Antimicrobial de-escalation is a highly recommended and widely practiced drug use strategy in intensive care units. It is believed to play important roles in reducing the development and transmission of antibiotic resistance, as well as reducing mortality and inappropriate empiric therapies. However, such benefits were not uniformly observed in clinical studies, making it hard to conclude the benefits and trade-offs of such a strategy. In this talk, we will present results from mathematical models, in terms of individual-based simulations and long-term behavior analysis, to infer the expected outcomes of clinical studies that compare de-escalation with traditional therapy. We believe that modeling could assist the design of many clinical studies to help researchers to obtain reasonable expectations of the outcomes, plan ahead analytical methods, and adjust data collection methods. (Received September 15, 2020)