A polygenic risk score (PRS) is a weighted sum of statistically significant disease/trait associated alleles of many genetic loci estimated from genome-wide association studies. In recent years, application of PRS has grown rapidly. Furthermore, some researchers have advocated for its use in clinical practice. Despite the promise of PRS in clinical translation, there is little consensus on the data input and methods for generating PRS. This presentation will include the history of the PRS, methods, available software, ethical and scientific challenges in clinical implementation of PRS, relevance of PRS across different ethnicities, and future research directions in methodological development of PRS.