



NOACs in the Hospital and Inter-professional Communication

Bayer Workshop 1

21st EAHP Congress 2016, Vienna, Austria

Wednesday 16 March, 16:15–17:45

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Which James Bond film uses Prater Park as its location?



Welcome and Introduction

Sotiris Antoniou, FRPharmS
Consultant Pharmacist, Cardiovascular, UK

 @santon74

sotiris.antoniou@bartshealth.nhs.uk

NOACs in the Hospital and Inter-professional Communication: Agenda

Time	Session title	Presenter/moderator
16:15–16:20	Welcome to the workshop and introduction of the expert faculty	Sotiris Antoniou (UK)
16:20–16:30	Challenges for hospital pharmacists in antithrombotic care: Real-world evidence matters – an overview	Sotiris Antoniou
16:30–16:45	Inter-professional communication matters – the role of pharmacists in multidisciplinary teams, patient pathways and responsible use of NOACs	Rodney Hughes (UK)/ Jannat Muen (UK)
16:45–16:50	Introduction to the Interactive Group Session	Trevor Nicholls (moderator)
16:50–17:10	Interactive scenario 1: Implementing a multidisciplinary team for managing anticoagulation services	Rodney Hughes/ Jannat Muen
17:10–17:30	Interactive scenario 2: Rationalisation of NOAC use in the hospital, using rivaroxaban as an example	Rodney Hughes/ Jannat Muen
17:30–17:40	Presentations by the Interactive Group Session winners and panel discussion	Sotiris Antoniou
17:40–17:45	Summary	Sotiris Antoniou



Challenges for Hospital Pharmacists in Antithrombotic Care Real-World Evidence Matters: An Overview

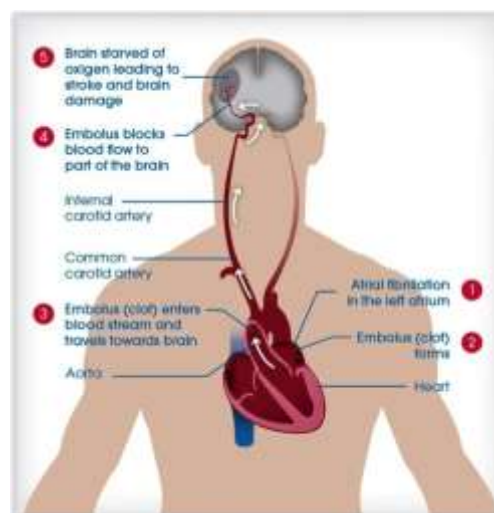
Sotiris Antoniou, FRPharmS
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Disclosures

- ◆ Received honoraria, speaker fees/research fees
 - Bayer, Boehringer, Pfizer/BMS, Daiichi Sankyo
- ◆ Chair of DRM Foundation/iPACT (international Pharmacist Anticoagulation Care Taskforce)
- ◆ Medical advisory board for Atrial Fibrillation Association

How AF Leads to Stroke



Stroke and AF. <http://www.strokeandaf.ca/af-you/af-stroke/> [accessed Oct 2015]

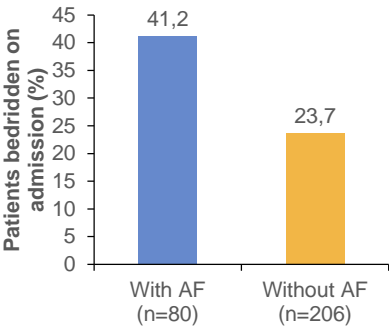
The Impact of AF on Stroke Outcomes

Survival rates are poorer, stroke recurrence rates are higher and functional outcomes are worse following AF-related stroke

◆ Framingham study (10-year follow-up from 1981)¹

	AF patients, % (n=30)	Non-AF patients, % (n=120)
1-year post-stroke recurrence	23	8
30-day post-stroke mortality	30	17
1-year post-stroke mortality	63	34

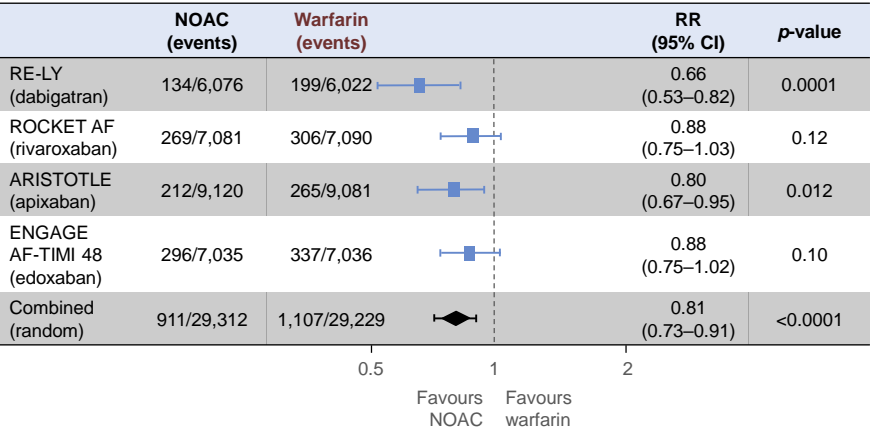
◆ Functional outcomes of stroke are worse in patients with AF²
OR=2.23 (95% CI 1.87–2.59); *p*<0.0005



1. Lin HJ *et al*, *Stroke* 1996;27:1760–1764; 2. Dulli DA *et al*, *Neuroepidemiology* 2003;22:118–123

Comparing Phase III Trials: Results are Consistent for Reduction in Stroke/SE

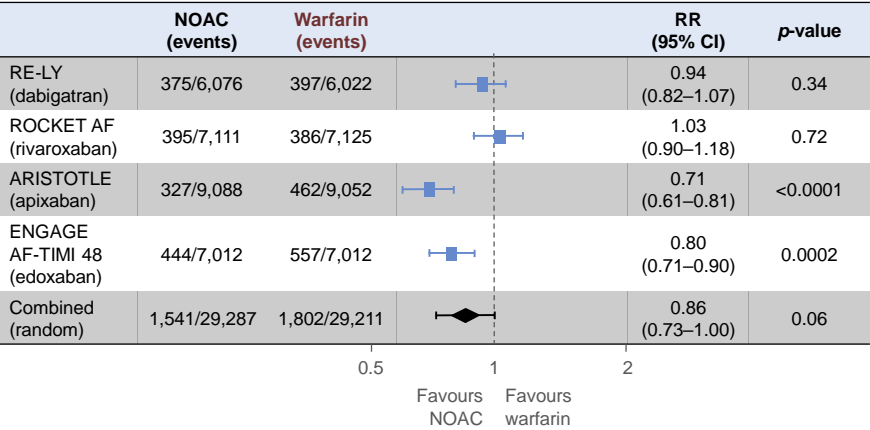
Meta-analysis of four phase III trials: stroke/SE



Heterogeneity: I²=47%; *p*=0.13
Different risk profiles
Ruff CT *et al*, *Lancet*. 2014;383(9921):955–962.

Comparing Phase III Trials: Results are Consistent for Major Bleeding

Meta-analysis of four phase III trials: major bleeding events



Heterogeneity: I²=83%; p=0.001
Different risk profiles
Ruff CT *et al. Lancet.* 2014;383(9921):955–962.

“After the Deluge” of SPAF Trials

Clinical trial

- ◆ Selected patients
- ◆ Strict inclusion and exclusion criteria
- ◆ Fixed dose options
- ◆ Strict study protocol



Real world

- ◆ Unselected patients (“all-comers”!)
- ◆ Relevant co-morbidities present
- ◆ Dose recommendations only
- ◆ Over- and under-reporting of events



“How does the evidence fit with the individual in front of me?”

Emergency Hospitalizations in the Pre-NOAC Era

Most commonly implicated medications	Annual national estimate of hospitalizations among older adults in the US, 2007–2009 (N=99,628)		Proportion of ED visits resulting in hospitalization
	n	% (95% CI)	%
Warfarin	33,171	33.3 (28.0–38.5)	46.2
Insulins	13,854	13.9 (9.8–18.0)	40.6
Oral antiplatelet agents	13,263	13.3 (7.5–19.1)	41.5
Oral hypoglycaemic agents	10,656	10.7 (8.1–13.3)	51.8
Opioid analgesics	4778	4.8 (3.5–6.1)	32.4
Antibiotics	4205	4.2 (2.9–5.5)	18.3
Digoxin	3465	3.5 (1.9–5.0)	80.5
Antineoplastic agents	3329	3.3 (0.9–5.8)	51.5
Antiadrenergic agents	2899	2.9 (2.1–3.7)	35.7
Renin-angiotensin inhibitors	2870	2.9 (1.7–4.1)	32.6
Sedative or hypnotic agents	2469	2.5 (1.6–3.3)	35.2
Anticonvulsants	1653	1.7 (0.9–2.4)	40.0
Diuretics	1071	1.1 (0.4–1.8)	42.4

Budnitz D et al, N Engl J Med 2011;365:2002–2012

Emergency Hospitalizations in the Pre-NOAC Era

Adverse events associated with haematological agents (not including non-VKA oral anticoagulants)	Annual national estimate of hospitalizations among older adults in the US, 2007–2009	Proportion of ED visits resulting in hospitalization
	% (95% CI)	%
Intracranial haemorrhage	5.6 (2.1–9.1)	99.7
Haemoptysis	2.0 (1.1–2.8)	73.6
Gastrointestinal haemorrhage	40.8 (29.9–51.7)	84.7
Genitourinary haemorrhage	4.7 (3.2–6.2)	42.4
Epistaxis	6.1 (4.3–8.0)	10.6
Skin or wound haemorrhage	6.8 (4.5–9.1)	24.5
Other type of haemorrhage	5.3 (2.7–8.0)	27.5
Elevated INR, abnormal laboratory values or drug toxicity not otherwise described	23.7 (16.8–30.6)	59.5

Budnitz D et al, N Engl J Med 2011;365:2002–2012

Pivotal Atrial Fibrillation Trials
Baseline Characteristics

	RE-LY (Dabigatran)	ARISTOTLE (Apixaban)	ENGAGE AF-TIMI 48 (Edoxaban)	ROCKET AF (Rivaroxaban)
Enrolled, N	18,113	18,201	21,105	14,264
Age, years	72±9*	70 (63–76) [†]	72 (64–78) [†]	73 (65–78) [†]
Female (%)	36	36	38	40
Mean CHADS ₂	2.1	2.1	2.8	3.5
CHADS ₂ ≥3 (%)	33	30	53	87
VKA naïve (%)	50	43	41	38
Paroxysmal AF (%)	33	15	25	18
Prior stroke/TIA (%)	20	19	28	55 [‡]
Diabetes (%)	23	25	36	40
Prior CHF (%)	32	36	57	63
Hypertension (%)	79	87	94	90

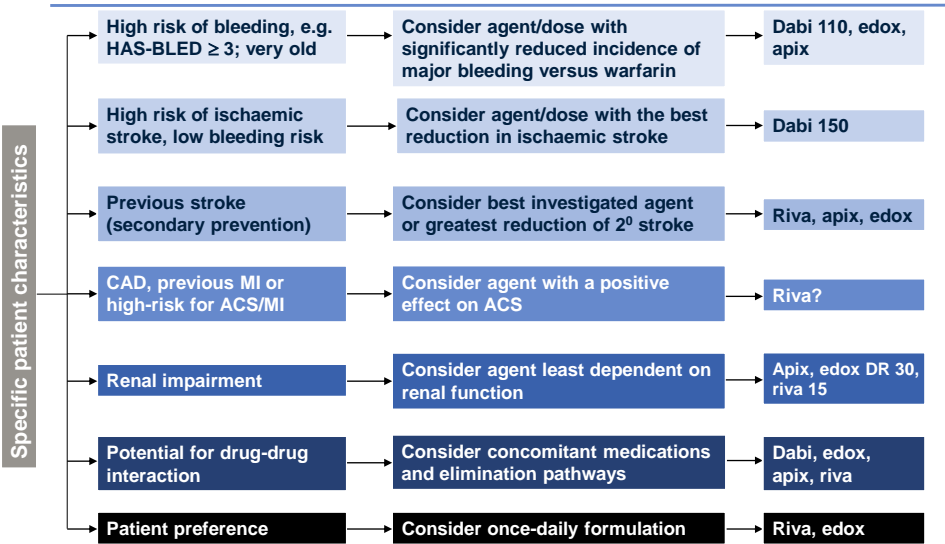
*Mean±standard deviation; [†]median (interquartile range); [‡]includes prior systemic embolism
Connolly SJ *et al*, *N Engl J Med* 2009;361:1139–1151; Patel MR *et al*, *N Engl J Med* 2011;365:883–891;
Granger CB *et al*, *N Engl J Med* 2011;365:981–992; Giugliano RP *et al*, *N Engl J Med* 2013;369:2093–2104;
Ruff CR *et al*, *Am Heart J* 2010;160:635–634; European Medicines Association (EMA), assessment report EMA/321083/2015

Pivotal Atrial Fibrillation Trials
Dose Comparison

	RE-LY (Dabigatran)	ARISTOTLE (Apixaban)	ENGAGE AF-TIMI 48 (Edoxaban)	ROCKET AF (Rivaroxaban)
Enrolled, N	18,113	18,201	21,105	14,264
Dose (mg)	150, 110	5	60, 30	20
Frequency	bid	bid	od	od
Initial dose adj*	No	5 → 2.5 mg	60 → 30 mg 30 → 15 mg	20 → 15 mg
Dose adj (%)	0	4.7	>25	21
Dose adj* after randomization	No	No	Yes	No
Design	PROBE	2 × blind	2 × blind	2 × blind

*Dose adjusted in patients with reduced drug clearance. PROBE = prospective, randomized, open-label, blinded end point evaluation
Connolly SJ *et al*, *N Engl J Med* 2009;361:1139–1151; Patel MR *et al*, *N Engl J Med* 2011;365:883–891;
Granger CB *et al*, *N Engl J Med* 2011;365:981–992; Giugliano RP *et al*, *N Engl J Med* 2013;369:2093–2104;
Fox KA *et al*, *Eur Heart J* 2011;32:2387–2394

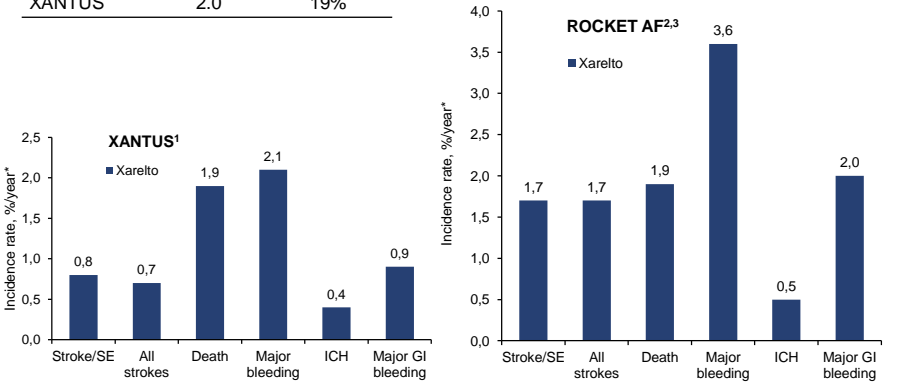
‘Pointers’* Towards Which NOAC to Choose



*All 'pointers' are debatable and direct comparisons between phase III clinical studies are not possible owing to differences in design/populations
Adapted from Savellieva I and Camm AJ. *Clin Cardiol* 2014;37:32–47 and Gonzalez-Quesada CJ and Giugliano RP. *Am J Cardiovasc Drugs* 2014;14:111–127

Comparison of Main Outcomes:
XANTUS versus ROCKET AF

	CHADS ₂	Prior stroke [#]
ROCKET AF	3.5	55%
XANTUS	2.0	19%

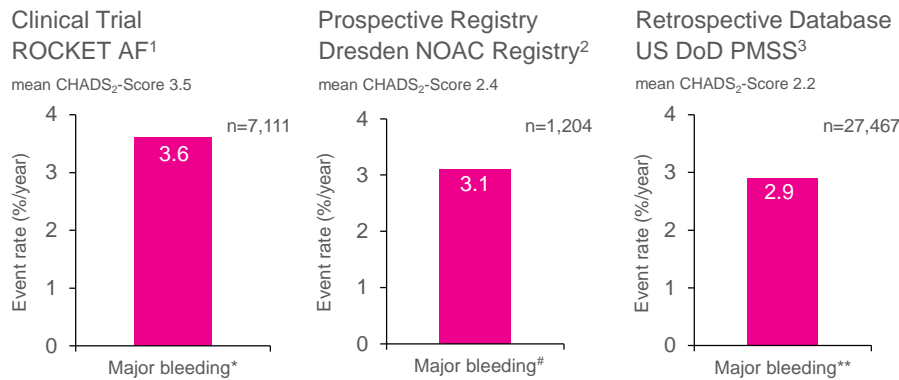


[#]Includes prior stroke, SE or TIA; *Events per 100 patient-years

1. Camm AJ et al, *Eur Heart J* 2015; doi: 10.1093/eurheartj/ehv466; 2. Patel MR et al, *N Engl J Med* 2011;365:883–891; 3. Sherwood MW et al. *J Am Coll Cardiol* 2015;66:2271–2281



Major Bleeding Rates with Rivaroxaban in Real World Studies were Consistent with Findings from ROCKET AF



Results are not intended for direct comparison

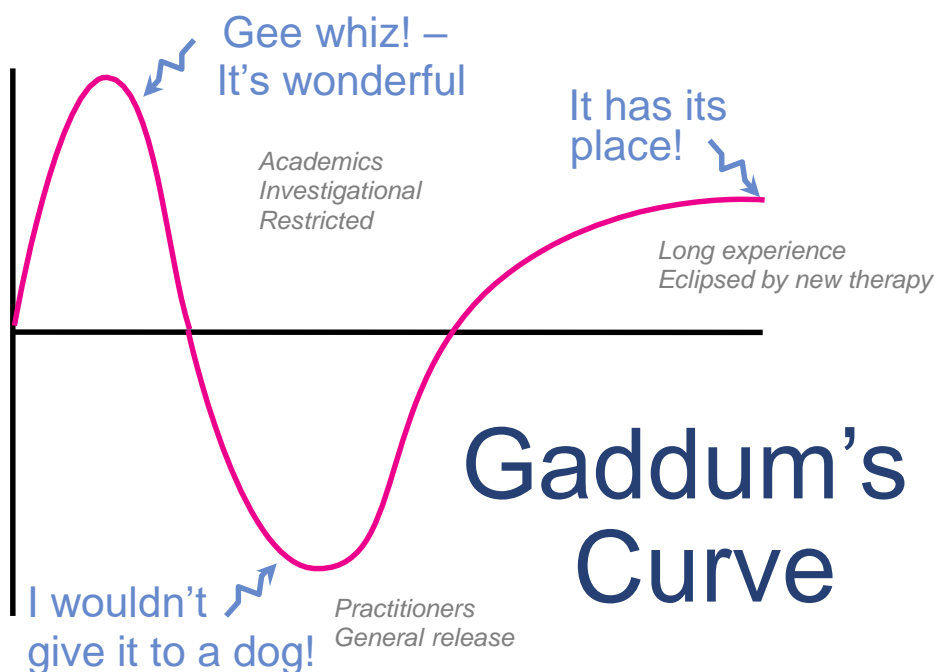
US DoD PMSS = US Department of Defense Post-Marketing Surveillance Study
*Major bleeding definitions according to ISTH; # modified ISTH definition (additionally included surgical revision from bleeding)
**Major bleeding was defined by the Cunningham algorithm*
1. Patel MR et al. *N Engl J Med* 2011; 365(10):883-891; 2. Beyer-Westendorf et al. *Blood* 2014;124(6): 955-962; 3. Tamayo S et al. *Clin Cardiol.* 2015;38(2):63-68; 4. Cunningham A et al. *Pharmacoepidemiol Drug Saf.* 2011;20(6):560-566

Lower Rates of ICB with NOACs but Similar GI Bleeding Rate with Rivaroxaban Compared to VKA

- ◆ Data from the US Market Scan Commercial and Medicare Supplemental databases in the period 2010-12
- ◆ Inclusion of patients initiating oral anticoagulants after NVAf diagnosis, and with at least 6 months of enrollment before first anticoagulant use
- ◆ Patients initiating dabigatran or rivaroxaban were matched with up to 5 warfarin users by age, sex, and time in the database

	Ischaemic stroke		Intracranial bleeding		GI bleeding	
	Events	HR (95% CI)	Events	HR (95% CI)	Events	HR (95% CI)
Warfarin N = 92,633	791	1 (ref.)	196	1 (ref.)	1293	1 (ref.)
Dabigatran N = 32,918	226	1.0 (0.8 – 1.1)	28	0.5 (0.3 – 0.7)	526	1.3 (1.2 – 1.4)
Rivaroxaban N = 3,301	18	1.2 (0.6 – 2.3)	1	0.4 (0.1 – 3.6)	23	0.9 (0.5 – 1.8)

Results are not intended for direct comparison. No head to head data comparing rivaroxaban to dabigatran
Bengtson et al. 2014, Presented at AHA 2014: Abstract 20218: Comparative Effectiveness of Dabigatran and Rivaroxaban versus Warfarin in Patients With Non-Valvular Atrial Fibrillation; Consider number of patients included when looking at event rates



Inter-professional Communication Matters – The Role of Pharmacists in Multidisciplinary Teams, Patient Pathways and the Responsible Use of NOACs

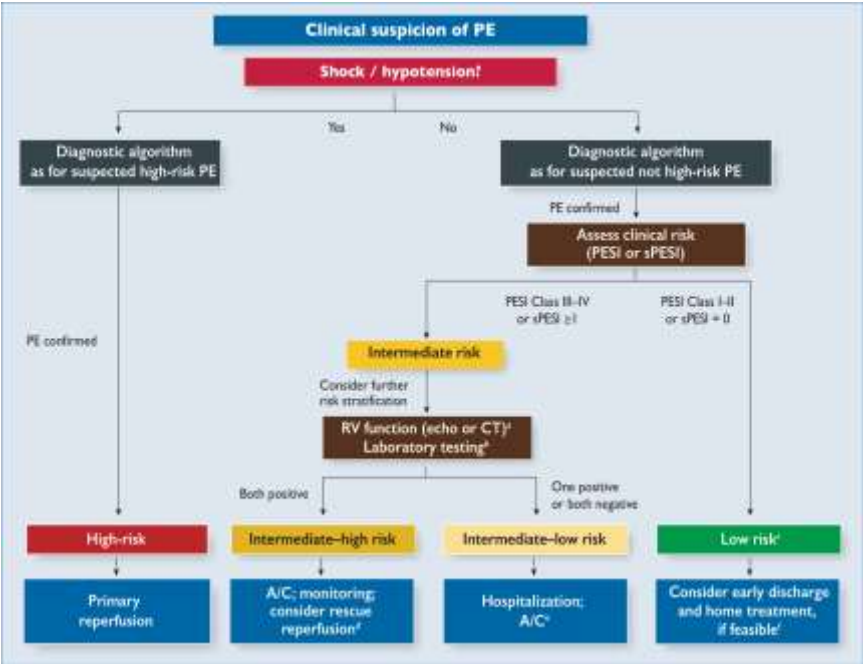
Rodney Hughes

Consultant Respiratory Physician

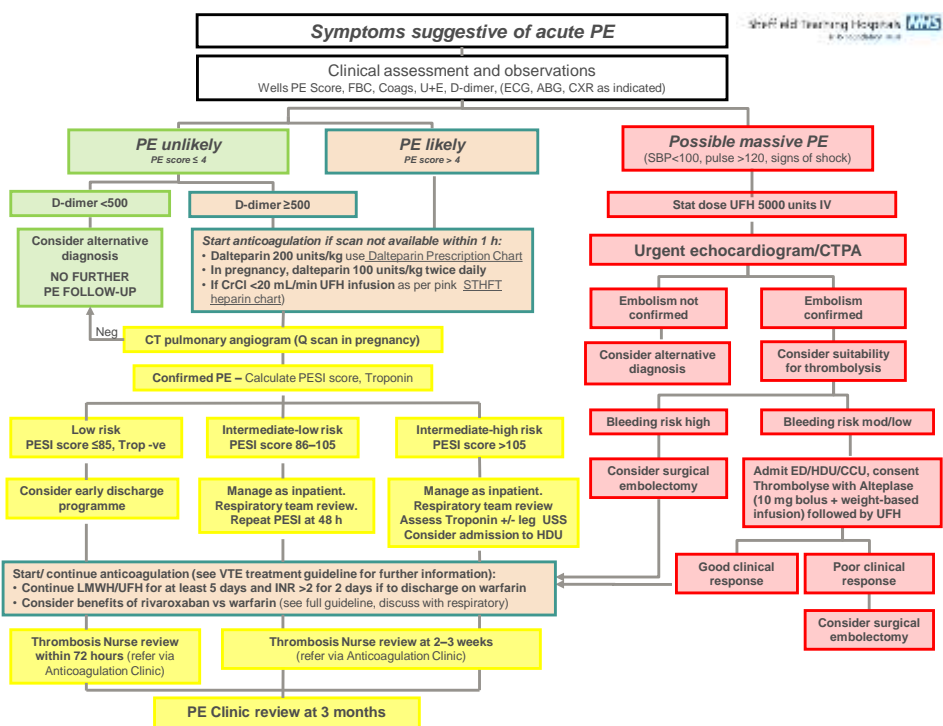
Jannat Muen

Anticoagulation & Thrombosis Prevention Pharmacist
Sheffield Teaching Hospitals, UK

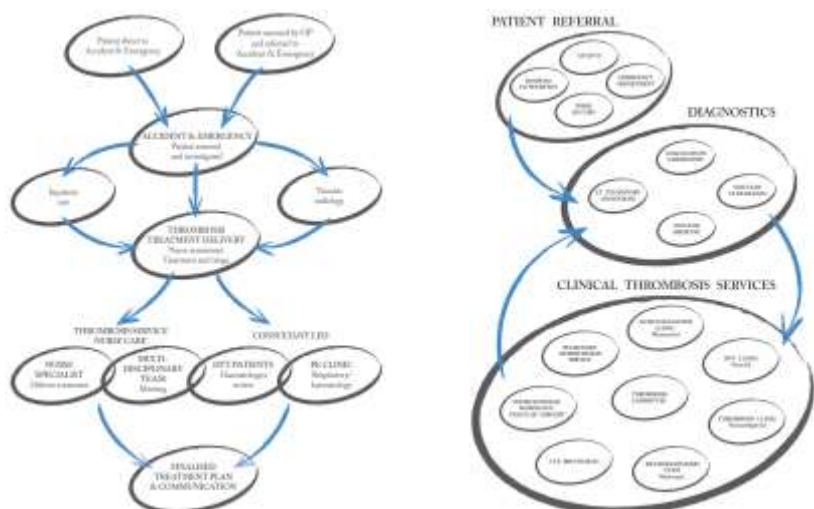
Maria's Story...



Konstantinides S et al. Eur Heart J 2014;35:3033–3069



Pathways



Traditional Role of the Hospital Pharmacist in the UK

- ◆ Supply medication
- ◆ Advise on suitability of medication
- ◆ 'Gate-keeper' of the formulary?
- ◆ Counselling patients
 - Warfarin
 - Self-injection of LMWH
- ◆ Warfarin dosing in clinic

Definition of Pharmaceutical Care

*“Pharmaceutical care is
the pharmacist’s contribution
to the care of individuals
in order to optimise medicines use
and improve health outcomes”*

Specialist Pharmaceutical Care in Anticoagulation

*“To lead, deliver, develop and evaluate
pharmacy services regarding
anticoagulant therapy in order to ensure
**safe, clinically effective and
cost-efficient use of anticoagulants**”*

‘Safe’ use of anticoagulants

- ◆ Clear, up-to-date, evidence-based guidelines
 - Prevention and treatment of VTE
 - Stroke prevention in atrial fibrillation
 - Bleeding/reversal guidelines
 - Perioperative bridging
 - Department specific: inpatient and ambulatory pathways
- ◆ Includes critical appraisal of trial data

'Clinically effective' use of anticoagulants

- ◆ Educating staff on the safe use of anticoagulants and reversal
- ◆ Educating patients on the correct use of anticoagulation
- ◆ Mechanical prophylaxis

'Clinically effective' use of anticoagulants – counselling patients

- ◆ Choice of agent – warfarin or NOAC?
- ◆ What to include in patient consultation:
 - Risks and benefits of rivaroxaban versus warfarin
 - Dosing schedule for rivaroxaban
 - Importance of taking it at the same time each day
 - What to do if a dose is missed
 - Take with food
 - Carry alert card

'Clinically effective' use of anticoagulants

- ◆ Advise clinicians how to switch between agents
- ◆ Advise on renal dosing and extremes of bodyweight
- ◆ Advise on treatment in pregnancy and cancer

'Cost-efficient' use of anticoagulants

- ◆ Over-labelled stocks (pre-packs) of low molecular weight heparin (LMWH) and rivaroxaban
- ◆ Dispensary stocks – correct pack sizes supplied
- ◆ A rational approach to the prescribing of NOACs
 - Treatment of first episode of VTE
 - Unstable patients on warfarin where indicated

Summary

- ◆ Pharmacists have a variety of skills which can be implemented at various points of the pathways
- ◆ Awareness of licensed indications, interactions and different dosing schedules are imperative
- ◆ The point of dispensing can be an excellent opportunity to educate
- ◆ Ensure you have a network of fellow HCPs you can refer to



Introduction to the Interactive Group Session

Trevor Nicholls



Which Countries Do We Come From?

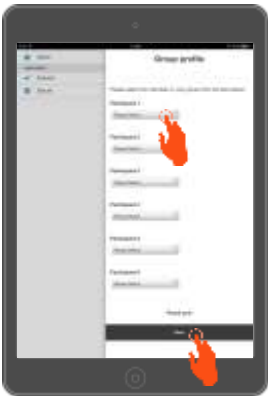


Please get into groups of 4–6 participants

Group iPads are being handed out

Pick Up Your Group iPad!

1. Tap **Group profile** on the home screen of the **Group iPad**
2. Select the group members from the dropdown list and tap **Save**



Pick Up Your Group iPad!

1. Tap **Interactive group exercise** on the home screen of the **Group iPad**
2. Wait for the exercise to be launched
3. Follow the on-screen instructions



Bayer Workshop: Implementing a multidisciplinary team for managing anticoagulation services

You have a maximum of **15 minutes** to complete the exercise

Scenario and task

Scenario

- ◆ A patient with a low-risk pulmonary embolism (sPESI score 0) and no further co-morbidities presents to your hospital

Task 1

- ◆ Please suggest an optimal multidisciplinary team (MDT) of healthcare professionals (HCPs) to manage this patient in your hospital
- ◆ Drag the HCP icons and drop them into the MDT box
- ◆ If a particular speciality is missing, you can add it using the free text field

Task 2

- ◆ Please create the optimal care pathway for this patient in your hospital
 - Drag the HCP icons and drop them next to the appropriate points on the left-hand side of the pathway when that HCP or the MDT group should be involved
 - At the places where you have assigned a role for a pharmacist, please add the appropriate actions for the pharmacist on the right-hand side of the pathway – **you can only put a pharmacist pharmacist actions where you have put a pharmacist**
 - Add the appropriate icons showing topics for patient education next to the relevant points in the pathway where that information should be given to the patient
- ◆ **You have a maximum of 15 minutes to complete the exercise!**

Awaiting results...

Please remember to evaluate the session!

Click on 'Evaluation' on your personal iPads

Bayer Workshop: non-medical demonstration exercise

You have a maximum of **5 minutes** to complete the exercise

How to play

- ◆ The aim of this interactive activity is to find the correct solution to the problem presented
- ◆ **The winning team will not only find the correct answer, but also ask the fewest questions needed to fully justify their choice in the shortest time**
- ◆ At the beginning of the exercise, you will be presented with a scenario, some basic information and the possible solutions – only one solution is correct
- ◆ Use the information to choose which question to ask first – then, based on the answer, choose which question to ask next, and so on
- ◆ Remember that some questions may not need to be asked because you may already have enough information to find the correct solution
- ◆ Once you think you have asked enough questions to gain the necessary information, select the solution you think is correct
- ◆ “Help!” With every answer there is a ‘Help’ button that provides additional guidance. If selected, this will count towards your total number of questions asked
- ◆ **You have a maximum of 5 minutes to complete the exercise!**

Scenario and task


Scenario

- ◆ You have tickets for tonight's performance of 'Carmen' at the Vienna State Opera House but you are late. It's 18:15 on a Monday and **the show starts in 45 minutes!**
- ◆ You are **at home in the busy northern suburbs** at rush hour, and **the Opera House is in the city centre, on the southern side** of the river
- ◆ You live next to a **metro station** that also has a **taxi rank**; you also have a **car**

Your task

- ◆ Get to the Opera House in time for the performance!

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Choose a solution

The order in which the solutions are shown is randomized on your iPads

Take the metro from home and then walk to the Opera House.

Take the metro from home and then a taxi to the Opera House.

Drive by car from home to the Opera House.

Walk to the Opera House from home on foot.

Take a taxi to the Opera House from home.

Awaiting results...

Optimal solution

The order in which the solutions are shown is randomized on your iPads

Take the metro from home and then walk to the Opera House.

Take the metro from home and then a taxi to the Opera House.

Drive by car from home to the Opera House.

Walk to the Opera House from home on foot.

Take a taxi to the Opera House from home.

Bayer Workshop: Interactive medical exercise Non-VKA oral anticoagulants on the formulary

You have a maximum of **10 minutes** to complete the exercise

How to play

- ◆ The aim of this interactive activity is to find the correct solution to the problem presented
- ◆ **The winning team will not only find the correct answer, but also ask the fewest questions needed to fully justify their choice in the shortest time**
- ◆ At the beginning of the exercise, you will be presented with a scenario, some basic information and the possible solutions – only one solution is correct
- ◆ Use the information to choose which question to ask first – then, based on the answer, choose which question to ask next, and so on
- ◆ Remember that some questions may not need to be asked because you may already have enough information to find the correct solution
- ◆ Once you think you have asked enough questions to gain the necessary information, select the solution you think is correct
- ◆ “Help!” With every answer there is a ‘Help’ button that provides additional guidance. If selected, this will count towards your total number of questions asked
- ◆ **You have a maximum of 10 minutes to complete the exercise!**

Scenario and task

Scenario

- ◆ Your hospital is considering whether to add rivaroxaban and potentially one or more other non-vitamin K antagonist oral anticoagulants (NOACs) to its drug formulary for patients with non-valvular atrial fibrillation (AF) and venous thromboembolism (VTE), and wants your advice

Your task

- ◆ Consider the arguments for the use of rivaroxaban in your hospital and make a recommendation

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Choose a solution

The order in which the solutions are shown is randomized on your iPads

Recommend replacing the existing anticoagulants on the formulary with all available NOACs.

Recommend adding rivaroxaban and another NOAC to the existing formulary.

Recommend against adding rivaroxaban to the existing formulary because the current standard therapy is more suited to our practice.

Recommend replacing the existing anticoagulants on the formulary with rivaroxaban alone.

Recommend against adding rivaroxaban to the existing formulary because adverse events and procedures are easier to manage with the current therapy.

Awaiting results...

Choose a solution

The order in which the solutions are shown is randomized on your iPads

- Recommend replacing the existing anticoagulants on the formulary with all available NOACs.
- Recommend adding rivaroxaban and another NOAC to the existing formulary.
- Recommend against adding rivaroxaban to the existing formulary because the current standard therapy is more suited to our practice.
- Recommend replacing the existing anticoagulants on the formulary with rivaroxaban alone.
- Recommend against adding rivaroxaban to the existing formulary because adverse events and procedures are easier to manage with the current therapy.

Please remember to evaluate the session!

Click on 'Evaluation' on your personal iPads

Thank you for your participation!

Please remember to

- ◆ Provide your email address on the profile screen on your iPad if you want to receive meeting content and your notes
- ◆ Complete the evaluation form on your iPad
- ◆ Return your iPad when you leave!

Bayer activities at EAHP tomorrow (Thursday 17 March)

- ◆ Meet-the-expert (Bayer booth, exhibition hall)
 - 10:30–11:00: Real-world evidence and adherence (Craig Coleman)
 - 16:30–17:00: AF screening (Sotiris Antoniou and Ben Freedman)
- ◆ 12:00–13:30: Interactive workshop (Hall N)
 - Real-World Adherence and Persistence – Patient Perspectives Matter (Sotiris Antoniou and Craig Coleman)