*SwERAS dagarna 17-18 Nov, 2022*

# Kognitiv dysfunktion och förvirringstillstånd

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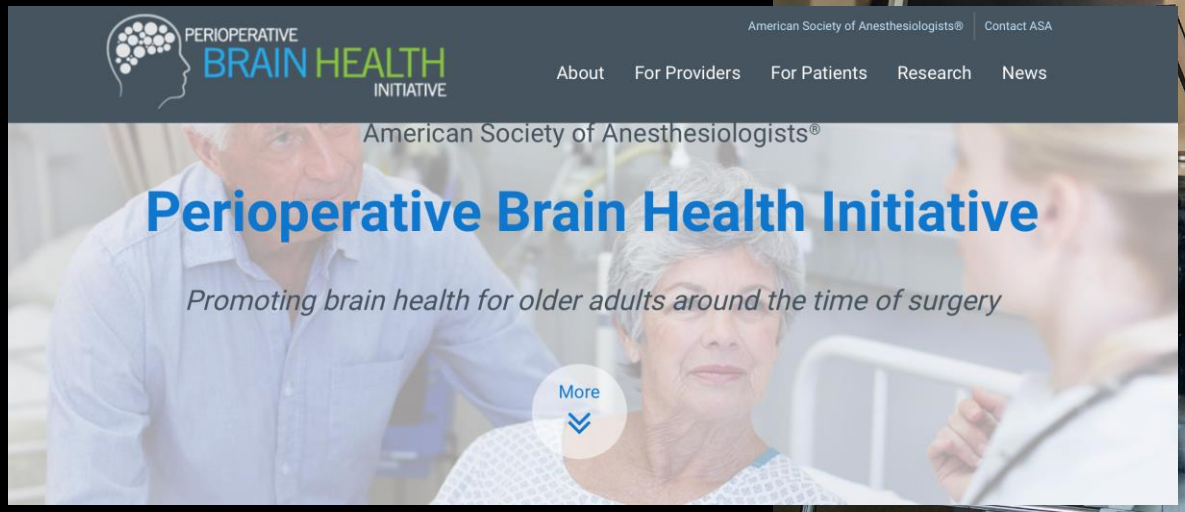
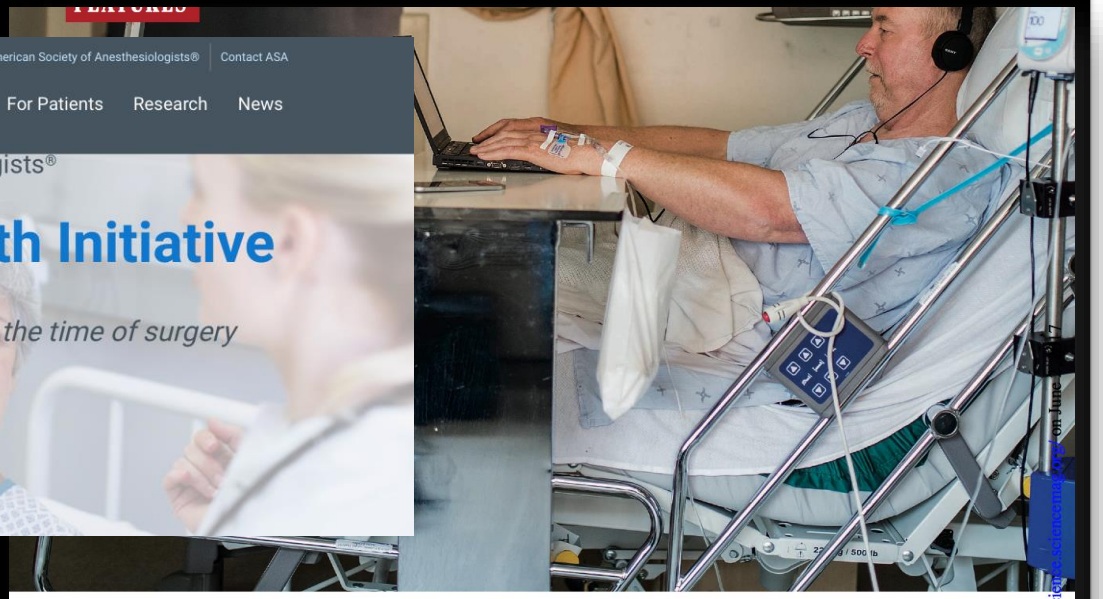
# Globally increased focus on postoperative neurocognitive outcomes



THE POST-OP BRAIN

Surgery can cure—but it may take a toll on cognition. Some scientists blame a body-wide inflammatory response

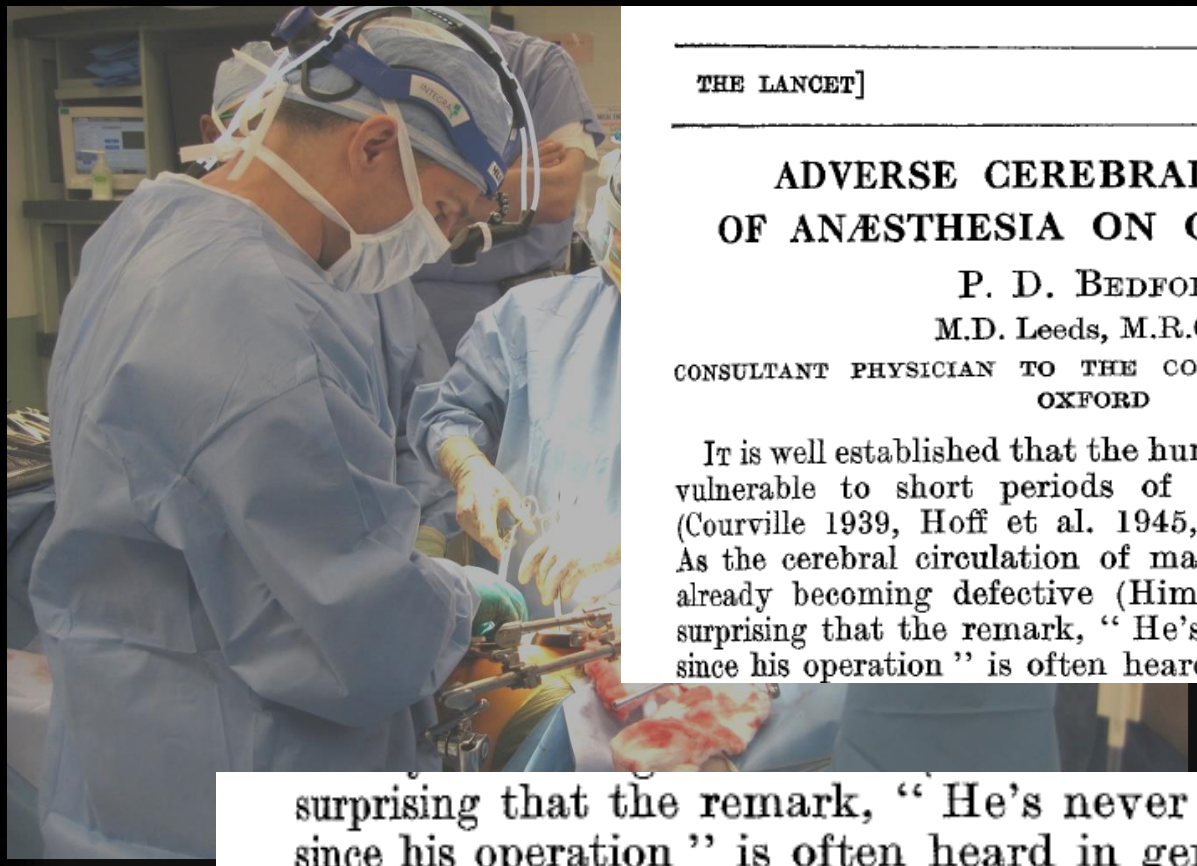
*By* **Mitch Leslie**



American Soc Anesthesiologists website

M Leslie, Science Magazine June 2, 2017

# The brain after anesthesia and surgery



THE LANCET] ORIGINAL

## ADVERSE CEREBRAL EFFECTS OF ANÆSTHESIA ON OLD PEOPLE*

P. D. BEDFORD
M.D. Leeds, M.R.C.P.
CONSULTANT PHYSICIAN TO THE COWLEY ROAD HOSPITAL, OXFORD

IT is well established that the human brain is extremely vulnerable to short periods of vascular insufficiency (Courville 1939, Hoff et al. 1945, Corday et al. 1953). As the cerebral circulation of many elderly patients is already becoming defective (Himwich 1951), it is not surprising that the remark, "He's never been the same since his operation" is often heard in geriatric practice.

surprising that the remark, "He's never been the same since his operation" is often heard in geriatric practice.

Bedford Lancet 1955

# Time course of brain dysfunction after surgery

**Delirium**

**Hours/days**

**DSM-code**

**Postoperative cognitive decline**

**Week/Month**

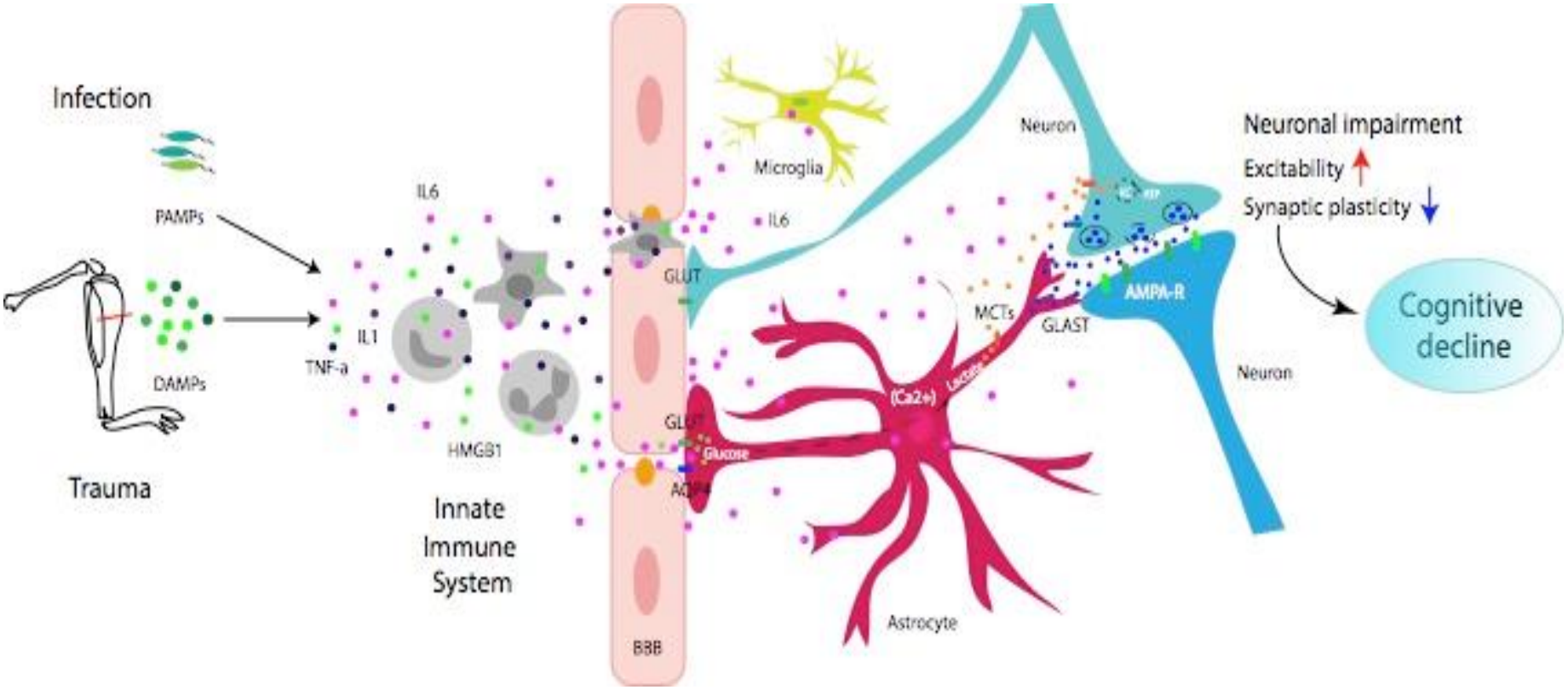
**DSM alignment with new nomenclature**

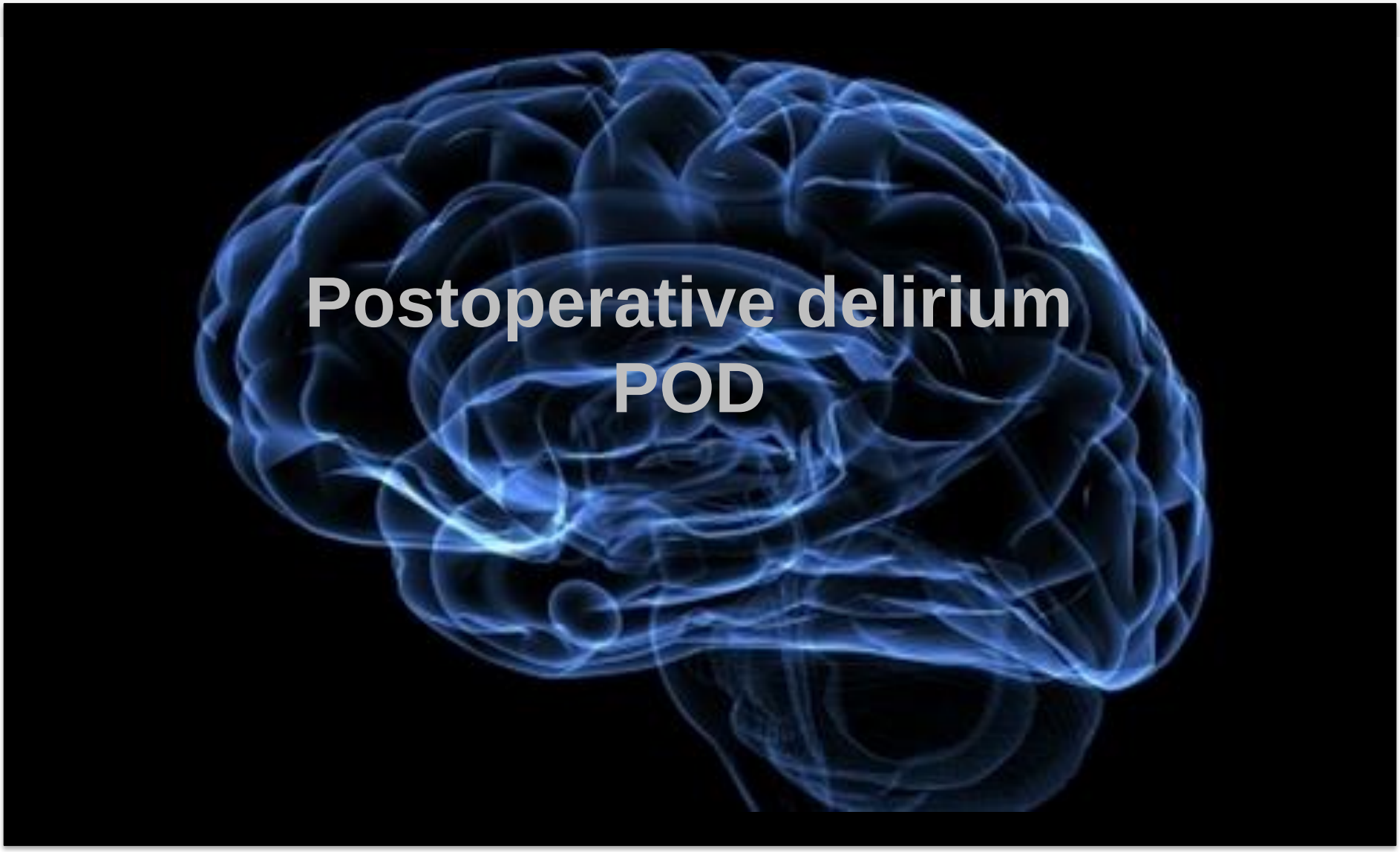
**Dementia**

**Permanent**

**DSM-code**

# Mechanisms behind surgery-induced neurocognitive decline




Postoperative delirium
POD

# Definition and types of POD

Acute onset of change in mental status
inattention, desorganised thinking, altered consciouness
Usually within 72 hours postop

**Hyperactive delirium (most common)**
agitation, confusion, combativeness

**Hypoactive delirium (less common)**
drowsiness, lethargy, slow speech, inattention

# Incidence of POD in the adult

**Overall incidence of POD at 35 % (n=1823 patients)**
Range 10 – 60 % in older patients

**POD is associated with**
- increased burden of postop care,
- longterm cognitive decline and dementia
- increased postoperative mortality

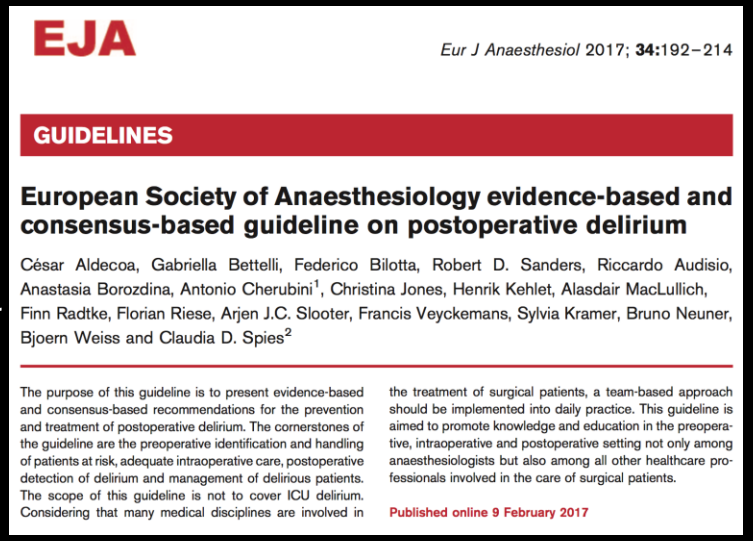
Patients developing POD cost on averege 2.5 times the care for patients without POD

Guenther et al Curr Op Anesthesiol 2011, Allen et al N Am Surg Clin 2013 Rudolph et al Anesth Analg 2011, Leslie et al *Arch Intern Med* 2008

# Risk factors for postoperative delirium

## Major preexisting risk factors

- age > 65 y
- preop cognitive impairment  or dementia
- poor vision or hearing
- severe illness, malnutrition, frailty
- Infection



EJA

*Eur J Anaesthesiol* 2017; **34**:192–214

GUIDELINES

**European Society of Anaesthesiology evidence-based and consensus-based guideline on postoperative delirium**

César Aldecoa, Gabriella Bettelli, Federico Bilotta, Robert D. Sanders, Riccardo Audisio, Anastasia Borozdina, Antonio Cherubini[1], Christina Jones, Henrik Kehlet, Alasdair MacLullich, Finn Radtke, Florian Riese, Arjen J.C. Slooter, Francis Veyckemans, Sylvia Kramer, Bruno Neuner, Bjoern Weiss and Claudia D. Spies[2]

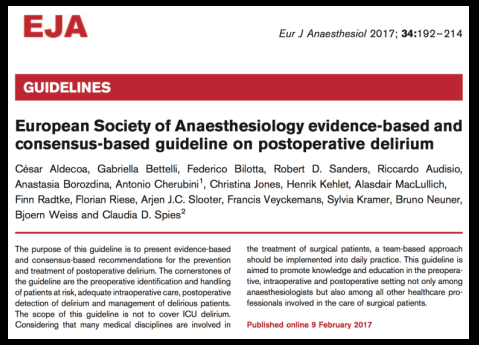
The purpose of this guideline is to present evidence-based and consensus-based recommendations for the prevention and treatment of postoperative delirium. The cornerstones of the guideline are the preoperative identification and handling of patients at risk, adequate intraoperative care, postoperative detection of delirium and management of delirious patients. The scope of this guideline is not to cover ICU delirium. Considering that many medical disciplines are involved in the treatment of surgical patients, a team-based approach should be implemented into daily practice. This guideline is aimed to promote knowledge and education in the preoperative, intraoperative and postoperative setting not only among anaesthesiologists but also among all other healthcare professionals involved in the care of surgical patients.

Published online 9 February 2017

Additional factor: sleep deprivation, poor functional status, metabolic derangements, polypharmacy, poorly controlled pain, dehydration, neuropsychiatric conditions, alcohol or drug abuse

ESA Guideline for POD, 2017 Am J Surg. 2010, Expert Panel on Postop delirium Journal of the American Geriatrics Society 2015

# Risk factors for postoperative delirium



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## Precipitating risk factors and drugs at-risk

- urgency, i.e. acute > elective
- long duration and invasiveness
- need admission to the ICU
- postop infection
- postop vascular adverse events

- anticholinergics
- opioids
- benzodiazepines
- dopaminergics
- metoclopramide
- barbiturates

ESA Guideline for POD, 2017 Am J Surg. 2010, Expert Panel on Postop delirium Journal of the American Geriatrics Society 2015

# POD and longterm cognition and morbidity

Preoperative MCI is associated with higher risk for POD

POD is associated with increased risk for postop morbidity (non-neurological)
and with POCD but lack of data on POD and risk for later dementia

Silverstein and Deiner Progress Neuropsychopharm Biol Psych 2013, Mahanna-Gabrielle Br J Anaesth 2019

# Assessment of POD

**Well-established diagnos within DSM V system**

**POD is typically studied with neuropsychological bedside tests**

**CAM (Confusion Assessment Method)**

**DRS (Delirium Rating Scale)**

**Box 2**
**The Confusion Assessment Method for the Intensive Care Unit (CAM-ICU)**

Delirium is diagnosed when both Features 1 and 2 are positive, along with either Feature 3 or Feature 4.

Feature 1. Acute onset of mental status changes or fluctuating course

- Is there evidence of an acute change in mental status from the baseline?
- Did the (abnormal) behavior fluctuate during the past 24 hours; come and go or increase or decrease in severity?

*Sources of information*: Serial Glasgow Coma Scale or sedation score ratings over 24 hours and available input from bedside critical care nurse or family.

Feature 2. Inattention

- Did the patient have difficulty focusing attention?
- Is there a reduced ability to maintain and shift attention?

*Sources of information*: Attention screening examinations by using either picture recognition or Vigilance A random letter test. Neither of these tests requires verbal response and are ideally suited for mechanically ventilated patients.

Feature 3. Disorganized thinking

- Was the patient's thinking disorganized or incoherent, such as rambling or irrelevant conversation, unclear or illogical flow of ideas, or unpredictable-switching from subject to subject?
- Was the patient able to follow questions and commands throughout the assessment?
  1. "Are you having any unclear thinking?"
  2. "[illegible] up this many fingers."
  3. "[illegible], do the same thing in the other hand." (Not repeating the number of fingers)

Feature 4. Altered level of consciousness

- Any level of consciousness other than "alert."
- Alert—normal, spontaneously fully aware of environment and interacts appropriately
- Vigilant—hyperalert
- Lethargic—Drowsy but easily aroused, unaware of some elements in the environment, or not spontaneously interacting appropriately with the interviewer; becomes fully aware and appropriately interactive when prodded minimally
- Stupor—Difficult to arouse, unaware of some or all elements in the environment, or not spontaneously interacting with the interviewer; becomes incompletely aware and inappropriately interactive when prodded strongly
- Coma— Unable to arouse, unaware of all elements in the environment, with no spontaneous interaction or awareness of the interviewer, so that the interview is difficult or impossible even with maximal prodding.

*Adapted from* Ely EW, Margolin R, Francis J, et al. Evaluation of delirium in critically ill patients: validation of the Confusion Assessment Method for the Intensive Care Unit (CAM-ICU). Crit Care Med 2001;29:1370; Copyright 2002, E. Wesley Ely, MD, MPH and Vanderbilt University, all rights reserved.

# Prevention and Treatment of POD

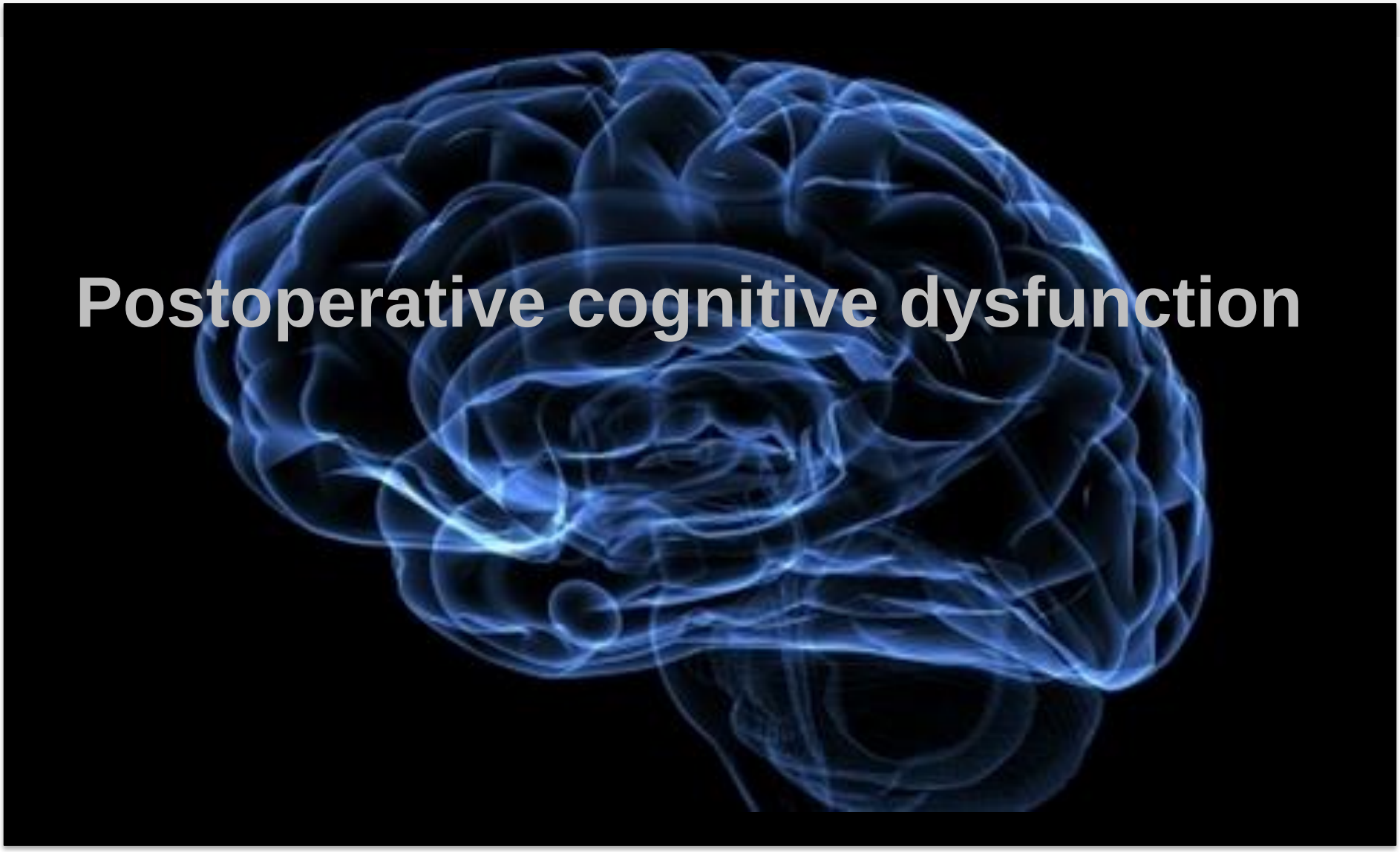
## *Non-pharmacological care process approach*

- **”ERAS” concept (provide clock, visual/hearing aids, day/night rythm, no indwelling catheters or IV lines, early mobilization and nutrition**

## *Perioperative management still under debate*

- **Raw EEG to avoid burst suppression - promising**
- **Processed EEG – still conflicting data**
- **NIRS-guided anesthesia, small size studies, methodological issues**
- **Dexmedetomidine perioperatively may reduce POD but not POCD**
- **Sedation at BIS > 80 vs < 50 during regional anesthesia**
- **Melatonin show conflicting results - unclear evidence**

Strom, Lancet 2010, Guenther,l Curr Op Anesthesiol 2011, Barnes-Daly CCM 2017, Hishieh JAMA Intern Med 2015, ESA Guidelines on POD 2017, Mahanna-Gabrielli Br J Anaesth 2019


Postoperative cognitive dysfunction

# Neurocognitive decline after non-cardiac surgery

- **Incidence is 20-40 % at 1 week and 10-15 % at 3 months > 60 y**

  *Möller et al, Lancet 1998, Monk et al Anesthesiology 2008 Mahanna Gabrielli 2019*

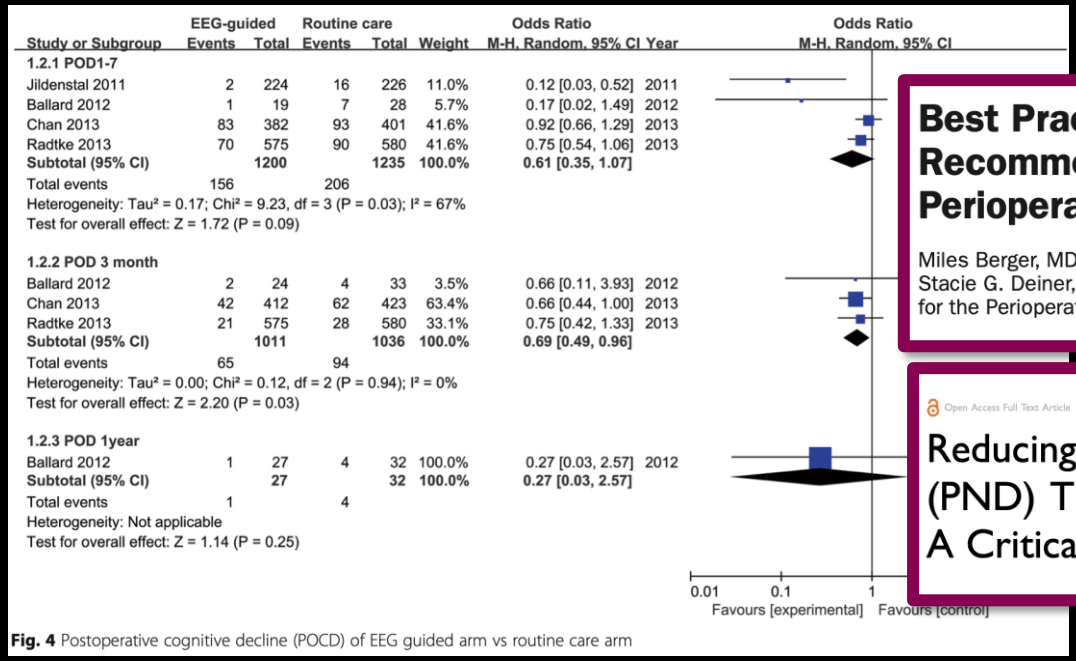
- **No or minimal difference in 3-months outcomes by general anesthesia v.s. regional techniques**

  *Rasmussen et al acta Anesthesiol Scand 2002*

- **No or minimal difference between IV versus inhaled anesthetics**

  *Shoen et al, Br J Anaesth 2011, Royse et al, Anaesthesia 2011, Qiao Anesthesiology 2015*

# Processed EEG-guided anesthesia - may reduce postop delirium but still unclear impact on postop neurocognitive decline (NCD)



| Study or Subgroup | EEG-guided Events | Total | Routine care Events | Total | Weight | Odds Ratio M-H, Random, 95% CI | Year |
|---|---|---|---|---|---|---|---|
| **1.2.1 POD1-7** | | | | | | | |
| Jildenstal 2011 | 2 | 224 | 16 | 226 | 11.0% | 0.12 [0.03, 0.52] | 2011 |
| Ballard 2012 | 1 | 19 | 7 | 28 | 5.7% | 0.17 [0.02, 1.49] | 2012 |
| Chan 2013 | 83 | 382 | 93 | 401 | 41.6% | 0.92 [0.66, 1.29] | 2013 |
| Radtke 2013 | 70 | 575 | 90 | 580 | 41.6% | 0.75 [0.54, 1.06] | 2013 |
| **Subtotal (95% CI)** | | **1200** | | **1235** | **100.0%** | **0.61 [0.35, 1.07]** | |
| Total events | 156 | | 206 | | | | |
| Heterogeneity: Tau² = 0.17; Chi² = 9.23, df = 3 (P = 0.03); I² = 67% | | | | | | | |
| Test for overall effect: Z = 1.72 (P = 0.09) | | | | | | | |
| **1.2.2 POD 3 month** | | | | | | | |
| Ballard 2012 | 2 | 24 | 4 | 33 | 3.5% | 0.66 [0.11, 3.93] | 2012 |
| Chan 2013 | 42 | 412 | 62 | 423 | 63.4% | 0.66 [0.44, 1.00] | 2013 |
| Radtke 2013 | 21 | 575 | 28 | 580 | 33.1% | 0.75 [0.42, 1.33] | 2013 |
| **Subtotal (95% CI)** | | **1011** | | **1036** | **100.0%** | **0.69 [0.49, 0.96]** | |
| Total events | 65 | | 94 | | | | |
| Heterogeneity: Tau² = 0.00; Chi² = 0.12, df = 2 (P = 0.94); I² = 0% | | | | | | | |
| Test for overall effect: Z = 2.20 (P = 0.03) | | | | | | | |
| **1.2.3 POD 1year** | | | | | | | |
| Ballard 2012 | 1 | 27 | 4 | 32 | 100.0% | 0.27 [0.03, 2.57] | 2012 |
| **Subtotal (95% CI)** | | **27** | | **32** | **100.0%** | **0.27 [0.03, 2.57]** | |
| Total events | 1 | | 4 | | | | |
| Heterogeneity: Not applicable | | | | | | | |
| Test for overall effect: Z = 1.14 (P = 0.25) | | | | | | | |

Odds Ratio M-H, Random, 95% CI

0.01 0.1 1

Favours [experimental] Favours [control]

**Fig. 4** Postoperative cognitive decline (POCD) of EEG guided arm vs routine care arm

**Best Practices for Postoperative Brain Health: Recommendations From the Fifth International Perioperative Neurotoxicity Working Group**

Miles Berger, MD, PhD,* Katie J. Schenning, MD, MPH,† Charles H. Brown IV, MD, MHS,‡ Stacie G. Deiner, MD,§ Robert A. Whittington, MD,‖ and Roderic G. Eckenhoff, MD,¶ for the Perioperative Neurotoxicity Working Group

Open Access Full Text Article

REVIEW

Reducing Perioperative Neurocognitive Disorders (PND) Through Depth of Anesthesia Monitoring: A Critical Review

Ding et al BOC Anesthesiology 2020, Berger M, et al Anesth Analg 2018, Evered L Goldstein P Internat J Gen Med 2021

# Perioperative protocols impact **early incidence** of NCD in orthopedics

Neuroscience in Anesthesiology and Perioperative Medicine

Section Editor: Gregory J. Crosby

**Cognitive Dysfunction After Fast-Track Hip and Knee Replacement**

Lene Krenk, MD, PhD,*† Henrik Kehlet, MD, PhD,*‡ Torben Bæk Hansen, MD, PhD,§ Søren Solgaard, MD, Dr Med,‖ Kjeld Soballe, MD, PhD,¶ and Lars Simon Rasmussen, MD, PhD#

| Incidence of NCD | 1 week | 3 months |
|---|---|---|
| n= 220, TKA or THA | 9.1 % | 8.0 % |
| *Orto part ISPOCD and others* | *20-40 %* | *6-15 %* |

Krenk et al, Anesth Analg 2014

# Is preop cognitive impairment a risk factor for NCD?

**Preexisting Cognitive Impairment Is Associated with Postoperative Cognitive Dysfunction after Hip Joint Replacement Surgery**

Brendan Silbert, M.B., B.S., F.A.N.Z.C.A., Lisbeth Evered, B.Sc., M.Biostat., Ph.D., David A. Scott, M.B., B.S., F.A.N.Z.C.A., Ph.D., Stephen McMahon, M.B.B.S., F.R.A.C.S.(Orth), F.A.(Orth), Peter Choong, M.B., B.S., M.D., F.R.A.C.S., David Ames, B.A., M.D., F.R.C.Psych., F.R.A.N.Z.C.P., Paul Maruff, Ph.D., Konrad Jamrozik, Ph.D.†

**Table 3.** Prevalence of Preexisting Cognitive Impairment and Incidence of Postoperative Cognitive Dysfunction and Cognitive Decline

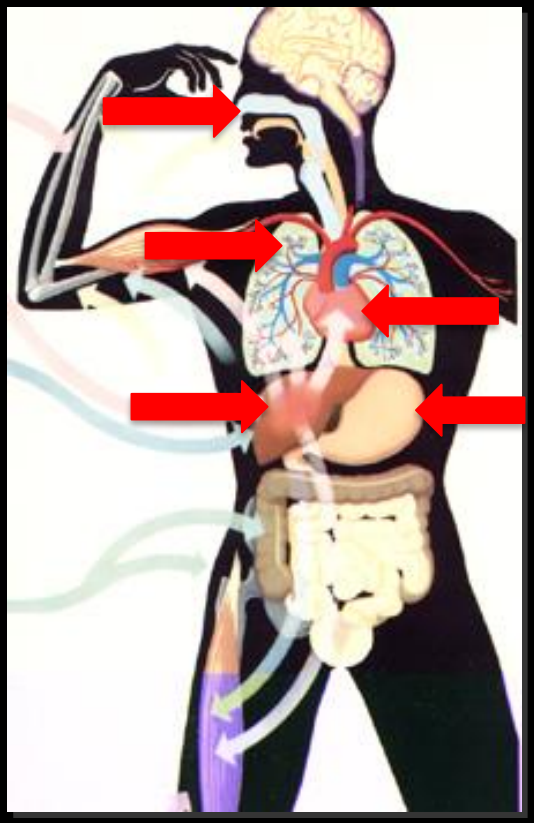
| | PreCI (n = 96) | No PreCI (n = 204) | *P* Value | 95% CI Difference |
|---|---|---|---|---|
| Day 7 | | | | |
| POCD | 23/91 (25.3%) | 26/195 (13.3%) | 0.012 | 12% (2%, 22%) |
| 95% CI | 16.7%, 35.5% | 8.9%, 18.9% | | |
| 3 months | | | | |
| POCD | 13/87 (14.9%) | 14/197 (7.1%) | 0.039 | 7.8% (1%, 16%) |
| 95% CI | 8.2%, 24.2% | 3.9%, 11.6% | | |
| 12 months | | | | |
| Cognitive decline | 5/83 (9.4%) | 2/188 (1.1%) | <0.001 | 8.3% (2%, 15%) |
| 95% CI | 2.0%, 13.5% | 0.1%, 3.8% | | |

Data are presented as n (%), 95% CI in percent.

POCD = postoperative cognitive dysfunction; PreCI = preexisting cognitive impairment.

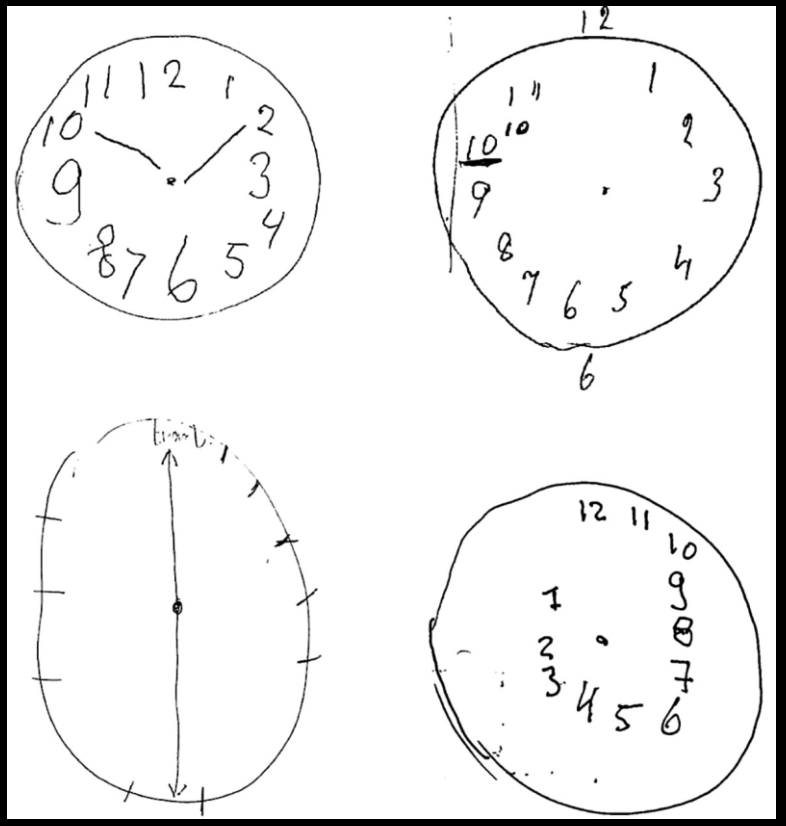
Silbert, Evered, Scott et al Anesthesiology 2015

## Preoperative assessment of vital organ function – except for the brain?



## Preoperative cognitive screening

### Mini Cog or the Clock-in-a-box test?



# Take-home messages

- Postoperative neurocognitive disorders continue to be a a common longterm adverse outcome after otherwise uneventful surgery. Major impact on patients, their families and health care system
- While underlying mechanisms for longterm cognitive decline are known, less is known about mechanisms underlying postop delirium.
- To avoid postop delirium: Assess brain function prior to surgery. Avoid trigger drugs and burst suppression during anesthesia. EEG monitoring show promising results, further studies are needed. Apply perioperative "ERAS" concept. Patients developing POD need follow-up
- While immune modulation is promising, no current prophylactic strategy available for neurocognitive decline