Post-Stroke Depression (PSD)

NIH StrokeNet Grand Rounds, April 26, 2018

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Objectives

- Describe the scope of the problem of depression and stroke
- Evaluate the evidence base for pharmacologic and non-pharmacologic treatment in post-stroke depression

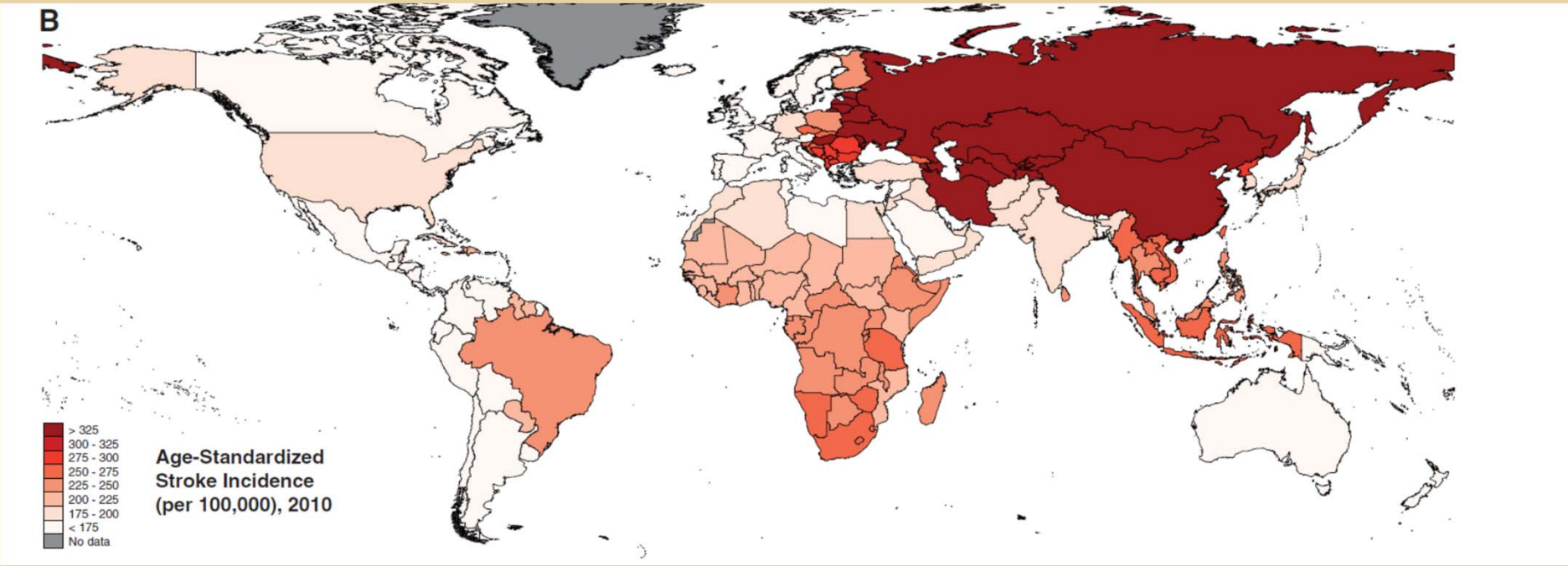
- **Take Home Message**
  - PSD is prevalent worldwide
  - PSD can be rapidly assessed
  - PSD can be treated

Stroke as a leading cause of disability

- ~795,000 new or recurrent strokes per year (US)
- 4th leading cause of death in US and 2rd worldwide
- A leading cause of long-term serious disability
  - Blacks more than whites
  - Women more than men

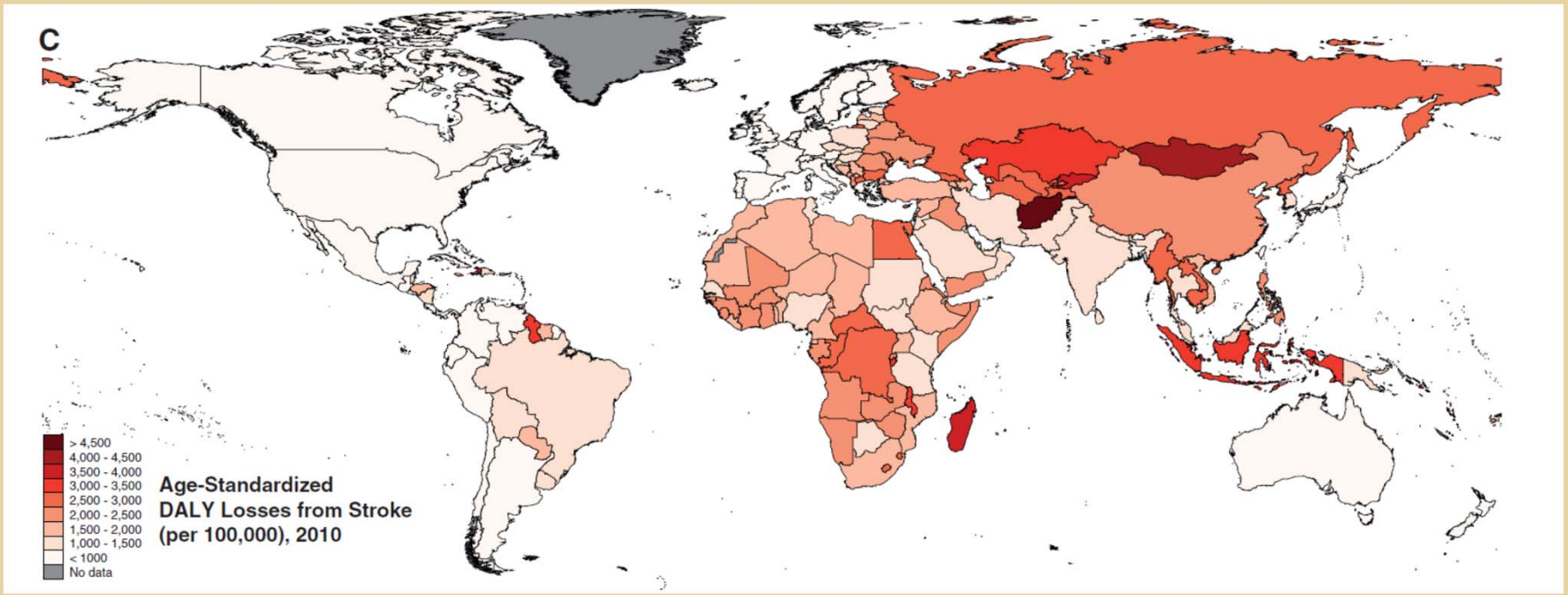
Heart Disease and Stroke Statistics – 2018 update
(Circulation. Online ahead of print January 31, 2018.
DOI: 10.1161/CIR.0000000000000558.

Global Stroke Incidence



troke. 2015;46:3564-3570. DOI: 10.1161/STROKEAHA.115.008226.)

Global Stroke Disability Adjusted Life Years (DALY) Lost



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Health Burden of Depression

- Depression is the ***leading*** global cause of years of life lived with disability
- Major contributor to the overall global burden of disease - disability-adjusted life-years (DALY).
  - Reduction in an individual's productive life
  - Takes into account premature mortality

Depression coupled with stroke is thus a double burden

WHO, 2016; Insel & Charney, JAMA 289, 3167-3168, 2003

Impact of Depression and Chronic Illness

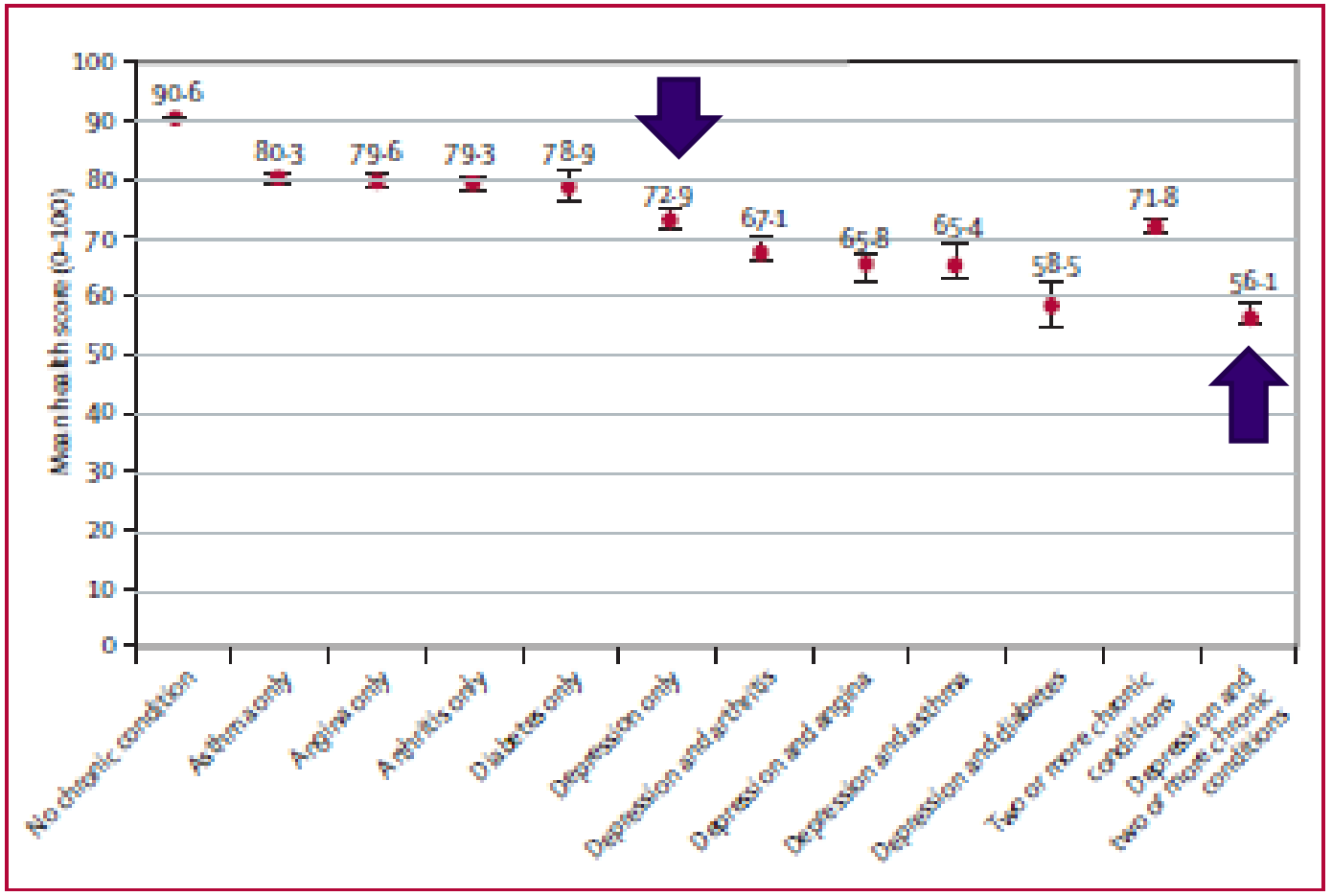
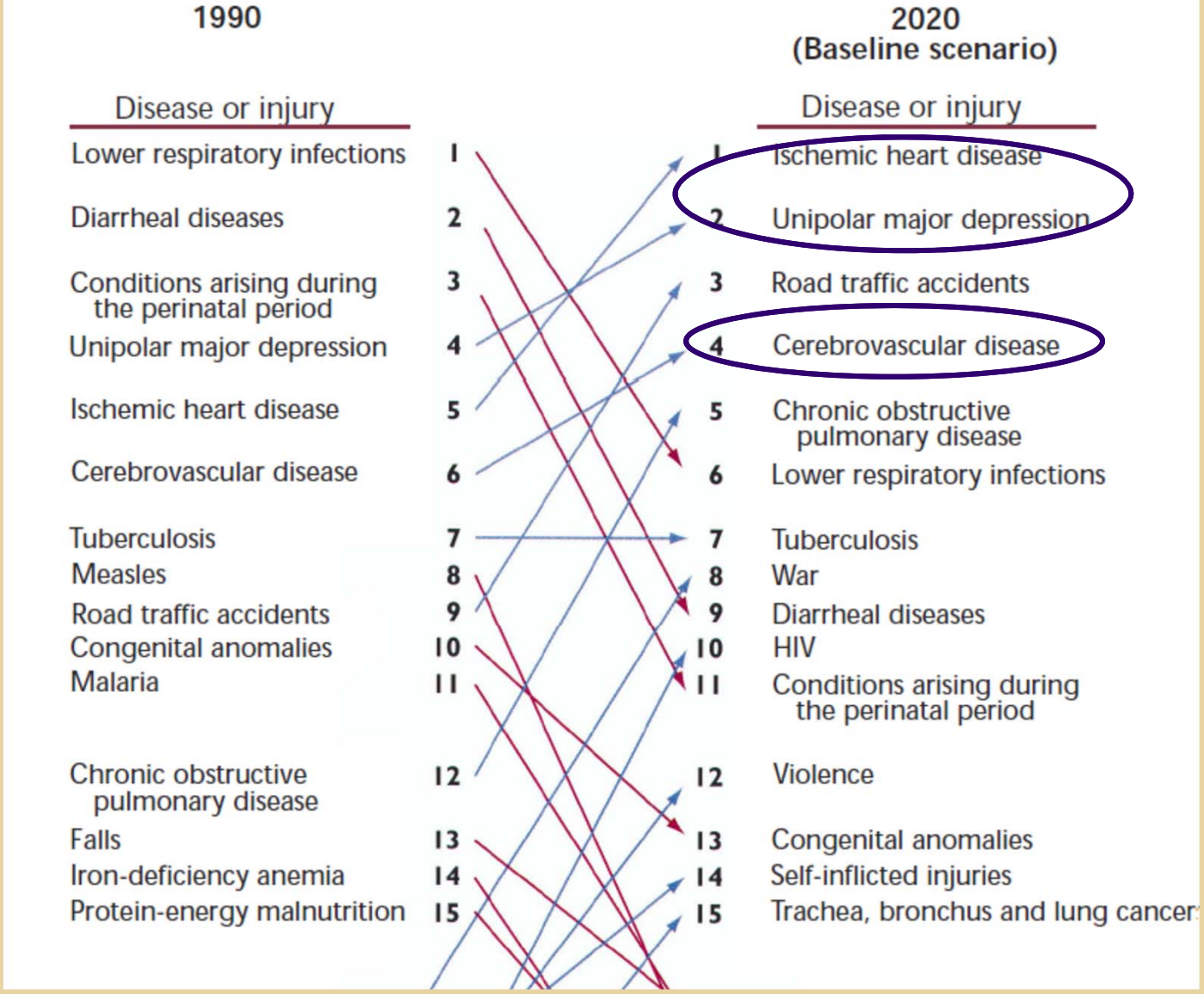


Figure: Global mean health by disease status
Data from WHS 2003.

www.thelancet.com Vol 370 September 8, 2007

Change in the rank order of disease burden for 15 leading causes worldwide, 1990–2020 (as measured by DALYS)



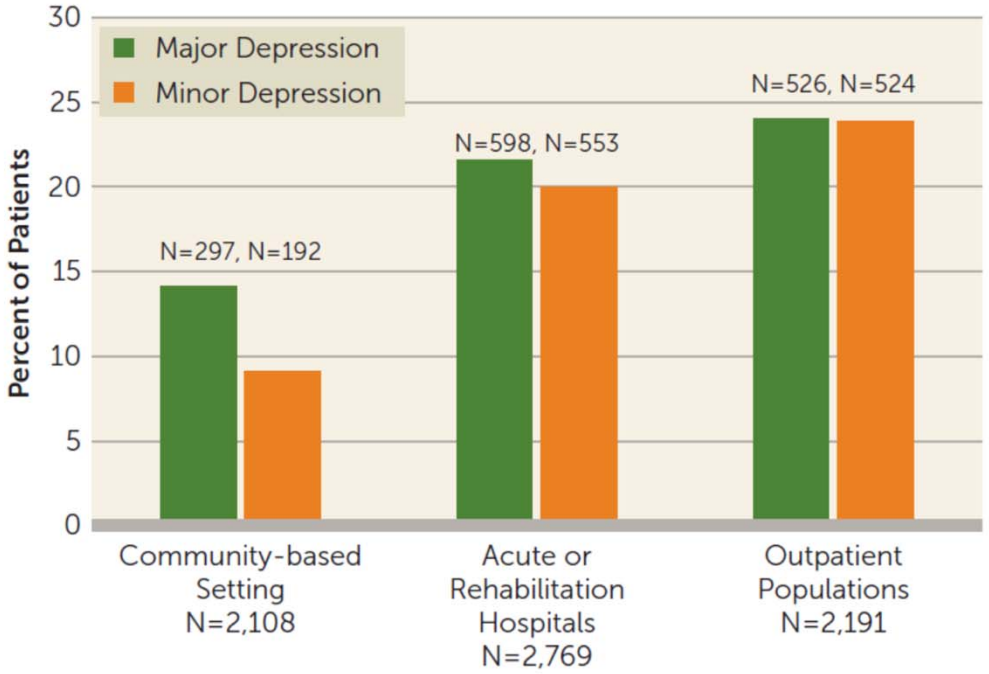
NATURE MEDICINE • VOLUME 4 • NUMBER 11 • NOVEMBER 1998

Frequency of depression after stroke

- 35% in > 65 year olds (Kelly-Hayes et al, J Stroke Cerebrovas Dis 12, 119-126, 2003)
- Synthetic review of studies conducted between 1977 and 2014.(Hacket et al, Stroke 2005, 36(6), 1330-40; Hackett & Pickles. Int J Stroke 9(8): 1017-1025 doi: 10.1111/ijs.12357. Epub 2014 Aug 12.
  - Pooled estimate was 33% (95% confidence interval, 26% to 39%) of all stroke survivors experiencing depression.
  - Range – 10% to 55%
  - Differences in case mix, method of mood assessment explains variation across studies
  - Reflects both incidence and prevalence

An alternative view

FIGURE 1. The Prevalence of Depression in Various Clinical Settings Following Stroke[a]



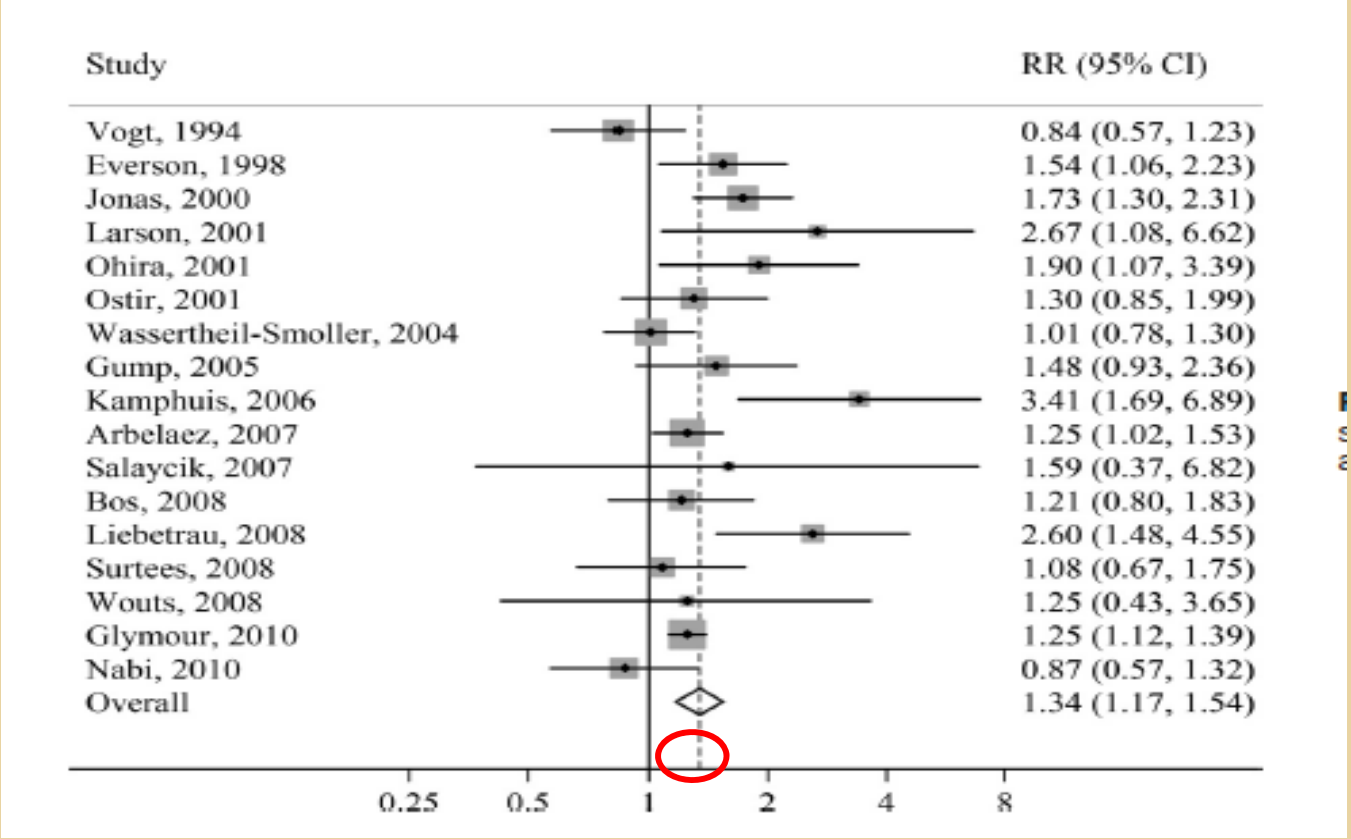
[a] Patients were examined using a standardized mental status examination and DSM-IV diagnostic criteria for depression following stroke with major depressive-like features or minor depression defined as more than two but less than five symptoms of major depression. Meta-analyses stating that the prevalence of poststroke depression is 31% miss these important clinical variables.

Post-Stroke Depression: A Review

Robert G. Robinson, M.D., Ricardo E. Jorge, M.D.

Am J Psychiatry 2016; 173:221–231; doi: 10.1176/appi.ajp.2015.15030363

Depression preceding stroke



Depression and Risk of Stroke : A Meta-Analysis of Prospective Studies
Jia-Yi Dong, Yong-Hong Zhang, Jian Tong and Li-Qiang Qin

Stroke 2012, 43:32-37: originally published online October 20, 2011
doi: 10.1161/STROKEAHA.111.630871

Consequences of post-stroke depression

- Poorer rehabilitation outcomes
- Reduced quality of life for stroke survivor *and* significant others
- Possibly increased risk of subsequent stroke, other CVD, death

Top 10 Things I want friends and family of stroke survivors to know about PSD

- 10: I don't have the words to tell you what's wrong. I really don't and I feel bad about it.
- 9: I'm not in control and I'm confused.
- 8: I feel like a burden. I was independent. I'm not now and it makes me sad.
- 7: I don't know what would help me feel better. But keep loving me.
- 6: I feel unlovable. I don't love myself. Touch heals. Hug me.
- 5: I don't recognize myself in the mirror.
- 4: I am working harder than you can imagine, at everything.
- 3: Are you afraid of me or are you afraid of having your own stroke? Stroke is scary. But I am not scary. Stay near.
- 2: Life can't go back to the way it was and neither can I. I'm changed. I didn't choose to change. I don't want to change. I can't deal with any more change.
- 1: ***I didn't survive a stroke to be miserable. I can be magnificent. But I need help and I need HOPE***!

Rachel Scanlon Henry, Stroke Connection, Spring 2018

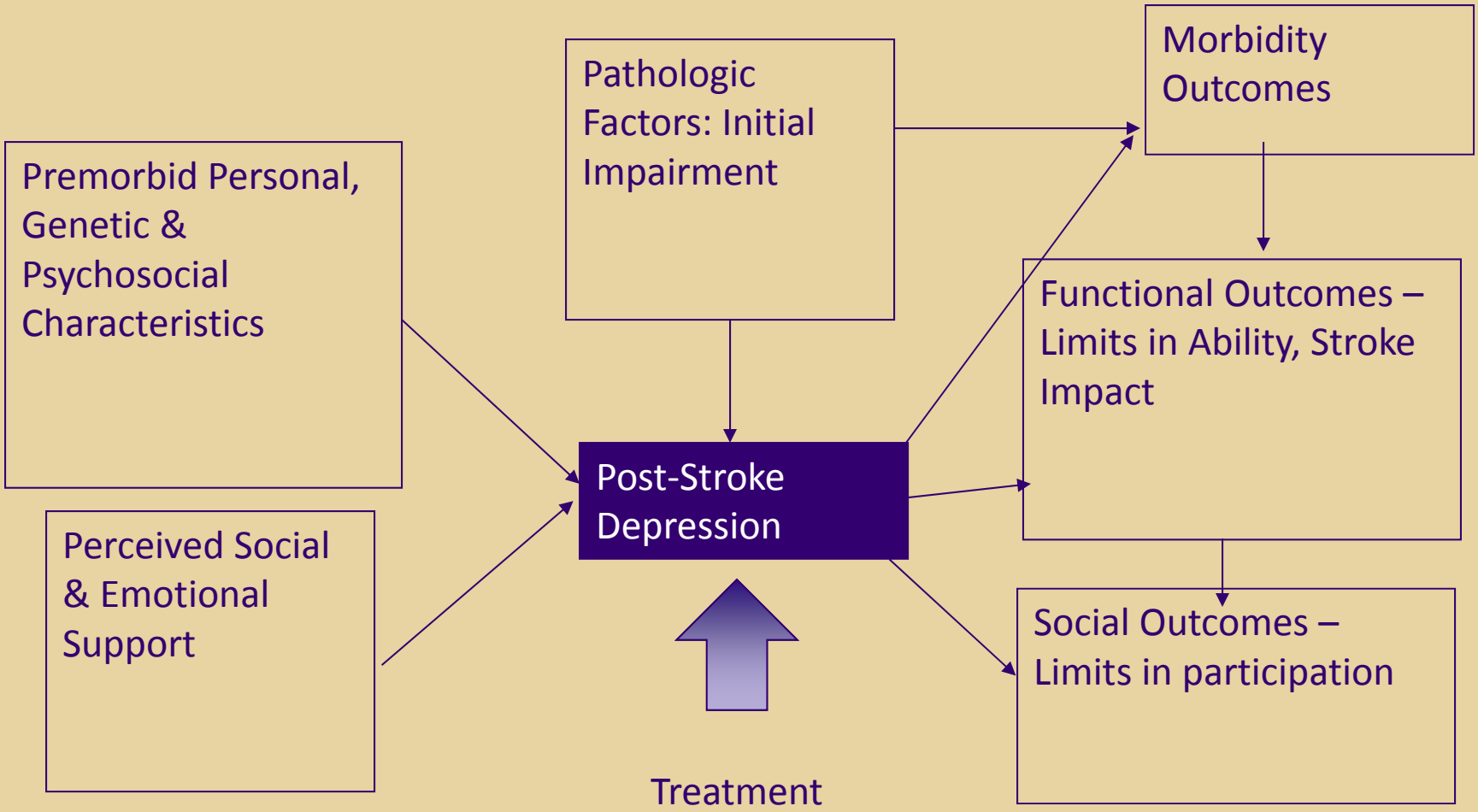
Postulated mechanisms linking depression and cardio-cerebrovascular disease

- Biological
  - Tissue injury (stroke)- damage to neural circuits regulating mood
  - Serotonin signaling disruption (genetic propensity?)
  - Inflammation – cytokines
    - Stroke leads to changes in the levels of pro-inflammatory cytokines which has been associated with depression in humans and in animal models
- Psychological
  - Stroke as stressor, 'reactive', chronic CVD as stressor OR life stresses lead to inflammatory response
- Bio-psycho-social
  - Combination of above

Towfighi et al Poststroke Depression *e33*

Stroke. 2017;48:e30-e43. DOI: 10.1161/STR.0000000000000113.

Conceptual Model



Identifying PSD – ask the patient!

- Clinically simple one question screen (Yale – Watkins et al 2001; Lachs et al 1990)
  - "Do you often feel sad or depressed?"
- Or two question -PHQ-2 (Kroenke et al 2003)
  - Over the last 2 weeks, how often have you been bothered by 1) "little interest or pleasure in doing things" and 2) "feeling down, depressed, or hopeless."
  - Rated: "not at all," "several days,""more than half the days,"or "nearly everyday" (scored as 0, 1, 2, and 3, respectively)

Formal Screening Tools

- Formal screening
  - Geriatric Depression Scale (GDS) – 30 or 15 items
  - Patient Health Questionnaire (PHQ-9)
  - Beck Depression Inventory (BDI) – 21 items
- DSM-IV criteria
  - Major depressive disorder: 5 or more of 10 depressive symptom; present at least “more than half the days”in the past 2 weeks, including depressed mood or anhedonia.
  - Other depressive disorder: 2 –4, including mood or anhedonia
  - Suicidal ideation always counts as one

UNDERSTANDING HOW POST-STROKE DEPRESSION AFFECTS YOUR LOVED ONE

American Heart Association | American Stroke Association
life is why

Just because someone is home from the hospital does not mean that all is normal and they are running on all cylinders. Their brains have been injured, and it takes time and the compassion and patience of friends and family for them to recover.

It is important to let survivors respond to this situation in their own way, without trying to meet the expectations of others who have not experienced a brain injury. It may not be possible to understand how they feel.

What to Understand About Post-Stroke Depression

- It is extremely common. Studies document that between one-third and two-thirds of stroke survivors experience depression.
- It can result from the stroke lesion itself. It may also be a reaction to their stroke deficits. Or it may be both.
- It can stymie recovery because it may prevent them from participating in therapy.
- It increases risk of another stroke.
- It generally responds well to treatment, which typically is a combination of medication and talk therapy.
- It is not a character flaw or moral failing.
- It is unlikely to go away by itself.

Things your loved one may be thinking and feeling when experiencing post-stroke depression:

- "I don't have the words to tell you what's wrong. I really don't, and I feel bad about it."
- "I'm not in control and I'm confused."
- "I feel like a burden. I was independent. I'm not now and it makes me sad."
- "I don't know what would help me feel better. But keep loving me."
- "I feel unlovable. I don't love myself. Touch heals. Hug me."
- "Life can't go back to the way it was and neither can I. I'm changed. I didn't choose to change. I don't want to change. I can't deal with any more change."

What Can Help

Family members and friends can help by coming from a position of compassion and understanding, rather than the expectation that everything should be better. Stroke support groups help both survivors and caregivers accept the new normal that stroke has brought to their family.

Treatment of PSD

- Pharmacologic (Hackett et al 2005, Stroke 36, 1098-)
  - Antidepressants
  - Psychostimulants
- Non-pharmacologic (Hackett et al 2004, Cochrane… CD003437)
  - Behavioral, psychosocial
  - Supportive therapy
  - Neuromodulation

Most recent scientific statement

AHA/ASA Scientific Statement

Poststroke Depression

A Scientific Statement for Healthcare Professionals From the American Heart Association/American Stroke Association

The American Academy of Neurology affirms the value of this statement as an educational tool for neurologists.

Amytis Towfighi, MD, Chair; Bruce Ovbiagele, MD, MSc, MAS, FAHA, Vice Chair; Nada El Husseini, MD, MHSc; Maree L. Hackett, PhD; Ricardo E. Jorge, MD; Brett M. Kissela, MD, MS, FAHA; Pamela H. Mitchell, PhD, RN, FAHA; Lesli E. Skolarus, MD; Mary A. Whooley, MD; Linda S. Williams, MD, FAHA; on behalf of the American Heart Association Stroke Council; Council on Cardiovascular and Stroke Nursing; and Council on Quality of Care and Outcomes Research

(*Stroke*. 2017;48:e30-e43. DOI: 10.1161/STR.0000000000000113.)

Antidepressants and PSD

- Antidepressants
  - Tricyclics – (nortriptaline, clomipramine)
  - Serotonin Selective Reuptake Inhibitors – SSRI (citalopram, fluoexetine, paroxetine, sertraline)
  - Norepinephrine Reuptake Inhibitors – NRI (reboxetine)
  - Serotonin-Norepinephrine Reuptake Inhibitor –
  - SNRI (venflaxine)

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Am J Psychiatry 2016; 173:221–231; doi: 10.1176/appi.ajp.2015.15030363

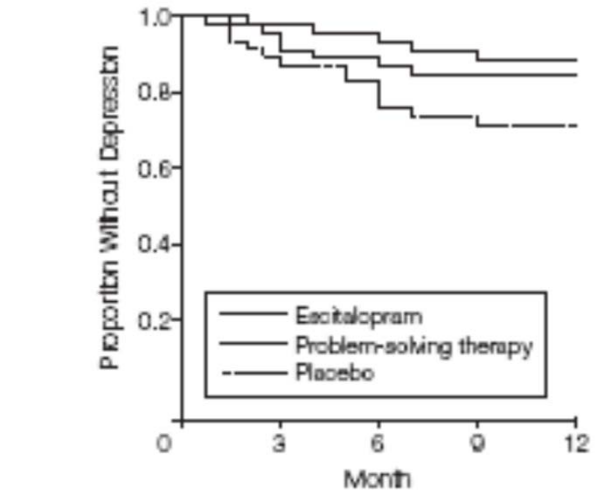
Interventions for management of post-stroke depression: A Bayesian network meta-analysis of 23 randomized controlled trials

Linghui Deng[1], Xuejun Sun[2], Shi Qiu[3], Yao Xiong[1], Yuxiao Li[1], Lu Wang[1], Qiang Wei[3], Deren Wang[1] & Ming Liu[1]

SCIENTIFIC REPORTS | 7: *16466* | DOI:10.1038/s41598-017-16663-0

Primary prevention

Figure 2. Risk Comparison of Depression Onset for Patients Receiving Escitalopram, Problem-Solving Therapy (PST), or Placebo Over 1 Year



No. at Risk					
Escitalopram	59	46	44	42	38
PST	59	49	46	41	38
Placebo	58	43	39	34	33

- (Anderson et al, 2004, Cochrane review)
  - no effect
- Escitalopram, problem-solving (Robinson et al, 2008 JAMA)
  effective
- Towfighi et al, 2017

Eight trials (n=776) suggest that pharmacological treatment may be effective in preventing PSD; however, further studies are needed in more representative samples of stroke survivors, and additional study is required to determine the optimal timing and duration of treatment.

Five trials (n= 1078) suggest that psychosocial therapies may prevent the development of PSD; however, the studies are not generalizable to all stroke survivors, given their narrow inclusion and exclusion criteria. Further research with more rigorous methods is needed to assess the effect of psychotherapy on prevention of PSD.

Non-pharmacologic Treatments

- Neuromodulation – repetitive transcranial magnetic stimulation rTMS (Deng et al, Scientific Reports, 2017, mostly in China)
- Behavioral, psychosocial (Towfighi et al, Stroke, 2017)
  - Cognitive Behavioral Therapy (+ effect)
  - Brief psychodynamic problem-solving (+ effect)
  - Motivational interviewing (+effect)
  - Collaborative care (+effect)
  - Stroke liasons (no effect on depression scores)

ASA Resources for Patients/Families

- http://strokeconnection.strokeassociation.org/Spring-2018/Helping-Others-Understand-Post-Stroke-Depression/

ASA Resource for Health Professionals

AHA/ASA Scientific Statement

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Table. Summary of Findings

Topic	Summary of Findings
Epidemiology	Approximately one third of stroke survivors develop PSD at some point after stroke. The frequency is highest in the first year, at nearly 1 in 3 stroke survivors, and declines thereafter.
Pathophysiology	The pathophysiology of PSD is complex and likely involves a combination of biological and psychosocial factors. Further research is needed to develop a better understanding of PSD pathophysiology with an aim to develop targeted interventions for prevention and treatment.
Predictors	A multitude of studies have evaluated predictors of PSD, but because of differences in inclusion and exclusion criteria, statistical methods, and inadequate sample sizes for multivariate analyses, generalizability is limited. The most consistent predictors of PSD have been physical disability, stroke severity, history of depression, and cognitive impairment. Further studies are needed to develop a better understanding of predictors of PSD.
PSD and functional outcomes	PSD is associated with poorer functional outcomes after stroke. Treatment with fluoxetine was associated with lower PSD occurrence rates and improvement in motor recovery in 1 RCT. Further research is needed to assess the effect of PSD on outcomes and to develop optimal strategies to counteract these effects.
PSD and QOL	A few studies suggest that PSD adversely affects QOL. Further research is needed to further elucidate the independent effect of PSD on QOL and to determine how to improve QOL in individuals with or at risk for PSD.
PSD and healthcare use	A few studies have shown an association between PSD and healthcare use. Further studies are needed to evaluate the effect of treatment of PSD on subsequent healthcare use.
PSD and mortality	PSD is associated with higher mortality after stroke.
Screening	Twenty-four studies (n=2907 participants) showed that the CES-D, HDRS, and PHQ-9 had high sensitivity for detecting PSD; however, the studies had several limitations, including generalizability. Systematic screening for PSD with the 9-item PHQ-9 is pragmatic, has high sensitivity for detecting PSD, and may improve outcomes, provided that processes are in place to assure accurate diagnosis, timely and effective treatment, and follow-up. Further research is needed to determine whether screening for PSD—in conjunction with collaborative care to ensure timely intervention, treatment, and follow-up—improves outcomes in diverse populations of stroke survivors.
Management: pharmacotherapy	Twelve trials (n=1121) suggest that antidepressant medications may be effective in treating PSD; further research is needed to determine optimal timing, threshold, and medications for treatment.
Management: neuromodulation	Further studies are needed to determine the efficacy of neuromodulation on treating PSD.
Management: psychosocial interventions	Seven trials (n=775) suggest that brief psychosocial interventions may be useful and effective in treatment of PSD. Whether antidepressant medication is a necessary or beneficial adjuvant cannot be established from these trials because of a lack of placebo controls.
Management: stroke liaison workers	Fifteen trials (n=2743) have not revealed a beneficial effect from stroke liaison workers on PSD; however, the trials included individuals without a diagnosis of PSD. Further studies are needed to determine the effect of liaison worker on those with established PSD.
Management: information provision	Seven trials (n=720) suggest that information provision provides a small benefit in depression scores; however, the clinical significance of this improvement is unclear.
Management: self-management	Few studies have assessed the effectiveness of self-management strategies on PSD; further studies are needed to determine whether these strategies are beneficial.
Prevention: pharmacotherapy	Eight trials (n=776) suggest that pharmacological treatment may be effective in preventing PSD; however, further studies are needed in more representative samples of stroke survivors, and additional study is required to determine the optimal timing and duration of treatment.
Prevention: psychosocial interventions	Five trials (n= 1078) suggest that psychosocial therapies may prevent the development of PSD; however, the studies are not generalizable to all stroke survivors, given their narrow inclusion and exclusion criteria. Further research with more rigorous methods is needed to assess the effect of psychotherapy on prevention of PSD.

CES-D indicates Center of Epidemiological Studies-Depression Scale; HDRS, Hamilton Depression Rating Scale; PHQ, Patient Health Questionnaire; PSD, poststroke depression; QOL, quality of life; and RCT, randomized controlled trial.

Questions and Comments