Published in final edited form as:

Anesthesiology. 2016 June ; 124(6): 1417. doi:10.1097/ALN.0000000000001097.

Effectiveness vs. Efficacy of Calabadiol and Sugammadex for Non-Depolarizing Neuromuscular Blocking Agent Reversal

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To the Editor

Haerter and colleagues recently published a study¹ on the comparison of calabadiol 2 to reverse non-depolarizing neuromuscular blocking agents (NMBAs) by binding and inactivation, which they described as comparative effectiveness. The study included *in vitro*, *ex vivo*, and *in vivo* experiments, including assessments of dose-response relationships. Although the article makes some important contributions, our concern focuses on the use of the term, and associated title that includes ‘comparative effectiveness.’ Instead, these studies should be described as efficacy, not effectiveness research. Although this distinction may seem to represent a minor issue, we feel that incorrectly defining the phase of research can lead to misconceptions about the study’s goals and objectives, and subsequent interpretation, and lead to misreporting on the current state of research (e.g. in a systematic review with searches based on titles and key terms).

Although they do not use the full term of ‘comparative effectiveness research,’ the idea of effectiveness, rather than efficacy, is well described by extensive literature on comparative effectiveness research (CER). The Institute of Medicine (IOM)² and Federal Coordinating Council on Comparative Effectiveness Research (FCC)³ describe CER as, “...the generation and synthesis of evidence that compares the benefits and harms of alternative methods to prevent, diagnose, treat, and monitor a clinical condition or to improve the delivery of care.” The IOM report goes on to state that, “The key elements of this definition are ... the study of patients in typical day-to-day clinical care.” In contrast, efficacy studies evaluate treatments under ideal conditions, with an emphasis on assessing the potential of the intervention to work under ideal or very specific conditions. The study by Haerter, et al. demonstrates which drugs work best in a laboratory setting and in controlled circumstances. While these findings are absolutely informative and significant, they do not demonstrate *effectiveness* in

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Conflicts of Interest: None.

that they do not reveal which drugs work well in a less controlled, “real-world” clinical setting.

The distinction between efficacy and effectiveness is also emphasized by the phases of translational research,⁴ where efficacy studies qualify as T1 or T2 research, but effectiveness studies fall under T3 research. Although the study by Haerter et al. compares treatments, the *in vitro*, *ex vivo*, and *in vivo* nature of experiments would still lead to its categorization as T1 research.

Acknowledgments

Funding: Dr. Lim is supported in part by a grant through the National Institutes of Health, T32GM075770.

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