et al (2000, 2001).

Cadilhac et al (2009) also estimated average subsequent year costs per stroke, using five years of patient follow-up data and a 3% annual discount rate. These costs were adjusted

for a recommended 5% discount rate (NHMRC, 2001) and are presented in Table 3.6, inflated to 2011 prices[2].

Excluding informal care, average annual costs per stroke in the second to fifth years following a stroke are estimated to be $5,798 for first-ever ischaemic strokes and $3,387 for intracerebral haemorrhagic strokes. This indicates that ischaemic strokes are more costly than intracerebral haemorrhages after the first year, reflecting the need for more intensive long term care.

Table 3.6: Annual subsequent year costs following a first-ever stroke ($) (a), 2011

	Ischaemic stroke	Intracerebral haemorrhage	All strokes (b)
	cost	*cost*	*cost*
Total costs exc. informal care	5,798	3,387	5,141
Total costs inc. informal care	7,098	4,687	6,441

Notes: (a) Costs presented in Cadilhac et al (2009) were discounted at a 3% rate. These costs were converted to costs discounted at a 5% discount rate (NHMRC 2001). (b) 'All strokes' costs were calculated by weighting ischaemic stroke costs and intracerebral haemorrhage stroke costs by their incidence shares, derived from NEMESIS data. From NEMESIS, 72.8% of strokes were ischaemic (Thrift et al, 2000; 2001).

Source: Deloitte Access Economics calculations using ABS (2011b), Cadilhac et al (2009) and Thrift et al (2000, 2001).

Five-year costs per stroke (excluding informal care) were calculated for first-ever strokes by summing the first year costs and four times the average cost for the subsequent four years. This conservatively assumes that the cost of a stroke does not extend beyond five years, in line with the reported cost data (Cadilhac et al, 2009).

The five-year costs were estimated to be $52,547 for an ischaemic stroke, $48,818 for an intracerebral haemorrhage, and $51,531 for any stroke. This indicates that ischaemic strokes are more costly to treat over five years than intracerebral haemorrhages due to greater ongoing costs (Table 3.7). These estimates are conservative because they restrict ongoing costs to five years (which may be considerably less than the life expectancy of stroke survivors) and exclude informal care costs.

[2] The majority of subsequent year costs for stroke are related to community services and rehabilitation (Cadilhac et al, 2009), rather than health care, thus costs were inflated at annual general inflation rather than health price inflation (ABS, 2011a).

Table 3.7: Five-year costs for first-ever strokes ($), 2011

	Ischaemic stroke	Intracerebral haemorrhage	All strokes (a)
	cost	*cost*	*cost*
A: Total exc. Informal care: first year	29,357	35,269	30,967
B: Total exc. Informal care per year: subsequent years (b)	5,798	3,387	5,141
C: Total five-year costs (A + [4 × B])	**52,547**	**48,818**	**51,531**

Notes: (a) 'All strokes' costs were calculated by weighting ischaemic stroke costs and intracerebral haemorrhage stroke costs by their incidence shares, derived from NEMESIS data. From NEMESIS, 72.8% of strokes were ischaemic (Thrift et al, 2000, 2001). (b) Costs presented in Cadilhac et al (2009) were discounted at a 3% rate. These costs were converted to costs discounted at a 5% discount rate (NHMRC, 2001).

Source: Deloitte Access Economics calculations using ABS (2011b), Cadilhac et al (2009) and Thrift et al (2000, 2001).

3.5 The cost of strokes in people with AF

Total strokes in people with AF including strokes specifically caused by AF, were estimated in Section 3.3. In this Section, these numbers are multiplied by the cost estimates in Section 3.4 to estimate the cost of first-ever strokes in people with AF.

By definition, strokes *caused* by AF are mainly ischaemic strokes. Haemorrhagic stroke is not generally associated with AF, unless hypertension is underlying both AF and haemorrhagic stroke or if haemorrhage occurs due to bleeding as a consequence of therapy for AF. Therefore, the estimated numbers of strokes due to AF were multiplied by the average cost of an ischaemic stroke and total strokes in people with AF were multiplied by the weighted average cost of any stroke.

Cost estimates are presented on a first year and five-year basis in Table 3.8 and Chart 3.1 for all strokes in the Australian population, strokes in people with AF, and strokes specifically due to AF. Costs of informal care have conservatively been excluded from these estimates and only direct costs are considered.

All first-ever strokes in 2011 are estimated to cost $1.4 billion in the first year and $2.4 billion over five years. We estimate that strokes in people with AF are expected to comprise 31.3% of first year ($444.8 million) and five-year ($740.2 million) costs of all strokes occurring in 2011.

Ischaemic strokes due to AF in 2011 are estimated to cost $314.4 million in the first year and $562.7 million over five years. These costs comprise just over one-fifth of first year and five-year costs of all strokes occurring in that year.

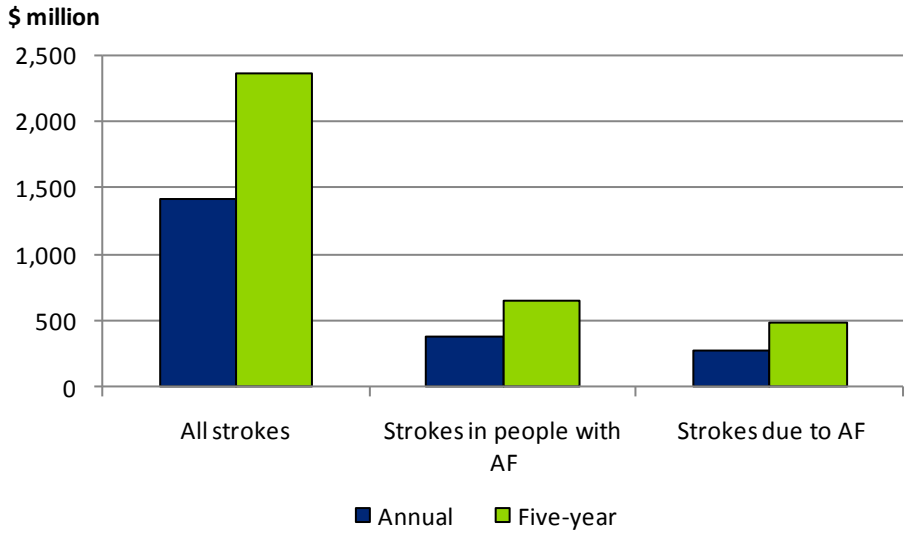
Table 3.8: Annual and five-year costs of first-ever strokes (a), 2011

	Incidence in 2011	First year costs	Five-year costs (b)
	number	*cost ($ million)*	*cost ($ million)*
All first-ever strokes	45,873	1,420.6	2,363.9
First-ever strokes in people with AF	14,364	444.8	740.2
First-ever strokes in people with AF due to AF (c)	10,709	314.4	562.7

Notes: (a) Includes health care costs, costs of community services and costs related to aged care. (b) Calculated by summing first year cost with four years worth of annual subsequent year costs. Subsequent year costs presented in Cadilhac et al (2009) were converted to costs discounted at a 5% rate (NHMRC, 2001). (c) Strokes due to AF were multiplied by the costs of ischaemic stroke. For other categories, relevant costs were weighted average costs of 'all strokes'.

Source: Deloitte Access Economics calculations using ABS (2011, 2011a, 2011b), AIHW (2010a), Cadilhac et al (2009), Thrift et al (2000, 2001) and Wolf et al (1991).

Chart 3.1: Annual and five-year costs of first-ever strokes occurring in 2011



Source: Deloitte Access Economics calculations using ABS (2011, 2011a, 2011b), AIHW (2010), Cadilhac et al (2009), Thrift et al (2000, 2001) and Wolf et al (1991).

4 Antithrombotic treatment in Australia

People with atrial fibrillation require treatment to prevent strokes as well as treatment to control sinus rhythm. In addition, around 25% of people with diagnosed atrial fibrillation do not receive any stroke prevention therapy.

Aspirin is commonly used for people at low-to-moderate stroke risk and warfarin for people at moderate-to-high stroke risk. Warfarin is more effective in stroke prevention than aspirin but increases the risk of major bleeds and requires regular blood monitoring tests. Warfarin is underused in Australian clinical practice due to the burden of frequent blood monitoring, fear of treatment-related bleeds, contraindications to treatment and multiple food-drug interactions, despite ongoing education initiatives. Only 40% of people with non-valvular atrial fibrillation at moderate-to-high stroke risk are estimated to use warfarin.

Warfarin imposes a cost burden on society including costs of monitoring tests, patient out-of-pocket travel costs to/from clinics, productivity losses and health care costs of warfarin related bleeds. The annual societal cost of warfarin-related monitoring and bleeding is estimated to exceed $95 million.

Newer stroke prevention treatments are becoming available which are more effective than warfarin and aspirin.

4.1 Stroke prevention in AF

Stroke prevention treatment for AF comprises anti-arrhythmic drugs (AADs) to control the pulse rate/rhythm and antithrombotic drugs to prevent blood clotting and associated cardiovascular events due to AF. The risk of stroke is similar with paroxysmal, persistent, or permanent AF and therefore the selection of antithrombotic prophylaxis should be independent of the rate/rhythm control strategy (Medi et al, 2007).

Aspirin is commonly recommended for people at a low-to-moderate stroke risk, and warfarin for people at a moderate-to-high stroke risk (Hankey et al, 2001). Although warfarin is around 2.5 times more effective than aspirin at reducing the risk of stroke, it is associated with a significantly higher rate of major bleeding and regular monitoring of a patient's blood levels is therefore required (Hart et al, 2007). Australian guidelines recommend that the selection of the optimal antithrombotic prophylaxis should depend on a patient's ischaemic stroke risk and the balance between the benefits and risks of long-term warfarin relative to aspirin (Medi et al, 2007).

The ischaemic stroke risk in a person with NVAF is generally based on their clinical risk factors for stroke other than AF. As outlined in Section 1.3, newer stroke prevention treatments are emerging. This has led to revised treatment guidelines in the US, Canada and Europe (Cairns et al, 2010; Wann et al, 2011).

4.2 How is AF managed in Australia?

Despite being recommended for people with AF at a moderate-to-high risk of stroke, warfarin is underutilised in Australian clinical practice. Warfarin was prescribed in only 44% of a random sample (n = 1,729) of GP encounters across Australia in which AF was managed in 2004-2006 (Fahridin et al, 2007). This is disproportionate to the 87% of AF patients at a moderate-to-high risk of stroke (see Chapter 2), which suggests under-prescribing.

A detailed study of antithrombotic use in Australian practice undertaken at Tasmania's largest hospital (Royal Hobart Hospital) between 2004-2006 audited the antithrombotic treatments used by patients with a primary or secondary diagnosis of AF on admission to the cardiology or medical wards (Jackson and Peterson, 2010). Among 135 patients who also underwent a stroke risk assessment (Hankey et al, 2001), only 31% of moderate-to-high risk stroke patients were using warfarin and 23% were not receiving any stroke prevention treatment. As discussed below, this study is believed to be representative of Australia-wide treatment practice.

Table 4.1 presents a profile of antithrombotic treatment practice for AF across Australia, which adjusts the Tasmania study data for the estimated undiagnosed proportion of people with AF. The key conclusions are:

- fewer than one-third of patients at a moderate-to-high stroke risk receive warfarin, including people who are not diagnosed with AF;
- around 40% of patients at a moderate-to-high stroke risk receive no treatment, which includes undiagnosed patients (around 20% of all AF patients) and around 25% of diagnosed patients; and
- treatment practice is similar for people at a moderate or high stroke risk.

Australian pharmacy data from IMS suggest the Tasmanian data are representative of the Australian population. The IMS data report 3.1 million warfarin packs totalling 373.6 million mg were dispensed via the Pharmaceutical Benefits Scheme (PBS) in 2009, with 53% of those prescriptions (198.0 million mg) attributable to AF. The average daily dose of adjusted-dose warfarin for stroke prevention in Australian practice is estimated to be 4.5mg (Gallus et al, 2000). Based on these data, PBS-dispensed warfarin in 2009 accounted for 44.0 million patient days or 120,547 patients on warfarin due to AF, which is nearly one-third of the estimated number of people with diagnosed or undiagnosed NVAF at a moderate-to-high stroke risk in Australia (397,596 people in 2011 – see Chapter 2). This extent of warfarin usage is very similar to the Tasmanian data.

Table 4.1: Antithrombotic use in Australian NVAF patients (adjusted for undiagnosed AF) (a)

Stroke risk	Warfarin	Aspirin only	No treatment
	%	%	%
High	37.0 (32.2)	33.0 (28.7)	22.0 (39.1)
Moderate	36.0 (30.3)	33.0 (27.8)	26.0 (41.9)
Low	16.0 (12.7)	16.0 (12.7)	69.0 (74.7)

Notes: (a) Data derived from the pre-intervention cohort on admission, which best represents general practice (Jackson and Peterson, 2010). The unadjusted figures are derived directly from Jackson and Peterson (2010) and do not sum to 100%. The adjusted figures are re-scaled to sum to 100% and then adjusted for undiagnosed AF. The undiagnosed proportion of AF is assumed to be 20% for all risk groups (Medi et al, 2007).

Source: Deloitte Access Economics calculations using Jackson and Peterson (2010) and Medi et al (2007).

4.3 Reasons for antithrombotic underuse

The underuse of warfarin reported above, despite initiatives to improve its use (Mandryk et al, 2008), is due to a range of disadvantages associated with its use, including:

- the burden of frequent INR monitoring on patients and the health care system;
- the fear of treatment-related bleeding, especially intracranial bleeding;
- limited access to INR testing facilities, especially in rural areas;
- the burden of drug and food interactions with warfarin; and
- contraindications to treatment.

Greater anticoagulation, whilst reducing the risk of blood clotting and hence ischaemic stroke, increases the risk of major bleeds including haemorrhagic strokes. Patients therefore require frequent monitoring of their INR levels to ensure they are maintained within a therapeutic range that balances these competing risks optimally (INR 2-3). Despite a substantial number of programs aimed at increasing time in the ideal therapeutic range for warfarin (National Prescribing Service, 2009), Australian patients are within their therapeutic INR range only 50-60% of the time (van Walraven et al, 2006).

Patients using warfarin are required to follow specific and consistent diets due to drug-food interactions, and in particular must avoid vitamin K rich foods and monitor their alcohol intake. There are also interactions between warfarin and many common prescription and over-the-counter medicines, which mean that patients on warfarin must avoid the use of certain medicines.

Because of these disadvantages, many patients and prescribers choose to use aspirin or no treatment even when warfarin is indicated, despite its stroke reduction benefits over aspirin.

Rural issues with warfarin treatment

Warfarin use is lower in rural areas and Aboriginal communities.

In a study of five Queensland hospitals, the proportions of ischaemic stroke/TIA survivors discharged on warfarin or no antithrombotic therapy were lower and higher, respectively, for regional hospital discharges compared with metropolitan hospital discharges (25% vs 83%, 33% vs 17%) (Read and Levy, 2005). These differences were not statistically significant, most likely due to the low sample size (n = 30). However, similar findings were reported in Missouri, US, where the proportions of patients hospitalised for AF and not contraindicated to warfarin who received warfarin or no treatment on discharged were lower and higher, respectively, for rural rather than urban hospital discharges (37% vs 48%, 45% vs 25%) (Flaker et al, 1999).

Good INR control is generally considered more difficult in warfarin clinics with fewer patients (Pickering and Thomas, 2007). For patients in rural (including some Aboriginal) communities, this may be due to delays for doctors receiving pathology results (Jackson et al, 2005). The time in therapeutic range has also been reported to be substantially below the recommended benchmark of 60% for urban Aboriginal communities, suggesting other unique problems also exist for INR control in Aboriginal people (Pickering and Thomas, 2007).

4.4 Burden of warfarin treatment

Patients receiving warfarin require their blood levels to be monitored at least monthly, however testing is more common if patients are not stabilised on warfarin, are sick, experience side-effects, or have had drug or food interactions. Australian clinical practice data suggest that patients undergo, on average, 20 INR tests each year (Bereznicki et al, 2005; Heller et al, 1998).

The Medicare Services Advisory Committee (MSAC) estimated the direct cost per INR test. This was based on the Medicare Benefits Scheme (MBS) fees for INR testing, a GP consultation every 6 INR tests and other administrative fees (MSAC, 2005). Based on the July 2011 MBS schedule this was expected to total $23.47 per test.

The MBS fees however, only consider direct costs to the Government. Some pathology providers charge patients additional fees to cover other related services and infrastructure. For example, QML Pathology (2010) charges an excess fee per test of $50.15 for laboratory blood collection or $56.95 for home blood collection (up to the fifth INR test) to cover a range of services required by patients using warfarin:

- specialist pathologists to monitor warfarin levels;
- a call centre to deal with warfarin dosing;
- a reminder and follow up process for urgent changes to warfarin doses;
- a reminder process for non-urgent patients; and
- patient access to a Warfarin Support Group.

After their fifth INR test, patients are billed an excess of $25 per test for blood samples not collected at home.

The burden of warfarin monitoring extends to patient out-of-pocket travel costs to/from the clinic, productivity losses for the time to undergo tests and the inconvenience of regular testing.

Furthermore, in 1999, the Quality in Australian Health Care Study estimated the cost of adverse events arising from warfarin use in Australia to be over $100 million in direct hospital costs alone (Rigby et al, 1999). Warfarin related injuries have a high preventable cost despite a relatively low incidence (Rigby et al, 2000).

The total annual cost (2011) of warfarin monitoring and bleeding per patient is estimated to be at least $720 (Table 4.2). The actual cost is likely to be much greater considering excess clinic fees and the full costs of warfarin-related bleeds. Further, the burden of warfarin also includes the cost of additional ischaemic strokes among people who choose to use less effective aspirin due to a fear of warfarin-related bleeding or to avoid the burden of regular blood testing. These costs are not included in Table 4.2.

Using the data in Section 4.2 it is estimated that 132,765 people in Australia with NVAF currently receive warfarin for stroke prevention[3]. The societal cost of warfarin-related monitoring and bleeding is therefore estimated to exceed $95 million each year for these people.

[3] Estimated as the sum of: 40.2% of 207,246 people with diagnosed NVAF at a high stroke risk; 37.9% of 110,831 people with diagnosed NVAF at a moderate stroke risk; 15.8% of 47,132 people with diagnosed NVAF at a low stroke risk. These percentages are those for people with diagnosed NVAF only, after re-scaling the proportions by therapy type to sum to 100%.

Table 4.2: Estimated annual cost of warfarin-related monitoring and bleeding (a)

Resource (cost bearer)	Cost per test or major bleed	Total annual cost	Source
	$	$	
INR testing and blood collection (government)	23.47	469.40	Based on current Medicare Benefits Schedule fees for pathology test (item 65120), patient episode initiation fee (item 73928), bulk-billing management fees and cost of a short GP consultation (item 3) (MSAC, 2005). Likely to be excess charges to patients
Travel costs (patient)	4.44	88.80	Middle rate of $0.74 per business kilometre for 2009-10 income year (ATO, 2010). Average distance travelled is 6km (Jowett et al, 2008)
Productivity losses (society)	7.70	153.93	Based on an average hourly wage of $32.43, 21% employment rate, and 13% of patients accompanied to clinic visits (ABS, 2011; Jowett et al, 2008). The employment rate for companions is conservatively assumed to also be 21%. Average travel and clinic time per visit is one hour (Jowett et al, 2008)
Total monitoring cost (society)	35.61	712.13	-
Warfarin-related bleeding (government)	2,907.53	8.72	Annual incidence of extracranial major bleeding 0.3% greater with warfarin than with no treatment i.e. treatment-related (Hart et al, 2007). The cost per bleed was multiplied by 0.3% to attain the cost of warfarin-related bleeding. Average public hospital inpatient cost per gastrointestinal bleed, AR-DRGs G61A/B (DoHA, 2010a)
Total per patient ($)			**720.85**
Total for NVAF population treated with warfarin ($)			**95.70 million**

Notes: (a) Total costs based on an average of 20 INR tests per year (Heller et al 1998, Bereznicki et al 2005) and a 0.3% increase in the annual incidence of major bleeding compared with no treatment (Hart et al 2007). Gastrointestinal bleeds are a common extracranial major bleeding event.

Source: Deloitte Access Economics calculations using ABS (2011), ATO (2010), Bereznicki et al (2005), DOHA (2010), Hart et al (2007), Heller et al (1998) and Jowett et al (2008).

5 The cost of preventable strokes

Diagnosis and the use of more effective stroke prevention treatment in patients with atrial fibrillation can prevent strokes and avert costs to patients and the Australian health care system.

Based on 2011 figures, it is estimated that 159,411 NVAF patients at a moderate-to-high stroke risk are currently untreated, with 7,403 annual strokes in this group. If these patients were treated with common treatments such as aspirin or warfarin it is estimated that 3,532 strokes could be prevented each year, resulting in cost savings of $103.7 million in the first year and $185.6 million over five years.

An important strategy to prevent more strokes and achieve higher cost savings will be to increase accessibility to newer, more efficacious stroke prevention treatments.

5.1 How many strokes due to AF are preventable?

The significant personal and economic costs of strokes create a critical need to manage patients with AF in line with best stroke prevention practice. However, around 10-30% of AF is undiagnosed (Section 2.3). Furthermore, Australian clinical practice data suggest under treatment of AF, with less than one third of AF patients at moderate-to-high stroke risk receiving warfarin and 40% of patients at moderate-to-high stroke risk receiving no treatment, including both undiagnosed patients and around one quarter of diagnosed and untreated patients (see Section 4.2).

This Section estimates the number of potential strokes that could be prevented by greater diagnosis of AF and better antithrombotic treatment of AF patients for stroke prevention. These calculations are only undertaken for people with NVAF in line with the underlying studies. Throughout this Section, 'treatment' and 'untreated patients' refers specifically to antithrombotic treatment (e.g. patients referred to as 'untreated' receive no antithrombotic stroke prevention treatment but may be using anti-arrhythmic drugs to control their heart rhythm).

5.1.1 Strokes preventable by getting untreated patients on treatment

Data from Section 4.2 (Table 4.1) on patients receiving no antithrombotic treatment for NVAF were applied to the NVAF prevalence (from Section 2.2) to estimate the numbers of untreated patients in each stroke risk group. The risks of stroke in untreated patients (Medi et al, 2007) were then applied to the number untreated in each risk group estimate the number of strokes occurring in untreated NVAF patients (Table 5.1). It is estimated that of all people with NVAF in 2011, 203,393 (40%) are receiving no treatment for NVAF including 159,411 people at a moderate-to-high stroke risk. The number of strokes estimated to

occur in 2011 in people untreated for NVAF is 8,239 strokes. People at a moderate-to-high stroke risk account for 7,403 of these strokes (90% of total strokes in people untreated for NVAF).

Table 5.1: Number of strokes in people with untreated NVAF, 2011

Stroke risk	Diagnosed but untreated	Undiagnosed	Total untreated	Probability of stroke if untreated	Number of strokes in untreated
	number	*number*	*number*	*%*	*number*
High	49,559	51,811	101,370	5.7	5,778
Moderate	30,333	27,708	58,041	2.8	1,625
Low	32,199	11,783	43,982	1.9	836
Total	**112,091**	**91,302**	**203,393**		**8,239**

Source: Deloitte Access Economics calculations using NVAF prevalence from Section 2.2, Jackson and Peterson (2010), Medi et al (2007), and a review of studies reporting the undiagnosed proportion of AF.

In Australia, people with NVAF receive either warfarin (moderate-to-high stroke risk) or aspirin (low-to-moderate stroke risk, or when warfarin is contraindicated or refused). Based on Jackson and Peterson (2010), 48% of moderate risk NVAF patients treated for stroke prevention received warfarin with the remainder receiving aspirin. Therefore, it is estimated that if previously untreated moderate stroke risk patients switched to stroke prevention treatments they would receive them in these proportions. Jackson et al (2001) estimated the proportion of high-stroke risk patients with a contraindication to warfarin to be 39%. Therefore, it was estimated that 39% of previously untreated high-risk patients would receive aspirin with the remainder receiving warfarin (Table 5.2).

Table 5.2: Untreated patients who should be treated for NVAF with either warfarin or aspirin

Stroke risk	No treatment to aspirin	No treatment to warfarin
	% of risk group	*% of risk group*
High	39	61
Moderate	52	48

Source: Deloitte Access Economics calculations using Jackson et al (2001) and Jackson and Peterson (2010).

The numbers of preventable strokes were estimated for people at a moderate-to-high risk of stroke only as only aspirin is indicated for the low risk population. Relative risks for stroke with warfarin and aspirin relative to no treatment (Section 1.3) were based on the estimates by Hart et al (2007) to be 33% and 79%, respectively.

Applying these fractions to the number of strokes predicted to occur in 2011 in untreated NVAF patients at a moderate-to-high stroke risk (Table 5.1), it is estimated that 3,532 strokes could be prevented though current commonly used treatments on the PBS (Table 5.3).

Table 5.3: Preventable strokes in patients currently receiving no antithrombotic therapy for NVAF at moderate-to-high stroke risk

Stroke risk	A: Weighted relative risk (switching to treatment)	B: Strokes in untreated patients	Preventable strokes (B × [1-A])
	%	*number*	*number*
High	50.9	5,778	2,835
Moderate	57.1	1,625	697
Total		**7,403**	**3,532**

Source: Deloitte Access Economics calculations using NVAF prevalence from Section 2.2, Jackson et al (2001), Jackson and Peterson (2010) and Medi et al (2007). Treatment is either warfarin or aspirin.

5.2 What is the cost of preventable strokes?

5.2.1 Cost savings from getting untreated patients onto treatment

The cost of preventable strokes from currently untreated patients receiving treatment was estimated using the health care, community services and aged care costs of ischaemic stroke reported in the NEMESIS study updated to current prices (Section 3.4).

Overall, it is estimated that 7,403 strokes will occur in 2011 in untreated AF patients at a moderate-to-high stroke risk. The cost of strokes in this untreated population will be $217.3 million in the first year and $389.0 million over five years (i.e. 2011-2015). Treating these people with current PBS-listed stroke prevention treatments would avert at least 3,532 strokes in 2011, resulting in cost savings of at least $103.7 million in the first year or $185.6 million over five years, when considering the direct costs of stroke only.

Currently, potentially preventable strokes in untreated people with NVAF at a moderate-to-high stroke risk comprise an estimated one fifth of the total cost of strokes in people with NVAF in Australia.

Table 5.4: Annual and five-year costs of preventable strokes in untreated NVAF patients at moderate-to-high stroke risk (a), 2011

Stroke risk	Strokes	First year costs	Five year costs
	number	*$ million*	*$ million*
Total strokes in untreated patients	7,403	217.3	389.0
Preventable strokes in untreated patients (b)	3,532	103.7	185.6

Notes: (a) Includes health care costs, costs of community services and costs related to aged care. (b) From switching untreated patients to treatment with aspirin or warfarin.

Source: Deloitte Access Economics calculations using ABS (2011, 2011a, 2011b), AIHW (2010), Cadilhac et al (2009), Hart et al (2007), Jackson et al (2001), Jackson and Peterson (2010), Medi et al (2007), Thrift et al (2000, 2001) and Wolf et al (1991).

These cost savings are conservative, as they only include strokes that are preventable by untreated patients receiving aspirin or warfarin treatment. Additional preventable strokes and cost savings are likely with newer, more effective treatments.

5.2.2 Total potential cost savings with better diagnosis and treatment

Overall, based on 2011 figures, estimated cost savings of $103.7 million in the first year and $185.6 million over five years may be realised in stroke costs alone, with better diagnosis and stroke prevention treatment for NVAF patients at a moderate-to-high stroke risk. Higher savings could be achieved with the use of newer more effective stroke prevention treatments.

These substantial cost savings indicate that at least 23% of the total cost of strokes in AF patients (Section 3.5) could be potentially be averted with better diagnosis and treatment.

6 Recommendations

Many people with atrial fibrillation need medicines to prevent strokes. However, many are undiagnosed or receive no stroke prevention treatment at all. Ineffective or no stroke prevention treatment leads to even more strokes, poor outcomes for patients and is costly to the Australian health care system.

In light of this, it is recommended that:

- awareness of the symptoms and effects of atrial fibrillation be increased among older Australians;
- GPs routinely check for heart arrhythmias in older patients; and
- new stroke prevention treatments with more favourable efficacy, safety and convenience compared to warfarin be made accessible.

This study estimates that, currently, over 500,000 people in Australia aged over 50 years have AF, a heart arrhythmia that increases the risk of stroke by up to five times. Almost 90% of these people are at a moderate-to-high risk of stroke due to AF and other risk factors. This study estimates that each year, nearly 11,000 ischaemic strokes occurring within the Australian population are due to AF.

A stroke is catastrophic for the individual. One in five people suffering a stroke will die within one month, and survivors experience prolonged and often permanent reductions in mobility, sensory perception, communication, social skills and quality of life. Strokes impose substantial costs on the Australian health care system, in particular hospitals and rehabilitation services. At current prices, this study estimates the cost of all strokes in people with AF to total $444.8 million in 2011 – nearly half a billion dollars.

The prevalence and risk of developing AF increase with age. The number of people with AF, the incidence of related strokes, and the costs of AF-related strokes are all likely to substantially increase in the future as the Australian population ages.

The significant personal and economic costs of strokes create a critical need to manage AF in line with best practice. On the PBS, warfarin is used for people at a moderate-to-high risk of stroke, and aspirin is used for people at a low-to-moderate risk of stroke or for whom warfarin is contraindicated or refused. Australian clinical practice data, however, suggest that around one quarter of patients with diagnosed AF and a moderate-to-high stroke risk are receiving no treatment.

This represents a high proportion of the AF population, despite ongoing educational initiatives to improve warfarin use (Mandryk et al, 2008) This is however not surprising given the significant burden of warfarin on patients and their prescribers. There is a clinical need for more effective stroke prevention treatments.

Further, international studies estimate that between 11% and 30% of AF is undiagnosed. This study proposes a most likely estimate of 20% for the proportion of AF cases in Australia

that are undiagnosed. These undiagnosed cases represent additional numbers of patients who receive no stroke prevention treatment for AF and are at significant risk of stroke.

Given the readily available stroke prevention treatments on the PBS (aspirin and warfarin), the proportions of AF cases that are undiagnosed and/or untreated, and the incidence rates of AF-related strokes in Australia are of concern. This study estimates that at least 3,532 strokes could be prevented each year through better diagnosis and treatment.

Finally, there is a need for newer stroke prevention medicines to be more convenient and safe, in order to reduce the overall cost and health burden of AF. Australian warfarin patients undergo at least monthly and on average 20 INR tests each year in an attempt to balance the conflicting risks of major bleeds and strokes within a narrow therapeutic window (INR 2-3). This study estimates that warfarin monitoring and bleeding in AF patients costs patients and the Australian health care system over $95 million annually, including costs of INR testing, treatment of bleeds and patient travel/time costs. There are additional warfarin burdens for patients in rural and regional areas.

In light of these findings, three key recommendations are proposed to improve the management of AF and reduce the impact of stroke in Australia:

- **Among older Australians, increasing awareness of the symptoms and effects of AF.**

  Targeted media campaigns should encourage older Australians to recognise and follow up possible symptoms of AF. These media could include leaflets and magazine articles targeted at the Australian demographic of people aged over 50 years (the at-risk group). These strategies would aim to increase the diagnosis (and therefore stroke prevention treatment) rates for AF.

- **Encouraging general practitioners (GPs) to routinely check for heart arrhythmias in patients aged over 50 years.**

  A simple diagnostic test using a stethoscope and some basic health questions should be carried out routinely by GPs at consultations with older patients. A patient should be referred for an ECG and/or a Holter monitor where AF is suspected. Again, this would increase the diagnosis and stroke prevention treatment rates for AF.

- **Making accessible any new stroke prevention treatments demonstrated to have more favourable efficacy, safety, and convenience on balance compared with warfarin.**

  Warfarin has several disadvantages relating to its narrow therapeutic window, and the need for close monitoring of blood levels in order to balance the risks of ischaemic stroke (due to under anticoagulation) and bleeding, including haemorrhagic stroke (due to over anticoagulation). Warfarin has been used in clinical practice for over 50 years and there is a clear need for superior treatments. Patients should receive the most effective stroke prevention treatments. A priority of Australian cardiovascular health care strategies should be the availability of such treatments to people with AF at a moderate-to-high stroke risk.

This report documents a significant unmet need for the prevention of strokes due to AF. More effective treatment of AF will prevent or postpone hundreds of new cases of disabling

or fatal strokes in Australia each year. Better stroke prevention will prevent much misery, relieve pressure on the acute hospital system, and save the health care system millions of dollars each year. Implementing optimum stroke prevention treatment in these patients should be an urgent priority for the Australian health care system.

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Limitation of our work

General use restriction

This report is prepared solely for the use of Boehringer Ingelheim. This report is not intended to and should not be used or relied upon by anyone else and we accept no duty of care to any other person or entity. The report has been prepared for the purpose of estimating the incidence and cost of stroke in people with atrial fibrillation in Australia. You should not refer to or use our name or the advice for any other purpose.

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About the report:

Deloitte Access Economics was commissioned by Boehringer Ingelheim to estimate the prevalence of atrial fibrillation, the incidence and cost of related strokes, and the impacts of improved diagnosis and treatment of atrial fibrillation in Australia. The impacts of improved diagnosis and treatment include the reductions in annual strokes and associated economic costs from proactively reducing stroke risks.

Expert advice was provided by Baker IDI, National Stroke Research Institute, Florey Neurosciences Institute and other relevant experts.

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