Secondary Prevention of Stroke and TIAs

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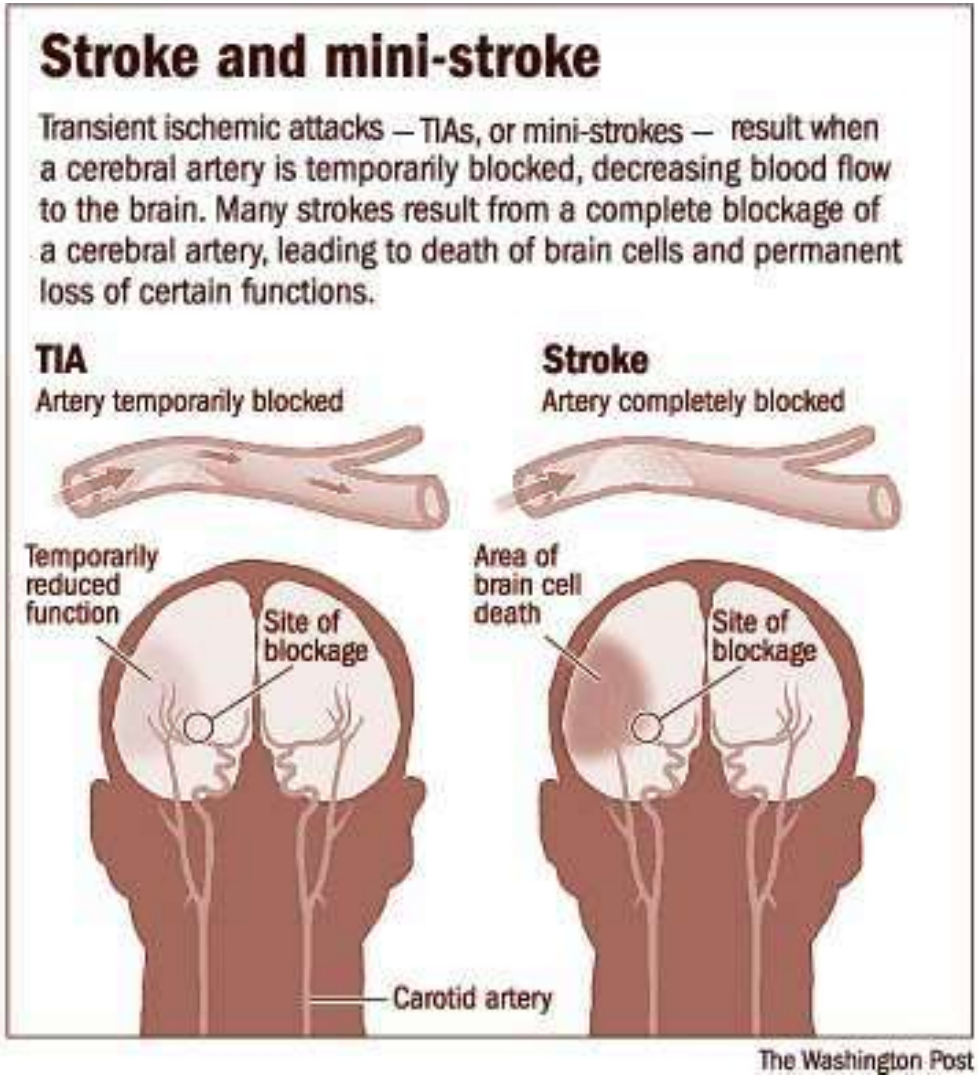
Objectives

- Distinguish between AIS and TIA
- Describe initial treatment strategies for TIA
- Highlight the $ABCD^2$ tool to identify patients at risk for future stroke
- Discuss secondary treatment and risk factor recommendations for patients who have had an ischemic stroke or TIA

Transient Ischemic Attack or "Mini Stroke"

- Prevalence rate ~ 2.3% of US population
  - True rate is probably higher!
- Defined as transient episode of neurological dysfunction caused by ischemia without acute infarction
  - S/Sx last < 24 hours (usually < 1 hour)
  - **Requires urgent treatment to reduce risk of stroke**



Benjamin EJ et al. Circ. 2019;139:e56-e528

Stroke vs. TIA

	Stroke	TIA
Symptoms	•Paralysis, weakness, speech difficulties, visual changes, ataxia •Symptoms can worsen, do not completely resolve	•Same presentation as stroke •Symptoms rapidly resolve
Damage	Infarction of brain tissue	None: tissue ischemic but no infarction
Diagnosis	Neurologic exam, areas of ischemia and infarction can be seen on imaging	Based on pt history only: symptoms resolved before seeking care; however areas of ischemia may be seen on imaging
Prognosis	Good to poor: death or permanent injury	Good, but increase risk for future stroke

ABCD² Stroke Risk Tool

Risk for Stroke at Various Time Points After TIA Based on ABCD² Score

Age:	≥60 years = 1 point
Blood pressure:	Systolic blood pressure ≥ 140 mm Hg and/or diastolic blood pressure ≥ 90 mm Hg = 1 point
Clinical features:	Unilateral weakness = 2 points
	Speech disturbance without weakness = 1 point
Duration of symptoms:	≥60 minutes = 2 points
	10–59 minutes = 1 point
Diabetes:	Yes = 1 point

ABCD² Score	*Risk Category*	*Stroke Risk*		
		2 Days	*7 Days*	*90 Days*
0–3	Low	1.0	1.2	3.1
4–5	Moderate	4.1	5.9	9.8
6–7	High	8.1	11.7	17.8

Johnston et al. Lancet 2007;369:283-92; Benjamin EJ et al. Circ. 2019;139:e56-e528

TIA Workup and Treatment

- **Work up: Patients with suspected TIA should be evaluated ASAP after an event** *(Class I)*
  - **Undergo MRI (preferable) or head CT within 24 hr of symptom onset**
  - Carotid testing: check for atherosclerosis
  - Cardiac testing: Afib, MI
    - EKG, holter monitor or inpatient telemetry:
    - ECHO: clot in atria or ventricle, diagnose cardiomyopathy
  - Lab tests: CBC, Chemistry, PTT/INR, FLP
  - **Hospital admission for any pt with $ABCD^2$ score $\geq$ 4**
- **Treatment: Follow secondary prevention guidelines to reduce risk for AIS**

Easton et al. Stroke 2009;40:2276-93; Kernan et al. Stroke 2014;45:1-77.

MRI in TIA

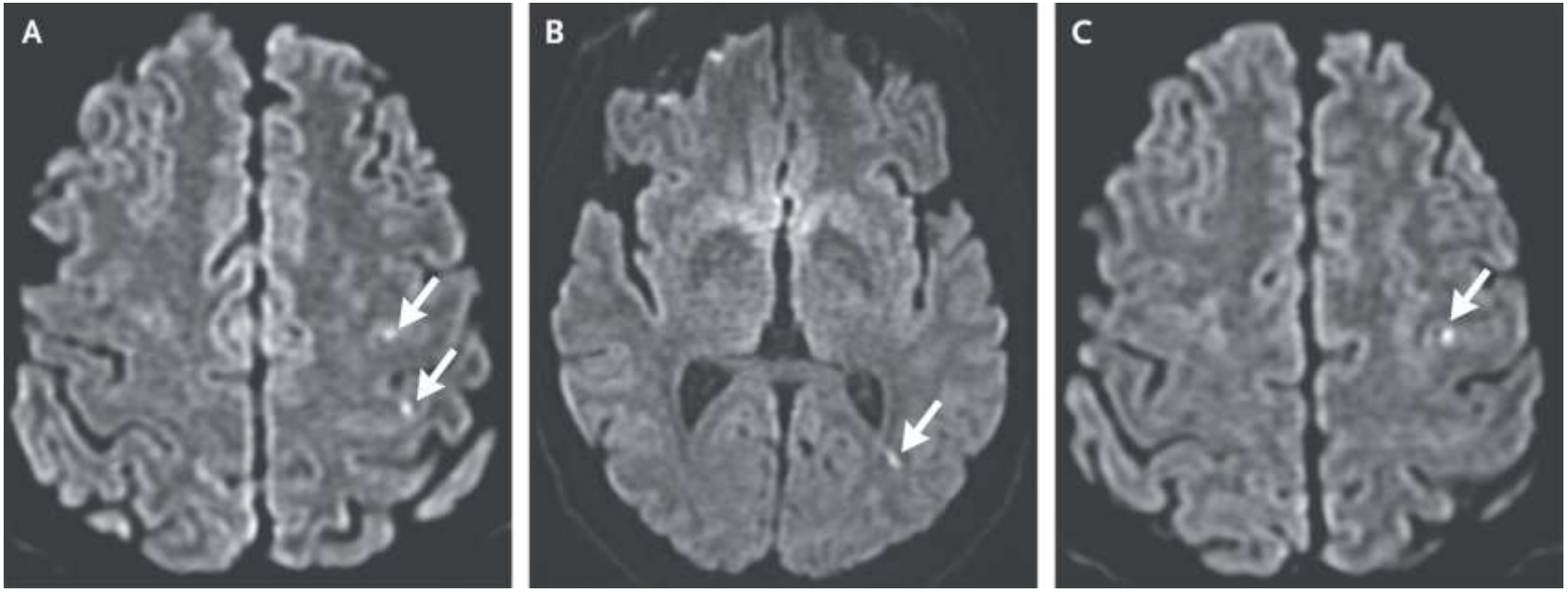


Figure 1 Neuroimaging Evaluation: An axial section of a diffusion-weighted image (MRI) of the brain shows multiple bright spots in the cortical territory of the right middle cerebral artery. Panel A shows two small brain infarctions (arrows), Panel B shows one small infarct (arrow), and Panel C shows one small infarct (arrow).

Amarenco P. NEJM 2020;382:1933-41

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TIA Questions

- How does TIA differ from ischemic stroke?
- What is the link between TIA and ischemic stroke?
- What is the purpose of the $ABCD^2$ tool? Which characteristics put a patient at higher risk for stroke?
- What recommendation do you have for a patient who reports TIA symptoms?

AHA/ASA Secondary Prevention Guidelines for Stroke/TIA

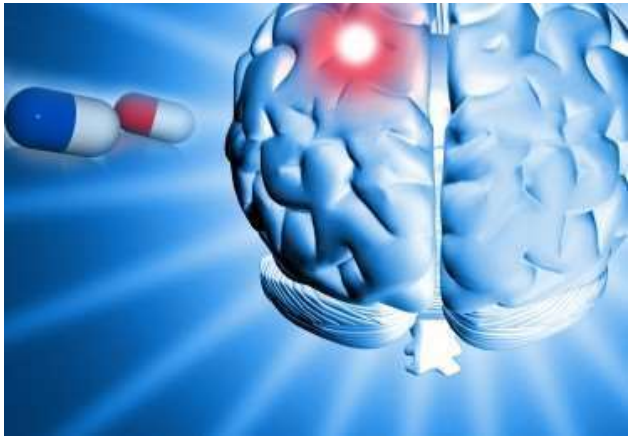
A: antiplatelet, anticoagulant, (sleep) apnea

B: blood pressure

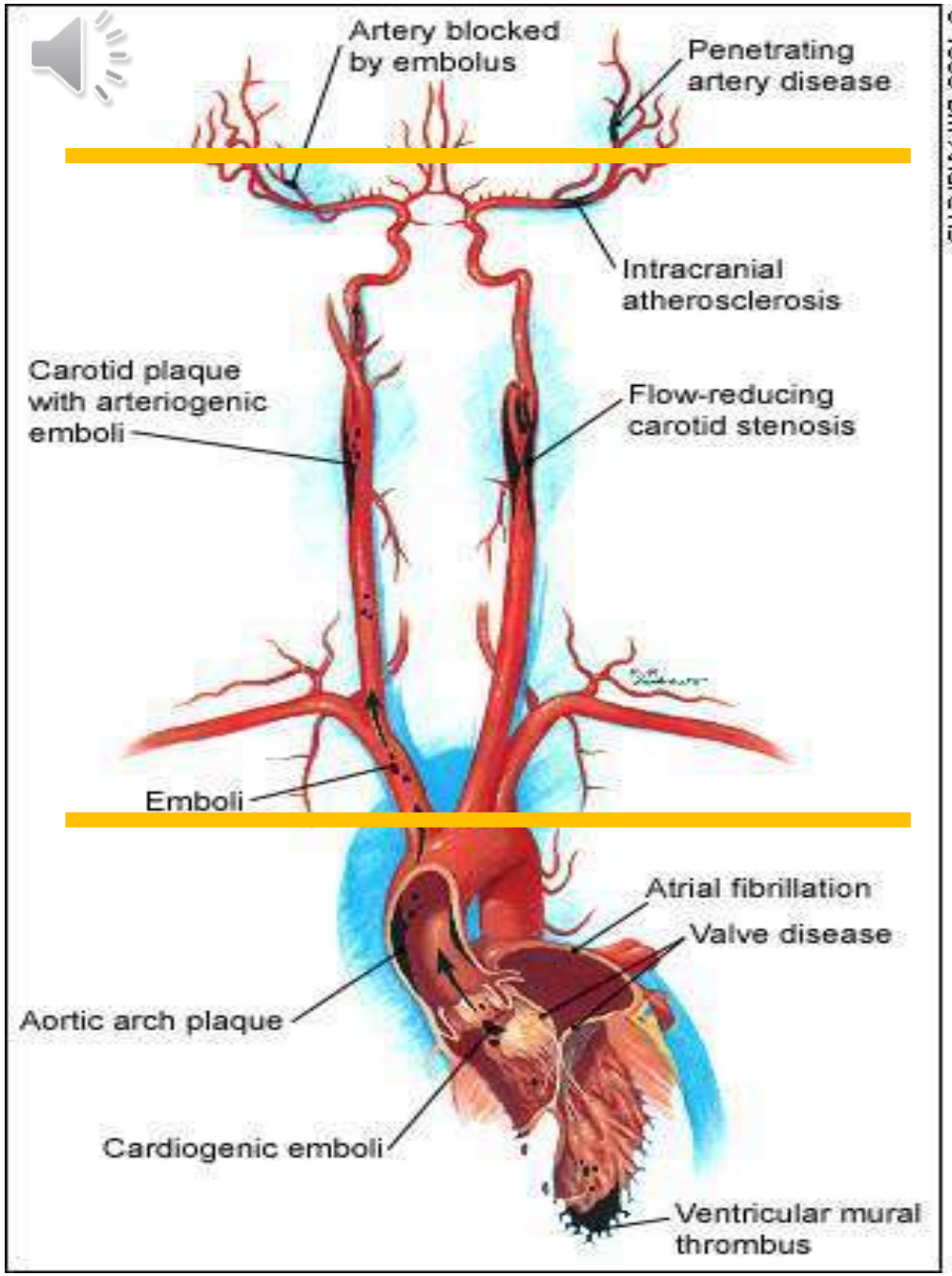
C: cholesterol, cigarettes

D: diabetes, diet, depression

E: exercise



Diener HC and Hankey GJ. JACC 2020;75:1804-14



Clot Source in Stroke/TIA

- **Noncardiogenic**
  - Carotid
  - Intracranial
- **Cardiogenic (embolism)**
  - Afib
  - Acute MI and LV thrombus
  - Cardiomyopathy
  - Valvular heart disease
  - Prosthetic heart valves

A: Antiplatelet

- **Noncardiogenic ischemic stroke/TIA:**
  - Clots that originate from carotids and intracranial arteries (may be in situ or embolic)
  - **Antiplatelet therapy recommended rather than oral anticoagulant** *(Class I)*
  - Selection should be based on individual patient: characteristics, risk factors, cost, tolerance
  - FDA approved agents: aspirin, Aggrenox, clopidogrel, ~~ticlopidine~~
  - **Aspirin 50-325 mg (81 mg) daily OR aspirin/dipyridamole 25mg/200mg BID (Aggrenox)**
    - Start within 24-48 hrs with loading dose 160-300 mg (po/pr)
    - For patients with stenosis of a major intracranial artery:
      - Aspirin 325 mg daily recommended *(Class I)*

A: Antiplatelet

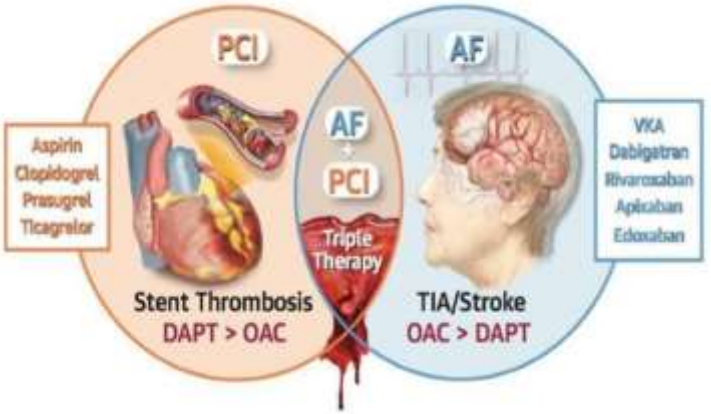
- **Noncardiogenic ischemic stroke/TIA continued:**
  - **Clopidogrel 75mg daily** is an option to aspirin or Aggrenox; recommended in patients w/asa allergy *(Class IIa)*
  - **DAPT (asa/clopidogrel)** for ***21 days of therapy*** can be beneficial in minor ischemic stroke and TIA *(Class IIa):*
    - Patients with NIHSS score ≤ 3 or TIA
    - **Start after 24 hours of stroke or TIA**
    - Followed by long-term single-agent AP therapy

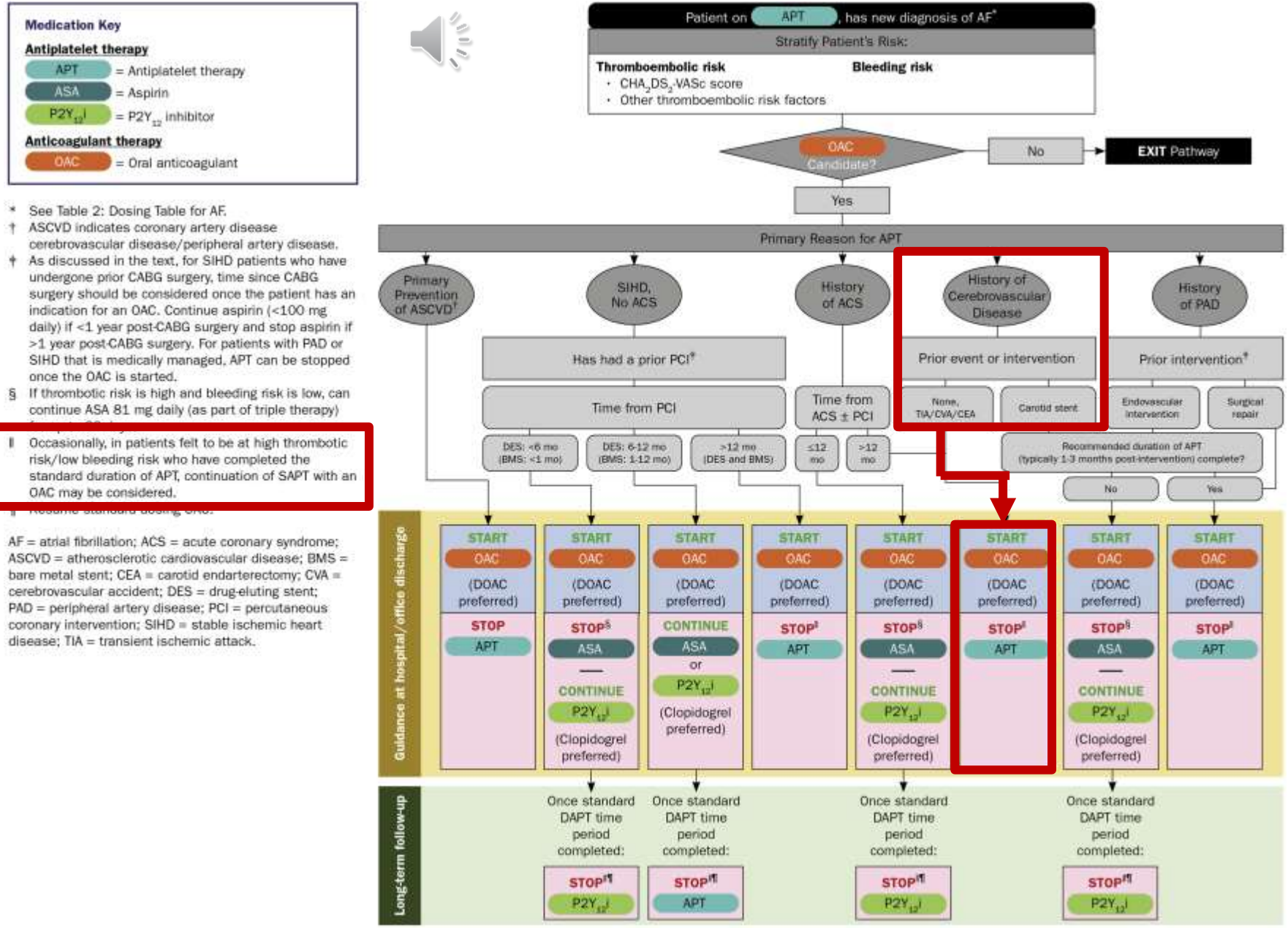
A: Anticoagulant

- **Cardiogenic ischemic stroke/TIA:**
  1. **Afib (nonvalvular):** VKA (target INR 2-3), apixiban, dabigatran, endoxaban, or rivaroxaban
     - Initiate within 4-14 days of event
       - Urgent anticoagulation is not recommended!
     - Bridging therapy for temporary interruption w/warfarin
     - **Aspirin monotherapy recommended in patients unable to take OAC**

A: Antiplatelet

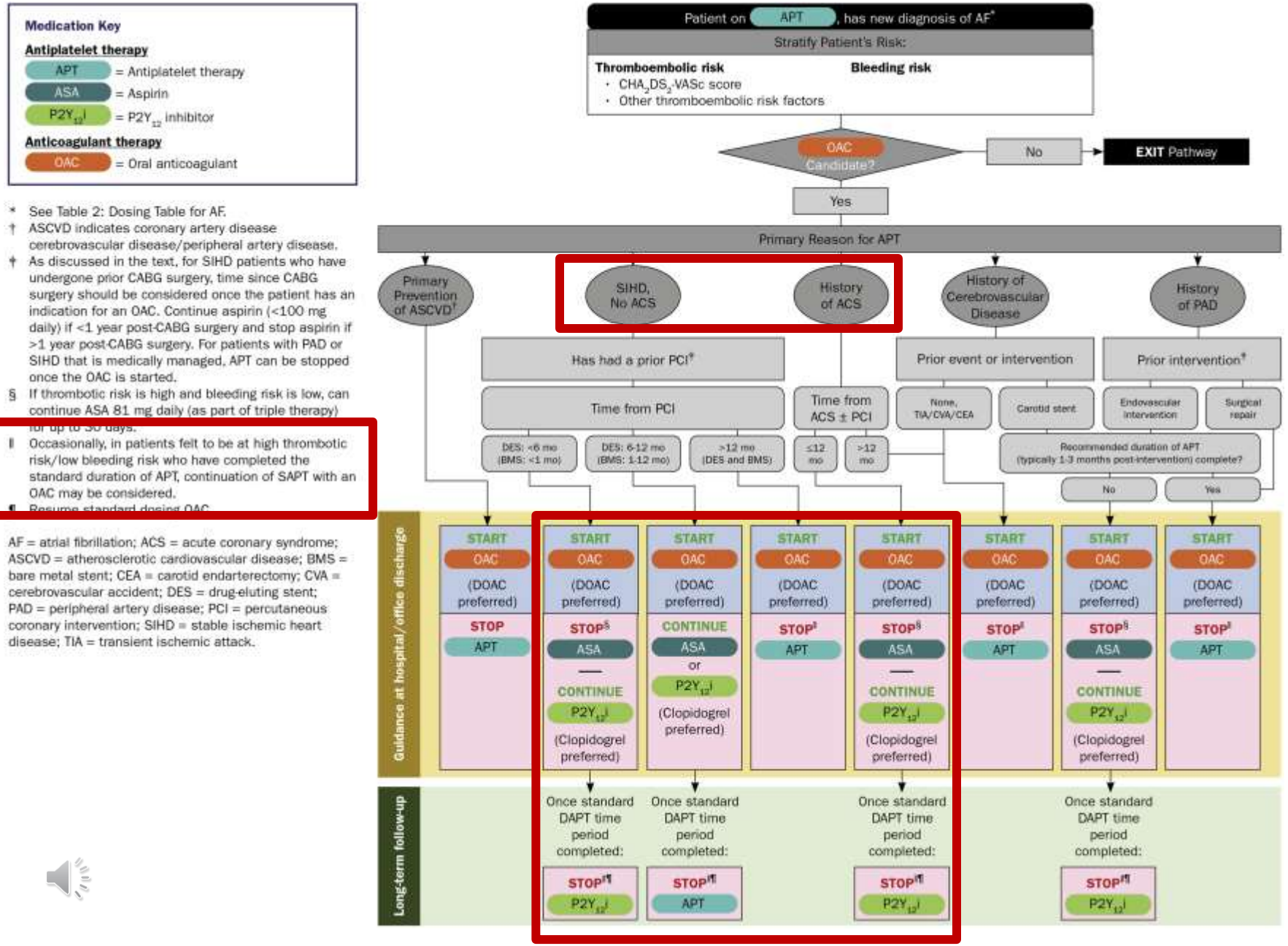
- **Cardiogenic ischemic stroke continued:**
  - Addition of antiplatelet therapy <u>not recommended</u> in the setting of AIS/TIA due to Afib unless patient has CHD and high risk for thrombosis/low risk for bleeding
    - Usefulness of adding aspirin to OAC is uncertain
    - Avoid triple therapy: drop daily aspirin, continue P2Y12 inh post ACS/PCI





Dharam J. Kumbhani et al. *J Am Coll Cardiol* 2021; 77:629-658.

JACC

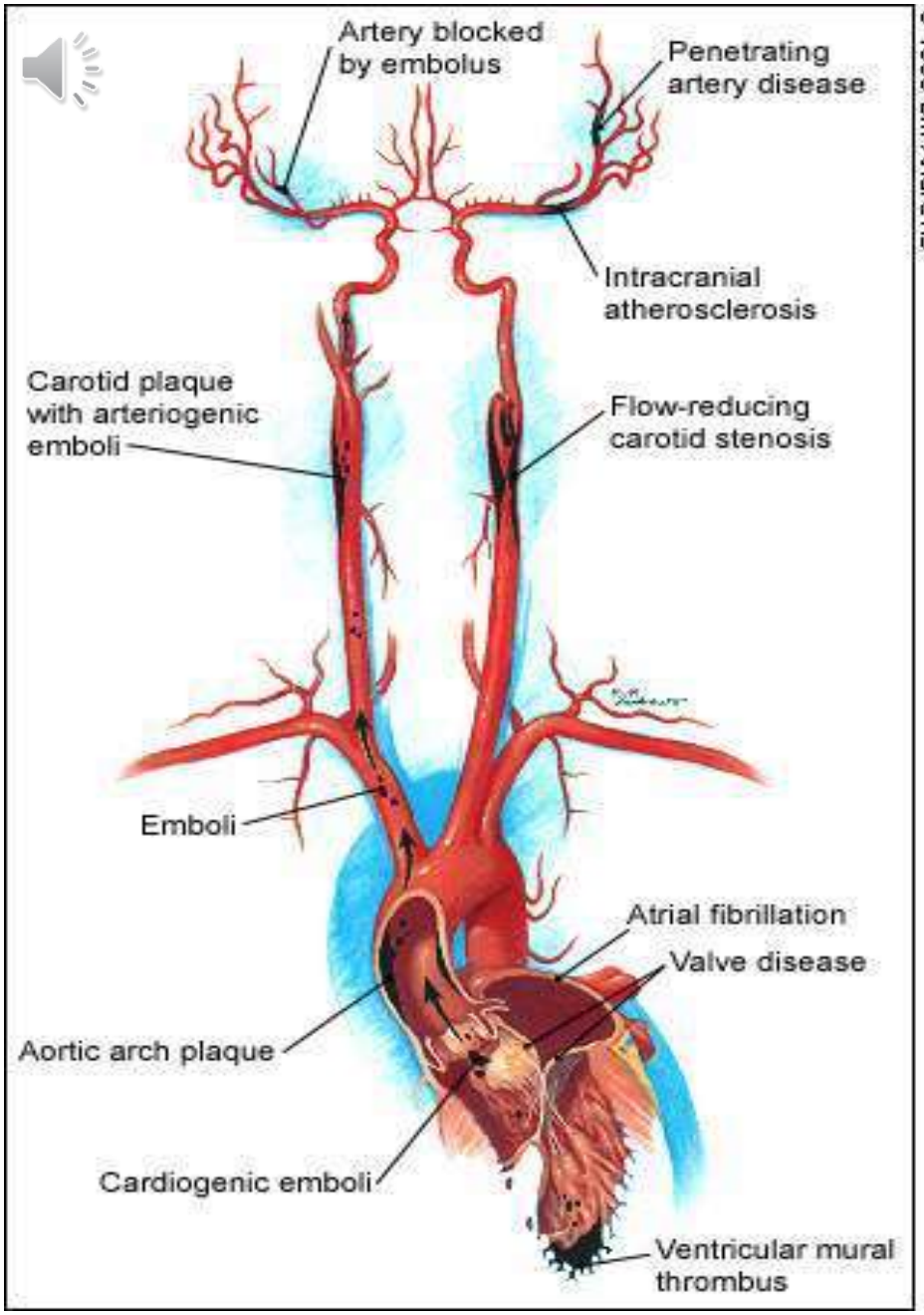


Dharam J. Kumbhani et al. *J Am Coll Cardiol* 2020; 77:629-658.

JACC

A: Anticoagulant

- **Cardiogenic ischemic stroke/TIA continued:**
  2. **Acute MI with LV thrombus:** VKA (target INR 2-3) for 3 months *(Class I)*
  3. **Dilated cardiomyopathy:**
     - With atrial/LV thrombus: VKA (target INR 2-3) for ≥ 3 months *(Class I)*
     - Without thrombus: VKA or antiplatelet therapy depending on risk of stroke vs bleeding
  4. **Valvular disease:** depends on which valve is diseased and type of prosthetic valve used



Clot Source in Stroke/TIA

- Cardiogenic-
  - Which drug class is recommended?
- Noncardiogenic-
  - Which drug class is recommended?
  - Which drugs are first line?
  - Is DAPT appropriate?

A: (Sleep) Apnea

- **Sleep apnea is present in 50-75% of patients with stroke/TIA**
- Associated with higher post-stroke mortality, delirium, depressed mood, and worse functional status
- **Consider sleep study and treatment with CPAP if sleep apnea diagnosed**

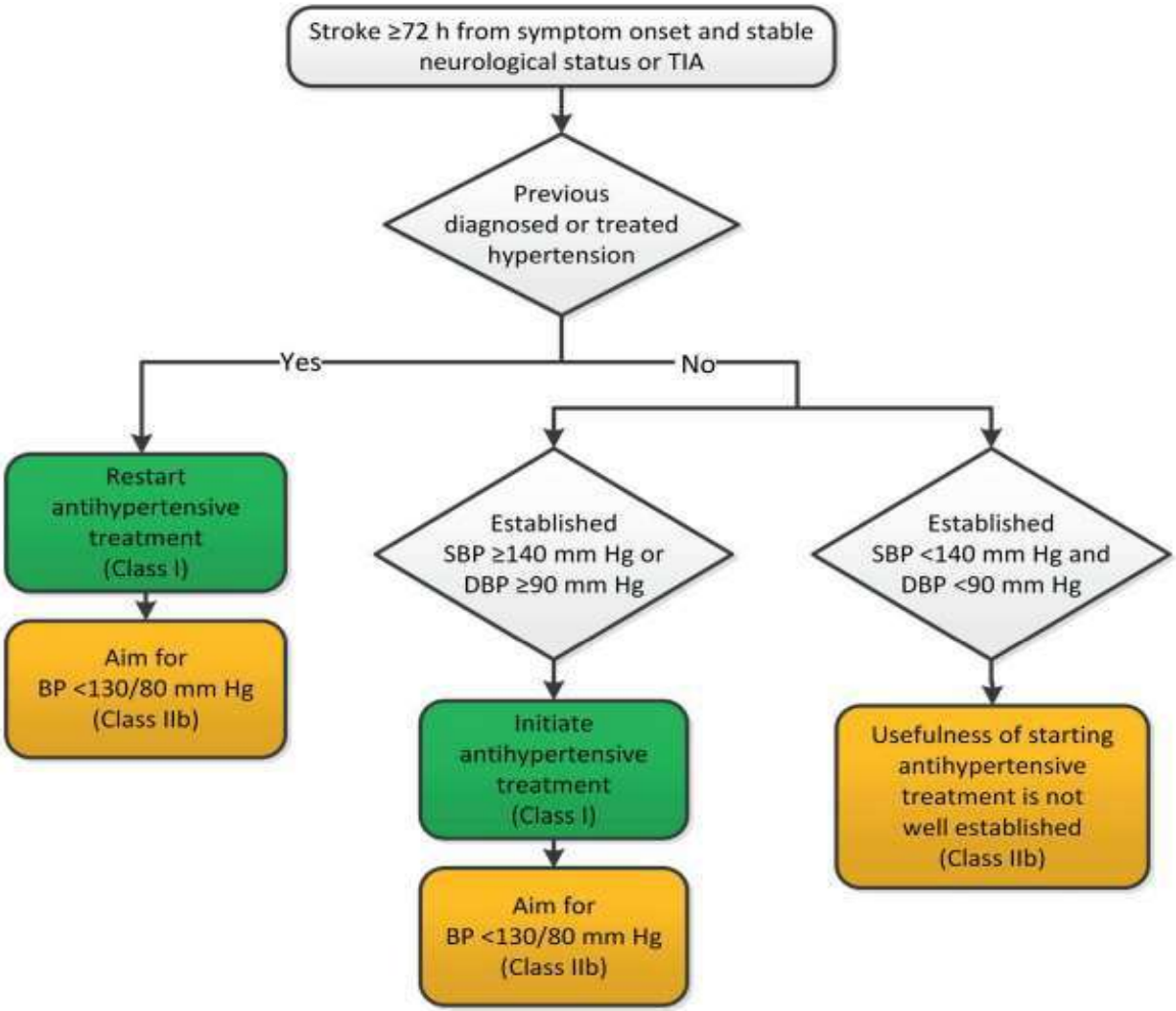
AHA Heart Disease and Stroke Statistics- 2017 Update

B: Blood Pressure

- Several studies demonstrate significant lower rates of recurrent stroke with lower BP
- Starting or restarting HTN therapy during hospitalization in patients with BP > 140/90 mmHg who are neurologically stable is safe and reasonable to improve long-term BP control *(Class IIa)*
- Target BP: see next slide
- Specific agents: **ACEI, ARB, thiazide diuretic, or ACEI/thiazide combination for BP lowering and endothelial protection** *(Class Ia)*

ACC/AHA 2017 HBP Clinical Practice Guideline

FIGURE 9 Management of Hypertension in Patients With a Previous History of Stroke (Secondary Stroke Prevention)



Whelton et al. JACC 2018;71:e127-248

B: Blood Pressure

- **Naïve patient with ischemic stroke:** Initiate HTN therapy a few days after the event in patients with BP ≥ 140/90 mmHg who are neurologically stable *(Class I)*
  - Why wait?

- **Patient with ischemic stroke and H/O HTN:** Resume previous BP med(s) after the first few days of event *(Class Ia)*
  - May require resuming at a lower dose to avoid hypotension

- **Patient with TIA:** start/resume BP therapy within 24 hours

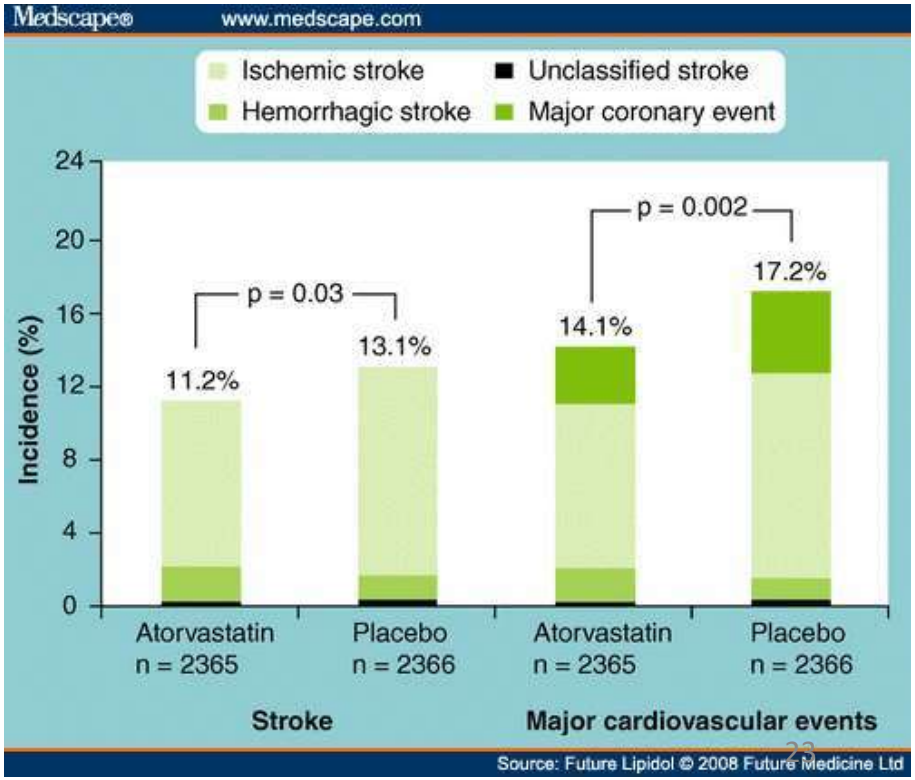
- **All patients:** Lifestyle modifications in addition to medications reasonable *(Class IIa)*

C: Cholesterol

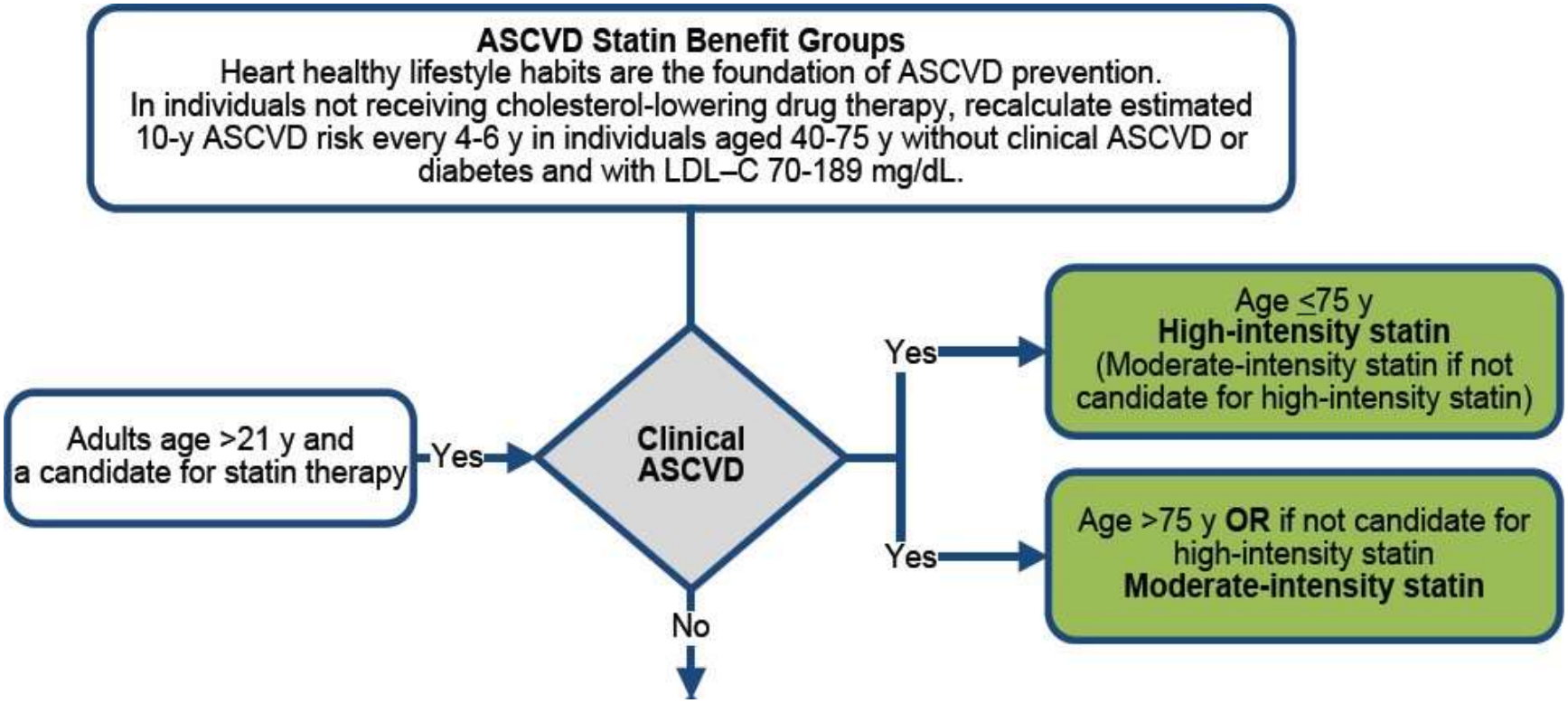
- Less evidence on use of statins in stroke/TIA compared to ACS/CCS
- Modest link between high LDL and risk of ischemic stroke, but also risk of ICH with low LDL
  - HPS *
  - SPARCL trial *
  - TST trial

* Increased risk of non-fatal hemorrhagic stroke during statin therapy most likely due to poorly controlled BP than too low LDL levels.

Dandapat S and Robinson JG. *Curr Neurol Neurosci Rep* 2016;16:24



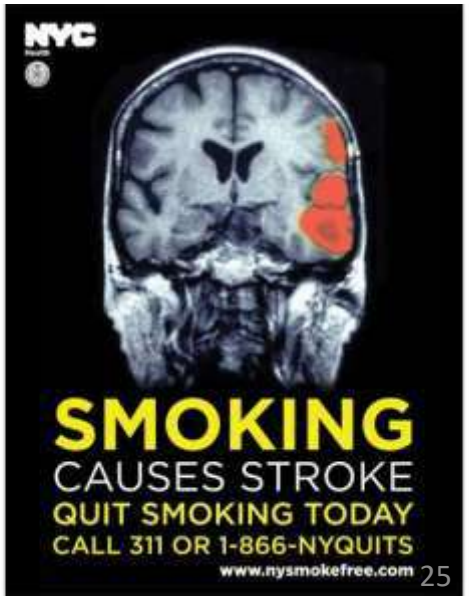
Clinical ASCVD: Secondary Prevention



- Clinical ASCVD includes patients with ACS, history of MI, stable or unstable angina, coronary or other arterial revascularization, **stroke, TIA** or PAD.
- *Class I recommendation*

C: Cigarettes

- Discontinuation of smoking reduces stroke risk across sex, race, and age groups
- **Patients should be strongly advised to quit** *(Class I)*
- Reasonable to advise patients to avoid passive tobacco smoke *(Class IIa)*
- **Counseling, NRT, and oral smoking cessation meds are effective** in assisting smokers to quit *(Class I)*

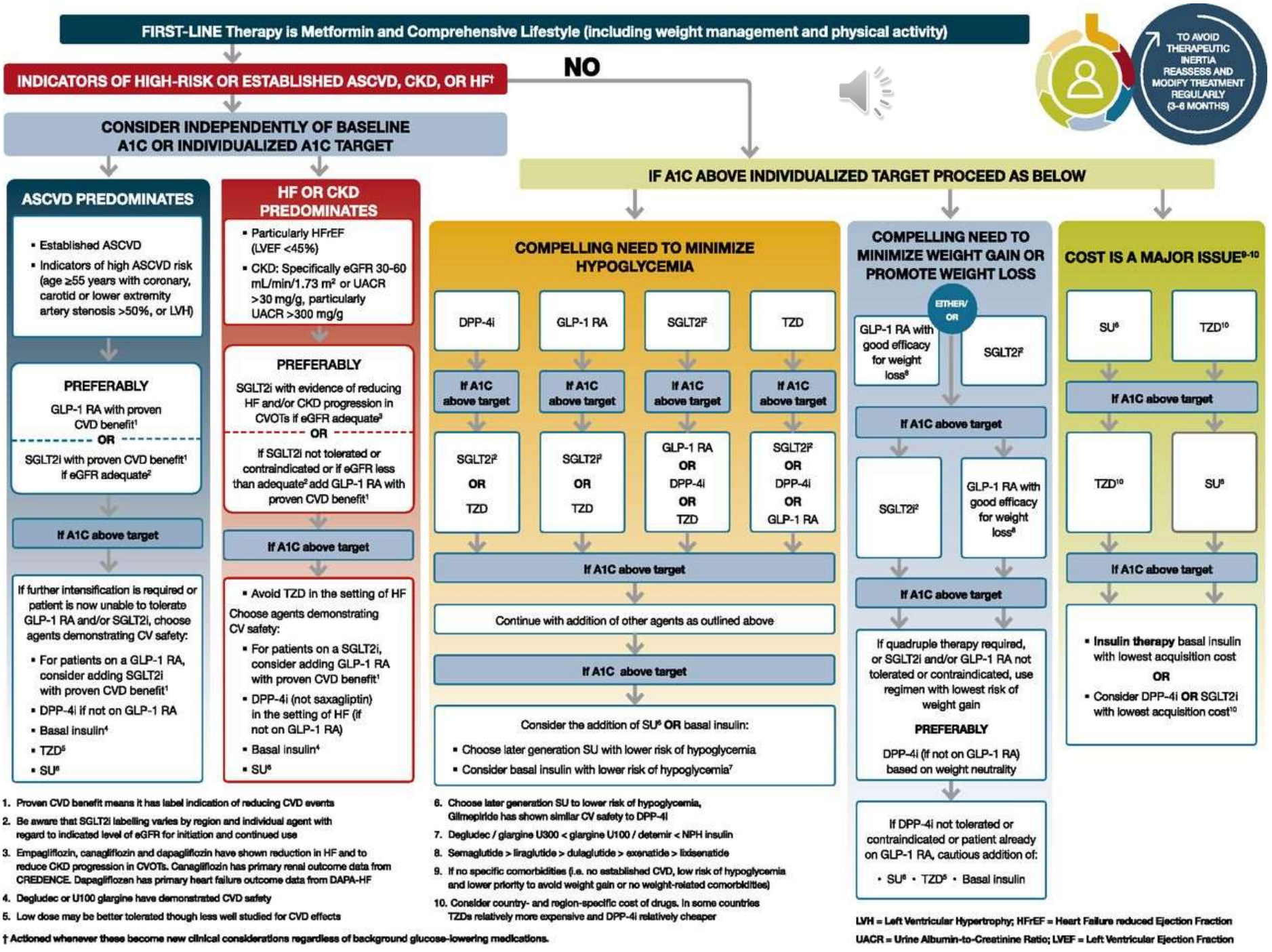


D: Diabetes

- No secondary prevention trials focused on pre-DM or DM management in patients with stroke
- In patients with H/O TIA or minor stroke, impaired glucose tolerance nearly doubles stroke risk compared to those with normal glucose levels
  - Triples the risk in patients with DM
- Patients with DM have higher risk of death after experiencing first stroke
  - Risk more pronounced in women and younger patients

D: Diabetes

- Screen all patients for DM after a TIA or ischemic stroke *(Class IIa)*
- **Follow ADA guidelines for glycemic control** and CV risk factor management *(Class I)*
- For patients with *metabolic syndrome*, management should focus on lifestyle modification (diet, exercise, weight loss) and treatment of individual components (HTN, dyslipidemia) *(Class I)*



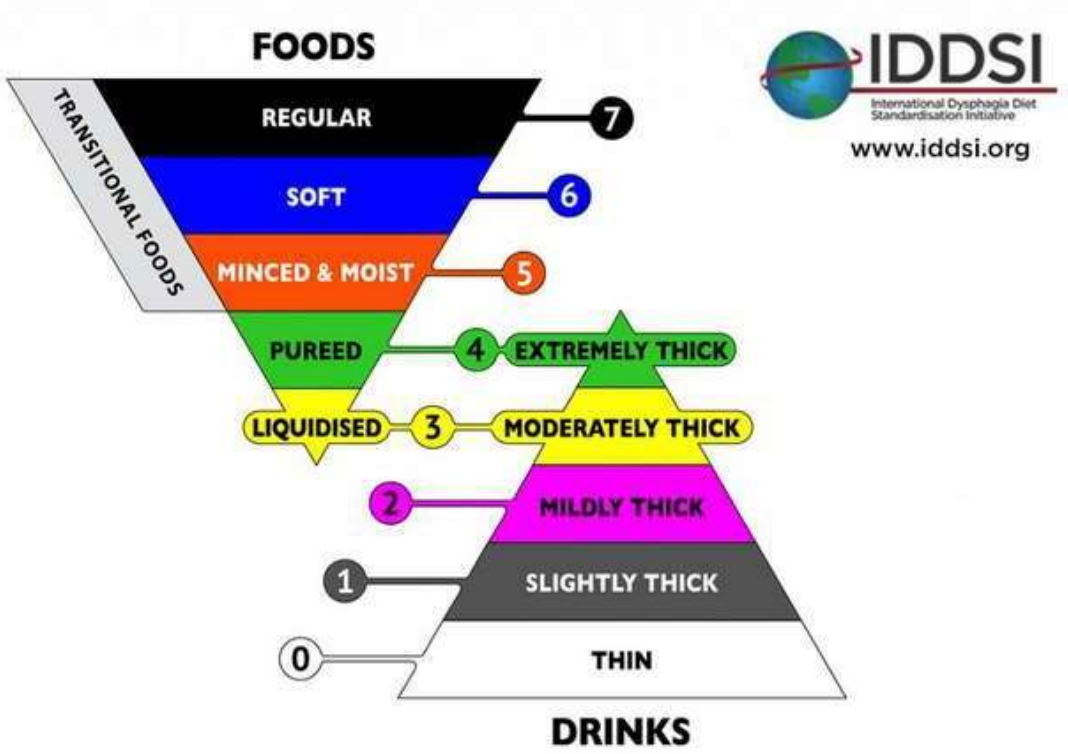
1. Proven CVD benefit means it has label indication of reducing CVD events
2. Be aware that SGLT2i labelling varies by region and individual agent with regard to indicated level of eGFR for initiation and continued use
3. Empagliflozin, canagliflozin and dapagliflozin have shown reduction in HF and to reduce CKD progression in CVOTs. Canagliflozin has primary renal outcome data from CREDENCE. Dapagliflozen has primary heart failure outcome data from DAPA-HF
4. Degludec or U100 glargine have demonstrated CVD safety
5. Low dose may be better tolerated though less well studied for CVD effects
6. Choose later generation SU to lower risk of hypoglycemia, Glimepiride has shown similar CV safety to DPP-4i
7. Degludec / glargine U300 < glargine U100 / detemir < NPH insulin
8. Semaglutide > liraglutide > dulaglutide > exenatide > lixisenatide
9. If no specific comorbidities (i.e. no established CVD, low risk of hypoglycemia and lower priority to avoid weight gain or no weight-related comorbidities)
10. Consider country- and region-specific cost of drugs. In some countries TZDs relatively more expensive and DPP-4i relatively cheaper

† Actioned whenever these become new clinical considerations regardless of background glucose-lowering medications.

LVH = Left Ventricular Hypertrophy; HFrEF = Heart Failure reduced Ejection Fraction
UACR = Urine Albumin-to-Creatinine Ratio; LVEF = Left Ventricular Ejection Fraction

D: Diet (Dysphagia)

- Before oral meds and diet started, patient must first pass swallow study to rule out aspiration



D: Diet

- **Evaluate patient with H/O stroke/TIA for signs of over nutrition and under nutrition** *(Class IIa)*
  - Patients with under nutrition should be referred for nutritional counseling
- Reasonable to **recommend sodium reduction to < 2.4 g/day**; further reduction to < 1.5g/day is also reasonable for further BP lowering *(Class IIa)*
- Heavy alcohol users should eliminate or reduce consumption *(Class I)*
  - Up to 2 drinks/day for men, up to 1 drink/day for women
- Reasonable to **recommend Mediterranean-type diet** *(Class IIa)*

Benjamin EJ et al. Circ. 2019;139:e56-e528

Depression

- Assess patient for depression using a validated screening tool
  - Optimal timing of screening is uncertain
- If diagnosed with post-stroke depression, treat with antidepressants in the absence of contraindications and closely monitor to verify effectiveness

E: Exercise

- Challenging due to weakness, cognitive impairment, and balance issues
- For those who are **capable of engaging in physical activity**:
  - 3-4 sessions (average 40 minutes) per week of moderate- to vigorous- intensity physical exercise
    - Moderate: break a sweat or increase HR (walking briskly or riding bicycle)
- For those **with disability after stroke**, referral to physical therapist or cardiac rehab for initiation

CENTRAL ILLUSTRATION: Treatment Options for Secondary Prevention After a Transient Ischemic Attack or Ischemic Stroke

Patients with TIA or Ischemic Stroke

- **Lifestyle** → Education; Treatment targets*; Weight loss; Physical activity; Stop smoking; Reduce alcohol
- **Hypertension** → **Treat to target: < 130/80 mmHg**
- **Lipids** → **Treat to target: Lower LDL by ≥ 50% from baseline with statins**
- **Diabetes** → Antidiabetics, diet, weight loss
- **Antiplatelet therapy** → Short term **(21 days):** aspirin plus clopidogrel; Long term: aspirin or clopidogrel or aspirin plus ER-dipyridamole
- **Cardiac embolism** → Oral anticoagulation; VKA-antagonists (INR 2.0-3.0); DOACs preferred; LAA occlusion (contraindication for OAC)
- **ESUS** → Aspirin
- **Patent foramen ovale** → PFO closure, <60 years, Non-lacunar stroke
- **Symptomatic carotid Stenosis 70%-99%** → Carotid endarterectomy or stenting
- **Intracranial stenosis Vertebral stenosis** → Best medical treatment

Diener, H.-C. et al. J Am Coll Cardiol. 2020;75(15):1804-18.

Thanks and good luck with finals!