



# COGNITIVE IMPAIRMENT FOLLOWING ISCHEMIC AND HEMORRHAGIC STROKE

A SCIENTIFIC STATEMENT FROM THE AMERICAN HEART  
ASSOCIATION/AMERICAN STROKE ASSOCIATION

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# Stroke Council Professional Education Committee

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# DEFINITIONS

- **Vascular cognitive impairment (VCI):** cognitive impairment of any severity associated with cerebrovascular disease irrespective of the occurrence of stroke symptoms.
  - Vascular injuries leading to VCI include insidious, progressive microvascular changes (i.e. diffuse white matter injury, cerebral microbleeds, enlarged perivascular spaces, cortical microinfarcts) as well as single or multiple clinical stroke events impacting brain structures critical for cognition
- **Vascular dementia (VaD):** end of a continuum of severity of clinical manifestations of VCI
- **Post-stroke cognitive impairment (PSCI):** any severity of cognitive impairment, irrespective of cause, noted after an overt stroke
- **Post-stroke dementia (PSD):** end of a continuum of severity of clinical manifestations of PSCI and refers to all types of dementia after stroke
- **ICH:** intracerebral hemorrhage
- **AIS:** acute ischemic stroke
- **SAH:** Subarachnoid hemorrhage

# EPIDEMIOLOGY

# PSCI : PREVALENCE AND INCIDENCE

- Substantial heterogeneity in reporting
- Impacted by multiple factors (timing of assessment, diagnostic criteria, demographics, etc.)
- Most common in first year after stroke
  - 60% cumulative incidence in first year
  - Highest rate right after stroke
  - Pooled prevalence of PSCI without dementia 38%
- Even if not meeting criteria for dementia, PSCI impacts quality of life
- Rates can be impacted by preexisting cognitive impairment

# PSD : PREVALENCE AND INCIDENCE

- Less frequent than milder forms of cognitive impairment after stroke
- Varies by stroke severity and recurrent stroke history
- Rates in first year 7.4% (first stroke, pre-stroke dementia excluded)-41.3% (recurrent stroke, pre-stroke dementia included)
- Overall estimates:
  - 10% have dementia before first stroke
  - 10% after first stroke
  - 1/3 after recurrent stroke

# RACIAL DISPARITIES

- Differences in frequency and severity of PSCI reported
  - Black patients have greater cognitive decline and more frequent post-stroke dementia within 5 years of ischemic stroke than White patients
  - This occurs despite Black patients having younger age at time of incident stroke

## PSCI AND PSD: ICH

- Frequent in patients with ICH
  - Higher in patients with lobar ICH
- New-onset dementia 14.2% 1 year after ICH
  - Lobar ICH 23.4% vs non-lobar ICH 9.2%
- New-onset dementia 28.3% at 4 years



# SAH AND COGNITION

- Common to have impairment in a least one neuropsychological domain
- Global mental status impairment 3 months after SAH 26-43%
  - 21% at 1 year

# PSCI NATURAL HISTORY

# NATURAL HISTORY

- Variable, can:
  - Start at stroke onset and stabilize
  - Start at stroke onset and progress
  - Develop after recurrent strokes
  - Develop at onset of stroke in presence of pre-existing cognitive impairment
  - Develop more than 3-6 months after stroke
- Estimates of impairment early in course may overestimate as improvement may occur
- Long-term data on PSCI limited

# DELAYED ONSET PSCI

- PSCI >3-6 months after stroke
  - Overall incidence of new dementia >1 year after stroke 1.7% per year
    - varies by stroke severity
- Risks differ from early PSCI
  - Recurrent stroke
  - Progression of small vessel disease/covert stroke
  - Older age
  - Baseline cognitive impairment
  - Hypertension
  - Diabetes
  - Brain atrophy

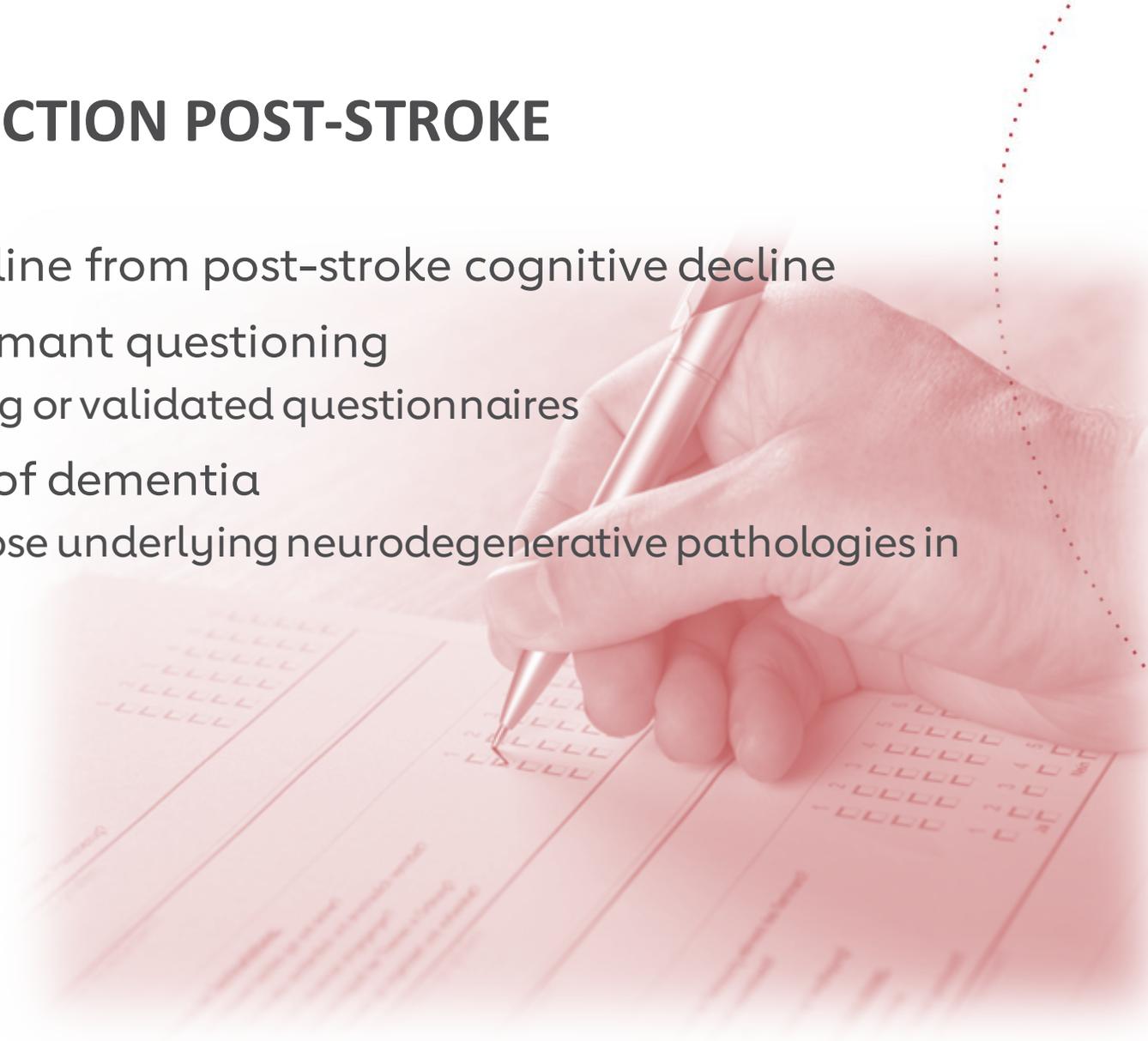
# DIFFERENTIAL DIAGNOSIS

# EVALUATION OF DECLINE IN COGNITIVE FUNCTION POST-STROKE

- Cognitive function post-stroke can be impaired by other complications, pre-stroke cognitive decline, and co-existing age-related neuropathologies
  - Delirium a common complication of stroke and should be differentiated from PSCI
    - Assess patients for delirium and for causes of delirium (medications, infection, pain, etc.)
  - Exclude reversible causes of cognitive impairment
    - TSH, vitamin B12
    - assess for mood disorders, hearing or vision impairments, sleep disorders, sedating and anticholinergic medications

# ASSESSMENT OF COGNITIVE FUNCTION POST-STROKE

- Differentiate pre-stroke cognitive decline from post-stroke cognitive decline
- Can be assessed by patient and informant questioning
  - Cognitive-related activities of daily living or validated questionnaires
- Common to have multiple etiologies of dementia
  - More research needed on how to diagnose underlying neurodegenerative pathologies in the setting of recent stroke



# **SYMPTOMS & COGNITIVE DOMAINS AFFECTED**

# STROKE LOCATION & COGNITION

- Location linked to type of deficits but not perfectly predictive of cognitive impairment
- Locations associated with increased risk of PSCI:
  - Left frontotemporal, left angular gyrus, left basal ganglia structures and surrounding white matter, left thalamus, right parietal lobe, left middle cerebral artery territory
- Given overlap of these regions and aphasia and cognitive screening dependence on language, severity of cognitive impairment may be overestimated in patients with aphasia

# COGNITIVE DOMAINS

- Executive function and attention difficulty common
  - Reported to show most improvement by 3-6 months
- Language does not tend to improve
- Global deficits described but may reflect use of global measures
- Deficits similar between ICH and AIS patients
- Executive function and verbal memory most affected in SAH

# PATHOPHYSIOLOGY

# PATHOPHYSIOLOGY

- Small vessel disease biggest contributor to VCID
- PSCI pathophysiology less well understood
  - Likely brain reserve and resilience play a role in degree of cognitive impairment

***Brain reserve:** difference between degree of brain damage observed and clinical manifestation of that damage*

***Brain resilience:** brain's capacity to counteract accumulated damage combined with compensatory mechanisms that can be used to mitigate effects*

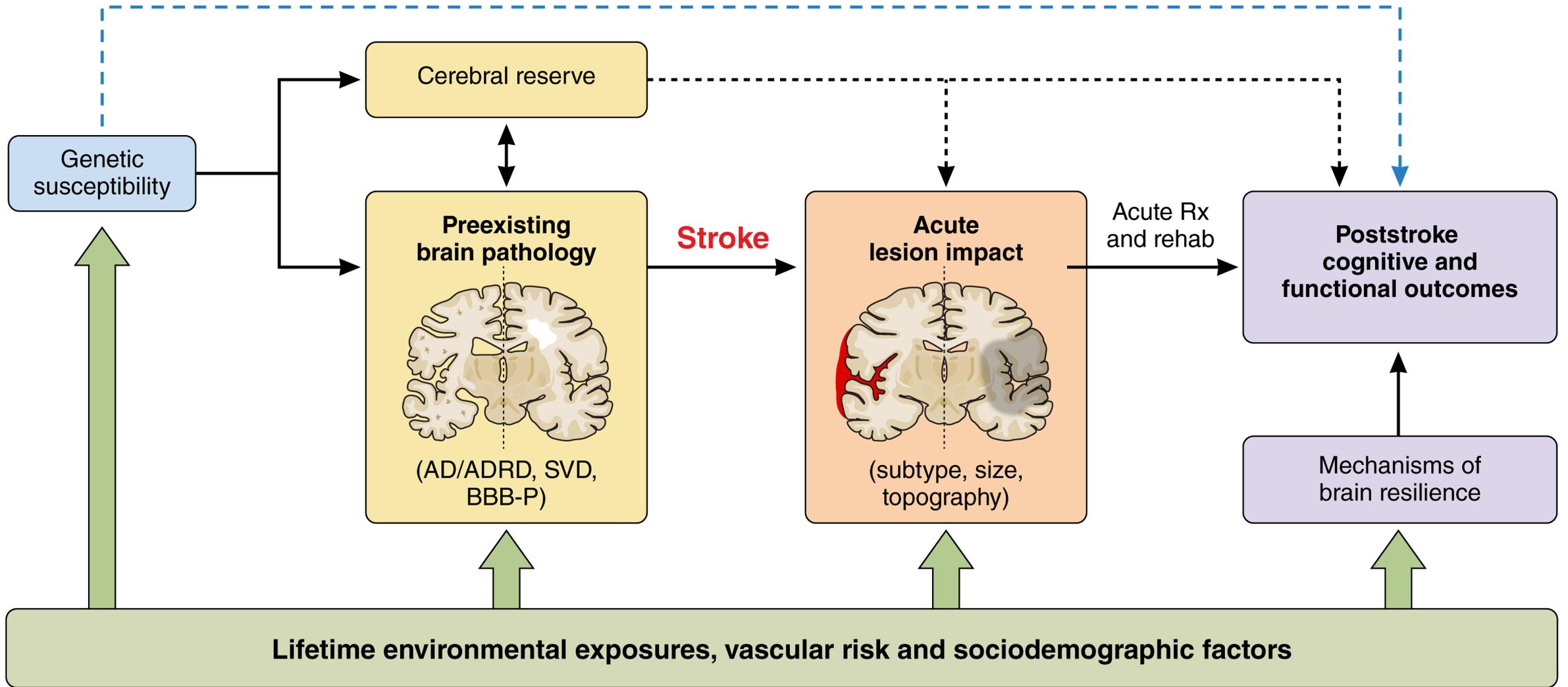
# BRAIN HEALTH & THE NEUROVASCULAR UNIT

- Brain health: brain's capacity to operate at its optimal state
- Neurovascular unit is the key structural element
  - Often damaged by stroke
  - Damage possibly leads to PSCI
  - Possible points of intervention for future treatment & prevention

## Neurovascular Unit

- *Neurons*
- *Astrocytes*
- *Pericytes*
- *Microglia*
- *Blood vessels*

# Brain susceptibility to poststroke cognitive impairment and dementia



# PSCI RISK FACTORS

# RISK FACTORS & VULNERABILITY FACTORS

## RISK FACTORS

- Pre-stroke cognitive decline
- Pre-existing cerebral vulnerability/reduced reserve
- Stroke impact

## VULNERABILITY

- Pre-existing reduced brain reserve
- Risks factors for increased vulnerability: age, small vessel disease, neurodegeneration

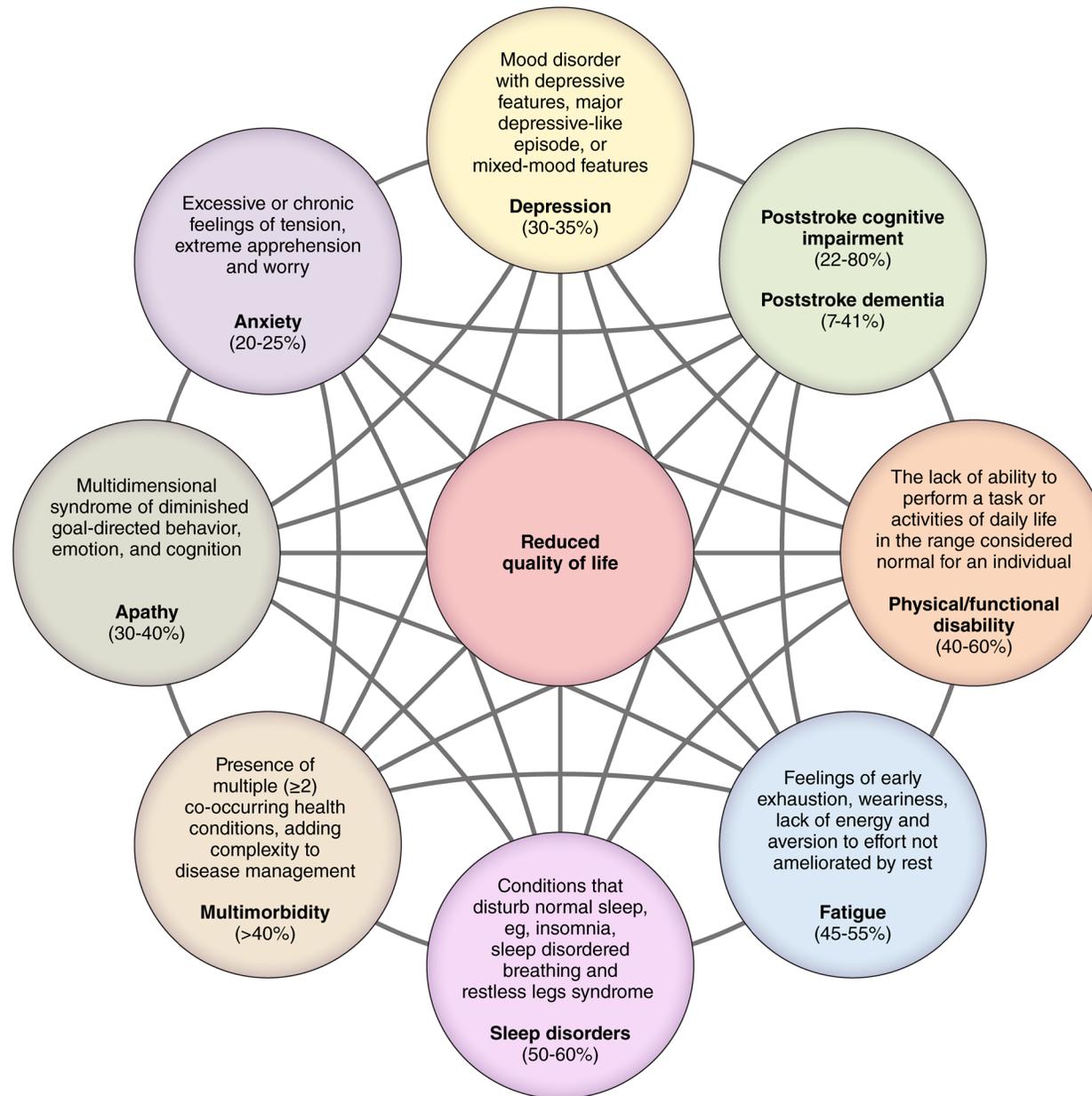
## OTHER ASSOCIATIONS

- PSCI frequently co-exists with post-stroke depression
- Strong social networks may be protective, though data sparse
- More common with higher stroke burden
  - Brain imaging can serve as a proxy, though extent of ability to predict unclear
- Rates higher in ICH, specifically lobar ICH
  - Likely related to underlying cerebral amyloid angiopathy
  - In SAH, linked to delayed cerebral ischemia and chronic hydrocephalus
- Post-stroke delirium associated with higher rates of post-stroke dementia

# ASSOCIATION WITH OTHER POST-STROKE OUTCOMES

## OTHER POST-STROKE OUTCOME ASSOCIATIONS

- Associated with other common post-stroke outcomes that contribute to lower quality of life
  - Physical disability, sleep disorders, depression, neuropsychological changes
  - These comorbidities can complicate or delay diagnosis
- Assessment of functional outcomes (mRS, Barthel, ADL assessments) are affected by cognitive impairment
- Poor cognition may impact participation in rehabilitation
- Along with cognition, patients should be assessed for these other conditions
- Improved physical activity and antidepressant use may benefit cognition, though minimal clinical trial data



# SCREENING AND DIAGNOSTIC MODALITIES

## SCREENING FOR PSCI

- Cognitive complaints are common
- Who to screen, when, and how often not clear
  - Need to screen if complaints or clinical concerns
- Informant report is insensitive to PSCI
- Objective assessment is critical
- No gold standard for cognitive screening post-stroke
- Early detection in acute setting essential for early planning and treatment
  - Reassessment important

## SCREENING TESTS

- Several brief tests have been used
  - Mini-Mental State Examination (MMSE)
  - Montreal Cognitive Assessment (MoCA)
    - Generally recommended, more sensitive to mild impairment, less ceiling effect
- Most screens not developed for heterogeneous presentations of PSCI
- Stroke deficits and individual patient factors (demographics, cultural, linguistic) may limit utility of standard tools

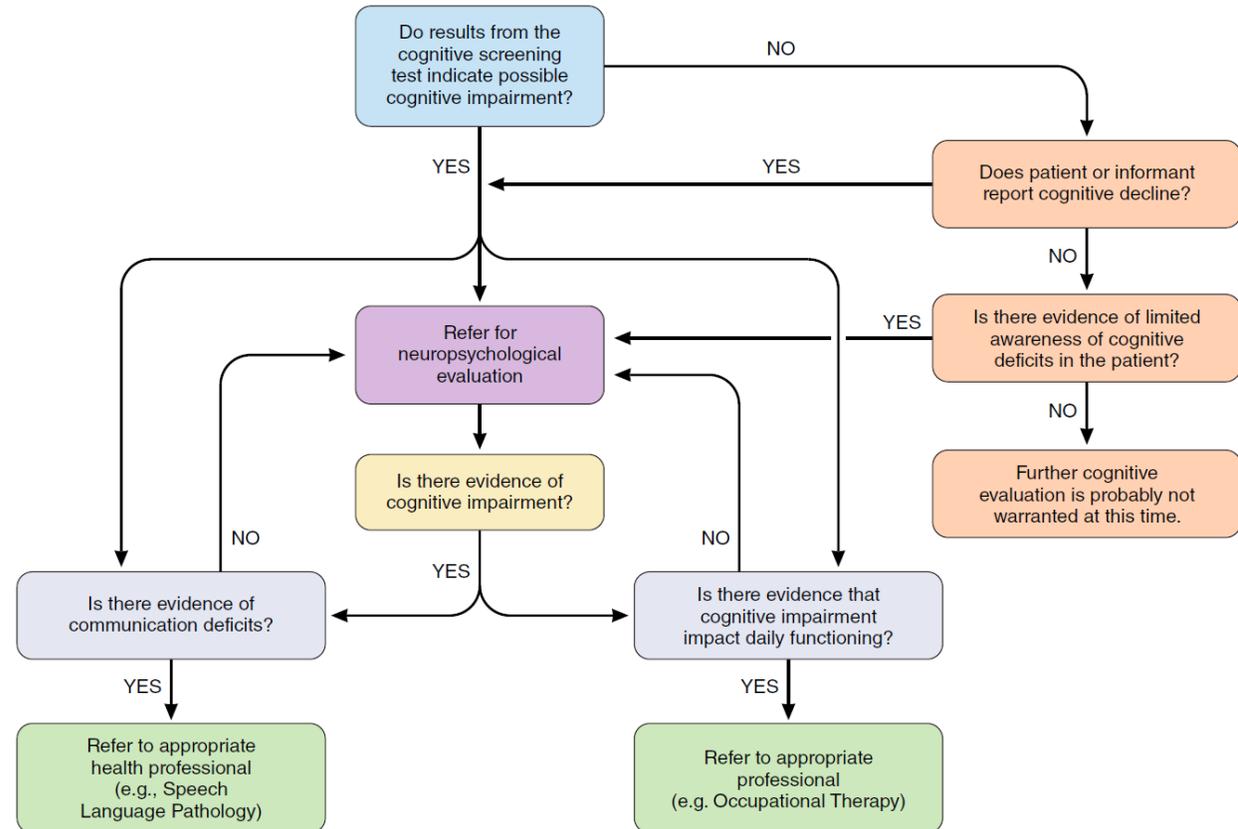
# MANAGEMENT OF POST-STROKE COGNITIVE IMPAIRMENT

# MANAGEMENT PEARLS – POST STROKE COGNITIVE IMPAIRMENT

## INTERDISCIPLINARY COLLABORATION

- Neurologists, gerontologists and PCPs can enlist many allied health professionals in post-stroke evaluation
- Examples include: SLP, OT, Neuro-Psych, RNs
- Not all patients will need all modalities – tailor the team to each individual patient
- Telehealth can assist with monitoring and management of cognitive deficits

## CARE PARADIGM



# MANAGEMENT PEARLS – POST STROKE COGNITIVE IMPAIRMENT

## COGNITIVE REHABILITATION

- Small gains in multiple domains identified in literature review
  - Memory, executive functioning and neglect
  - Attention training has inconsistent benefits
- Virtual tools may be beneficial for cognitive rehab
  - Patient's own device – gamified tools
  - Caregiver training and education

## PHYSICAL ACTIVITY

- Small studies suggest aerobic activity may improve cognitive function
- Tai Chi, boxing and resistance training studied in small sample sizes
- Virtual tools (e.g. Wii Fit, Oculus Rift) have inconclusive evidence

# MANAGEMENT PEARLS – POST STROKE COGNITIVE IMPAIRMENT

## MEDICAL MANAGEMENT

- Secondary Stroke prevention is paramount
  - Risk of PSCI increases with subsequent strokes
- BP control is associated with lower risk of dementia in general population
  - Also associated with lower risk of primary and secondary strokes
- Integrated vascular risk factor modification has been effective in slowing progression of AD
  - Further research needed to establish impact in PSCI
- Reduction in final lesion size via acute stroke intervention may reduce risk of PSCI
  - Improved functional and cognitive outcomes among EVT and thrombolysis recipients c/w no treatment
- No consistent benefits of SSRIs or dopamine agonists following stroke
- Studies of cholinesterase inhibitors and memantine have shown small positive effect in
  - complicated by high rates of adverse events and patient discontinuation

## COMPLIMENTARY AND INTEGRATIVE TREATMENTS

- Transcranial magnetic stimulation (TMS) shows small improvement in cognitive and attention performance
- Other modalities plagued by poor quality studies
  - Acupuncture
  - Neuromodulation
  - Herbal supplements & vitamins
  - DASH and Mediterranean diets

# ANTICIPATORY GUIDANCE – FOR CLINICIANS

## WHEN COGNITIVE IMPAIRMENT DETECTED

- Characterize affected domains
- Assess for safety issues
- Connect with Community Resources
- Address Caregiver Fatigue
- Introduce Advanced care planning tools

## HOME SAFETY CONCERNS

- Toileting
  - Grab bars, raised toilet seats
- Mobility and Communication
  - Provide mobility tools
  - Simplify access to emergency help
- Transitional Care processes increase home safety
  - Reduce Falls
  - Reduce readmissions

# ANTICIPATORY GUIDANCE – FOR CLINICIANS

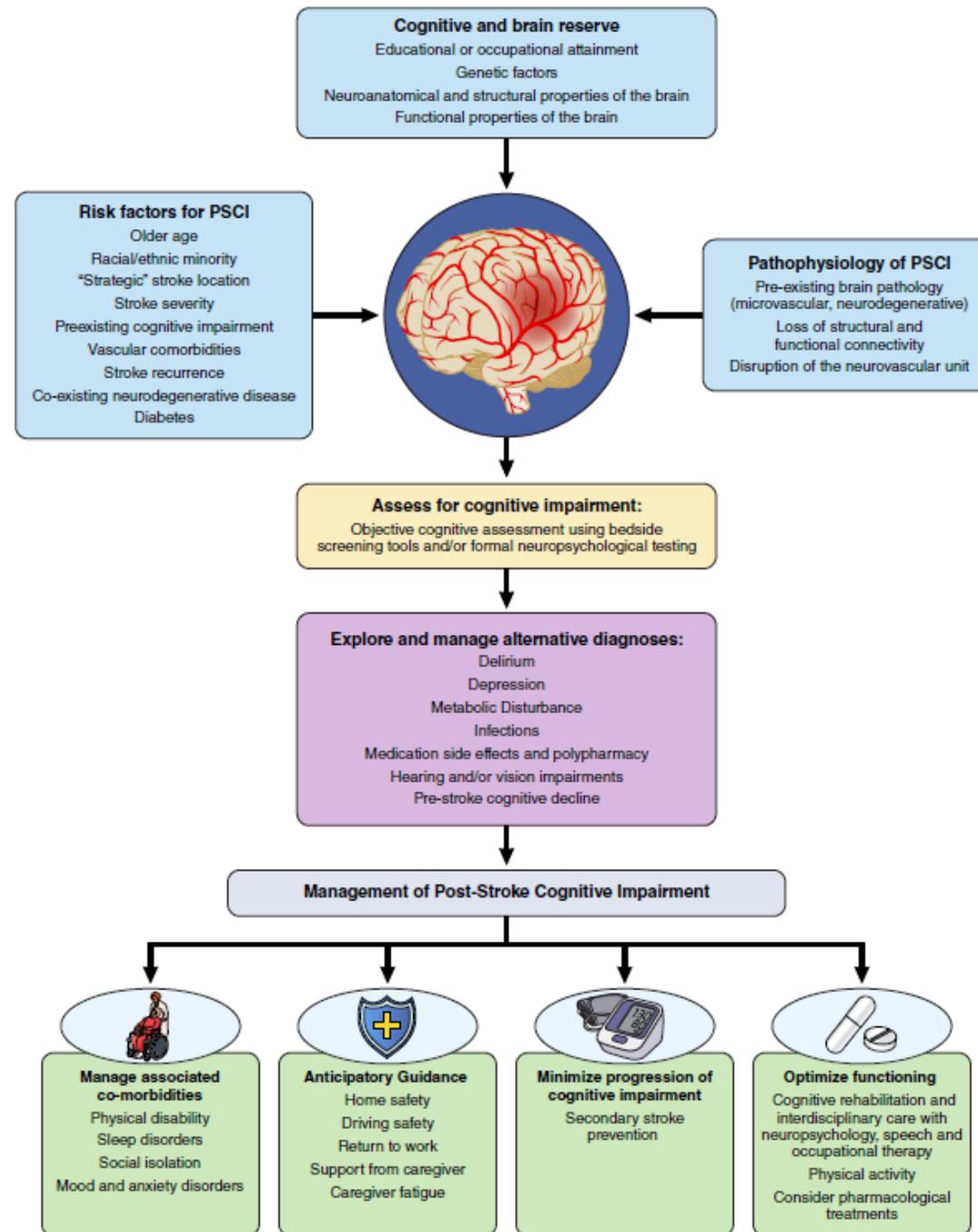
## RETURN TO WORK

- Cognitive decline risk higher in those who do NOT return to work or those who were unemployed before stroke
- Cognitive/vocational rehab can assist
- Lack of knowledge of invisible deficits hinders return to work and staying employed

## DRIVING

- Common source of pride and independence
- 1/3 of stroke patients require training or rehab before resuming driving
- Attention and executive functioning performance linked to resuming driving
- Limited data supporting any particular intervention to improve performance

# SUMMARY



# SUMMARY & FUTURE DIRECTIONS

## MULTIPLE AREAS OF FUTURE INVESTIGATION

- Mechanisms of PSCI
- Stroke subtypes, preexisting pathology
- Social/cultural factors
- Cognitive Screening
- Need for adequately powered trials of rehab, lifestyle modification, and pharmaceuticals
- Further study of multidisciplinary clinics & other care models

## DISCOVERY STUDY (DETERMINANTS OF INCIDENT STROKE COGNITIVE OUTCOMES AND VASCULAR EFFECTS ON RECOVERY)

- 8,000 patient multicenter study of ischemic and hemorrhagic stroke patients
- Patients with no dementia history enrolled and followed for 2 years
- Serial cognitive and functional assessments, MRI, PET imaging, genetics and biomarker tests