HEALTH STATE UTILITY VALUES FOR ATRIAL FIBRILLATION AND ASSOCIATED TREATMENT-RELATED ADVERSE EVENTS

Scott Doyle[1], Andrew Lloyd[1], Ann-Marie Craig[2], Mark Davis[3]
[1]Oxford Outcomes, Oxford, UK; [2]Sanofi Aventis, Guildford, UK; [3]Moorfield House Surgery, Leeds, UK

1. Objectives

- The study aimed to describe common adverse events (AE) associated with atrial fibrillation medications, as well as atrial fibrillation (AF) itself. The AF and adverse event descriptions were used to estimate societal utility values in the UK.

2. Intro

- Atrial fibrillation is a common cardiac arrhythmia affecting approximately 6 million patients in Europe and 2.3 million in the United States (Kannel & Benjamin 2008). Estimates in the general population suggest a prevalence rate of 0.4-1.0%, with a marked increase with age, increasing to approximately 10% by 80 years (Go et al. 2001).
- AF is characterized by an atrial heart rhythm which occurs when the normal sinus rhythm of the heart is overwhelmed by randomly generated electrical discharges from the atrium. This leads to an irregular and inefficient beating and pumping of the blood through the heart, causing pooling and clotting. It is this clotting that is responsible for the substantial morbidity and mortality associated with AF, mainly from stroke (Lip & Boos 2006).
- AF typically presents as one of three states: 1) Paroxysmal: recurrent episodes that self-terminate in less than 7 days; 2) Persistent: recurrent episodes that last more than 7 days; and 3) Permanent: an ongoing long-term episode (Fuster et al. 2006).
- Although the health outcome and health related quality of life (HRQL) implications of AF are well known (Hart et al. 1999), few studies have explored the HRQL impact of treatment-related adverse events. Information on this aspect of AF would help inform medical decisions for untreated AF, as well as provide an evidence base for assessing the economic impact of AF therapy.

3. Methods

- The AF health states were developed from a variety of sources, including existing EQ-5D results from the Euro Heart Survey (Nieuwlaat et al. 2008), a literature review and qualitative interviews with AF patients (N=6) and specialist AF clinicians (N=5).
- The health states described both paroxysmal/persistent and permanent AF along with 14 adverse events (Figure 1). Adverse event descriptions were bolted to the EQ-5D derived base AF health states so that the associated disutility of specific treatment adverse events could be described.
- To assess the content and face validity of the draft AF health states, an additional review was undertaken with a further 5 cardiology clinical experts. The health states were then piloted with 5 members of the general public in a cognitive debriefing exercise to assess comprehension and discernability of the descriptions. No revisions were required as a result of these reviews.
- In total, 127 members of the UK general public assessed the health states in a Time Trade-Off (TTO) interview and ranking task.

4. Results

- The study revealed the public preferences for atrial fibrillation and associated adverse event health states. Each of the AE values was associated with a disutility from their respective base state. The disutility of each AE was very similar whether the AE was added to the paroxysmal/persistent base state or the permanent base state. Pulmonary AE (interstitial lung disease) was associated with the greatest disutility (-0.17 paroxysmal/persistent base; -0.15 permanent base) and circulatory issues had the least impact (-0.01 paroxysmal/persistent; -0.02 permanent) (see Table 2).
- The sample population was a good match to the UK population sets (ONS 2001), but with higher employment and female representation (Table 1). The study sample also reported less moderate and extreme problems than those described in the societal reference study (Kind et al. 1998).

5. Conclusions

- **To our knowledge, this is the first study that focuses on the utility impact of adverse events associated with treatments of atrial fibrillation. As atrial fibrillation is a largely asymptomatic condition, the impact of treatment adverse events on health related quality of life are amongst the most important factors considered in treatment decisions. The utility values collected in this study may prove useful in populating cost-effectiveness analyses.**

6. References

- Fuster V, Rydén LE, Cannom DS, et al. 2006 Guidelines for the Management of Patients with Atrial Fibrillation. Circulation. 2006 Aug 15;114(7):e257-354.
- Go AS, Hylek EM, Phillips KA, et al. 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 2001;285:2370–5.
- Hart R G, Benavente O, McBride R. et al Antithrombotic therapy to prevent stroke in patients with atrial fibrillation: a meta-analysis. Ann Intern Med 1999. 131:492–501
- Kannel WB, Benjamin EJ. Status of the epidemiology of atrial fibrillation. Med Clin North Am. 2008 Jan;92(1):17-40.
- Kind P, Dolan P, Gudex C, Williams A. Variations in population health status: results from a United Kingdom national questionnaire survey. British Medical Journal 1998; 316: 736-41.
- Lip G, Boos CJ. Antithrombotic treatment in atrial fibrillation. Heart. 2006 February; 92(2): 155–161.
- Nieuwlaat R, Prins MH, Le Heuzey JY, Vardas PE, Aliot E, Santini M, Cobbe SM, Widdershoven JW, Baur LH, Lévy S, Crijns HJ. Prognosis, disease progression, and treatment of atrial fibrillation patients during 1 year: follow-up of the Euro Heart Survey on atrial fibrillation. Eur Heart J. 2008 May;29(9):1181-9. Epub 2008 Apr 7.
- Office of National Statistics, National Statistics "Census 2001 Information" statistics.gov.uk/StatBase/Product.asp?vlnk=9343

Figure 1: AF Base and Adverse Event Health States

PAROXYSMAL/PERSISTENT AF (EQ-5D BASE STATE)
- You have some problems in walking about
- You have no problems with washing or dressing yourself
- You have no problems performing your usual activities (e.g. work, study, housework, family or leisure activities)
- You have no pain or discomfort
- You are moderately anxious or depressed

PERMANENT AF (EQ-5D BASE STATE)
- You have some problems in walking about
- You have no problems with washing or dressing yourself
- You have some problems performing your usual activities (e.g. work, study, housework, family or leisure activities)
- You have no pain or discomfort
- You are moderately anxious or depressed

ADVERSE EVENTS (each added as last bullet point to base states)
- HYPERTHYROIDISM: You have an overactive thyroid gland which causes your metabolism to speed up. You have lost weight and experience hot flushes. You need to take medication and regularly have blood tests done.
- HYPOTHYROIDISM: You have an underactive thyroid gland which causes your metabolism to slow down. You have gained weight and often feel cold. You need to take medication and regularly have blood tests done.
- LIVER DEPOSITS: You have developed problems with your liver. This is not likely to be serious and should get better in time, but it means you need to have regular blood tests done.
- PULMONARY ISSUES: You have developed problems with your lungs that affect your breathing and can leave you feeling breathless or tired.
- SLEEP DISTURBANCE: You have trouble falling asleep or staying asleep.
- NEUROPATHY: You have an uncomfortable 'pins and needles' sensation in your hands and feet. Sometimes it can be a painful tingling that can be sensitive to touch. Other times you may have trouble feeling with your fingertips.
- DERMATOLOGICAL ISSUES: You are sensitive to sunlight and sun-burn easily. Your skin has taken on a blotchy, slightly bluish-grey tinge.
- OPTIC ISSUES: Your eyes are sensitive to bright light, particularly sunlight. Your vision can be slightly blurry in places and you see halos around objects in dim-lighting or darkness.
- NAUSEA: You have mild nausea and occasional vomiting.
- DIARRHOEA: You have mild diarrhoea and need to go to the bathroom several times per day.
- CIRCULATORY ISSUES: You have poor circulation, which often leads to cold hands and feet.
- FATIGUE: You feel fatigued and tire easily
- RASH: You have a mild rash that is red and itchy.
- DIZZINESS: You get occasionally experience spells of dizziness

Table 1: Demographics (N=127 total interviews)

	Study sample	UK Census 2001
Age Mean (std. dev.)	41.45 (12.81)	38.2
Gender (N/ Tot, % female)	76 (59.8%)	51% Female
Ethnic group (N / %)		
White	122 (96.1%)	92.1%
Black	1 (0.8%)	2.0%
Asian	1 (0.8%)	4.0%
Other	3 (2.4%)	1.9%
Employment status (N / %)		
Full time	61 (48.0%)	48.6%
Part time	29 (22.8%)	11.7%
Home maker	8 (6.3%)	6.5%
Student	10 (7.9%)	7.3%
Retired	5 (3.9%)	13.6%
Disabled	0 (0.0%)	5.8%
Other	14 (11.0%)	6.5%
Education (N / %)		
No Formal Qualifications	5 (3.9%)	-
GCSE/ O' Levels	26 (20.5%)	-
A' Levels	20 (15.7%)	-
Vocational or work based	14 (11.0%)	-
University degree	47 (37.0%)	-
Other	15 (11.8%)	-
EQ-5D (Moderate / Extreme problems)		Kind et al. 1998
Mobility	4.7% / 0.0%	18.3% / 0.1%
Self care	0.0% / 0.0%	4.1% / 0.1%
Usual activity	3.1% / 0.0%	14.2% / 2.1%
Pain - discomfort	18.9% / 0.0%	29.2% / 3.8%
Anxiety/ depression	13.4% / 1.6%	19.1% / 1.8%

Table 2: Disutility of Treatment-Related Adverse Events from Base State

	Paroxysmal/ Persistent	*Permanent*
Circulatory issues	0.01	0.02
Dizziness	0.01	0.03
Rash	0.03	0.03
Liver deposits	0.03	0.03
Sleep disturbances	0.04	0.04
Fatigue	0.04	0.05
Nausea	0.06	0.05
Dermatological changes	0.06	0.09
Hyperthyroidism	0.08	0.06
Neuropathy	0.08	0.07
Diarrhoea	0.08	0.08
Optical issues	0.08	0.08
Hypothyroidism	0.10	0.10
Pulmonary issues	0.17	0.15

Funding for this study was provided by sanofi-aventis R&D.

Oxford Outcomes

ISPOR