Research on the risks associated with prescription opioid treatment has received significant attention, establishing the basis for interventions aimed at reducing opioid prescribing as part of the effort to curb the addiction and overdose crises. Prescription characteristics linked to adverse opioid-related outcomes are commonly observed in chronic pain treatment. However, recent evidence indicates that reductions in opioid prescribing, particularly abrupt discontinuation, are also associated with negative outcomes. This seminar examines the relationship of prescription opioid use and discontinuation with incident opioid-related outcomes.