Norwegian Twin Registers and Norwegian Twin Studies — An Overview

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The Norwegian Twin Registers include several sets of population-based sub-registers, and covers twin pairs born between 1895 and today. Except for the missing birth years 1960 to 1967, the register is almost complete. Most of the register contains information about both same-sexed and opposite-sexed twin pairs, except for twin pairs born between 1946 and 1960, where only same-sexed twins are registered. In a substantial part of the register, information about zygosity is obtained, mainly by a mailed questionnaire and in some cases supported by DNA testing. These are the birth years 1915 to 1960 and the birth years 1967 to 1979. Zygosity information is further obtained in the different twin studies derived from the twin register. In 1990 the whole register was made available in a computerized form. Several twin studies have been derived from the different parts of the register. In this article, studies from the two earliest parts of the register are reviewed and grouped by recruitment specifics. Finally, future plans for the register and twin studies are discussed.

The Norwegian twin data are not centralized in a single register, but rather organized in sets of population-based sub-registers established for research purposes by investigators at separate institutes. Part I covers all twins born between 1895 and 1945 (Bergem, 1997; Kringlen, 1968a), Part II overlaps somewhat with the first, but contains additional data in the overlapping years, and covers same-sexed twins in the period 1915–1960 (Berg 1984; Magnus 1983). Part III is based on all twins born between 1967 and 1979 (Harris et al., this issue). Additionally, all twins born after 1967 are registered in the Medical Birth Registry of Norway (Irgens, 2000). These collective databases are referred to as the Norwegian Twin Registers. Unfortunately, twins born in the period 1960 to 1967 are not included in any part of the Norwegian Twin Registers.

The History of the Norwegian Birth Register and the Norwegian Twin Registers

For several hundred years all births in Norway were registered in the parish registers by local clergymen. The Central Bureau of Statistics (CBS) was founded in 1876 and obtained the data from the parish registers. In 1916 the birth registration became a civil affair by the "Act of Castbergian". Before that time, children were not registered unless they were born within marriage and baptized in the State Church. The report from the parish registers to CBS was the normal procedure until 1946, when the National Population Register of Norway (NPRN) was finally established in all Norwegian communities. Between 1946 and 1967 the NPRN obtained the data from the parish registers, and passed on the information to the CBS. In 1967 the NPRN took over the responsibility of registering all births and passing on the information to both the parish registers and the CBS. This double registration took place until 1983, when the parish registers were shut down. In 1990 the name of CBS was changed to Statistics Norway.

Part I

In connection with twin research on functional psychoses, a national population based twin register covering the birth years 1901–1930 was compiled in 1963 (Kringlen, 1968a, 1968b, 1978). The information was obtained from The Central Bureau of Statistics. This register was later extended both forward and backward by Kringlen, and now covers twin births during the period from 1895 to 1945. Except for the years 1895–1900, the register is almost complete, and includes same-sexed and opposite-sexed twin pairs, in total 37,000 pairs (Table 1).

Until 1990, the register was maintained manually and was not computerized. In connection with a twin research on senile dementia, Bergem (1997, 1999) made the register operative for computer use to facilitate matching with other national databases. The register now contains full names of the twins, day and place of birth and whether the parents of the twins were married. The sex of both twins is recorded as well as whether the co-twin was born alive or dead. In a few cases, zygosity is determined by blood tests. There is also information regarding full names and year of birth for both parents and the father's occupation. This twin register is not updated regarding the date or cause of death of those who have passed away.

In a subset of Part I, covering twin pairs born between 1905 and 1945, there is information about personal identity number (Table 1). The 11-digit unique personal identity number for every individual has been in use in Norway since the autumn of 1964, based on the 1960 national census. The twin register was matched against the personal identity register, and among twins born between 1905 and 1945, a total of 23,334 individuals with personal identity numbers were identified (Iversen et al., 2001). These were twin pairs where both twins were alive in 1960,

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in other words about 11,650 pairs, representing 40% of the twin pairs born in Norway in the actual period. A substantial number of women who changed their last name through marriage were lost in this process. The twin register includes names given by birth, and the personal identity number register does not record maiden names.

Part II

The second part of the twin register has its origin from the Institute of Medical Genetics, University of Oslo, and is named the Norwegian Twin Panel. This register is also population-based, but covers only same-sexed twins born in Norway in the period 1915–1960. Part II is partly overlapping Part I, since the data covering the years 1915–1945 were obtained from Part I, whereas the data from 1946 to 1960 were collected from the Central Bureau of Statistics. All pre-existing register information on these twins was updated and computerized. Magnus et al. (1983) scored a population of 11,175 same-sexed twin pairs born between 1915 and 1960 for zygosity by means of a mailed questionnaire. Of the estimated 20,200 same-sexed twins born in this period, 12,752 complete pairs were still alive after their 20th birthday, and 87.6% (11,175) responded to the questionnaire. To assess the accuracy of the zygosity classifications, genetic markers were examined for a subsample of 207 pairs. The authors concluded that zygosity could be predicted with satisfactory reliability for intact pairs (correctly classified 97.6%) and for pairs where only one of the twins had responded (correctly classified 96.1%) to the questionnaire. Compared with blood testing, the authors found the questionnaire method sufficient to adequately score twin pairs for zygosity.

Part III

The third part of the Norwegian Twin Registers is maintained by the Norwegian Institute of Public Health. It comprises its own program of research in genetic epidemiology of mental and physical health and is described in a separate article in this issue (Harris et al., 2002). This Twin Panel is routinely expanded by recruiting pairs from the Medical Birth Registry of Norway (MBRN). This final part of the Norwegian Twin Registers is a complete population based register, which includes all same-sexed and opposite-sexed twins born after 1967, registered in the MBRN. Initially, the MBRN was run by the Central Bureau of Statistics. Some years later the MBRN was established as a separate body affiliated to the University of Bergen. Since 1976, the State Health Inspectorate has been involved as the owner and the National Institute of Public Health as the register-responsible institution and finally, the University of Bergen as the body responsible for running the MBRN (Irgens, 2000). The data in the MBRN includes sex, birth weight and length, complications during delivery, maternal health before and during pregnancy, vital status of the twins at birth and in the actual years after birth and some background information on the parents. Zygosity information is not included in the MBRN, but zygosity is assessed among the participants in the studies at the Norwegian Institute of Public Health and these data are now available for the cohorts born from 1967 through 1979 (Harris et al., 1995). The complexity of the different parts of the register is listed in Table 1.

Are the Norwegian Twin Registers complete?

When a twin register is based on the birth register, all twins in the population are most likely to be included, and the register is valuable for obtaining unselected samples. Although all parts of the Norwegian Twin Registers are population based in the sense of being based upon birth registers, there are still some limitations regarding population representation. In Part I the birth years 1895–1900 are incomplete, because the birth register was inaccurate in early years. Also, it is difficult and sometimes impossible to identify females who have changed their maiden name. Parts I and III include both same-sexed and opposite-sexed twin pairs. The opposite-sexed twin pairs are missing only in the birth period 1946–1960. Twins born between 1960 and 1967 are totally missing. Part III of the register seems to be complete.

Table 1

The Norwegian Population Based Twin Registers

	Birth years	No of pairs	Zygosity known	Same -sex and opposite -sex	11-digit personal identity number	Twin pairs included	Drawbacks/bias
Part I Main register	1895–1945	37,000	No, except for a few cases	Yes	No	All	Incomplete before 1900. No information about death
Sub-set	1905–1945	11,650	No	Yes	Yes	Only those alive after 1960	Females changing maiden name missing
Part II	1915–1960	11,175	Yes	No, same -sexed only	No	88% of living twins	Opposite-sexed pairs missing
Part III	1967–1979	7685	Yes, if participating in questionnaire studies	Yes	Yes	Depends on questionnaire or substudy	

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How Representative Are the Twin Samples in the Studies Derived from the Norwegian Twin Registers?

The twin method is a valuable contribution to genetic research. An unselected sample and a good study design can provide information about the importance of hereditary and environmental factors for the development of a disease or a trait. Still, after important breakthroughs in molecular genetics, twin research has not lost its value. However, there are limitations in twin research. A review of the literature of twin studies reveals high variability in MZ/DZ ratios and in concordance rates for a given disease. Sampling problems may be the reason for this variability. According to Torgersen (1987) the main sampling problems include small samples, self-selection and non-representative ascertainment.

The problems of small samples and self-selection in twin research are usually ruled out when the sample is derived from a population based twin register. In this way, most of the Norwegian twin studies have avoided the major problems of sampling. When the twin register is cross-checked with another register, there could be an ascertainment problem if the other register is not complete. Some of the twin studies suffer to a certain degree from this problem. Torgersen (1987) demonstrated that the concordance of certain psychiatric diseases depends on the severity of the disease in selected patient populations.

A larger part of the Norwegian twin studies are based on only same-sexed twin pairs (Table 2), which means that a substantial part of DZ twins are excluded from the sample. The zygosity distribution in Norwegian twins is 30% MZ and 70% DZ. According to Weinberg's differential method, there will be equal numbers of same-sexed and opposite sexed pairs in the DZ group (Stern 1960), which means 35% same-sexed DZ pairs. Thus, a sample of same-sexed twins covers 65% of the total twin population. In clinical twin studies with relatively small samples, the sample size of DZ twins is particularly critical, because the genetic variation is relatively large among DZs. In some of the reviewed Norwegian studies the samples were rather small, while other samples were large enough to cover up for the missing opposite-sexed pairs.

In a few studies most of the criteria for an unselected sample was met, which means that the proportion between MZ and DZ twins, between same sexed and opposite-sexed DZ twin pairs, and between females and males in the different age groups corresponded to the population. Further, the age group was appropriate for the observed disease, and the number of twin pairs was large enough to compare MZs and DZs in order to obtain statistical significant differences.

The Use of the Norwegian Twin Registers in Twin Research — Major Achievements

Several twin studies have been conducted on the data in different parts of the Norwegian Twin Registers. Most of the studies based upon the older cohorts (Parts I and II) concern psychiatric, psychological or cardiovascular outcomes (Table 2). Some studies ascertained cases by checking the twin register against a disease register, others used mailed questionnaires in order to screen for specific diseases or traits. The latter studies are often large-scale studies with no personal contact. In other studies, all the selected twin pairs were personally examined and clinically diagnosed. These clinical studies have smaller sample sizes but are valuable because the validity of diagnoses is rather high, especially when the same clinicians rated the whole sample. Some studies were based on a combination of screening and personal examination. In a few studies, blood samples were collected and DNA testing was performed (Berg 1983; Bergem & Lannfelt, 1997; Magnus, 1981). The following section describes studies based on Parts I and II of the register (Table 2), grouped by specifics of the recruitment. Studies based on Part III, containing twins born after 1967, are described in a separate paper.

Partly Screening, Partly Clinical Twin Study

Functional psychoses. The first Norwegian twin study based on Part I of the Norwegian Twin Registers was published by Kringlen in 1968 (a,b). In this study 25 000 pairs aged 35–64 were cross-checked against the National Register of Psychoses. A major part of the 342 same-sexed and opposite-sexed psychotic twin pairs was personally investigated. The diagnoses were schizophrenia, manic-depressive disorder and reactive psychosis. Zygosity was determined by blood testing and by a mailed questionnaire. Concordance for schizophrenia was 25% (14/55) in the MZ and 8% (14/172) in the DZ twin pairs, based on registered hospitalised cases, increasing to 38% (21/55) for MZs and 10% (9/90) for DZs, based on personal investigation, supporting a genetic factor in the etiology of schizophrenia, but the genetic factor seemed to be weaker than previously thought. One important statement from this study was that problems in sampling techniques in earlier studies of schizophrenia resulted in overestimation of the genetic factors.

Clinical Twin Studies with Personal Interviews

In this group of twin studies a large number of twins from the twin registers were screened for a certain disease, by cross-checking against another register. Then the samples were selected by personal interviews and diagnostic classification of the cases. The final samples were relatively small compared to the total number of twins screened.

Schizophrenia. The study of functional psychoses (Kringlen, 1968) was later followed up by Onstad et al. (1991). The sample originated from both Part I and II of the Norwegian twin register. Approximately 12,000 names of same-sex twin pairs born between 1936 and 1960 were cross-checked with the National Register for Mental Disorder, which is now closed. In total 52 schizophrenic twin pairs were interviewed and studied. There was a preponderance of females in the MZ group. Zygosity was measured by applying a questionnaire developed by Torgersen (1979). The proband-wise concordance for schizophrenia was 48% (15/31) in MZ and 4% (1/28) in DZ, which supported Kringlen's conclusions from 1968.

Psychiatric nosology and personality disorders. To study psychiatric nosology, Torgersen (1978) cross-checked 91,318 names of patients from the patient registers of inpatient and outpatient psychiatric clinics all over Norway with same-sexed twin pairs born between 1910 and 1955 from Part I and II of the Norwegian Twin Register. He personally

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Table 2

Twin Studies Originated from Part I and II of the Norwegian Twin Registers

Authors	Subjects	Birth years covered	No. of twin pairs screened	No. of pairs investigated	Personal interview	DNA testing	Same-sexed and opposite-sexed	Evidence for heritability
Part I								
Kringlen 1968	Functional psychoses	1901–1930	25,000	75MZ 257DZ	Partly	No	Both	Yes
Dalgard & Kringlen 1976	Criminality	1921–1930	2500	49MZ 89DZ	Yes	No	Same-sexed males	No
Kringlen 1978	Coronary heart disease	1905–1935	25,000	9MZ 22DZ	Yes	No	Same-sexed	No
Bergem et al. 1997	Senile dementia	1895–1925	26,000	21MZ 51DZ	Yes	Yes	Both	Yes, Strongly
Iversen et al. 2001	Cancer	1905–1945	11,650	11.650 MZ/DZ?	No	No	Both	Not investigated
Part II								
Magnus 1981	Cholesterol	1915–1960	?	97MZ	No	Yes	MZ only	Modifying factor
Magnus 1983	Zygosity	1915–1960	11,175	4.402MZ 6.773DZ	No	Yes (207)	Same-sexed	—
Magnus 1984	Birth weight	1915–1960	5850	5.650 offspring	No	No	Same-sexed	Yes
Berg 1987	Coronary Heart Disease hypertension	1915–1960	8500 8500	41MZ 61DZ, 268MZ 437DZ	No No	Yes (198) No	Same-sexed Same-sexed	Yes Yes
Tambs et al. 1987	Left-handedness	1925–1955	1244	469MZ 507DZ	No	No	Same-sexed	No
Corey et al. 1991	Epilepsy	1915–1960	8395 +5952	79MZ 201DZ	No	No	Partly both	Yes
Part I and II								
Torgersen 1978	Nosology anxiety/ depression	1910–1955	20,000	299MZ & DZ	Yes	No	Same-sexed	Inconclusive
Torgersen 1983	Anxiety disorders	1910-1955	20,000	32MZ 53DZ	Yes	No	Same-sexed	Yes, partly
Torgersen 1984	Personality disorders	1910-1955	20,000	28MZ 41DZ	Yes	No	Same-sexed	Yes, partly
Torgersen 1986a & b	Affective & Somatoform	1910-1955	20,000	57MZ 65DZ	Yes	No	Same-sexed	Yes
Onstad et al. 1991	Schizophrenia	1936–1960	12,000	24MZ 28DZ	Yes	No	Same-sexed	Yes
Skre et al. 1993	Anxiety Disorder	1936–1960	12,000	32MZ 49DZ	Yes	No	Same-sexed	Yes
Torgersen et al. 2000	Personality Disorder	1936–1960	12,000	92MZ 129DZ	Yes	No	Same-sexed	Yes

interviewed 299 MZ and DZ same-sexed female and male twin pairs. Zygosity diagnoses were determined by means of blood and serum typing in 215 pairs. The author concluded that the etiology of chronic anxiety neurosis is different from the etiology of neurotic depressive states. However, in milder states, it is not possible to differentiate the two diseases etiologically.

Several studies originated from the same sample. In 1984 Torgersen published a study of schizotypal personality disorder (SPD) and borderline personality disorder (BPD). Torgersen concluded that SPD was genetically determined, whereas BPD was a result of environmental risk factors. In 1993 Torgersen et al. repeated the study design with a different sample, studying the cotwins and relatives of the schizophrenic probands collected in the twin study of schizophrenia (Onstad et al., 1991). Recently, a considerably larger sample of twins (92 MZ pairs and 129 DZ pairs) with different types of personality disorders was studied by means of a model-testing program based on tetrachoric correlations (Torgersen et al., 2000). The sample was drawn

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from different sources, a larger part from the Norwegian Twin Registers, and a smaller number of twins from the inpatient and outpatient wards of two different psychiatric hospitals. The results supported the conclusions from 1984. The authors concluded that most personality disorders (PD) except passive-aggressive PD are genetically influenced. Most genetic proportions of the variance were between 0.5 and 0.6 for single disorders, clusters and for PD in general.

Anxiety disorders. Another sub-sample of 32 MZ and 53 DZ twin pairs suffering from anxiety disorder was studied by Torgersen in 1983. In the group of generalized anxiety disorder (GAD) there was no statistically significant difference in concordance among the two zygosity groups. Ten years later another twin study of anxiety disorder was carried out by Skre et al. (1993). The sample of this study consisted of three sub-samples from other twin studies by Onstad (1991), Torgersen (1984) and Kringlen (1968). The sampling procedure and the zygosity testing are described earlier for each of these studies. The total sample of this particular study counted 81 same-sexed twin pairs. The results indicated a genetic contribution to panic disorder, generalized anxiety disorder and posttraumatic stress disorder, whereas environmental factors seemed to be important in the etiology of simple and social phobia.

A large-scale twin- and family study of anxiety and depression was published by Tambs and Moum in 1993. They reported only a weak degree of heritability. The twin sample was obtained from Part III of the twin register and will be presented in more detail elsewhere.

Affective and somatoform disorders. Further, another subsample of 57 MZ and 65 DZ same-sexed twins with moderate depression was studied (Torgersen, 1986a). The zygosity was determined by means of ten genetic markers in about 75% of the sample. The concordance rate was 51% in MZ and 20% in DZ, indicating heredity to be of considerable importance for the development of depression. The genetic factors were most important for bipolar disorder, a little less for psychotic major depression, less for non-psychotic major depression and least for dysthymic disorder and depressive adjustment disorder. Also in the study of somatoform disorder, Torgersen (1986b) concluded that the development of the disease was influenced by genetic factors.

Criminality. The criminality twin study published in 1976 by Dalgard and Kringlen was carried out using Part I of the Norwegian Twin Registers. A sample of 138 same-sexed male twin pairs aged 40–50 years was obtained by cross checking all male twins in the Norwegian Twin Register born in the years 1921–1930 with the National Criminal Register. Zygosity was based on blood and serum typing in 60% of the sample. A questionnaire to determine zygosity was applied to the whole sample as well. The authors remarked that the questionnaire had a tendency to classify MZ twins incorrectly as DZs. All twins were personally interviewed. The difference in concordance rates between MZ and DZ was not statistically significant, supporting the view that hereditary factors are not significant in the etiology of common crime.

Senile dementia. This is one of the few studies where both same-sexed and opposite-sexed twin pairs were studied. Twin studies of high age are rare, because it is more and more difficult to trace complete twin pairs as they grow older.

Names of 26,000 twin pairs from the twin register born between 1895 and 1925 were checked against 23,000 names of cognitively impaired subjects from Norwegian institutions for the elderly (Bergem et al., 1997; 1999). The final sample consisted of 72 twin pairs, mean age 79.5 years, located all over Norway. The sex distribution and zygosity proportion corresponded to the general population for this age (Lykken et al., 1987). There were 38 AD, 24 Vad, 5 mixed and 5 miscellaneous probands. There was no significant age difference between MZ and DZ pairs, or between concordant and discordant pairs. All together, this was close to an unselected sample of demented twins. The same-sexed pairs were DNA tested to verify preliminary zygosity diagnoses (Jeffreys, 1985). DNA was also analyzed in the search of candidate genes for dementia (Bergem, 1997b). Each twin was investigated clinically and tested by a standard test battery. There were obtained approximately 30 post-mortem cerebral autopsies to verify clinical diagnoses.

The probandwise concordance rate for AD was 83% (10/12) among MZ twins and 46 % (12/26) for DZ twins, indicating that heredity is of major importance in the etiology of late-onset AD. These concordance rates are higher compared with other studies (Breitner, 1995; Gatz et al., 1997; Raiha et al., 1996), probably due to differences in sampling. The heritability factor calculated by tetrachoric correlation was 0.6. Results from molecular genetic research have so far not been able to identify genes responsible for this major heritability factor, which verifies the valuable contribution of clinical twin studies in genetic research. In the VaD group, there was no significant difference in concordance rate between the two zygosity groups, indicating that environmental factors have a major impact on the development of VaD. A further support to the theory of AD as a genetically determined disease, was that 68% of the AD pairs had a positive family history in first- and second-degree relatives. It is well known that APOE e4 is a risk factor for developing AD. Thus, family history and APOE was studied in 25 twin pairs (Bergem & Lannfelt, 1997). In AD cases lacking the e4 allele, 73% were definite familial cases (at least 2 affected first-degree relatives). Among all the AD cases with a definite positive family history, 44% had no e4 in their genotypes. This indicates that there is no causality between family history and the APOE e4 allele.

Coronary heart disease (I). The Norwegian Twin Register was checked against approximately 10,000 coronary disease patients of both sexes in the age group 40–70 years admitted to general hospitals in Norway during the period 1971–75. In this way 78 twin pairs were identified. In a sub-sample of 31 same-sexed twin pairs cholesterol and zygosity were determined by blood tests. Since the concordance difference between MZs and DZs was not statistically significant, the author concluded that the genetic disposition seemed to play a minor role in the etiology of coronary heart disease (Kringlen, 1981). However,

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the numbers were too small to draw any certain conclusion. Heavy work pressure was correlated to myocardial infarction in both DZ and MZ discordant twins.

Screening with Mailed Questionnaire

The following groups of twin studies are all derived from Part II of the Norwegian Twin Registers, named the Norwegian Twin Panel. The cases were selected by screening the twin register by a mailed questionnaire in order to obtain a sample suffering from a particular disease or symptom. These cases were not interviewed personally, and the results are dependent on correct response from each case. The study of zygosity testing (Magnus et al., 1983) is described earlier in this paper, and is the basis for all the other studies carried out from this part of the twin register.

Coronary heart disease(II) and hypertension. In 1984 Berg reported a twin study of premature coronary heart disease (CHD) with a different conclusion from Kringlen (1978). Extensive health questionnaires were sent to the 11,175 responders in the zygosity prediction study of the Norwegian Twin Panel (Part II) described earlier (Magnus et al., 1983). The basis for the coronary heart disease study comprised more than 8,500 same-sexed pairs under the age of 60 from Part II. Concordance rates of CHD were 29% in the 41 MZs and only 8% in the 61 DZs, which indicates that genetic factors are of importance in the etiology of early onset CHD. Concordance rate for reported hypertension was also found to be significantly higher in MZ than in DZ pairs, namely 34% in the 268 MZs versus 9% in the 437 DZs. Bergs group further reported that significantly more DZ than MZ twin pairs were discordant for death caused by coronary heart disease between 40 and 60 years of age. The findings indicated a significant genetic effect on premature death, coronary heart disease and hypertension.

The Norwegian Twin Panel has further been the base for molecular genetic research associated with coronary heart disease. The first part of the study included 198 twin pairs (Berg, 1983). Levels of serum cholesterol, triglycerides, apolipoprotein B (apoB), apolipoprotein A-I (apoA-I) and apolipoprotein A-II (apoA-II) were studied. The author reported high heritability for all three parameters; 0.66 for apoB, 0.53 for apoA-I and 0.69 for apoA-II. Some years later a study of 156 MZ pairs was completed with data on the same lipoprotein parameters as those previously reported (Berg, 1987). The results confirmed that there are high heritability levels for serum concentrations of these 3 apolipoproteins.

Some years earlier Magnus et al. (1981) suggested that there was a restrictive effect of the M allele in the MNS blood group system on environmentally caused variation in serum cholesterol level. To study this effect, 97 MZ twin pairs from the Twin Panel living close to Oslo were grouped by marker system genotypes.

Birth weight. There are several studies and publications about birth weight based on samples from the Norwegian Twin Panel. Birth weights of 13,970 offspring belonging to 5850 same-sexed MZ and DZ twins were analyzed in order to explain the causes of variation in birth weight within and between families (Magnus, 1984, 1985a). Offspring of both twins were available in 2826 pairs. More than 50% of the total variation in birth weight was found to be caused by variation in fetal genes, and less than 20% was caused by variation in maternal genes.

In another study by Magnus et al. (1985b) a questionnaire on smoking habits during pregnancy was performed on 341 MZ and 321 DZ female twin pairs. The intra-pair correlation was 0.8 in MZ and 0.4 in DZ twin pairs, indicating a substantial genetic influence on liability to smoke during pregnancy. They also found that the offspring of smoking MZ twins weighted significantly less compared with offspring of the non-smoking co-twins.

Epilepsy. This twin study is the only reported study where twin registers from two different countries, namely Norway and Virginia, are combined. In order to examine the importance of genetic and environmental factors in the etiology of epilepsy and febrile seizures, the total of 11,175 twin pairs from Part II and 9 733 pairs from the Virginia Twin Registry were contacted (Corey et al., 1991). The Virginia Twin Registry is based on birth records of both same-sexed and opposite-sexed twin pairs born in Virginia between 1915 and 1975. Health history information was solicited from 8395 Norwegian twin pairs and 5,957 Virginia-born pairs. Zygosity information was made on the basis of a questionnaire.

There was a history of epilepsy in one or both members of 280 pairs and febrile seizures were reported in 252 pairs. Analyses of questionnaire data revealed no significant difference in concordance rates between Virginian and Norwegian twins for either of the two disorders. The concordance rate of epilepsy was 19% in 79 MZ twins and 7% in 201 DZ twins. For febrile seizures the average concordance rate was 33% in 95 MZ twins and 11% in 157 DZ twins. The results provided evidence that genetic factors have a role in the expression of epilepsy and febrile seizures.

Left-handedness. This study is different from the others in the sense of sample selection. All same-sexed twin pairs within the age group 30 to 60 years, living in a defined county of Norway, were selected from the Norwegian Twin Panel, and requested by mail to participate. In total 469 MZ pairs and 507 DZ pairs responded positively. The sex distribution was equal in both groups. Zygosity was earlier determined by Magnus et al. (1983), and is described separately in this paper. Information about the dominant writing-hand was collected from the twin pairs, their parents, spouses and children. No significant associations for twins were found, indicating that there is no genetic effect for left-handedness (Tambs et al., 1987).

Cross-checking the Twin Register Against Another Register

In the reported cancer study the method used was cross-checking the twin register against a disease register in some sort of a prevalence study. If the registers are ready to be matched, this is less time consuming compared to the other methods earlier described.

Cancer. Iversen et al. (2001) examined cancer risk among twins compared with the general population. From Part I of the Twin Registers computerized by Bergem (1997a), 12,000 same-sexed and opposite-sexed twin pairs identified with personal identity numbers born between 1905 and

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1945 were matched against the National Cancer Registry, which is practically complete for all kinds of solid tumours. A substantial part of married women changing their family name through marriage, were lost in the sampling procedure when cross-checking names from the twin register with the personal identity number register. To improve the match of the two registers, the whole twin register was washed out manually by Bergem and co-workers. Since Part I of the twin register lacked information about zygosity, the zygosity of this actual twin sample was unknown.

A reduced risk of malignant disease among twins for all tumour sites combined was demonstrated, standardized incidence rate (SIR) 0.90 (95% CI 0.85–0.94) in females and 0.95 (95% CI 0.90–0.99) in males. A significant reduction of colon cancer in male twins and of rectal cancer in female twins was observed. In both sexes, there was a reduced incidence of malignant melanomas of the skin and of non-solid tumours (leukaemia, lymphoma and myeloma). In females, the incidence of tumours of the central nervous system and lungs were also reduced. Except for ovary cancer, no other cancer showed a significant increased incidence.

Current Major Research Focus and Future Plans

Currently, there is a collaboration project between the National Institute of Public Health, the Department of Psychiatry and the Department of Psychology, where all types of *DSM-IV* Axis I and Axis II disorders are studied in a large sample of several thousand twin pairs. Genome testing is planned as well.

The twin study on senile dementia is not finished. More data will be analyzed regarding computer tomography, cerebral autopsy, environmental risk factors and candidate genes. When it comes to DNA testing of demented twins, there is an ongoing international collaboration between Norway, Sweden and other countries. Further, the offspring of all demented twin pairs have been identified, and there are plans to start a twin/family genetic study of dementia. A Nordic collaboration of twin studies have been discussed, similar to the Norway-Virginia project. For senile dementia, this could easily be done, because the methods and samples are quite similar in Norway and Sweden.

A large part of the current major research has its base in the youngest population of the Norwegian Twin Register, and will be described elsewhere.

In this paper, the major twin studies derived from the Norwegian Twin Register are described. Although there are some limitations in sampling and diagnostic procedures, these studies have contributed to the understanding of genetic influence and environmental risk factors in the development of different diseases. However, the cancer study suffered from the fact that the Norwegian Twin Registers is divided into three parts. The three different organizations responsible for the different parts of the register do not collaborate very well. Because of this, the cancer study did not have access to zygosity data, and they did not get permission from the authorities to contact the twins personally. A plan for the near future is to organize the three parts of the twin register appropriately, in order to run one complete twin register covering every birth year from 1900 up to now, and also to fill out the missing 7 years. The register should be a research register, possible to use in every serious research project, and run by a coordinated steering group.

Part III of the register, derived from the Medical Birth Registry of Norway (MBRN) and run by the Norwegian Institute of Public Health, is already organized very well. Norway has a number of epidemiological registries with a rather loose affiliation to the central authorities. The MBRN is situated between the central health authorities and the Central Bureau of Statistics on one side and various research centres on the other side. A paramount aim of the MBRN is that the users should have access to data, both for health management and health research purposes. This unique organizational position is one reason why the MBRN is probably the medical birth registry in the Nordic countries with the widest application of its data both in research and management (Bakketeig, 2000; Irgens, 2000).

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