



Acta Genet Med Gemellol 39: 441-446 (1990)  
©1990 by The Mendel Institute, Rome

Sixth International Congress  
on Twin Studies

## **Selection Bias in Disease-Related Twin Studies Data on 11,154 Adult Finnish Twin Pairs from a Nationwide Panel**

**K. Romanov<sup>1</sup>, M. Koskenvuo<sup>2</sup>, J. Kaprio<sup>1</sup>, S. Sarna<sup>1</sup>, K. Heikkilä<sup>1</sup>**

*Departments of Public Health, <sup>1</sup>University of Helsinki and <sup>2</sup>University of Turku, Finland*

---

**Abstract.** The effect of migration on pairwise concordance for disease was assessed in 11,154 twin pairs of the Finnish Twin Cohort Study by comparing the pairs living in the same province to the pairs which members were living in different provinces of Finland. The cumulative incidence of psychosis and hypertension for the years 1972-1985 were analyzed. The cumulative concordance of psychosis for those MZ twin pairs living in the same province were higher than for those MZ pairs living further apart. Similar findings were found among DZ pairs for psychosis. The cumulative concordance of hypertension was only slightly higher among those MZ and DZ pairs living in the same province compared with pairs living in different provinces. These results indicate an overestimation of concordance of psychosis caused by selective migration. This bias in twin studies is likely to influence heritability estimates in a sample of limited geographical area.

**Key words:** *Twins, Concordance, Selection bias, Psychosis, Hypertension*

---

### **INTRODUCTION**

Migration studies of various diseases have continuously been a special interest of epidemiologists to assess the difference of patterns of morbidity and mortality between those who migrate and those who stay. Studies of migrant populations have aimed primarily toward the separation of factors associated with place from those that are characteristic of persons. However, the circumstances of migration are often exceptional and there is usually a strong selectional effect causing unrepresentativeness of migrants compared with the population of the area from which they migrate. It is possible that

the more active, stronger or more unstable subjects are those who migrate and as a result migration will bias the results [12,18].

The migrant studies have usually analyzed the population moving from one geographical area to another. However, this selection caused by migration may also have an effect on the results of those epidemiologic studies utilizing the population which remain in a certain geographical area. Obviously this bias might affect the results of twin studies designed to assess concordance of a disease among twin pairs. For example, a healthy member of a twin pair is likely to be more active to migrate away from the geographical area studied than his/her chronically ill cotwin. A consequence of this selection would be the overestimation of the proportion of concordant pairs studied in a limited geographical area because discordant pairs are more likely to be separated by migration. Moreover, it is possible that this selection operates only when an individual is affected by some debilitating chronic illness.

The purpose of this study was to estimate the effect of migration on concordance figures of psychosis and hypertension by the comparison of pairs of twins living both in the same province with those living in different provinces in Finland. In the present study, psychosis is considered as a serious chronic disease and as more likely to produce selection bias than hypertension, which should not usually restrict migration of an individual to a considerable degree. Factors that possibly affect the dynamics of migration, ie, age and cohabiting status of twins when migrating to another province, are not included in this study.

## SUBJECTS AND METHODS

The Finnish Twin Cohort consists of all Finnish twin pairs of same gender born before 1958 and with both cotwins alive in 1967 [6]. The twin pairs were selected from the Central Population Registry of Finland in 1974. A questionnaire was mailed to all pairs in 1975. The overall response rate was 89%. Twin zygosity was determined by examining the responses of both members of each twin pair to two questions on the similarity of appearance at school age. The validity of the questionnaire method of zygosity determination was assessed in a subsample by eleven blood markers [19]. Some 93% of all respondent pairs could be classified as MZ or DZ with only a slight probability of misclassification (1.7%). Those pairs in which either cotwin had moved abroad or was dead in 1987 were excluded, thus the total number of pairs included in the present study was 11,154.

The information of diagnosis of hypertension (ICD 400-404) and nonorganic psychosis (ICD 295-299) was obtained from the nationwide Hospital Discharge Registry for the years 1972-1985. This registry covers all discharges from the hospitals in Finland. The discharge diagnosis are assigned by the physician treating the patient using the International Statistical Classification of Diseases (ICD 1967).

The reliability of the nationwide Hospital Discharge Registry of Finland has been found to be satisfactory for epidemiologic studies [5,15].

In addition, information on hypertension was obtained from the Registry for the Reimbursement of Free-of-charge Medication of the Social Insurance Institution. In

Finland, since 1970, patients with chronic hypertension are provided with a free of charge medication. The prerequisite is the detailed medical certification, which is then approved by the Institution.

The effect of migration on the pairwise concordance of these diseases was assessed by comparing the pairs whose both members were living in the same province to those living in different provinces in 1987. Administratively, Finland is divided into twelve provinces. The mean number of inhabitants in each province is 407,800 (range 23,000-1,175,000). The province of each twin living in 1987 was determined with the home address obtained from the Central Population Registry.

The results of psychosis and hypertension were analyzed separately to produce the percentage of concordance and discordance by home province. The heritability was estimated by doubling the difference between MZ and DZ intraclass correlation; accordingly, the SE of this estimate was calculated [17].

## RESULTS

In 1987 MZ cotwins were living slightly more frequently in the same province (73%) than DZ cotwins (67%). Among MZ pairs, the pairwise concordance of psychosis was 15.3% of affected pairs living in the same province and 0% of those living in different provinces ( $p < 0.05$ ). The corresponding values for DZ pairs were 2.9% and 1.0% ( $p > 0.05$ ) (Table 1).

**Table 1 - Cumulative incidence of psychosis in twin pairs**

	MZ pairs				DZ pairs			
	Concordant		Discordant		Concordant		Discordant	
	N	%	N	%	N	%	N	%
Pairs living in the same province	13	15.3	72	84.7	7	2.9	234	97.1
Pairs living in different provinces	0	0	35	100	1	1	102	99

The pairwise concordance of cumulative incidence of hypertension was higher in MZ pairs living in the same province (37.3%) than in those living in different provinces (30.4%) ( $p > 0.05$ ). Similar results were obtained among DZ pairs (19.1% vs 15.5%,  $p > 0.05$ ) (Table 2).

The heritability estimate for psychosis was considerably higher among the twins living in the same province than in the total sample ( $0.44 \pm 0.05$  vs  $0.32 \pm 0.04$ ). However, the heritability estimate for hypertension was the same irrespective of province status (Table 3).

**Table 2 - Cumulative incidence of hypertension in twin pairs**

	MZ pairs				DZ pairs			
	Concordant		Discordant		Concordant		Discordant	
	N	%	N	%	N	%	N	%
Pairs living in the same province	114	37.3	191	62.7	143	19.1	605	80.9
Pairs living in different provinces	31	30.4	71	69.6	51	15.5	287	84.5

**Table 3 - Heritability for cumulative incidence of psychosis and hypertension in twins**

	Both cotwins live in the same province (N = 7,682)	All twin pairs in Finland pooled together (N = 11,154)
Psychosis	0.44	0.32
Hypertension	0.48	0.48
Heritability = $2(r_{MZ} - r_{DZ})$		

## DISCUSSION

**Sample.** The Finnish Twin Cohort was compiled from the Central Population Registry of Finland, because an unlimited representative sample is the most reliable type of twin studies to investigate the genetic component in the etiology of diseases [1]. In most studies of twins the proportion of concordant pairs has varied considerably according to the completeness with which cases are ascertained in the sample [2]. The present study was based on the data of the hospital discharge registry of this cohort compiled from the entire population. This method makes it possible to ascertain the cases independently from the health status of the cotwin. The hospitalizations for psychosis and hypertension covered, in principle, all admissions to hospitals during the follow-up of 14 years. The actual coverage of this method seems to be good, as demonstrated in another study using the same procedure of record-linkage [5]. For hypertensive probands, there were probably only occasional hospital discharge data, since hospitalization for uncomplicated hypertension is seldom needed. However, the representativeness of the follow-up data, including the National Drug Registry, can be considered good when compared to the cumulative incidence of a large Finnish population study of hypertension [3]. The prevalence in the cohort of other chronic diseases, eg, coronary heart disease, multiple sclerosis and Parkinson's disease, has been found to correspond to that of the general population [9,11,13].

**Results.** Concordance for psychosis was considerably higher, and concordance for hypertension was slightly higher, among pairs with both twins living in the same province, among both MZ and DZ pairs. It can be speculated that hypertension combines with ill health in reducing individual mobility. In a longitudinal study of sociocultural mobility as a precursor of hypertension among former university students geographical mobility was associated with a slightly reduced risk of hypertension [4].

In a study investigating migration from one township to another in Finland, the most frequent reason for migration was getting a new job, getting new housing or getting married [14]. A chronic, especially debilitating disease may inhibit this kind of life-event which involves vigorous efforts. In the present study, migration included exclusively changing residence from one province to another. This may represent an even more remarkable life-event when the distance between former and new residence is longer than that from one municipality to another. Hence, it is possible that the slightly lower incidence of hypertension among the migrant group reflects the selective process of interprovincial migration as a major change in life conditions, which requires more strength and activity and, consequently, better health.

Differences in place of residence, such as living in different provinces, also reflect differences in the amount of shared environment within twin pairs. It is likely that co-twins who live in different provinces see and contact each other less often than those who live in the same province. We have previously shown that the frequency of intrapair social contact is a significant modulator of pairwise similarity for personality traits, such as neuroticism, and alcohol use [7,8,16,17]. The present study shows that this applies also to hospitalization for psychosis, for which pairwise similarity is modulated by shared environment. The causal relation between shared environment and pairwise similarity could not be assessed in this analysis, for it was not known which event preceded the other, migration or hospitalization. For the etiology of hypertension, shared environment apparently has only a minor role according to this analysis, as we have previously shown for extraversion [8,17].

## CONCLUSIONS

These findings indicate that migration bias confounds heritability estimates for chronic diseases affecting the individual's general condition. Heritability estimates of psychotic disorders, eg, schizophrenia, vary greatly between repeated studies [10]. The bias caused by migration might play an important role in that variation, with studies based on geographically restricted samples yielding higher heritability estimates than those based on a nationwide sample.

## REFERENCES

1. Aho K, Koskenvuo M, Tuominen J, Kaprio J (1986): Occurrence of rheumatoid arthritis in a nationwide series of twins. *J Rheumatol* 13:899-902.
2. Allen G, Hrubec Z (1979): Twin concordance. A more general model. *Acta Genet Med Gemellol* 28:3-13.
3. Aromaa A (1981): Epidemiology and public health impact of high blood pressure in Finland (summary in English). *Kansaneläkelaitoksen julkaisuja AL 17*, Helsinki.
4. Gillum RF, Paffenbarger RS (1978): Chronic disease in former college student, XVII. Sociocultural mobility as a precursor of coronary heart disease and hypertension. *Am J Epidemiol* 108:289-298.
5. Heliövaara M, Reunanen A, Aromaa A et al (1984): Validity of hospital discharge data in a prospective study on stroke and myocardial infarction. *Acta Med Scand* 216:309-316.
6. Kaprio J, Sarna S, Koskenvuo M, Rantasalo I (1978): The Finnish Twin Registry: Formation and compilation, questionnaire study, zygosity determination procedures and reasearch program. *Prog Clin Biol Res* 24B:179-184.
7. Kaprio J, Koskenvuo M, Langinvainio H, Romanov K, Sarna S, Rose RJ (1987): Genetic influences on the use and abuse of alcohol: A study of 5638 adult Finnish twin brothers. *Alcoholism Clin Exp Res* 11:349-356.
8. Kaprio J, Koskenvuo M, Rose RJ (1989): Changes in cohabitation and intra-pair similarity of MZ cotwins for alcohol use, extraversion and neuroticism. *Behav Genet*.
9. Kinnunen E, Juntunen J, Ketonen L, Koskimies S, Konttinen YT, Salmi T, Koskenvuo M, Kaprio J (1988): Genetic susceptibility to multiple sclerosis. A co-twin study of a nationwide series. *Arch Neurol* 45:1108-1111.
10. Koskenvuo M, Langinvainio H, Kaprio J, Lönnqvist J, Tienari P (1984): Psychiatric hospitalization in twins. *Acta Genet Med Gemellol* 33:321-332.
11. Koskenvuo M, Kaprio J, Rose RJ, Kesäniemi A, Sarna S, Heikkilä K, Langinvainio H (1988): Hostility as a risk factor for mortality and ischemic heart disease in men. *Psychosom Med* 50:330-340.
12. Krueger DE, Moriyama IM (1967): Mortality of the foreign born. *Am J Publ Health* 57:496-503.
13. Marttinen RJ, Kaprio J, Koskenvuo M, Rinne UK (1988): Parkinson's disease in a nationwide twin cohort. *Neurology* 38:1217-1219.
14. Nieminen M (1983): Internal migration in Finland in 1977-78. A Survey Investigating the Reasons for Migration. *Yearbook of Population Research in Finland*, Vol 21.
15. Poikolainen K (1983): Accuracy of hospital discharge data: Five alcohol-related diseases. *Drug and Alcohol Dependence* 12:315-322.
16. Rose RJ, Kaprio J (1988): Frequency of social contact and intra-pair resemblance of adult MZ co-twins: Does shared experience influence personality after all? *Behav Genet* 18:309-328.
17. Rose RJ, Koskenvuo M, Kaprio J, Sarna S, Langinvainio H (1988): Shared genes, shared experience, and similarity of personality. Data from 14288 adult Finnish cotwins. *J Personal Soc Psychol* 54:161-171.
18. Sackett DL (1979): Bias in analytical research. *J Chron Dis* 32:51-63.
19. Sarna S, Kaprio J, Sistonen P, Koskenvuo M (1978): Diagnosis of twin zygosity by mailed questionnaire. *Hum Hered* 28:241-254.

**Correspondence:** Dr. K. Romanov, Department of Public Health, University of Helsinki, Haartmaninkatu 3, SF-00290 Helsinki 29, Finland.