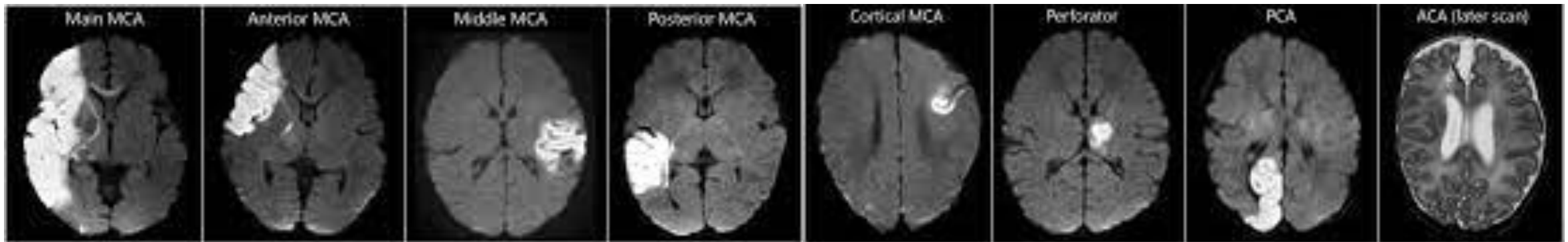# Ischemic Stroke prevention

The 5th Family Medicine Review Course

Athari Salmeen

Stroke neurologist, JAH

- No disclosure

Objectives

A. Stroke classification

B. Secondary prevention

C. Post-stroke sequelae

Stroke/TIA

- Type of stroke
- Mechanism of stroke

Stroke risk factors
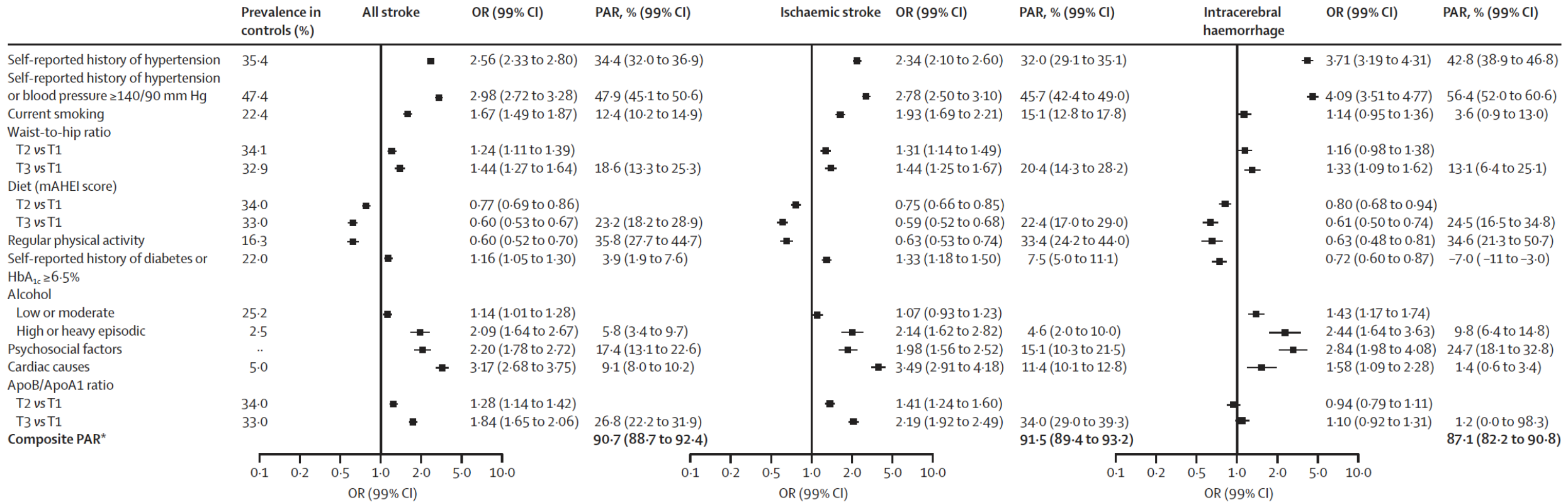
- History
- Investigations
- Optimizing targets

Post-stroke sequelae

- History and examination
- Investigations
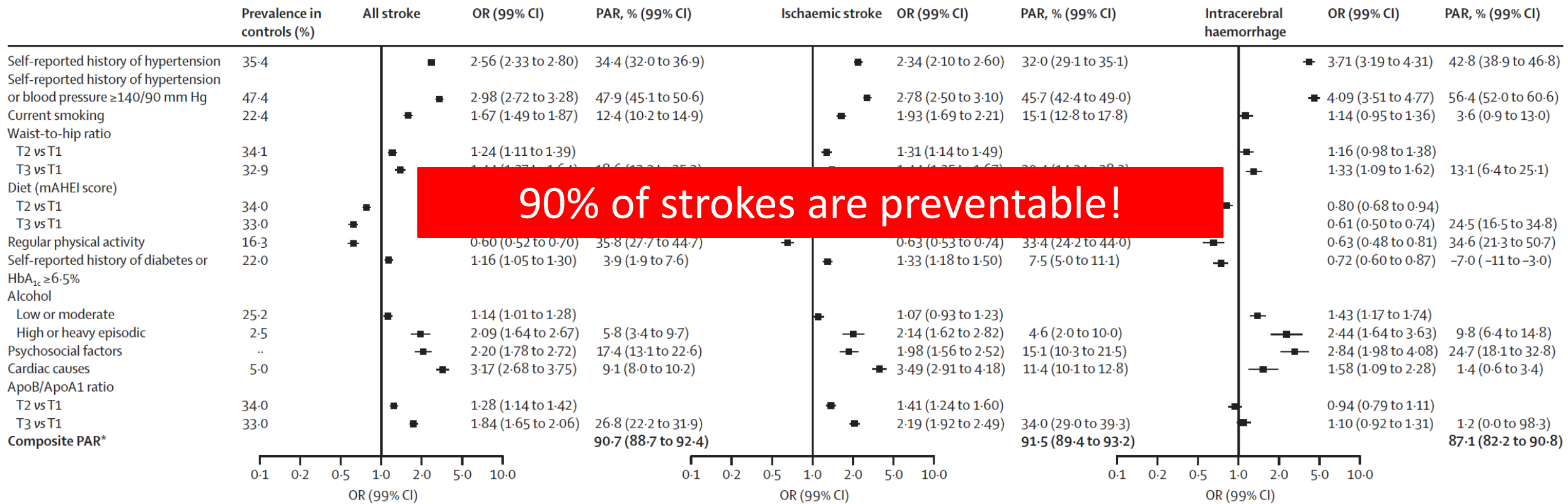- Management (including referrals)

Global and regional effects of potentially modifiable risk factors associated with acute stroke in 32 countries (INTERSTROKE): a case-control study

Martin J O'Donnell, Siu Lim Chin, Sumathy Rangarajan, Denis Xavier, Lisheng Liu, Hongye Zhang , Purnima Rao-Melacini, Xiaohe Zhang,
Prem Pais, Steven Agapay, Patricio Lopez-Jaramillo, Albertino Damasceno, Peter Langhorne, Matthew J McQueen, Annika Rosengren,
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Zvonko Rumboldt, Shahram Oveisgharan, Fawaz Al Hussain, Daliwonga Magazi, Yongchai Nilanont, John Ferguson, Guillaume Pare, Salim Yusuf;
on behalf of the INTERSTROKE investigators*

	Prevalence in controls (%)	All stroke	OR (99% CI)	PAR, % (99% CI)	Ischaemic stroke	OR (99% CI)	PAR, % (99% CI)	Intracerebral haemorrhage	OR (99% CI)	PAR, % (99% CI)
Self-reported history of hypertension	35·4		2·56 (2·33 to 2·80)	34·4 (32·0 to 36·9)		2·34 (2·10 to 2·60)	32·0 (29·1 to 35·1)		3·71 (3·19 to 4·31)	42·8 (38·9 to 46·8)
Self-reported history of hypertension or blood pressure ≥140/90 mm Hg	47·4		2·98 (2·72 to 3·28)	47·9 (45·1 to 50·6)		2·78 (2·50 to 3·10)	45·7 (42·4 to 49·0)		4·09 (3·51 to 4·77)	56·4 (52·0 to 60·6)
Current smoking	22·4		1·67 (1·49 to 1·87)	12·4 (10·2 to 14·9)		1·93 (1·69 to 2·21)	15·1 (12·8 to 17·8)		1·14 (0·95 to 1·36)	3·6 (0·9 to 13·0)
Waist-to-hip ratio										
T2 vs T1	34·1		1·24 (1·11 to 1·39)			1·31 (1·14 to 1·49)			1·16 (0·98 to 1·38)	
T3 vs T1	32·9		1·44 (1·27 to 1·64)	18·6 (13·3 to 25·3)		1·44 (1·25 to 1·67)	20·4 (14·3 to 28·2)		1·33 (1·09 to 1·62)	13·1 (6·4 to 25·1)
Diet (mAHEI score)										
T2 vs T1	34·0		0·77 (0·69 to 0·86)			0·75 (0·66 to 0·85)			0·80 (0·68 to 0·94)	
T3 vs T1	33·0		0·60 (0·53 to 0·67)	23·2 (18·2 to 28·9)		0·59 (0·52 to 0·68)	22·4 (17·0 to 29·0)		0·61 (0·50 to 0·74)	24·5 (16·5 to 34·8)
Regular physical activity	16·3		0·60 (0·52 to 0·70)	35·8 (27·7 to 44·7)		0·63 (0·53 to 0·74)	33·4 (24·2 to 44·0)		0·63 (0·48 to 0·81)	34·6 (21·3 to 50·7)
Self-reported history of diabetes or HbA$_{1c}$ ≥6·5%	22·0		1·16 (1·05 to 1·30)	3·9 (1·9 to 7·6)		1·33 (1·18 to 1·50)	7·5 (5·0 to 11·1)		0·72 (0·60 to 0·87)	−7·0 (−11 to −3·0)
Alcohol										
Low or moderate	25·2		1·14 (1·01 to 1·28)			1·07 (0·93 to 1·23)			1·43 (1·17 to 1·74)	
High or heavy episodic	2·5		2·09 (1·64 to 2·67)	5·8 (3·4 to 9·7)		2·14 (1·62 to 2·82)	4·6 (2·0 to 10·0)		2·44 (1·64 to 3·63)	9·8 (6·4 to 14·8)
Psychosocial factors	··		2·20 (1·78 to 2·72)	17·4 (13·1 to 22·6)		1·98 (1·56 to 2·52)	15·1 (10·3 to 21·5)		2·84 (1·98 to 4·08)	24·7 (18·1 to 32·8)
Cardiac causes	5·0		3·17 (2·68 to 3·75)	9·1 (8·0 to 10·2)		3·49 (2·91 to 4·18)	11·4 (10·1 to 12·8)		1·58 (1·09 to 2·28)	1·4 (0·6 to 3·4)
ApoB/ApoA1 ratio										
T2 vs T1	34·0		1·28 (1·14 to 1·42)			1·41 (1·24 to 1·60)			0·94 (0·79 to 1·11)	
T3 vs T1	33·0		1·84 (1·65 to 2·06)	26·8 (22·2 to 31·9)		2·19 (1·92 to 2·49)	34·0 (29·0 to 39·3)		1·10 (0·92 to 1·31)	1·2 (0·0 to 98·3)
Composite PAR*				90·7 (88·7 to 92·4)			91·5 (89·4 to 93·2)			87·1 (82·2 to 90·8)

0·1 0·2 0·5 1·0 2·0 5·0 10·0
OR (99% CI)

0·1 0·2 0·5 1·0 2·0 5·0 10·0
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Diet (mAHEI score)										
T2 vs T1	34·0								0·80 (0·68 to 0·94)	
T3 vs T1	33·0			**90% of strokes are preventable!**					0·61 (0·50 to 0·74)	24·5 (16·5 to 34·8)
Regular physical activity	16·3		0·60 (0·52 to 0·70)	35·8 (27·7 to 44·7)		0·63 (0·53 to 0·74)	33·4 (24·2 to 44·0)		0·63 (0·48 to 0·81)	34·6 (21·3 to 50·7)
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Composite PAR*				**90·7 (88·7 to 92·4)**			**91·5 (89·4 to 93·2)**			**87·1 (82·2 to 90·8)**

OR (99% CI)   OR (99% CI)   OR (99% CI)

Case

62 years old male recently discharged from hospital for stroke

He presented for refill his prescription but while talking to the patient, he describes transient right face and arm weakness today morning

Past medical history: smoking, and coronary artery disease

Medications: aspirin, atorvastatin 10 mg

Review discharge summary:
  CT head: ischemic infarct in right pons.
  ECG: sinus rhythm
  HbA1c 6; LDL 2.5
  Carotid ultrasound: diffuse atherosclerotic changes bilaterally without significant stenosis.

How will you approach this patient with stroke?

Investigations	HbA1c, fasting glucose	Lipid profile	Cardiac work up ECG, 24h Holter, loop recorder Echocardiogram (±bubble)	**Vascular imaging Ultrasound carotid CTA arch to vertex MRA arch to vertex**	Others Toxicology Autoimmune (APLS) Hypercoagulable state OSA screen
Medications	anti-thrombotics (antiplatelet/anticoagulation)	statin, others	blood pressure medications	hypoglycemic agents	
Others	education	Lifestyle modification: weight loss, physical activity, alcohol consumption and smoking cessation	appropriate referrals		

Polypill

Case

62 years old male recently discharged from hospital for stroke

He presented for refill his prescription but while talking to the patient, he describes transient right face and arm weakness today morning

Past medical history:, smoking, and coronary artery disease

Medications: aspirin, atorvastatin 10 mg

Review his discharge summary:

CT head: ischemic infarct in right pons.

ECG: sinus rhythm

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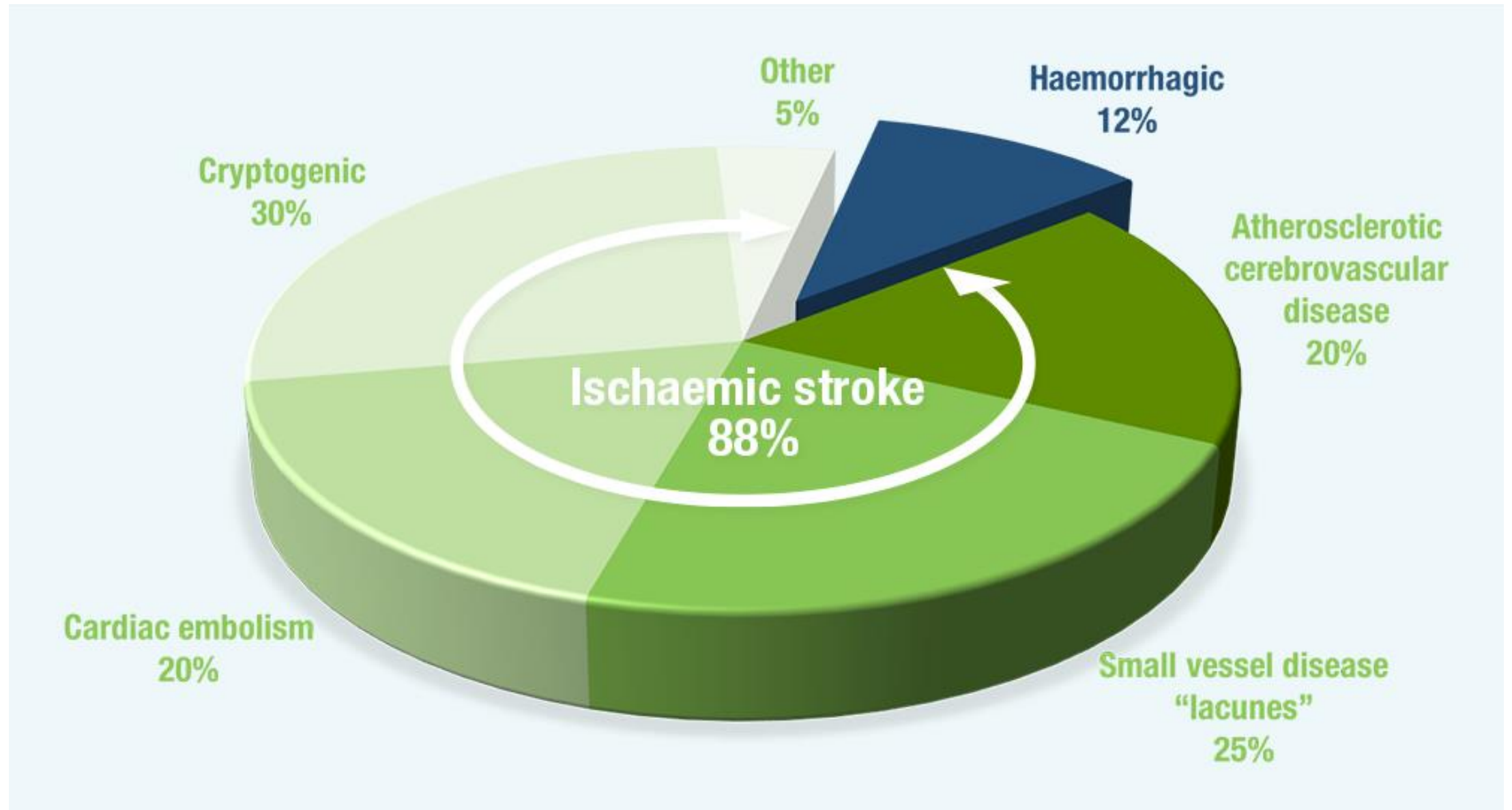
TABLE 1. TOAST Classification of Subtypes of Acute Ischemic Stroke

Large-artery atherosclerosis (embolus/thrombosis)*

Cardioembolism (high-risk/medium-risk)*

Small-vessel occlusion (lacune)*

Stroke of other determined etiology*

Stroke of undetermined etiology

   a. Two or more causes identified

   b. Negative evaluation

   c. Incomplete evaluation

TOAST, Trial of Org 10172 in Acute Stroke Treatment.
*Possible or probable depending on results of ancillary studies.

TABLE 3. TOAST Classification of High- and Medium-Risk Sources of Cardioembolism

High-risk sources
   Mechanical prosthetic valve
   Mitral stenosis with atrial fibrillation
   Atrial fibrillation (other than lone atrial fibrillation)
   Left atrial/atrial appendage thrombus
   Sick sinus syndrome
   Recent myocardial infarction (<4 weeks)
   Left ventricular thrombus
   Dilated cardiomyopathy
   Akinetic left ventricular segment
   Atrial myxoma
   Infective endocarditis
Medium-risk sources
   Mitral valve prolapse
   Mitral annulus calcification
   Mitral stenosis without atrial fibrillation
   Left atrial turbulence (smoke)
   Atrial septal aneurysm
   Patent foramen ovale
   Atrial flutter
   Lone atrial fibrillation
   Bioprosthetic cardiac valve
   Nonbacterial thrombotic endocarditis
   Congestive heart failure
   Hypokinetic left ventricular segment
   Myocardial infarction (>4 weeks, <6 months)

TOAST, Trial of Org 10172 in Acute Stroke Treatment.

TABLE 3. TOAST Classification of High- and Medium-Risk

TABLE I—POTENTIAL BENEFITS OF SUBCLASSIFYING CEREBRAL INFARCTION

More accurate prediction of prognosis

Identification and modification of underlying pathophysiological process to reduce acute damage and risk of recurrent stroke

Planning immediate supportive care and longer term rehabilitation programme

Putting results of clinical trials into context of individual physician's practice

Enabling acute intervention trials to be done with the best chance of demonstrating benefit if present

Development of more sensitive measures of case-mix for comparative audit and contracting purposes

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Strok
a.
b.
c.
TC
*P

lation)

Myocardial infarction (>4 weeks, <6 months)

TOAST, Trial of Org 10172 in Acute Stroke Treatment.

Case

62 years old male

Past medical history: hypertension, dyslipidemia, smoking

He presented to ED with acute onset left face/arm/leg weakness. He was diagnosed with ischemic stroke.

He underwent investigations in hospital while being admitted and was referred to PMR for further rehabilitation.

You see him in your clinic for first follow up since discharge from hospital.

What's his likely stroke subtype?

Table 5. Stroke Syndromes

Syndrome	Localization	Symptoms
Major Cerebral Artery Syndromes		
Anterior cerebral artery	Median frontoparietal	Contralateral anesthesia, leg > arm hemiparesis, abulia; dominant hemisphere: mutism; nondominant hemisphere: acute confusional state; bilateral infarction: urinary incontinence, akinetic mutism
Middle cerebral artery, complete	Lateral frontoparietal, superior temporal	Contralateral hemianesthesia, hemiparesis, hemianopia with gaze preference; dominant hemisphere: aphasia and apraxia; nondominant hemisphere: aprosodia, hemineglect
Middle cerebral artery, superior division	Lateral frontal	Contralateral hemiparesis, expressive aphasia
Middle cerebral artery, inferior division	Lateral parietal and superior temporal	Contralateral hemianopia, receptive aphasia
Gerstmann	Dominant hemisphere angular gyrus area	Agraphia, acalculia, right-left confusion, finger agnosia, ideomotor apraxia
Distal posterior cerebral artery	Inferior temporal and occipital	Hemianopia
Alexia without agraphia	Dominant occipital lobe and splenium of corpus callosum	Alexia without agraphia
Anton	Bilateral occipital	Cortical blindness with denial of deficit
Balint	Bilateral parieto-occipital	Oculomotor apraxia, optic ataxia, simultagnosia
Recurrent artery of Heubner	Head of caudate and anterior limb of internal capsule	Contralateral face and arm weakness, motor aphasia
Anterior choroidal artery	Posterior limb of internal capsule, posterior corona radiata	Contralateral hemiparesis (severe), hemianesthesia, hemianopia (uncommonly)
Lacunar Syndromes		
Pure motor	Posterior limb of internal capsule or thalamus	Contralateral hemiparesis
Sensorimotor	Posterior limb of internal capsule or thalamus	Contralateral hemiparesis, hemisensory loss
Pure sensory	Posterior limb of internal capsule or thalamus	Contralateral hemisensory loss
Dejerine-Roussy	Thalamus	Contralateral hemisensory loss with hemibody pain
Hemiballismus	Subthalamic nucleus	Contralateral hemiballismus
Ataxic hemiparesis	Corona radiata, internal capsule, basal ganglia, or pons	Contralateral hemiparesis with prominent ataxia
Dysarthria–clumsy hand	Corona radiata, internal capsule, basal ganglia, or pons	Contralateral dysarthria and upper limb ataxia
Brainstem Syndromes		
Weber	Cerebral peduncle and ventral midbrain (sparing red nucleus and cerebellothalamic tract)	Ipsilateral oculomotor palsy, contralateral body weakness
Claude	Ventral midbrain and superior cerebellar peduncle (near red nucleus)	Ipsilateral oculomotor palsy, contralateral tremor
Benedikt	Cerebral peduncle and ventral midbrain (including red nucleus and cerebellothalamic tract)	Ipsilateral oculomotor palsy, contralateral body weakness and tremor
Locked-in	Bilateral median pontine	Quadriplegia with bulbar plegia sparing some eye movements
Marie-Foix	Lateral pons	Ipsilateral ataxia, contralateral weakness and loss of pain and temperature
Raymond	Ventral pons	Ipsilateral abducens palsy, contralateral hemiparesis
Millard-Gubler	Mid pons	Ipsilateral facial weakness, contralateral body weakness
Foville	Dorsal pons	Ipsilateral lateral gaze palsy and facial weakness
Dejerine	Medial medulla	Ipsilateral tongue weakness, contralateral hemiparesis and loss of vibration and proprioception
Wallenberg	Lateral medulla	Ipsilateral facial sensory loss, Horner's syndrome, palatal weakness, dysphagia and ataxia, contralateral body pain and temperature loss

Case

62 years old male

Past medical history: hypertension, dyslipidemia, smoking

He presented to ED with acute onset left face/arm/leg weakness. He was diagnosed with ischemic stroke. Pure motor syndrome

He underwent investigations in hospital while being admitted and was referred to PMR for further rehabilitation.

You see him in your clinic for first follow up since discharge from hospital.

- Clinic:
  - Compliance
  - Vitals/examination
  - Review investigations
  - *post-stroke sequelae*

	Nonmodifiable Risk Factors	Modifiable Risk Factors
Ischemic stroke	Age	Hypertension
	Sex	Current smoking
	Race/ethnicity	Waist-to-hip ratio
		Diet
		Physical inactivity
		Hyperlipidemia
		Diabetes mellitus
		Alcohol consumption
		Cardiac causes
		Apolipoprotein B to A1
	Genetics*	
Hemorrhagic Stroke	Age	Hypertension
	Sex	Current smoking
	Race/ethnicity	Waist-to-hip ratio
		Alcohol consumption
		Diet
	Genetics*	

Table 1. The Framingham Stroke Risk Profile: 10-Year Stroke Probability for Men and Women Aged 70 Y With Systolic Blood Pressure of 160 mm Hg

% Probability							
Men	8	15	18	30	40	60	85
Women	6	10	16	34	42	80	90
Impact of other risk factors							
Hypertension medication	None	+	+	+	+	+	+
Diabetes mellitus	None		+	+	+	+	+
Cigarette use	None			+	+	+	+
Cardiovascular disease	None				+	+	+
Atrial fibrillation	None					+	+
ECG_left ventricular hypertrophy	None						+

Hypertension	high BP in non hypertensive Intra-individual variability	**Target < 130/80 (neurologically stable patient)** ⭐
Diabetes mellitus	Duration of diabetes Prediabetes	**Target HbA1c <7%**
Dyslipidemia	Complex relation with stroke Hypertriglyceridemia	**Target LDL < 1.8 mmol/L (<70mg/dL)**
Lifestyle modification (sedentary behavior, diet, obesity, alcohol and smoking)	Diet BMI/waist to hip ratio physical activity Smoking cessation (alcohol/substance use) OCP or hormonal replacement therapy	**Mediterranean diet or high in fruits/vegetables** **Waist circumference of <88 cm for women and <102 cm for men, or BMI of 18.5 to 24.9 kg/m²** **Aerobic exercise 4 to 7 days per week, to accumulate at least 150 minutes per week in episodes of 10 minutes or more, in addition to routine activities of daily living**
OSA	Polysomnography calculating apnea-hypopnea index (AHI)	**CPAP improve sleep apnea, BP, sleepiness and other apnea related outcomes**
Antithrombotics	anti-platelet vs anticoagulation Contraindication	**Aspirin vs clopidogrel vs aspirin-dipyridamole** **Dual anti-platelet** **DOAC vs warfarin**

Case

59 years old women who presented with unilateral arm weakness associated with sensory symptoms in right face and arm of 1 hour duration

Past medical history: diabetes

She went to emergency department where she was evaluated

she was discharged after negative CT head. She was given aspirin. She did ECG that showed AF. Blood glucose 9 mmol/L

What's the likely diagnosis?
What's the likely underlying etiology?

Case

68 years old women who presented with unilateral arm weakness associated with sensory symptoms in right face and arm of 1 hour duration TIA or minor non-disabling stroke

Past medical history: diabetes

She went to emergency department where she was evaluated

she was **discharged** after negative CT head. She was given aspirin. She did ECG that showed AF. Blood glucose 9 mmol/L

List other cardioembolic source of stroke

List other cardioembolic source of stroke

- <u>Atrial fibrillation</u>
- Valvular disease
- LV thrombus
- Cardiomyopathy
- Patent foramen ovale
- Congenital heart disease
- Cardiac tumors

Valvular disease
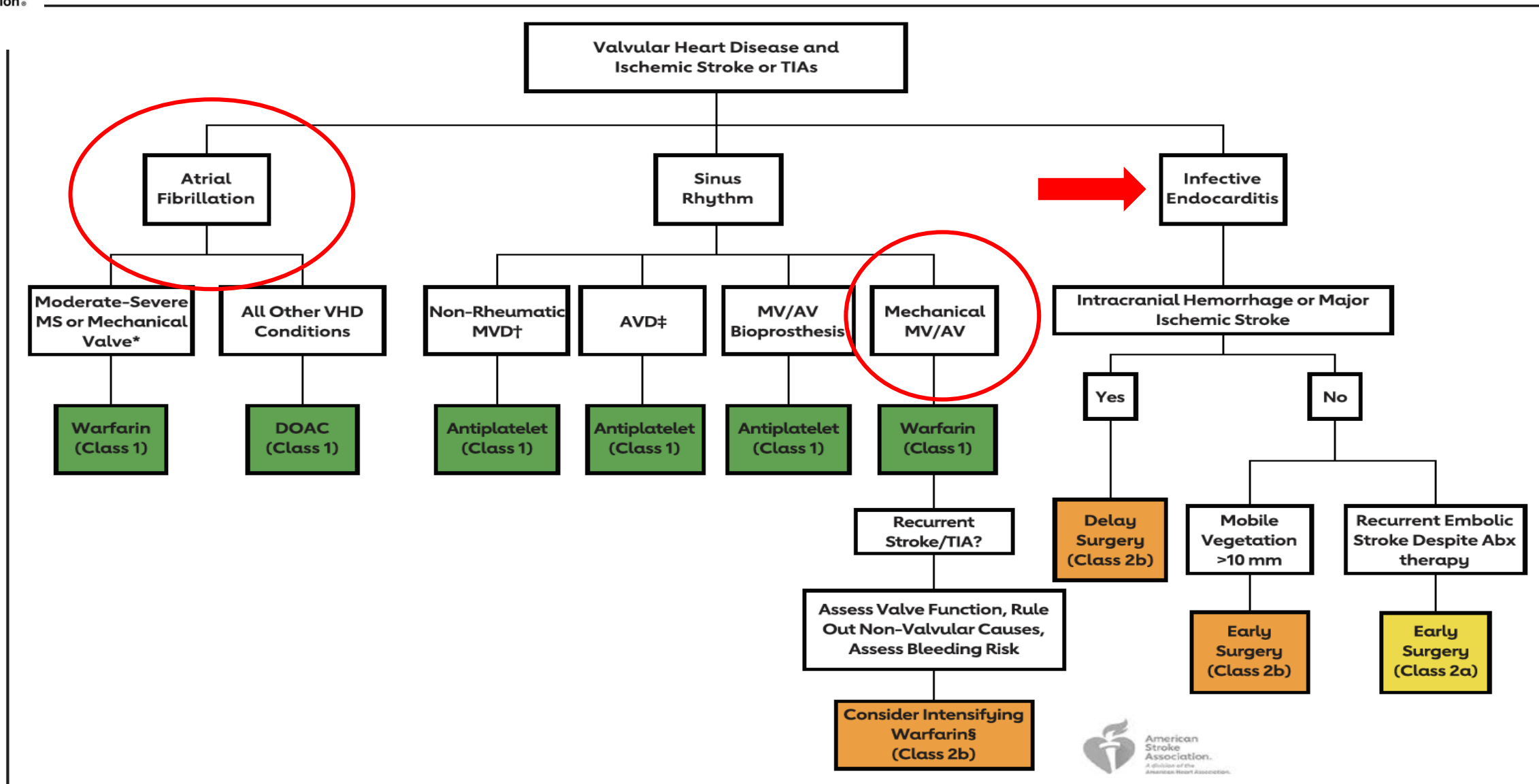
Case

59 years old women who presented with unilateral arm <mark>numbness</mark> associated with sensory symptoms in right face and arm <mark>5 minutes</mark> duration

Past medical history: diabetes

She went to emergency department where she was evaluated

she was discharged after negative CT head. She was given aspirin. She did ECG that showed AF. Blood glucose 9 mmol/L

What's the likely diagnosis?
What's the likely underlying etiology?

Risk Factor	Points	Score
Age		
≥ 60 years	1	
Blood pressure		
Systolic BP ≥ 140 mm Hg *OR* Diastolic BP ≥ 90 mm Hg	1	
Clinical features of TIA (*choose one*)		
Unilateral weakness with or without speech impairment *OR*	2	
Speech impairment without unilateral weakness	1	
Duration		
TIA duration ≥ 60 minutes	2	
TIA duration 10-59 minutes	1	
Diabetes	1	
Total ABCD² score	0-7	

ABCD² Score	2-day Stroke Risk	Comment
0-3	1.0%	Hospital observation may be unnecessary without another indication (e.g., new atrial fibrillation)
4-5	4.1%	Hospital observation justified in most situations
6-7	8.1%	Hospital observation worthwhile

- Low risk ABCD and ABCD2 scores
  - May have substantial stroke risk
  - May have other high-risk cause of stroke (high DWI signal, LAA, Afib)
  - 25% of strokes occurred in patients with ABCDs score < or = 4
  - Risk in low-risk patients was 5.9%
  - Low-risk ABCD<4 category
    - 5.8% had strokes within 7 days
- Prospective observational study
  - There was no relationship between ABCD2 score at presentation and subsequent stroke risk after TIA

Bhatt and Jani 2011

ABCD2

Risk Factor	Points	Score
Age		
≥ 60 years	1	
Blood pressure		
Systolic BP ≥ 140 mm Hg *OR* Diastolic BP ≥ 90 mm Hg	1	
Clinical features of TIA (*choose one*)		
Unilateral weakness with or without speech impairment *OR*	2	
Speech impairment without unilateral weakness	1	
Duration		
TIA duration ≥ 60 min		
TIA duration 10-59 m		
Diabetes		
Total ABCD² score		

- Low risk ABCD and ABCD2 scores

Does not incorporate variables known to predict short term risk of stroke
- DWI
- Large artery stenosis
- Atrial fibrillation

stroke (high D
ts with ABCD

- Prospective observational study
  - There was no relationship between ABCD2

ABCD² Score	2-day Stroke Risk	
0-3	1.0%	Hospital observation may be unnecessary without another indication (e.g., new atrial fibrillation)
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Case

72 years old male smoker presenting with 3 episodes of right arm shaking and confusion of 2 minutes duration.

Those episodes tend to occur mostly while standing.

He is awake during the spell, he can talk but he is not answering his family properly. He does have recall of those events after they stop. He thought his speech was normal. No history of generalized shaking. No previous history of seizure

What's the likely diagnosis?
What's the likely underlying etiology?

Extracranial carotid stenosis

- Revascularization AND medical management
- Revascularization
  - CEA
  - CAS
  - Extracranial to intracranial bypass for ICA occlusion has not ben demonstrated to reduce risk of recurrent stroke

- Medical management
  - Antiplatelet therapy recommended for symptomatic carotid stenosis
  - Antihypertensive therapy and statin recommended
  - Target LDL < 70 mg/dL

Carotid stenosis

- CEA preferred procedure for symptomatic carotid stenosis 70-99% with small but still significant benefit in 50-69% symptomatic stenosis
  - 16% absolute benefit over 5 years of CEA
  - Rothwell et al: mild benefit in patients with 50-69% ICA stenosis (4.6% over 5 yr)
    - NASCET analysis found no clear benefit of CEA in women and in patients with retinal ischemic events
- Preference for CEA in patients who undergo early revascularization
  - CEA associated with reduced complication rate relative to CAS in patients who undergo procedure within 1 week of stroke or TIA
  - Post hoc analysis: greater benefit of CEA when surgery was done in patients who were enrolled within 2 weeks of their last nondisabling ischemic event (if patient suitable for operation, early CEA preferred)

Surgery should typically be done within 2 weeks of index event

CEA vs CAS

- CAS was associated with higher periprocedural stroke rate
  - similar results have been seen with CEA and CAS beyond immediate periprocedural period.
  - Stenting in patients eligible for CEA shown consistently higher risk of periprocedural stroke than CEA (possible exception of patients < 70 years)
    - Consider patient age in selection of procedure
- Carotid stenting
  - unfavorable anatomy
  - restenosis of CEA
  - high perioperative risk
  - previous radiotherapy
- Transcarotid stenting: lower perioperative stroke risk than transfemoral carotid stenting

Optimal Medical Management of Asymptomatic Carotid Stenosis

Daniel G. Hackam 🄔, BSc, MD, PhD

Clinical/imaging features associated with increased risk of late stroke in patients with asymptomatic 50-99% stenosis treated medically

- Vulnerable plaque: incidence rate of 4.3% per year combined ipsilateral stroke or TIA
- Presence of microemboli on transcranial doppler monitoring (15.6% during first year follow up vs 1%)
- Other high risk features:
    - Plaque echolucency on duplex ultrasound
    - Progression in severity of ACS
    - Silent embolic infarcts on brain imaging
    - Reduced cerebrovascular reserve
    - Large juxta-luminal hypoechoic area
    - Intraplaque hemorrhage
    - Carotid ulceration
- *Ongoing trials to guide revascularization*

Modality	Details
Diet	Mediterranean diet
Exercise	Moderate intensity (such as brisk walking, jogging, swimming, or cycling) 4 to 7 days per week, for a total of at least 150 min per week
Smoking	Smoking cessation with varenicline or bupropion and nicotine replacement therapy
Antithrombotic therapy	Options
	ASA 75–325 mg/d
	ASA+rivaroxaban 2.5 mg bid
	Clopidogrel 75 mg OD or ticagrelor 90 mg BID (if ASA-intolerant or allergic to ASA)
Lipid-lowering therapy	Goal LDL <1.8 mmol/L (70 mg/dL; <1.4 mmol/L [54 mg/dL] for very high risk)
	High-dose statin
	Add ezetimibe or
	Add PCSK9 inhibitor
	Consider icosapent ethyl (high-dose EPA) for fasting triglycerides 1.52–5.63 mmol/L
Antihypertensive therapy	Goal BP <130/80
	Prefer ACE inhibitor/ARB due to high prevalence of renovascular hypertension
	May require combination therapy
Glucose-lowering therapy	Goal HbA1c <7.0%
	Metformin, GLP-1 agonist, SGLT-2 antagonist are preferred
Consider referral for carotid revascularization	TCD+ for microemboli, plaque ulcer, reduced cerebrovascular reserve, intraplaque hemorrhage, silent embolic infarcts on CT/MRI, plaque echolucency, large JBA, progression in severity of stenosis

Intracranial Large artery atherosclerosis

- Common cause of stroke worldwide with **high rate of recurrent stroke**
  - risk of recurrent stroke from ICAS extends well beyond 30 days

- Management plan:
  - Antiplatelet*
  - Blood pressure control (sBP <140 mm Hg)
    - Patients with documented hemodynamic impairment, or those treated to sBP <120 mmHg early after stroke, may not benefit and the lower threshold associated with increased stroke risk is not known
  - High intensity statin; target LDL
    - Optimal target LDL for patients with ICAS not determined, WASID and SAMMPRIS post hoc analyses show lower LDLs associated with lower vascular event rates in patients with ICAS
    - TST trial <70 with athero
  - Moderate physical activity at least 3-5 times per week
- Given lack of efficacy data, PTAS is considered investigational in this population
  - No RCTs have directly compared PTAS with medical therapy in pts with symptomatic 50-69% stenosis

Case

49 years old woman with depression, hypertension and diabetes presents to the ED with sensory deficits affecting her right face/arm/trunk and leg.

The symptoms started the night prior and peaked today morning on presentation. There are no motor deficit

What's the likely diagnosis?
What's the likely underlying etiology?

Case

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Small vessel disease

- 20-30% of ischemic stroke
- Subcortical infarcts < 15 mm in diameter or lacunes in patients presenting with lacunar stroke syndromes
- Small vessel disease and lacunar strokes are leading cause of vascular dementia and vascular cognitive impairment
- BP control and antiplatelet
  - In patients with ischemic stroke related to small vessel disease, usefulness of cilostazol for secondary stroke prevention is uncertain

Case

You are in clinic. You see a 34 years old man complaining of vertigo and neck pain after riding "a very wild" roller coaster last night. The examination demonstrates anisocoria with mild ptosis on the left side, nystagmus and left sided ataxia.

What is the next step?

Risk For Recurrent Stroke	Time from Stroke Symptom Onset to Healthcare Presentation	Presenting Symptoms	When Patients Should be Seen by Healthcare Professional	Where Patients Should be Seen	Tests to be Done on Initial Assessment
Very HIGH RISK	Within 48 hours	- Transient, fluctuating or persistent unilateral weakness (face, arm and/or leg) - Transient, fluctuating or persistent speech disturbance/aphasia. - Fluctuating or persistent symptoms **without motor weakness or speech disturbance** (e.g. hemi-body sensory symptoms, monocular visual loss, hemifield visual loss, ± other symptoms suggestive of posterior circulation stroke such as diplopia, dysarthria, and/or ataxia).	Immediately	Emergency Department [ideally ED with brain imaging onsite and access to alteplase (tPA)]	CT/CTA or MRI/MRA (aortic arch to vertex), ECG, Lab Work (Table 3)
HIGH RISK	Between 48 hours and 2 weeks	- Transient, fluctuating or persistent unilateral weakness (face, arm, and/or leg), or speech disturbance/aphasia	As soon as possible, ideally within 24 hours	Stroke Prevention Clinic with Neurologist or Stroke Specialist, Nurse Practitioner	CT/CTA or MRI/MRA (aortic arch to vertex), ECG, Lab Work (Table 3)
Moderate (INCREASED) RISK	Between 48 hours and 2 weeks	- Fluctuating or persistent symptoms *without motor weakness* or speech disturbance (e.g., hemibody sensory symptoms, monocular vision loss, binocular diplopia, hemifield vision loss, or ataxia)	As soon as possible, ideally within 2 weeks	Stroke Prevention Clinic with Neurologist or Stroke Specialist, Nurse Practitioner	CT/CTA or MRI/MRA (aortic arch to vertex), ECG, Lab Work (Table 3)
LOWER RISK	More than 2 weeks	- Any typical or atypical symptoms of stroke or transient ischemic attack	Ideally within 1 month	Ambulatory Clinic with access to Neurologist or Stroke Specialist, Nurse Practitioner	As appropriate based on assessment by health care team

Case

40 years old female with past medical history significant for provoked right leg DVT 2 years ago (not on current antithrombotic).

She presented with acute onset left leg weakness. She had a recent flight from Australia.

Examination: Leg is normal temperature and calf is of normal size.

She has mild weakness (4+/5) of her left shoulder abduction.

She is weak (4/5) in her hip flexion, knee flexion and dorsiflexion

What's the likely diagnosis?
What's the likely underlying etiology?

Stroke in young

- Age definition
  - less than **50 years**
  - less than 45-65

- Acute management
  - IVT/EVT, admission, hemicraniectomy if malignant MCA infarction

- Diagnostic process? ➡

- Blood work:
  - CBC, RFT, coagulation profile
  - Lipid profile
  - HbA1c, fasting glucose
  - **Toxicology screen (blood and urine)**
  - **Blood c/s x3 q1h apart, CRP/ESR**
- Vessel imaging: CTA or MRA with contrast
- **Cardiac work up including echocardiogram with bubble study (TEE preferred over TTE)**
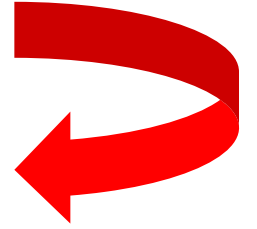
Carotid duplex is NOT sufficient in stroke in young

Vascular risk factors	Hypertension. Hypercholesterolemia. Diabetes mellitus. Smoking. Obesity (waist to hip ratio) and low physical activity. Psychosocial factors
Migraine	Controversial
Malignancy	50% higher than expected incidence of ischemic stroke after malignancy (age 15-39 yo) 8% found occult malignancy in young adults with stroke (4% diagnosed pre-stroke, 4% median time from stroke to post stroke cancer 6.7 years)
Illicit drug use	Cannabis, opioids, ecstasy, LSD Cocaine and amphetamine
Pregnancy and puerperium	
Genetic risk factors	
cardioembolic	PFO, cardiomyopathy, congenital heart disease Low incidence of AF
Vasculopathy	cervical artery dissection, vasculitis, moyamoya
RCVS	
ESUS	
Others	metabolic/mitochondrial (Fabry disease, MELAS) Hematologic (sickle cell disease)

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Traditional risk factors combined account for 80% of all ischemic stroke in young

Patients age 18-60 y with non-lacunar stroke and PFO

↓

Evaluation for cause by combined neurology/cardiology team →

- MRI of brain confirming ischemic stroke
- MRI or CT of intracranial and extracranial vessels with contrast
- Contrasted echocardiography or other advanced cardiac imaging
- Early evaluation for DVT, including lower extremity doppler and consideration of pelvic MRV
- Prolonged cardiac monitoring to screen for intermittent atrial fibrillation
- Consider toxicology screen, C-reactive protein, antiphospholipid antibodies, other labs as indicated
- Low threshold for blood cultures, hypercoagulable evaluation, vasculitis workup including catheter angiogram and LP, consideration of rare causes of stroke including genetic etiologies

◇ **Alternative etiology found?**

YES → **Treat underlying etiology**

NO → **Potential paradoxical embolism**

↓

◇ **Atrial septal aneurysm or large right-to-left shunt**

YES →

High Risk PFO

PFO closure is reasonable

Factors reducing potential benefit of closure:

- Low RoPE score, including older age and multiple risk factors
- Need for anticoagulation

(Class 2a)

NO →

Low Risk PFO

Benefit of PFO closure is not well established

Factors increasing potential benefit of closure:

- High RoPE score, including young age and no risk factors
- History of DVT or prothrombotic condition
- Prior non-lacunar stroke or cortical TIA
- Failure of antiplatelet treatment

(Class 2b)

Case

62 years old male recently discharged from hospital for stroke

He presented for refill his prescription but while talking to the patient, he describes transient right face and arm weakness today morning

Past medical history: smoking, and coronary artery disease

Medications: aspirin, atorvastatin 10 mg

Review discharge summary:
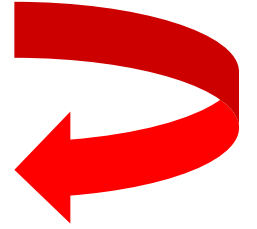>   CT head: ischemic infarct in right pons.
>   ECG: sinus rhythm
>   HbA1c 6; LDL 2.5
>   Carotid ultrasound: diffuse atherosclerotic changes bilaterally without significant stenosis.

How will you approach this patient with stroke?

Case

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Case

50 years old female

Past medical history: migraine with aura, hypertension

One week ago, patient diagnosed with left anterior cerebral artery stroke

She is on apixaban 5 mg

She is a lawyer (sick leave currently), she is a mother of 3 children (youngest 18 years old)

How will you approach this patient with stroke?

	Risk factors
Anxiety[110]	Lower educational level, history of depression, unemployment, and alcohol consumption
Central post-stroke pain[111]	Severe infarctions with haemorrhagic transformation
Cognitive impairment[112,113]	Supratentorial infarction
Depression[110]	Lower educational level and unemployment
Mortality[10,34]	Older age (40–50 years), male sex, history of cardioembolic stroke, and coexisting cause of stroke
Post-stroke epilepsy[114]	Severity of stroke, history of stroke caused by large-artery atherosclerosis, early seizures (within 7 days of stroke), cortical involvement, and territory of middle cerebral artery involvement
Post-stroke fatigue[115]	Post-stroke depressive symptoms, anxiety, and recurrent cerebrovascular events
Recurrent stroke[12,34]	Older age (40–50 years), male sex, history of cardiovascular risk factors, atherothrombotic stroke, cardioembolic stroke, and lacunar stroke
Risk of suicide attempts[116,117]	Male sex, living alone at stroke onset, low income, lower educational level, severe stroke (being drowsy or unconscious on hospital admission), and post-stroke depression
Sexual dysfunction[118]	Depression and use of angiotensin-converting-enzyme inhibitors
Unemployment[3,119]	Higher NIHSS at admission, a longer duration of follow-up, female sex, self-employment before stroke, and lower occupational status

Approach to patient with stroke?

Prevent another event

- Identify stroke type

- Review patient's risk factors
  - Review patient's compliance and risk factors management plan

- Screen for other risk factors
  - Control other risk factors

Sequelae of stroke

- Mood/depression and fatigue

- Disability assessment
  - Rehab (mobility/motor skill/speech and swallowing)
  - Driving and sexual relationship

- Caregiver burden

- Seizure post stroke and other stroke related complications

It's ok to give a sick leave to patient with stroke even if we think clinically patient is intact

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Case

50 years old female

Past medical hist

One week ago, p   rtery stroke

She is on apixaba

She is a lawyer (s   ren (youngest
18 years old)

A. Stroke classification: Anterior cerebral artery
   (atherosclerosis vs embolic)

B. Stroke risk factors: known HTN. Review
   other risk factors. Why apixaban? OCP?

C. Post-stroke sequalae: patient is young.
   Review motor status, review cognitive
   status. Relation with family

Intracerebral hemorrhage

Recognize mechanism of ICH

- CT angiogram
  - Exclude most aneurysms, AVM
- MRI with contrast at 3 months
  - Ensure evolution of hematoma
  - Exclude underlying mass lesion or vascular malformation that was initially compressed by hematoma
  - underlying deep perforating vasculopathy or amyloid angiopathy
- In absence of evidence of angiopathy, further investigations with catheter angiography might be warranted to exclude small vascular malformation

Schrag, M. et al. J Am Coll Cardiol. 2020;75(15):1819–31.
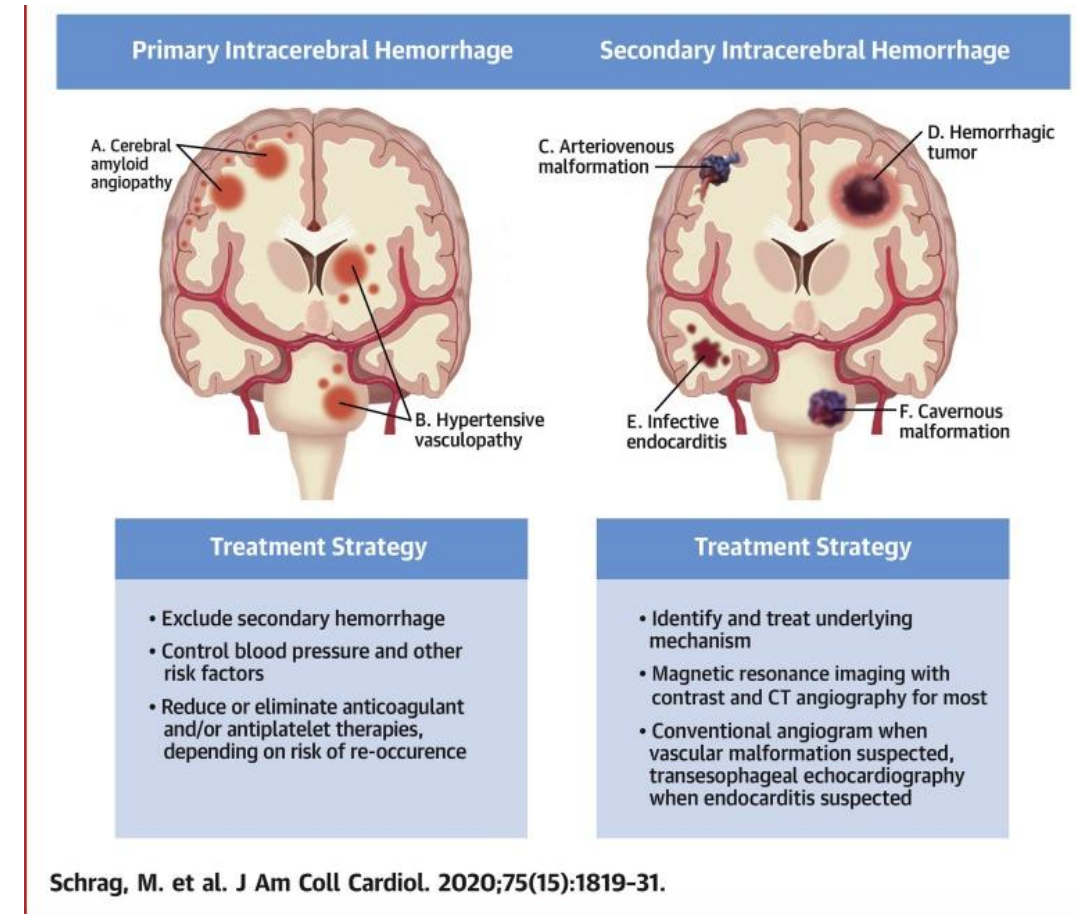
Intracerebral hemorrhage

- Lowering BP
  - Reduction of ~ 9mm Hg in SBP associated with 50% (95% CI 26-67) relative reduction in risk of intracerebral hemorrhage, with no lower threshold for benefit identified

- Antithrombotic after ICH
  - RESTART trial – restarting antiplatelets associated with non-significant reduction in recurrent ICH events (adjusted HR 0.51 (95% CI 0.25-1.03, P=0.06) → substantial increase in bleeding related to antiplatelet use appears unlikely
  - Ongoing trials of restarting AC in AF with ICH (balance of risk might favor AC overall)
    - There is no benefit of using antiplatelet agent rather than AC
  - Patients with CAA, large number of microbleeds and cortical hemosiderosis on MRI most likely indicated group high risk for restarting AC
  - Time to restart AC 4-8 weeks might be reasonable.
    - Optimal balance of risks occurred with recommencement 1-2 weeks following ICH
  - NOAC favored over warfarin

Thank you

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American Stroke Association
A division of the American Heart Association.
Together to End Stroke®

American Stroke Association®

ESO
EUROPEAN STROKE ORGANISATION

Canadian Stroke Best Practices

Secondary Stroke Prevention Checklist

Taking Steps to *Prevent Another Stroke*

QUESTIONS	YES	RISK / RECOMMENDATION
1. Has the patient had a **stroke** or **TIA**?	☐	Approximately 23% of strokes each year are recurrent. Risk of recurrent stroke or TIA is high (5% at 1 year) but can be mitigated with appropriate prevention strategies.
2. Does the patient need to undergo **diagnostic evaluation** to determine the etiology of the stroke?	☐	Given the relatively high risk of recurrent stroke, a diagnostic evaluation is recommended for gaining insights into the etiology and planning optimal prevention strategies, with testing completed or underway within 48 hours of stroke symptom onset.
3. Does the patient have **blood pressure** greater than 130/80 mm Hg?	☐	Treatment of hypertension is possibly the most important intervention for secondary prevention of ischemic stroke. An office blood pressure goal of <130/80 mm Hg is recommended for most patients. Antihypertensive medication is useful.
4. Has the patient been screened for **diabetes mellitus** (DM)?	☐	DM is an independent risk factor for stroke recurrence. After a TIA or ischemic stroke, all patients should be screened for DM. New cases of Type 2 DM have been detected in about 11.5% of patients presenting with acute ischemic stroke and prediabetes in 36.2%. For most patients, achieving a goal of hemoglobin A1c ≤7% is recommended.
5. Does the patient's **cholesterol level** need to be lowered?	☐	Patients with ischemic stroke and no known coronary heart disease, no major cardiac sources of embolism, and LDL-C >100 mg/dL, should be treated with atorvastatin 80 mg daily to reduce risk of stroke recurrence. Patients with ischemic stroke or TIA and atherosclerotic disease should be treated with a statin and also ezetimibe, if needed, to a goal LDL-C of <70 mg/dL.
6. Is the patient **physically inactive**?	☐	Regular physical activity reduces stroke risk, positively impacts stroke risk factors and aids in recovery. Patients who are able should engage in at least moderate-intensity aerobic activity for a minimum of 10 minutes 4 times a week or vigorous-intensity aerobic activity for a minimum of 20 minutes twice a week. For patients with deficits that impair their ability to exercise, a supervised exercise program can be beneficial.
7. Does the patient **smoke**?	☐	Smoking approximately doubles the risk of stroke. Counseling with or without drug therapy should be recommended to help patients quit smoking.
8. Does the patient need to make **dietary changes**?	☐	It is reasonable to recommend that patients follow a diet emphasizing vegetables, fruits, whole grains, low-fat dairy products, fish, legumes and nuts, and limits sodium, sweets and red meats.
9. Does the patient drink large amounts of **alcohol**?	☐	Patients who are heavy drinkers should be counseled to eliminate or reduce their consumption of alcohol. Light to moderate amounts of alcohol consumption (up to 2 drinks per day for men and up to 1 drink per day for nonpregnant women) may be reasonable.
10. Has the patient been screened for or diagnosed with **atrial fibrillation** (AF)?	☐	AF is a powerful risk factor for ischemic stroke, increasing the risk 4- to 5-fold. In patients with non-valvular AF or atrial flutter and stroke or TIA, oral anticoagulation is recommended.
11. Is this an **ischemic stroke** or **TIA** patient who should be on aspirin or other antiplatelet therapy?	☐	In patients with noncardioembolic ischemic stroke or TIA, antiplatelet therapy is indicated in preference to oral anticoagulation. More specifically, Guidelines recommend aspirin 50-325mg daily, or clopidogrel 75mg, or the combination of aspirin 25mg and extended release dipyridamole 200mg twice daily. Dual antiplatelet therapy is only recommended short-term and in very specific patients.
12. Does the patient have **sleep apnea**?	☐	Sleep apnea affects about 38%-40% of patients with stroke. Treatment with positive airway pressure can be beneficial.