Anticoagulation….it is important to all of us

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Faculty/Presenter Disclosure

- Danielle Hart, nurse practitioner Cardiac program/ Atrial fibrillation (AF) care
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- Discussion based on guidelines and current literature which supports anticoagulation in the AF patient population to prevent stroke
- no disclosures

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Objectives

- Examine motives to anticoagulate in the AF patient population to prevent stroke
- Evidence and ease of anticoagulation
- Review of stroke risk assessment
- Case study
- Concerns surrounding anticoagulation

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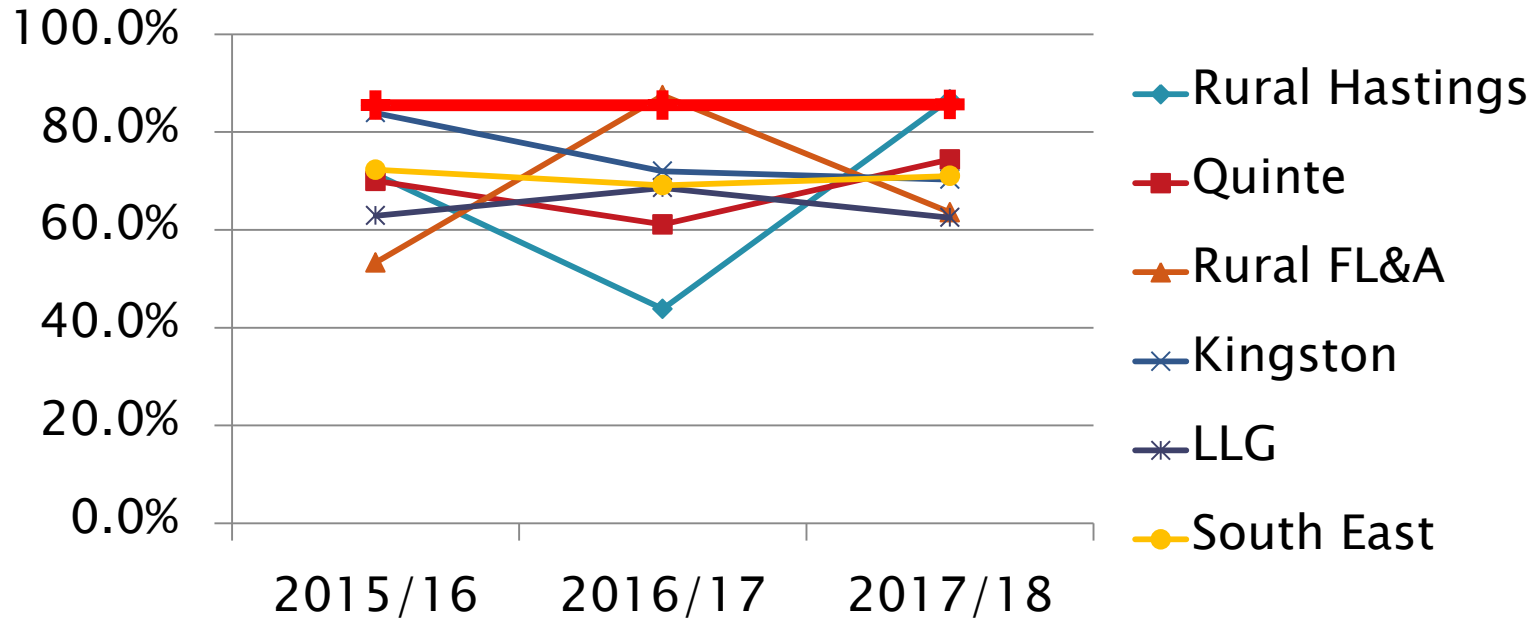
% Ischemic Stroke/TIA + Afib ≥ 65 yrs Who Filled Anticoagulant Rx ≤ 90 days



	Rural Hastings	Quinte	Rural FL&A	Kingston	LLG	South East	ON Benchmark
2015/16	71.4%	70.0%	53.3%	83.9%	62.9%	72.3%	85.5%
2016/17	43.8%	61.1%	87.5%	72.0%	68.6%	69.1%	85.5%
2017/18	86.7%	74.4%	63.6%	70.3%	62.5%	71.0%	85.6%

Reference: CorHealth Ontario Stroke Report Card;
Data Source: CIHI DAD & ODB Database

Why anticoagulate ?

- In Canada, stroke is the leading cause of adult neurological disability with 400,000 Canadians living from its effects
- AF found to be responsible for more than 15% of all ischemic strokes
- Ischemic strokes caused by AF are twice as likely to be fatal and associated with more impairment compared to non-AF strokes
- Several randomized trials have established the efficacy of anticoagulation for stroke protection

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Most patients should receive NOAC

- We recommend that when OAC-therapy is indicated for patients with non-valvular AF, most patients should receive dabigatran, rivaroxaban, apixaban or edoxaban in preference to warfarin *(Strong Recommendation, High-Quality Evidence)*.

Values and preferences: This recommendation places a relatively high value on the greater ease of use of the NOACs in comparison to warfarin, and the results of large RCTs showing that the NOACs are either non-inferior or superior to warfarin in stroke prevention; the drugs have no more major bleeding or less bleeding vs warfarin and especially less intracranial hemorrhage. The recommendation places less value on the shorter clinical experience, lack of a specific antidote, and lack of a simple test for intensity of anticoagulant effect with the NOACs. The preference for one of the NOACs over warfarin is less marked among patients already receiving warfarin with stable therapeutic INRs, no bleeding complications, and who are not requesting a change in OAC therapy.

Canadian Cardiovascular Society

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	RE-LY[2]	ROCKET AF[1]	ARISTOTLE[3,4]	ENGAGE-AF
No. of patients	18,113	14,264	18,201	21,105
Statistical objective	Non-inferiority	Non-inferiority	Non-inferiority	Non-inferiority
Study drugs	Two doses of double-blind dabigatran	Double-blind rivaroxaban	Double-blind apixaban	Double-blind edoxaban
Control	Open-label warfarin (INR 2–3)	Double-blind warfarin (INR 2–3)	Double-blind warfarin (INR 2–3)	Double-blind warfarin (INR 2–3)
Primary Dose(s) Studied	110 mg BID and 150 mg BID	20 mg OD	5 mg BID	60 mg OD and 30 mg OD
Adjusted Dose Studied	None (~85% renal excretion)	15 mg OD For patients with CrCl = 30-49 mL/min (~33% renal excretion)	2.5 mg BID For patient with any two of the following: - Age ≥80 years - Body weight ≤60 kg - Serum creatinine ≥1.5 mg/dL (133 µmol/L) (27% renal excretion)	30 or 15mg Dose adjustment at randomization (or throughout) for ≥1 of the following: – CrCl = 30-49 mL/min – Weight ≤60 kg – Cardiac medications that are strong P-gp inhibitors (50% renal excretion)

Anticoagulation options

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Warfarin

- for those with mechanical valve or mitral stenosis
- an option in renal dysfunction
- reasonable to continue if INR stable
- **But** many are challenged with INR monitoring, attaining and achieving therapeutic range
- many interactions to consider

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Warfarin Interactions

Increase INR

Specific Drugs Reported		
acetaminophen	fenoprofen	oxymetholone
alcohol†	fluconazole	pantoprazole
allopurinol	fluorouracil	paroxetine
aminosalicylic acid	fluoxetine	penicillin G, intravenous
amiodarone HCl	flutamide	pentoxifylline
argatroban	fluvastatin	phenylbutazone
aspirin	fluvoxamine	phenytoin†
atenolol	gefitinib	piperacillin
atorvastatin†	gemfibrozil	piroxicam
azithromycin	glucagon	pravastatin†
bivalirudin	halothane	prednisone†
capecitabine	heparin	propafenone
cefamandole	ibuprofen	propoxyphene
cefazolin	ifosfamide	propranolol
cefoperazone	indomethacin	propylthiouracil†
cefotetan	influenza virus vaccine	quinidine
cefoxitin	itraconazole	quinine
ceftriaxone	ketoprofen	rabeprazole
celecoxib	ketorolac	ranitidine†
cerivastatin	lansoprazole	rofecoxib
chenodiol	lepirudin	sertraline
chloramphenicol	levamisole	simvastatin
chloral hydrate†	levofloxacin	stanozolol
chlorpropamide	levothyroxine	streptokinase
cholestyramine†	liothyronine	sulfamethizole
cimetidine	lovastatin	sulfamethoxazole
ciprofloxacin	mefenamic acid	sulfinpyrazone
cisapride	methimazole†	sulfisoxazole
clarithromycin	methyldopa	sulindac
clofibrate	methylphenidate	tamoxifen
COUMADIN overdose	methylsalicylate ointment (topical)	tetracycline
cyclophosphamide†	metronidazole	thyroid
danazol	miconazole (intravaginal, oral, systemic)	ticarcillin
dextran	moricizine hydrochloride†	ticlopidine
dextrothyroxine	nalidixic acid	tissue plasminogen activator (t-PA)
diazoxide	naproxen	tolbutamide
diclofenac	neomycin	tramadol
dicumarol	norfloxacin	trimethoprim/sulfamethoxazole
diflunisal	ofloxacin	urokinase
disulfiram	olsalazine	valdecoxib
doxycycline	omeprazole	valproate
erythromycin	oxandrolone	vitamin E
esomeprazole	oxaprozin	zafirlukast
ethacrynic acid		zileuton
ezetimibe		
fenofibrate		

Decrease INR

Specific Drugs Reported		
alcohol†	COUMADIN underdosage	phenobarbital
aminoglutethimide	cyclophosphamide†	phenytoin†
amobarbital	dicloxacillin	pravastatin†
atorvastatin†	ethchlorvynol	prednisone†
azathioprine	glutethimide	primidone
butabarbital	griseofulvin	propylthiouracil†
butalbital	haloperidol	raloxifene
carbamazepine	meprobamate	ranitidine†
chloral hydrate†	6-mercaptopurine	rifampin
chlordiazepoxide	methimazole†	secobarbital
chlorthalidone	moricizine hydrochloride†	spironolactone
cholestyramine†	nafcillin	sucralfate
clozapine	paraldehyde	trazodone
corticotropin	pentobarbital	vitamin C (high dose)
cortisone		vitamin K

Table 6 Absorption and metabolism of the different NOACs

	Dabigatran[158,182]	Apixaban[183]	Edoxaban[184]	Rivaroxaban[185,186]
Bioavailability	3–7%	50%	62%	15 mg/20 mg: 66% without food, 80–100% with food
Prodrug	Yes	No	No	No
Clearance non-renal/renal of absorbed dose	20%/80%	73%/27%	50%/50%	65%/35%
Plasma protein binding	35%	87%	55%	95%
Dialysability	50–60% (in part dialysable)	14% (in part dialysable)	n.a. (in part dialysable)	n.a. (in part dialysable)
Liver metabolism: CYP3A4 involved	No	Yes [elimination, moderate contribution (≈25%)[a]]	Minimal (<4% of elimination)	Yes (hepatic elimination ≈18%)[131]
Absorption with food	No effect	No effect	6-22% more; minimal effect on exposure	+39% more (see above)
Absorption with H2B/PPI	-12% to 30% (not clinically relevant)	No effect	No effect	No effect
Asian ethnicity	+25%[166]	No effect	No effect	No effect
Elimination half-life	12–17 h	12 h	10–14 h	5–9 h (young)
				11–13 h (elderly)
Other	Dyspepsia (5–10%)			Intake of 15 mg/20 mg with food mandatory

- **CHADS2**: measured and validated 1733 patients and repeatedly validated but weak tool to differentiate low-risk individuals
- **CHADS65**: derived from Danish data which revealed age stronger predictor than hypertension and diabetes for stroke
- **CHA2DS2VASc**: consideration of female sex, age and vascular

Stroke Risk as a Function of Atrial Fibrillation Duration and CHA_2DS_2-VASc Score

Rachel M. Kaplan, Jodi Koehler, Paul D. Ziegler, Shantanu Sarkar, Steven Zweibel, and Rod S. Passman

Originally published 30 Sep 2019 | https://doi.org/10.1161/CIRCULATIONAHA.119.041303 | Circulation. ;0:null

Stroke risk tools

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TABLE 3. $CHADS_2$ stroke risk stratification scheme for patients with nonvalvular AF

Risk factors	Score
C Recent congestive heart failure	1
H Hypertension	1
A Age ≥75 yrs	1
D Diabetes mellitus	1
S_2 History of stroke or transient ischemic attack	2

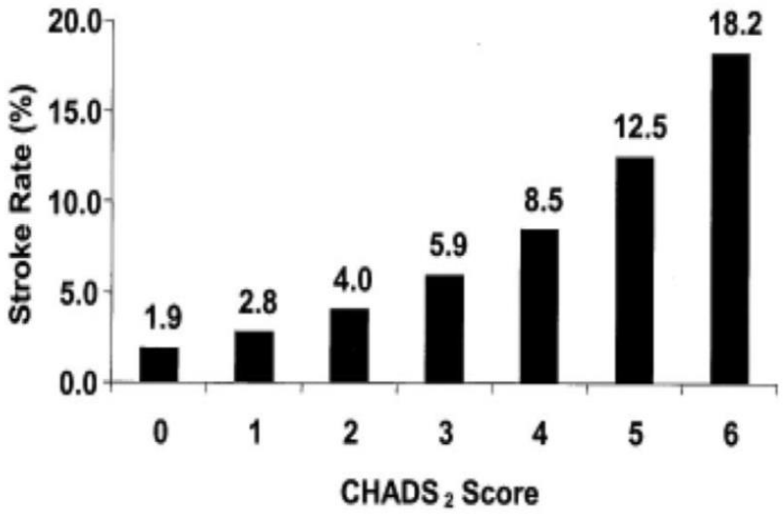

FIG 6. Relationship between $CHADS_2$ score and annual risk of stroke (reproduced with permission[61]).

Risk factors	
C Congestive Heart Failure	+1 point
H Hypertension	+1 point
A_2 Age ≥75	+2 point
D Diabetes	+1 point
S_2 Stroke/TIA History	+2 point
V Vascular Disease	+1 point
A Age 65-74	+1 point
S Sex (Female)	+1 point

Stroke risk per year	
SCORE	% RATE PER YEAR
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%

Reference: European Heart Rhythm Association. Guidelines for the management of atrial fibrillation: the Task Force for the Management of Atrial Fibrillation of the European Society of Cardiology (ESC). *Eur Heart J*. 2010;31(19):2369-2429.

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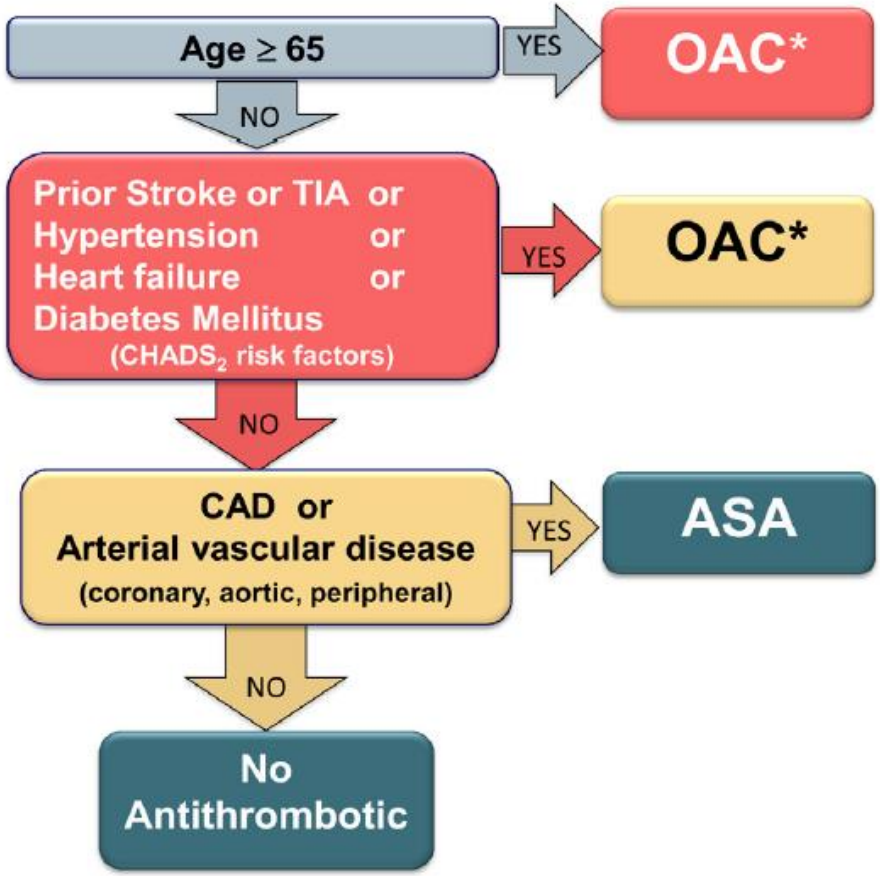
Society Guidelines

2014 Focused Update of the Canadian Cardiovascular Society Guidelines for the Management of Atrial Fibrillation

The "CCS Algorithm" for OAC Therapy in AF



Consider and modify (if possible) all factors influencing risk of bleeding during OAC treatment (hypertension, antiplatelet drugs, NSAIDs, excessive alcohol, labile INRs) and specifically bleeding risks for NOACs (low eGFR, age ≥ 75, low body weight).†

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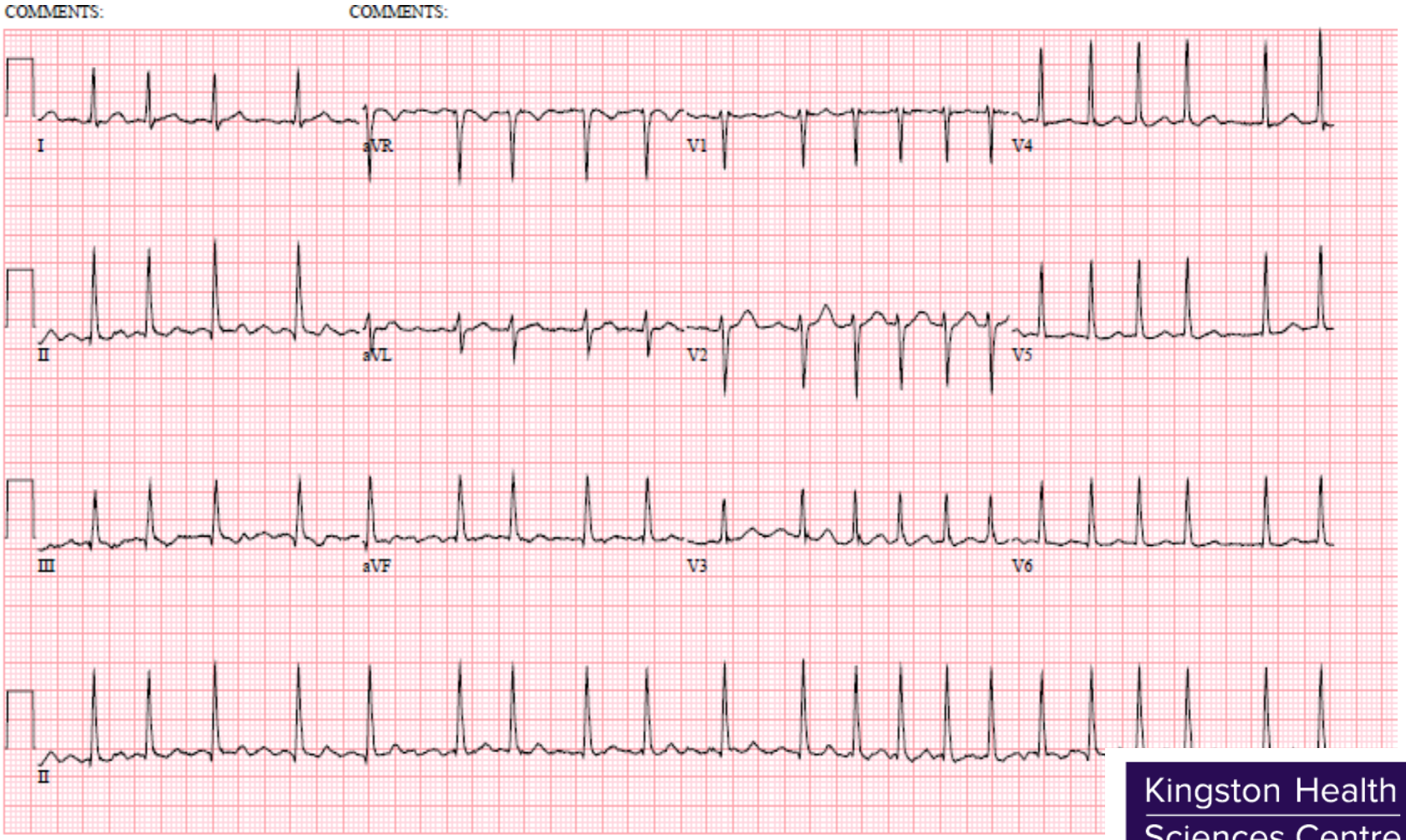
True Case

- Ms.B 76 year old female with atrial fibrillation, smoking history and hypertension
- Referred to arrhythmia clinic after an assessment at rapid cardiac clinic post ED visit
- CHA2DS2VASc=3 (maybe 4 if HTN)
- Discussion re: rate control and anticoagulation
- Patient reluctant to start anticoagulation
- “believes in living off the land” and “AF only happens once in awhile”



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- Started Apixaban but in a follow up call…

Patient Assessment

[redacted]d today to ask my advice about a "blood thinner". She states she saw he family doctor that was "adamant" that she take something more than ASA. She states her atrial fibrillation is generally settled at present and she has not been taking the metoprolol or apixaban and she will not take these medications again. She states she is having blood work to prepare for cataract surgery and has an appointment with arrhythmia on Nov 21st.

Analysis and Plan
(including consultation, education, and referrals)

Protocol/Guideline Used: ☐ Yes Specify _____ ☐ No ☐ Not applicable

I explained to [redacted], as I had in the past, that an ASA is only 20 % effective to prevent stroke and that I had contacted her doctor about my concerns of not taking "full anticoagulation". I offered to review various anticoagulants with her but she said she would discuss further in clinic…or maybe with her family doctor

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EMERGENCY DEPARTMENT RECORD **MD Attending:** Graham, Karen, MD

Mode of Arrival: Ambulance **Accompanied By:** Self

CTAS: 2 **Rm:** **FRI Screening Result:** NEG

Reason for Visit: Confusion/Headache

Recent International Travel (21 days): No recent travel
Are these injuries the result of someone hurting you? No **SADV Offered:** No **SADV Called:** No
Trauma Team Activated?
Farm Injury?

Diagnosis

Diagnosis 1: Stroke

Consultant Diagnosis: right frontal infarct

Disposition: Admit to Critical Care/OR:06
Time Left ED: 2016/11/16 0200

Unfortunate events

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- onset of stroke symptoms unknown, found by neighbours, unable to speak
- Persistent AF
- Global aphasia No hemiparesis
- CT: Right MCA subacute stroke/left superior cerebellar stroke/right PCA chronic stroke

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Anticoagulation Predicaments in practice

- Patient and caregiver beliefs, fears/refusal
- Health care provider beliefs and experiences
  - Proper dosing
- Bleeding risk or bleeding in patient history even before anticoagulation…NASH,GAVE, hematological disorders
- Stopping for procedures/surgery
- Antiplatelet and anticoagulation (post CAD, post aneurysm, post stroke)
- Cost and LU code

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More Predicaments in practice

- Patients with frequent falls
- Antiepileptic medication may decrease efficacy (Dilantin)
- Deteriorating kidney function and dialysis
- Liver dysfunction and alcohol
- What to do after intracerebral hemorrhage
  - Intracranial hemorrhage is a risk factor for stroke
- Cardiac ablation…to continue or not...
- How much AF = anticoagulation

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- scoring tools available
  - ATRIA, HAS BLED, HEMORR$_2$HAGES
- antiplatelet and anticoagulation (does patient need both)
- Plavix and ASA…not less bleeding and not as effective for stroke protection
- No robust studies have shown benefit in withholding anticoagulation
- Avoid bridging unless mechanical valve
- Low dose of anticoagulation not necessarily lower bleeding…need to treat underlying issue

Avoid Bleeding

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- Atrial appendage closure may be option
- Discuss with patient bleeding risks versus stroke… be transparent
- Bleeding is often treatable BUT stroke can leave life long disability or be fatal
- Collaborate with partners to find balance between stroke risk and bleeding (hematology, gastroenterology, neurology)
- Educate about the importance of restarting anticoagulation if held

Summarizing Stroke and Bleeding

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Take home messages

- Provide knowledge of what we know regarding AF and stroke…**BUT** we do not know daily risk
- ASA not enough protection against stroke in AF
- Urge patients to be active in decision making and ensure they understand anticoagulation “life long”
- Educate all care providers and patients regarding proper dosing
- Collaboration between patient and health care members is a key for success

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More on Predicaments & Potential Interventions

Perspectives from Community Pharmacist
Rapid Response Nurse
Family Physician

Community Pharmacist

Barriers/Predicaments:

- **Financial** – Patients that do not qualify for LU criteria or have a drug plan, **DOACs can be quite cost prohibitive** & going back to the prescriber to recommend warfarin & monitoring can be time consuming & delays treatment
- **Tracking down prescribers** –It is sometimes quite difficult to track down prescribers **to clarify prescriptions or for missing LU codes.** Discharge papers often do not have direct numbers to prescribers or fax numbers. This delays therapy

Interventions/Tips:

- **Re-educating patient's on importance of anticoagulation** & stroke risk at first dispensing
- Offering **compliance packaging**
- **Tracking down missing LU codes & clarifying pre**scriptions
- **Sending refill requests to primary care provider** to avoid gaps in care **once hospital Rx has run out**

Rapid Response Nurse

Barriers/Predicaments:

- Patient **fears**
- **Lack of education/understanding**
- **Cost** (Drug cards)
- When there is **no medical practitioner**
  - It's challenging to ensure patient will go to after-hours or walk-in clinic for medication renewals

Interventions/Tips:

- **Health teaching** using the ***Stroke Journey*** guide
- **Reviewing medications** with the patient emphasizing that they are to continue for life
- If there are **financial issues, linking with SE LHIN CC** and request drug card &/or social work if not already authorized

Family Physician

Barriers/Predicaments:

- **Coumadin- need for blood work**
- **NOAC- no routine monitoring to show that patient is taking as prescribed**
- As Dr Gregory House says… "everybody lies" i.e. about taking their meds

Interventions/Tips:

- **Regular follow up & review of benefits**
- **Bring meds to every visit**
- **Blister pack** for those with many meds
- **PrescribeIT ®**
- Coumadin was difficult… but at least we knew patients were taking it
- **For those on few meds, consider single daily dosing**

Questions/Discussion

Questions for the Panel?

Sharing from the Audience:

1. What are the top predicaments or barriers you see in your practice for patients taking anticoagulation medication?
2. What are the top tips or interventions you use to support or ensure patients taking anticoagulation medication daily?