

## The authors reply:

### Citation for published version (APA):

Donnelly, J., Smielewski, P., Menon, D. K., & Aries, M. J. H. (2018). The authors reply: Individualizing Cerebral Perfusion Pressure Targets. *Critical Care Medicine*, 46(2), E176-E176. <https://doi.org/10.1097/CCM.0000000000002857>

### Document status and date:

Published: 01/02/2018

### DOI:

[10.1097/CCM.0000000000002857](https://doi.org/10.1097/CCM.0000000000002857)

### Document Version:

Publisher's PDF, also known as Version of record

### Document license:

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## The authors reply:

We appreciate the comments of Bernard et al (1) about our recent article (2), published in *Critical Care Medicine*, on individualizing cerebral perfusion pressure (CPP) targets. The authors highlight several pertinent issues that deserve explication as they relate to this study (2) and to neurocritical care in general.

As correctly pointed out by the authors, arterial blood pressure (ABP) zeroing has implications with regard to the guideline thresholds. The vast majority of data reported in our study (2) is from the period where ABP was zeroed at right atrium level (1996–2015); however, from March of 2015, the zero level was adjusted to Monro level (3). Thus, the reported absolute CPP values for periods before 2015 will be somewhat higher than the CPP values thereafter; however, it should be noted that the difference between actual CPP and a position on the CPP-pressure reactivity index (PRx) curve (CPPoptimal [CPPopt], CPP lower limit of reactivity [LLR], or CPP upper limit of reactivity [ULR]) will not depend on ABP transducer zero level. Complicating matters, the final cerebral arterial blood pressure will depend on additional, generally unmeasured factors such as wave reflection, vessel geometry, and luminal obstructions. For example, if a patient has a significant carotid stenosis, the pressure measured at the level of the radial artery would be significantly higher (~50 mm Hg) than at middle cerebral artery level (4).

The current method of estimating CPPopt and limits of (vascular) reactivity uses a series of heuristic constraints in attempt to produce reliable values that fit the autoregulation concept (5). This selection process has the obvious clinical disadvantage of decreasing the CPPopt yield. To increase the yield, we used a multiple window averaging algorithm (6), which uses data from multiple time windows of different length to give an averaged CPPopt, LLR, or ULR. Using this algorithm, the yield of LLR, ULR, and CPPopt increased to 93% of monitoring time. The proportion of time that LLR or ULR were extrapolations, rather than values experienced by the patient within the time window, was not calculated.

Completely disturbed autoregulation represents a challenge for an automated CPP target recommendation algorithm such as ours. As stated in the methods, if autoregulation was impaired across all levels of CPP (i.e., the whole autoregulation curve is above PRx of 0.3—occurring on average 6.07% [SD, 13.73%] of the valid monitoring time), then the value for CPPopt was taken to be both the LLR and ULR. This insured that any CPP value during globally impaired autoregulation was classified as “outside” the CPP limits of reactivity. However, one could also argue that no LLR, ULR, or CPPopt recommendation should be given when no CPP is associated with adequate cerebral autoregulation.

Although a CPP that is too low is clearly detrimental in that it leads to cerebral ischemia, the cerebral effects of high CPP are less clearly defined. In addition, theoretical risks of maintaining high CPP include damage to other organs. The unknown feasibility, effectiveness, and potential risks of a CPPopt guided therapy are the impetus for the upcoming CPPopt-Guided Therapy trial of Target Effectiveness in traumatic brain injury patients (COGITATE, www.cppopt.org, clinical trial number: NCT02982122).

Dr. Donnelly received funding from Woolf Fisher Trust (PhD scholarship). Dr. Smielewski disclosed that he receives part of the licensing fee for the software ICM+ used for data collection and analysis in this project. Dr. Menon’s institution received funding from GlaxoSmithKline and NeurotraumaSciences; he received funding from Pfizer; he disclosed that he has collaborative research or consultancy agreements with Ornim Medical, Shire Medical, Calico, Pressura Ltd, Glide Pharma Ltd, and Lantasma AB; and he received support for article research from the National Institute for Health Research, United Kingdom. The remaining authors have disclosed that they do not have any potential conflicts of interest.

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DOI: 10.1097/CCM.0000000000002857

## Heparin-Free Regional Anticoagulation: There Are Significant Differences Between Citrate-Containing Dialysate and Regional Citrate Anticoagulation

### To the Editor:

Faguer et al (1), in a recent issue of *Critical Care Medicine*, described a new method of heparin-free regional anticoagulation during intermittent hemodialysis using calcium-free and citrate-containing dialysate. Since