

# Objectives of Session

- Project Background – Why the need
- Decision Support Tool – summary of key evidence
- Promotion Key Messages

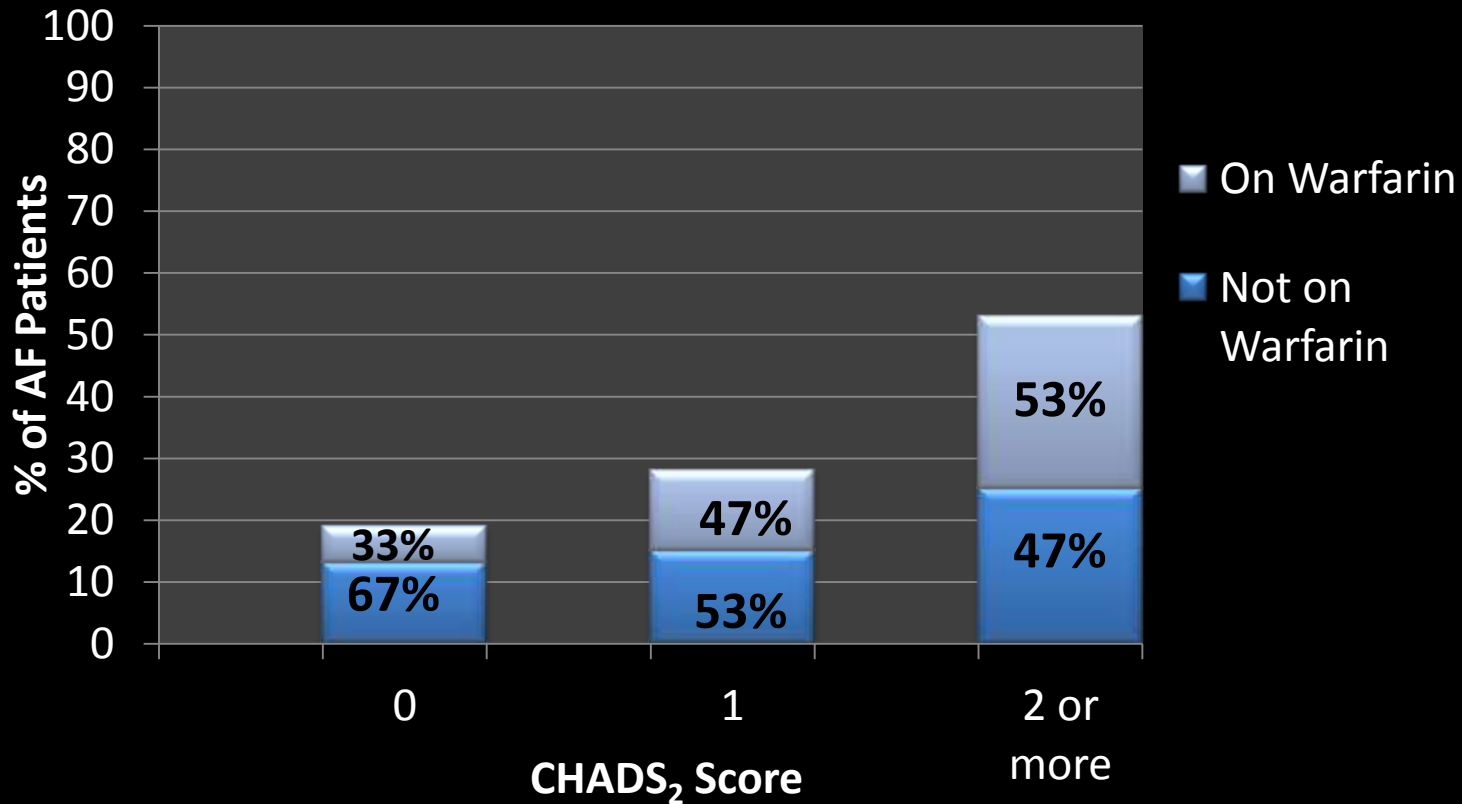
# Project Background

## Grasp AF Audit

- Initial Grasp AF project undertaken in NHS Buckinghamshire in 2010 as an ST4 project
- 52 out of 59 practices run Grasp AF tool during April-Sept 2010
- 50 of the 52 practices agreed to share their data
- From shared Grasp data prevalence of AF in sample =1.61% (actual no patients= 7094)

# Grasp AF Project Results

Grasp AF Data for NHS Buckinghamshire  
Initial Project Results - September 2010



# Grasp AF Project Findings

- Misperceptions about relative safety & efficacy of aspirin versus warfarin for AF in primary care
  - ❖ Bleeding risk with anti-platelets and well controlled warfarin not being recognised as comparable
  - ❖ Lack of awareness that the efficacy of aspirin in reducing stroke risk in AF declines with age
  - ❖ Older patients put on aspirin in preference to warfarin - some with warfarin CI noted
  - ❖ 'Falls risk' common reason cited for not initiating OACS
  - ❖ General reluctance to prescribe warfarin in primary care
- Recent changes in national guidance on use of anti-platelets in 1<sup>o</sup> & 2<sup>o</sup> prevention CVD

# Way Forward

- Pragmatic GP decision guide tool on CI to anti-thrombotics
  - ❖ a 'catch all' set of guidance - unable to find a single source that was available to GPs
  - ❖ Not the resources to look at each practice or leverage to get practices to provide feedback about their decision making locally.

AIM



‘To promote change in prescribing behaviour towards increased uptake in use OACs in AF management’

## Contraindications to The Initiation of Oral Anticoagulants & Anti-platelet Agents in Patients with Atrial Fibrillation in Primary Care

As a patient's relative stroke & bleeding risk can change, it is essential that all AF patients are reviewed at LEAST annually for a re-assessment of their stroke versus bleeding risk & the anti-thrombotic treatment option of choice.

Contraindications listed below apply to BOTH anti-platelet agents (e.g. aspirin, clopidogrel, dipyridamol) & ALL oral anticoagulants (e.g. warfarin, phenindione, dabigatran, rivaroxaban) except where indicated.

### Absolute Contraindications

- Known large oesophageal varices.
- Significant thrombocytopenia (platelet count < 50 x 10<sup>9</sup>/L) - refer to haematologist.
- Within 72 hours of major surgery with risk of severe bleeding - defer & reassess risk postoperatively.
- Previously documented hypersensitivity to either the drug or excipients - consider cardiology opinion.
- Acute clinically significant bleed - defer & re-assess stroke versus bleeding risk within 3 months.
- Decompensated liver disease or deranged baseline clotting screen (INR > 1.5) - refer to Gastroenterology /Hepatology. **Contraindication applies to oral anticoagulants only**
- Pregnancy or within 48 hours post partum - seek urgent haematological advice. **Contraindication applies to oral anticoagulants only.**
- Severe renal impairment (GFR < 30 mL/min/1.73 m<sup>2</sup> or on dialysis). **Contraindication applies to dabigatran only.**

### Relative Contraindications

- Previous history intracranial haemorrhage - as some AF patients especially those considered at higher stroke risk (i.e. CHADS<sub>2</sub> score ≥3) may benefit from anti-thrombotic therapy, seek the opinion of a stroke specialist.
- Recent major extracranial bleed within the last 6 months where the cause has not been identified or treated - decision for oral anti-thrombotic therapy should be deferred.
- Recent documented peptic ulcer (PU) within last 3 months - decision for oral anti-thrombotic therapy should be deferred until treatment for PU completed. In all cases with history PU give PPI cover whilst on anti-thrombotic.
- Recent history recurrent iatrogenic falls in patient at higher bleeding risk.

A patient at higher bleeding risk is assessed by having 3 or more of the following risk factors:-

- age > 65 years
- previous history bleed or predisposition to bleeding (e.g. diverticulitis)
- uncontrolled hypertension
- severe renal impairment (i.e. serum creatinine > 200µmol/L, GFR < 30 mL/min/1.73 m<sup>2</sup> or on dialysis)
- acute hepatic impairment (e.g. bilirubin > 2x ULN + LFTS > 3x ULN), chronic liver disease (e.g. cirrhosis)
- low platelet count < 80 x 10<sup>9</sup>/L or a thrombocytopenia or anaemia of unknown cause
- on concomitant drugs associated with an increased bleeding risk e.g. SSRIs, oral steroids, NSAIDs, methotrexate or other immune-suppressant agents.

**N.B.** A risk of falls is not a contraindication to initiating oral anticoagulation, (e.g. a patient with an annual stroke risk of 5% (CHADS<sub>2</sub> score 2-3) would need to fall 205 times for fall risk to outweigh stroke reduction benefit of warfarin).

- Dementia or marked cognitive impairment with poor medicines compliance & no access to carer support.
- Chronic alcohol abuse - especially if associated with binge drinking.

**N.B.** Poor compliance with any oral anticoagulant agent will reduce benefits and may increase risks associated with use.

## Contraindications to the Initiation of Oral Anticoagulant & Anti-Platelet Therapy for Atrial Fibrillation in Primary Care - Supporting Information & Acknowledgements.

### Summary

The aim of this document is to give GPs a pragmatic decision guide on the absolute and relative contraindications to oral anticoagulants and anti-platelet agents in AF management in primary care. The information given has been drawn from "expert clinical opinion" together with established documented clinical evidence where available.

The key message is that although aspirin or aspirin/clopidogrel combinations may be chosen in preference to oral anticoagulants to reduce stroke risk in AF, the contraindications to using anti-platelet agents almost mirror those of oral anticoagulants. In addition the reduction in stroke risk in AF conferred by antiplatelets has never been shown to be as effective as oral anticoagulants.

### Key Supporting References

- European Society of Cardiology (ESC) Guidelines for the management of atrial fibrillation. Eur Heart J. Aug 29 2010. <http://www.escardio.org/Guidelines-surveys/escardio-guidelines/GuidelinesDocuments/guidelines-af-ff.pdf>
  - > Recommendation that selection of anti-thrombotic therapy should be based upon the absolute risks of stroke, thrombo-embolism and bleeding and the relative risk and benefit for a given patient. Highlights the use of the 'HAS-BLED' bleeding risk score as a tool to assess bleeding risk in AF patients.
- Keeling D, Baglin T et al; Guidelines on oral anticoagulation with warfarin - 4<sup>th</sup> Ed 2011; British Journal of Haematology 136:5-2141. [http://www.bshguidelines.com/documents/warfarin\\_4th\\_ed.pdf](http://www.bshguidelines.com/documents/warfarin_4th_ed.pdf)
  - > Latest updated BSH guidance - includes statement re concomitant use of anticoagulants & anti-platelets
- Mant J, Hobbs FDR, et al, Warfarin versus aspirin for stroke prevention in an elderly community population with atrial fibrillation (AF): (BAFTA RCT study). Lancet. 2007;370: 493-503.
  - > BAFTA study showed clear superiority of warfarin over aspirin with no increase in risk of major haemorrhage. Mean age of population was 81.5 years.
- Bailey RD, Hart RG, Benevento O, Pearce LA. Recurrent brain hemorrhage is more frequent than ischemic stroke after intracranial hemorrhage. Neurology 2001;56:773-7.
  - > Recurrent stroke among survivors of primary intracranial hemorrhage (ICH) occurs at a rate of about 4% per patient year and most are recurrent ICH. Survivors of ICH likely to have a higher risk of recurrent ICH than of ischemic stroke with CHADS<sub>2</sub> score < 3 [Adjusted annual stroke rate risk with CHADS<sub>2</sub> score 3 is 3.9%]
- Man-Son Hing M, Nichol G, Lu A, Laupeis A. Choosing antithrombotic therapy for elderly patients with atrial fibrillation who are at risk of falls. Arch Intern Med 1999; 159: 677-83.
  - > Showed a calculated risk of a subdural haemorrhage from falling in patients with annual stroke risk 3% would require a patient to fall 293 times for falls risk to outweigh stroke reduction benefit of warfarin.
- The ACTIVE Writing Group on behalf of the ACTIVE Investigators. Lancet 2006;367:1903-12
  - > Study found incidence of bleeding was significantly greater with aspirin + clopidogrel compared with warfarin (19.3% vs. 16.3%; NH 33; RR=1.21, 95% CI 1.08-1.35, P=0.001).
- Wehinger C, Stollberger C, Lammer T et al. Evaluation of risk factors for stroke/embolism & of complications due to anticoagulant therapy in atrial fibrillation. Stroke 2001;32(10):2246-2252
  - > Study found significant difference in bleeding complications between those patients prescribed at least three additional medicines & those prescribed less than three.
- Shireman TI, Howard PA, Kresowik TF et al. Combined anticoagulant-antiplatelet use and major bleeding events in elderly atrial fibrillation patients. Stroke.2004;35(10):2362-2367.
  - > Found history of bleeding to be a significant independent predictor of future bleeding events.
- PROGRESS Collaborative Group. RCT of a perindopril-based BP-lowering regimen among 6,103 individuals with previous stroke or transient ischaemic attack. Lancet. 2001 Sep 29;358(9287):1033-41
  - > study showed importance of BP control in patients with cerebrovascular disease in significantly lowering risk of first ICH
- Laupeis A, Boysen G, Connolly S et al. Risk factors for stroke & efficacy of antithrombotic therapy in AF: analysis of pooled data from five randomized controlled trials. Archives of Internal Medicine. 1994;154(13):1449-1457.
  - > Study found both systolic and diastolic BP to be significantly higher in those patients with bleeding complications than in those without bleeding complications.
- Dite PD, Labrecque D et al. World Gastroenterology Organisation Practice Guideline Oesophageal Varices 2008.
  - > Oesophageal varices develop in patients with cirrhosis at an annual rate of 3-6%, but varices large enough to pose a risk of bleeding occur in only 1-2% of cases. Approx 4-30% of pts with small varices will develop large varices each year & therefore be at risk of bleeding. Mortality resulting from bleeding depends on the severity of the underlying liver disease.
- UK Teratology Information/Toxicology database report on use of Warfarin in Pregnancy. National Poisons Information service commissioned by HPA. March 2011 <http://www.toxbase.org>
- Summary Product Characteristics for Marevan (warfarin) Pradaxa (Dabigatran); Plavix (Clopidogrel). Electronic Medicines Compendium @ <http://www.medicines.org.uk>

### Acknowledgements

This document was written in collaboration with Dr Matthew Fay, GP & NHS Heart Improvement Clinical Lead and Dr Paul Guyler, Lead Stroke Consultant Southend University Hospital NHS Foundation Trust and Stroke Improvement Program Associate, with contributions received from various clinical healthcare professionals in cardiology, neurology, haematology and gastroenterology.

# Absolute Contraindications (CI)

- **Known large oesophageal varices**
- **Decompensated liver disease /deranged baseline clotting screen (INR>1.5)** – refer to *Gastroenterology /Hepatology*. CI applies to OACs only
- **Within 72 hours of major surgery with risk of severe bleeding** defer & reassess risk postoperatively.
- **Acute clinically significant bleed**  
- defer & re-assess stroke versus bleeding risk within 3 months.
- **Significant thrombocytopenia (platelet count < 50 x 10<sup>9</sup>/L)** refer to haematologist.
- **Severe renal impairment (GFR < 30 mL/min/1.73 m<sup>2</sup> or on dialysis).**  
CI applies to dabigatran only.
- **Pregnancy or within 48 hours post partum**  
- seek urgent haematological advice. CI applies to OACs only.
- **Previously documented hypersensitivity to drug or excipients** consider cardiology opinion.

# CI Liver Disease & Oesophageal Varices – World Gastroenterology Org Practice Guideline 2008

- Variceal bleeds account for 30% of all upper GI bleeds
- Bleeding associated with high mortality rate
- Oesophageal varices develop in patients with cirrhosis at annual rate of 5-8%
- 4-30% pts with small varices develop large varices each year
- At time of diagnosis 30% of cirrhotic patients have varices, reaching 90% after approx 10 years
- INR > 1.5 predictive indicator for likelihood of varices to be present in cirrhosis

# Absolute Contraindication - Pregnancy

- Good evidence from UK Teratology Service
- All VKAs contraindicated. No data with newer OACs
- Fetal warfarin syndrome well recognised complication following exposure during pregnancy
- Critical period gestational weeks 6-12
- Advice from Royal College Obstetricians & Gynaecologists

**To use LMWH duration of pregnancy & for at least 6 weeks post partum**

# Relative Contraindications

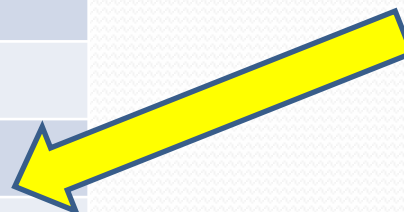
- **Previous history intracranial haemorrhage**
- **Recent major extracranial bleed within the last 6 months where cause has not been identified or treated**
- **Recent history recurrent iatrogenic falls in patient at higher bleeding risk.**
- **Dementia or marked cognitive impairment with poor medicines compliance & no access to carer support.**
- **Recent documented peptic ulcer (PU) within last 3 months**
- **Chronic alcohol abuse**

# Risk of Ischaemic Stroke versus ICH

Absolute stroke rate in AF depends on age & co-morbid conditions

Pop<sup>n</sup> based studies of survivors of a 1<sup>st</sup> ICH have identified rates of recurrent ICH of 2.1 to 3.7% per patient year

CHADS <sub>2</sub> Score	Adjusted Annual Stroke Rate (%) <sup>*</sup> (95% CI)	Number Needed to Treat (NNT)
0	1.9	53
1	2.8	36
2	4.0	25
3	5.9	17
4	8.5	12
5	12.5	8
6	18.3	5



<sup>\*</sup>Adapted from Gage BF et al. JAMA 285: 2864-2870

# BAFTA STUDY

## Risk of primary event & Major Haemorrhage by Tx Allocation

Primary Event	Warfarin		Aspirin		W vs A
	N	Risk /yr	N	Risk/yr	
Death					RR (95%CI)
All causes	107	8.0%	108	8.4%	0.73 (p=0.73)
All strokes	33	2.5%	61	4.9%	0.52 (p=0.002)
<b>All major haemorrhages</b>	25	1.9%	25	2.0%	0.96 (p=0.9)
Primary events + major haem	39	3.0%	64	5.1%	0.59 (p=0.008)

# Active A & Active W Trials

	ACTIVE-A		ACTIVE-W	
	Aspirin (n=3,782)	A + C (n=3,772)	A + C (n=3,335)	Warfarin (n=3,371)
Total strokes (%/yr)	3.3	2.4	2.4	1.4
Disabling & fatal strokes (%/yr)	2.1	1.6	1.7	1.3
Major bleeding (%/yr)	1.3	2.0	2.4	2.2
Net clinical benefit	-	+	+	++

## **Bleeding Risk In Patients with Hx Falls**

***A risk of falls is not a contra-indication to OACs***

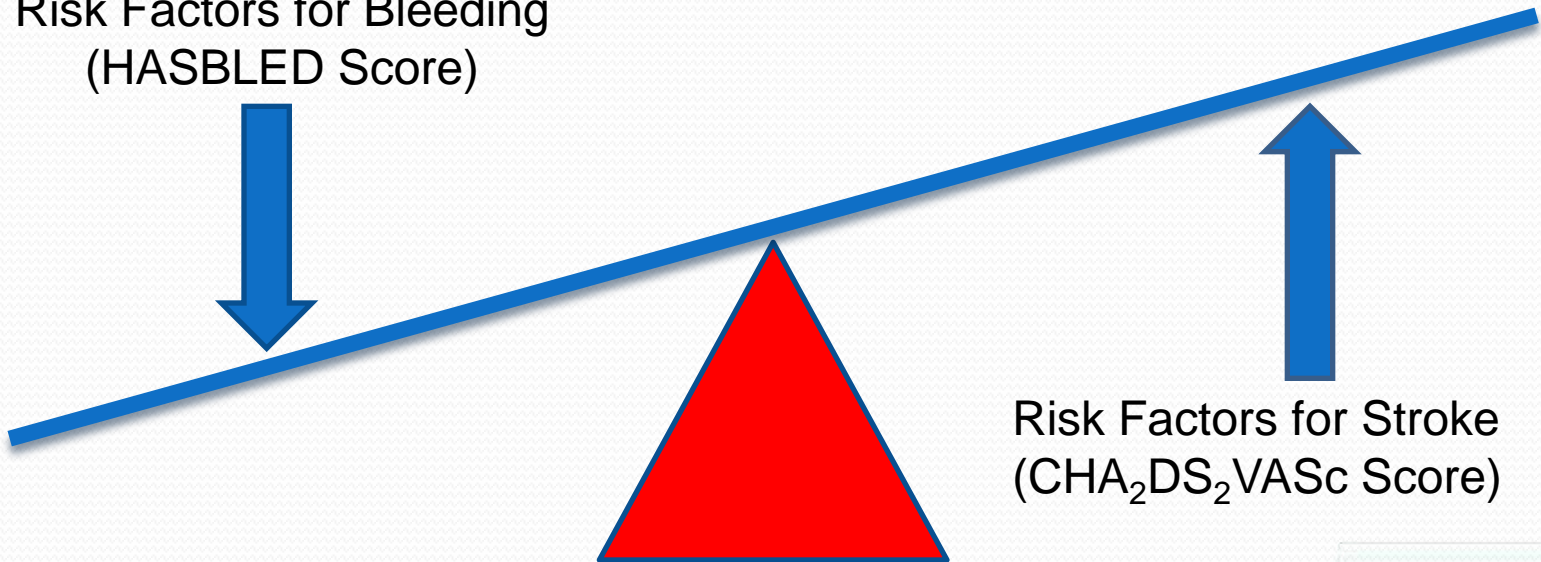
### ***Factors associated with increased bleeding risk-***

- *age > 65 years*
- *previous history bleed or predisposition to bleeding*
- *uncontrolled hypertension*
- *severe renal impairment*
- *acute hepatic impairment*
- *low platelet count <  $80 \times 10^9/L$  or a thrombocytopenia or anaemia of undiagnosed cause*
- *on concomitant drugs associated with an increased bleeding risk*

# KEY MESSAGES

- Contraindications to OACs apply to both newer OACs & anti-platelets
- Anti-thrombotic therapy should be based on absolute risks stroke and bleeding and relative risk and benefit for a given patient with AF
- Essential that all AF patients are reviewed at **LEAST** annually to assess stroke versus bleeding risk & HENCE anti-thrombotic treatment of choice.

Risk Factors for Bleeding  
(HASBLED Score)



Risk Factors for Stroke  
(CHA<sub>2</sub>DS<sub>2</sub>VASc Score)

# What Next

- Delivering the messages in promotion decision support tool – part of education package
- Work continued collaboration across primary & secondary care interface
- Assess impact on anticoagulation services delivery & potential introduction newer oral anti-thrombotics



**DESIRED OUTCOME**

**Changes in prescribing practice → fewer strokes !**

# Acknowledgements

Document produced in collaboration with

- Dr Matthew Fay GP& NHS Heart Improvement Clinical Lead
- Dr Paul Guyler Lead Stroke Consultant Southend University Hospital NHS Foundation Trusts & Stroke Improvement Programme Association

Endorsed by Atrial Fibrillation Association (AFA).

Available to download on AFA website

<http://www.atrialfibrillation.org.uk/medical-professionals/articles-submitted.html>