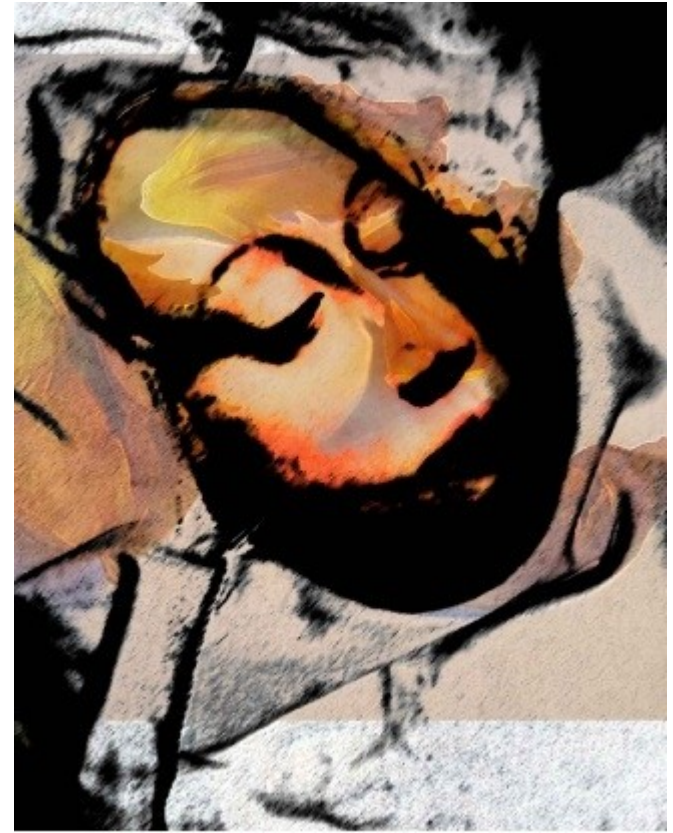


# Inflammasjon og delirium

Leiv Otto Watne, lege/stipendiat  
Geriatrisk avd, OUS - Ullevål

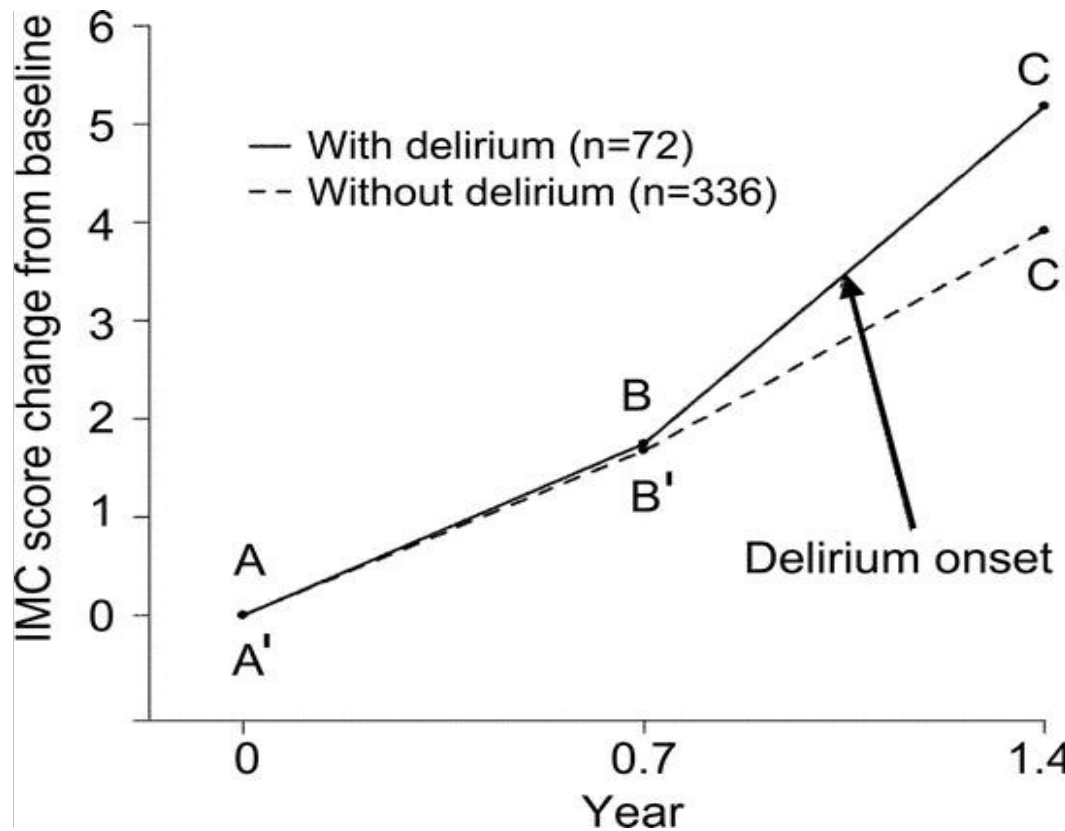
# Delirium

- An acute change in cognition and attention
- Common condition:
  - At hospital admittance: 14-24%
  - Incident delirium among general hospital populatons: 6-56 %
  - Hip fracture patients: 35-65 %
  - ICU patients: 70 – 83 %



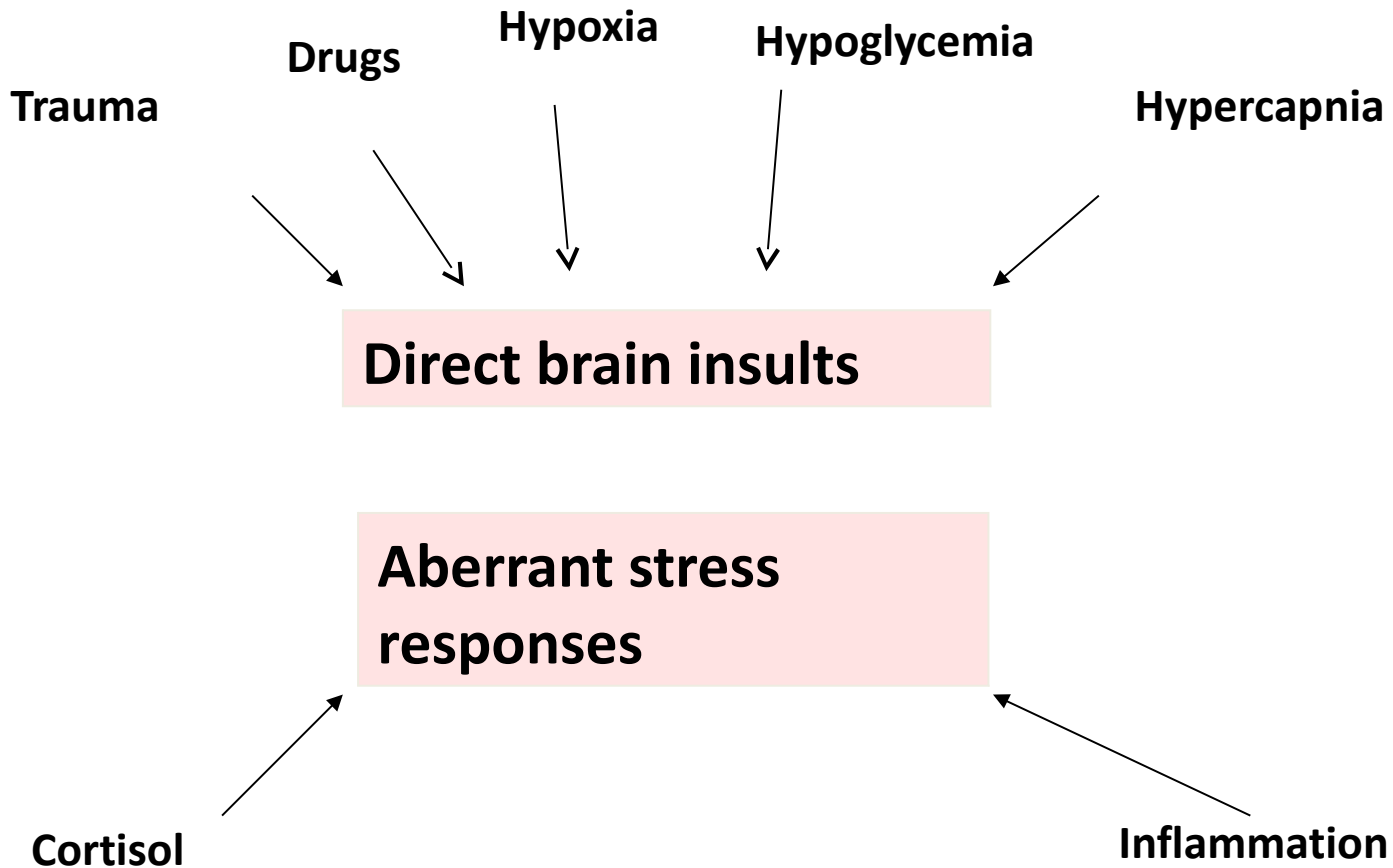
Inouye, SK. N Engl J Med 2006  
Rudolph, J. Anesthesia & Analgesia 2011

# Delirium and long-term effects on cognition



Fong, T. Neurology. 72(18):1570-1575,  
May 5, 2009.

# Delirium pathophysiology



MacLulich AM. J Psychosomatic Res 2008

Khan, B. JAGS 2011

Tomas C. BMC Neuroscience 2008

MacLulich AM. JAGS 2011

Hshieh, T. A Biol Sci Med Sci. 2008

Cerejeira J. JAGS 2012

**Table 1. Summary of Recent Evidence on the Role of Bi**

**Biomarkers for Delirium—A Review**

Babar A. Khan, MD, MS,<sup>\*†‡</sup> Mohammed Zawabiri, MD,<sup>†‡</sup> Noll L. Campbell, PharmD,<sup>†‡§||</sup> and Malaz A. Boustani, MD, MPH<sup>†‡#</sup>

Study	Service	Sample Size	Age, Mean ±SD	Category	Diagnosis Asses	Biomarker	Findings
Wilson <sup>16</sup>	Medicine	100	84.5 ± 4.2	Risk*	CAM, DSM-III	IGF-1	Low IGF-1 increases the risk of delirium
Macdonald <sup>15</sup>	Medicine	86	82.7 ± 6.6	Risk	CAM	CRP	High levels predict the incidence of delirium
de Rooij <sup>4</sup>	Medicine	185	80	Risk	CAM	Cytokines	Cytokines may contribute to pathogenesis of delirium
Tagarakis <sup>10</sup>	Surgery	154	70.1 ± 7.7– 67.8 ± 7.4	Risk	DRS	ApoE	No correlation between ApoE and postoperative delirium
Leung <sup>7</sup>	Surgery	190	72.5 ± 6	Risk	CAM	ApoE	ApoE carrier status was associated with greater risk of early postoperative delirium
Van Munster <sup>9</sup>	Medicine	264	81.4–76.7	Risk	CAM	ApoE	No evidence that ApoE carriers have higher
Van Munster <sup>16</sup>	Surgery	98	84.6 ± 7.				delirium have
Lemstra <sup>22</sup>	Surgery	68	83.2 ± 6. 78.5–80				8 in preoperative and
Van Munster <sup>8</sup>	Medicine, surgery	656	77.4 ± 7. 82.3 ± 7.				presence of ApoE-4
Van Munster <sup>13</sup>	Surgery	120	84.8 ± 6. 82.9 ± 7.				may have a role um. S-100 β is marker
Adamis <sup>11</sup>	Medicine	164	84.6 ± 6.				low IGF-1, and
Ely <sup>12</sup>	ICU	53	53.2 ± 21 – 65.4 ± 13				tly associated delirium
Adamis <sup>5</sup>	Medicine	67	84.2 ± 6.				ed with delirium
Thomas <sup>18</sup>	Medicine	61	86.2 ± 4.				with ameters in
Van Munster <sup>23</sup>	Medicine	412	81.6 ± 7.9– 76.6 ± 7.6	Diagnosis	CAM, DOS, DRS-R-98	S-100 β	Higher levels of S-100 β were found in patients with delirium than in those without
Van Munster <sup>24</sup>	Surgery	120	84.8 ± 6.9– 82.9 ± 7.0	Diagnosis	CAM, DOS, DRS-R-98	S-100 β, NSE	Delirium associated with high levels of S-100 β but not with NSE
Plaschke <sup>21</sup>	ICU	114	73.3 ± 6.0– 67.3 ± 9.3	Diagnosis	CAM-ICU	Cortisol, IL-6	Early postoperative delirium after cardiac surgery associated with higher cortisol and IL-6 levels

**Serum: Totalt 835 pasienter i studier der en undersøker sammenheng mellom inflammasjon og delirium**

# A Systematic Literature Review of Cerebrospinal Fluid Biomarkers in Delirium

Roanna J. Hall<sup>a, b</sup> Susan D. Shenkin<sup>a, b</sup> Alasdair M.J. MacLulich<sup>a, b</sup>

Study/provenance	Design/setting	Biomarker(s) studied	Causes of delirium	Cases	Controls
Koponen et al. [16, 18, 22, 23] Finland, 1990, 1994	prospective cohort study, with external control group; psychogeriatric hospital	SLI, BLI, 5-HIAA, AChE	stroke (n = 15), infection (n = 9), metabolic (n = 8), epileptic fit (n = 6), medication (n = 6), life change in dementia (n = 5), myocardial infarction or ischaemia (n = 4), carcinoma (n = 4), functional psychosis (n = 2), subdural haematoma (n = 2), intracerebral haemorrhage (n = 2), trauma (n = 2)	n = 67 for SLI (41.8% male); n = 69 for other biomarkers (42% male); n = 56 at 2 weeks; n = 33 at 1 year; n = 16 at 4 years; (11 I.P.)	n = 13 (38.5% male) for SLI, 5-HIAA, AChE n = 19 (31.6% male) for BLI
Ramirez-Bermudez et al. [24], Mexico, 2008	prospective cohort study; general hospital	HVA			
Pearson et al. [25] Scotland, 2010	prospective cohort study; general hospital	cortisol			
Caplan et al. [26] Australia, 2010	prospective cohort study; general hospital	lactate, NSE, S100B, glucose, protein			
MacLulich et al. [13] Scotland and The Netherlands, 2011	prospective cohort study; general hospital	TNF- $\alpha$ , IL-1 $\beta$ , IL-6, IL-8, IL-10 and IL-12p			

CSF: Totalt 56 pasienter i studier der ein undersøker sammenhengen mellom inflammasjon og delirium

SLI = Somatostatin-like immunoreactivity; 5-HIAA = hydroxyindole-acetic acid; AChE = acetyl-cholinesterase; HVA = homovanillic acid; BLI =  $\beta$ -endorphin-like immunoreactivity; NSE = neuron-specific enolase; TNF- $\alpha$  = tumour necrosis factor-alpha; IL = interleukin.

Hall, R. Dement Geriatri Cogn Disord 2011

# Delirium og inflammasjon

- Serum:
  - IL-6 ↑ (de Rooij, van Munster, MacLulich)
  - IL-8 ↑ (de Rooij, van Munster)
  - CRP ↑ (Macdonald)
  - Neopterin ↑ (Osse)
- CSF:
  - IL-8 ↑ (MacLulich)

Van Munster, JAGS 2008

De Rooij, Psychosomatic Res 2007

MacLulich, JAGS 2011

Macdonald, Age and Ageing, 2007

Osse, JAGS 2012

## **Inclusion and randomization**

Patients are included and randomized in the emergency department by the orthopaedic surgeon on call.

## **Intervention**

Patients are screened daily for delirium. Background information is collected while patients are admitted

## **Assessment**

After 4 and 12 months the patient will be assessed by a specially trained research assistant blinded to allocation.

Primary endpoint: Cognitive function

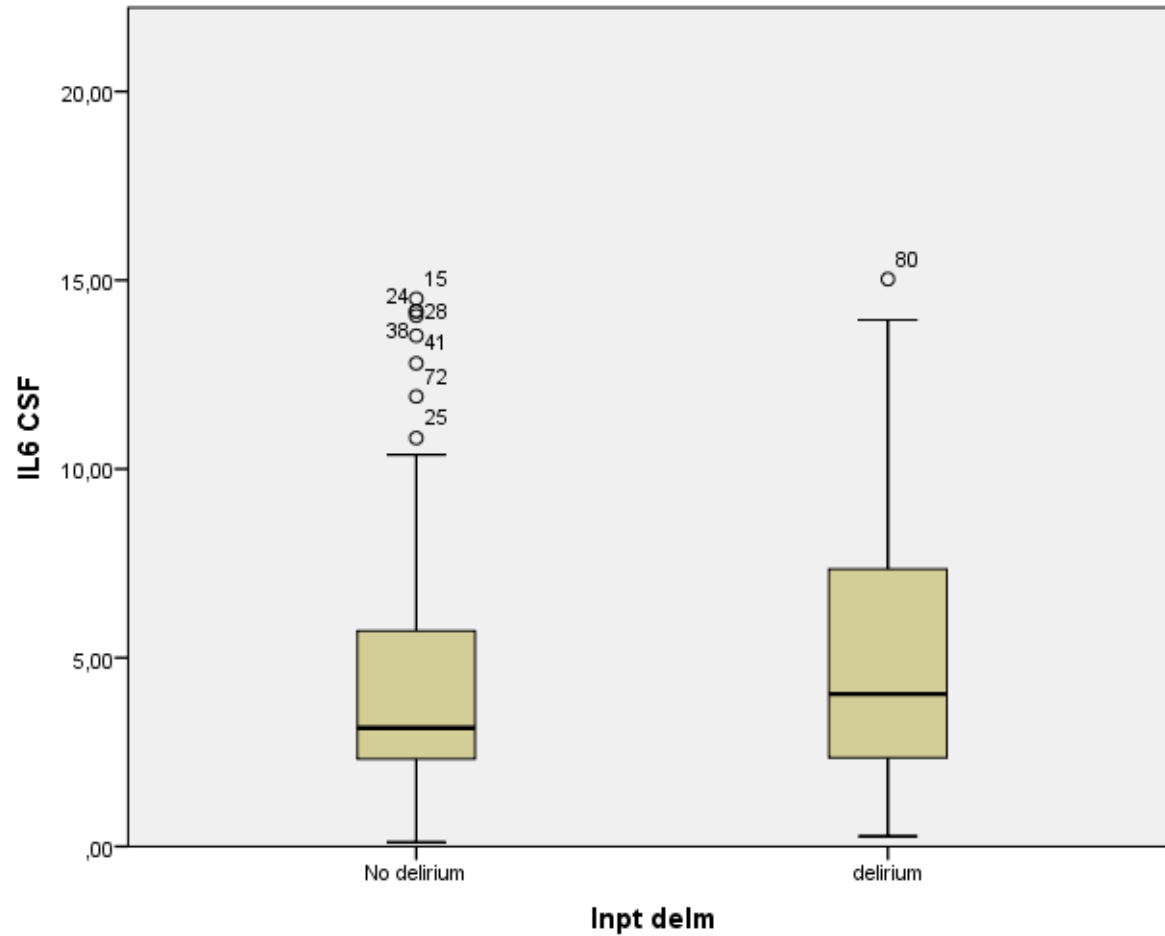




# CRP, IL-6, IL-6R

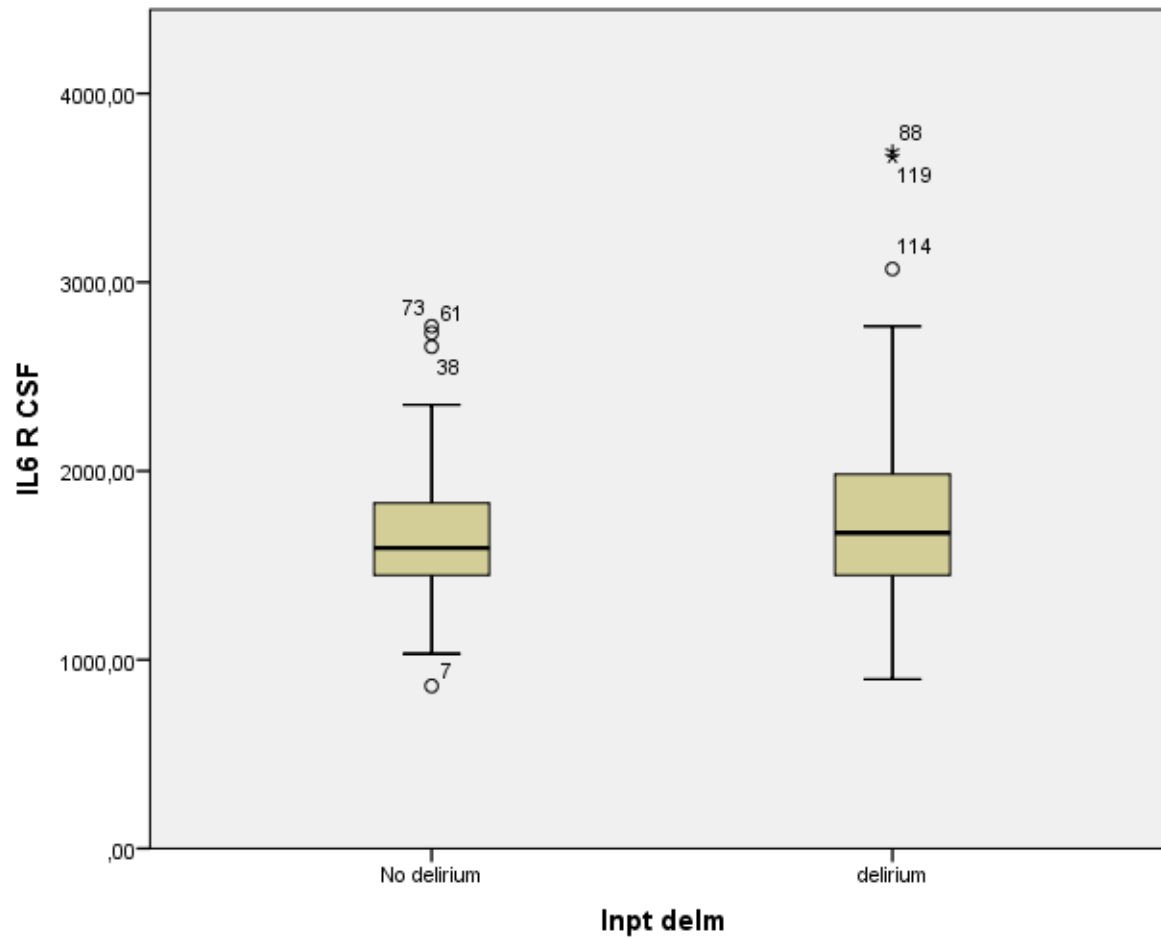
- N=147 (Oslo University Hospital N=95; Royal Infirmary of Edinburgh N=52)
- Patients were assessed by the Confusion Assessment Method (pre-op and over two weeks post-op) and the IQCODE.
- ELISAs were used for the assays

# IL6 CSF



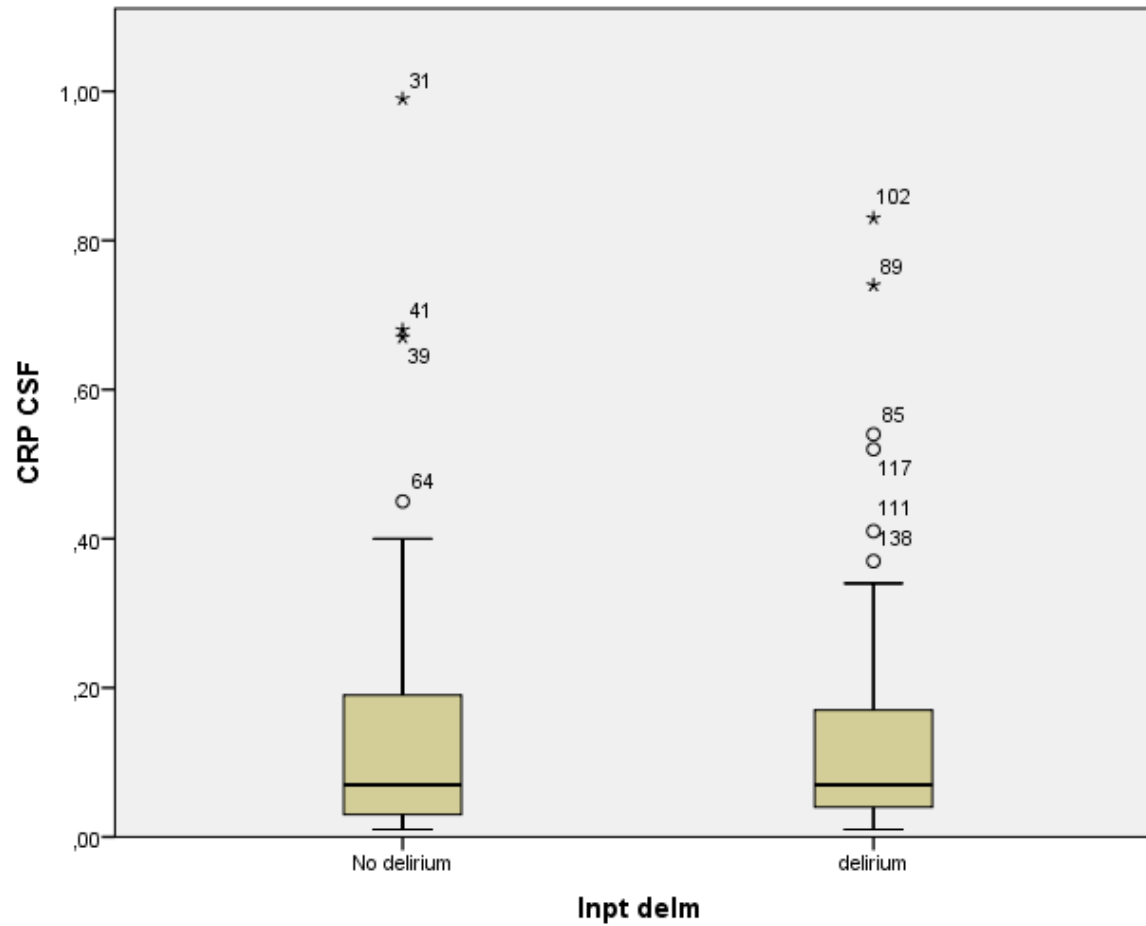
$p = 0.31$

# IL6R CSF



p = 0.22

# CRP CSF



p = 0.58