Count data plays an important role in biomedical and clinical research, especially with the rapid biomedical technique progresses including next generation sequencing. However, using routine statistical model to analyze counts, such as Poisson model, often results in biased or even misleading conclusions. Primary challenges when applying Poisson model to count data include over-dispersion and zero-inflation, which are commonly encountered in practice. In addition, the repeated measures and incomplete observations in modern clinical trials and survey studies add to complexity. This talk will review these challenges in count data analysis and methodology progresses made by the speaker's group. In addition, the application of counting process method to the cutting-edge single-molecule localization microscopy image analysis and recently developed innovative statistical methods will also be introduced.