# LONG TERM COGNITIVE OUTCOME OF ICU PATIENTS

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SAINT-LUC
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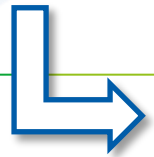
# INTRODUCTION

Progress in (ICU) Medicine

Increased survival and survivors

**LONG TERM DYSFUNCTION and DISABILITIES**

- ICU-AW
- Cognitive Dysfunction
- …



Costs

# INTRODUCTION

## COGNITIVE DYSFUNCTION IN THE ICU

- Delirium
- Anxiety
- Acute stress disorder
- Depression

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## COGNITIVE DYSFUNCTION IN THE ICU

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## COGNITIVE DYSFUNCTION AFTER ICU

- Cognitive dysfunction
- Anxiety
- Post traumatic stress disorder
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## COGNITIVE DYSFUNCTION IN THE ICU

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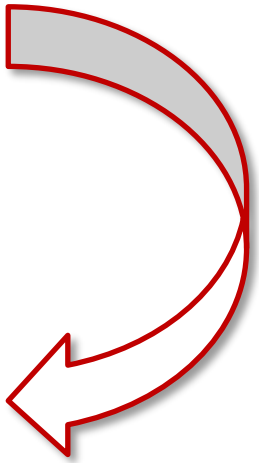

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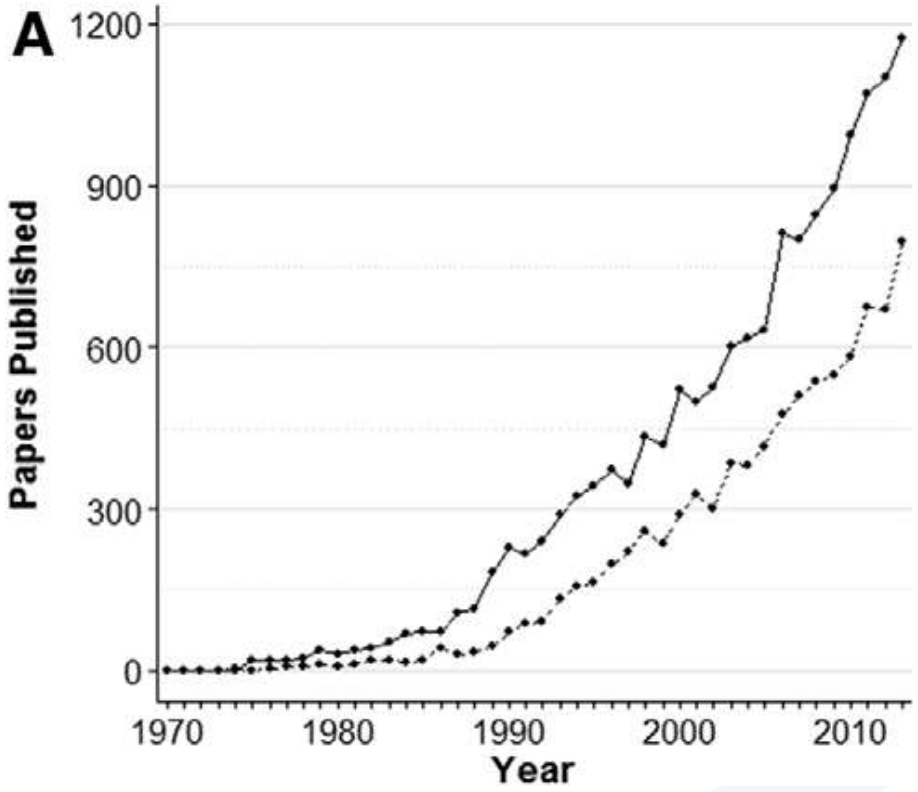
## COGNITIVE DYSFUNCTION AFTER ICU

- Cognitive dysfunction
- Anxiety
- Post traumatic stress disorder
- Depression

# Outcome Measurement in ICU Survivorship Research From 1970 to 2013: A Scoping Review of 425 Publications*




*Turnbull A et al^. Crit Care Med.2016;44:1267-77*

# HOW TO DIAGNOSE ?

**Table 1** Summary of common functional and walk tests applicable for assessing survivors of a critical illness.

| Instrument | Description | Interpretation | Comments |
|---|---|---|---|
| *Functional tests* | | | |
| Physical Function ICU Test (PFIT)[12] | 4 domains once patient able to sit out of bed: sit to stand, marching on the spot, shoulder flexion, muscle strength[e] | No total score calculated; enables prescription of activities based on results | Inter-rater reliability (ICC > 0.99 for all domains); responsiveness ($p = 0.02–0.005$);[12] intra-rater reliability: participants unable to repeat test because of fatigue |
| Barthel Index (BI)[100,97] | 10 ADLs[a] measured on a 0–2 scale | Dependence: total = 0–4; severe = 5–12; moderate = 6–18; slight = 19; independent = 20 | Used to assess patients in the post-ICU period[24] |
| Functional Independent Measure (FIM)[11] | 18 ADLs in motor and cognitive themes[b]; 7-point ordinal scales; performed by a multi-disciplinary team over 72-hour period | Score range 18–126 (fully dependent–functional independence) | Acceptable levels of reliability and validity[14]; possible ceiling effects, particularly in outpatient settings[98] |
| Functional Ambulation Categories (FAC)[99] | 6-point ordinal scale[c] assessing ambulation | Descriptive categories reflect function | Can be used to assess progress in walking in ICU cohort |
| Glittre ADL Test[13] | 5 laps of a 10-metre walk with steps and carrying, lifting and bending activities[d] | Time-measurement; 4–5 min for in-patient pulmonary rehabilitation; ADL-time associated with disease severity[13] | Responsive to intervention[13]; used for patients with COPD, but not currently with survivors of a critical illness |
| *Walk tests* | | | |
| Six Minute Walk Test (6MWT)[18] | Distance walked in six minutes on a 30 m flat track or circuit. Requires the person to walk as far as possible in the six minutes. Standardised encouragement provided each minute. Rests permitted but rest time is included in the six minute period. Heart rate and oxygen saturation should be measured during the test. | The minimum important difference for the 6MWT based on changes following pulmonary rehabilitation has been variously reported as 10% or 35 m (95%CI 30–42)[100] and 14% or 25 m (95%CI 20–61)[101] | Reflects functional capacity in respiratory or cardiac diseases |
| Incremental Shuttle Walk Test (ISWT)[28] | Participants walk round a 10 m track (1 shuttle) in time with audio prompts. Walking speed increases each minute; 12 levels of speed (0.5–2.37 m/s). Number of shuttles and distance walked recorded. Heart rate and oxygen saturation should be measured during the test. | The minimum clinically important improvement in ISWT after pulmonary rehabilitation in COPD is reported as 47.5 m (95% CI 38.6–56.5)[30] | Used to assess patients in the post-ICU period[102] |
| Timed Up and Go (TUG)[31] | Stand from sitting in a chair, walk 3 m at regular pace and return to sit in the chair | Normal ≤10 s; good mobility, independent ≤20 s; requires supervision/walk aid = 21–30 s | Used to assess patients in the post-ICU period[102] |

*Elliott D et al. Austr Crit Care.2011:24:155-66*

**Table 3** Summary of generic HRQOL instruments used for patients following a critical illness (adapted from[103]).

| Instrument | Items; domains/concepts examined |
|---|---|
| Medical outcomes study (SF-36)[74,104] | 36 items in 8 domains; physical: functioning, role limitations, pain, general health; mental: vitality, social, role limitations, mental health; health transition; variable response levels (2–5); Mental and Physical Component Summary calculated from domains |
| Assessment of quality of life (AQoL)[67] | 15 items in 5 domains: illness (3 items); independent living (3 items); physical senses (3 items); social relationships (3 items); psychological well-being (3 items); 4 response levels; measured on a scale from 0.04 (state worse than death) to 1.00 (full health) where 0.0 is death equivalent; enables cost-utility analysis |
| 15D[92,105] | 15 items/domains: mobility, vision, hearing, breathing, sleeping, eating, speech, elimination, usual activities, mental function, discomfort, distress, depression, vitality, and sexual activity; 5-point ordinal scale (1 = full function; 5 = minimal/no function) |
| EuroQol 5D[68,92,106] | Adapted from 15D; 5 items: mobility, self-care, usual activities, pain/discomfort, anxiety/depression; 3 response levels; cost-utility index calculated |
| Nottingham Health Profile (NHP)[69] | 45 items; experience: energy, pain, emotional reactions, sleep, social isolation, physical mobility; daily life: employment, household work, relationships, home life, sex, hobbies, and holidays |
| Quality of life – Italian (QOL – IT)[70] | 5 items: physical activity; social life; perceived quality of life; oral communication; functional limitation; varied response levels (4–7) |
| Quality of life – Spanish (QOL – SP)[71] | 15 items: basic physiological activities (4 items); normal daily activities (8 items); emotional state (3 items) |
| Perceived quality of life (PQOL)[72] | 11 items on satisfaction with: bodily health; ability to think/remember; happiness; contact with family and friends; contribution to the community; activities outside work; whether income meets needs; respect from others; meaning and purpose of life; working/not working/retirement; each scored on 0–100 scale |
| Sickness impact profile (SIP)[73,107] | 68 item short-version/136 items in 6 domains; physical: body movement, mobility, ambulation; psychosocial: intellectual, social interaction, emotional behaviour, communication; sleep and rest; daily work; household; leisure and recreation |

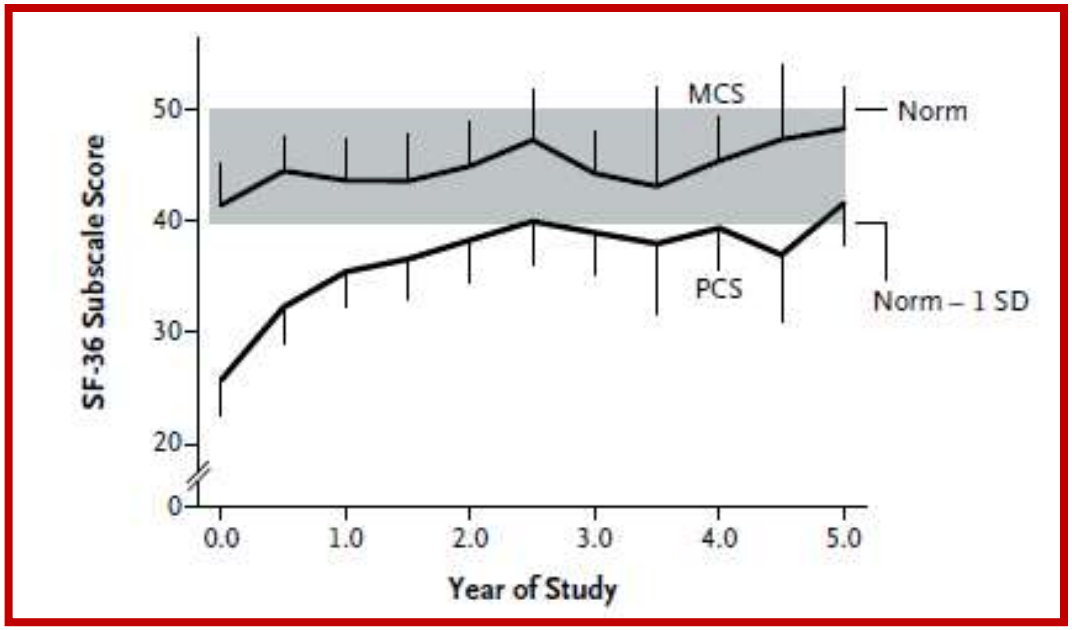
*Elliott D et al. Austr Crit Care.2011:24:155-66*

# Outcome Measurement in ICU Survivorship Research From 1970 to 2013: A Scoping Review of 425 Publications*

**Conclusions:** Peer-reviewed publications reporting patient outcomes after hospital discharge for ICU survivors have grown from 3 in the 1970s to more than 300 since 2000. Although there is evidence of consolidation in the instruments used for measuring participation restriction and quality of life, the ability to compare results across studies remains impaired by the 250 different instruments used. Most articles described cohort studies of modest size with a single follow-up assessment using patient-reported measures of participation restriction and quality of life. Development of a core outcome set of valid, reliable, and feasible measures is essential to improving the outcomes of critical illness survivors. (*Crit Care Med* 2016; 44:1267–1277)

*Turnbull A et al^. Crit Care Med.2016;44:1267-77*

# Functional Disability 5 Years after Acute Respiratory Distress Syndrome




*Herridge M et al. NEJM.2011:364(14):1293-304*

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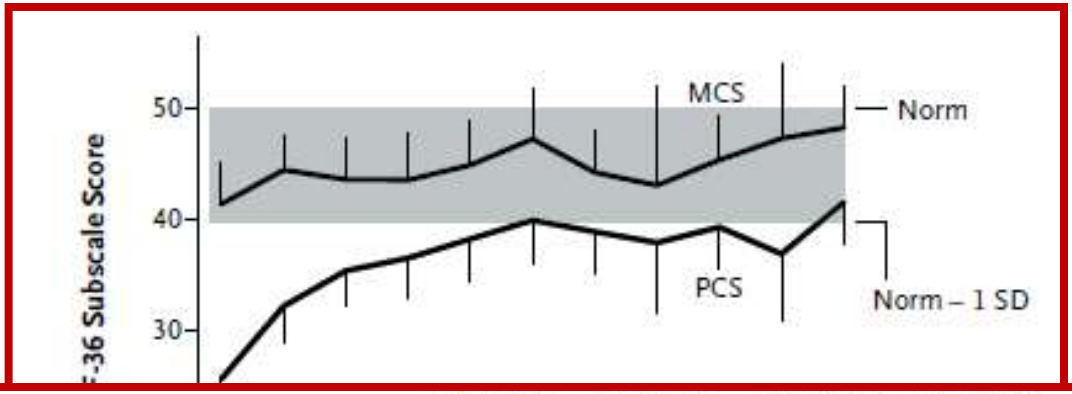



| Clinical Outcomes | At 1 Year (N=83) | At 2 Years (N=69) | At 3 Years (N=71) | At 4 Years (N=63) | At 5 Years (N=64) |
|---|---|---|---|---|---|
| Median SF-36 score | | | | | |
| Physical functioning | 60 | 70 | 70 | 75 | 75 |
| Role, physical | 25 | 50 | 100 | 75 | 88 |
| Bodily pain | 62 | 62 | 72 | 74 | 74 |
| General health | 52 | 62 | 55 | 59 | 62 |
| Vitality | 55 | 55 | 50 | 50 | 55 |
| Social functioning | 63 | 75 | 75 | 69 | 75 |
| Role, emotional | 100 | 100 | 100 | 100 | 100 |
| Mental health | 72 | 76 | 72 | 76 | 76 |

*Herridge M et al. NEJM.2011:364(14):1293-304*

# The Adult Respiratory Distress Syndrome Cognitive Outcomes Study

## Long-Term Neuropsychological Function in Survivors of Acute Lung Injury

Subset of **FACTT: Fluid and Catheter Treatment Trial:**
**Liberal vs conservative fluid management in ALI**

➡ **ventilation days -2.5d (P=0.04)**

75 patients from the initial 1001 patients included in the FACTT trial
Telephone-based neuro-psychological evaluation

- Test battery: 45-60 minutes
- Memory, verbal fluency, Executive function

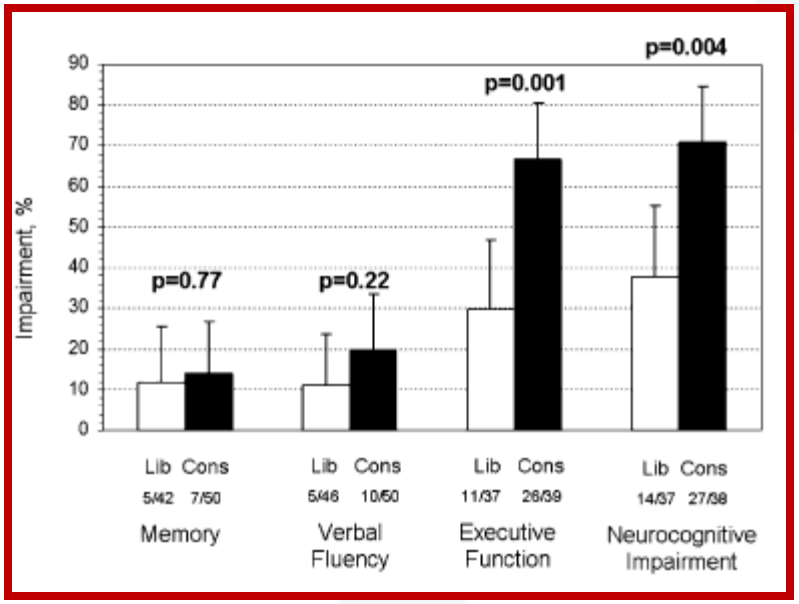
- Memory impairment: 13%
- Verbal fluency impairment: 16%
- Executive functions impairment: 49%

*Mikkelsen ME et al. AJRCCM.2014:185(12):1307-15*

# The Adult Respiratory Distress Syndrome Cognitive Outcomes Study

## Long-Term Neuropsychological Function in Survivors of Acute Lung Injury

| | |
|---|---|
| **DEPRESSION** | **36% (37/102)** |
| **PTSD** | **39% (40/102)** |
| **ANXIETY** | **62% (63/102)** |

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# The Adult Respiratory Distress Syndrome Cognitive Outcomes Study

## Long-Term Neuropsychological Function in Survivors of Acute Lung Injury

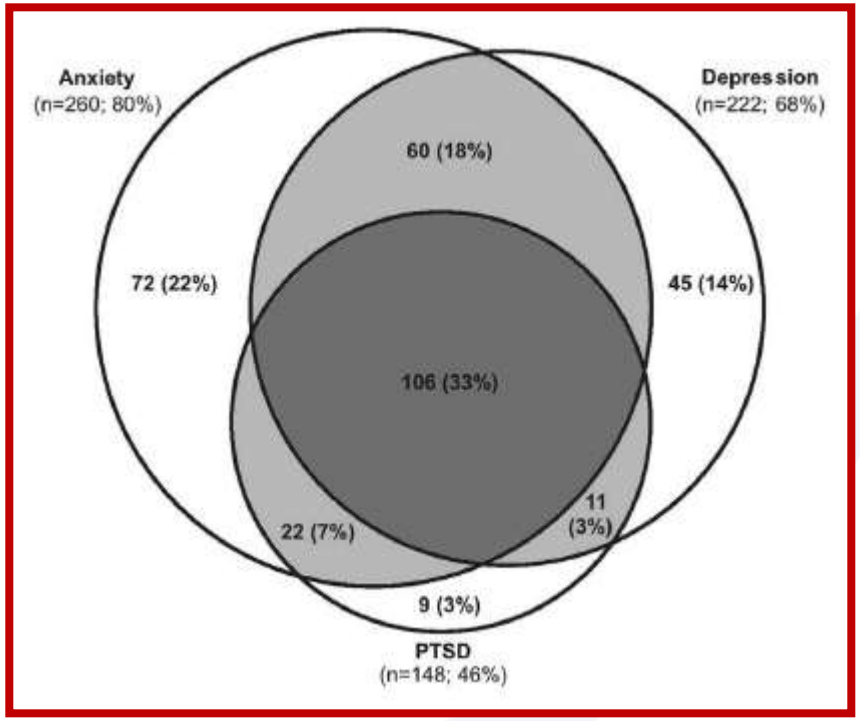
| | Psychiatric Morbidity | | |
|---|---|---|---|
| | Not Present ($n = 35$) | Present ($n = 67$) | *P* Value |
| Baseline characteristics | | | |
| Age, yr | 51 (38–64) | 50 (44–57) | 0.58 |
| Male sex, % | 40 | 45 | 0.64 |
| Race or ethnic group, % | | | 0.19 |
| White | 94 | 81 | |
| Black | 6 | 15 | |
| Hispanic | 0 | 4 | |
| Level of education, yr | 14 (12–16) | 12 (12–15) | 0.15 |
| Medical ICU, % | 49 | 58 | 0.44 |
| APACHE III | 88 (63–108) | 77 (60–99) | 0.31 |
| Conservative strategy, % | 46 | 60 | 0.18 |
| Pulmonary artery catheter, % | 57 | 52 | 0.64 |
| On-study variables* | | | |
| Hemodynamic variables† | | | |
| Systolic blood pressure (mm Hg) | 111 (102–116) | 104 (98–111) | 0.05 |
| Shock, % | 37 | 30 | 0.46 |
| Respiratory variables | | | |
| $Pa_{O_2}$‡ | 86 (72–98) | 72 (68–90) | 0.02 |
| Metabolic variables | | | |
| Glucose, mg/dl | 123 (107–140) | 119 (109–136) | 0.99 |
| Hypoglycemia‡, <60 mg/dl, % | 0 | 13 | 0.03 |
| Hyperglycemia‡, >180 mg/dl, % | 34 | 30 | 0.65 |
| Corticosteroid therapy§ | | | |
| Corticosteroids (mg of methylprednisolone, cumulative) | 0 (0–60) | 0 (0–140) | 0.58 |
| Corticosteroids received, % | 29 | 33 | 0.66 |
| ICU length of stay (d) | 11 (7–20) | 12 (8–16) | 0.92 |
| Duration of mechanical ventilation (d) | 7 (4–15) | 7 (4–10) | 0.94 |

*Mikkelsen ME et al. AJRCCM.2014:185(12):1307-15*

# Psychiatric Symptoms in Acute Respiratory Distress Syndrome Survivors: A 1-Year National Multicenter Study

606 patients

**416 patients (66%) with at least 1 psychiatric disorder**




*Huang et al. Crit Care Med.2016:44:954-65*

# Psychiatric Symptoms in Acute Respiratory Distress Syndrome Survivors: A 1-Year National Multicenter Study

| Variables | Prevalence Ratio (95% CI) of Substantial Psychiatric Symptoms[a–c] | | | | | |
|---|---|---|---|---|---|---|
| | Depression | | Anxiety | | Post-Traumatic Stress Disorder | |
| | Bivariable | Multivariable | Bivariable | Multivariable | Bivariable | Multivariable |
| Age quartile (younger vs older)[d] | 1.03 (0.95–1.12) | | 1.13 (1.05–1.21) | **1.16 (1.07–1.26)** | 1.22 (1.10–1.36) | **1.23 (1.08–1.41)** |
| Female | 1.24 (1.02–1.50) | **1.26 (1.01–1.58)** | 1.41 (1.19–1.66) | **1.43 (1.18–1.74)** | 1.78 (1.37–2.32) | **1.80 (1.31–2.48)** |
| Unemployed | 1.50 (1.24–1.83) | **1.35 (1.09–1.69)** | 1.31 (1.11–1.55) | **1.26 (1.05–1.52)** | 1.51 (1.17–1.95) | **1.40 (1.03–1.90)** |
| Body mass index, per 10 kg/m$^2$ | 1.07 (0.96–1.20) | | 1.11 (1.01–1.22) | **1.14 (1.03–1.26)** | 1.07 (0.93–1.24) | |
| Alcohol misuse | 1.22 (0.99–1.50) | **1.39 (1.09–1.77)** | 1.19 (0.99–1.44) | **1.45 (1.18–1.79)** | 1.35 (1.02–1.79) | **1.79 (1.31–2.46)** |

*Huang et al. Crit Care Med.2016:44:954-65*

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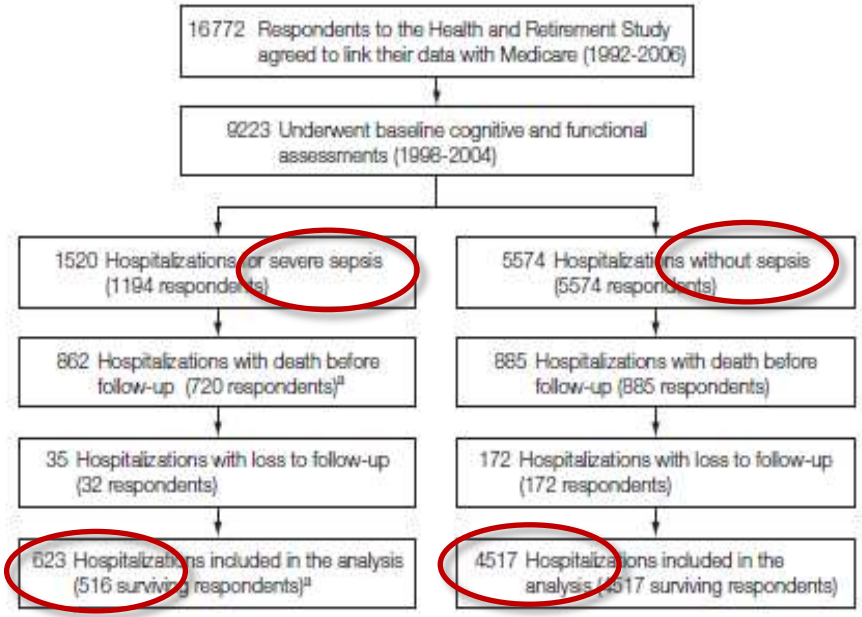
| Variables | Prevalence Ratio (95% CI) of Substantial Psychiatric Symptoms[a–c] | | | | | |
|---|---|---|---|---|---|---|
| | Depression | | Anxiety | | Post-Traumatic Stress Disorder | |
| | Bivariable | Multivariable | Bivariable | Multivariable | Bivariable | Multivariable |
| Acute Physiology and Chronic Health Evaluation III, per 20 unit | 0.90 (0.83–0.97) | **0.90 (0.82–0.99)** | 0.89 (0.84–0.96) | 0.95 (0.88–1.02) | 0.89 (0.80–0.98) | **0.88 (0.79–0.98)** |
| % of days with opioids, per 20% | 1.10 (1.02–1.19) | **1.11 (1.03–1.20)** | 1.07 (1.01–1.14) | **1.08 (1.01–1.15)** | 1.13 (1.02–1.25) | 1.09 (0.98–1.22) |
| % of days with corticosteroids, per 20% | 1.02 (0.96–1.08) | | 1.02 (0.97–1.07) | | 1.05 (0.98–1.13) | 1.04 (0.96–1.12) |
| % of days with neuromuscular blocker, per 20% | 1.00 (0.87–1.17) | | 1.12 (1.02–1.24) | 1.12 (0.99–1.27) | 1.14 (0.96–1.35) | **1.23 (1.02–1.49)** |

*Huang et al. Crit Care Med.2016:44:954-65*

# Long-term Cognitive Impairment and Functional Disability Among Survivors of Severe Sepsis




- Prospective cohort
- 9223 patients with baseline cognitive assessement
- 1194 patients / 1520 hospitalisation for severe sepsis
- 4517 survivors of non sepsis ICU stay and 516 survivors of sepsis

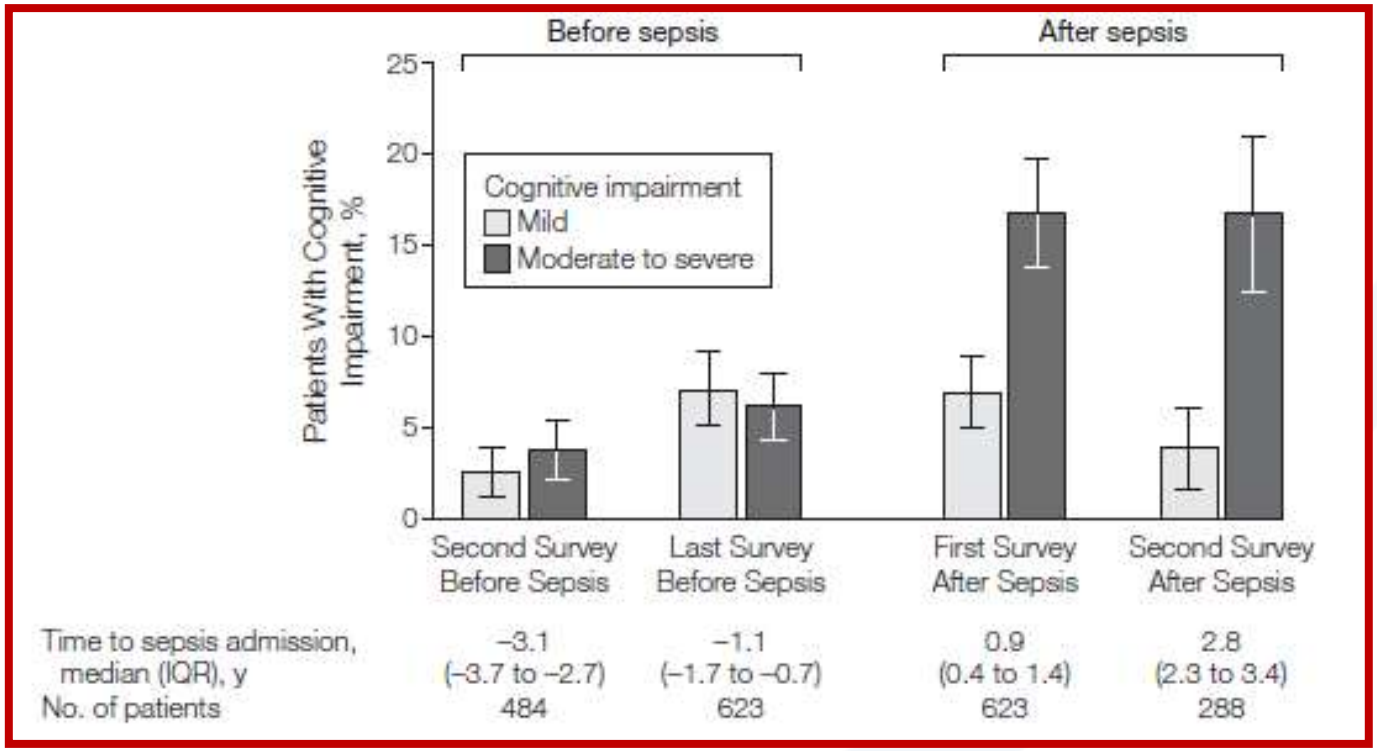
- Personal interviews to
  - assess cognitive impairment
  - assess activities of daily living

- Cognitive impairment:
  - specific questionnaire (<65y or > 65y)

*Iwashyna et al. JAMA.2010:304(16):1787-94*

# Long-term Cognitive Impairment and Functional Disability Among Survivors of Severe Sepsis

Cognitive Impairment Among Survivors of Severe Sepsis at Each Survey Time Point

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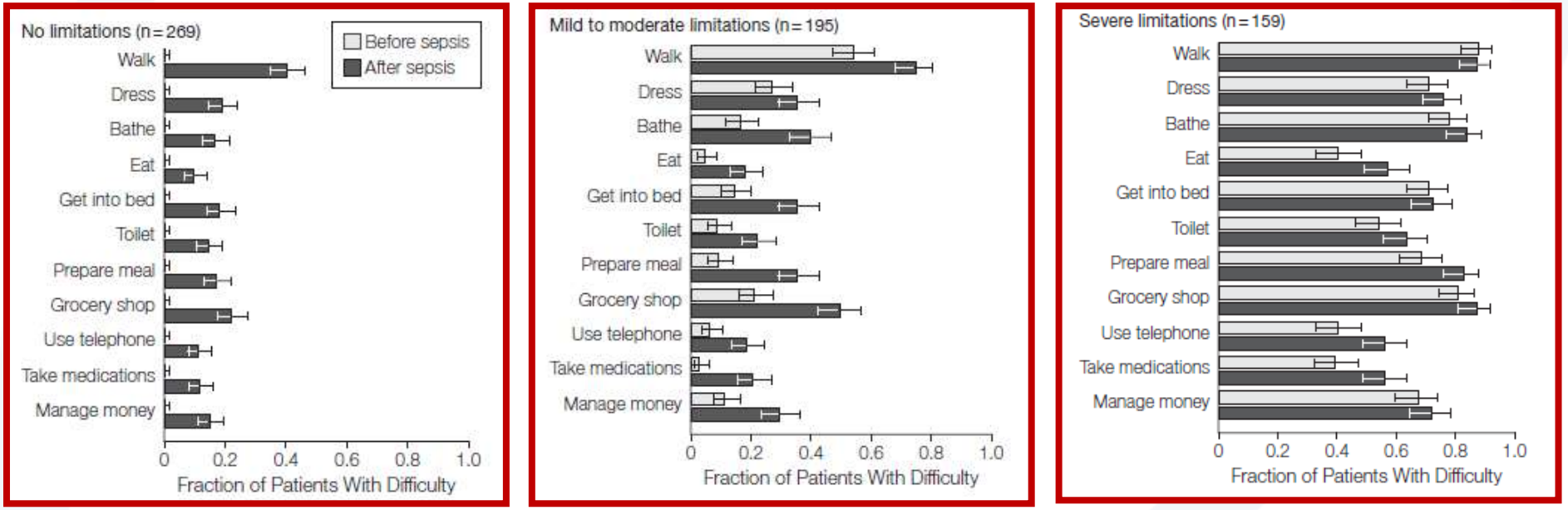


Wide range of new or worsening difficulties

*Iwashyna et al. JAMA.2010:304(16):1787-94*

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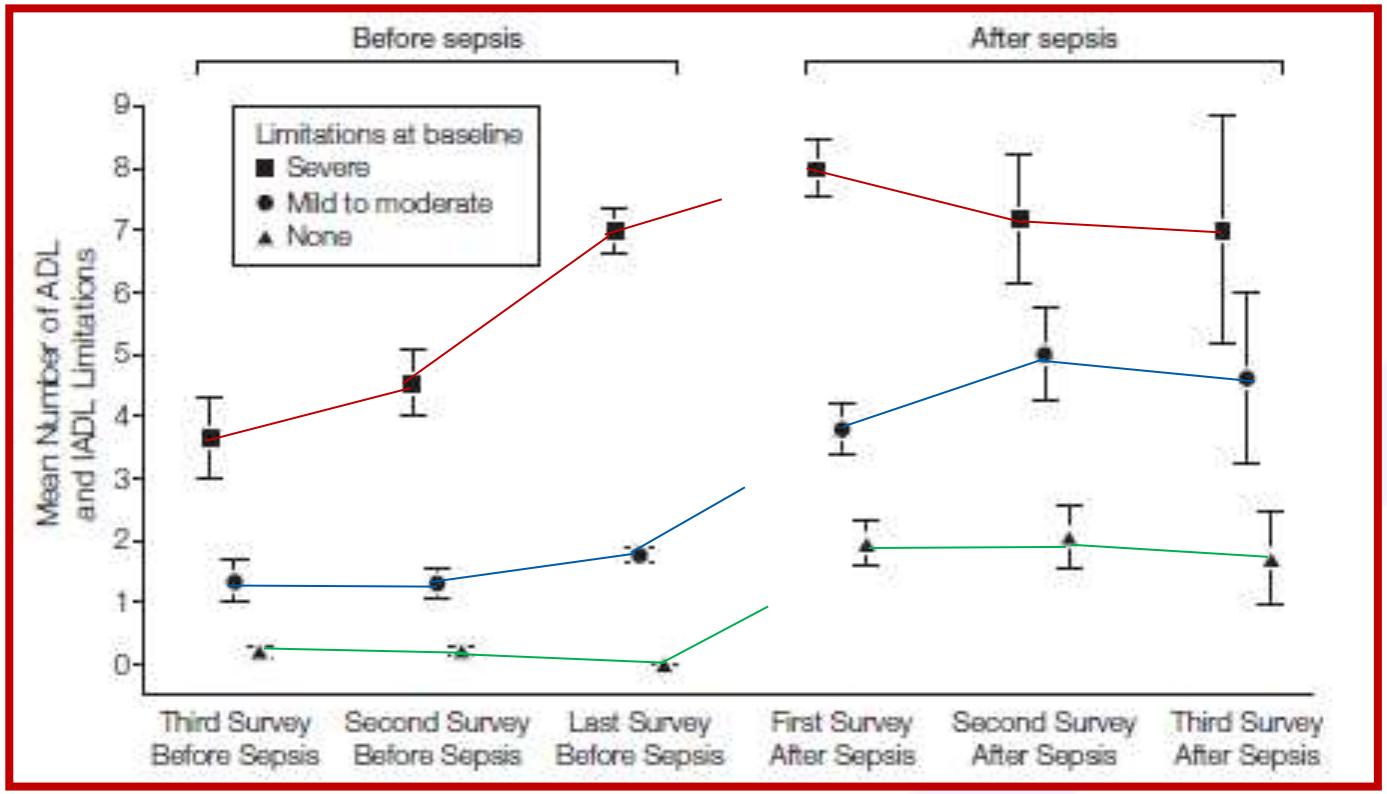


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# Long-Term Cognitive Impairment after Critical Illness

the BRAIN-ICU Study Investigators*

- In hospital cohort: 821 patients with shock or respiratory failure
- Follow-up cohort: 467 patients

Evaluation of in-hospital delirium (CAM-ICU)

Assessment of global cognition at M3 and M12 after discharge

- Repeatable Battery for the Assessmemt of Neuropsychological Status
- Trial Making Test (part B)

- 6% of patients had cognitive impairment at baseline
- 74% of patients developed delirium

*Pandharipande PP et al. NEJM.2013:369:1306-16*

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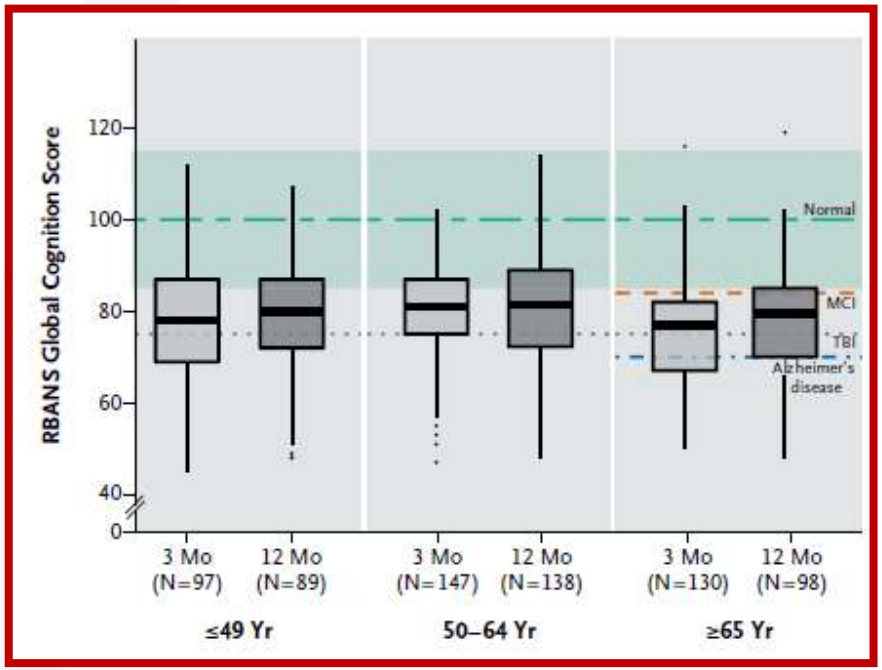
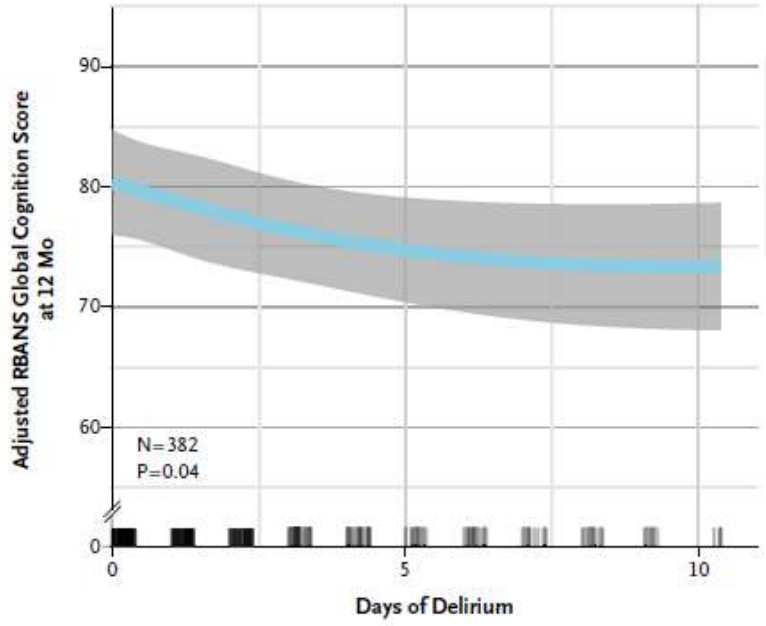



Independent from the use of sedatives or analgesics, or organ failure during ICU

*Pandharipande PP et al. NEJM.2013:369:1306-16*

# Long-Term Cognitive Impairment after Critical Illness

the BRAIN-ICU Study Investigators*

**At M3:**

- **40% of patients** had global cognition score that were 1,5 SD below the population means ( similar to scores for patients with **moderate TBI**)
- **26 % of patients** had global cognition score that were 2 SD below the population means ( similar to scores for patients with **mild Alzheimer's disease**)

**At M12:**

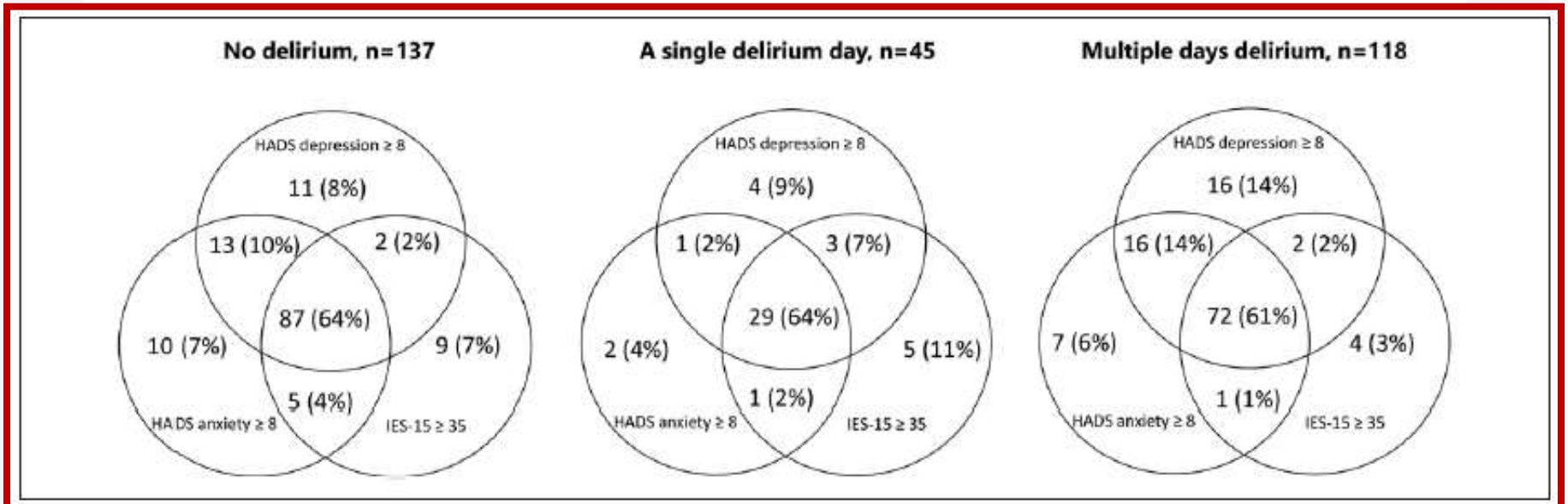
- **34% of patients** had global cognition score that were 1,5 SD below the population means ( similar to scores for patients with **moderate TBI**)
- **24 % of patients** had global cognition score that were 2 SD below the population means ( similar to scores for patients with **mild Alzheimer's disease**)

*Pandharipande PP et al. NEJM.2013:369:1306-16*

# Long-Term Mental Health Problems After Delirium in the ICU*

2669 patients

| Study population 567 subjects | | |
|---|---|---|
| No delirium | 270 | (48%) |
| A single delirium day | 86 | (15%) |
| Multiple days delirium | 211 | (37%) |




*Wolters AE et al. Crit Care Med.2016:44:1808-13*

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2669 patients

| Study population 567 subjects | | |
|---|---|---|
| No delirium | 270 | (48%) |
| A single delirium day | 86 | (15%) |
| Multiple days delirium | 211 | (37%) |

| Outcome | ICU Delirium | Risk Ratio (95% CI) Crude | Adjusted[a] |
|---|---|---|---|
| HADS anxiety (≥ 8) | No | Reference | Reference |
| | Single day | 0.96 (0.72–1.28) | 1.01 (0.76–1.33) |
| | Multiple days | 1.07 (0.87–1.31) | 1.08 (0.87–1.35) |
| HADS depression (≥ 8) | No | Reference | Reference |
| | Single day | 0.97 (0.73–1.30) | 0.99 (0.74–1.31) |
| | Multiple days | 1.20 (0.99–1.46) | 1.21 (0.98–1.50) |
| Impact of Event Scale 15 item (≥ 35) | No | Reference | Reference |
| | Single day | 1.16 (0.87–1.54) | 1.23 (0.93–1.63) |
| | Multiple days | 0.98 (0.78–1.24) | 1.04 (0.82–1.34) |

HADS = Hospital Anxiety and Depression Scale.

*Wolters AE et al. Crit Care Med.2016:44:1808-13*

# Outcome of delirium in critically ill patients: systematic review and meta-analysis

Jorge I F Salluh,[1] Han Wang,[2] Eric B Schneider,[2] Neeraja Nagaraja,[2] Gayane Yenokyan,[3] Abdulla Damluji,[4] Rodrigo B Serafim,[1,5] Robert D Stevens[6]

Despite the small number of studies that evaluated outcomes at more than one time point, available data suggest an association between delirium and cognitive impairment and mortality after discharge.

*BMJ.2015;350:h2538*

# The association between brain volumes, delirium duration, and cognitive outcomes in intensive care unit survivors: The VISIONS cohort magnetic resonance imaging study*

- Prospective study
- 47 ICU pts with sepsis / respiratory failure
  70% had delirium during ICU stay,
  > 25% during at least 3 days
- MRI and cognitive functions at discharge, 3 and 12 m post-ICU

Results:

- Duration delirium / brain volume (hospital discharge, M3)
  Frontal lobe
  Hippocampal atrophy (Executive functions, memory)
- Worsening brain atrophy at 3 months ~ cognitive deficit 12 months

*Gunther et al. Crit Care Med.2012;40:2022-32*

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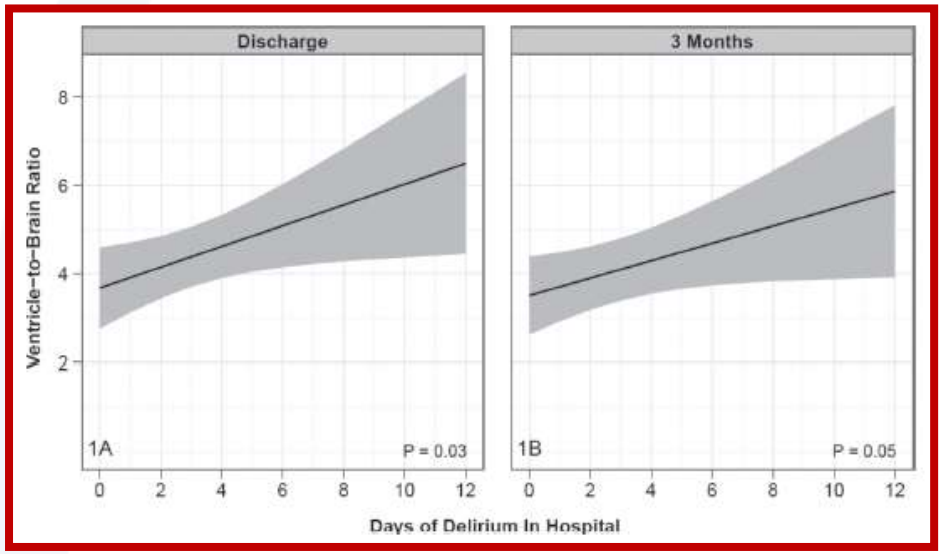


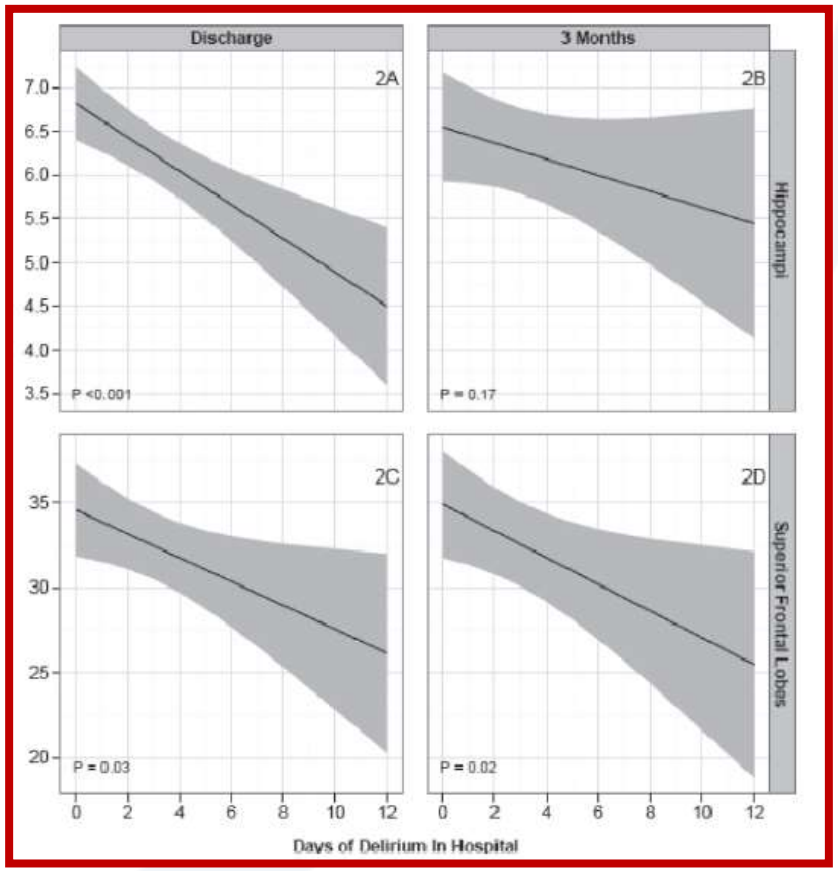


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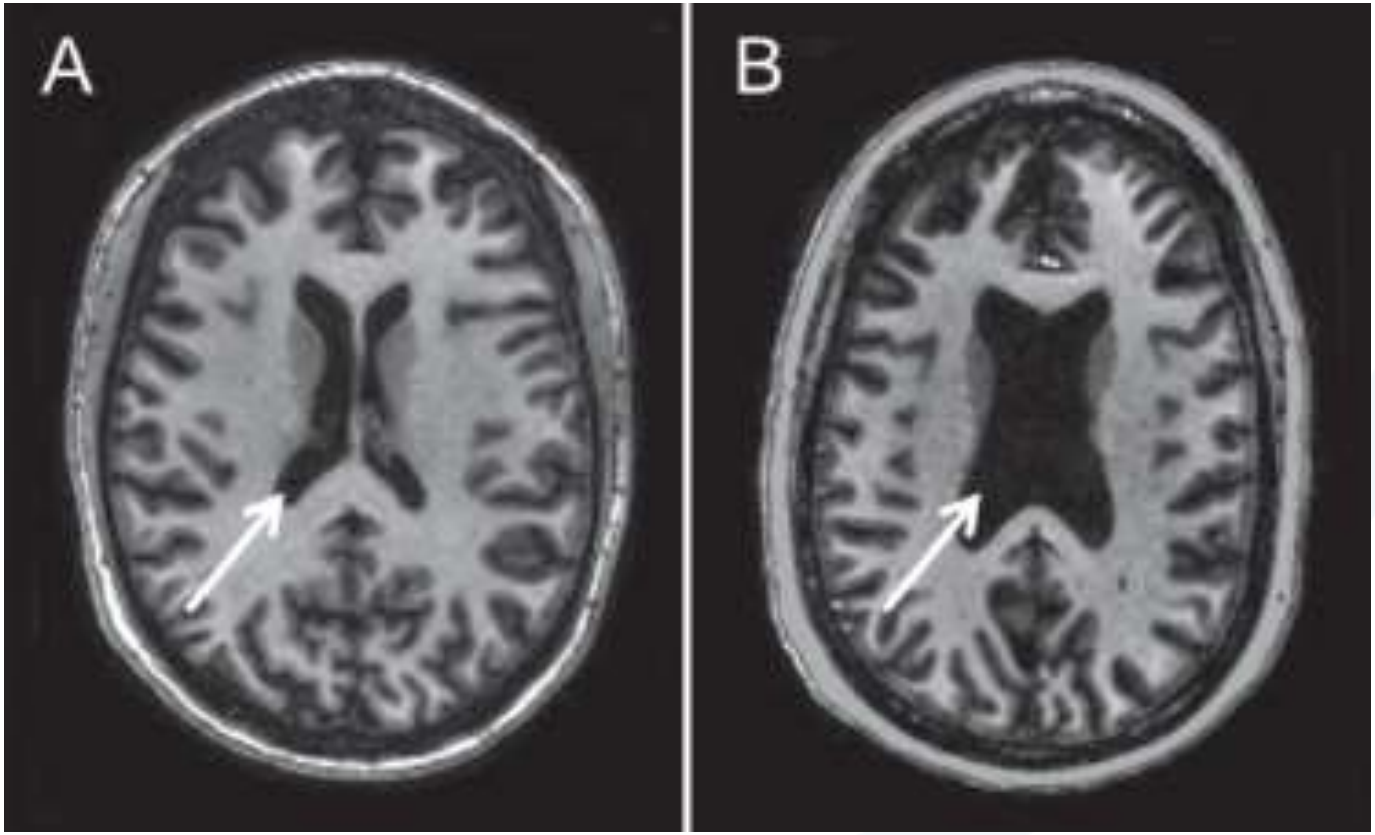
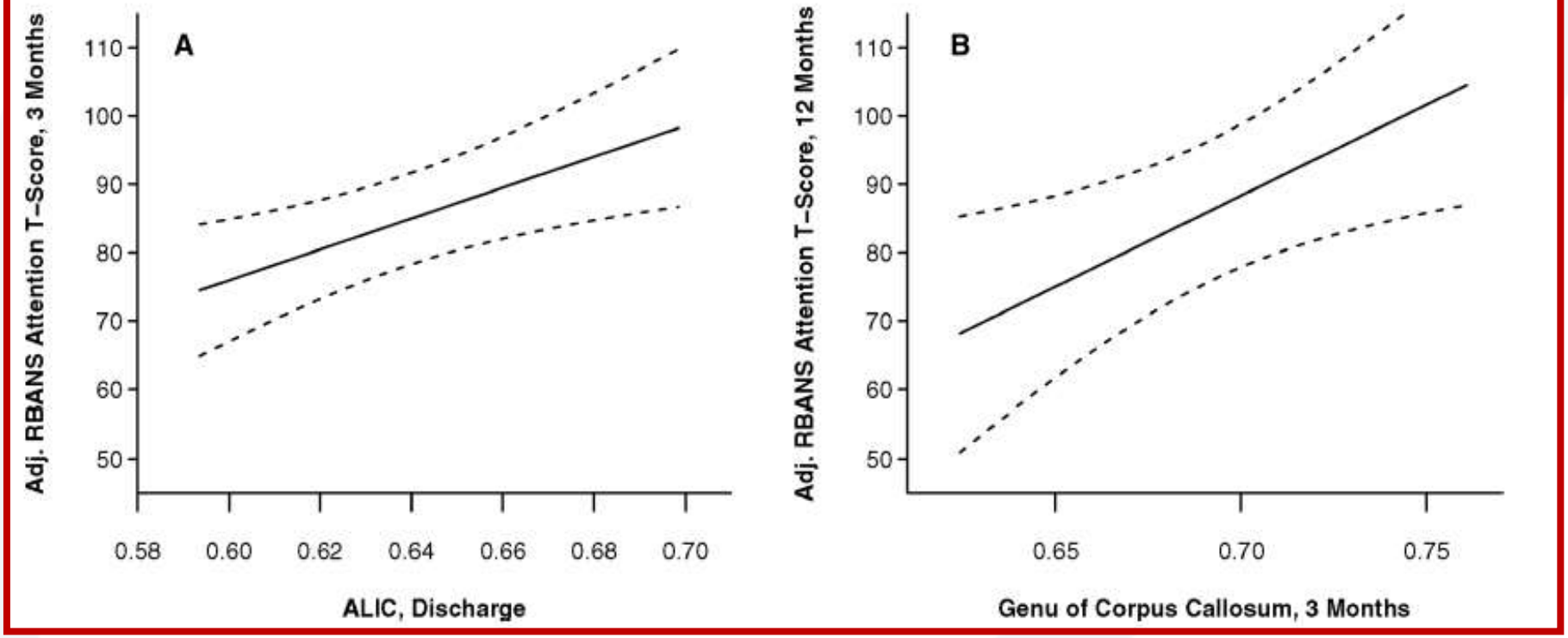



*Gunther et al. Crit Care Med.2012;40:2022-32*

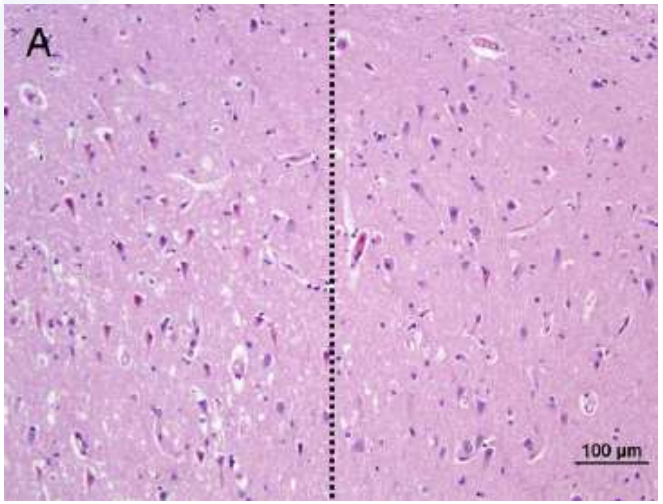
# The relationship between delirium duration, white matter integrity, and cognitive impairment in intensive care unit survivors as determined by diffusion tensor imaging: The VISIONS prospective cohort magnetic resonance imaging study*




*Morandi et al. Crit Care Med.2012;40:2182-9*

Journal of Critical Care

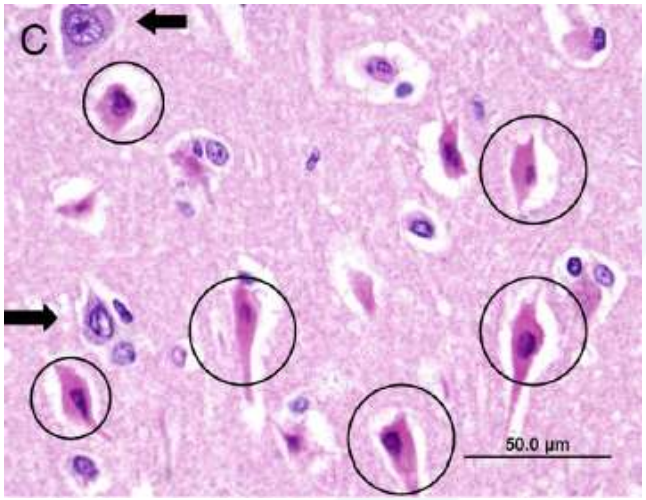
# Brain autopsy findings in intensive care unit patients previously suffering from delirium: A pilot study ☆



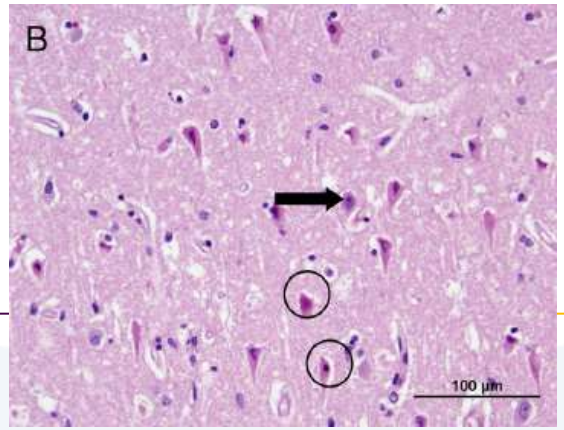

Irreversibly injured pyramidal neurons

Healthy neurons

## Acute hippocampal hypoxic injury




Condensed nuclei and eosinophilic cytoplasm im imjured neurons

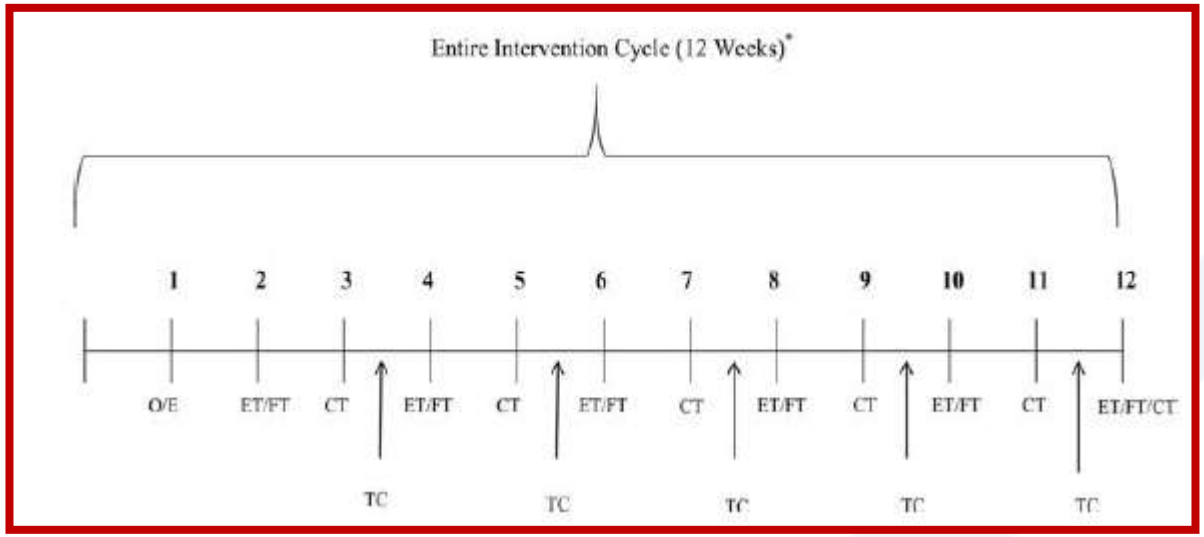



*Janz J et al. J Crit Care.2010;538.e7-538.e12*

# Cognitive and physical rehabilitation of intensive care unit survivors: Results of the RETURN randomized controlled pilot investigation*

8 controls / 13 intervention-patients

**Intervention:** in-home cognitive, physical and functional rehabilitation program via a social worker or a master's level psychology technician utilizing telemedicine (6 in-person visits and 6 televisits)




*Jackson et al. Crit Care Med.2012;40:1088-97*

# Cognitive and physical rehabilitation of intensive care unit survivors: Results of the RETURN randomized controlled pilot investigation*

| Test | N | Baseline | | | 3-Month Follow-Up | | |
|---|---|---|---|---|---|---|---|
| | | Control (n = 8) | Intervention (n = 7) | *p* | Control (n = 8) | Intervention (n = 7) | *p* |
| Tower | 15 | 7.5 (4.5–9.0) | 8.0 (6.5–10.0) | .37 | 7.5 (4.0–8.5) | 13.0 (11.5–14.0) | <.01 |
| Timed Up and Go | 15 | 15 (12–20) | 18 (15–20) | .47 | 10.2 (9.2 –11.7) | 9.0 (8.5–11.8) | .51 |
| Katz Activities of Daily Living | 15 | | | .88 | | | .78 |
| Little/no dependency | | 75% (6) | 71% (5) | | 75% (6) | 100% (7) | |
| Moderate/severe dependency | | 25% (2) | 29% (2) | | 25% (2) | 0% (0) | |
| Functional Activities Questionnaire | 15 | 7.0 (1.5–14.2) | 0.0 (0.0–4.0) | .14 | 8.0 (6.0–11.8) | 1.0 (0.0 –2.5) | .04 |
| Activities Balance and Confidence Scale | 15 | 54 (28–75) | 68 (36–81) | .58 | 83 (38–91) | 82 (78–89) | .35 |
| Dysexecutive Questionnaire | 15 | 27.0 (13.5–31.0) | 13.0 (8.0–15.0) | .12 | 16.0(7.8–19.2) | 8.0 (6.0–13.5) | .74 |
| Mini-Mental State Examination | 15 | 27.0 (22.5–28.2) | 28.0 (25.0–29.0) | .54 | 26.5 (24.8–28.5) | 30.0 (29.0–30.0) | .25 |

*Jackson et al. Crit Care Med.2012;40:1088-97*

# Feasibility and safety of early combined cognitive and physical therapy for critically ill medical and surgical patients: the Activity and Cognitive Therapy in ICU (ACT-ICU) trial

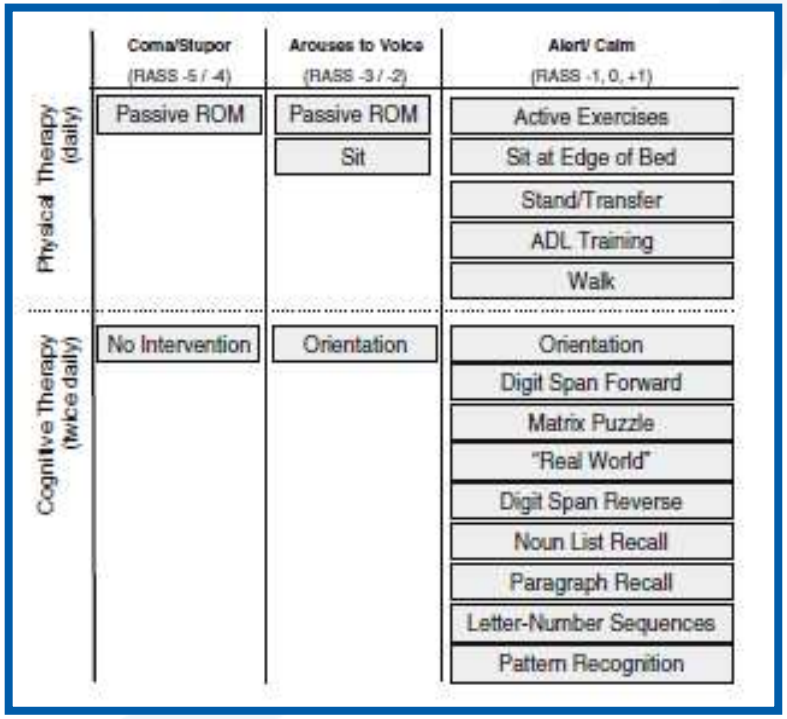
87 medical or surgical ICU patients
Randomization 1/1/2

- Usual care
- Usual care + Early physical therapy (1/d)
- Usual care + Early PT + Cognitive therapy (2/d)

Cognitive Therapy :

**Orientation**
**Memory**
**Attention**
**Problem-solving**

} Exercices




*Brummel et al. Intensive Care Med.2014;40:370-9*

# Feasibility and safety of early combined cognitive and physical therapy for critically ill medical and surgical patients: the Activity and Cognitive Therapy in ICU (ACT-ICU) trial

**Table 3** 3-month follow-up outcomes

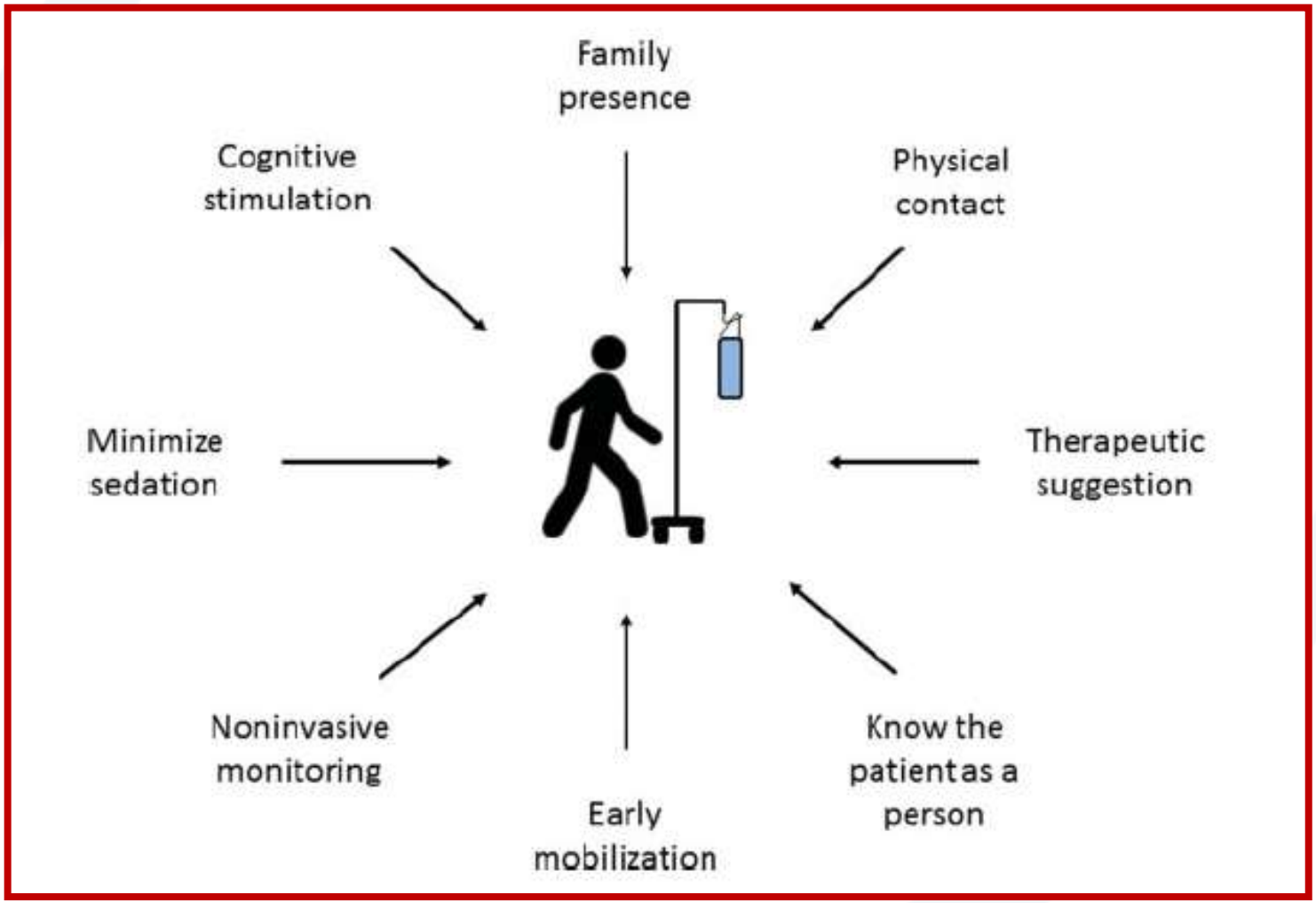
| | Usual care ($n = 12$) | Physical therapy ($n = 14$) | Cognitive + physical therapy ($n = 18$) | $P$ |
|---|---|---|---|---|
| Primary follow-up outcome | | | | |
| Tower test (executive functioning)[a] | 10.0 (8.8–12.2) | 11.0 (11.0–12.0) | 10.0 (8.0–11.0) | 0.20 |
| Secondary follow-up outcomes | | | | |
| DEX (executive functioning)[b] | 17.5 (8.5–28.8) | 10.0 (5.0–17.0) | 9.0 (2.0–17.5) | 0.08 |
| MMSE (global cognition)[c] | 28.0 (26.8–29.0) | 29.0 (27.0–30.0) | 29.0 (27.9–29.8) | 0.64 |
| TUG (functional mobility)[d] | 8.0 (7.5–13.5) | 10.0 (8.0–13.0) | 11.0 (9.0–13.0) | 0.79 |
| Katz ADL (activities of daily living)[e] | 0 (0–0) | 0 (0–1) | 0 (0–2) | 0.69 |
| FAQ (instrumental activities of daily living)[f] | 2.5 (0.8–5.5) | 2.0 (0.0–4.8) | 1.0 (0.0–3.8) | 0.67 |
| EQ-5D VAS (health-related quality of life)[g] | 75 (61–86) | 80 (62–89) | 75 (54–80) | 0.44 |

*Brummel et al. Intensive Care Med.2014;40:370-9*

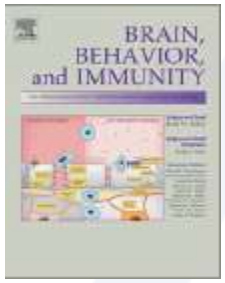
Trials

Non-sedation versus sedation with a daily wake-up trial in critically ill patients recieving mechanical ventilation - effects on long-term cognitive function: Study protocol for a randomized controlled trial, a substudy of the NONSEDA trial

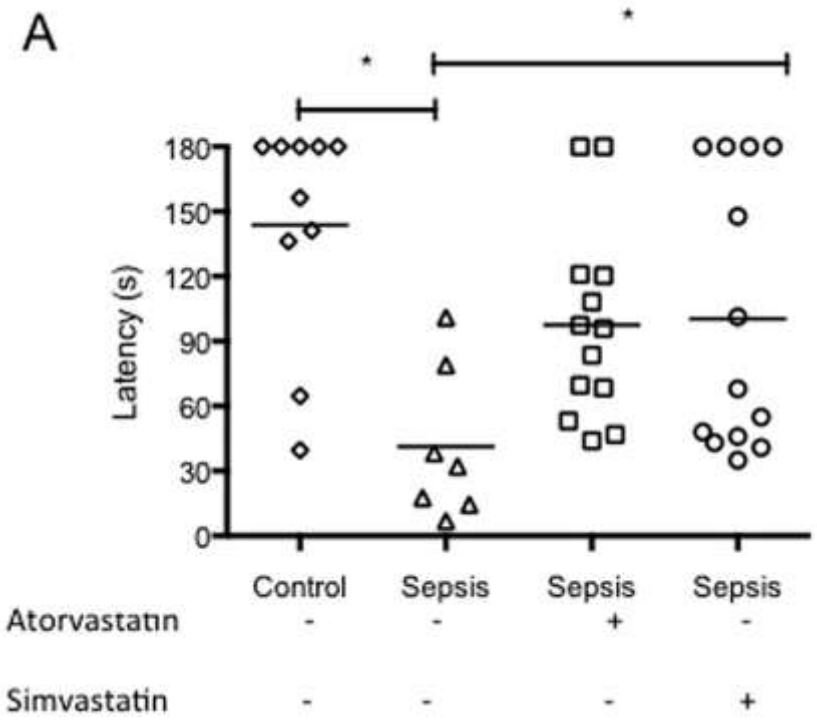
*Nedergaard et al. Trials.2016;17:269*



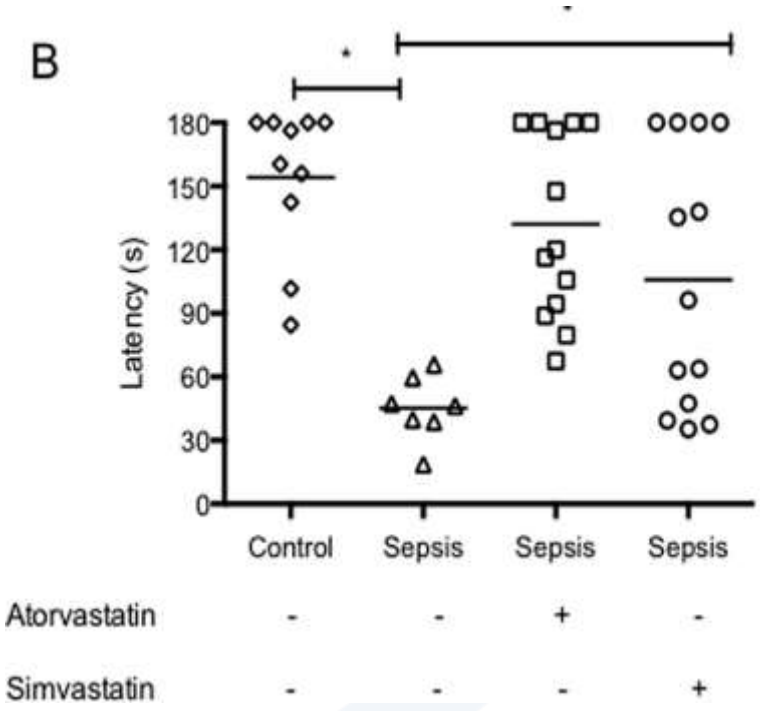

*Karnatovskaia L et al. Sem Respir Crit Care Med.2016;37:136-42*




# Statins prevent cognitive impairment after sepsis by reverting neuroinflammation, and microcirculatory/endothelial dysfunction




Short term memory




Long term memory

*Reis PA et al. Brain Behav Immun.2017;60:293-303*

# Predictors of posttraumatic stress and quality of life in family members of chronically critically ill patients after intensive care

- Cross-sectional design nested within a prospective longitudinal cohort study
- Post-traumatic stress symptoms and QOL in family members
- Post-traumatic Stress Scale-10 – Euro-Quality of life-5D-3L questionnqires
- By phone

*Wintermann et al. Ann Intensive Care.2016;6:69*

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**Conclusions:** Posttraumatic stress and HRQL should be routinely assessed in family members of CCI patients at regular intervals starting early at ICU. Preventive family-centered interventions are needed to improve posttraumatic stress and HRQL in both patients and their family members.

*Wintermann et al. Ann Intensive Care.2016;6:69*

# TAKE HOME MESSAGE

For those patients who survive ICU
Do never say again:
« Don’ t worry, he’ s gonna be fine »