Transient ischemic attack & secondary vascular prevention

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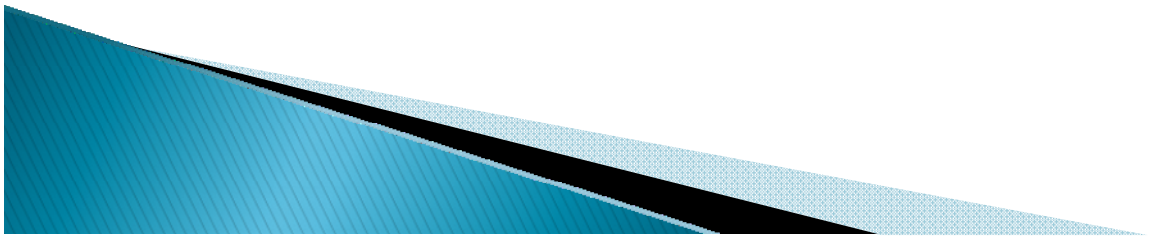
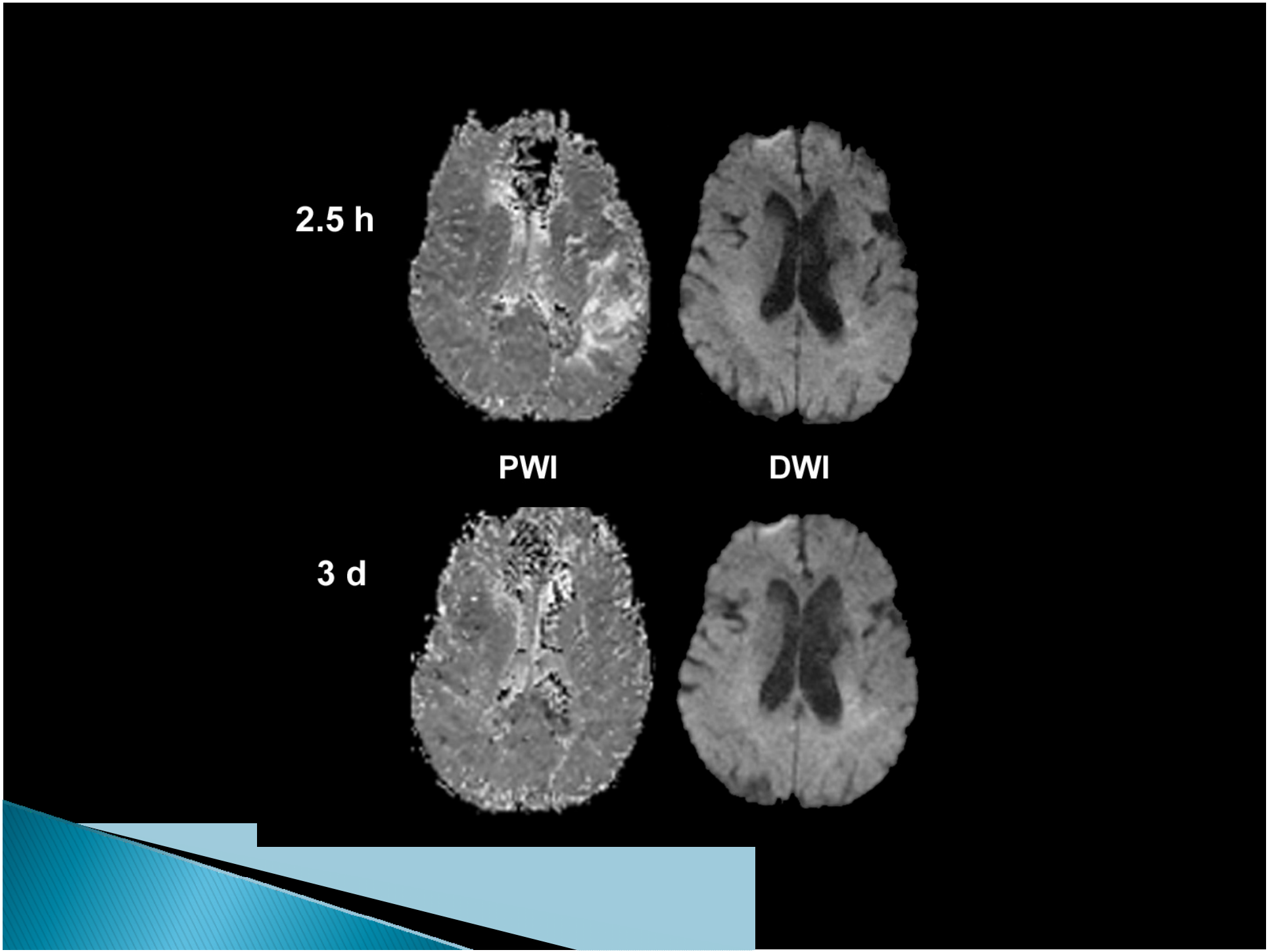
CENTRE FOR BRAIN RESEARCH
THE UNIVERSITY OF AUCKLAND
Te Whare Wānanga o Tāmaki Makaurau

Independent 79 yr old man

- Presented with
  - L numbness & slurred speech
  - 2 episodes; 10 mins & 2 hrs
- Hypertension
- Type II DM
- Examination
  - pulse 80/min reg, BP 160/95
  - neurology normal




2.5 h
PWI
DWI
3 d

What's a TIA

What's a TIA

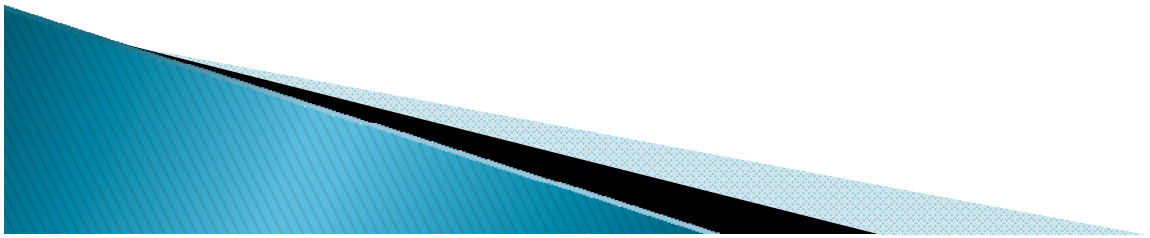
- Loss of focal brain (or eye) function
- Of presumed vascular origin
  - temporary loss of blood flow to brain/eye
- Symptoms resolve <24 hours

What's a TIA?

A TIA is where stroke symptoms disappear within 24 hours

But

- most TIA's last only minutes
  - 60% <1 hour
  - 71% <2 hours
  - 14% 2-24 hours



What's a TIA?

A TIA is where stroke symptoms disappear within 24 hours

But

- 1/3 of TIA patients have acute cerebral infarction on MRI scans

New definition of TIA

"a transient episode of neurological dysfunction caused by focal brain, spinal cord or retinal ischemia, without evidence of acute infarction"

- Tissue based definitions useful
  - infarction distinguishes MI from angina
  - focuses on pathophysiology, not temporal factors

New definition of stroke

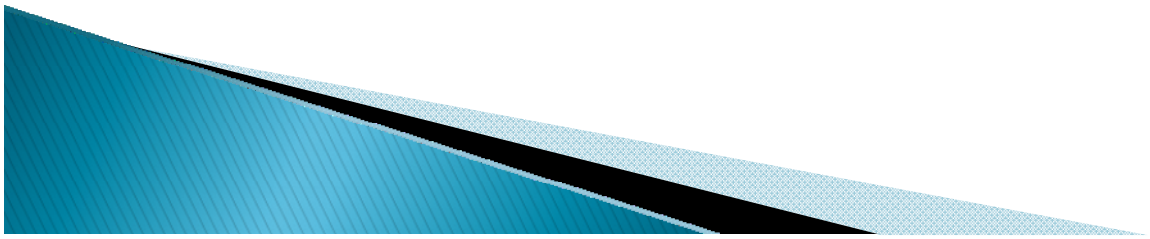
"an infarction of central nervous system tissue"

TIA pointers

- TIAs
  - don't precede cerebral hemorrhage
  - don't cause loss of consciousness
- TIAs almost never cause
  - isolated focal symptoms
    - double vision or dysphagia
  - non-focal symptoms
    - faintness, dizziness, confusion

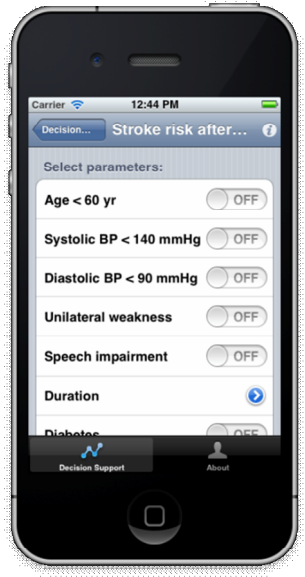
TIAs carry a poor prognosis

- 1 in 5 people with stroke have had a TIA first
- The risk of stroke following a TIA is high
  - up to 10% by 3 months
- Strokes after TIA are severe
  - 1 in 5 fatal
  - 2 in 3 survivors are disabled
- Not all TIAs carry the same stroke risk



ABCD^2 score

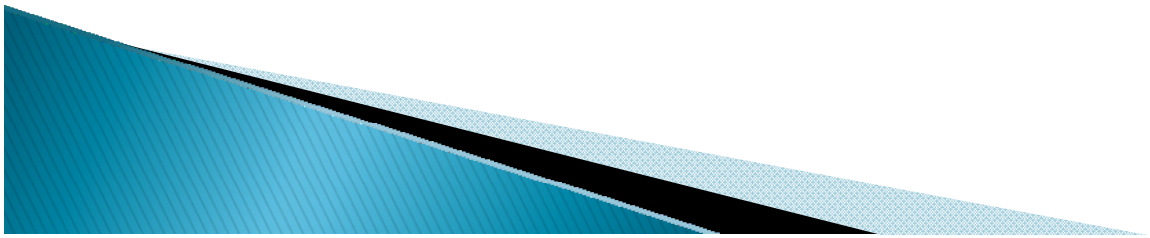
Age ≥ 60		1
Blood pressure high		1
Clinical	no weakness	0
	speech/no weakness	1
	unilateral weakness	2
Duration	<10 mins	0
	10–59 mins	1
	≥ 1 hour	2
Diabetes		1



Independent 79 yr old man

- Presented with
  - L numbness & slurred speech
  - 2 episodes – 1st 10 mins, 2nd 2 hrs
- Hypertension
- Type II DM
- Examination normal but BP 160/95

ABCD2 = 6

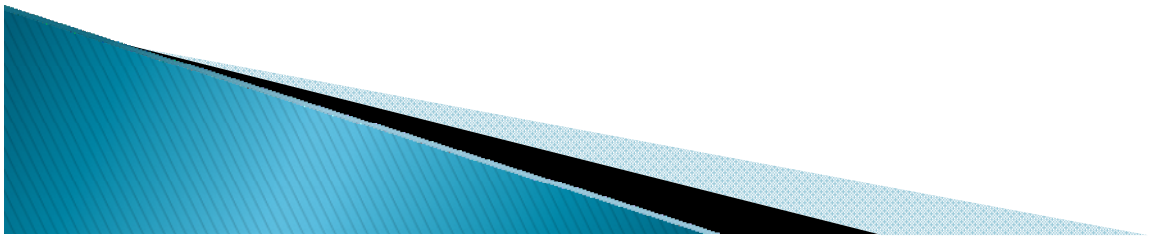


Stroke risk by ABCD^2 score

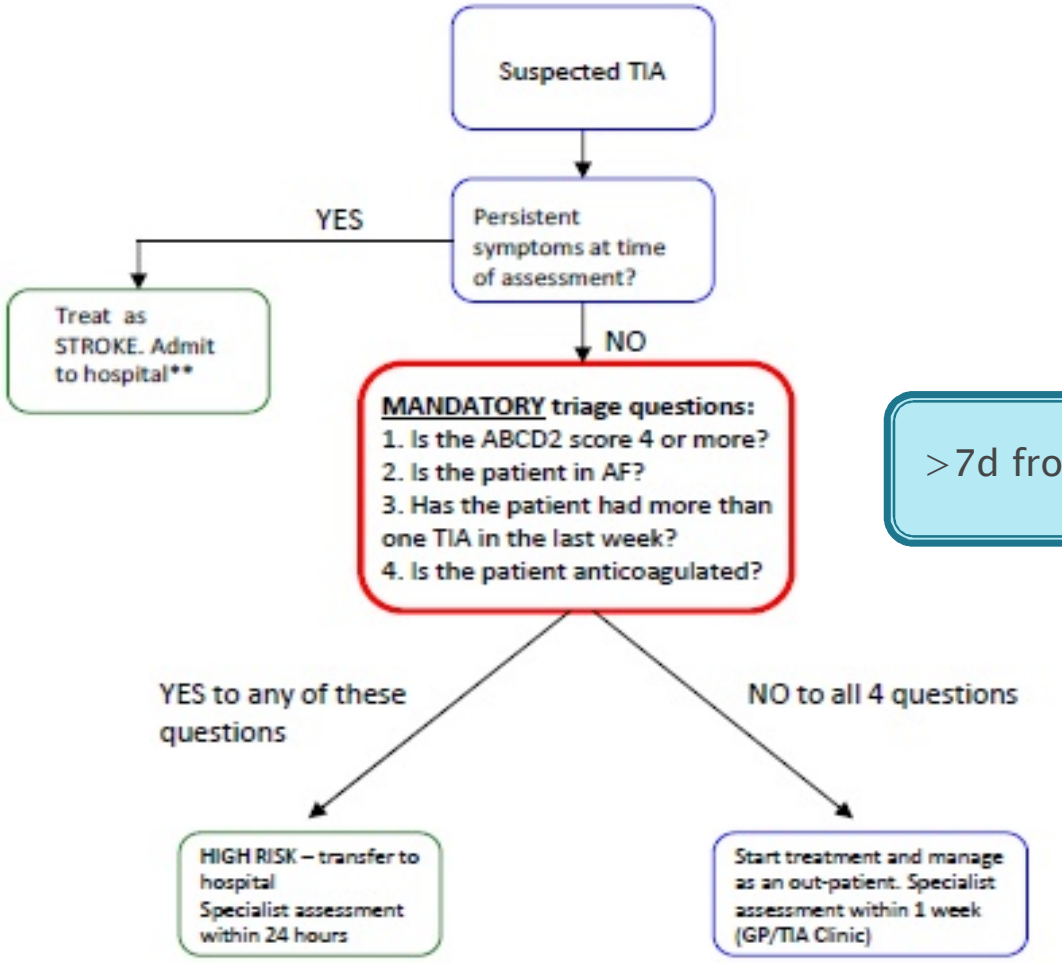
ABCD2 score:	0 – 3	4 – 5	6 – 7
Proportion of TIAs	34%	45%	21%
Stroke risk at			
2 days	1	4	8
7 days	1	6	12
3 months	3	10	18

Independent 79 yr old man

- Discharged from hospital
  - outpatient appointment at stroke clinic
- Represented 4 days later with severe stroke
  - left hemiparesis, sensory loss and neglect



TIA pathway



>7d from onset = 'lower risk'

Secondary stroke prevention

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Mr M 77 years

- Presented with
  - Non-fluent dysphasia
  - R facial weakness
- Background
  - Ischaemic heart disease
  - Hypertension
  - Hyperlipidemia

Mr M 77 years

- L MCA branch territory infarct due to large artery disease
- What secondary vascular prevention?

Anti-platelet therapy

- All people with ischemic stroke or TIA
  - unless patient needs to be anti-coagulated
- Clopidogrel alone
- Low dose aspirin plus dipyridamole
- Aspirin alone if can't tolerate A+D or C

Anti-platelet therapy

	RRR	ARR	NNT
A vs placebo	13%	1%	100
A+D vs A alone	18%	1	104
C vs A	10%	0.6	166
A+D vs C alone	no difference		

A	Aspirin
A+D	Aspirin plus Dipyridamole
C	Clopidogrel

Anti-hypertensive therapy

- All patients
  - Ischemic stroke or TIA
  - Intracerebral hemorrhage
- Regardless if normotensive or hypertensive

Anti-hypertensive therapy

	RRR	ARR	NNT
Stroke/TIA If hypertensive	31%	2%	45
Stroke/TIA If not hypertensive	24%	0.9	230

Lipid lowering therapy

Statins

- All patients after ischemic stroke or TIA
- *Not* routinely with intracerebral hemorrhage

Lipid lowering therapy

	RRR	ARR	NNT
Statins vs placebo	16%	0.4%	230

Carotid endarterectomy

After non-disabling stroke

- 70-99% ICA stenosis
  - NNT = 6 to prevent stroke/surgical death
- 50-69% ICA stenosis in *selected* patients
  - NNT = 14 to prevent stroke/surgical death
- Benefit of surgery
  - halved if delay >2 weeks
  - halved again if delay > 4 weeks

Mrs N 68 years

- Woke
  - slurred speech & L facial droop
- Stepwise deterioration
  - L lower limb weakness
  - L hand weakness

Mrs N 68 years

- Background
  - Paroxysmal Afib/Aflutter
    - 2010 cardioversion but recurred
    - 2010 ablation procedure & warfarin stopped
    - irregular palpitations for 4 weeks
  - Hypertension
  - Increased BMI
  - Impaired glucose tolerance

Mrs N 68 years

- Examination
  - Pulse 72/min irreg irreg (Afib/flutter on ECG)
  - Mild L weakness

Mrs N 68 years

- Cardioembolic R MCA territory infarction
- Treated with iv heparin
  - (stepwise deterioration)
- What oral anti-thrombotic agent?

Warfarin reduces stroke risk

	All strokes/year	RRR
Placebo	12%	
Aspirin	10%	14%
Warfarin	4%	66%

EAFT Lancet 1993; 342:1255

Warfarin problematic

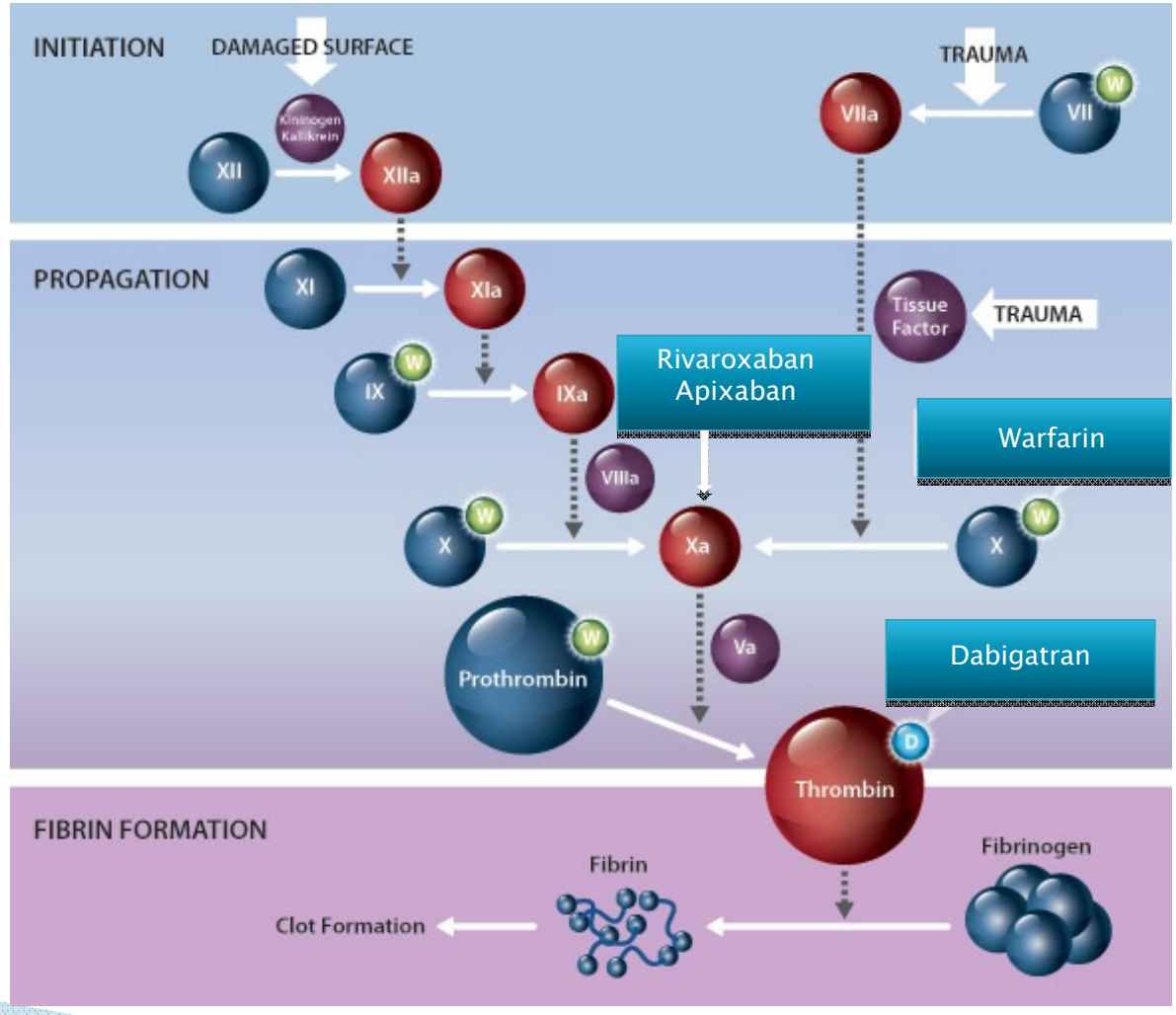
- In 2006 in Auckland
  - only 20% of stroke patients with known AF were taking Warfarin
- In 2010 in Northland
  - only 31% of stroke patients with known AF were taking Warfarin

Bang & McGrath NZMJ 124;28

Warfarin problematic

- Even if treated with Warfarin
  - INR only therapeutic 1/2 – 2/3 of time
- In Auckland 2006
  - only 15% stroke patients on Warfarin had INR 2-3
- In Northland 2010
  - only 8% stroke patients on Warfarin had INR 2-3
- 2-3% risk of major bleeds per year
  - 10% in 1st year if ≥80 years

Coagulaton cascade



Dabigatran

- Direct competitive inhibitor of thrombin
- 80% excreted by kidneys
- C_{max} 0.5–2 hours
- Half life = 12–17 hours
- RELY study

RELY study

- 18 113 patients
  - 71 years, $CHADS_2$ =2.1
- Randomized to
  - Warfarin (open label)
  - Dabigatran 110 mg bd or 150 mg bd
- Non-inferiority study

NEJM 2009; 361:1139

RELY study

	Warfarin %/year	Dabi 110 %/year	Dabi 150 %/year
Ischemic stroke	1.2	1.3	0.9*
Death	4.1	3.8	3.6*

* = superior to warfarin

NEJM 2009; 361:1139

RELY study

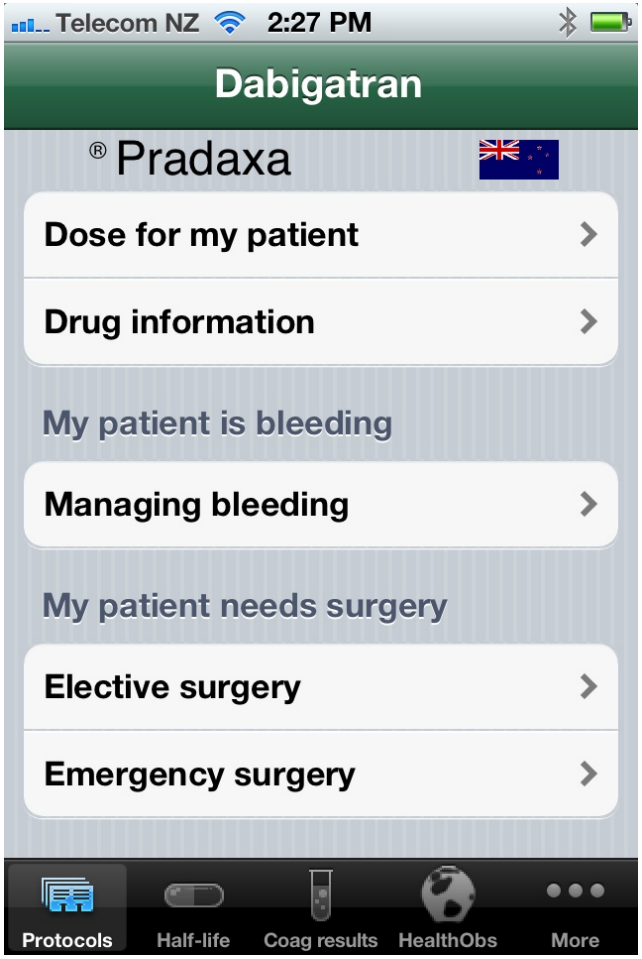
	Warfarin %/year	Dabi 110 %/year	Dabi 150 %/year
Major bleeding	3.4	2.7*	3.1 ns
Gastrointestinal	1.0	1.1 ns	1.5**
Intracranial bleeding	0.7	0.2*	0.3*

* superior to warfarin
** inferior to warfarin

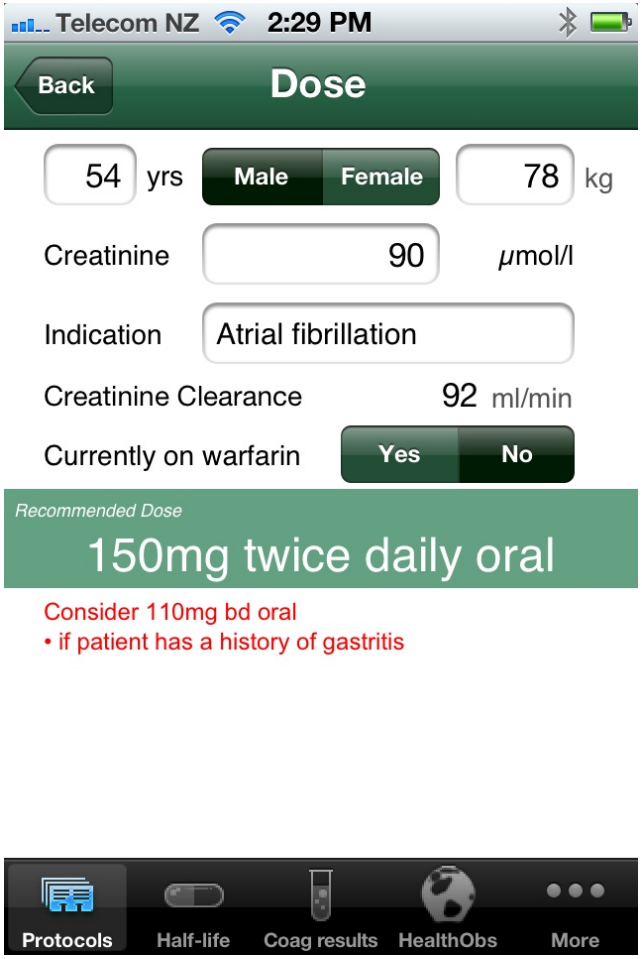
How to avoid problems?

- Discuss risk-benefits with patients
- Know in advance
  - when to start
  - what dose to use
    - elderly/renal impairment
  - what to do if patient comes in bleeding

How to avoid problems?



How to avoid problems?



Mr D 45 years

- Presented (while driving) with
  - Left upper limb “fat & heavy”
  - Had to steer with right hand
  - Then involuntary jerking left arm over 45 mins
  - No alteration of awareness or other symptoms

Mr D 45 years

- Left parietal infarct at 30 years
  - R homonymous hemianopia
  - R upper limb sensory loss
  - PFO & atrial septal aneurysm on echo
  - recurrent R upper limb sensory symptoms
- Left MCA TIA 2008
  - normal carotid ultrasound scan
- Smoker
- Migraine

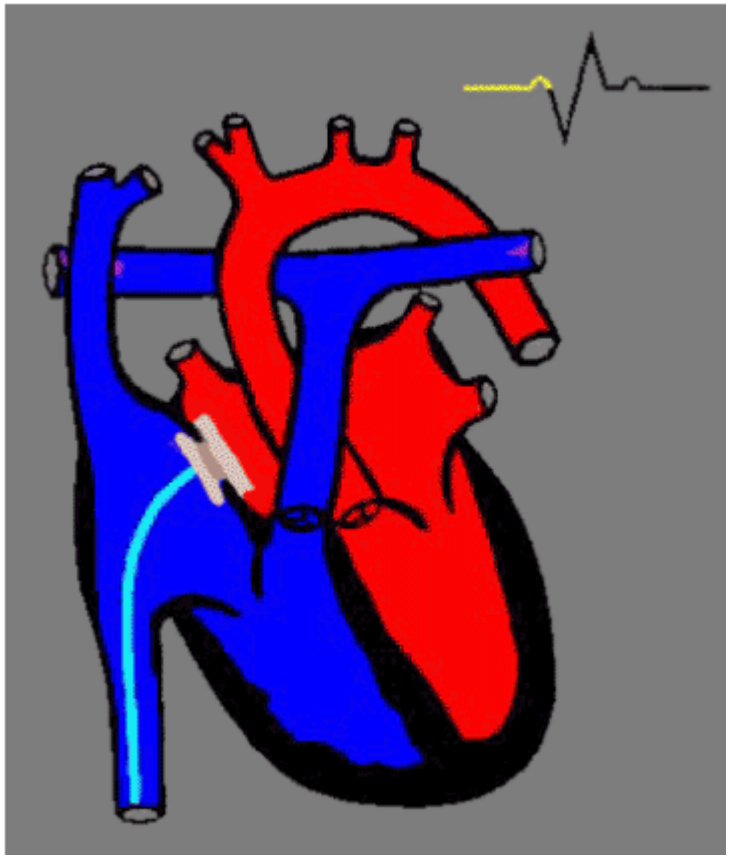
Mr D 45 years

- What's going on?
- Focal onset seizures
- What do you do?
  - Lamotrigine; increasing to 100 mg BD
  - Driving restriction

Mr D 45 years

- What about the PFO?
  - increased stroke risk
- L parietal infarct at 30 years
  - PFO & smoking only risk factors
  - L MCA TIA 2008
- Should the PFO have been closed?

PFO closure



Patent foramen ovale

CLOSURE 1 study

- 909 stroke & TIA patients
  - randomized to PFO closure or best medical therapy
  - no difference in stroke/TIA/death at 2 yrs
  - 3% major procedural complications
  - 6% had post procedure atrial fibrillation

N Eng J Med 2012; 366:991

Patent foramen ovale

RESPECT study

- 980 stroke patients (took 69 centres 8 yrs)
- randomized to PFO closure or best medical therapy
- 25 strokes (2.5%) over 8 years
  - intention to treat
    - 9 strokes closed vs 16 medical p=0.08
  - per protocol
    - 6 strokes closed vs 14 medical p=0.03
- Not a clinically meaningful difference