

## The Swedish Twin Registry

### *Past and future use*

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The Swedish Twin Registry of the Karolinska Institute comprises about 10 000 sets of twins, and was built up in 1961-1962. It covers about 95% of all Swedish same-sexed twins that were born in the country in 1886-1925 and were still living as unbroken pairs at the time of compilation.

The compilation procedure has been presented in detail by Cederlöf (1966a), and will be summarized as follows. Since the middle of the last century, a rather unique system for population registration has existed in Sweden. It is based not only on birth records, but also on migration records. As soon as an individual moves away from the place he lives, he has to notify the authorities as to where he moves. This system made it possible for us to follow-up any individual from his place of birth to his next place of living, and so on, until we found his current address or had to discard him as deceased. We started, in that way, with about 41 000 multiple birth records, handscreened from about 3½ million birth records from all Sweden during the period in question, and ended with a series of about 12 000 located sets of twins. Of the remainder, about 26 000 had to be discarded, due to death of one or both partners; 1 000, due to emigration to foreign countries; and 100, due to hospitalization in mental asylums, or home for aged people, etc. In the compilation procedure we lost track of about 1 100 individuals, or 1.5%.

The zygosity of the twins has been determined with the aid of some similarity questions contained in a questionnaire, mailed to all the twins in the registry. Out of several questions, one proved to be of high reliability, namely the very simple question whether the twins as children were as alike as two peas in a pod, or of family likeness only. We assumed that if both twins in a set agreed in saying that they had been as alike as two peas in a pod, the pair was MZ. If they, on the other hand, agreed in saying that they had been of family likeness only, we regarded the pair as DZ. We validated this questionnaire diagnosis by analyzing the outcome from a subsample of 200 pairs who had also been examined serologically in regard to five markers, A<sub>1</sub>A<sub>2</sub>BO, MN, Rh, Hp, and Gm. The results were reported here in Rome in 1961 and showed an agreement in diagnoses of 95% for MZ and 90% for DZ (Cederlöf et al, 1961).

About 3-4% of the pairs could not be evaluated by the questionnaire method as they gave conflicting answers to the peas-in-the-pod question. In another 15% of the pairs, one or both cotwins failed to return their questionnaires; hence, the working files of the registry comprise exactly 10 508 pairs, of whom 3 656, or 35%, are MZ.

The Twin Registry was originally set up with the intention of studying differences in mortality rates between smokers and nonsmokers in smoking discordant twin pairs, especially in regard to coronary heart disease and nonspecific chronic lung disease. The background to this study-design was the fact that, in spite of the well established differences in disease rates between smokers and nonsmokers in general, many critics have advanced the argument that smokers and nonsmokers are too different in too many habitual and possibly also constitutional factors to warrant unbiased estimates of a smoking effect. The twin approach no doubt enhances the possibility to evaluate the effect of smoking, as twins belonging to the same pair — even if smoking discordant — have been shown to differ far less in a series of environmental and habitual variables (Cederlöf, 1966a; Cederlöf et al, 1969b).

The original aim of reporting mortality has, during the years, been extended to include some morbidity investigations. These were all carried through with data collected by mailed questionnaires and using methods of diagnosis that originate from Rose (1962), in regard to “angina pectoris” as an indication of coronary heart disease, and from the British College of General Practitioners (1960), in regard to “cough” and “prolonged cough”. All data on morbidity and smoking in the twin registry have been published (Cederlöf et al, 1966a; Lundman, 1966) and show that the lung symptoms persist among the smokers in the comparable groups of smoking discordant MZ, while the angina pectoris symptom fails to do so in the comparable groups, although it is significantly higher among smoking twins as compared to nonsmoking twins in general, i. e., when the twin method is not applied, and smokers and nonsmokers belong to different pairs.

The questionnaire data on morbidity have undoubtedly given interesting results, especially in regard to the coronary heart disease question, where the results imply that smoking is not causally associated with the symptom angina pectoris. Data from questionnaire studies have to be regarded as comparatively soft, however, and attempts to verification are necessary, and have also been carried out in subsamples. Thus, Lundman (1966) carried through an intensive clinical investigation on 200 pairs of smoking discordant twins. He did not find any difference between smokers and nonsmokers in regard to coronary heart disease — a finding which by and large confirmed the results of the questionnaire study and also elucidated the validity of the questionnaire diagnosis (Cederlöf et al, 1966b). Another clinical investigation has recently been carried out by Liljefors, who studied pairs with coronary heart disease and used the questionnaire diagnosis as a screening method. Some preliminary findings have been reported at this meeting (Liljefors, 1969). Another study further elucidated the sensitivity and specificity of the questionnaire method; its results have also been presented at this meeting (Cederlöf et al, 1969d).

In the category of hard data we now also have some preliminary results on mortality among smokers and nonsmokers in the registry. These have been reported at this meeting in regard to gross mortality and — very preliminary — in regard

to mortality in coronary heart disease (Cederlöf and Friberg, 1969). Further, an analysis has been carried out in regard to cancer morbidity and mortality. These results have also been reported at this meeting (Cederlöf et al, 1969c).

The twin registry has also been used in other context than the smoking-disease issue. Thus, an evaluation of the effect of urban/rural residence on disease was published in 1966 (Cederlöf, 1966b), and hereditary aspects of angina pectoris and bronchitis were reported in 1966 (Cederlöf et al, 1967a, 1967b). Further, some work has been done in regard to diabetes (Serasi and Luft, 1967) and atopic allergy (Lubs, 1970).

It should also be mentioned that two of us (R. C. and L. F.), during our stay as visiting researchers in USA in 1967, got the opportunity to work together with the National Academy of Science, Washington, D.C.; the Dept. of Environmental Health, University of Cincinnati, Ohio; and the National Air Pollution Control Administration of the US Public Health Service, in carrying out a questionnaire study on the American Twin Registry of the National Research Council. This registry contains white male twins who serve or served in the US Armed Forces, and was obtained by matching birth records from all but nine of the continental States with the Veteran Administration files. The sample used in our study comprised 4311 sets of twins born in 1917-1927. The study was designed in the same way as the Swedish questionnaire study on smokers and nonsmokers. The results confirmed very closely the Swedish findings, and were published in 1968 (Cederlöf et al, 1969a). A cooperative effort is now being made to compare and pool information from the two registries. A preliminary report on the background of certain coronary symptoms has been read at this meeting (Cederlöf et al, 1969b).

The future of the epidemiological research on the Swedish and American twin registries seems to be promising. We think that the twin approach in epidemiology considerably enhances the possibility of studying cause-effect relationships, thanks to the improved group comparability. So far, however, most data from the registries — with the exception of studies on small subsamples and the up to now occurred mortality — are of the softer type. We intend, if possible, to supplement these data by clinical investigations on larger groups, either within hospitals or in field studies.

In view of the considerable costs involved, if thousands of individuals should be clinically investigated, it is of course very important to design such studies with the utmost care. Before embarking on a larger study of this kind, we strongly feel a need for cooperation with well known researchers in the field of epidemiology. The Karolinska Institute has (with financial support from the Tobacco Research Council, USA) therefore invited a group of about 15 people to a planning conference in USA this fall. The outcome of this conference will be decisive as to what will be the future program of the registries.

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