The importance of anticoagulation?

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Declaration of Interest

Received honararia from Boehringer Ingelheim, pfizer, Bayer, Daiichi Sankyo

Case history

- Mrs RC
- 76 year old lady reviewed in hypertension
- known AF
- Drug history
  - Amlodipine 10mg
  - Losartan 25mg daily
  - Simvastatin 20mg daily
  - **Aspirin 75mg daily**

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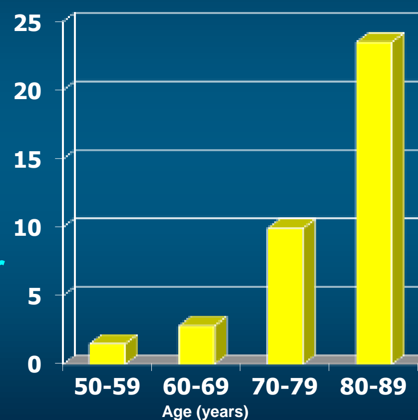
AF and stroke risk

- AF is the leading cause of embolic stroke
- Risk increases with ⇑ age
- **Without preventive treatment, approximately 1 in 20 patients (5%) with AF will have a stroke each year**
- AF related strokes are associated with higher mortality and more disability

% of strokes attributable to AF



Kannel WB et al. *Am J Cardiol* 1998; 82 (8A): 2N–9N.

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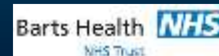
Think of a patient……. (1)

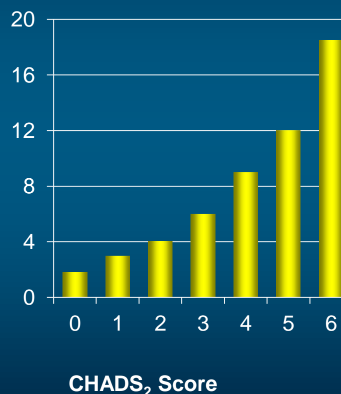
- 76 year old female
- Irregular pulse → AF confirmed on ECG
- Relevant PMH
  - Hypertension
- ***How do we know if she is at risk….?***



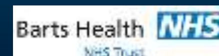
Atrial Fibrillation

Stratification of Stroke Risk: $CHADS_2$ Score

	Score
CHF or LV dysfunction	1
Hypertension	1
Age > 75 years	1
Diabetes	1
Stroke/TIA	2



Gage BF et al. JAMA 2001;285: 2864–2870



CHA_2DS_2-VASc

- Congestive heart failure/ LV dysfunction 1
- Hypertension 1
- Age ≥ 75 2
- Diabetes mellitus 1
- Stroke/TIA/TE 2
- Vascular disease (CAD, CArD, PAD) 1
- Age 65-74 1
- Sex category (female) 1

Score 0 – 9

Score	Annual stroke rate, %
0	0
1	1.3
2	2.2
3	3.2
4	4.0
5	6.7
6	9.8
7	9.6
8	6.7
9	15.2

Validated in 1084 NVAF patients not on OAC with known TE status at 1 year in Euro Heart Survey

OR for stroke if: Female: 2.53 (1.08 – 5.92), p=0.029; Vascular disease: 2.27 (0.94 – 5.46), p=0.063

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Approach to thromboprophylaxis in AF

Risk category	CHA_2DS_2-VASc score	Recommended antithrombotic therapy
One 'major' risk factor or ≥ 2 'clinically relevant non-major' risk factors	≥ 2	OAC
One 'clinically relevant non-major' risk factor	1	Either OAC or aspirin 75-325 mg daily. Preferred: OAC rather than aspirin.
No risk factors	0	Either aspirin 75-325 mg daily or no antithrombotic therapy. Preferred: no antithrombotic therapy rather than aspirin.

AF = atrial fibrillation; CHA_2DS_2-VASc = cardiac failure, hypertension, age ≥ 75 (doubled), diabetes, stroke (doubled)-vascular disease, age 65–74 and sex category (female); INR = international normalized ratio; OAC = oral anticoagulation, such as a vitamin K antagonist (VKA) adjusted to an intensity range of INR 2.0–3.0 (target 2.5).

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For our patient……

CHADS2 Score for Atrial Fibrillation Stroke Risk

Congestive Heart Failure history? ☐ Yes +1

Hypertension history? ☑ Yes +1

Anticoagulate!

The adjusted stroke rate was the expected stroke rate per 100 person-years derived from the multivariable model assuming that aspirin was not taken.

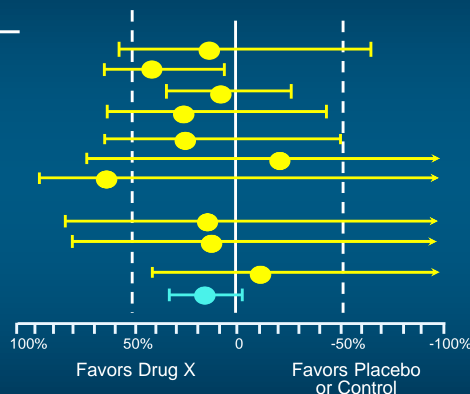
76 year old female with hypertension

Efficacy of drug X Compared With Placebo

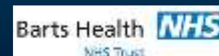
Drug X cf placebo/control

Study	Year
	1989; 1990
	1991
	1993
	1997
	1997
	1999
	2006

Relative Risk Reduction (95% CI)



Hart RG et al. *Ann Intern Med.* 2007;146:857-867

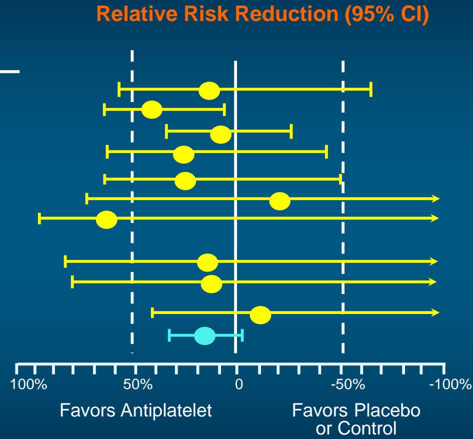


Efficacy of aspirin Compared With Placebo

Aspirin cf placebo/control

Study	Year
AFASAK I	1989; 1990
SPAF I	1991
EAFT	1993
ESPS II	1997
LASAF	1997
Daily	
Alternate day	
UK-TIA	1999
300 mg daily	
1200 mg daily	
JAST	2006
Aspirin trials *(n=7)*	

Relative Risk Reduction (95% CI)



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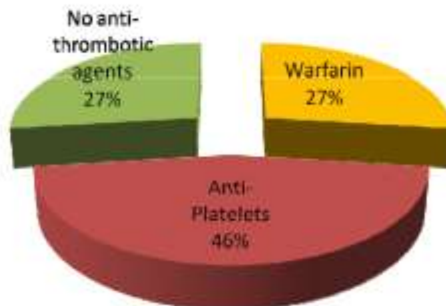
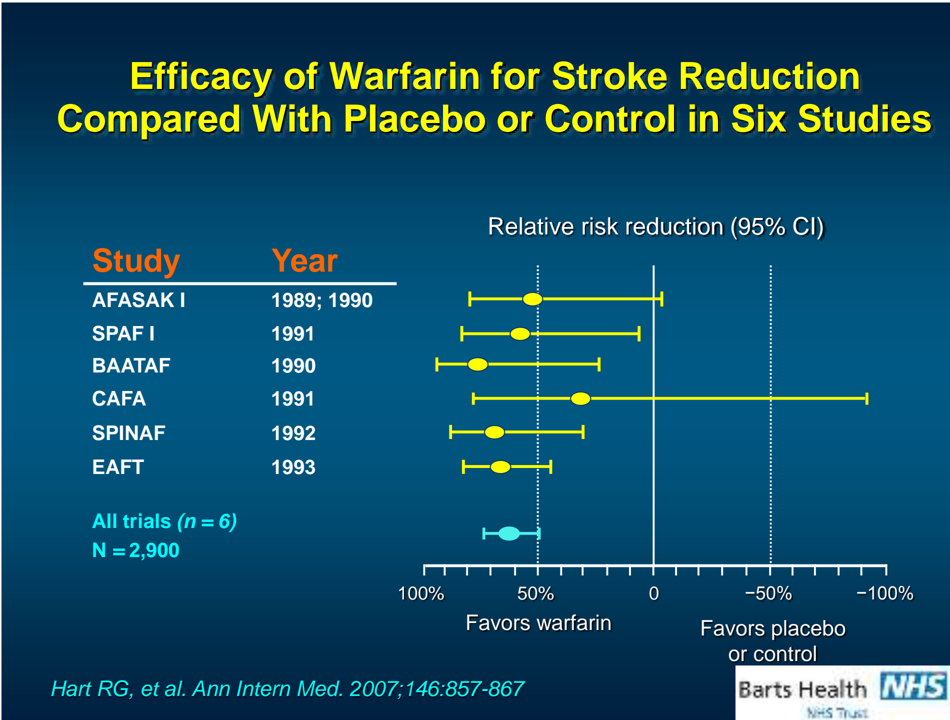
StrokeImprovement

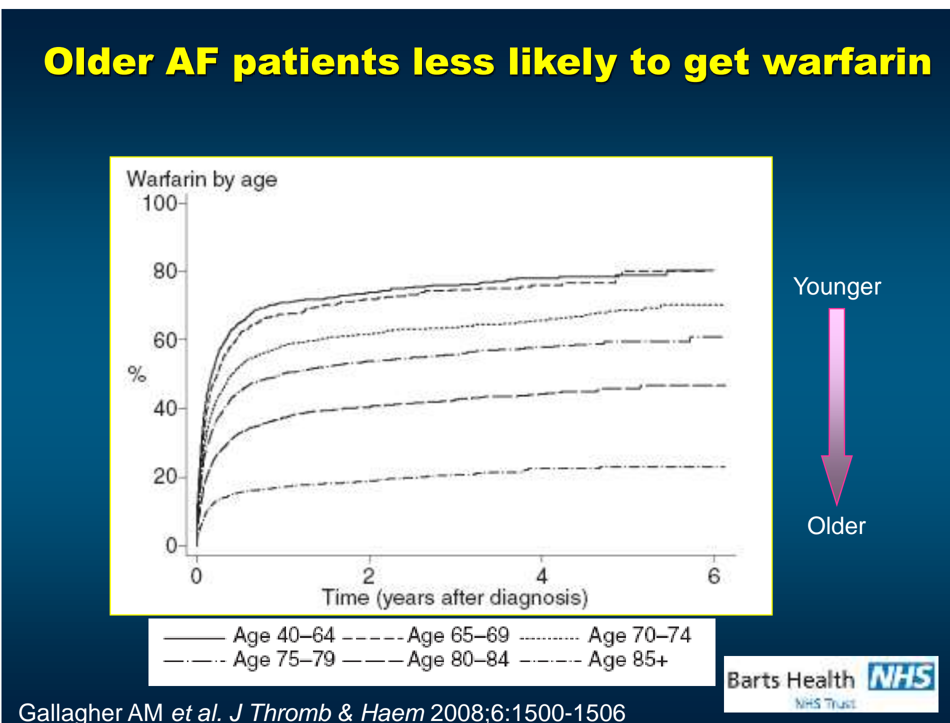
NHS Improvement NHS

RESULTS

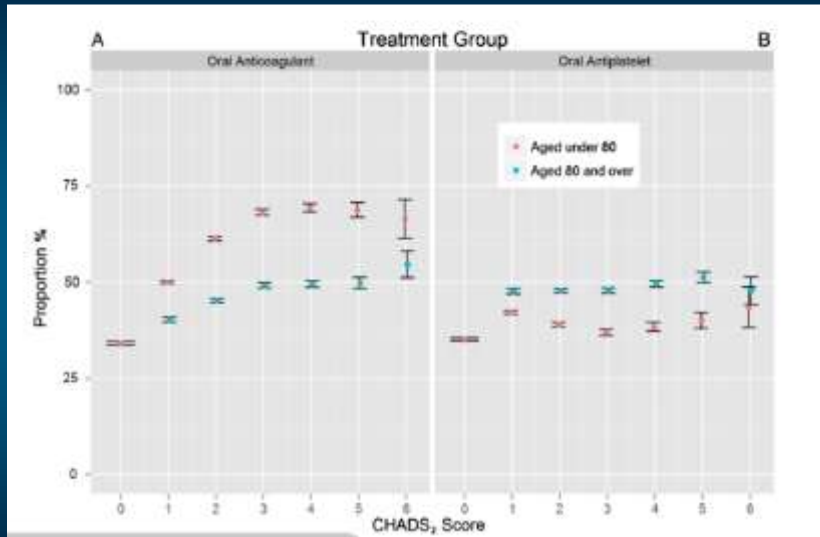
High risk patients with no contra-indication to warfarin : (n=131)




Efficacy of Warfarin for Stroke Reduction Compared With Placebo or Control in Six Studies
Relative risk reduction (95% CI)
Study
Year
AFASAK I
1989; 1990
SPAF I
1991
BAATAF
1990
CAFA
1991
SPINAF
1992
EAFT
1993
All trials (n = 6)
N = 2,900
100%
50%
0
−50%
−100%
Favors warfarin
Favors placebo or control
Hart RG, et al. Ann Intern Med. 2007;146:857-867
Barts Health NHS


Older AF patients less likely to get warfarin
Warfarin by age
100
80
60
40
20
0
%
0
2
4
6
Time (years after diagnosis)
Age 40–64
Age 65–69
Age 70–74
Age 75–79
Age 80–84
Age 85+
Younger
Older
Gallagher AM et al. J Thromb & Haem 2008;6:1500-1506
Barts Health NHS

Older AF patients less likely to get warfarin



Cowan C, et al Heart 2013;0:1-7

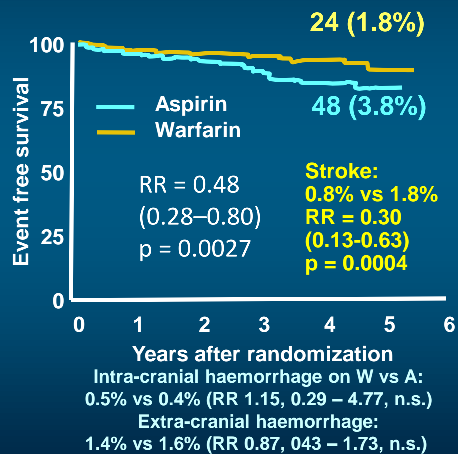
BAFTA:

Birmingham Atrial Fibrillation Treatment of the Aged

- 2001-2004; 260 GPs in England and Wales
- 973 pts ≥ 75 years (81.5 ± 4.2)
- 72% $CHADS_2 \leq 2$
- Warfarin (target INR 2–3) or aspirin (75 mg per day)
- 1^0 endpoint - fatal or disabling stroke (ischaemic or haemo-rrhagic), other intracranial haemorrhage, or clinically significant arterial embolism

INR > 3.0 14% of the time

Mant J, et al. Lancet 2007;370:493-503

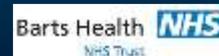


Intra-cranial haemorrhage on W vs A:
0.5% vs 0.4% (RR 1.15, 0.29 – 4.77, n.s.)
Extra-cranial haemorrhage:
1.4% vs 1.6% (RR 0.87, 043 – 1.73, n.s.)

Falls

- Markov decision analytic model was used to determine the preferred treatment strategy in patients > 65 yrs/old
- Patients need to fall >295 times per year for risk to outweigh benefit
- Mean number of falls/ year of elderly people who fall: 1.8

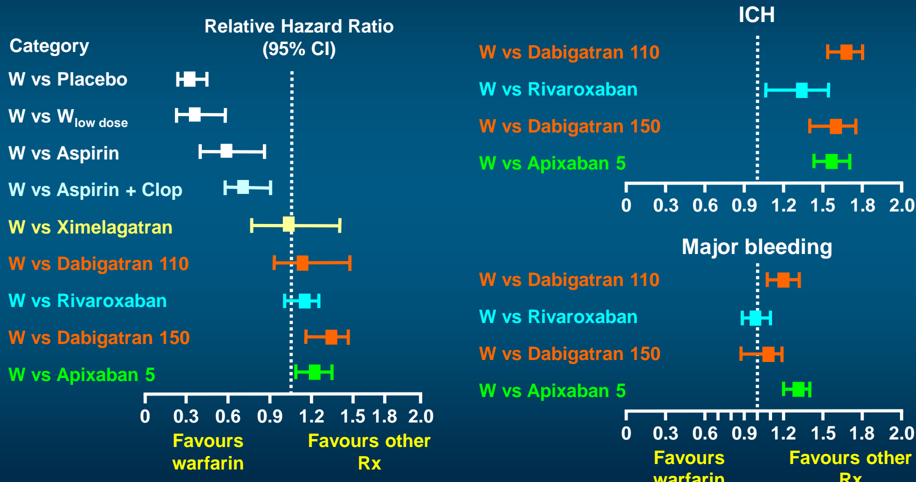
Man-Son-Hing et al *Arch Intern Med.* 1999;159:677-685



QIPP agenda

Provided by the Stroke Improvement Programme

- Atrial fibrillation – detection and optimal therapy in Primary care
  - Identifying new patients
  - Ensuring appropriate pathways
  - Appropriate assessment of anticoagulation
  - Cost of NOT prescribing anticoagulant
    - 46% who should be are not on warfarin
    - RRR with warfarin 50 – 70% ….. That's good!
    - 4500 strokes and 3000 deaths could be prevented if anticoagulated
    - Direct cost of strokes £3b (£8b indirect)



Stroke Prevention: Anticoagulant Effect
Meta-analysis of stroke or systemic embolism
Category
Relative Hazard Ratio (95% CI)
W vs Placebo
W vs W low dose
W vs Aspirin
W vs Aspirin + Clop
W vs Ximelagatran
W vs Dabigatran 110
W vs Rivaroxaban
W vs Dabigatran 150
W vs Apixaban 5
0 0.3 0.6 0.9 1.2 1.5 1.8 2.0
Favours warfarin
Favours other Rx
Modified from Camm AJ. EHJ 2009;30:2554-5
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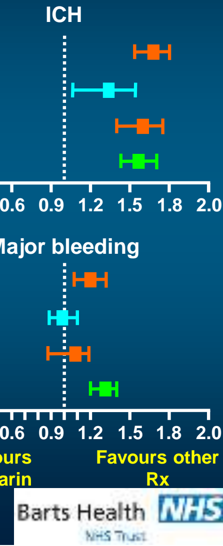

ICH
W vs Dabigatran 110
W vs Rivaroxaban
W vs Dabigatran 150
W vs Apixaban 5
0 0.3 0.6 0.9 1.2 1.5 1.8 2.0
Major bleeding
W vs Dabigatran 110
W vs Rivaroxaban
W vs Dabigatran 150
W vs Apixaban 5
0 0.3 0.6 0.9 1.2 1.5 1.8 2.0
Favours warfarin
Favours other Rx

Case history

- Mrs RC
- 76 year old lady reviewed in hypertension
- known AF
- Drug history
  - Amlodipine 10mg
  - Losartan 25mg daily
  - Simvastatin 20mg daily
  - **Aspirin 75mg daily**

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Case history

- Mrs RC
- Previously been on warfarin but felt that in view of poor TIR, warfarin was not suitable

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Case history

- Mrs RC
- Previously been on warfarin but felt that in view of poor TIR, warfarin was not suitable
- Referred to haematology
  - CrCl 30mls/min
  - Rivaroxaban 15mg daily
  - How would we counsel this lady?

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Rivaroxaban patient counselling checklist

- **Indication for anticoagulation**
  - Explanation of AF, risk of stroke
- **Name of drug**
  - Rivaroxaban (Xarelto® is trade name)
- **Give rivaroxaban information leaflet**
- **Action of rivaroxaban**
  - Makes blood less sticky, takes longer to clot
- **Difference with warfarin (if applicable)**
  - No INR monitoring; unable to monitor anticoagulant effect
  - Same dose to be taken once each day
- **Dosing**
  - Take specified dose once each day
  - Swallow whole with water, do not open capsule
  - Must be taken with food
  - Same time every day
  - Action on missed dose: take as soon as you remember, within 12 hours, do not double up
- **Importance of concordance**
  - Unable to monitor anticoagulant effect
  - Implications of poor concordance: increased risk of stroke
  - Implications of overdose: increased risk of bleed
  - If problems with remembering to take, discuss with GP

- **Bleeding/Unexplained bruising**
  - Mild, self-terminating episodes to be expected due to nature of medicine (similar to warfarin)
  - Regular or excessive ongoing bleeding go to A&E, inform of symptoms and that rivaroxaban being taken
- **Other side effects**
  - Likely to experience dizziness, weakness and gastro upset
  - Report side effects to MHRA via Yellow card/website
- **Concomitant Medicines**
  - Avoid long-term use of NSAIDs
  - Check with GP/pharmacist before starting any new medicines
- **Alert card**
  - Keep with you at all times e.g. in wallet
  - Show to healthcare professionals
- **Pregnancy and Breastfeeding**
  - Avoid
- **Contact Sports (e.g. boxing, rugby, football)**
  - Avoid (risk of internal bleeding)
- **Inform all healthcare professionals**
  - Inform hospital doctors, pharmacists, dentists etc. prior to any treatment
  - Surgical interventions can increase risk of bleeding, request GP to seek specialist advice
- **Repeat Prescriptions, Follow up appointments**
  - Initiated in hospital, will be given full supply for trial purposes
  - Ensure do not run out of medicine

Signature of Patient (or representative or advocate).. date...............

Patient or advocate name..

Signature of BLT practitioner: ....date.................

Name of practitioner and designation ....

- How would the counselling differ if prescribed dabigatran?

Counselling

- Reduces the chance of unwanted blood clots forming which helps prevent strokes
- Take regularly ,
  - any time is ok – when would be easiest for you
  - Warfarin – evening to coincide with INR test
  - Forgotten doses
    - W – if before midnight
    - D – if within 6 hrs of next dose (miss)
    - R/A – take immediately, do not double within the same day
- Like all medicines – unwanted side effects
  - If unusual bleeding, such as dark or bloody stools, urine or unexplained bruising tell your doctors
  - NSAIDs can't be taken with anticoagulants
  - Specifics Dabigatran – Indigestion

NHS
National Patient Safety Agency

Oral
Anticoagulan
Therapy
Important information
for patients

Patient Card

Xarelto

NHS
National Patient Safety Agency

Oral
Anticoagulan
Therapy
Important information
for patients

Patient Card

Xarelto

PATIENT
ALERT CARD

Xarelto® 15mg
Xarelto® 20mg

- KEEP THIS CARD WITH YOU AT ALL TIMES
- PRESENT THIS CARD TO EVERY PHYSICIAN OR DENTIST PRIOR TO TREATMENT

National Patient Safety Agency

Oral
Anticoagulan
Therapy
Important information
for patients

PATIENT
ALE

Patient Card

Xarelto

PRADAXA®
PATIENT ALERT CARD

National Patient Safety Agency

Oral
Anticoagulan
Therapy
Important information
for patients

PATIENT
ALE

Patient Card

Xarelto

PRADAXA®
PATIENT ALERT CARD

Important patient instructions

Take your drug exactly as prescribed (once or twice daily).
No drug is no protection!

Never stop your medicine without consulting your physician.

Never add any other medication without consulting your physician, not even short-term painkillers that you can get without prescription.

Alert your dentist, surgeon or other physician before an intervention.

Concomitant medication

Name:	Dose:

Emergency information

Standard tests do no quantitatively reflect level of anticoagulation!

Name & telephone of patient relative to contact if emergency:

Patient blood group (+ physician signature):

Atrial Fibrillation
Oral Anticoagulation Card

for non-vitamin-K anticoagulants

Patient name: DOB:

Patient address:

Oral anticoagulant, dosing, timing, with or without food:

Treatment indication:

Treatment started:

Name and address of anticoagulant prescriber:

Telephone number of prescriber or clinic:

More info:
www.NOACforAF.eu
www.noacforaf.eu

Planned or unplanned visits

Date (or date range):	Site (GP; clinic; cardiologist; ...):	To do / findings:

Recommended follow-up

(see EHRA at www.NOACforAF.eu for information & practical advice)

Check each visit:
1. Compliance (pt. should bring remaining meds)?
2. Thrombo-embolic events?
3. Bleeding events?
4. Other side effects?
5. Co-medications and over-the-counter drugs.

Blood sampling:
- monitoring of anticoagulation level is not required!
- yearly: Hb, renal and liver function
- if CrCl 30-60 ml/min, >75y, or fragile: 6-monthly renal function
- if CrCl 15-30 ml/min: 3-monthly renal function
- if intercurring condition that may have impact: renal and/or liver function

Date	Serum creatinine	Creatinine clearance	Hemo-globin	Liver tests

Reducing Risk of Bleeding

1. **Address uncontrolled hypertension**
2. **Review benefit/risk of concomitant aspirin**:
   - Hypertensives, diabetics, CHD and no acute ischemic event or intervention in the last year
   - **Stop aspirin when INR in therapeutic range**
3. **Risk of bleeding is greatest in first 90 days of OAC therapy**
   - Caution : drug interactions and new drugs
   - Close or more frequent monitoring
4. **Review concomitant use of NSAIDS**
5. **Consider a PPI**

Hylek, E.M., Evans-Molina, C, Shea, C. et al. (2007), Major hemorrhage and tolerability of warfarin in the first year of therapy among elderly patients with atrial fibrillation, Circulation, 115, 2689-2696.