Institution: University of Birmingham

Unit of Assessment:UoA1

Title of case study: Improving the management of patients with atrial fibrillation

1. Summary of the impact (indicative maximum 100 words)

Atrial fibrillation (AF) is the commonest heart rhythm abnormality, affecting around 8.8 million people in the European Union, and confers a substantial risk of stroke and death. It accounts for one third of hospital admissions for cardiac rhythm disturbances, and the rate of AF-related admissions has continued to rise in recent years. The work of Prof Gregory Lip and Dr Deirdre Lane has made Birmingham an internationally-respected centre of excellence for research in AF, delivering crucial impacts in international clinical practice guidelines and improvements in patient care within three main areas: treatment decisions related to stroke and bleeding risk, screening practice in primary care, and stroke and bleeding risk assessment, ultimately reducing morbidity and mortality for a significant proportion of the population, particularly among the elderly.

2. Underpinning research (indicative maximum 500 words)

Atrial fibrillation (AF) is characterised by an irregular, often rapid heartbeat, due to a malfunction in the heart's electrical system. AF is the most common heart rhythm irregularity, or 'arrhythmia'. Over the last 15 years' research led by Professor Gregory Lip (Professor of Cardiovascular Medicine at the University of Birmingham and consultant cardiologist at City Hospital; Honorary Professor 1999-2009 and returned as Cat C in 2008 RAE; full Professor since 2009) and Dr Deirdre Lane (Lecturer in Cardiovascular Health at the University of Birmingham since 2010) into AF has developed and validated new tools for assessing stroke and bleeding risk among patients with AF who are treated with antithrombotic therapy, re-evaluated treatment approaches, and provided crucial insights into the most effective practices in screening for the condition.

Assessing stroke risk

Due to the irregularity in the beating of the heart in patients with AF, the flow of blood is affected. This can cause blood cells to stick together and increases the risk of a blood clot forming in the upper chambers of the heart (the atria). In people with AF, the most common place for these blood clots to travel to is the brain and this can result in a stroke. AF increases the risk of stroke five-fold.

Many risk scoring systems have been developed over the years to predict stroke, thromboembolism and transient ischemic attack (TIA), using various clinical and diagnostic features, typically stratifying patients into high-, intermediate-, or low-risk categories. However, these risk schemas did not clearly take into account many other potential risk factors, and so were not completely predictive or reliable in many cases. A scoring system called $CHADS_2$ (acronym for Congestive heart failure, Hypertension, Age >75 years, Diabetes mellitus, and prior Stroke or TIA), developed in 2001 was widely used internationally to assess stroke risk in AF. Led by Lip, Birmingham's regional AF Clinical Effectiveness Topic Group refined risk stratification specifically for a local primary care population, and in 2006 – after demonstrating its comparable effectiveness to $CHADS_2$ – the Birmingham schema was refined for dissemination in the evidence-based UK National Institute for Health and Clinical Excellence (NICE) guidelines on AF management, which outlined this algorithm-based approach to stroke risk stratification. In 2009, this was then further developed by the Lip team into a risk factor-based approach by reclassifying and incorporating additional new risk factors. The revised schema was then compared with other existing stroke risk stratification schema in a real-world cohort of AF patients from the Euro Heart Survey for AF. This new approach (abbreviated to CHA_2DS_2-VASc) [1] was able to demonstrate improvement in predictive value for thromboembolism over the $CHADS_2$ schema, with low event rates in low-risk subjects and the classification of only a small proportion of subjects into the intermediate-risk category, offering a clear way to improve stroke risk stratification in AF.

Prescription of oral anticoagulation therapy needs to balance the benefit of stroke prevention against the risk of bleeding, but a lack of recommendations on bleeding risk assessment hampered antithrombotic guidelines for AF management. The Birmingham team developed a practical risk score for bleeding, known as HAS-BLED (Hypertension, Abnormal Renal/Liver Function, Stroke, Bleeding History or Predisposition, Labile INR, Elderly, Drugs/Alcohol Concomitantly)) [2] to estimate the 1-year risk of major bleeding, and validated it in several independent patient cohorts.

AF treatment decisions relating to risk

While anticoagulation therapy with warfarin is highly effective in reducing stroke risk in AF, it is associated with high monitoring costs and increased risk of serious haemorrhage. Ongoing uncertainties about whether these benefits and risks were applicable to elderly populations led to work between Lip and colleagues in primary care at the University of Birmingham (Profs David Fitzmaurice, Richard Hobbs (based at Birmingham until 30/4/2011), and Jonathan Mant (at Birmingham until 1/10/2008)) for the BAFTA (Birmingham Atrial Fibrillation Treatment of the Aged) study (£740kMRC, 1999-2004). This compared the efficacy of warfarin with that of aspirin for the prevention of stroke in a primary care population of 973 patients with AF aged 75 years or over. The BAFTA study clearly showed the superiority of anticoagulation for stroke prevention, with no increased risk of serious haemorrhage between warfarin versus aspirin in the elderly [3,4].

Screening in primary care

Again working with colleagues in primary care (Profs Fitzmaurice, Hobbs, Mant), Lip looked at systematic screening (targeted and total population screening) versus routine practice for the detection of AF in the over 65s, known as the Screening for Atrial Fibrillation in the Elderly (SAFE) study (£485k NIHR HTA-funded 1999-2003). Evaluating the relative benefits of whole population, targeted, and opportunistic screening for the presence of AF, SAFE showed that opportunistic screening improved on standard practice, and was likely to be cost-effective in terms of the patient benefits of identifying new cases [5]. In addition, SAFE identified that many primary care professionals could not accurately detect AF with standard electrocardiograms, and that additional interpretative software was unable to address this problem even when combined with interpretation by a GP [6]. Their subsequent recommendation was that diagnosis of AF in the community must include reading of electrocardiograms by appropriately trained people.

3. References to the research (indicative maximum of six references)

1: Lip GY, Nieuwlaat R, Pisters R, Lane DA, Crijns HJ. Refining clinical risk stratification for predicting stroke and thromboembolism in atrial fibrillation using a novel risk factor-based approach: the euro heart survey on atrial fibrillation. *Chest*. 2010;137(2):263-72 *doi: 10.1378/chest.09-1584*

2: Pisters R, Lane DA, Nieuwlaat R, de Vos CB, Crijns HJ, Lip GY. A novel user-friendly score (HAS-BLED) to assess 1-year risk of major bleeding in patients with atrial fibrillation: the Euro Heart Survey. *Chest*. 2010;138(5):1093-100. *doi: 10.1378/chest.10-0134*

3: Hobbs FD, Roalfe AK, Lip GY, Fletcher K, Fitzmaurice DA, Mant J; on behalf of the Birmingham Atrial Fibrillation in the Aged (BAFTA) investigators and Midland Research Practices Consortium (MidReC) network. Performance of stroke risk scores in older people with atrial fibrillation not taking warfarin: comparative cohort study from BAFTA trial. *BMJ*. 2011;342:d3653. *doi: 10.1136/bmj.d3653*

4:Mant J, Hobbs FD, Fletcher K, Roalfe A, Fitzmaurice D, Lip GYet al. BAFTA investigators; Midland Research Practices Network (MidReC). Warfarin versus aspirin for stroke prevention in an elderly community population with atrial fibrillation (the Birmingham Atrial Fibrillation Treatment of the Aged Study, BAFTA): a randomised controlled trial*. Lancet*. 2007;370(9586):493-503. *doi:10.1016/S0140-6736(07)61233-1*

5: Fitzmaurice DA, Hobbs FD, Jowett S, Mant J, Murray ET, Holder Ret al. Screening versus routine practice in detection of atrial fibrillation in patients aged 65 or over: cluster randomised controlled trial. *BMJ*. 2007;335(7616):383. *doi: http://dx.doi.org/10.1136/bmj.39280.660567.55*

6:Mant J, Fitzmaurice DA, Hobbs FD, Jowett S, Murray ET, Holder R et al. Accuracy of diagnosing atrial fibrillation on electrocardiogram by primary care practitioners and interpretative diagnostic software: analysis of data from screening for atrial fibrillation in the elderly (SAFE) trial. *BMJ*. 2007;335(7616):380. *http://dx.doi.org/10.1136%2Fbmj.39227.551713.AE*

4. Details of the impact (indicative maximum 750 words)

Birmingham-based research led by Lip and Lane has had international impacts in AF risk assessment, screening and treatment. This has been primarily delivered by their roles with national and international organisations as expert consultants on AF management, positions which have been based on the expertise developed through the research described here. Professor Lip was the previous Clinical Adviser for the current UK NICE guidelines (2006) and is co-authoring the 2014 revision on AF management. He has served as Deputy Editor ("content expert") for the 2012 American College of Chest Physicians (ACCP) guidelines on antithrombotic therapy for AF [1] and in similar capacities for various guidelines and/or position statements from European Heart Rhythm

Association (EHRA), including Task Force Chair for a Position Statement on Bleeding Risk in AF Patients [2]. He also served on the writing committee of the European Society of Cardiology (ESC) guidelines on AF (2010) and the 2012 focused update. Dr Lane is also a member of the ACCP and EHRA document writing committees. Both Professor Lip and Dr Lane were part of the BMJ Writing group (2013) for NHS Shared Decision Making in the development of a patient decision aid for stroke prevention for AF or atrial flutter [3] and were recently part of the task force that developed a patient education website for the EHRA (Lip was Chair) [4]. Along with these changes to clinical guidance for patient care, the team have delivered the following impacts in three key areas:

Assessing stroke and bleeding risk

Professor Lip and Dr Lane have developed and validated two risk stratification scores, CHA_2DS_2-VASc and HAS-BLED, based on common clinical information that provide well-validated approaches for clinicians to assess their patients' risk of stroke and bleeding, respectively. These scores have helped clinicians to formally assess stroke risk and identify 'truly low risk' patients who do not need antithrombotic therapy, and effectively capture those patients who should be considered for oral anticoagulation therapy. CHA_2DS_2-VASc is easily available for use by GPs as part of the Guidance on Risk Assessment and Stroke Prevention for Atrial Fibrillation (GRASP-AF) risk stratification tool for stroke to guide oral anticoagulation treatment, which is freely available and compatible for use with all GP clinical systems in England [5]. The simple, user-friendly HAS-BLED score, comprising risk factors either readily available from the clinical medical history or routinely tested in (new) patients, allows clinicians to formally assess bleeding risk, identifying modifiable risk factors (optimising blood pressure control, removing concomitant anti-platelet, reducing alcohol intake, and optimising time in therapeutic range for those patients receiving warfarin), and those who require regular review (patients at higher bleeding risk).

The CHA_2DS_2-VASc score has become the principal tool to assess stroke risk and decide on anticoagulant therapy in the most recent ESC2010 guidelines on atrial fibrillation [6] and their focused update in 2012[2], both used in Europe and throughout most parts of the world. This score is also used by the Asia Pacific Heart Rhythm Society guideline, which recommends that the CHA_2DS_2-VASc score should be used to assess the risk of stroke for all patients with nonvalvular AF in the Asia-Pacific region[7]. A narrative form of CHA_2DS_2-VASc is used in the 2012 ACCP guideline [1].The HAS-BLED score is similarly used in international AF treatment guidelines (Europe, Canada) – notably those issued by the ESC in 2010/12 (noted above) and the 2012 Canadian Cardiovascular Society [8]. Both scores are recommended in the UK Consensus Statement on AF issued by the Royal College of Physicians of Edinburgh [9].The significant worldwide impact of this work with CHA_2DS_2-VASc and HAS-BLED on the management of AF has recently been acknowledged by two prestigious awards, the Arrhythmia Alliance Team of the Year 2012 and the BMJ Awards Cardiovascular Medicine Team of the Year 2013.

AF treatment decisions relating to risk

One quarter of all strokes in people aged ≥75 years result from AF, and therefore improving the provision of stroke prevention in elderly people with AF is a critical aspect of management. The BAFTA study clearly led to a change in guidelines and clinical practice by providing clear evidence for health professionals of the benefit of using oral anticoagulation therapy in over 75s. The NHS Quality and Outcomes Framework guidance in 2009 and 2013/14 [10,11] highlighted that *"there is clearly a need to encourage the use of this treatment for AF patients at high risk of stroke"*, and both stated *"recent evidence from the BAFTA trial…suggests not only is warfarin much more effective than aspirin, but that it is not as unsafe – in terms of risk of serious haemorrhage – as previously thought"*. The 2013/14 guidelines also noted that *"It is advised that patients with stroke associated with AF are reviewed for long-term treatment with warfarin".*

Screening in primary care

The SAFE study helped to define best practice with respect to AF screening in the elderly population, comparing the effectiveness (including cost-effectiveness, i.e. value for money) of different approaches of systematic or ad-hoc screening to best diagnose AF. Together with the BAFTA trial this has changed the way that AF is now managed at a national and international level:
UK clinical guidance: The National Institute for Health and Care Excellence (NICE) sets accepted

practice for patient healthcare, used by groups ranging from NHS, Local Authorities, employers, voluntary groups and others involved in delivering care or promoting wellbeing. Results of the BAFTA and SAFE studies were incorporated into the 2006 National Atrial Fibrillation Clinical Guideline for Management in Primary and Secondary Care [12]. These directly reference SAFE, and importantly remain the current guidance informing clinical practice and patient care throughout the assessment period.The British Committee for Standards in Haematology Guidelines on oral anticoagulation published in 2011 also draw on the results of the BAFTA study [13]

International clinical guidelines: The ESC published guidelines in 2010 for AF management [6] referencing the work of Lip, and a 2012 update [2] stating "*"We therefore recommend that, in patients aged 65 years or over, opportunistic screening for AF by pulse palpation, followed by recording of an ECG to verify diagnosis, should be considered for the early detection of AF"*. This work also reached the USA, with the American College of Chest Physicians [1] published evidence-based guidelines on antithrombotic therapy in AFin 2012, incorporating BAFTA results. Utilising this work for primary care was also part of the World Heart Federation/International Atrial Fibrillation Association 2012 guidelines [15] (Lip part of Steering Committee).

5. Sources to corroborate the impact (indicative maximum of 10 references)

1. You JJ, Singer DE, Howard PA, Lane DA, Eckman MH, Fang MC et al. Antithrombotic therapy for atrial fibrillation, 9th edition: American College of Chest Physicians evidence-based clinical practice guidelines. Chest 2012; 141(2) (Suppl):e531S-e575S. *doi: 10.1378/chest.11-2304*
2. Lip GYH, Andreotti F, Fauchier L, Huber K, Hylek E, Knight E et al. Bleeding risk assessment and management in atrial fibrillation patients: a position document from the European Heart Rhythm Association, endorsed by the European Society of Cardiology Working Group on Thrombosis. Europace 2011;13: 723-746. *doi: 10.1160/TH11-10-0690*
3. NHS Shared Decision Making. Patient Decision Aid for Stroke Prevention for atrial fibrillation or flutter. http://sdm.rightcare.nhs.uk/pda/stroke-prevention-for-atrial-fibrillation.
4. European Heart Rhythm Association atrial fibrillation patient website. http://afibmatters.org.
5. Guidance on Risk Assessment and Stroke Prevention for Atrial-Fibrillation (GRASP-AF) .Query and risk stratification toolavailable for use within all GP clinical systems in England. http://www.improvement.nhs.uk/graspaf/documents/resources/GRASP-AF_2012_flyer.pdf
6. Camm AJ, Kirchhof P, Lip GY, Schotten U, Savelieva I, Ernst S et al. Guidelines for the management of atrial fibrillation. The Task Force for the management of atrial fibrillation of the European Society of Cardiology. *European Heart Journal* 2010; 31: 2369-2429. *doi:10.1093/eurheartj/ehq278*
7. APHRS News July 2013: http://www.aphrs.asia/news_images/2013_08/APHRS-No.8-final.pdf
8. Canadian Cardiovascular Society Atrial Fibrillation Guidelines Committee. Focused 2012 Update of the CCS Atrial fibrillation Guidelines: recommendations for stroke prevention and rate/rhythm control. Can J Cardiol 2012;28:125–136. *doi: 10.1016/j.cjca.2012.01.021.*
9. Stott DJ, Dewar RI, Garratt CJ, Griffith KE, Harding NJ, James MA et al. Royal College of Physicians of Edinburgh. RCPE UK Consensus Conference on 'Approaching the comprehensive management of atrial fibrillation: evolution or revolution?'.*J R Coll Physicians Edinb*. 2012;42 Suppl 18:3-4.http://www.rcpe.ac.uk/sites/default/files/files/Final_statement.pdf
10. BMA/NHS Employers. Quality and Outcomes Framework guidance for GMS contract 2009/10. Delivering investment in general practice. March 2009 (AF Indicator 3, pp.107-109).
11. 2013/14 general medical services (GMS) contract quality and outcomes framework (QOF) Guidance for GMS contract 2013/14. (Indicators AF003-004, pp.33-38).
12. National Collaborating Centre for Chronic Conditions. Atrial fibrillation. National Clinical Guideline for management in primary and secondary care. London: Royal College of Physicians; 2006. *http://www.nice.org.uk/nicemedia/live/10982/30055/30055.pdf*
13. Keeling D, Baglin T, Tait C, Watson H, Perry D, Baglin C et al. British Committee for Standards in Haematology Guidelines on oral anticoagulation with warfarin. Fourth edition. *British Journal of Haematology* 2011; 154(3): 311-324 *http://www.bcshguidelines.com/documents/warfarin_4th_ed.pdf*
14. Atrial fibrillation in primary care (AFIP). Bringing atrial fibrillation practice closer to guidelines. A Tool for Primary Care Physicians. International Atrial Fibrillation Association. 2012 http://www.world-heart-federation.org/fileadmin/user_upload/documents/AF-Aware/GAFA/AFIPtoolUpdated23July212.pdf