

## Adoption of a single-page best practice algorithm improves outcomes in patients with acute atrial fibrillation: a multi-disciplinary quality improvement project

Edd Maclean (MBBS)<sup>1,2\*</sup>, Daniella de Block Golding (MBBS)<sup>2</sup>, Samantha Maden (MBBS)<sup>2</sup>, Shreena Patel (MBBS)<sup>2</sup>, Ola Joseph (MBBS)<sup>2</sup>, Max Denning (BMBCh)<sup>2</sup>, Jesca Boot (MBBS)<sup>2</sup>, Roger Rear (MBBS)<sup>2</sup>

<sup>1</sup>Queen Mary University of London, Mile End Road, London E1 4NS.

<sup>2</sup>North Middlesex Hospital Sterling Way, London, N18 1QX.

ARTICLE INFO	ABSTRACT
<p><i>Article type:</i> Original article</p> <hr/> <p><i>Article History:</i> Received: 11-Apr-2019 Accepted: 23-Jun-2019</p> <hr/> <p><i>Key words:</i> Atrial Fibrillation, Algorithm, Quality Improvement, Stroke</p>	<p><b>Introduction:</b> In response to a serious incident involving an atrial fibrillation (AF) associated stroke, a quality improvement project was established to examine and improve all aspects of patient care for individuals presenting with acute AF to London's North Middlesex University Hospital (NMUH).</p> <p><b>Materials and Methods:</b> The presenting complaint was examined for 2,105 consecutive medical admissions to identify 100 patients (4.7%) with acute AF. For each patient, 36 indices and performance indicators were collected and analysed against international standards. Deficiencies were identified in documentation, risk stratification, anticoagulation and arrhythmia management decisions. With cross-specialty collaboration, a single-page AF management algorithm was established using sequential PDSA methodology, and a further 100 consecutive patients with acute AF were analysed prospectively. A composite endpoint of adverse outcomes (AF-associated readmission, stroke, cardiac death or major bleeding) was examined.</p> <p><b>Results:</b> Algorithm implementation significantly reduced the proportion of patients exposed to unnecessary stroke risk (30% vs 4%, <math>P &lt; 0.0001</math>); improved identification and documentation of thromboembolic potential (50% vs 88%, <math>P &lt; 0.0001</math>), reduced incorrect drug decisions (12% vs 2%, <math>P = 0.01</math>), reduced contraindicated rhythm control (8% vs 0%, <math>P = 0.007</math>), and increased direct oral anticoagulant (DOAC) prescribing (38% vs 86%, <math>P &lt; 0.0001</math>) over warfarin. After a mean follow-up of 248 +/- 91 days, there was a significant reduction in composite adverse outcomes (22% vs 6%, <math>P = 0.0018</math>).</p> <p><b>Conclusion:</b> Using established quality improvement methodology and cost-neutral multi-disciplinary expertise, this novel management algorithm has significantly improved the quality and safety of care for patients with acute AF at NMUH.</p>
<p>► <b>Please cite this paper as:</b> Maclean E, de Block Golding D, Maden S, Patel S, Joseph O, Denning M, Boot J, Rear R. Adoption of a Single-page Best Practice Algorithm Improves Outcomes in Patients with Acute Atrial Fibrillation: A Multi-disciplinary Quality Improvement Project. Journal of Patient Safety and Quality Improvement. 2019; 7(3):87-94. Doi: 10.22038/PSJ.2019.39546.1220</p>	

### Introduction

Atrial fibrillation (AF) remains the most common heart rhythm disturbance; across

Europe, an estimated 18 million individuals will be affected by 2060(1).

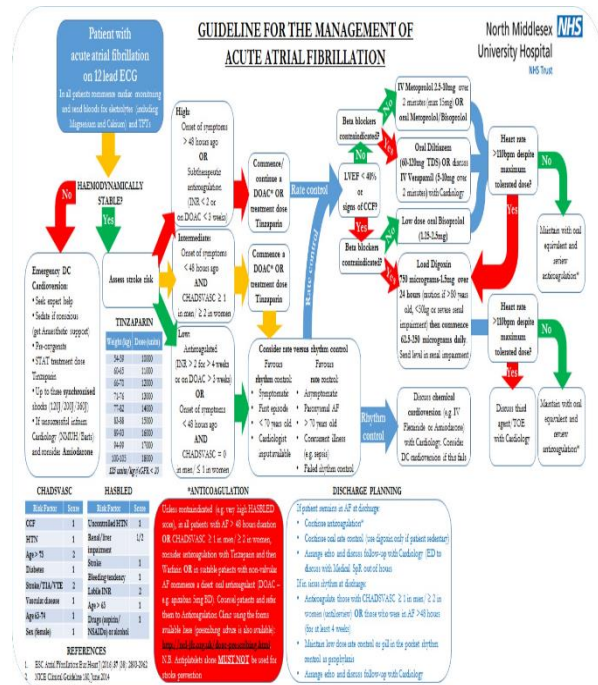
\* Correspondence Author: Edd Maclean, Queen Mary University of London, Mile End Road, London, United Kingdom. Tel: 02078825555; Email: e.maclean@qmul.ac.uk

© 2019 mums.ac.ir All rights reserved.

This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/3.0>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

AF is associated with both cardiac decompensation and embolic events and, despite recent advances in thromboembolic risk assessment and anticoagulation, each year it remains implicated in around 30% of ischaemic strokes(2). It is accepted that the management of AF should therefore be twofold: 1) Either re-establish the normal heart rhythm or control the heart rate and 2) Assess and reduce the risk of embolic stroke if safe to do so. Whilst the former is often the most acute – sometimes life-threatening – clinical issue, the most significant morbidity from AF results from a failure to safely address the latter. International (ESC) and National (NICE) guidelines are well-evidenced and facilitate important decision-making regarding anticoagulation, rate, and rhythm control strategies in AF (3-4). Whilst these documents are well-referenced and explicitly detailed, they do not specifically cater for local resources or populations and, consequently, can be difficult to use as an immediate reference guide for the non-specialist in everyday practice. In addition, even with established guidelines, physicians’ compliance can be variable depending on factors such as awareness, familiarity, agreement, and the inability to overcome the inertia of previous practice(5). The initial management of acute AF presents challenging permutations of clinical findings, investigations, drugs and procedures, and consequently incorporates several potentially high-risk steps. For example, the physician’s decision to attempt reversion to a normal (sinus) rhythm – a ‘rhythm control’ strategy – requires careful assessment of thromboembolic risk and cardiac function. Inappropriate rhythm control carries a significant stroke association and incorrect drug decisions can cause cardiovascular instability. Likewise, the decision to slow down the patient’s pulse rate in acute AF – a ‘rate control’ strategy – must be guided in particular by haemodynamic status, co-morbidities and medication history. Drug selections and dosages have significant ramifications on patient safety; overzealous rate control may cause haemodynamic deterioration, whilst overly cautious drug administration can delay recovery and potentiate cardiac failure. In all patients, an assessment of

thromboembolic and bleeding risk is essential; this can be estimated using validated risk scoring tools such as the CHA<sub>2</sub>DS<sub>2</sub>-VASc and HASBLED scores respectively(6-7) (Figure 1).



**Figure 1:** The NMUH acute atrial fibrillation guideline (modified to remove contact details). Abbreviations: CCF -congestive cardiac failure; HTN – hypertension; LVEF - left ventricular ejection fraction; TIA-transient ischaemic attack; VTE-venous thromboembolism; TOE-transoesophageal echocardiogram; DOAC- direct oral anticoagulant

These registry-derived indices respectively inform clinicians of the likelihood of embolic stroke in the absence of anticoagulation, and the chance of significant haemorrhage following initiation of anticoagulation. In challenging cases, the two measures are often combined with patient choice to form a risk/benefit decision. Importantly, it has been demonstrated that patients with AF consider moderate to severe stroke as at least equal to or worse than death, and would accept on average four gastrointestinal bleeds to prevent one stroke(8). It is therefore paramount that both physicians and patients are provided with the necessary information to engage with appropriate anticoagulation therapy. Oral anticoagulants for the prevention of stroke in patients with non-valvular AF include the Direct Oral Anticoagulants (DOACs) such as apixaban, and the vitamin

K antagonists such as warfarin. In recent years, landmark trials such as ARISTOTLE, ROCKET-AF and RE-LY have demonstrated at least equal efficacy of the DOACs when compared with warfarin for stroke prevention in AF, and there is increasing evidence of a superior safety profile in DOAC agents, particularly apixaban (9-12). In addition, when compared with warfarinised patients, DOAC users require fewer blood tests, clinic visits and dose changes, and are at lower risk of significant drug interactions. Consequently, the ESC guidelines now recommend DOACs over vitamin K antagonists in suitable patients with non-valvular AF.

### Quality Improvement

As an Acute Trust in North London with over 500 inpatient beds, North Middlesex University Hospital (NNUH) encounters individuals with AF across all clinical areas, including in Accident & Emergency (A&E), via the acute medical take, in outpatient and pre-assessment clinics, peri-operatively, and incidentally on the wards. Following a serious incident at NNUH in which a patient with sub-optimally managed AF suffered an ischaemic stroke, the decision was made to review local procedures and establish a best practice guideline which condensed, simplified and standardised the optimum care of these patients.

### Aims

Using a SMART objectives framework, we aimed to use expertise from across grades and specialities (including Cardiology, Haematology, A&E, Stroke, Internal Medicine and Pharmacy) to create an indicative guideline for managing patients presenting with acute AF. This document would be a comprehensive but concise, single-page algorithm suitable for use at the point of consultation throughout the trust, and the recommendations would be applicable to patients with either new onset or decompensated tachycardic AF. We sought early quantitative improvements in the proportion of these patients who were adequately protected from stroke, and safely and appropriately rate or rhythm controlled. We hypothesised that improvements in

these areas would translate into a reduction of adverse events long term.

## Materials and Methods

### Baseline data

A baseline survey repeated over 3 distinct weeks determined the inpatient prevalence of AF at NNUH to be 8-10%. Further detailed data collection was performed for 100 consecutive patients admitted via NNUH A&E with acute AF during December 2016-March 2017. 36 indices were recorded for each patient including date of birth, sex, CHA2DS2-VASc constituents, choice of rate or rhythm controlling or anticoagulant drugs, contraindications, adverse effects, echocardiographic and ECG data, and length of stay. These indices were derived from the patient data required to effect appropriate decision making as per the ESC and NICE AF guidelines. Deficiencies table 2 were identified regarding administration of anticoagulation, choice of rate or rhythm controlling drug, documentation and stroke risk stratification.

### Algorithm design

Our first PDSA cycle consequently consisted of an examination of any pre-existing local guidance and a review of similar projects (neither were identified), and thereafter a condensation of international guideline-derived best practice into a simple AF treatment algorithm. Initial recommendations were then reviewed by a panel of 10 Cardiology Doctors and Specialist Nurses (FY1-Consultant/Band 8 level) who assessed the safety of the proposed arrhythmia management strategies and refined them according to their own clinical experiences. Following revision, a subsequent PDSA cycle tested the draft algorithm theoretically in a series of 20 historic patients. This evaluation demonstrated that the new guideline would have had positive ramifications on patient safety and experience. The guidance was then passed to the Stroke and Haematology Specialist Doctors and Nurses, who were integral in guiding risk stratification (particularly in specialist cases) and advising on safe follow-up pathways for patients on anticoagulation. Clinical

applicability was then evaluated by the 'frontline' A&E and Acute Medical staff, who gave feedback on the utility of the algorithm's assisted decision-making and any information additionally required.

A significant barrier was encountered at this stage whereby frontline staff felt the guidance lacked explicit details in parts, and that it assumed a specialist-level of knowledge. The algorithm was subsequently revised in accordance with their direct feedback to provide more reference information (such as the doses of particular medications), and to further simplify decision-making (such as recommending Cardiology input in all patients considered for rhythm control).

With the clinicians who practise the guidance subsequently in agreement, the Pharmacists assessed the feasibility and safety of the treatment algorithms. The Medicines Management Committee ultimately gave their approval prior to finalisation.

### Algorithm introduction

A third PDSA cycle examined the guideline 'going live' in a controlled environment; via the acute medical take supervised by a Cardiology registrar. This pilot demonstrated the successful uptake of the algorithm over a weekend in A&E, with optimal anticoagulation and arrhythmia-management outcomes achieved in a series of six acute AF patients.

The guideline was published in May 2017 with assistance from the trust's communications team who disseminated the document via the trust news, via an upload on the intranet, and via sequential group emails. The Cardiology team also presented the guidance at the trust's grand round.

The finished guideline is composed of an interactive PDF file available on the trust intranet, and is also printed and displayed at key acute care locations throughout NNUH (such as A&E Resuscitation, The Acute Medical Unit and the Medical Wards). The PDF contains a direct hyperlink to relevant additional prescribing resources on the internet (the local Joint Formulary Committee Guidance on DOAC prescribing, counselling and follow-up).

The algorithm itself is a bold, colourful, and simple decision aid, with boxes of additional

information (such as CHA<sub>2</sub>DS<sub>2</sub>-VASc assessment and discharge advice) in free text provided for users who require greater detail at the point of use. The algorithm incorporates recommendations for all patients, ranging from haemodynamically unstable emergencies to chronic heart failure patients with significant co-morbidities (see Figure 1). Specific drug choices and dosages (including in special cases) are drawn from the ESC guidelines and local best practice, and are indicated throughout.

Critically, the algorithm encourages stroke risk assessment and consideration of anticoagulation at the point of admission. Given that – in suitable patients – the ESC guidelines now recommend the use of a DOAC ahead of vitamin K antagonists, DOACs (such as apixaban) are listed as the first line anticoagulant. The algorithm also removes the possibility of unsafe rhythm control, and provides second- and third-line rate control therapies in the event of initial treatment failure. The contact details of Senior Clinicians are provided for assistance 24 hours a day.

To monitor the trust's progress (particularly after key players left the trust in late 2017), two 'AF Champions' were appointed – they remain responsible for repeat data collection in September 2019 and for the ongoing quality assurance of the guidance.

### Follow-up data

After a run-in period and a short safety pilot of the new guideline, prospective data collection was subsequently performed in a series of consecutive AF patients from June 2017 (n=100). As well as baseline data and performance indices, the incidence of a composite of adverse outcomes (AF-associated hospital readmission, stroke, cardiac death and major bleeding) was examined.

### Statistical analysis

Follow-up statistical analysis was performed using SPSS software (v. 26, IBM Corporation, New York, USA).

The Shapiro-Wilk test distinguished normally and non-normally distributed data. Categorical group parameters were compared using Z-tests. Continuous

parameters were analysed using two-tailed unpaired T tests for normally distributed data or the Mann-Whitney U test for non-normally distributed data. Grouped outcomes were compared using Fisher's exact test. The level of significance for all tests was set at P<0.05.

### Results

Key baseline characteristics including age, sex, haemodynamic status, stroke risk (CHA<sub>2</sub>DS<sub>2</sub>-VASc score) and echocardiographic findings (which guide treatment decisions) were similar between the two patient groups (Table.1).

**Table 1:** Baseline characteristics for patients admitted before and after the introduction of our best practice algorithm

Parameter	Before algorithm (n=100)	After algorithm (n=100)	P value
Mean age (years)	71.4	73.4	0.72
Male (%)	54	48	0.48
CHA <sub>2</sub> DS <sub>2</sub> -VASc score (mean)	3.2	3.4	0.34
Haemodynamically unstable at presentation	3	2	1
Echocardiogram performed (%)	79	84	0.46
LV impairment on echo (LVEF <55%) (%)	44	41	0.76
Left atrial enlargement on echo (%)	82	90	0.15

Comparative performance indicators and outcome variables are shown numerically in table 2 and graphically in figure 2. Patients with an indication for – and no documented

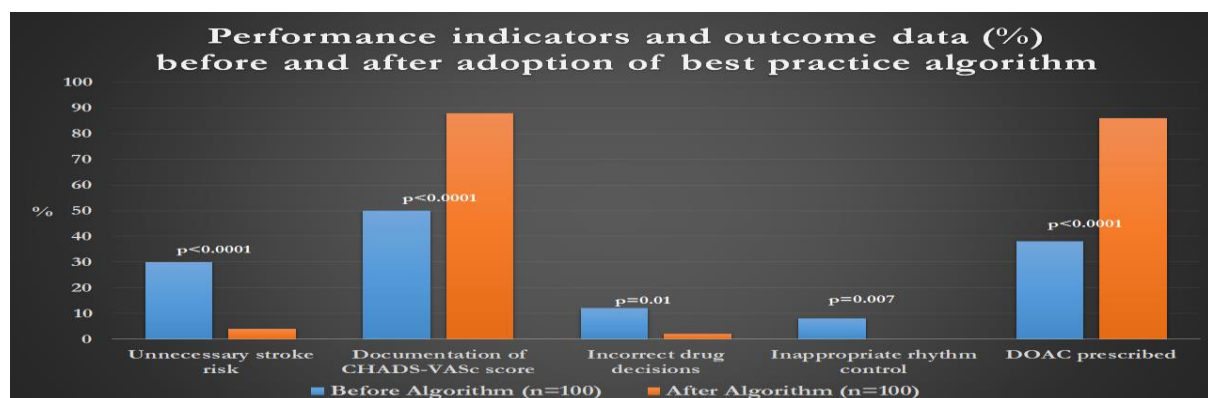
contraindication to – anticoagulation that did not receive anticoagulation were deemed to have been put at unnecessary risk of stroke.

**Table 2:** Performance indicators for patients admitted before and after the introduction of our best practice algorithm

Parameter	Before algorithm (n=100)	After algorithm (n=100)	P value
Unnecessary risk of stroke	30%	4%	<0.0001
CHA <sub>2</sub> DS <sub>2</sub> -VASc score documented	50%	88%	<0.0001
Incorrect drug prescribed	12%	2%	0.01
Contraindicated rhythm control attempted	8%	0%	0.007
% DOACs used	38%	86%	<0.0001
Significant inpatient haemorrhage	2	3	1
Mean Length of stay (days)	4.7	3.5	0.11

Since guideline implementation, there has been a significant reduction in patients exposed to unnecessary stroke risk, fewer treatment strategy and medication errors, and a significant increase in the proportion

of DOACs being prescribed instead of warfarin. There was no change seen in anticoagulation-related complications, and there was also a trend towards reduced inpatient length of stay.



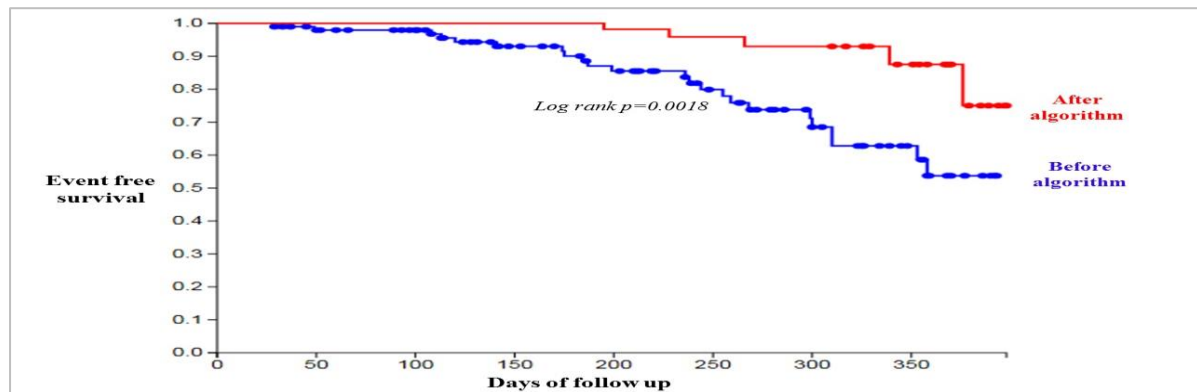
**Figure 2:** Comparative performance indicators and outcome data (%) before (blue) and after (red) adoption of the best practice algorithm

After a mean follow-up of 248 +/- 91 days, a reduction in a composite of adverse outcomes

was seen (22% vs 6%, p=0.0018 – see figure 3 and table 3).

**Table 3:** Adverse outcomes in patients before and after adoption of the best practice algorithm

Outcome	Before algorithm (n=100)	After algorithm (n=100)	p value
Cardiac Death	1%	0%	1
AF-associated hospital readmission	18%	6%	0.015
Stroke	3%	0%	0.27
Major bleeding	0%	0%	1
Composite endpoint	22%	6%	0.0018



**Figure 3:** Kaplan Meier plot of event free survival between groups (Before algorithm n=100, After algorithm n=100) after a mean follow-up of 248 +/- 91 days

**Discussion**

The management of acute AF is multifactorial and presents well-established pitfalls. In our analysis, the finding that 30% of patients were put at unnecessary risk of stroke may appear striking, but similar results have been documented in other observational studies. Pisters et al (2010) found that 22% of AF-associated ischaemic strokes at their institution could have been prevented with improved antithrombotic guideline adherence (13). Likewise, Xian et al. (2016) analysed 94,474 patients with AF who suffered ischaemic strokes and found that 83.5% were not appropriately anticoagulated prior to stroke incidence (14). In their 2016 review, Vallakati and Lewis attribute the underuse of therapeutic anticoagulation by clinicians predominantly to the fear of causing harm, or ‘omission bias’ (15). Encouragingly however, this trend appears to be improving; the FibStroke study (Palomäki et al, 2016) found that appropriate OAC prescribing in AF improved from 49% in 2003 to 65% in 2012(16). Brown et al. (2016) documented a similar increase in OAC use (42% to 52%), accrediting this to the favourable clinical trial results for the DOACs

in particular (17). Accordingly, we found that the introduction of a novel treatment algorithm improved the proportion of patients receiving appropriate anticoagulation from 70% to 96%. We ascribe this improvement to the algorithm’s design, which provides decision-makers with the tools to make early – but comprehensive – risk assessments. The corresponding transition towards increased DOAC prescribing has so far proved both efficacious and safe, and may also improve patient satisfaction by reducing the number of outpatient anticoagulation clinic visits. In long term analyses, DOACs have also been found cost effective when compared to warfarin (18). Our trend towards reduced mean hospital stay has also been observed in similar studies, and appears to be mediated by the relatively short initiation period of DOACs when compared with warfarin (19). Following our intervention, we also found that decisions regarding rhythm versus rate control had moved in-line with international guidance, and accordingly there were significantly fewer errors regarding initial drug choice and dose. A significant reduction in the composite endpoint was

predominantly mediated by fewer hospital re-admissions. Whilst this may reflect the use of more appropriate rate or rhythm control strategies – and therefore fewer subsequent arrhythmia-associated decompensations – the change in anticoagulation prescribing patterns may also be implicated. Bhattarai et al (2018) examined readmission risk in 1781 discharges from a single centre, and found that warfarin therapy was associated with 30-day hospital readmission, whereas DOAC therapy was not (20).

## Reflections

Devising a guideline sufficiently comprehensive to cover the bulk of acute AF scenarios, and yet acceptably concise as to be useful as a ‘quick reference’ guide, is challenging. Despite this, there appears to have been excellent engagement with our algorithm which we attribute to its simplicity, availability and scope. Our key reflection is of the need to involve important stakeholders earlier. Whilst it seemed prudent to source initial best practice from Cardiologists, gauging the level of experience and assistance required for the most frequent practitioners of the guidance (i.e. A&E and General Medicine) would have been far more useful at an earlier stage. The guideline consequently required extensive revision during a relatively advanced PDSA cycle, whereas these practitioners’ needs could have been addressed at project inception. Likewise, pharmacological recommendations were initially sourced directly from ESC and NICE guidelines, however the local pharmacists subsequently advised that certain drugs were not available at NMUH. Their expertise regarding local resources would have proved a useful adjunct at the outset of our quality improvement project.

## Limitations

An important limitation in our project is its potential for selection bias; the follow-up analysis was performed by the clinicians who both recruited the patients and devised the algorithm. However, the ongoing and cyclical review process that is required by quality improvement work necessitated that the authors were unmasked to patients’ clinical data throughout. The generalisability of our data to other

inpatient settings is not guaranteed; NMUH has a unique patient population, close Cardiology (including Electrophysiology) input and excellent echo availability, which may facilitate (and skew) decision-making, particularly in complex cases.

## Conclusion

In the wake of a serious incident, and as a result of multi-disciplinary collaboration, our best practice guideline for AF is improving the safety and efficacy of care for a large inpatient population in North London. This intervention relied only on the experience, knowledge and dedication of our staff body and delivered a low-cost solution to an increasingly prevalent problem.

The guideline is unique in its design and its incorporation of arrhythmia management with early anticoagulation strategies. It has potentiated quantitative improvements in patient outcomes in-line with international standards. In addition, the observed trend towards a reduction in length of stay has significant cost-saving implications and spreads the benefits of our project beyond patients with AF. Consolidative measures remain in place to sustain this improvement.

## Acknowledgements

With thanks to Dr. Chris Mitchell (NMUH Haematology) and Dr. Bob Luder (NMUH Stroke Physician)

## References

1. Rahman F, Kwan GF, Benjamin EJ. Global epidemiology of atrial fibrillation. *Nat Rev Cardiol.* 2014; 11(11):639-54.
2. Friberg L, Rosenqvist M, Lindgren A, Terént A, Norrving B, Asplund K. High prevalence of atrial fibrillation among patients with ischemic stroke. *Stroke* 2014.45(9): 2599-605.
3. Kirchhof P, Benussi S, Kotecha D, Ahlsson A, Atar D, Casadei B et al. 2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS *Eur Heart J* 2016 37(38):2893-2962.
4. National Institute for Health and Care Excellence Atrial Fibrillation: Management, Clinical Guideline 180, June 2014.
5. Cabana MD, Rand CS, Powe NR, Wu AW, Wilson MH, Abboud PC et al. Why don't physicians follow clinical practice guidelines? *JAMA* 1999 282(15):1458-65.

6. Shariff N, Aleem A, Singh M, Li YZ, Smith SJ AF and Venous Thromboembolism - Pathophysiology, Risk Assessment and CHADS-VASc score J Atr Fibrillation. 2012 5(3): 649.
7. Lip GYH, Frison L, Halperin JL and Lane DA Comparative Validation of a Novel Risk Score for Predicting Bleeding Risk in Anticoagulated Patients With Atrial Fibrillation J Am Coll Cardiol. 2011 57(2): 173-80
8. Potpara TS; Lane DA; Lip GY Optimizing stroke prevention in atrial fibrillation: better adherence and compliance from patients and physicians leads to better outcomes Europace 2015 17(4):507-8
9. Granger CB, Lopes RD, Hanna M, Ansell J, Hylek EM, Alexander JH et al. Clinical events after transitioning from apixaban versus warfarin to warfarin at the end of the Apixaban for Reduction in Stroke and Other Thromboembolic Events in Atrial Fibrillation (ARISTOTLE) trial. Am Heart J. 2015 169(1):25-30.
10. ROCKET AF Study Investigators. Rivaroxaban-once daily, oral, direct factor Xa inhibition compared with vitamin K antagonism for prevention of stroke and Embolism Trial in Atrial Fibrillation: rationale and design of the ROCKET AF study. Am Heart J.2010 159(3):340-7.
11. Connolly SJ, Ezekowitz MD, Yusuf S, Eikelboom J, Oldgren J, M.D., Parekh A et al. Dabigatran versus Warfarin in Patients with Atrial Fibrillation. N Engl J Med 2009 361:1139-1151.
12. Bai Y, Shi X, Ma C, Lip GYH Meta-Analysis of Effectiveness and Safety of Oral Anticoagulants in Atrial Fibrillation With Focus on Apixaban The American Journal of Cardiology 2017 120(9): 1689-1695
13. Pisters R, van Oostenbrugge RJ, Knottnerus ILH, de Vos CB, Boreas A, Lodder J et al. The likelihood of decreasing strokes in atrial fibrillation patients by strict application of guidelines Europace 2010 12: 779-784
14. Xian Y, O'Brien EC, Liang L, Xu H, Schwamm LH, Fonarow GC et al. Association of Preceding Antithrombotic Treatment With Acute Ischemic Stroke Severity and In-Hospital Outcomes Among Patients With Atrial Fibrillation. JAMA. 2017 317(10):1057-1067
15. Vallakati A, Lewis WR Underuse of anticoagulation in patients with atrial fibrillation Postgrad Med. 2016;128(2):191-200
16. Palomäki A, Mustonen P, Hartikainen JE, Nuotio I, Kiviniemi T, Ylitalo A Underuse of anticoagulation in stroke patients with atrial fibrillation - the FibStroke Study Eur J Neurol. 2016 23(1):133-9
17. Brown JD, Shewale AR, Dherange P, Talbert JC. A Comparison of Oral Anticoagulant Use for Atrial Fibrillation in the Pre- and Post-DOAC Eras. Drugs Aging. 2016 33(6):427-36.
18. López-López JA, Sterne JAC, Thom HHZ, Higgins JPT, Hingorani AD, Okoli GN et al. Oral anticoagulants for prevention of stroke in atrial fibrillation: systematic review, network meta-analysis, and cost effectiveness analysis. BMJ. 2017 359:j5058
19. Basto AN, Fewel NP, Vo K, Stock EM, Ta M. Initiation of direct oral anticoagulants versus warfarin for venous thromboembolism: impact on time to hospital discharge. J Thromb Thrombolysis. 2018 45(1):51-55
20. Bhattarai M, Hudali T, Robinson R, Al-Akchar M, Vogler C, Chami Y Impact of oral anticoagulants on 30-day readmission: a study from a single academic centre. BMJ Evid Based Med. 2019 24(1):10-14.