An ever growing number of medical organizations, societies, working groups and governmental agencies issue algorithms i.e. guidelines, of decision making flowcharts in diagnosis and treatment in a variety of diseases. In the field of evidence-based diagnosis and treatment of breast cancer, a large number of guidelines are available both from medical associations and national health departments. Among the most appreciated and utilized comprehensive guides is the European Society for Medical Oncology (ESMO) Breast Cancer Guidelines and from the other side of the Atlantic the National Comprehensive Cancer Network (NCCN) Guidelines in Breast Cancer. Although there is much concordance between the guidelines from these two organizations, it is intriguing to locate their discrepancies also. The aim of this talk is to present a number of different points between ESMO and NCCN in the whole spectrum of breast cancer management, from prevention and diagnosis to treatment and follow up and to summarize in detail, the differences between ESMO and NCCN guidelines regarding genetic risk evaluation and screening, surgery, chemotherapy, endocrine treatment, targeted biological agents, radiotherapy, pregnancy and fertility and follow-up.