Using results from modern genome-wide association studies (GWAS), we and others have now unequivocally demonstrated that complex traits are extremely polygenic, with each individual trait potentially involving thousands to tens of thousands of genetic variants. While each individual variant may have a small effect on a given trait, in combination, they can explain substantial variation of the trait in the underlying population. In the past, analyses of GWAS have mainly focused on modelling genetic susceptibility one-variant-at-a-time, and identifying those which reach stringent statistical significance for association. In the future, however, we advocate that analysis needs to focus more on polygenic modelling to exploit the power of diffused signals in GWAS. In this talk, I will review recent advances in statistical methods for polygenic analysis, as well as scientific knowledge gained through their applications, in three areas of major interest (i) understanding biology through genomic enrichment analysis (ii) exploring causality through Mendelian Randomization (Genetic Instrumental Variable) analysis and (iii) and informing precision medicine through development of risk prediction models.