this number is typically from about 20 genes to up to about 20,000 different genes. Microarray analysis has been used to assess gene expression in tumor biopsies in oncology studies (139) atherosclerosis (macrophages taken from atherosclerotic plaques) (140) skin biopsies in studies of psoriasis (141) cells in inflamed joints in studies of arthritis (142) biopsies from lesions in multiple sclerosis (143) and immune disorders in general, including diabetes (144).

In microarray analysis, it is usually not the case that increased expression of any one particular gene is important in defining the subgroup. Instead, the contribution of the entire, predetermined group of genes is used for this definition. In the words of one investigator, "It's really not possible to focus on what are the 'most important genes' from this analysis, the prediction is based on a large number of genes whose expression in total defines the prediction. In short, it is the pattern of gene expression, rather than the expression of any single or few genes, that has the power to do the prediction (145)."

Examples of microarray analysis for defining subgroups, in the context of clinical trials and in ordinary clinical practice, are provided in this textbook in the chapter on biomarkers and personalized medicine.

h. Recommending dropping one subgroup from the trial, rather than stopping the entire trial

Where one particular subgroup in a trial is experiencing severe adverse drug reactions, such as death, the investigator can drop that particular subgroup from the trial (146). Dropping one subgroup from a trial is preferable to stopping the entire trial. Hence, in configuring the subgroups in the study population, the investigator or medical writer should contemplate various risk factors that might be expected in the study population, and for each risk factor, and include in the Clinical Study Protocol criteria that can be used to identify subjects as high, moderate, and low risk. An example

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