One in nine men will be diagnosed with prostate cancer and will weigh treatment decisions against the unknown course of their disease. Treatment too can carry significant comorbidities. There is a need to better match screening and treatment to the risk that the disease poses for the individual. Like other cancers, it is driven by both inherited and acquired genetic changes with a domino effect of pathology. Knowledge of the drivers can guide effective personalized care. Even though prostate cancer is the most heritable of all common cancers (twice that of breast cancer), the underlying genetic determinants of its risk and severity have been challenging to decipher and remain largely unknown. We will discuss a local (and global) study of prostate cancer with a novel family-based design, investigate one of the principal inherited risk factors, and uncover an unexpected twist of determinants of severity.