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# Generalizability of randomized control trials

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Sir: I appreciate N. Petrucci's comments but feel they bring an excessive degree of skepticism about multicenter randomized controlled trials (RCTs). It is indeed true that we treat individual patients rather than patient populations, and it is, therefore, important to define how the results obtained in an RCT apply to any particular patient:

1. I do not agree that we study patients "not to find out anything about them": The RCT's primary aim is to serve the population being studied. This is why any patient suffering from a severe disease state should be keen to be enrolled in an RCT. N. Petrucci suggests that we need to extend our barriers and request a lower statistical *p* value. I disagree, because such a strategy would only slow down the development of new therapeutic interventions. The RCTs, which would then require larger patient populations, would be harder to conduct and more expensive, so that people might be more hesitant about starting them. Also, ethically speaking, more patients would be treated with the placebo when the active product has already been shown to be beneficial. That is why RCTs, such as the PROWESS study, may, and should, be ended before the target number of patients is reached if efficacy is already established at the time of an interim analysis.
2. It is true that RCTs usually include a number of exclusion criteria to increase the chances of finding a beneficial effect. Post-marketing surveillance may be helpful to support the administration of a new intervention in patient populations that were not considered in the initial trial, although the power of such analyses is limited by the lack of a control group [1]. As recently outlined by Califf and DeMets [1], the best thing we can do is to perform additional studies targeting particular patient populations.

While the results from any RCT must, of course, be considered in the light of study design, population, and analysis (as must the results from any other study type), the RCT is the best method we currently have to establish the efficacy of therapeutic interventions; denying it would be to deny progress. Placing overly restrictive barriers on RCT development and performance would potentially deprive us of the discovery of exciting developments. Indeed, the intensive care community can be proud of its recent achievements in the conduct of good clinical trials [2, 3].

## References

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