

## Post Stroke Cognitive Decline

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## Presenter Disclosure Information

Deborah A. Levine, MD, MPH  
Post Stroke Cognitive Decline

**FINANCIAL DISCLOSURE:**

Grants/Research Support: NIH/NIA R01  
Consultant / Advisory Board: Astra Zeneca and UCSF  
(SOCRATES trial event adjudicator), UCSF (POINT trial event  
adjudicator), Member, Program Advisory Committee of the  
Kaiser Permanente Northern California - University of  
California San Francisco Stroke Prevention/Intervention  
Research Program.

**UNLABELED/UNAPPROVED USES DISCLOSURE:**

Use of citocholine in patients with stroke is  
investigational only

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## Teaching Points

1. Incident stroke is associated with an acute decline in cognitive function and also accelerated and persistent cognitive decline over years.
2. Any cognitive domain can be affected.
3. Preventing recurrent strokes may reduce risk of poststroke cognitive decline.

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### Outline

- Epidemiology
- Clinical presentation
- Pathogenesis
- Management

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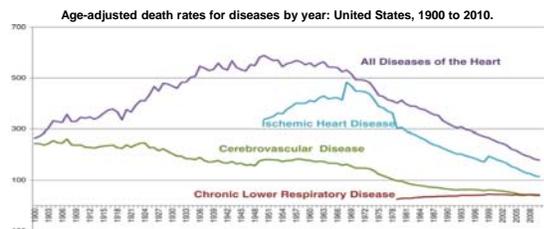
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### Stroke mortality is declining.



Lackland DT et al. Stroke. 2014;45:315-353.

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### Poststroke dementia is increasing.

- Up to 30% of stroke survivors have poststroke dementia.
  - 10% have dementia before stroke.
  - 10% have dementia after first stroke.
  - 33% have dementia after recurrent stroke.
- Prevalence of poststroke cognitive decline (both dementia and cognitive impairment) is increasing in older adults.

Pendlebury ST, Rothwell PM. Lancet Neurol 2009;8:1006-18. Ukrainitseva S et al. Stroke 2006;37:1155-59. Edwards JD et al. Stroke 2010;41:996-1000.

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### Stroke disability is increasing.

- Stroke disability is increasing.
  - Over the last twenty years, disability rates—years lived with disability—for stroke rose 40%, the *only major disease* showing a significant increase.
- Cognitive decline is a major cause of disability in stroke survivors.

Murray CJ et al. JAMA 2013;310:591-606. Tatemichi TK et al. J Neurol Neurosurg Psychiatry 1994;57:202-7. Patel MD et al. J Am Geriatr Soc 2002;50:700-6.

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### Cognitive decline has risks.

Poststroke cognitive decline is associated with:

- Mortality
- Disability
- Institutionalization
- Recurrent stroke
- Poorer quality of life

Dhamoon MS et al. Neurology 2010;75:328-34. Moroney JT et al. J Am Geriatr Soc 1999;47:824-9. Barba R et al. Stroke 2002;33:1993-8. Patel MD et al. J Am Geriatr Soc 2002;50:700-6. Moroney JT et al. Neurology 1997;48:1317-25.

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**What are risk factors for PSCD?**

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**What are risk factors for PSCD?**

- Older age
- Low education level
- Atrial fibrillation
- Prestroke cognitive decline
- Diabetes?
- Hypertension?
- Left hemisphere stroke
- Stroke severity
- Recurrent stroke
- Cerebral atrophy on brain imaging

Pendlebury ST, Rothwell PM. Lancet Neurol. 2009;8:1006-18. Dhouri A et al. Circulation 2013;128:1341-8. del Ser T et al. Stroke 2005;36:2670-5. Ankolakar S et al. J Stroke Cerebrovasc Dis 2014;23:1821-9.

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**Cognitive effects of stroke are variable.**

All cognition domains can be affected:

- Executive function/processing speed
- Learning and Memory (working and verbal)
- Language
- Visuospatial function
- General mental status

Sachdev PS et al. Neurology 2004;62:912-919. Hachinski V et al. Stroke 2006;37:2220-2241. Reed BR et al. Brain 2007;130:731-9.

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**Does cognitive decline after stroke persist for years?**

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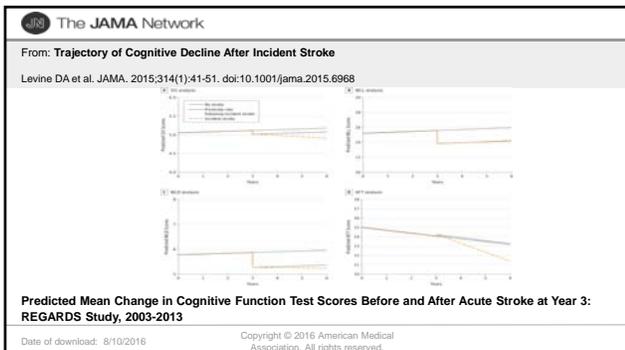
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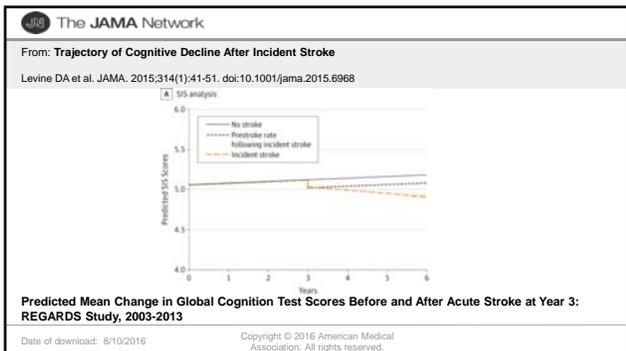
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**Does cognitive decline after stroke persist for years?**

- Incident stroke is associated with an acute decline in cognitive function and also accelerated and persistent cognitive decline over 6 years.

Levine DA et al. JAMA 2015;314:41-51.

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**Diagnosis requires testing.**

- Clinical practice guidelines and quality improvement programs recommend cognitive assessments for stroke patients before hospital discharge and also in postacute settings.
- Our work suggests stroke survivors warrant monitoring for mounting cognitive impairment years after the event.

Advanced Disease-Specific Care Certification Requirements for Comprehensive Stroke Center (CHC). Joint Commission website. <http://www.jointcommission.org>. Miller EL et al. Stroke 2010;41:2402-48. Levine DA et al. JAMA 2015;314:41-51.

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**Cognitive tests are recommended.**

- Montreal Cognitive Assessment (MoCA)
- Addenbrooke's Cognitive Examination-Revised
- Neuropsychological battery
- Mini-Mental State Examination (MMSE)
  - Highly correlated with MoCA (r=0.8) but has ceiling effect and less detects visuoexecutive dysfunction.

Mai M et al. Int J Stroke 2016;11:420-4. Pendlebury ST et al. Stroke 2010;41:1290-3. Pendlebury ST et al. Stroke 2012;43:464-9. Hachinski V et al. Stroke 2006;37:2220-41.

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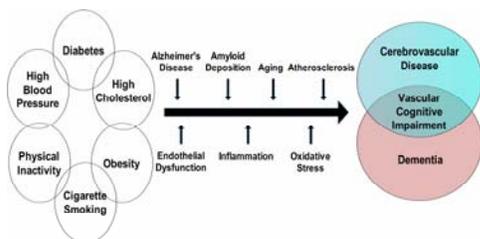
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**Shared mechanisms may contribute to poststroke cognitive decline.**



Levine DA, Langa KM. Neurotherapeutics. 2011;8:361-73.

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**Most dementia is mixed.**

- There are contributions by neurodegenerative disease, cerebrovascular disease, and comorbidity.
- Microinfarcts, microbleeds, and atrophy play key role.

Langa KM, Levine DA. JAMA 2014;312:2551-61. Knopman DS et al. Stroke. 2015;46:433-40. Launer L et al. Ann Neurol 2011;70:774-80.

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**Evidence-based treatment is lacking.**

- Currently, no drug has proven effective in treatment of poststroke cognitive decline.
- Cognitive rehabilitation may help.
- Preventing recurrent strokes likely is effective.

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### Cognitive rehabilitation may help.

- Cognitive training and rehabilitation represent possible therapies for PSCD.
- Cochrane reviews have found unclear effectiveness of cognitive rehabilitation and occupational therapy and insufficient evidence to evaluate individualized treatment.

Loetscher T. Cochrane Database Syst Rev. 2013;(5):CD002842. Chung CS et al. Cochrane Database Syst Rev. 2013;(4):CD008391. Hoffmann T, et al. Cochrane Database Syst Rev 2010;(9):CD006430. Nair RD, Lincoln NB. Cochrane Database Syst Rev 2007;(3):CD002293.

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### Computer training is promising.

- Computer-assisted cognitive training may improve cognitive scores perhaps by increasing functional connectivity of the hippocampus with the frontal lobe.
- Larger trials with longer follow-up are needed.

Lin Z et al. J International Medical Research 2014;42:659-68. Prokopenko SV. J Neurol Sci 2013;325:148-53.

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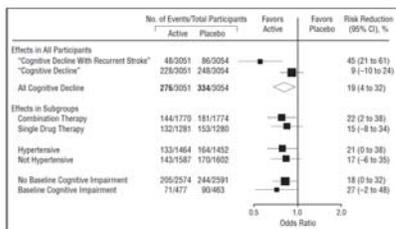
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### Hypertension treatment is associated with lower risk of cognitive decline related to recurrent stroke.

#### PROGRESS trial



Tzourio C et al. Arch Intern Med 2003;163:1069-75.

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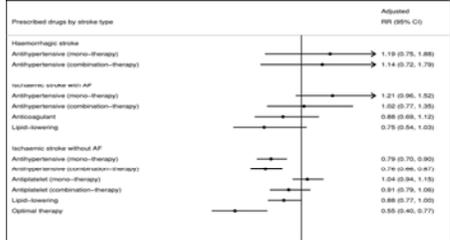
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**Secondary prevention is associated with lower risk of cognitive impairment in patients with ischemic stroke without atrial fibrillation. South London Stroke Register**



American Heart Association. Abdel Douiri et al. *Circulation*. 2013;128:1341-1348. Copyright © American Heart Association, Inc. All rights reserved.

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**Some studies are negative.**

- The SPS3 trial (n=2916) found that short-term dual antiplatelet treatment or blood pressure reduction in patients with recent lacunar stroke was not associated with lower risks of cognitive decline.

Pearce LA et al. *Lancet Neurol* 2014;13:1177-85.

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**Clinical trials have been negative.**

- The ASPIS trial (n=202) found no benefit of a 24-month multi-domain intervention focused on improving lifestyle and vascular risk factors on the incidence of poststroke cognitive decline compared with standard stroke care.
- Studies with a larger sample size are needed.

Matz K et al. *Stroke* 2015;128:1341-8.

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**Other interventions may help.**

- Diagnosis and treatment of depression.
- Reduction of polypharmacy.
- Aerobic exercise, mental activity, and social engagement.

Langa KM, Levine DA. JAMA 2014;312:2551-61. del Ser T et al. Stroke 2005;36:2670-5. Jorge RE et al. Arch Gen Psychiatry 2010;67:187-196.

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**The future is bright.**

- Many trials are ongoing.
- Some results are intriguing.
  - Citicoline: Although the drug seems to be safe and well tolerated, more study of its disease-modifying effects and mechanisms are needed.

Alvarez-Sabin J. Cerebrovasc Dis 2013;35:146-54. Jorge RE et al. Arch Gen Psychiatry 2010;67:187-96.

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