Multicentre Clinical Registries
Establishment of multicentre clinical registries as a basis for comparative evaluation of rare diseases

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1. THE NEED FOR MULTICENTRE CLINICAL REGISTRIES IN RARE DISEASES

The study of diseases, whether in the framework of controlled clinical trials or observational clinical studies faces the problem of heterogeneity of subjects. Heterogeneity usually is tackled by the application of statistical methods which lead to general results valid for populations but not for single individuals. In statistical models, the true heterogeneity is viewed as a random variation produced by a stochastic mechanism. This approach has been proven successful in many medical applications concerned with frequent diseases in the second half of the twentieth century.

However, apart from systematic errors, for rare diseases, the statistical error produced by random variation of results may be considerable. In the following tableau, we demonstrate the statistical precision of an observed proportion (e.g. a specific finding among a group of patients) depending on the number of subjects in the study. Results are based on the statistical convention that erroneous inferences from samples to populations should be limited to maximal one of 20 studies.

We present results for observed proportions of 50% and observed proportions of 10%. Due to the mathematical symmetry, proportions of 90% lead to equivalent results to those of 10%, as one can simply exchange the labels of “finding” and “absence of finding” (Table 1).
From this table it can be clearly seen that in most clinical questions, sample sizes below 100 will not allow valid conclusions. For specific problems, especially in the multifactorial setting, even sample sizes of thousands of patients will be necessary to obtain sufficient evidence.

Thus, the need of multicentre approaches for rare diseases is obvious. This, however, is not only true for controlled clinical trials but also for clinical epidemiology working with data from hospital based registries.

2. CHALLENGES TO THE IMPLEMENTATION OF A MULTICENTRE CLINICAL REGISTRY OF ADAMANTIADES-BEHÇET’S DISEASE

2.1 Definition of manifest Adamantiades-Behçet’s disease according to clinical findings

Still there is no commonly accepted diagnostic scheme for Adamantiades-Behçet’s disease. This fact seems to provide a major problem for the establishment of a multicentre registry. However, the different diagnostic schemes for Adamantiades-Behçet’s disease are essentially composed of the same manifestations with different weighing or different hierarchical classifications. Among others, these manifestations are ocular, oral, genital, or skin-related. Additionally, the pathergy test is used as a valid diagnostic criterion.\(^1\)\(^2\)

In an analysis from the German Registry of Adamantiades-Behçet’s disease, the comparison of different diagnostic schemes leads to less than 10% “inconsistent” cases, i.e. the diagnosis of manifest Adamantiades-Behçet’s disease was identical in more than 90% of cases. Additionally, the sheer information needed to classify patients according to different definitions of Adamantiades-Behçet’s disease should be available in many centres, working with one specific diagnostic scheme.