What's new in assessment, triage and treatment of TIA?

"Holding back the floodgates – Approaches to stroke prevention"

Dr. Albert Jin PhD MD FRCPC
Associate Professor, Queen's University
Department of Medicine, Division of Neurology

February 16, 2022

Disclosures

- I have no commercial conflicts of interest or commercial disclosures
- I receive a stipend for my role as Regional Medical Director of the Stroke Network of Southeast Ontario
- I am the site PI for the ESCAPE-NEXT trial. I do not receive any money for this.

TIA: Clinical vs imaging assessment

- TIA has traditionally been defined as a neurological deficit which is referable to a vascular origin lasting less than 24 hours.

- About half of these cases actually have MRI evidence of tissue damage, even when symptoms had resolved.

- Conversely, some cases with deficits lasting more than 24 hours have no MRI lesion

TIA: Current definitions

- American Heart Association defines TIA as a transient episode of neurological dysfunction caused by focal brain, spinal cord or retinal ischemia, without acute infarction and without a time limit specified for the symptom duration

- Canadian Stroke Best Practices define TIA the same way except that if the symptoms last more than 24 hours the episode is called a “minor stroke”
  - Is it really minor if the symptoms are disabling?

What to do with the TIA/minor stroke patient who comes to your office?

- If the episode happened less than 48 hours ago, send the patient to the Emergency Department for rapid assessment.
  - CT angiography to rule out critical stenosis which would require urgent CEA

- If the episode happened more than 48 hours ago, send a referral to the Stroke Prevention Clinic
  - Initial assessment and contact with a stroke physician is typically within 72 hours.

Effect of urgent treatment of transient ischaemic attack and minor stroke on early recurrent stroke (EXPRESS study): a prospective population-based sequential comparison

Peter M Rothwell, Matthew F Giles, Arvind Chandratheva, Lars Marquardt, Olivia Geraghty, Jessica N E Redgrave, Caroline E Lovelock, Lucy E Binney, Linda M Bull, Fiona C Cuthbertson, Sarah J V Welch, Shelley Bosch, Faye Carasco-Alexander, Louise E Silver, Sergei A Gutnikov, Ziyah Mehta, on behalf of the Early use of Existing Preventive Strategies for Stroke (EXPRESS) study

Lancet Neurol 2009; 8: 235–43

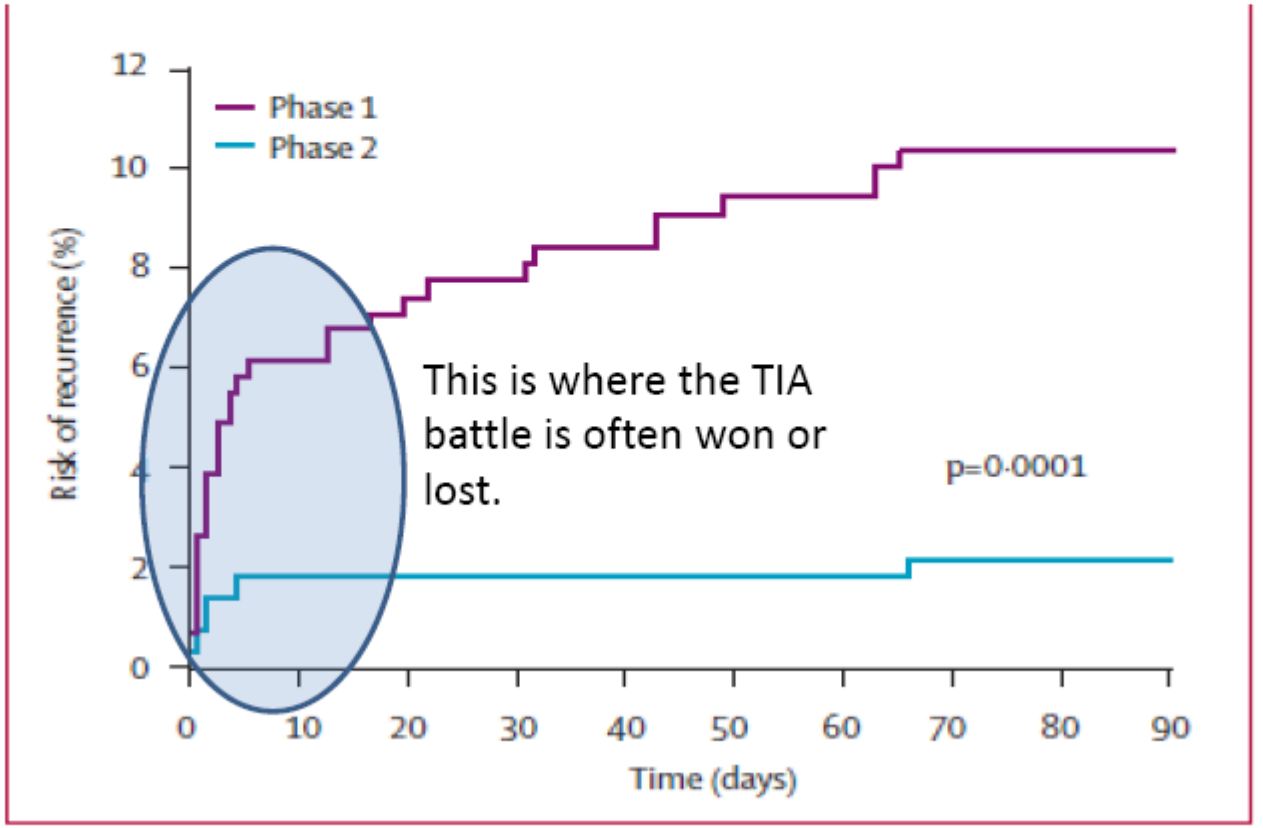


Figure 2: **Risk of recurrent stroke after first seeking medical attention in all patients with TIA or stroke who were referred to the study clinic**

But not all TIA patients will go on to have a stroke. So how do we identify those who are most at risk?

BMJ 2021;372:n49

Prospective validation of Canadian TIA Score and comparison with ABCD2 and ABCD2i for subsequent stroke risk after transient ischaemic attack: multicentre prospective cohort study

Jeffrey J Perry,[1,2] Marco L A Sivilotti,[3] Marcel Émond,[4,5] Ian G Stiell,[1,2] Grant Stotts,[6] Jacques Lee,[7,8] Andrew Worster,[9] Judy Morris,[10] Ka Wai Cheung,[11] Albert Y Jin,[12] Wieslaw J Oczkowski,[13] Demetrios J Sahlas,[13] Heather E Murray,[3] Ariane Mackey,[4,14] Steve Verreault,[4,14] Marie-Christine Camden,[4,14] Samuel Yip,[15] Philip Teal,[15] David J Gladstone,[16] Mark I Boulos,[16] Nicolas Chagnon,[17] Elizabeth Shouldice,[18] Clare Atzema,[8] Tarik Slaoui,[10] Jeanne Teitlebaum,[10] Kasim E Abdulaziz,[2] Marie-Joe Nemnom,[2] George A Wells,[2] Mukul Sharma[13]

- The Canadian TIA Score was previously derived from 4000 patients at 8 Canadian hospital emergency departments
- Predicts risk of subsequent stroke, risk range 0.01% to 28%
- Score ranges from -3 to 23

Table 1 | Canadian TIA Score

Items	Points
Clinical findings:	
1) First transient ischaemic attack (in lifetime)	2
2) Symptoms ≥10 minutes	2
3) Past history of carotid stenosis	2
4) Already on antiplatelet therapy	3
5) History of gait disturbance	1
6) History of unilateral weakness	1
7) History of vertigo	−3
8) Initial triage diastolic blood pressure ≥110 mm Hg	3
9) Dysarthria or aphasia (history or examination)	1
Investigations in emergency department:	
1) Atrial fibrillation on electrocardiogram	2
2) Infarction (new or old) on computed tomography	1
3) Platelet count $\geq 400 \times 10^9$/L	2
4) Glucose ≥15 mmol/L	3
Total score (−3 to 23):	X

- **Setting and participants**: 7607 patients seen in 13 Canadian ED's over 5 years

- **Primary outcome**: subsequent stroke or CEA/CAS within 7 days
- **Secondary outcome**: subsequent stroke within 7 days

Results

- Of 7607 patients, 182 patients met the primary outcome (2.4%).
- 108 (1.4%) had subsequent stroke within 7 days
- 83 (1.1%) had CEA/CAS
- 9 had both stroke and CEA/CAS

Risk stratification of TIA using the Canadian TIA Score

Risk	Canadian TIA Score range	Observed risk of 1º outcome	Observed risk of stroke	% patients
Low	-3 to 3	0.5%	0.2%	16.3
Medium	4 to 8	2.3%	1.5%	72.1
High	9 or greater	5.9%	2.7%	11.3

Canadian TIA score vs ABCD2 score

- ABCD2 score
  - Age ≥ 60
  - BP ≥ 140/90
  - Clinical features (2 pts unilateral weakness, 1 point speech disturbance)
  - Duration of symptoms (< 10 min, 10-59 min, ≥ 60 min)
  - Diabetes

- The ABCD2 score was unable to classify anyone as low risk and all but 3% of patients were categorized as medium risk.

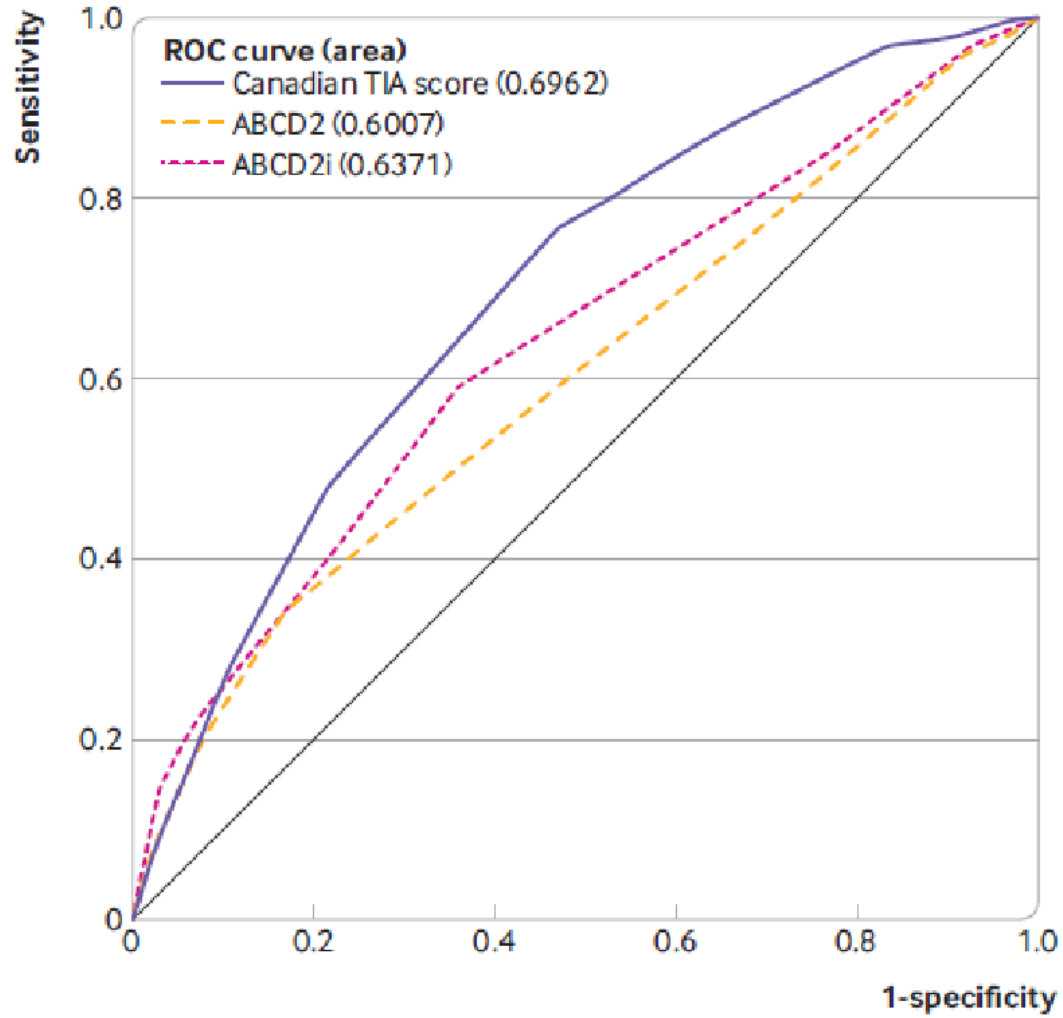


Fig 1 | Receiver operating characteristic (ROC) curve for comparison of Canadian TIA Score with ABCD2 and ABCD2i scores for subsequent stroke or carotid revascularisation within 7 days (n=7607)

Will this replace ABCD2?

- This was designed for use with an ED assessment so maybe not directly translatable to the outpatient office
  - Different patient population

- A modified and simpler version of the Canadian TIA Score is currently being evaluated

What about patients with symptoms which are a bit uncertain?

- Motor or speech deficits that are very short-lived
- Non-motor and non-speech symptoms
- Symptoms which take more than ten minutes to evolve

Research

JAMA Neurology | Original Investigation

Rate and Prognosis of Brain Ischemia in Patients With Lower-Risk Transient or Persistent Minor Neurologic Events

Shelagh B. Coutts, MD; Francois Moreau, MD; Negar Asdaghi, MD; Jean-Martin Boulanger, MD; Marie-Christine Camden, MD; Bruce C. V. Campbell, PhD; Andrew M. Demchuk, MD; Thalia S. Field, MD; Mayank Goyal, MD; Martin Krause, MD; Jennifer Mandzia, MD; Bijoy K. Menon, MD; Robert Mikulik, MD; Andrew M. Penn, MD; Richard H. Swartz, MD; Michael D. Hill, MD; for the Diagnosis of Uncertain-Origin Benign Transient Neurological Symptoms (DOUBT) Study Group

JAMA Neurol. 2019;76(12):1439-1445. doi:10.1001/jamaneurol.2019.3063
Published online September 23, 2019. Corrected on January 13, 2020.

DOUBT Study: **D**iagnosis of Uncertain-**O**rigin **B**enign **T**ransient Neurological Symptoms Study

- 1028 patients (≥ 40 yo) enrolled within 8 days of symptoms onst
- All had diffusion-weighted imaging

- Non-motor or non-speech minor focal neurological events of any duration
- Motor or speech symptoms of less than 5 minutes duration
- No previous stroke

Table 1. Baseline Patient Characteristics

Variable	No. (%) (N = 1028)
Medical history	
Age, median (IQR), y	63.0 (54.1-71.5)
Hypertension	480 (46.7)
Type 1 or 2 diabetes	140 (13.6)
Current smoker	105 (10.2)
Ischemic heart disease	87 (8.5)
Atrial fibrillation	51 (5.0)
Hyperlipidemia	342 (33.3)
Taking aspirin prior to event	347 (33.8)
Taking statin prior to event	285 (27.7)
Taking antihypertensive medication prior to event	419 (40.8)
No known vascular risk factors	352 (34.2)

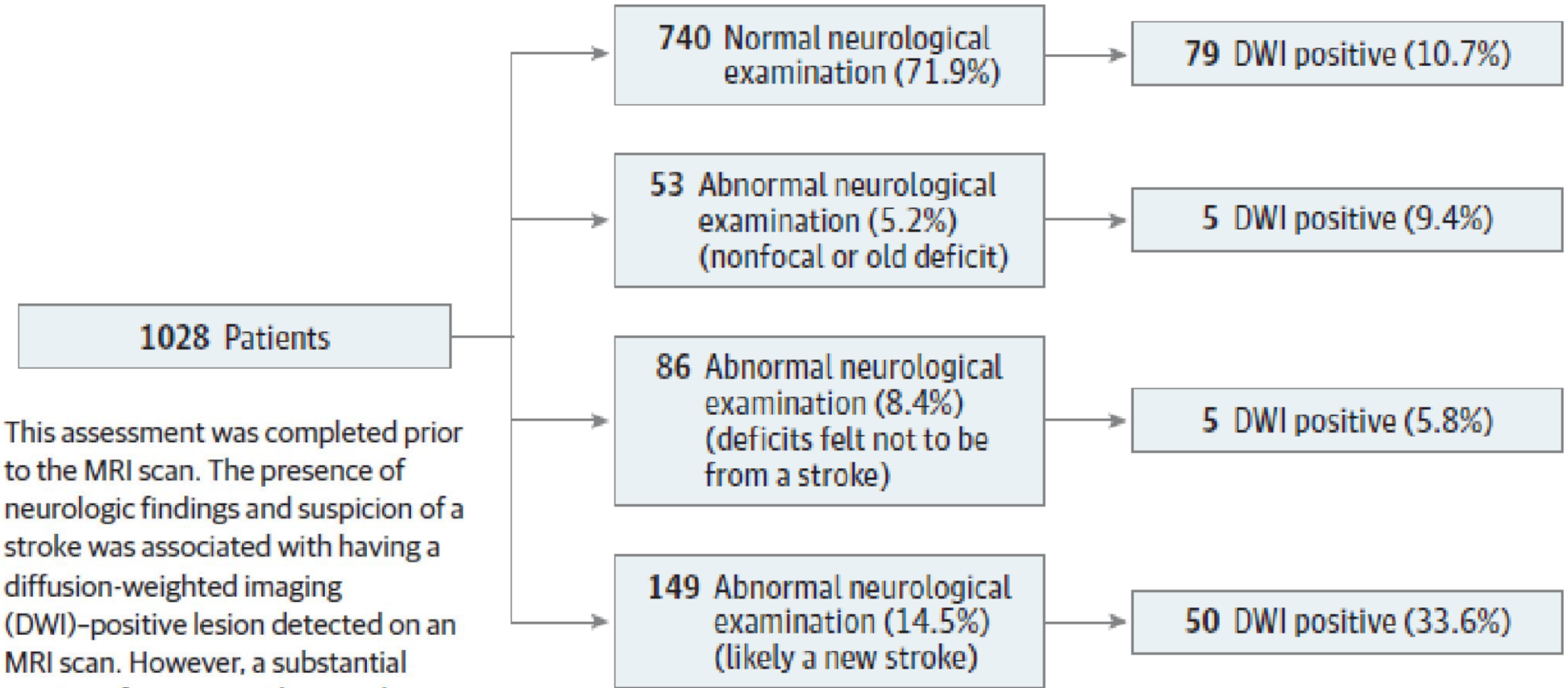
Historical and clinical features of the transient neurologic event	
Any migraine history	256 (24.9)
History of migraine with aura	80 (7.8)
Any reported stress by patient	158 (15.4)
Any motor or speech symptoms	218 (21.2)
Isolated sensory symptoms	482 (46.9)
Symptom duration <5 min	122 (11.9)
Progression of first to last symptoms >10 min	179 (17.4)
Ongoing symptoms at time of assessment	370 (36.0)
Previous identical event	238 (23.2)
Initial neurologic examination results normal	740 (72.0)

DOUBT Study Results

- **13.5% of patients had infarcts on DWI!**
  - 8.9% had single infarcts and 4.6% had multiple infarcts

- Infarct was associated with:
  - Age > 60
  - Male
  - Motor or speech symptoms
  - Deficits present on assessment

Figure. Association Between Neurologist's Assessment of Results of the Neurologic Examination and Magnetic Resonance Imaging (MRI)



This assessment was completed prior to the MRI scan. The presence of neurologic findings and suspicion of a stroke was associated with having a diffusion-weighted imaging (DWI)–positive lesion detected on an MRI scan. However, a substantial portion of patients with normal examination results or abnormal examination results with another explanation also had a DWI-positive lesion detected on an MRI scan.

Table 3. Multivariable Analysis of Variables Associated With DWI-Positive Lesion Detected on MRI Scan[a]

Variable	OR (95% CI)
Age (per year)	1.02 (1.00-1.04)
Male sex	2.03 (1.39-2.96)
Any motor or speech symptoms	2.12 (1.37-3.29)
Ongoing symptoms	1.97 (1.29-3.02)
Abnormal results of initial neurologic examination	1.71 (1.11-2.65)
No prior identical symptomatic event	1.87 (1.12-3.11)

Abbreviations: DWI, diffusion-weighted imaging; MRI, magnetic resonance imaging; OR, odds ratio.

What happened to these patients?

Table 4. Brain MRI and 1-Year Clinical Outcome Rates

Outcome	Patients, No. (%) (N = 1028)
Primary outcome	
Stroke on MRI results (DWI positive)	139 (13.5)
Secondary outcomes	
Recurrent ischemic stroke	7 (0.7)
Death	9 (0.9)
Myocardial infarction	4 (0.4)
Transient ischemic attack	9 (0.9)
Composite of ischemic stroke, MI, or death	20 (1.9)

Abbreviations: DWI, diffusion-weighted imaging; MRI, magnetic resonance imaging.

DOUBT: A normal MRI is reassuring

- In this patient population, normal MRI had a high negative predictive value (99.8%) for future stroke
- The key finding is that a detailed neurological history and examination are only partly helpful to rule out/rule in infarct on MRI
- A migraine history, or slow symptom evolution, or short symptom duration did not predict a benign outcome

We still have blindspots in TIA diagnosis…

- Prior studies have shown that women are more likely to be diagnosed with a stroke mimic than men
- But from studies like DOUBT we know that many stroke mimics, or “doubtful” cases actually have an infarct on MRI
- Are we underdiagnosing TIA/stroke in women?

Research

JAMA Neurol. 2019;76(8):962-968. doi:10.1001/jamaneurol.2019.1305
Published online May 22, 2019.

JAMA Neurology | Original Investigation

Sex Differences in Presentation and Outcome After an Acute Transient or Minor Neurologic Event

Amy Y. X. Yu, MD, MSc; Andrew M. Penn, MD; Mary L. Lesperance, PhD; Nicole S. Croteau, MSc; Robert F. Balshaw, PhD; Kristine Votova, PhD; Maximilian B. Bibok, PhD; Melanie Penn, BScN, RN, CNN(C); Viera Saly, MD, MSc; Janka Hegedus, MD, PhD; Charlotte Zerna, MD, MSc; Evgenia Klourfeld, MD; Lisa Bilston, BSc; Zachary M. Hong, BSc; Shelagh B. Coutts, MD, MSc; for the SpecTRA Study Group

OBJECTIVE To evaluate sex differences in the symptoms, diagnoses, and outcomes of patients with acute transient or minor neurologic events.

DESIGN, SETTING, AND PARTICIPANTS This prospective cohort study of patients with minor ischemic cerebrovascular events or stroke mimics enrolled at multicenter academic emergency departments in Canada between December 2013 and March 2017 and followed up for 90 days is a substudy of SpecTRA (Spectrometry for Transient Ischemic Attack Rapid Assessment). In total, 1729 consecutive consenting patients with acute transient or minor neurologic symptoms were referred for neurologic evaluation; 66 patients were excluded for protocol violation (n = 46) or diagnosis of transient global amnesia (n = 20).

MAIN OUTCOMES AND MEASURES The main outcome was the clinical diagnosis (cerebral ischemia vs stroke mimic). Secondary outcomes were 90-day stroke recurrence and 90-day composite outcome of stroke, myocardial infarction, or death. The association between presenting symptoms (focal vs nonfocal) and clinical diagnosis was also assessed. Research hypotheses were formulated after data collection.

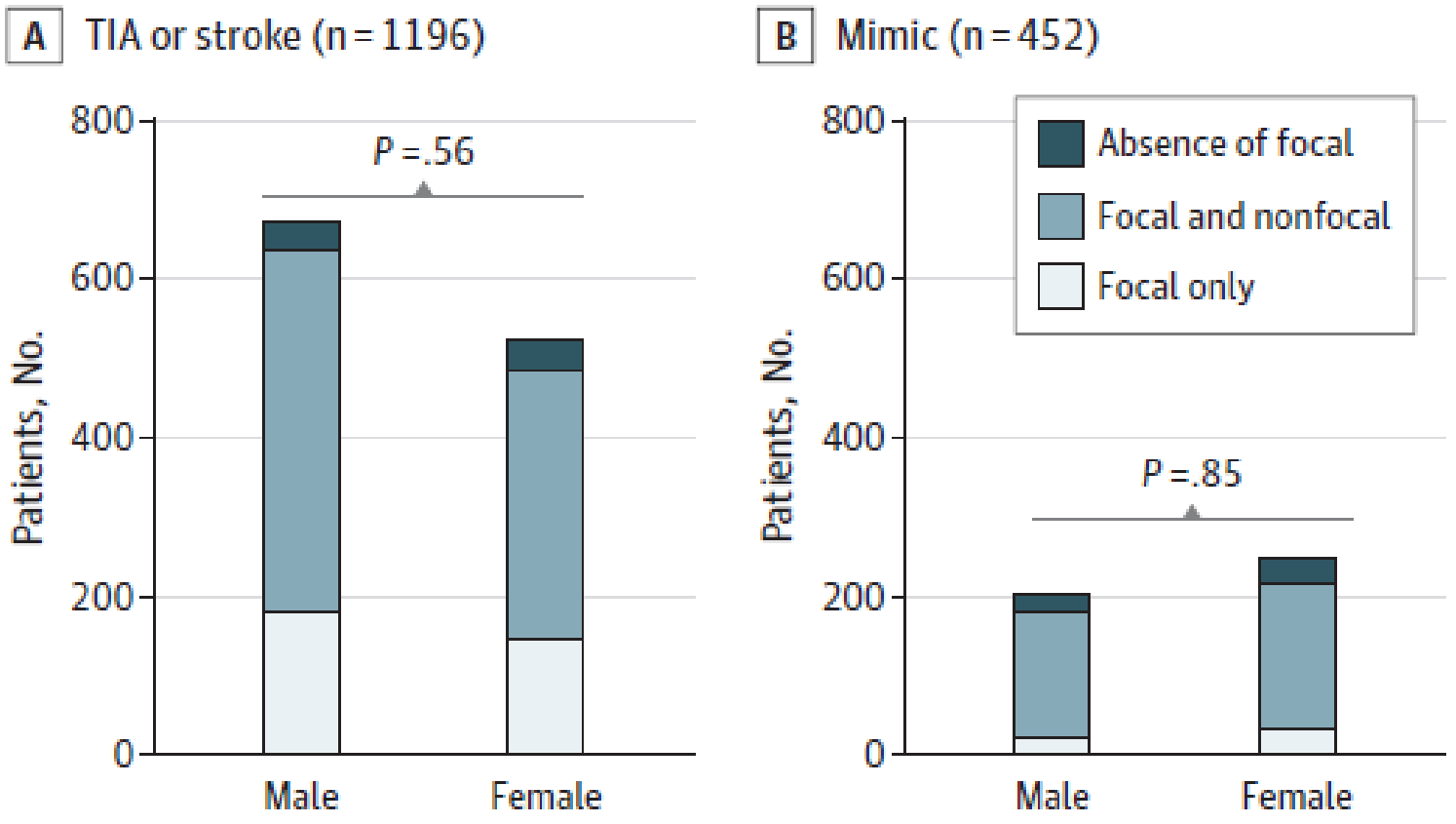
Table 1. Baseline Characteristics and Investigations of 1648 Patients by Sex

Characteristic or Investigation	No. (%) of Patients		P Value
	Women (n = 770)	Men (n = 878)	
Age, median (IQR), y	71 (58-81)	69 (59-79)	.09
Race/ethnicity			
White	705 (91.6)	791 (90.1)	.03
Black	7 (0.9)	7 (0.8)	
Asian	25 (3.2)	52 (5.9)	
Aboriginal	19 (2.5)	10 (1.1)	
Other	14 (1.8)	18 (2.0)	
Hypertension	401 (52.1)	513 (58.4)	.01
Diabetes	118 (15.3)	179 (20.4)	.01
Dyslipidemia	227 (29.5)	351 (40.0)	<.001
Coronary artery disease	74 (9.6)	166 (18.9)	<.001
Atrial fibrillation	92 (11.9)	115 (13.1)	.53
Active smoking	91 (11.8)	126 (14.4)	.15
History of stroke	59 (7.7)	87 (9.9)	.13
History of migraines	193 (25.1)	107 (12.2)	<.001
Self-reported psychiatric condition or recent stressor	177 (23.0)	158 (18.0)	.01

Women are more likely to be diagnosed with a stroke mimic, less likely to have DWI-positive scan but carry the same recurrent stroke risk compared to men

- Women are less likely to receive a diagnosis of stroke or TIA (adjusted RR 0.88, 95% CI 0.82-0.95)
- Women were less likely to have acute infarct on MRI (adjusted RR 0.77, 95% CI 0.67-0.87)
- But, women and men had similar recurrence of stroke within 90 days (adj RR 0.90, 95% CI 0.48-1.66) and a similar 90-day composite outcome of stroke, MI, or death
- Among patients with 90-day recurrent stroke
  - 88.9% of women received an initial diagnosis of minor stroke/TIA whereas 100% of men did
  - 33.3% of women had DWI-positive scan, 73.9% of men did
  - Of patients with DWI-negative scan, women were more likely to be incompletely investigated than men

Figure. Presenting Symptoms by Sex and Final Diagnosis



Symptom distribution by sex among patients with transient ischemic attack (TIA) or minor stroke (A) or with stroke mimic (B).

Table 2. Multivariable Analysis of Diagnosis and 90-Day Outcomes Comparing 1648 Female vs Male Patients

Diagnosis or Outcome	No. (%) of Patients		Unadjusted RD, % (95% CI)	Adjusted RR (95% CI)[a]
	Women (n = 770)	Men (n = 878)		
Minor ischemic cerebrovascular event	522 (67.8)	674 (76.8)	−9.0 (−13.4 to −4.5)	0.88 (0.82 to 0.95)
Infarct evident on MRI	275 (35.7)	406 (46.2)	−10.5 (−15.4 to −5.7)	0.77 (0.67 to 0.87)
Stroke recurrence within 90 d	18 (2.3)	23 (2.6)	−0.25 (−1.94 to 1.45)	0.90 (0.48 to 1.66)
90-d Stroke, myocardial infarction, or death	35 (4.5)	46 (5.2)	−0.63 (−2.93 to 1.67)	0.86 (0.54 to 1.32)

Abbreviations: MRI, magnetic resonance imaging; RD, risk difference; RR, risk ratio.

[a] Adjusted for baseline covariates of age, hypertension, diabetes, atrial fibrillation, coronary artery disease, smoking, and history of stroke.

- I think the main point of this study is that even with a negative DWI scan in women, and an initial diagnosis of stroke mimic in women, the risk of recurrent stroke is the same as in men

- There are sex differences in the stroke workup for those with a negative DWI scan and a diagnosis of a stroke mimic, as reflected in a high rate of incomplete investigation in women than men

Summary

1. For TIA presenting within 48 hours, send the patient to the ED for rapid workup, and for patients beyond 48 hours, refer to the Stroke Prevention Clinic.
2. The Canadian TIA Score has greater ability to risk stratify TIA than the ABCD2 score.
3. Many patients with unusual symptoms actually have infarction on MRI.
4. There are sex differences in the diagnosis of TIA/minor stroke despite similar outcomes for stroke recurrence at 90 days.