UNIVERSITY OF CAMBRIDGE

Improving TBI outcome

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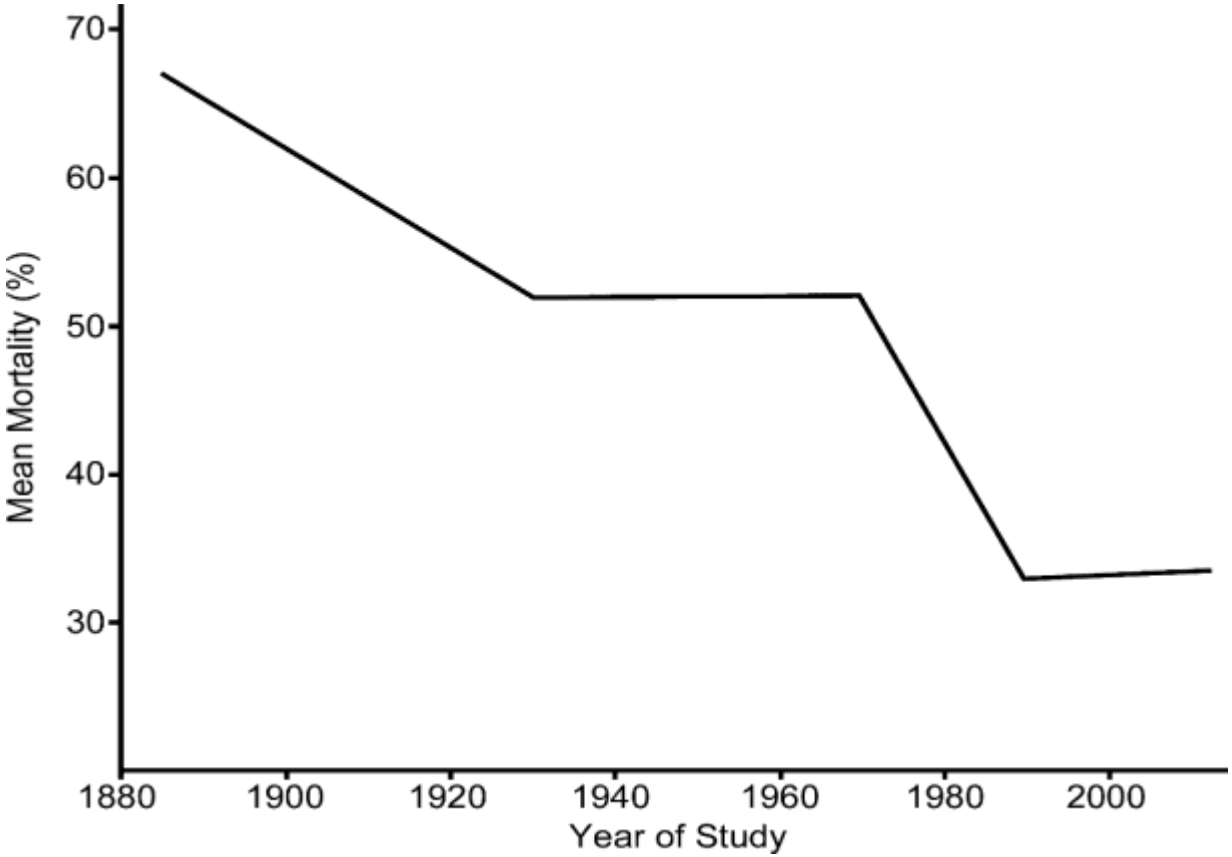
20/10/2017

Division of Neurosurgery, Department of Clinical Neurosciences

Brain Physics Lab

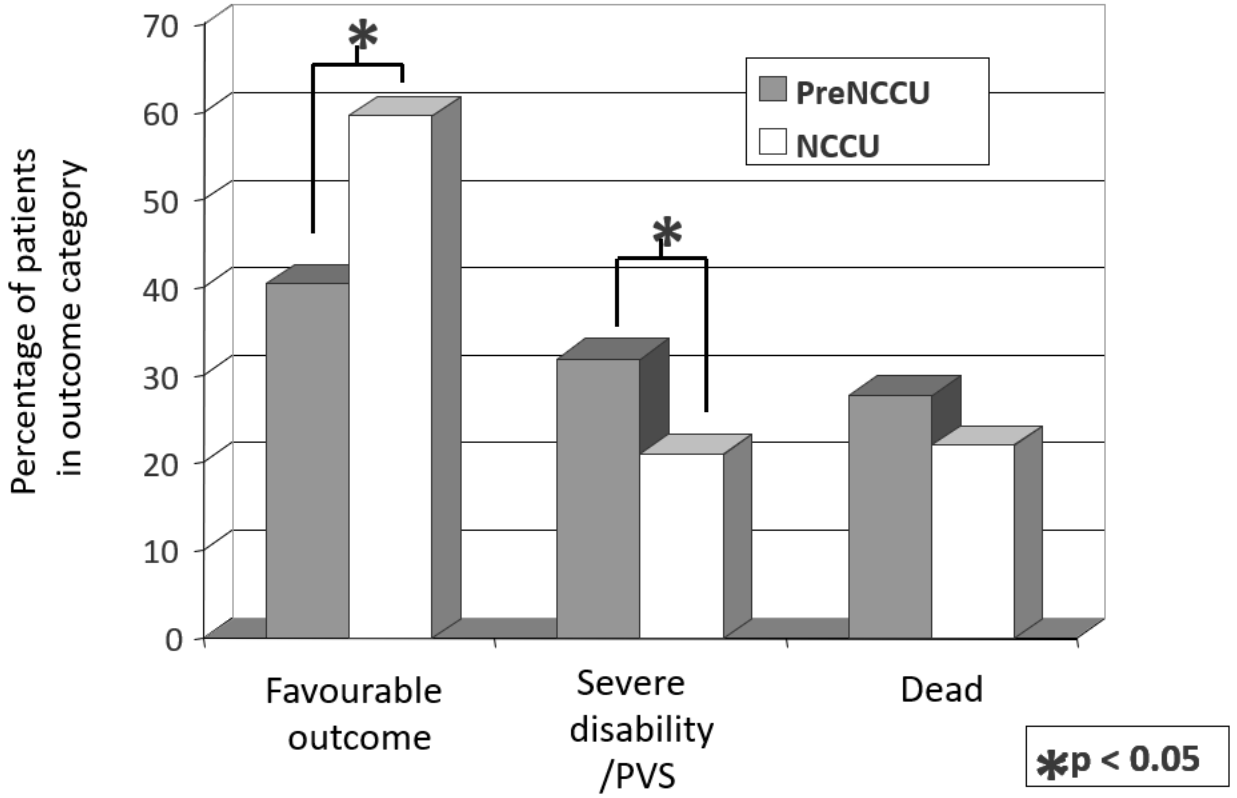
Background



Stein, S. C., Georgoff, P., et al. (2010). *Journal of Neurotrauma*

Thanks to Joseph Donnelly

The impact of specialised neuro-critical care



Thanks to David Menon

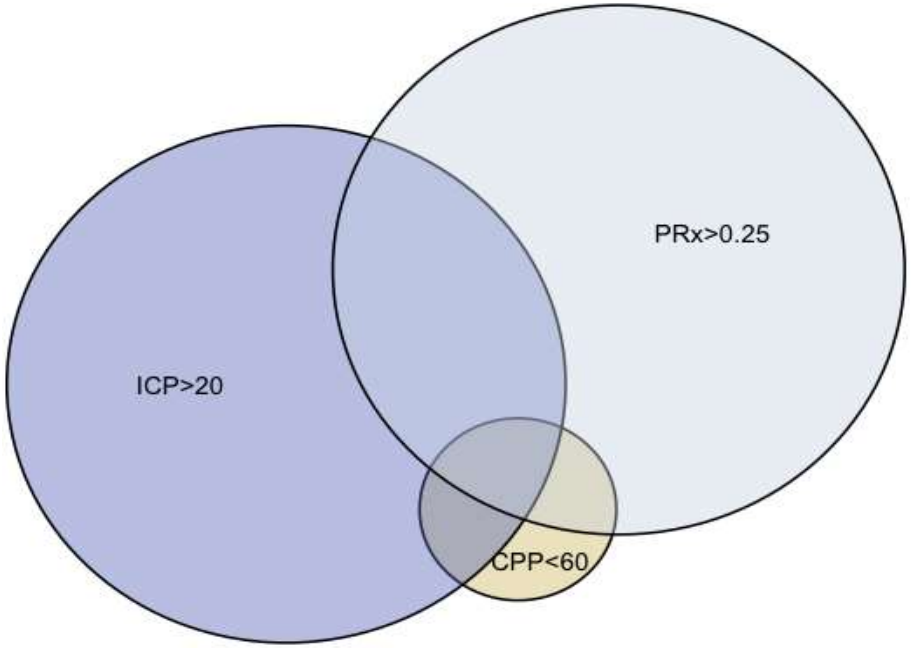
TBI secondary insults

Definition of insults

- ICP > 20
- CPP < 60

Potential exacerbating condition

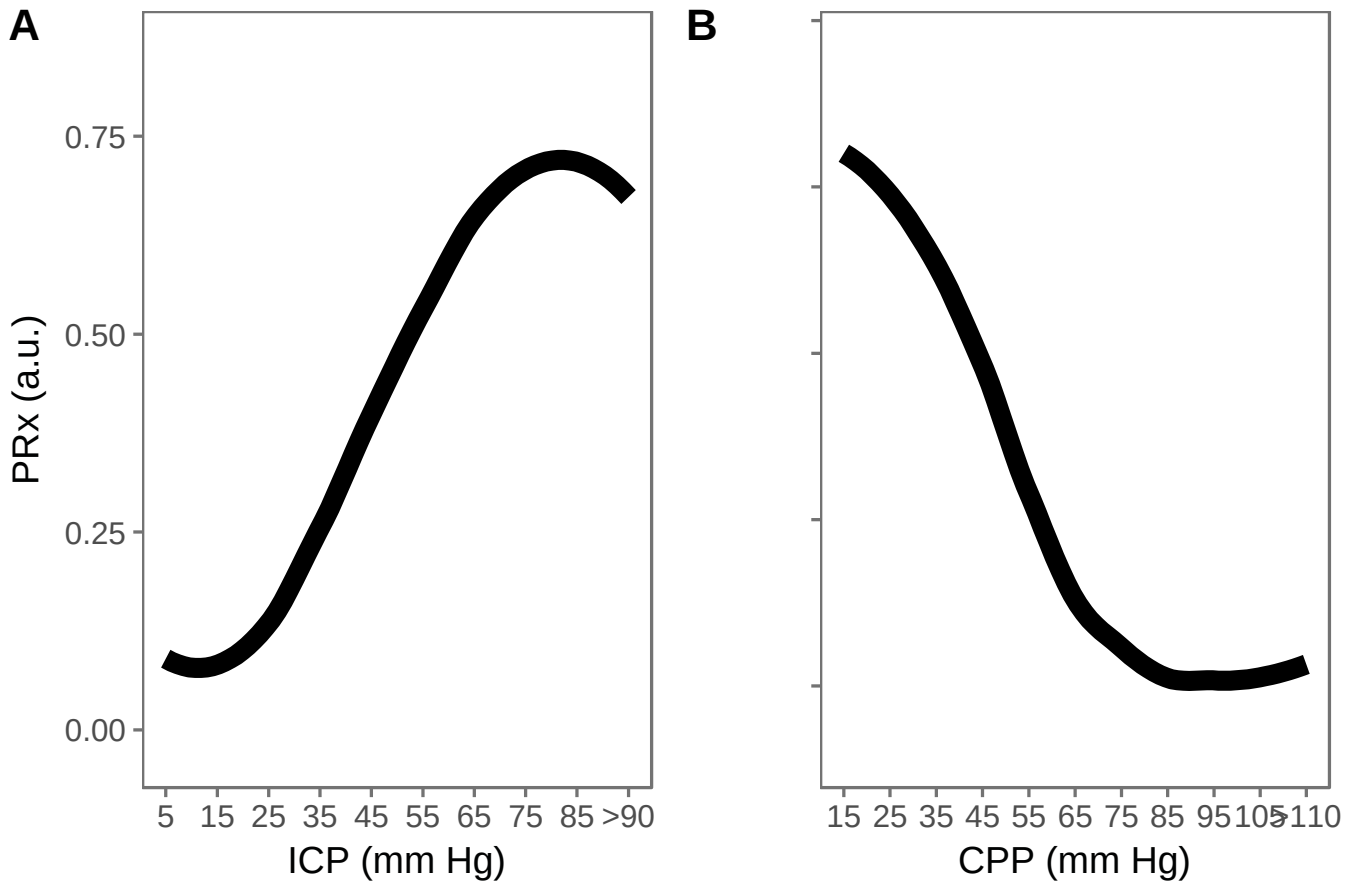
- PRx > 0.25



Thanks to Joseph Donnelly

Associations and consequences of clinical high ICP

N=37



Thanks to Joseph Donnelly

Associations and consequences of clinical high ICP

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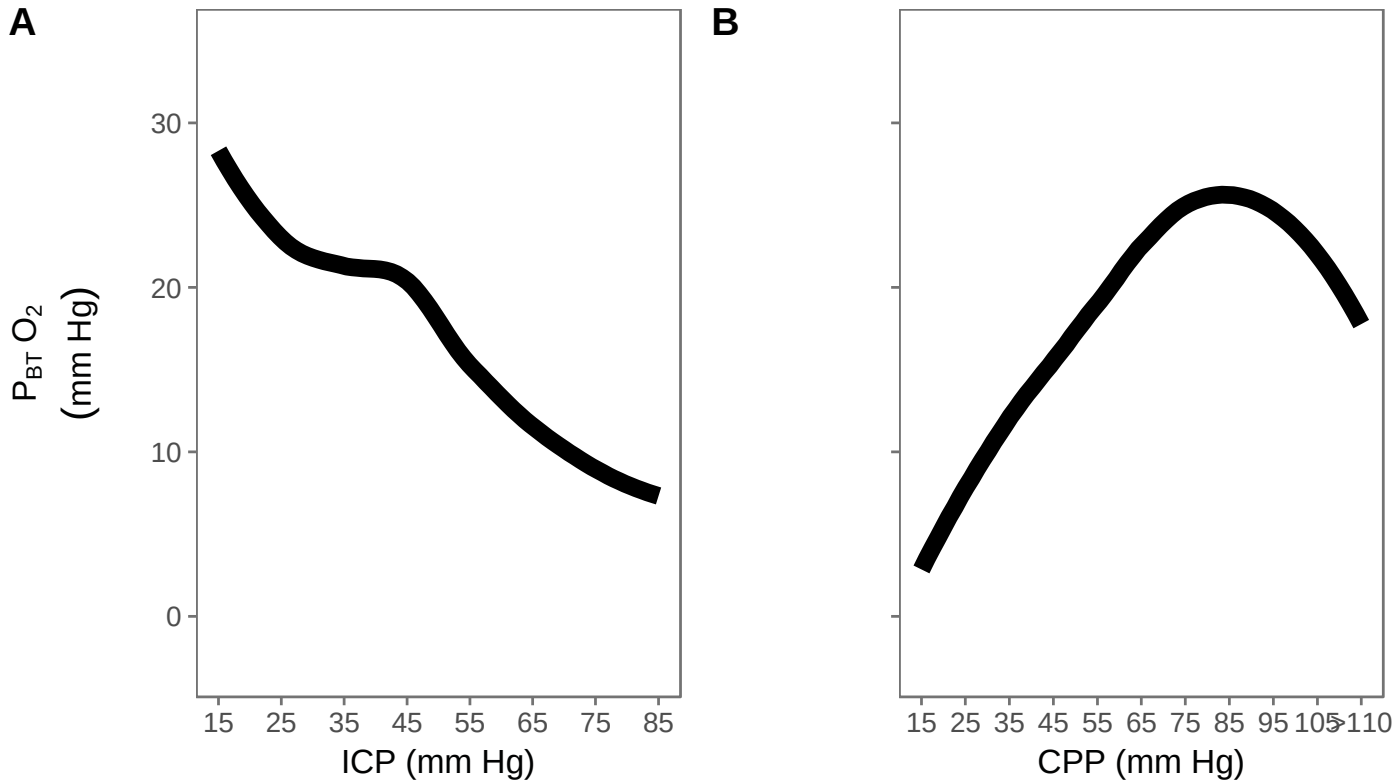

Associations and consequences of clinical high ICP

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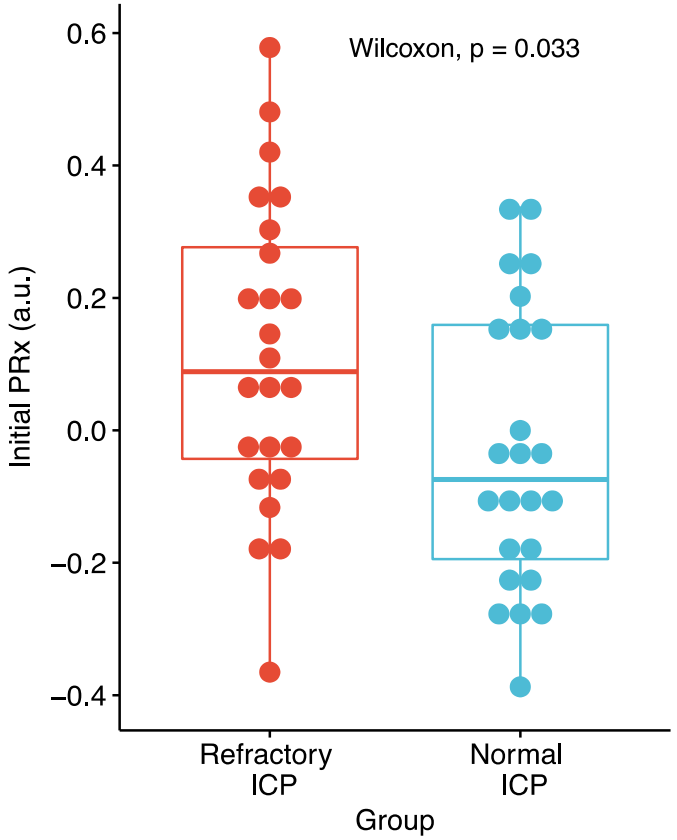
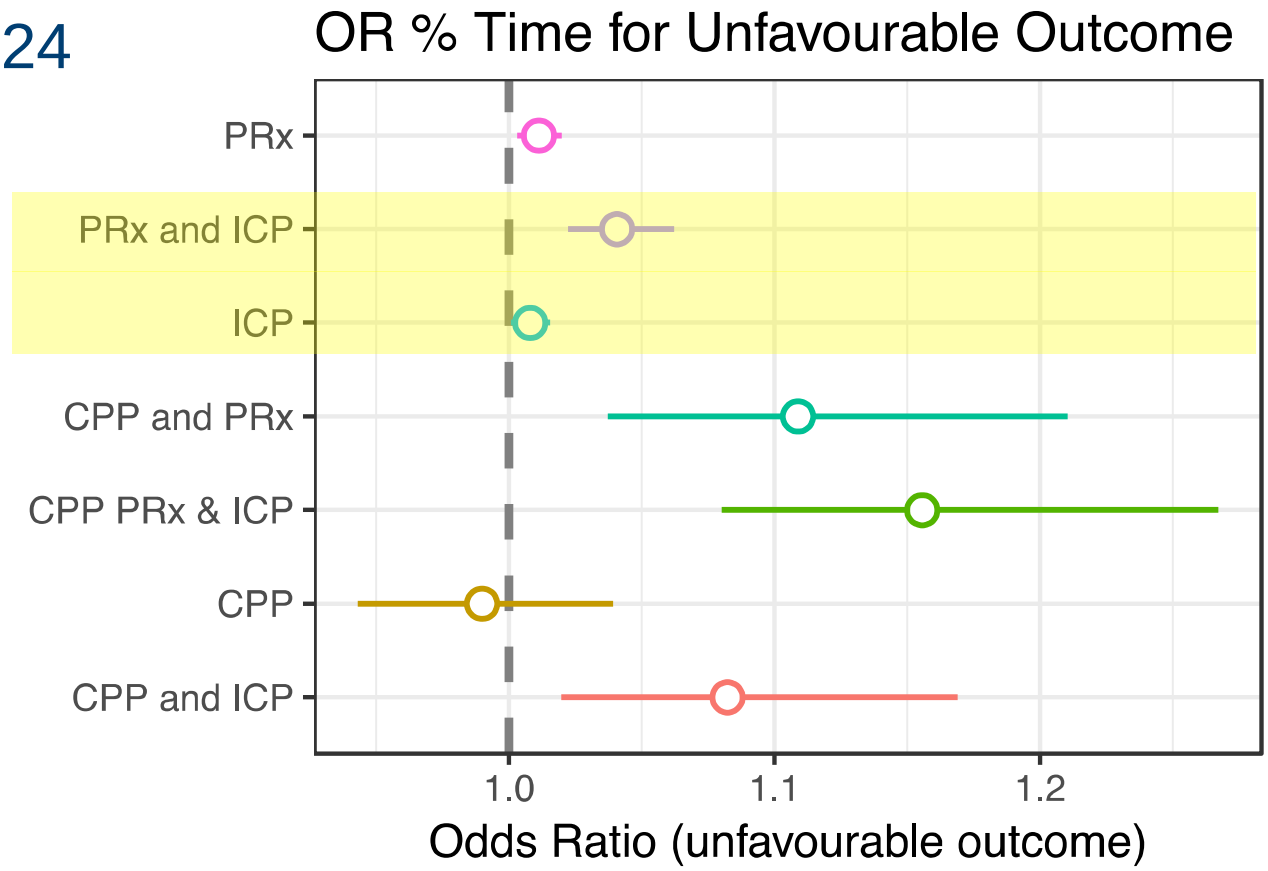


Impact of ICP insults on outcome

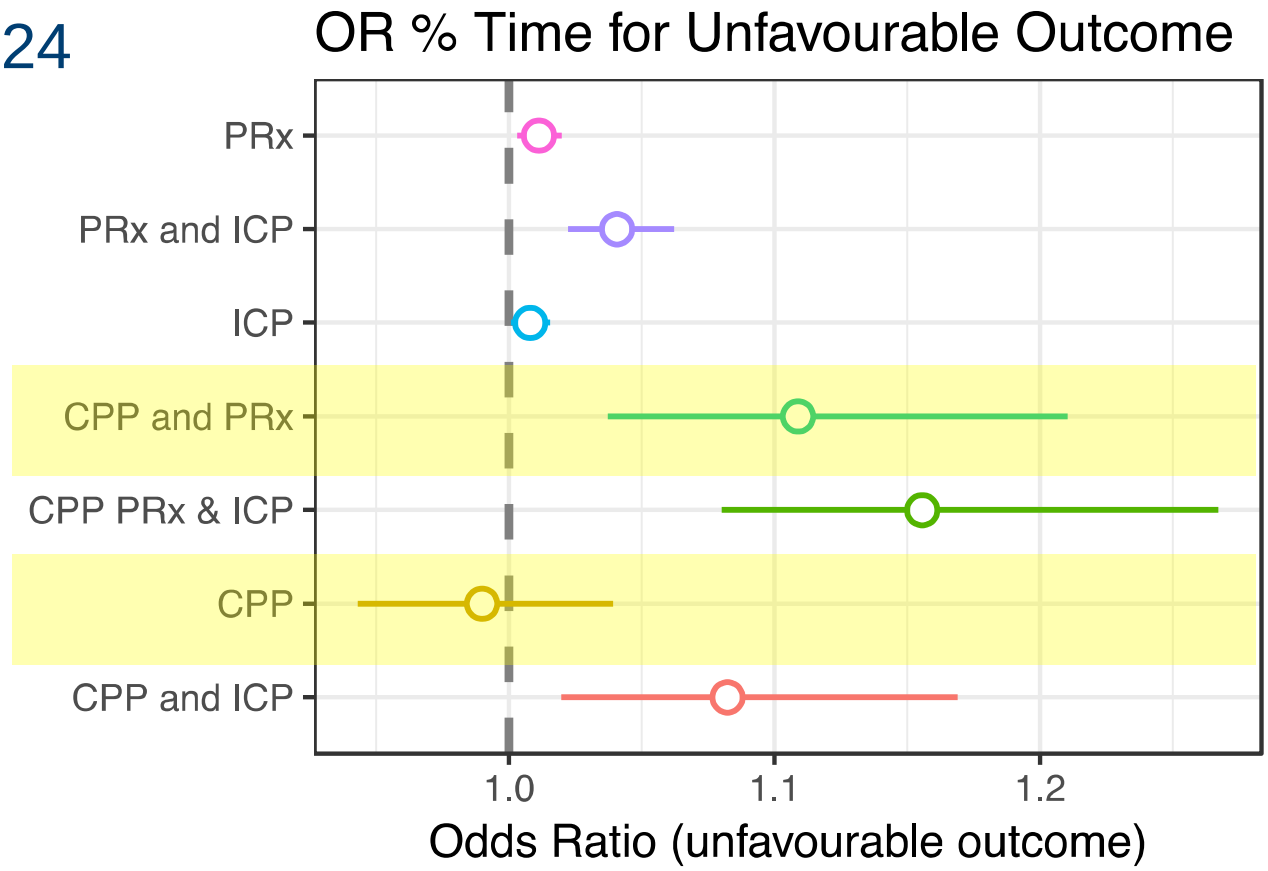
N=824



Thanks to Joseph Donnelly

Impact of CPP insults on outcome

N=824

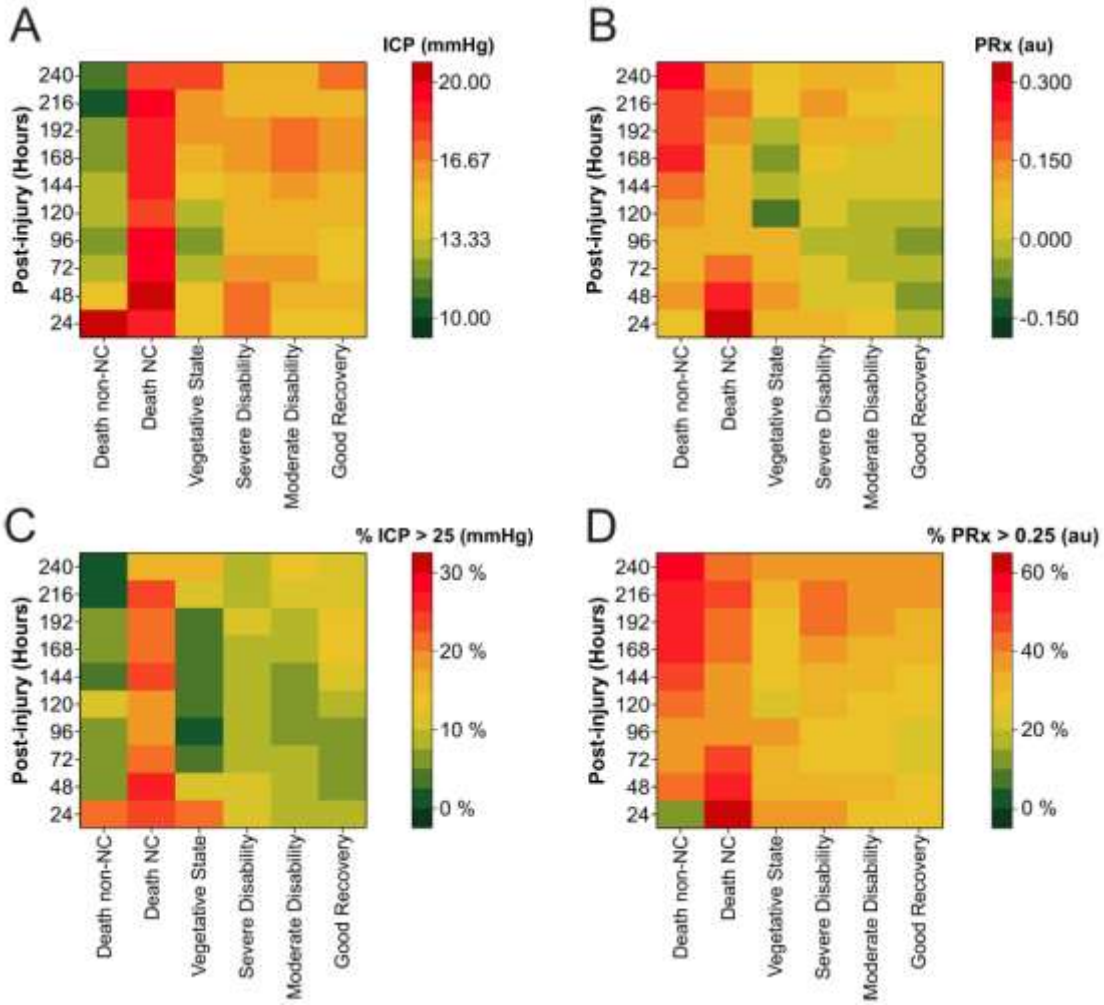


Thanks to Joseph Donnelly

Heatmaps of time profile of ICP and PRx stratified by different levels of functional outcome.

N=601

No DC



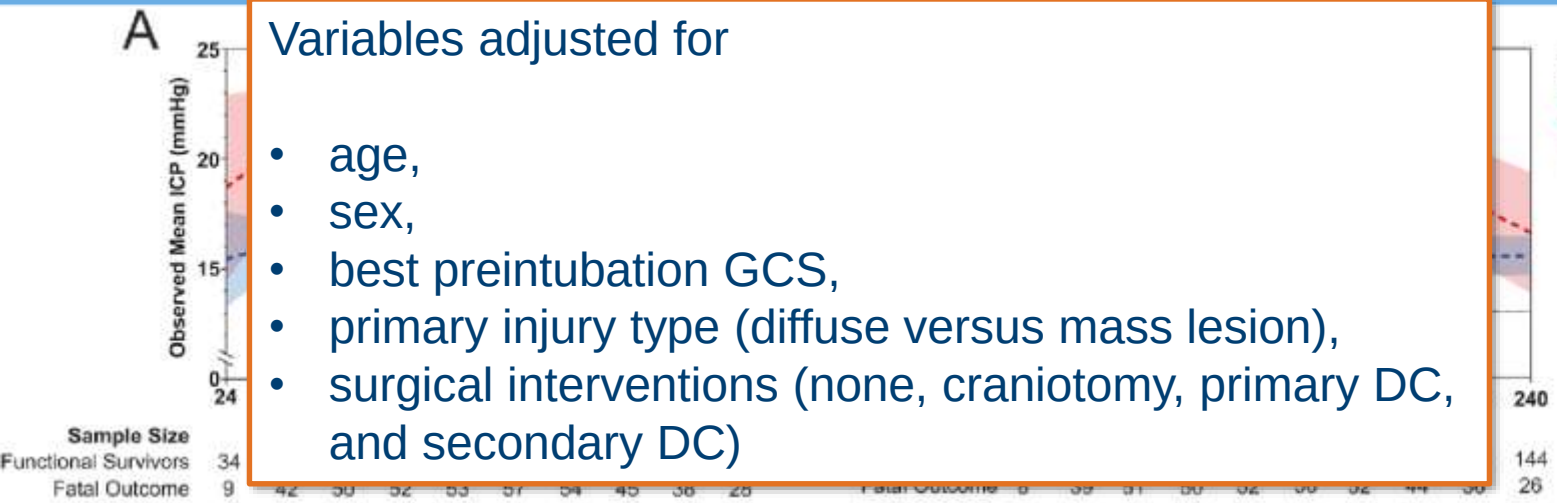
Time profile of ICP and PRx

Variables adjusted for

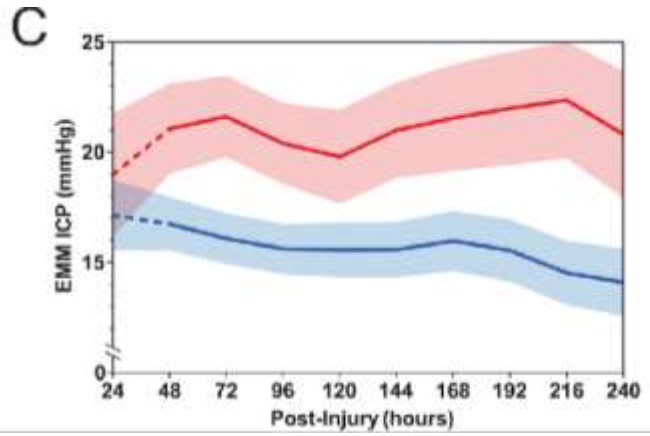
- age,
- sex,
- best preintubation GCS,
- primary injury type (diffuse versus mass lesion),
- surgical interventions (none, craniotomy, primary DC, and secondary DC)

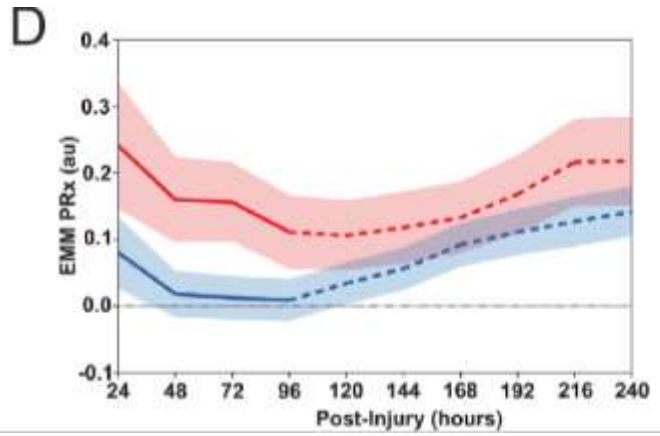
N=601

No DC



Adjusted for patient, injury, and treatment characteristics.

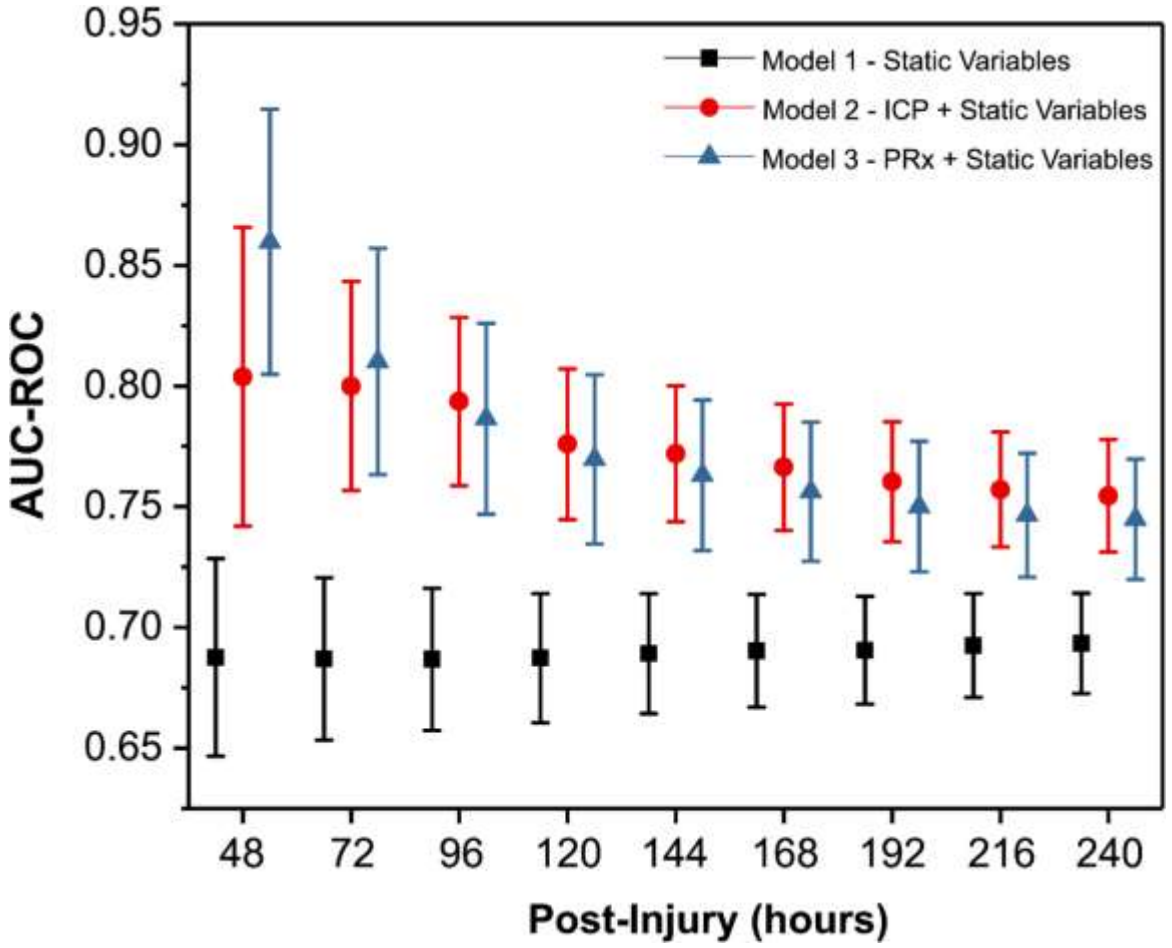




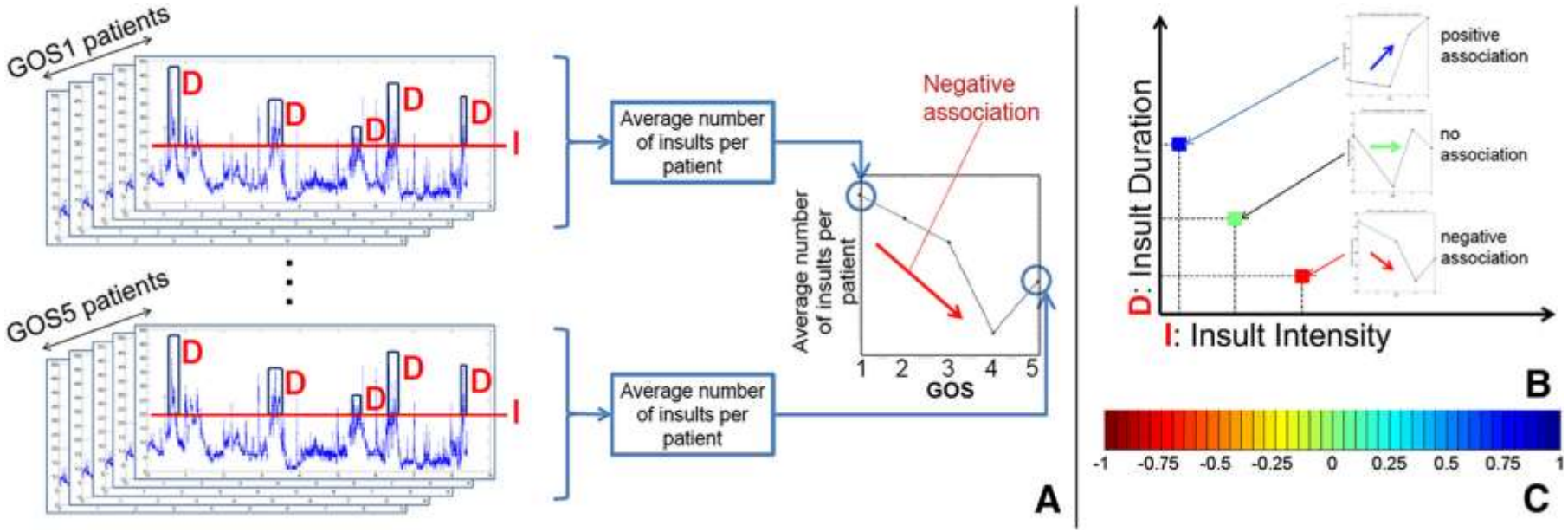
(ROC) curve analysis for prediction of fatal outcome due to neurological causes.

N=601

No DC



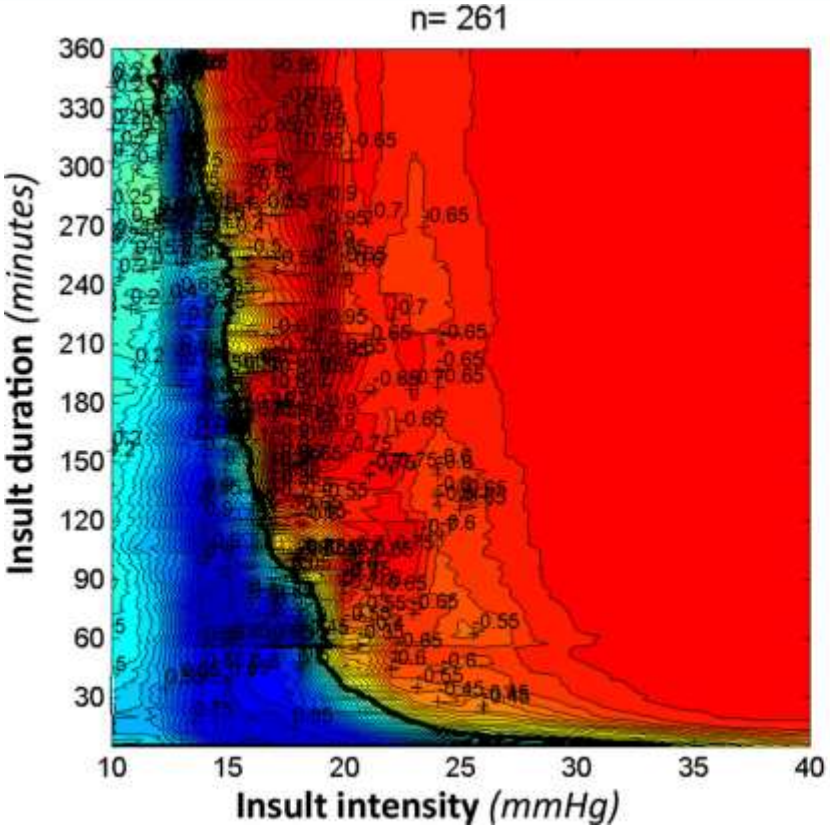
Limits of reactivity visualisation



Güiza, F. et al., 2015. Visualizing the pressure and time burden of intracranial hypertension in adult and paediatric traumatic brain injury. *Intensive Care Medicine*.

Visualising the ICP insults burden

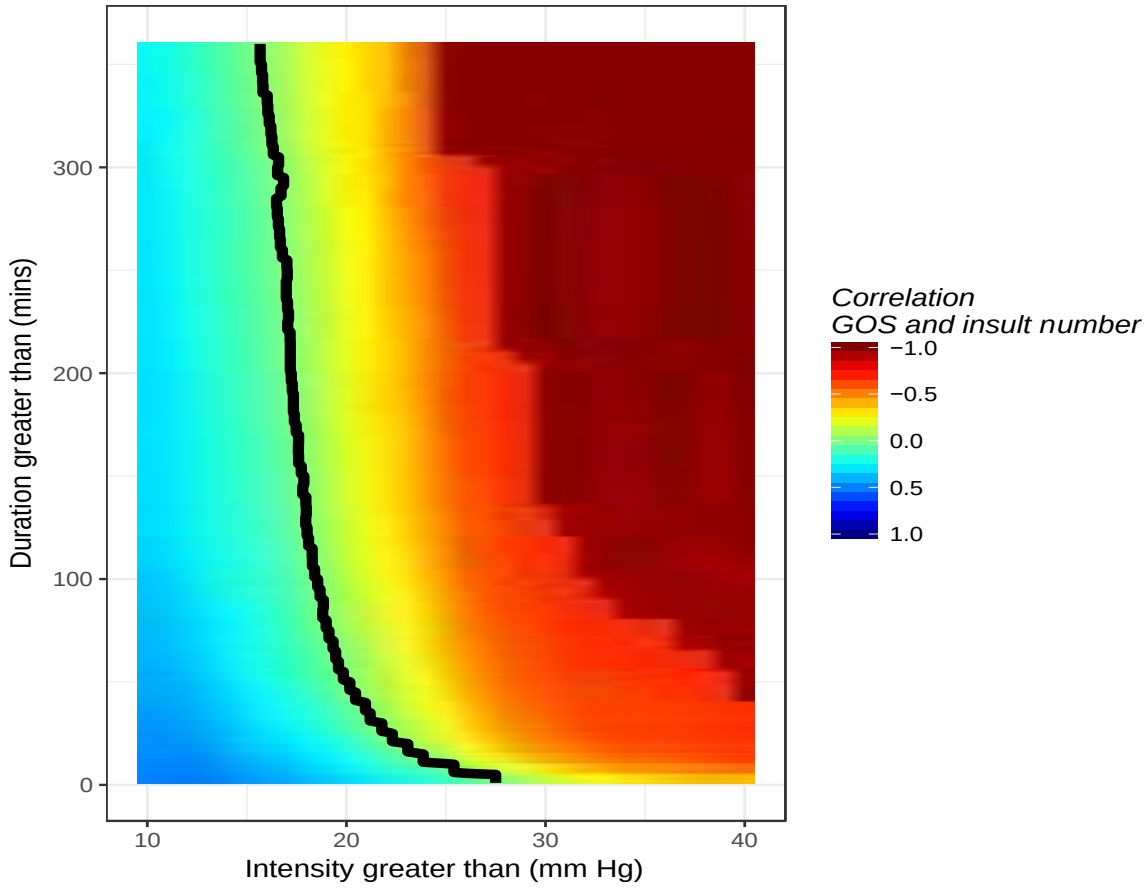
N = 261



Güiza, F. et al., 2015. Visualizing the pressure and time burden of intracranial hypertension in adult and paediatric traumatic brain injury. *Intensive Care Medicine*.

Visualising the ICP insults burden (Cambridge cohort)

n=748

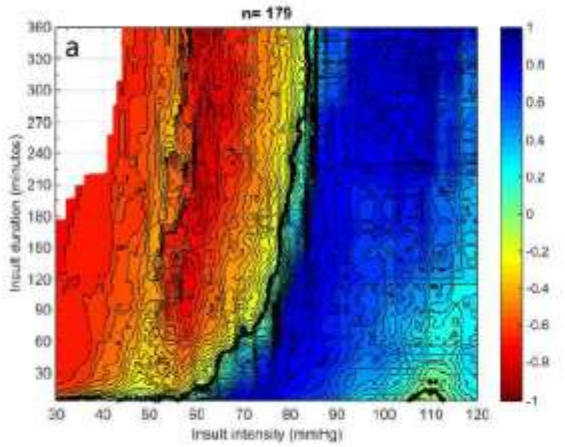


24 million episodes

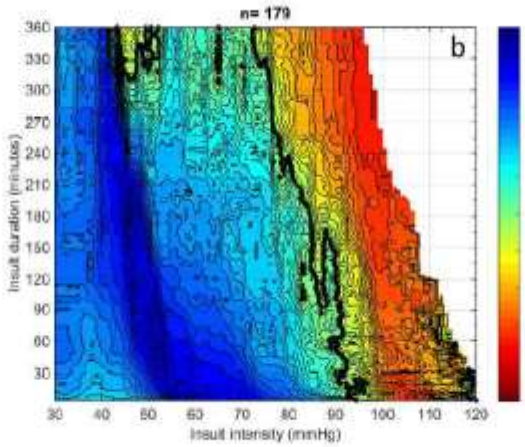
Donnelly J at al, in press

Visualising CPP insults

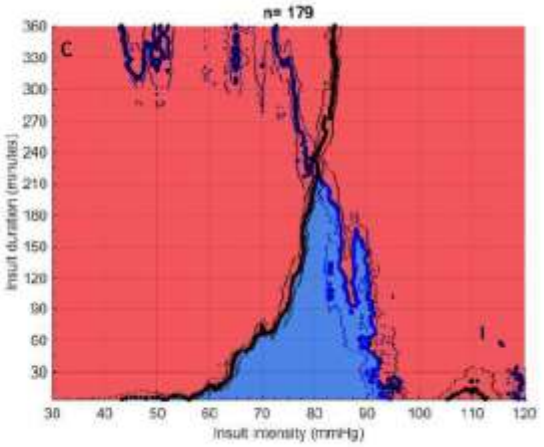
Hypo-perfusion



Hyper-perfusion



Combined
(transition curves only)



Guiza et al. Cerebral perfusion pressure insults and associations with outcome in adult traumatic brain injury. J Neurotrauma 2017

J Neurosurg 83:949–962, 1995

Cerebral perfusion pressure: management protocol and clinical results

MICHAEL J. ROSNER, M.D., SHEILA D. ROSNER, R.N., M.S.N., AND ALICE H. JOHNSON, R.N., B.S.N.

Division of Neurological Surgery, Department of Surgery, University of Alabama at Birmingham, Birmingham, Alabama

Intensive Care Med (2006) 32:1475–1484
DOI 10.1007/s00134-006-0294-3

REVIEW

Per-Olof Grände

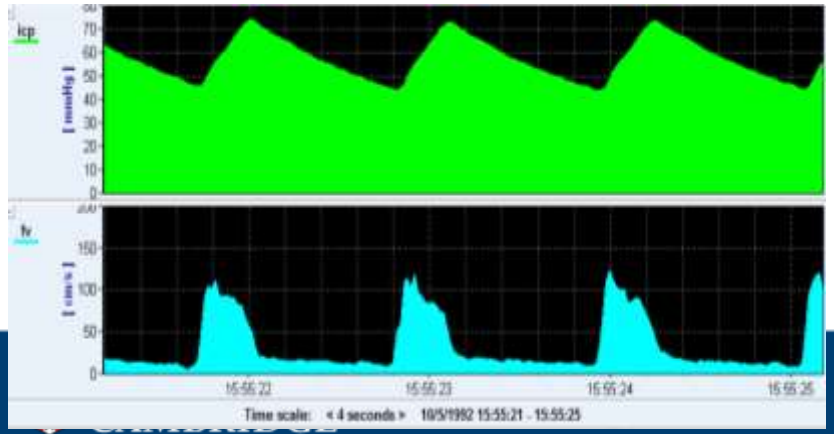
The "Lund Concept" for the treatment of severe head trauma – physiological principles and clinical application

CPP above : 70? ....65?...

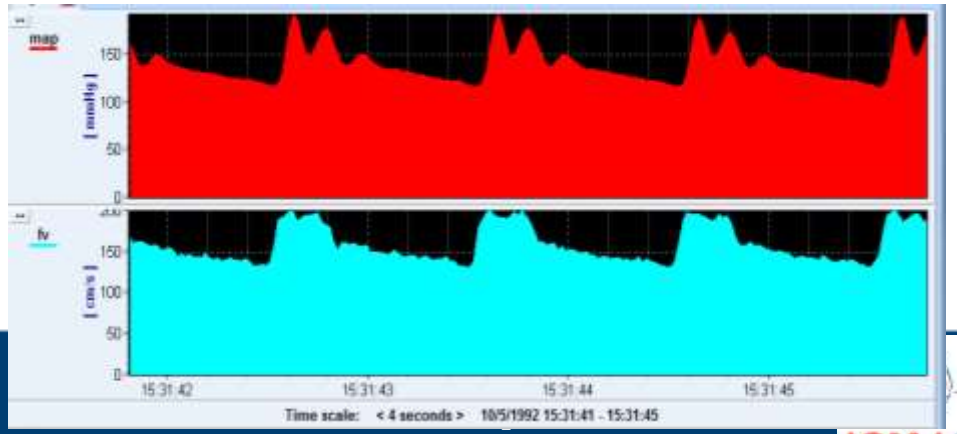
CPP may be low; ICP<15 mmHg

Set thresholds: Is it wise?

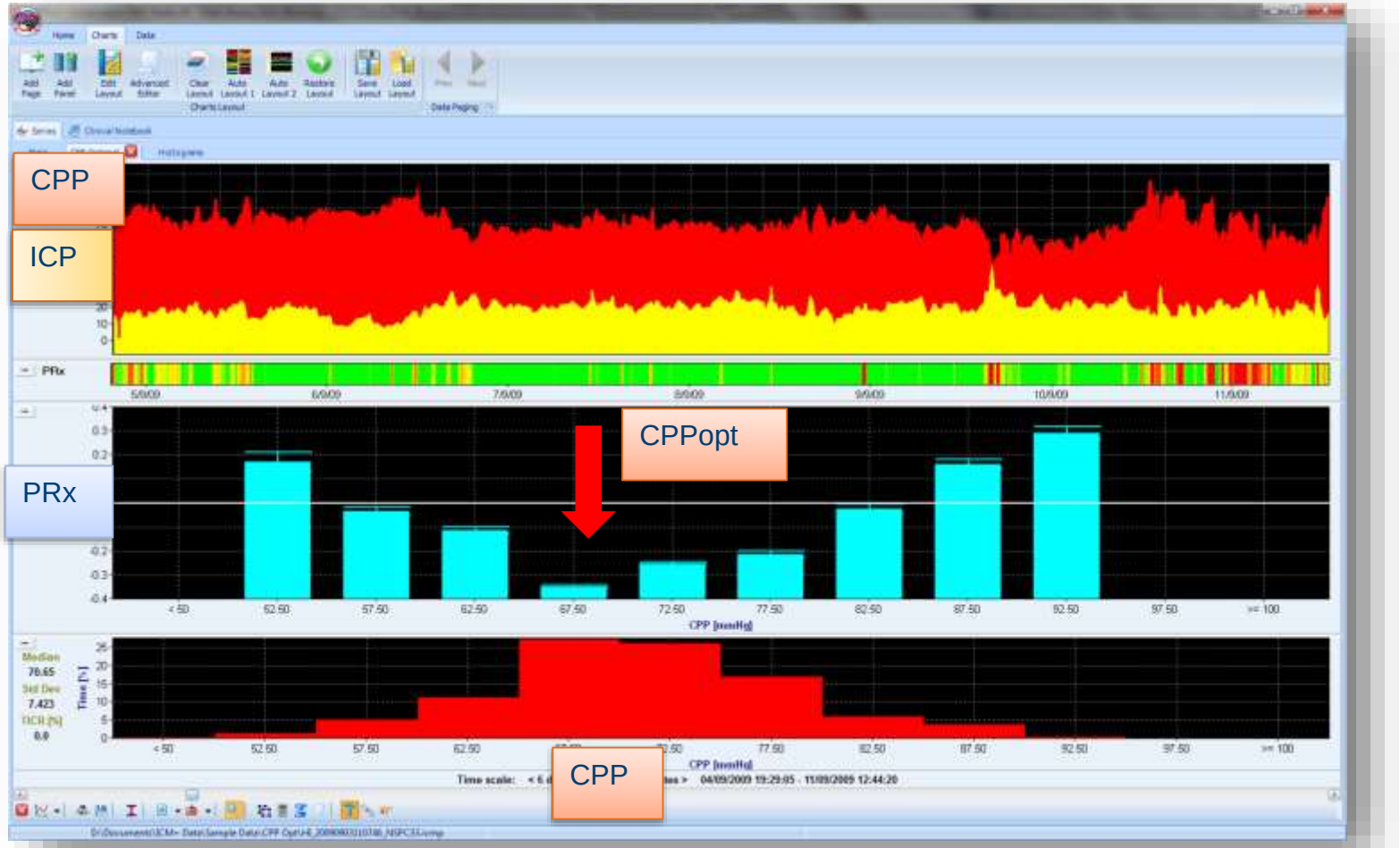
Too low CPP: ischaemia



Too high CPP: hyperaemia



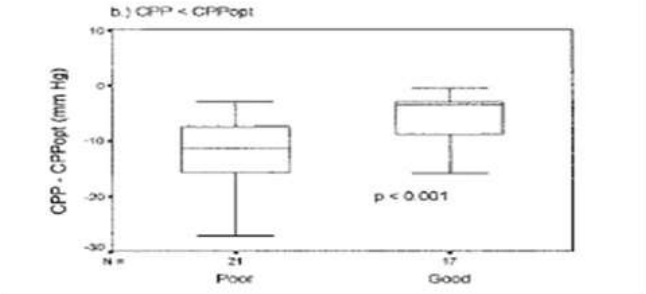
Individual CPP target based on PRx/CPP relationship



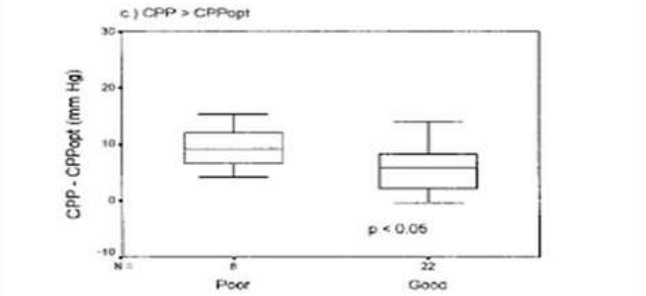
Risk of managing CPP above or below continuously updated CPP opt

N = 100

'Hypoperfusion' (CPP < optimal CPP)

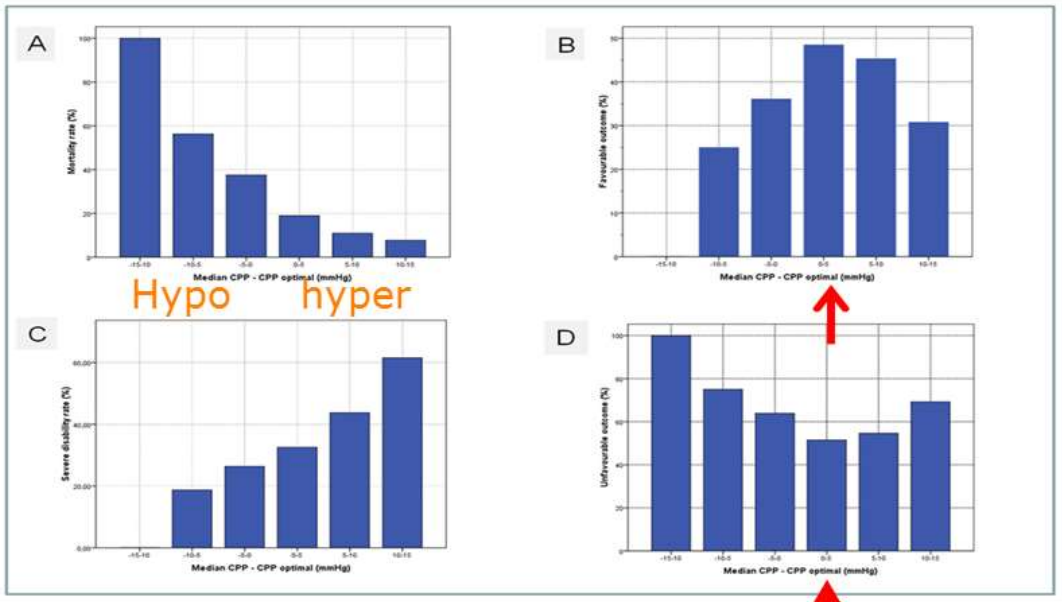


'Hyperperfusion' (CPP > optimal CPPopt)



Steiner et al. 2002

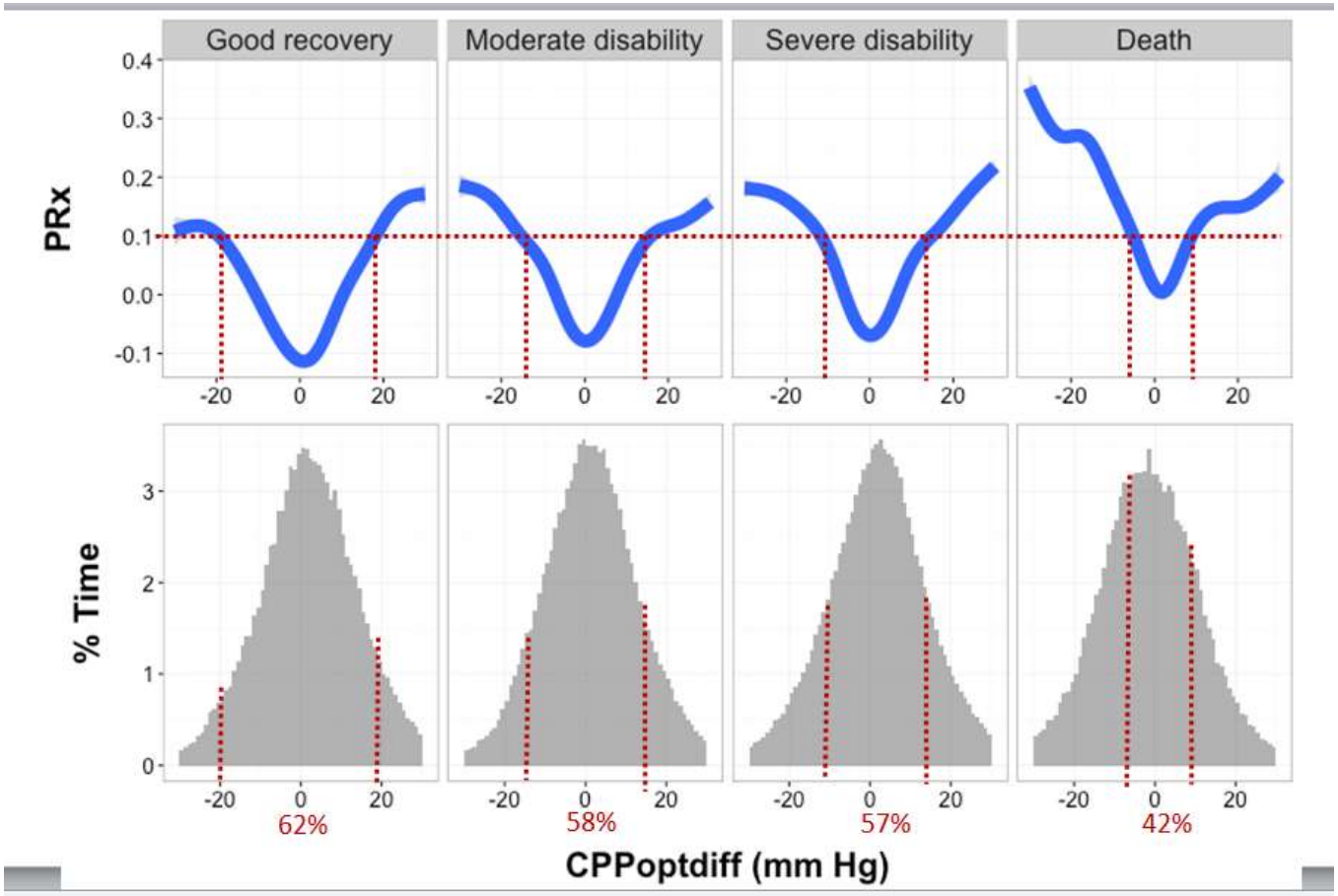
Aries et al. 2012



N = 327 pts

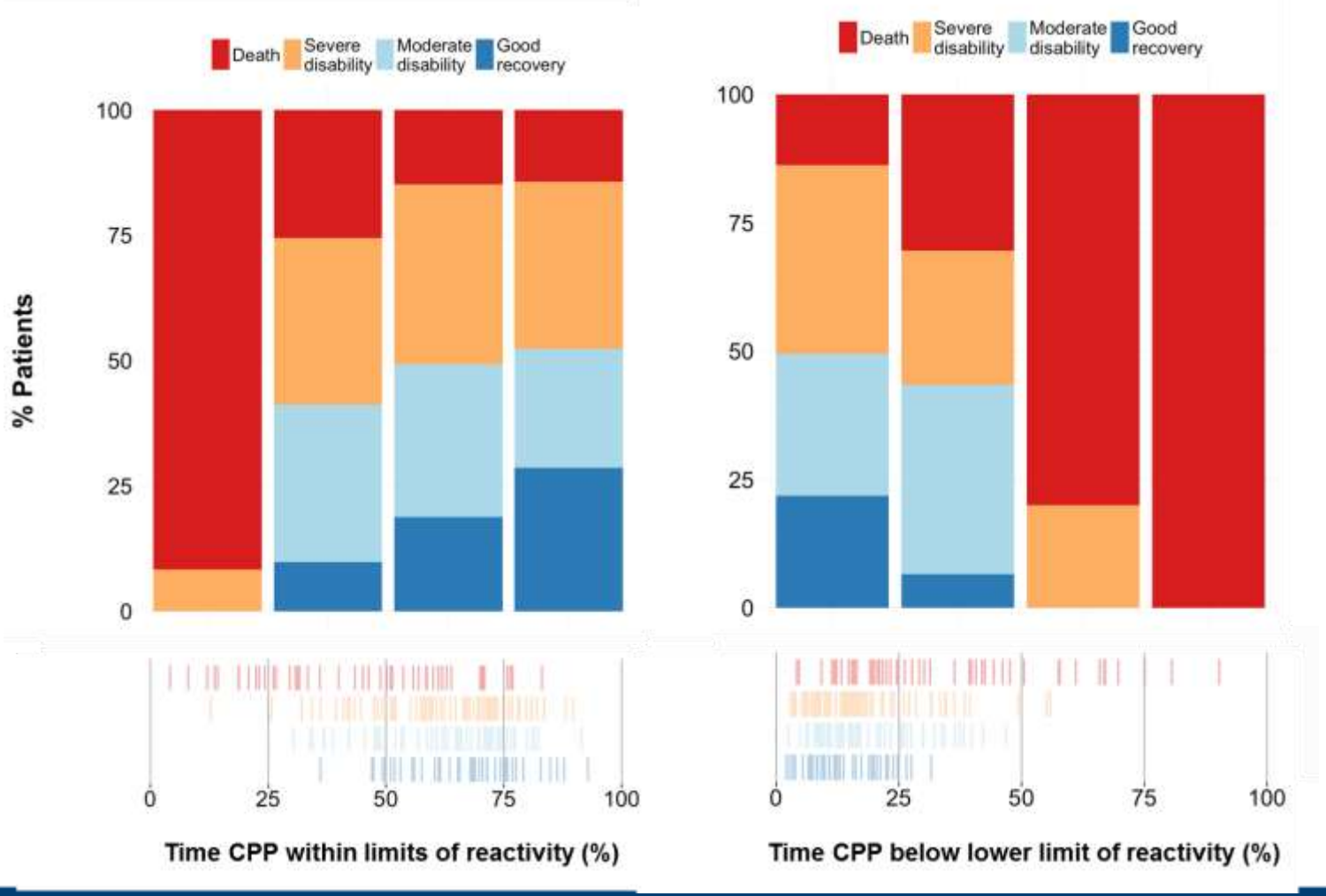
Target

Vascular reactivity range

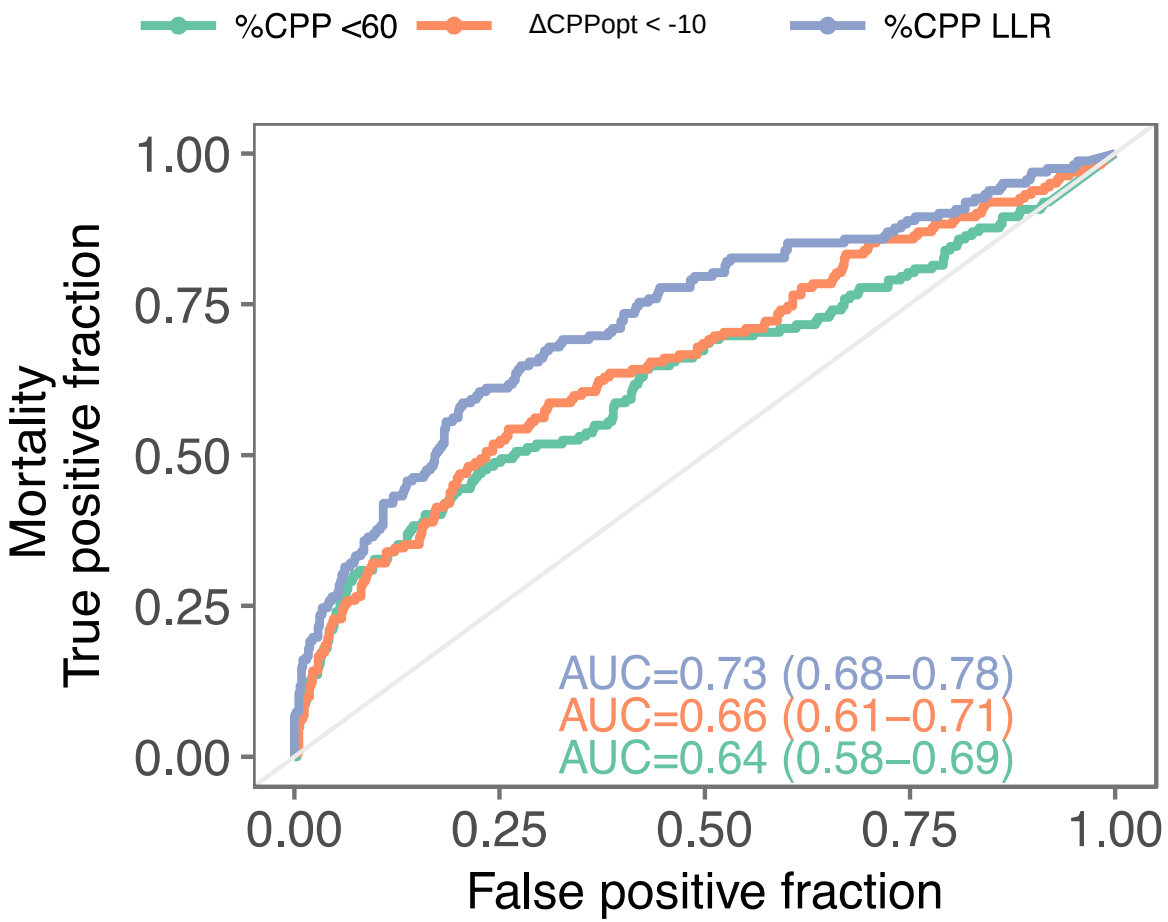


Thanks to Joseph Donnelly

Most recent data: 2016

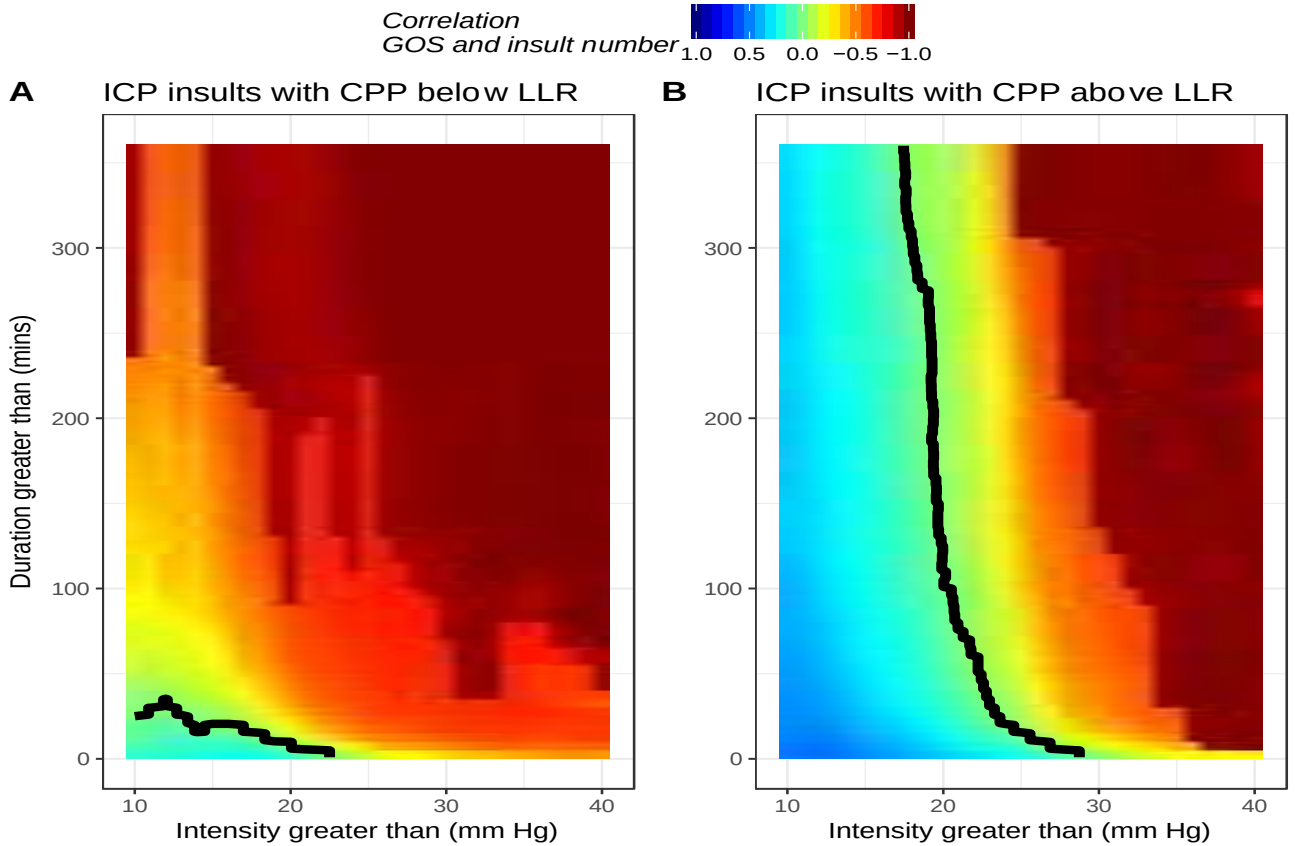


Limits of autoregulation and mortality



ICP insults stratified by the limits of reactivity

n=748



3 million episodes

21 million episodes

How can we use the information at the bedside?

- Time spent below estimated lower limit of reactivity associates with patient outcome
- Having a CPP above the estimated lower limit of reactivity is protective during episodes of raised ICP

CPP optimal in real time on NICU
How I do it with "ICM+" in Moscow

Neurosurgery Institute named after Burdenko, Moscow

Oshorov AV

Methods of ICP corrections

relatively short-term

- HOB
- EVD
- HV
- Sedation
- Hyperosmolar therapy

relatively long-term

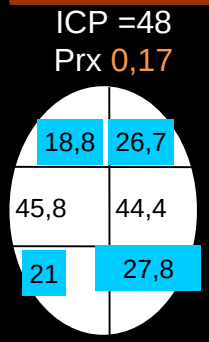
- removal of mass-effect
- optimization of CPP
- Hypothermia
- DC
- Barbiturates

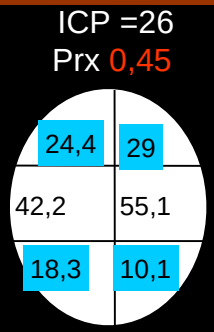
Optimization of CPP

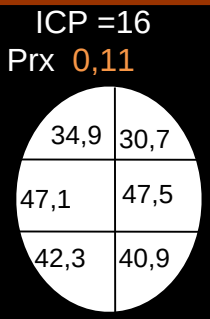
Primary through manipulation with ABP

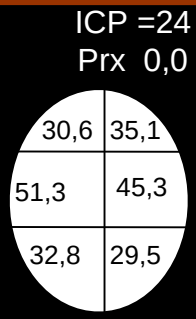
Secondary: through decreasing ICP

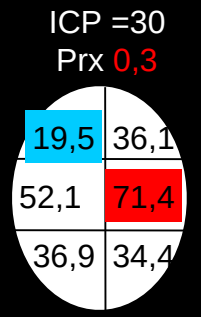
Data of rCBF, ICP and Prx in severe TBI pts (GCS < 9)

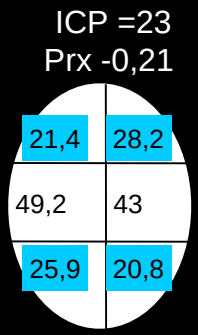


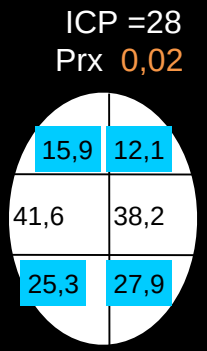


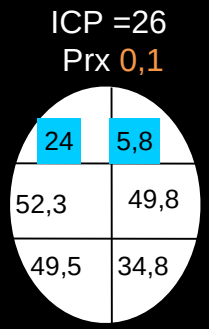


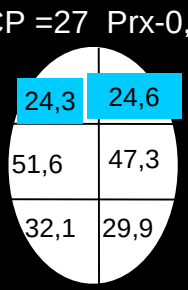


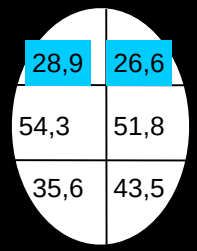


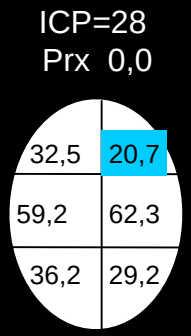


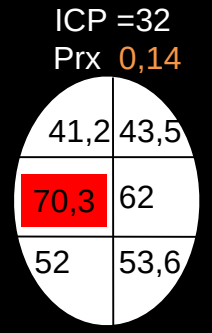


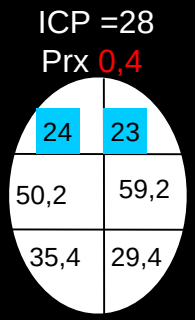


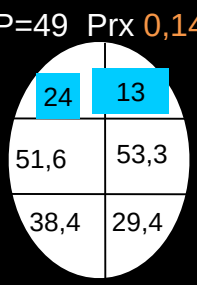


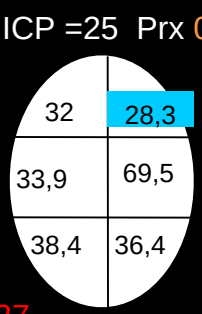


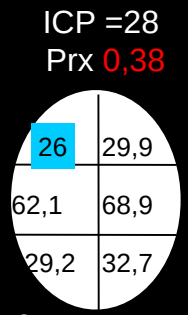


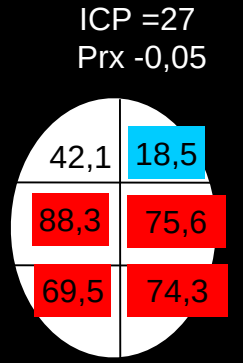


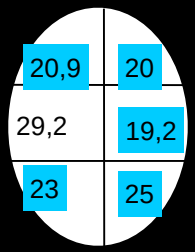


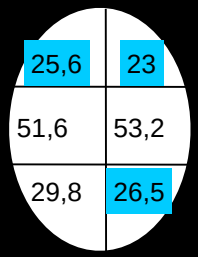


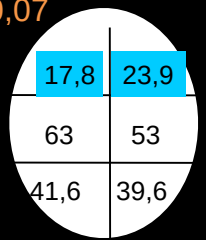


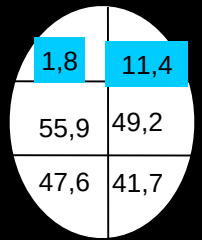


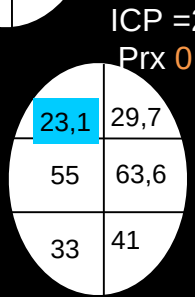






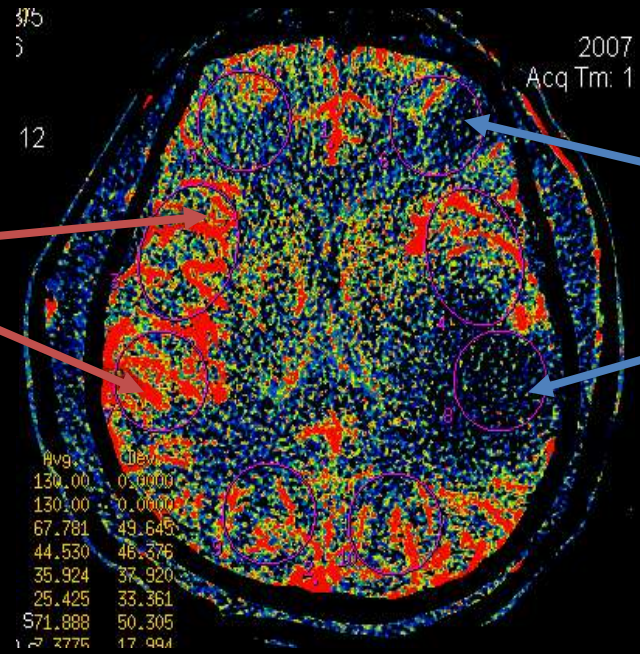






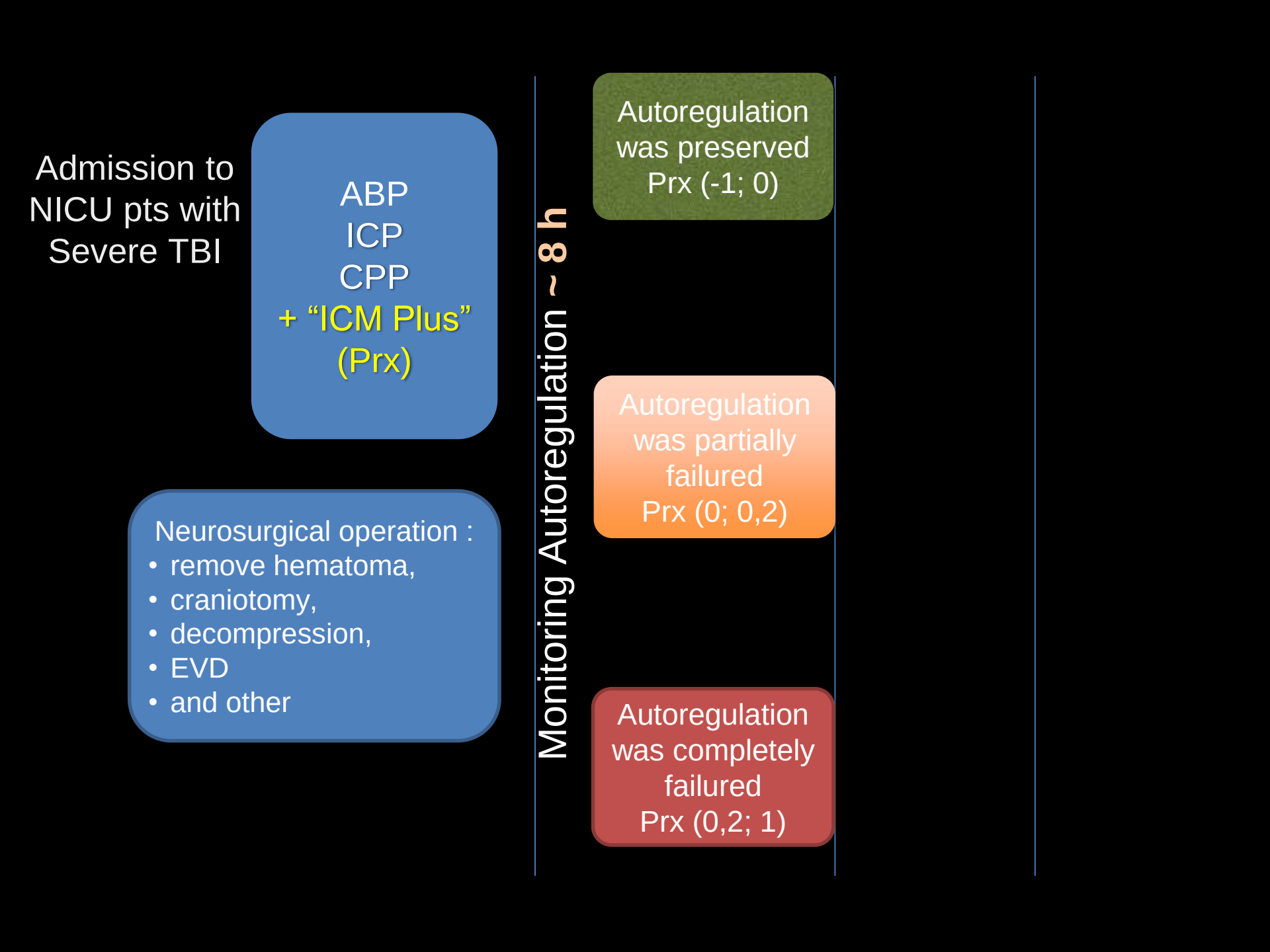
Data of rCBF in patient with focal injury in left hemispheric GCS – 7, GOS – 3 (severe disability)

Mean CBF in intact region: 46,0±10,0 ml100g/min

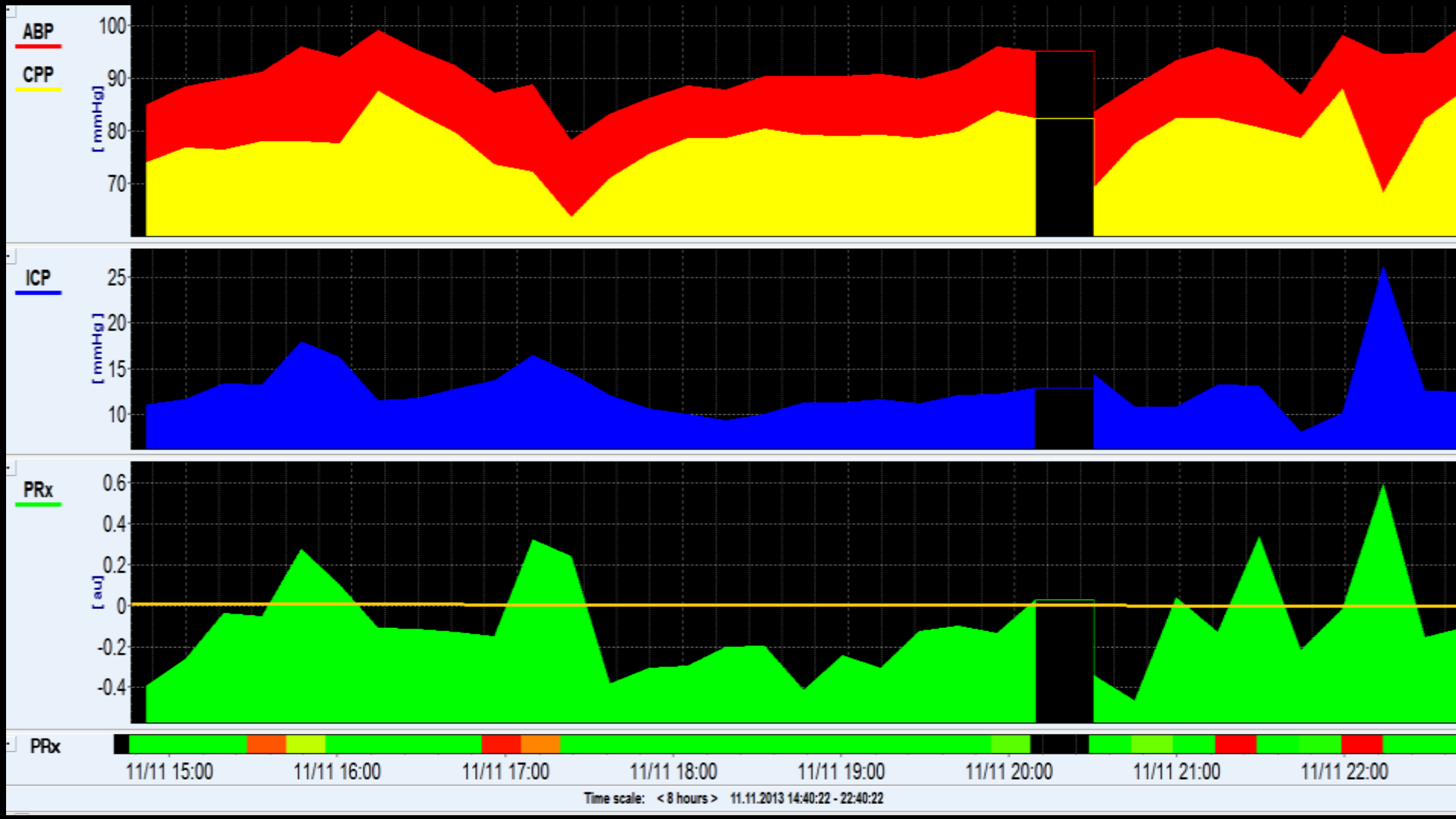


Mean CBF in region of contusions: 16,3±6,0 ml/100g/min (p <0,01)

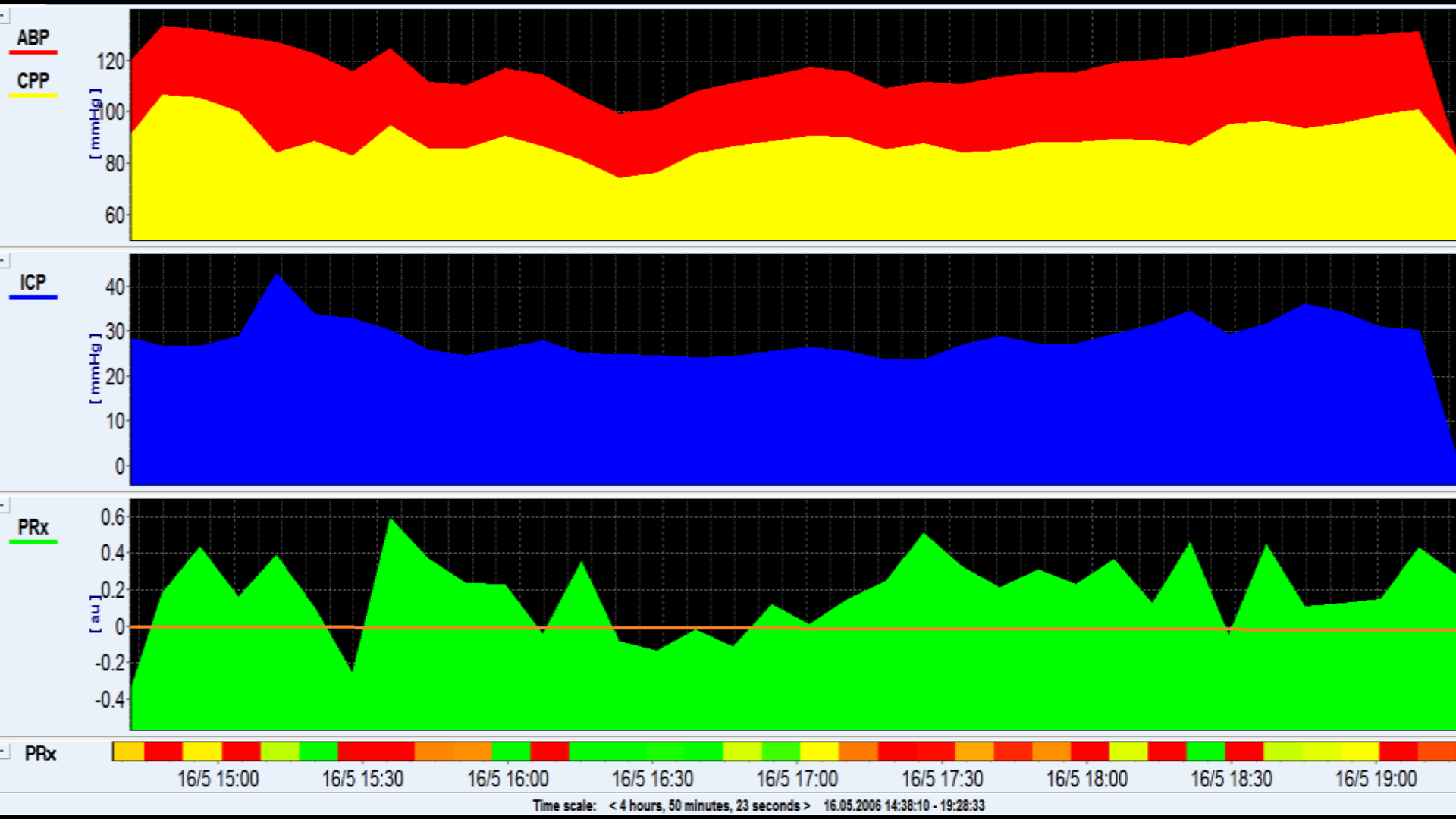
Potapov AA, Zaharova NE, Pronin IN et al. (2011)
Zh Vopr Neirohir Im N N Burdenko


Admission to NICU pts with Severe TBI
ABP
ICP
CPP
+ “ICM Plus”
(Prx)
Neurosurgical operation :
• remove hematoma,
• craniotomy,
• decompression,
• EVD
• and other
Monitoring Autoregulation ~ 8 h
Autoregulation was preserved
Prx (-1; 0)
Autoregulation was partially failured
Prx (0; 0,2)
Autoregulation was completely failured
Prx (0,2; 1)

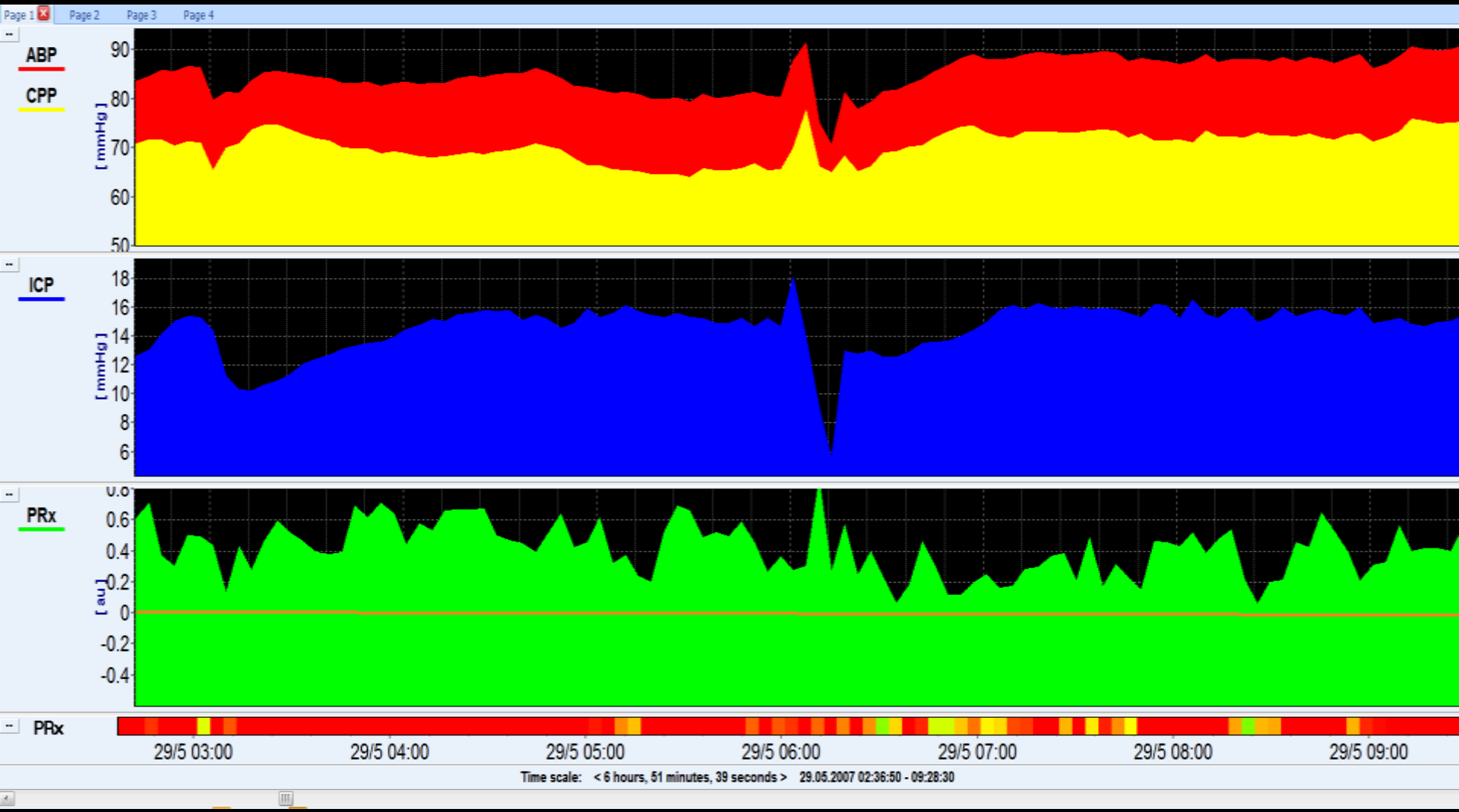
1) Autoregulation was preserved Prx (-1; 0)



2) Autoregulation was partially failure Prx (0; 0,2)



3) Autoregulation was completely failure Prx (0,2; 1)

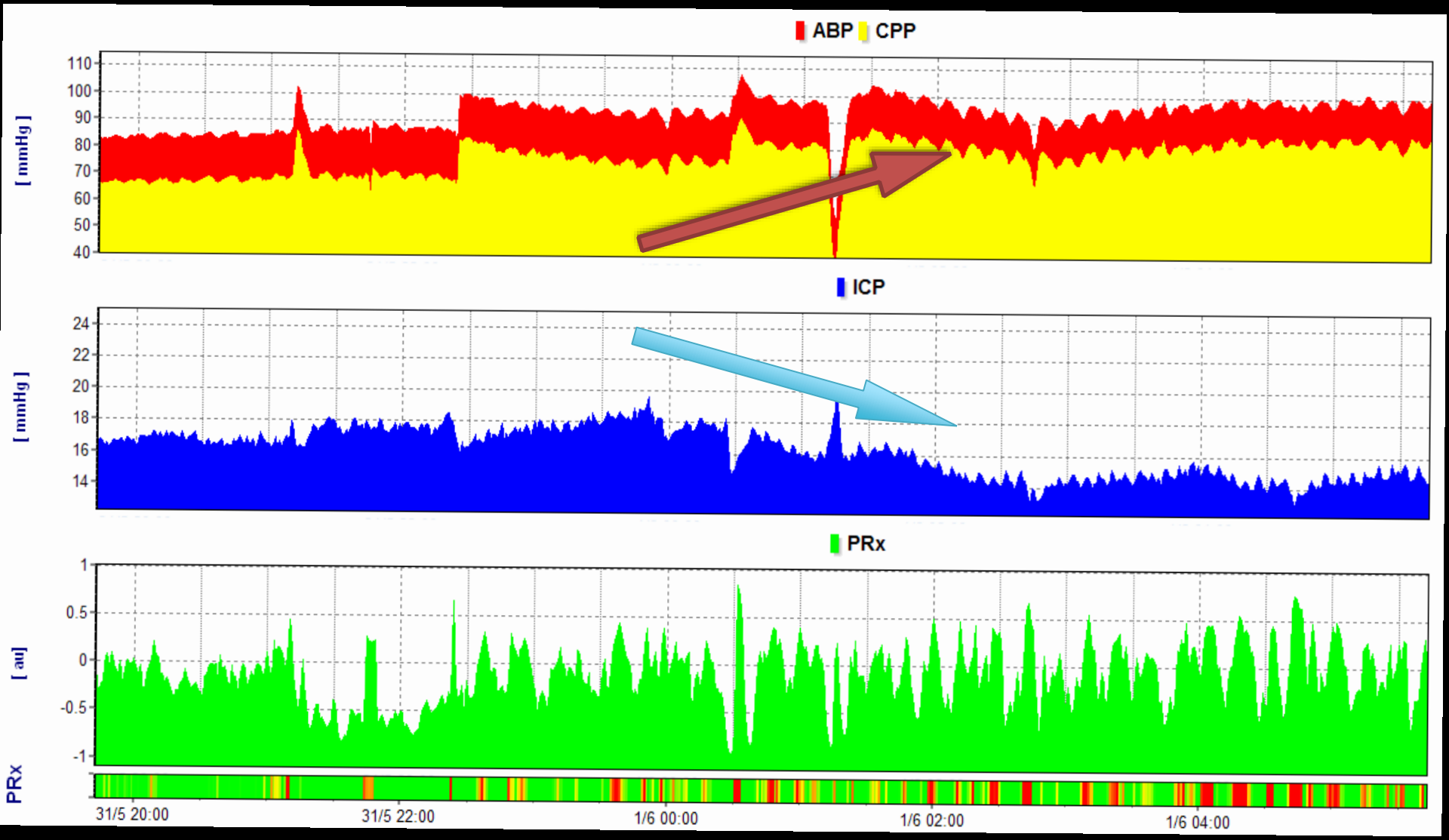


ABP
ICP
CPP
+ “ICM Plus”
(Prx)

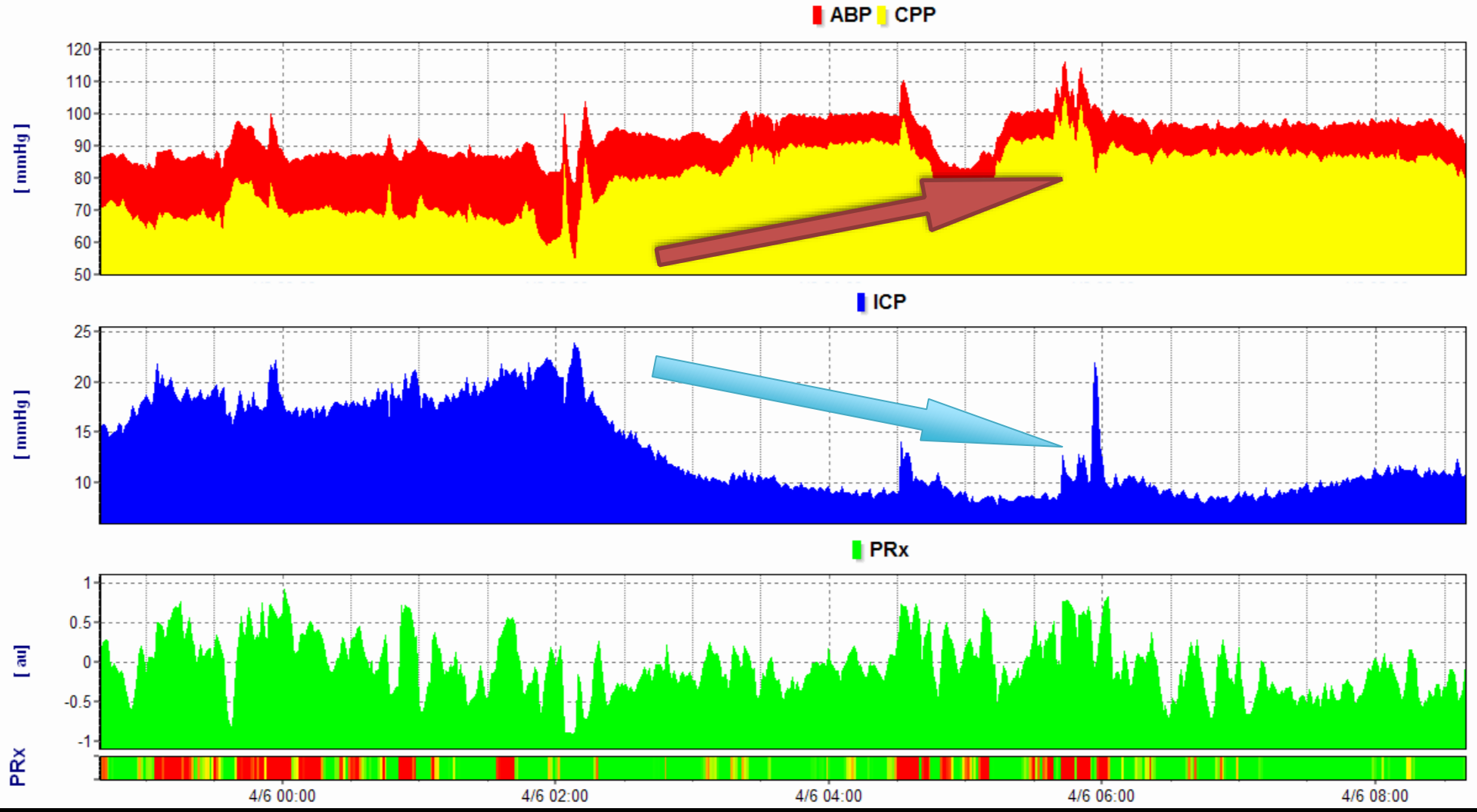
Neurosurgical operation :
remove hematoma,
craniotomy,
decompression,
EVD and other

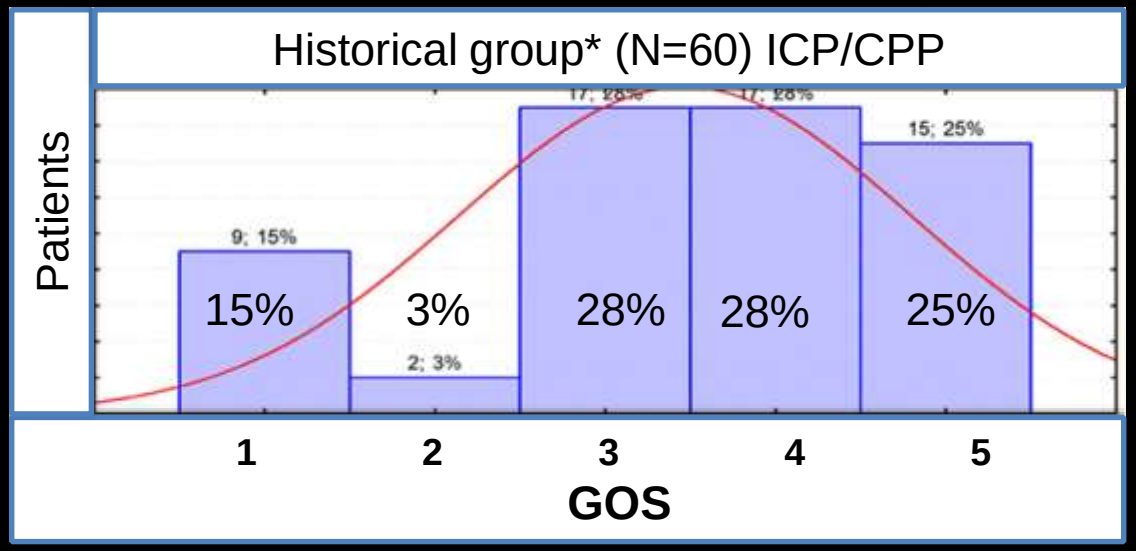
Autoregulation was preserved Prx (-1; 0)	ICP < 20	CPP 50-70
	ICP > 20	CPP 50-90
Autoregulation was partially failured Prx (0; 0,2)	ICP < 20	CPP 50-70
	ICP > 20	CPP 70-90
Autoregulation was completely failured Prx (0,2; 1)	ICP < 20	CPP 50-70
	ICP > 20	CPP 50-70

Optimization CPP in patient with preserved autoregulation from 65 to 75-80 mmHg



Optimization CPP in patient with partially failured autoregulation from 70 to 90 mmHg

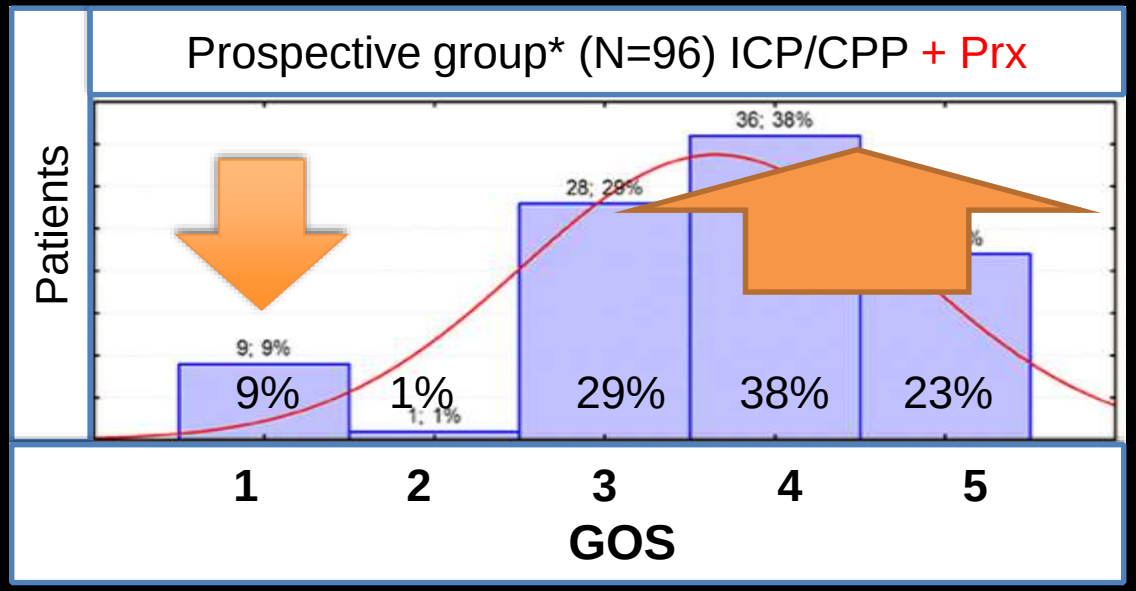




Tendency (but p>0,05)

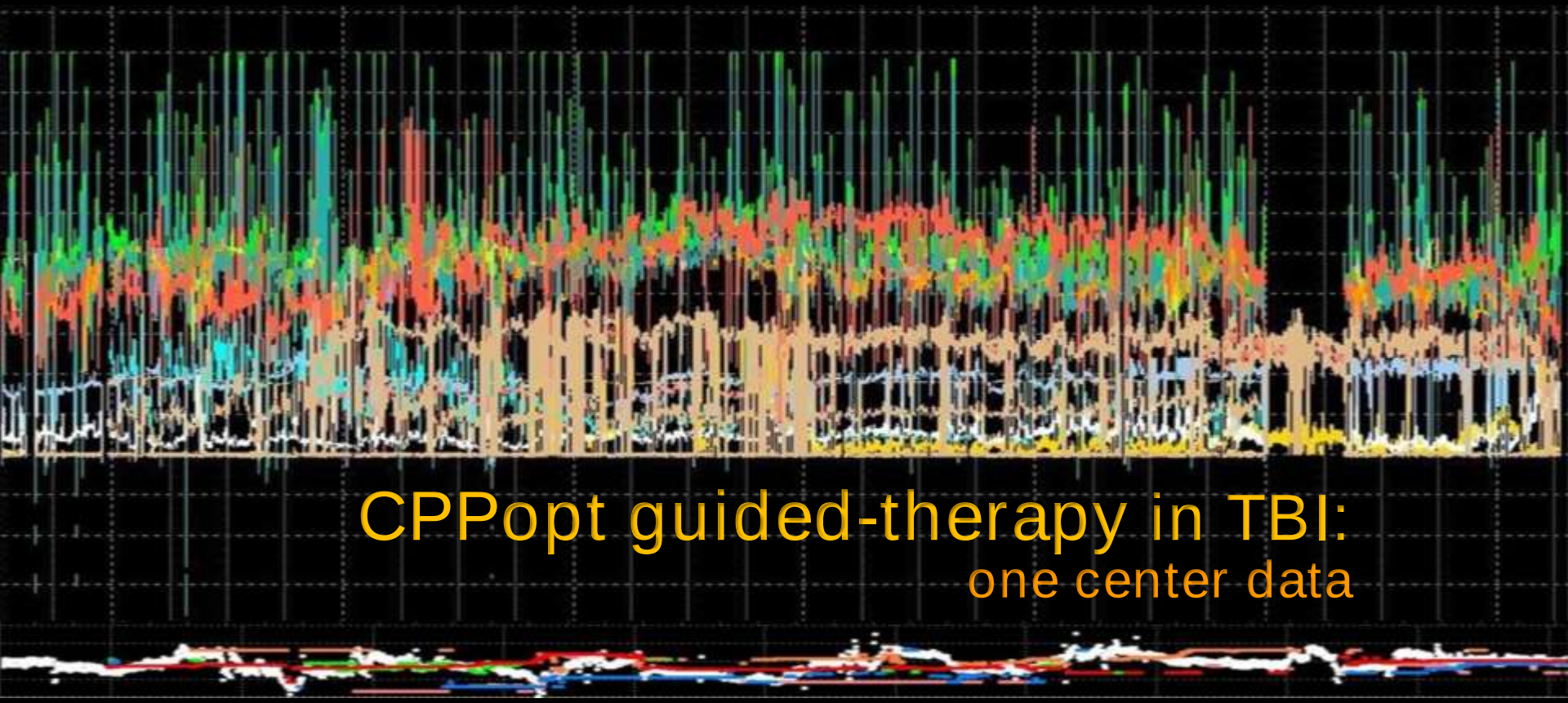
Decreasing death from 15% to 9%

Increasing Favorable outcome from 53% to 61%



In conclusion:
we need more data to define a best strategy

* - pts with decompression were excluded from analysis



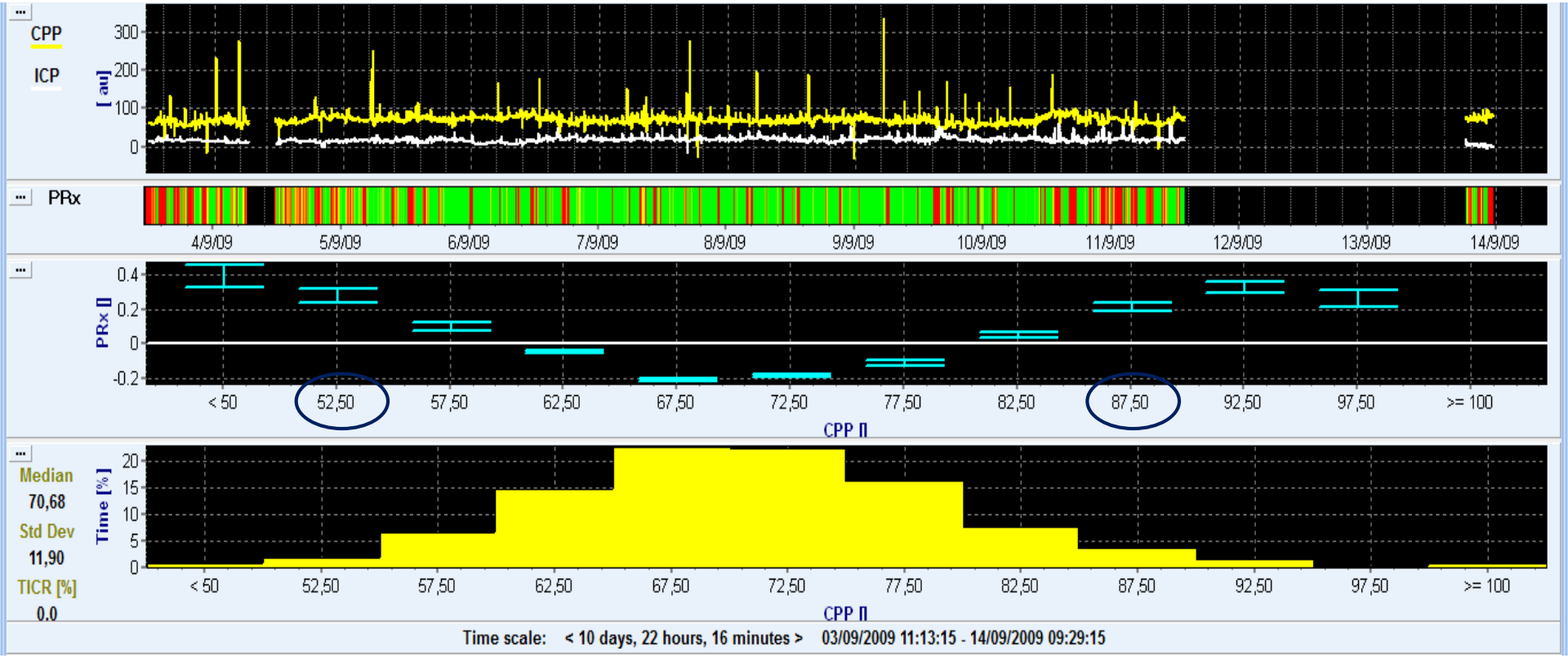
CPPopt guided-therapy in TBI:
one center data

Celeste Dias

CELESTE.DIAS@MED.UP.PT

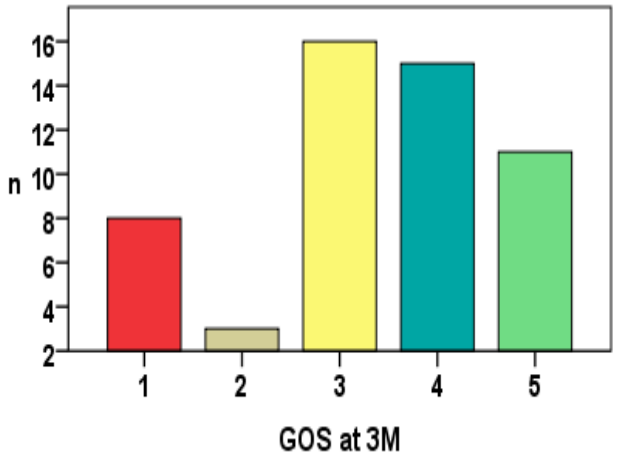
CPPopt - decision steps

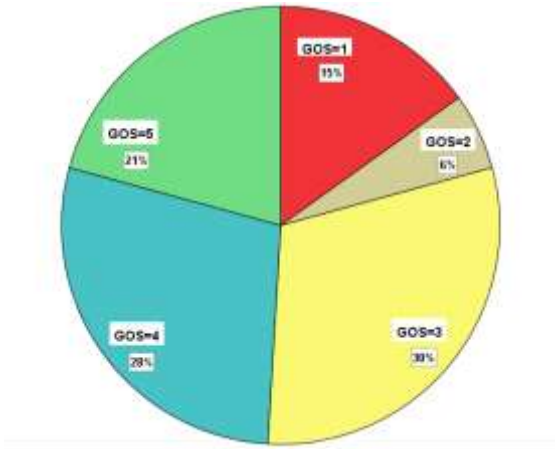
- 30º head up elevation and ABP transducer at heart level.
- CPPopt value and curve, updated every minute, in a 4 hr calculation window.
- at least 75% of time good recordings of CPP and ICP values available in the 4hr calculation window
- average PRx values had to be < 0.25 the past 4hrs
- select the CPP value with most negative PRx value covered by the curve.
- U-shaped, ascending and descending curves were accepted in case the overall PRx<0.25.



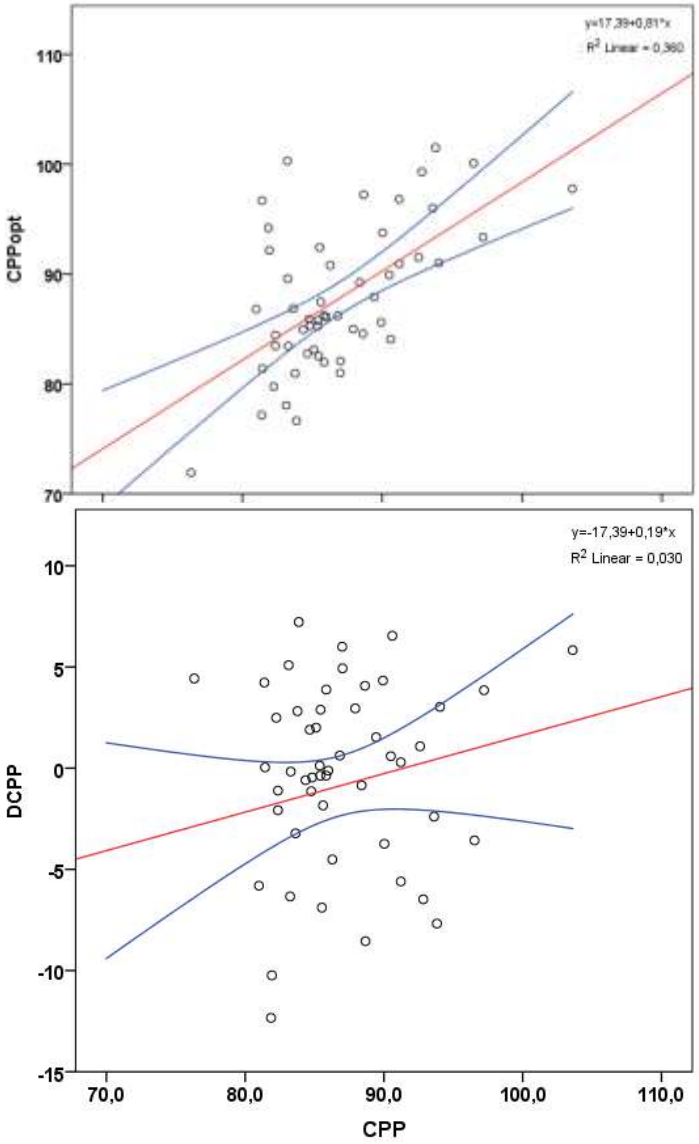
CPPopt – demographic data

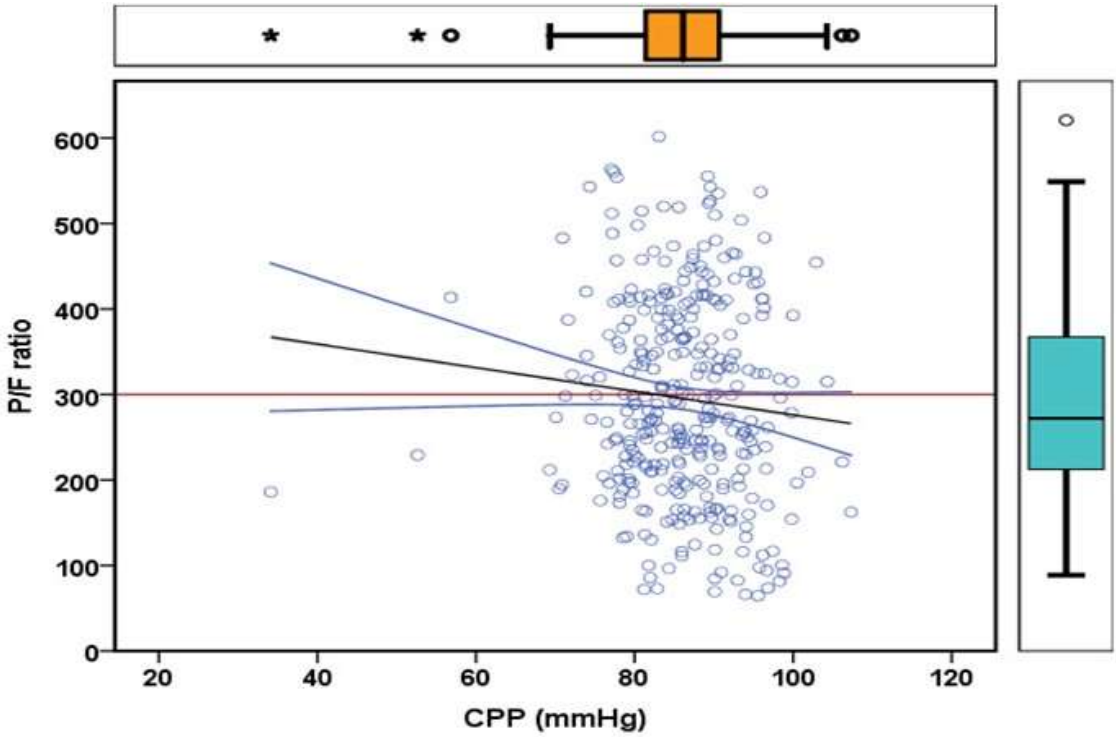
From Jul 2011 to Jan 2016	n; % median (min-max)
n	53
Age (years)	44 (20-88)
Gender (n; %male)	47; 89% M
in local GCS	7 (3-13)
SAPSII	43 (22-66)
SAPSII mortality (%)	31 (5-78)
NCCU mortality rate	7; 13%
Hospital mortality rate	8; 15%
LOS at NCCU (days)	20 (5-65)
LOS at Hospital (days)	37 (8-138)
GOS at 3M	3 (1-5)
Decompressive craniectomy (n; %)	15; 28%





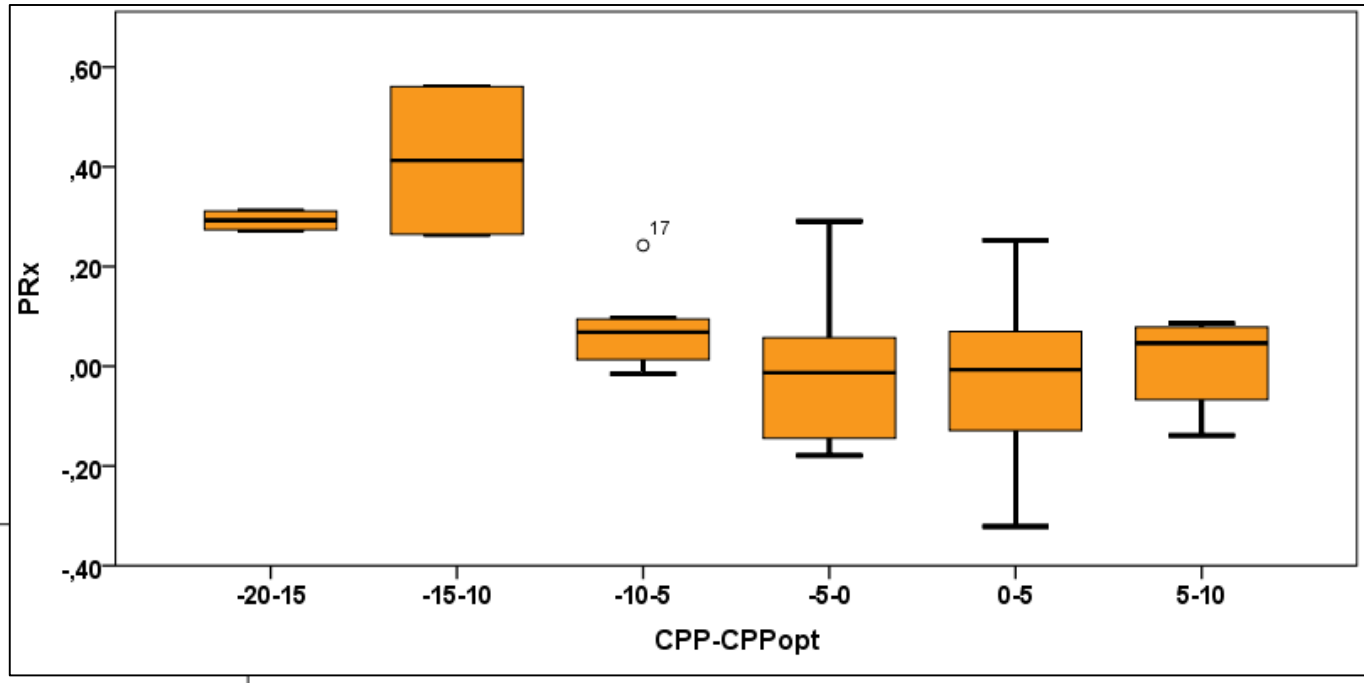
CPPopt vs real CPP

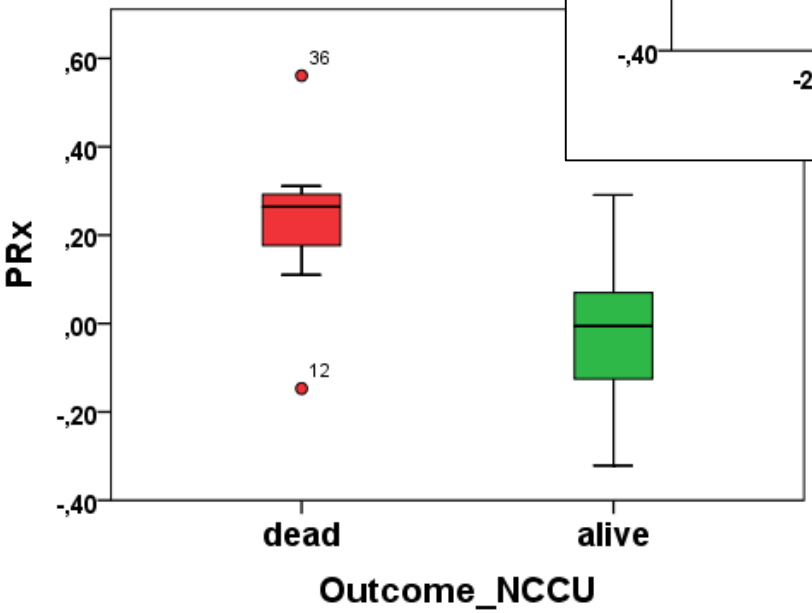




30º head up elevation and ABP transducer at heart level.

PRx, delta-CPP and mortality at NCCU



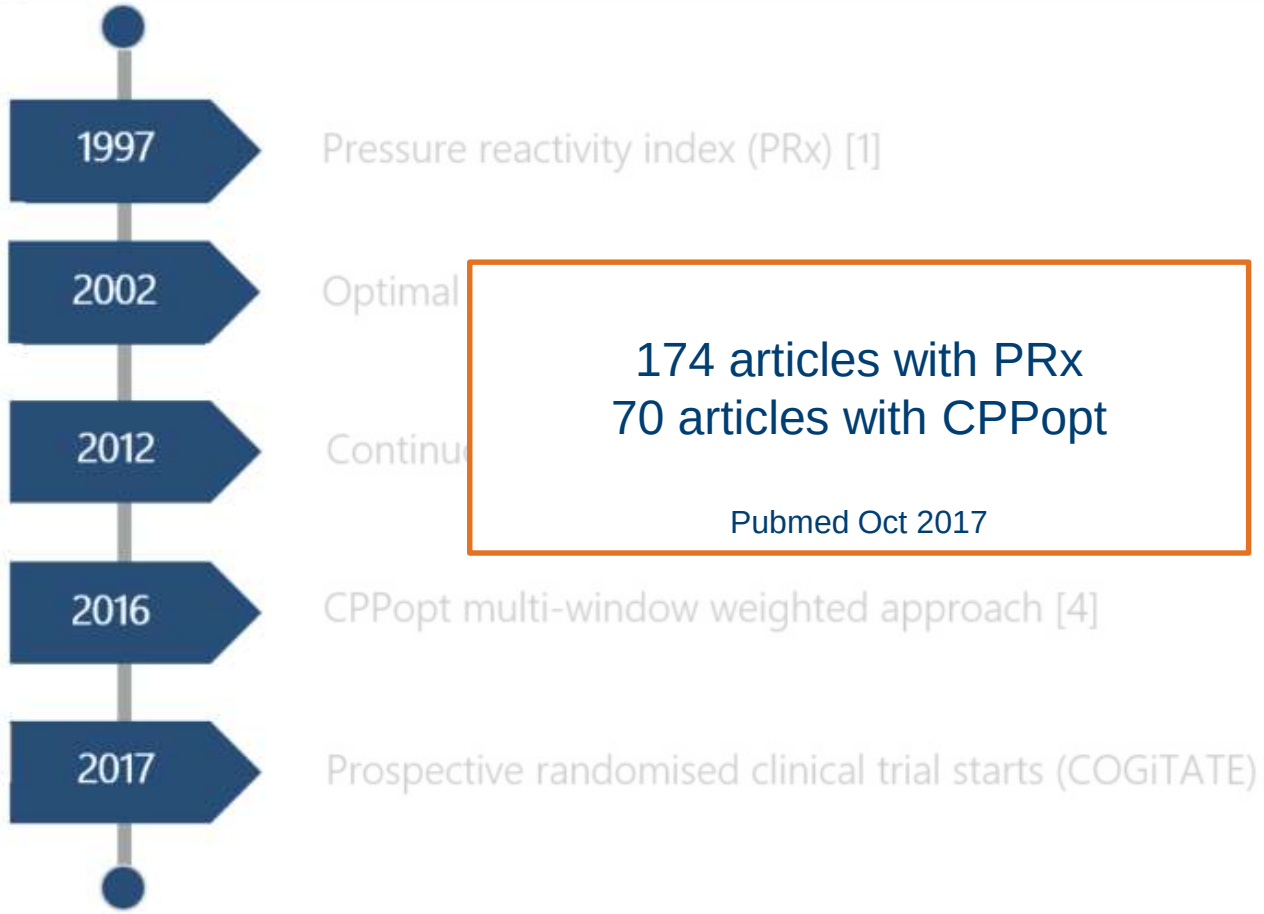


Conclusions

- Online monitoring data (CPP, ICP) is suitable for online assessment of autoregulation (PRx)
- CPPopt guided-therapy needs to applied with a strict protocol
- CPPopt algorithm may be applied by trained nurses
- Results show that patients with impaired autoregulation have worse outcomes
- CPP-CPPopt around zero is related to best outcomes

Thanks to Dr Celeste Dias, Porto

Pressure reactivity index and CPPopt work so far



174 articles with PRx
70 articles with CPPopt

Pubmed Oct 2017

Unanswered fundamental questions

- How does CPPopt behave prospectively?
- Is CPP management according to CPPopt safe ?
- How do clinicians interpret and act on CPPopt recommendations ?
- What is the best end point for the subsequent RCT ?

Further questions to address

- Should CPPopt be targeted outright or be a guide given other parameters (and if so, how)?
- Is CPPopt the most appropriate target or some other associated parameter (such as the lower limit of autoregulation)?
- Should we target CPPopt even if autoregulation at CPPopt is still absent?
- Is CPPopt guided therapy beneficial in all TBI patients?
- Is CPPopt guided therapy equally beneficial in contusional, pericontusional and 'normal' TBI brain

Upcoming CPP feasibility and safety study

CPPOpt Guided Therapy: Assessment of Target Effectiveness

A randomized trial assessing the safety and effect of "optimal" cerebral perfusion pressure directed treatment.

The study protocol

CPP treatment arm

- CPP: 60-70 mmHg
- No CA information is displayed

CPPopt treatment arm

- Target the CPPopt
- CA information is provided
- CPP > 50 and < 100

In common

- ICP<22 protocol
- Review every 4 hours (3x review by research team)
- Clinicians might decide/choose different CPP targets
- Simple CPP treatment protocol

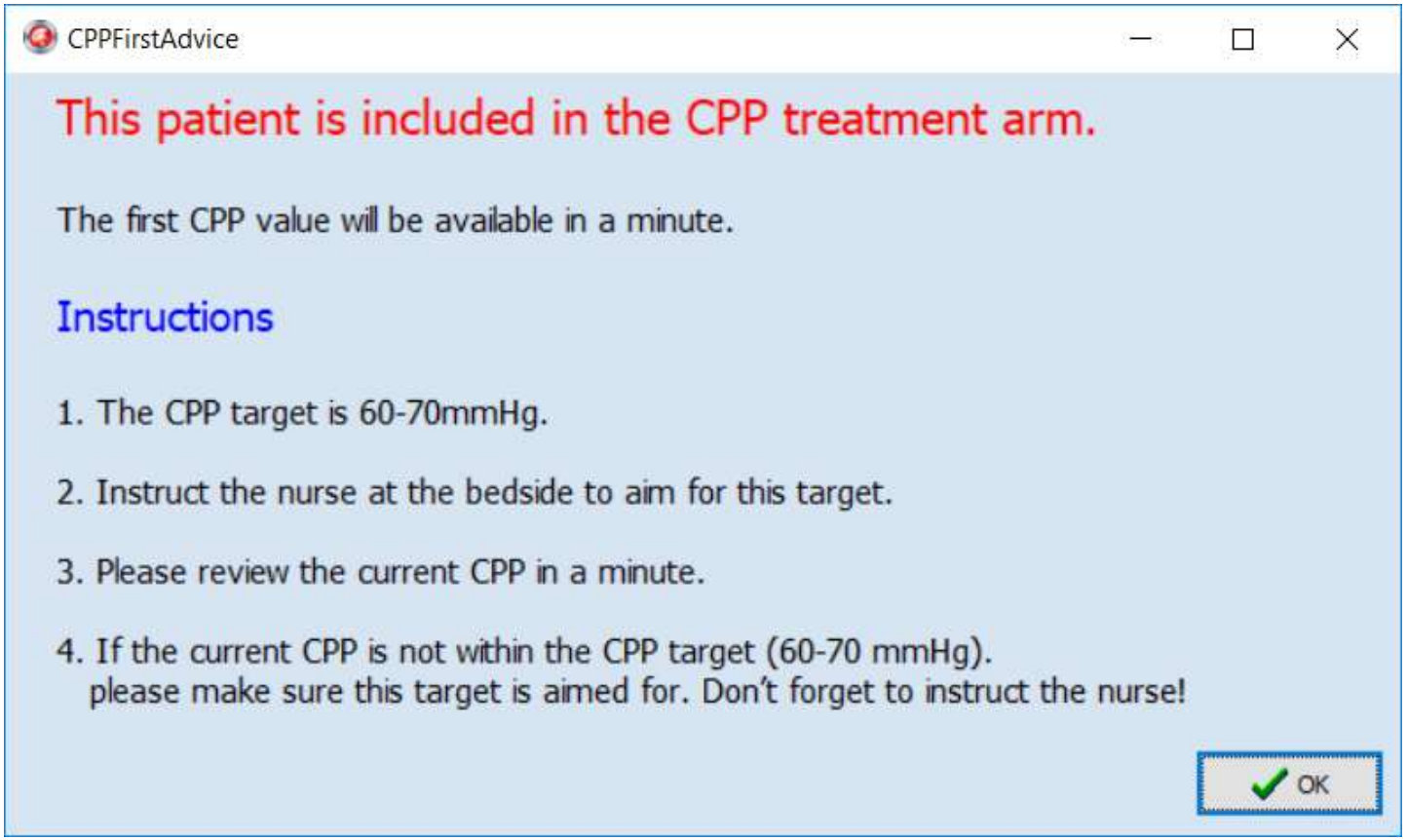
N = 30

N = 30

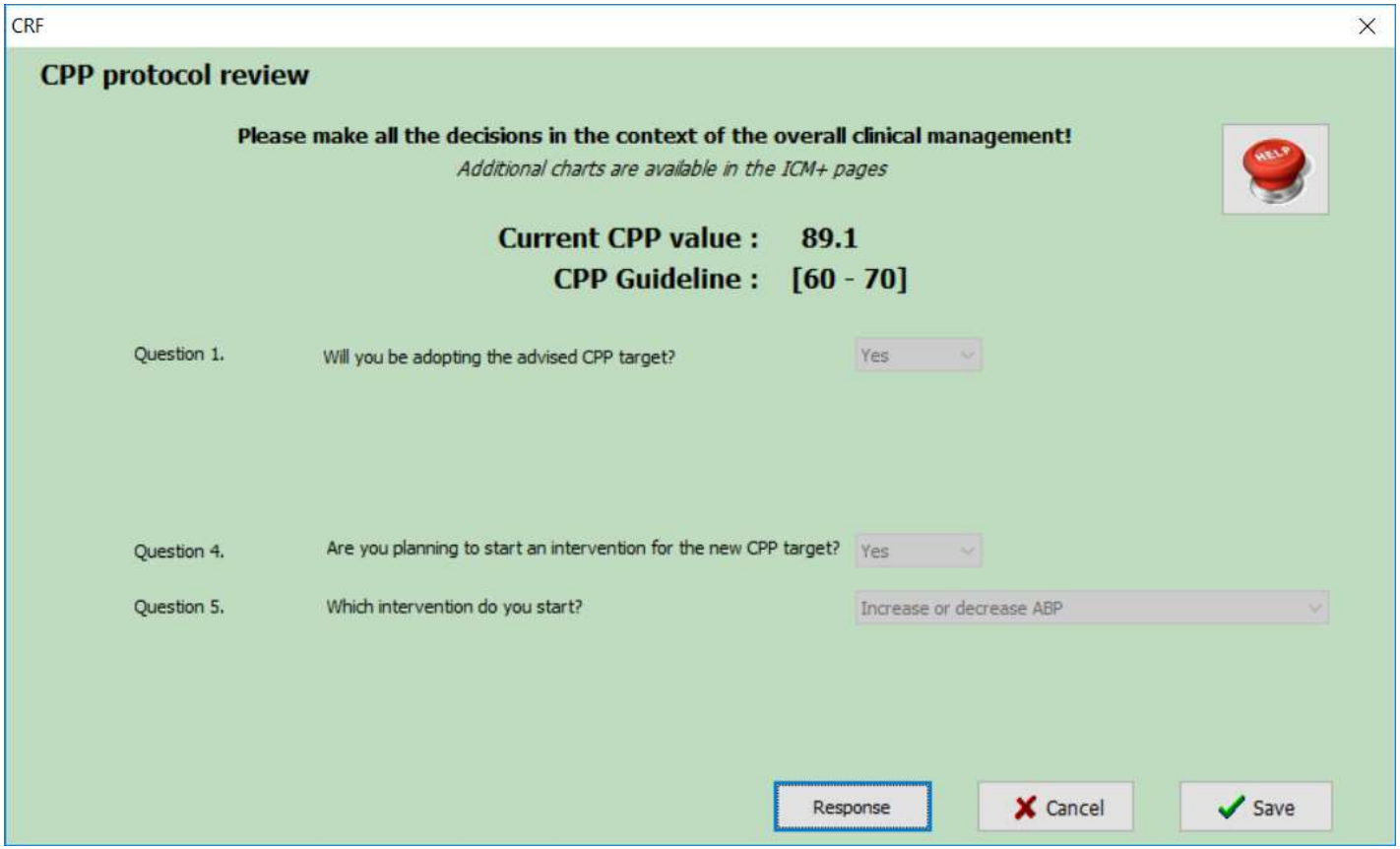
Covering 5 days after admission

COGiTATE tool - Randomisation

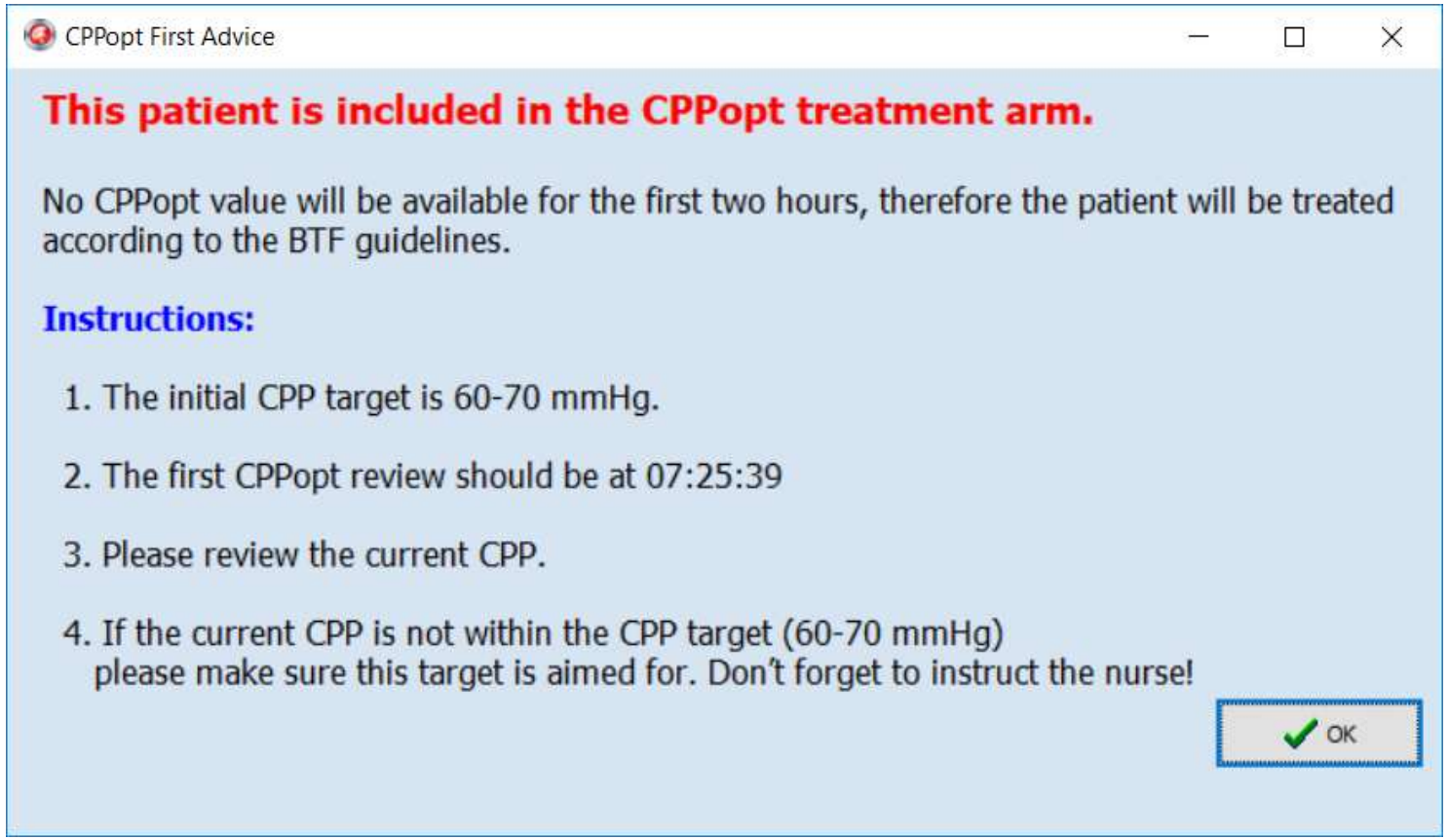
COGiTATE tool – CPP treatment arm



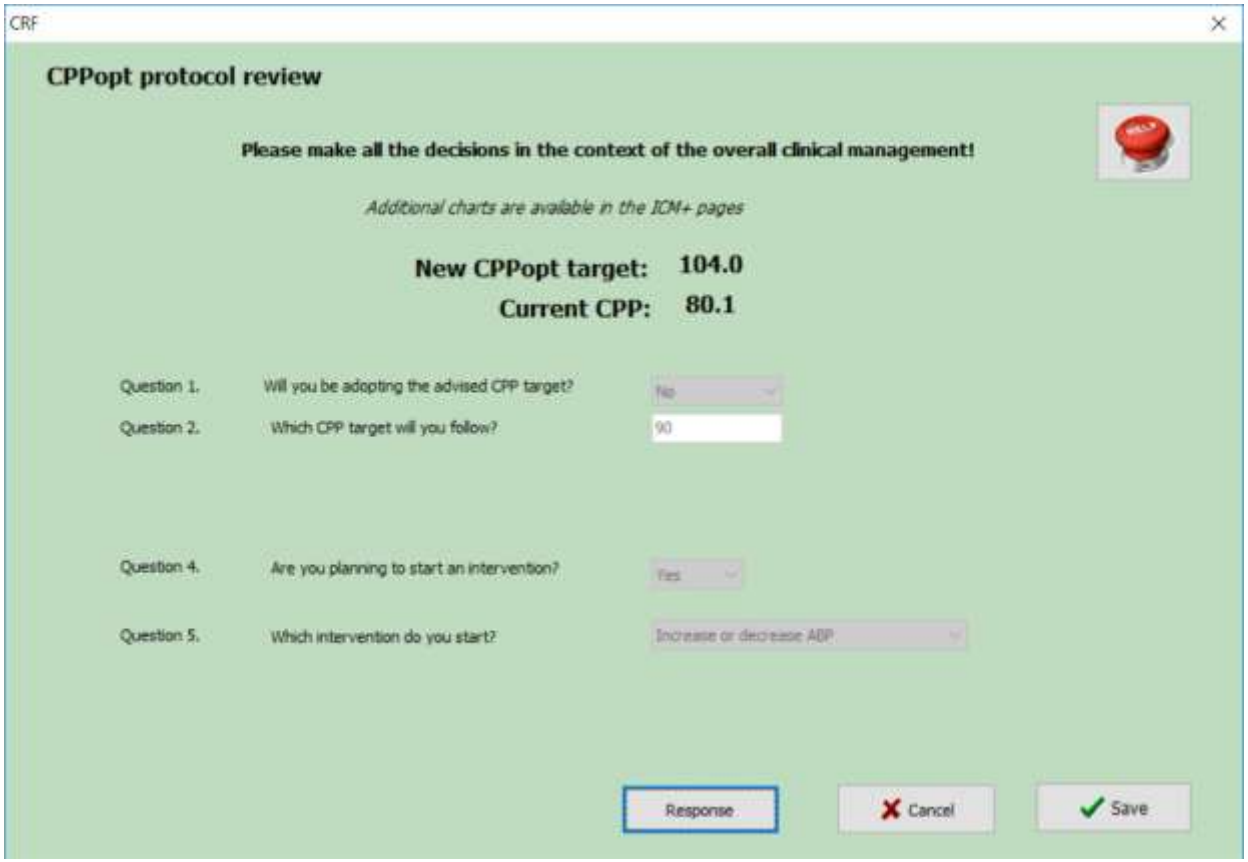
COGiTATE tool – 4 hourly review



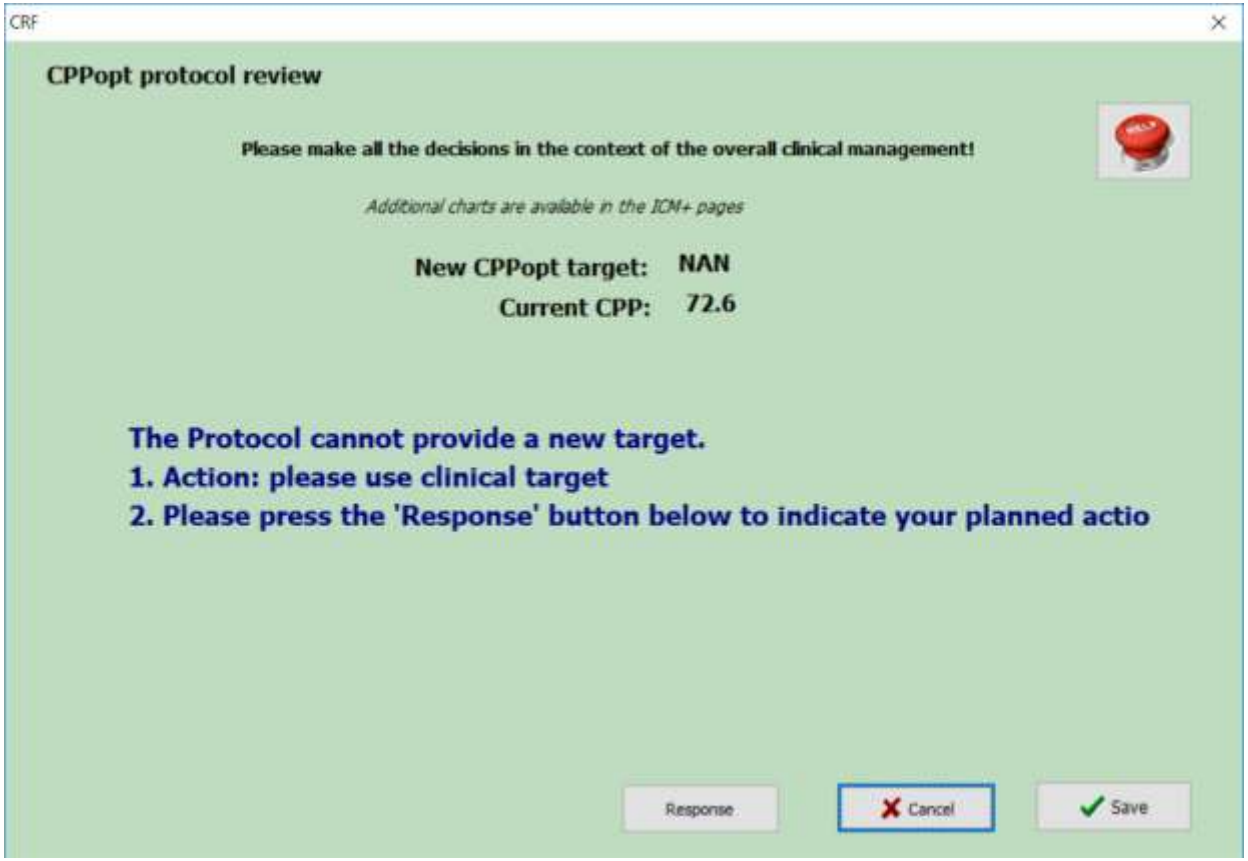
COGiTATE tool – CPP Opt treatment arm



COGiTATE tool – 4 hourly review



COGiTATE tool – review with no CPPopt target



Treatment (local) protocol

CPP target	ICP	Action	Interventions
↑	> 20 mmHg	Decrease ICP	ICH treatment ↑
↑	< 20 mmHg	Increase ABP	Fluids Vasopressor ↑ (as per clinician)
↓	> 20 mmHg	Decrease ABP	Vasopressor ↓
↓	< 20 mmHg	Decrease ABP	Vasopressor ↓

Study main endpoints

Feasib

- Differ
  - Me
  - Me

Safety

- A cha
  repres
  mana
  harmf

sic ICP

Therapy Intensity Level Scale*

Item	Details	Specifics	Score	Max	Patient
Positioning	Head elevation for ICP control		1	1	.....
	Nursed flat (180°) for CPP management		1		
Sedation and neuromuscular blockade	Low dose sedation (as required for mechanical ventilation)		1	8	.....
	Higher dose sedation for ICP control (but not aiming for burst suppression)		2		
	High dose propofol or barbiturates for ICP control (metabolic suppression)		5		
	Neuromuscular blockade (paralysis)		3		
CSF drainage	CSF drainage–low volume	< 120 mL/day (<5 mL/h)	2	3	.....
	CSF drainage–high volume	> 120 mL/day (>5 mL/h)	3		
CPP management	Fluid loading for maintenance of cerebral perfusion		1	2	.....
	Vasopressor therapy required for management of cerebral perfusion		1		
Ventilatory management	Mild hypocapnia for ICP control, based on arterial CO2 in mmHg,	>35, <40	1	4	.....
	Moderate hypocapnia for ICP control,	>30, <35	2		
	Intensive hypocapnia for ICP control,	<30	4		
Hyperosmolar Therapy	Mannitol	< 2g/kg/24h	2	6	.....
	Mannitol	> 2g/kg/24h	3		
	Hypertonic saline	0.3g/kg/24h	2		
	Hypertonic saline	>0.3g/kg/24h	3		
Temperature control	Treatment of fever	(T>38°C or spontaneous T<34.5°C)	1	5	.....
	Cooling for ICP control,	(>35°C)	2		
	Hypothermia	(<35°C)	5		
Surgery for intracranial hypertension	Intracranial operation for progressive mass lesion, NOT scheduled on admission		4	9	.....
	Decompressive craniectomy		5		
Maximum (daily) total possible score				38	.....

*Zuercher P, Groen JL, Aries MJ, Steyerberg EW, Maas AI, Ercole A, Menon DK. Reliability and Validity of the Therapy Intensity Level Scale: Analysis of Clinimetric Properties of a Novel Approach to Assess Management of Intracranial Pressure in Traumatic Brain Injury. J Neurotrauma. 2016;33:1768-1774.

Secondary aims/endpoints

Between group differences in

- ICP variability
- Frequency and average duration of spikes > 20mmHg
- Mean daily RAP (cerebral compliance index).
- Mean daily vasopressor dose.
- Incidence of troponin rise stratified by day.
- Mean daily fluid balance.
- Mean daily P/F ratio (pulmonary complications).
- Survival and GOSE at 3 months.

Physiological effectiveness / effect of targeting CPPop

Differences in

- Mean daily MAP.
- Mean daily PRx at CPPopt.
- Mean daily L/P ratio, PbO2 (and PbO2/PaO2 ratio), brain tissue glucose

COGiTATE website