AKI

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The author replies: Stratil[1] cites the influence of both our publication[2] and its accompanying commentary[3] on the recent decision by the German Parliament not to implement a presumed consent model for organ donation, believing our study limitations led to flawed decision-making by the Bundestag.

In response to the specific points made in the letter, we note the following. First, our main analysis did indeed utilize the latest year of available data (2016), but we also conducted additional work utilizing 5 years of cumulative data (2012–2016), with no change in outcomes. Second, we clearly justify categorizing Spain as an opt-in country, a choice with which the Spanish would agree,[4] but sensitivity analyses are shown for both categorizations. Third, we avoid bias in our statistical approach by utilizing forward stepwise multiple linear regression models to avoid cherry-picking variables. Finally, we specifically avoid making any causal link with any associations, and state ". . . as with any observational data, association does not automatically imply causality, and we caution against such interpretation of our data. Numerous pitfalls with regards to insufficient control for confounders or selection bias can affect observed associations such as the link between opt-out countries and reduced living donor rates."[2]

Organ donation rates in Germany are some of the lowest in the developed world, owing to multifactorial reasons, and are genuinely concerning. However, simple legislative tinkering of explicit versus presumed consent will not achieve meaningful change on its own, as shown by both empirical research analysis and real-world evidence. We stand by our conclusion that interventions beyond short-sighted legislation change are warranted to boost organ donation.

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AKI: an enlightening acronym with a shadow side

To the editor: Skrypnyk *et al.*[1] describe elegantly and convincing that in ischemic acute kidney injury (AKI) in mice, interleukin-6 mediates the production of neutrophil gelatinase–associated lipocalin in the liver and not in the kidney. They extend and generalize this finding to AKI of all etiologies, especially sepsis-induced AKI, in their title and discussion. The AKI concept has advantages for epidemiologic studies, yet this symptom-based definition does not account for etiology or associated pathophysiological mechanisms. Considerable evidence now suggests that the pathophysiological mechanisms of sepsis-induced AKI are different from those seen in AKI of other etiologies.[2] Moreover, sepsis-induced AKI is a heterogonous syndrome driven by multiple different mechanisms acting simultaneously, but not all to the same extent or at the same time in individual patients.[3] We previously identified heterogeneous neutrophil gelatinase–associated lipocalin mRNA and protein levels in kidneys of patients with lethal sepsis.[4] Hence, clearly not all AKIs are alike, and even within a common etiology of AKI, such as sepsis-induced AKI, heterogeneous findings can be found. Using the name AKI makes talking about it easier as if we understand it. However, it can blur our vision of the details.

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4. Jou-Valencia D, Koeze J, Popa ER, et al. Heterogenous renal injury biomarker production reveals human sepsis-associated acute kidney injury subtypes. *Crit Care Expl*. 2019;1:e0047.

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The author replies: We agree entirely with the comments by Zijlstra *et al.*,[1] who note that the heterogeneity of different causes of acute kidney injury (AKI), particularly sepsis-induced AKI, can be misrepresented by the use of the general term AKI. The complex nature of AKI demands more precise terminology—and we note that the term AKI itself can be utterly