International Journal of Epidemiology

Vol. 24, No. 3
Printed in Great Britain

The New Danish Twin Register: Establishment and Analysis of Twinning Rates

KIRSTEN OHM KYVIK,* ANDERS GREEN* AND HENNING BECK-NIELSEN†

Kyvik K O (Genetic Epidemiology Research Unit, Institute of Community Health, University of Odense, Odense, Denmark), Green A and Beck-Nielsen H. The new Danish Twin Register: Establishment and analysis of twinning rates. *International Journal of Epidemiology* 1995; **24:** 589–596.

Background. Twin registers provide a valuable source for research into disease causation. The existing population-based registers comprise mostly old twins. In order to be able to study diseases which occur in childhood and youth a new Danish twin register has been established.

Methods. The register is based on the Danish Civil Registration, with information on number of twin births from the Danish Vital Statistics Office as the source of validation. All twins resident in Denmark at 1 March 1991 were sent a one-side questionnaire asking about diabetes, willingness to participate in other research projects and similarity in the twins.

Results. The register, comprising 20 888 twin pairs, covers 74.4% of all twin pairs born 1953–1967 (incl.) and 97.4% of those born 1968–1982 (incl.). The response rate to the questionnaire study was 92.3%. The responders represented 19 180 twin pairs distributed as 5304 monozygotic pairs, 6861 same-sex dizygotic pairs, 6244 opposite-sex dizygotic pairs and 771 pairs of unknown zygosity. Of the respondent twins, 96% declared their willingness to participate in additional studies. An analysis of trends in the twinning rates for the years 1968–1982 showed that the rate of monozygotic twinning is increasing and the twinning rate of opposite-sex twin pairs is decreasing.

Conclusions. Earlier estimated trends in twinning rates have been confirmed. Due to the high response rate and opportunities for linkage with other Danish registers, the present material provides a valuable resource for twin studies in diseases and human traits.

Since the days of Sir Francis Galton[1] research in twins has been an accepted method of discriminating between the relative contribution of genetic and environmental factors to phenotypic variance.

The biological mechanisms behind multiple births are largely unknown. There is evidence that during at least the last 20 years there has been a decreasing rate of dizygotic (DZ) and an increasing rate of monozygotic (MZ) twin births.[2] Most studies have estimated MZ and DZ twinning rates indirectly only, by Weinberg's rule, due to lack of reporting of zygosity in the vital statistics. Weinberg's rule states that the total number of DZ twin pairs is twice the number of opposite-sex (OS) twin pairs; the rest of the total number of twin pairs being MZ.[3] The application of this rule has been questioned.[4] Further elucidation of the possible changes in twinning rates and the validity of Weinberg's rule requires access to a large and population-based sample of twins with established zygosity diagnosis.

Research in twins has been subject to criticism due to potential biases.[5] Twins experience a different perinatal, and in some cases postnatal (e.g. family size), environment from singletons. The implicit assumption that the intra-pair difference in environment is approximately similar in monozygotic and dizygotic pairs has also been regarded with concern. Possibly, such biases may be of greater importance when studying psychological or behavioural traits as compared with disease.

A more serious bias concerns the ascertainment of twins for a study. Case stories have only limited value, showing a tendency towards an overrepresentation of MZ and concordant twin pairs.[6] Series of self-reported twins have been a popular method of identifying twin cohorts with specific diseases, but self-selection is a very serious potential bias. The validity of results from studies of twins performed in consecutive patient data depends on to what extent the twin pairs may be regarded as representative. Population-based twin

* Genetic Epidemiology Research Unit, Institute of Community Health, University of Odense, Odense, Denmark.
† Department of Endocrinology (M), Clinical Research Institute, Odense University Hospital, Odense, Denmark.
Reprint requests to: Kirsten Ohm Kyvik, Genetic Epidemiology Research Unit – ISH, Winsløwparken 15, DK-5000 Odense C, Denmark.

registries avoid these biases.[7] Due to the complete registration of the populations in the Scandinavian countries, population-based twin registries have existed in Norway, Sweden, Finland and Denmark for several decades.[8–11] With the exception of a young cohort of twins in the Finnish Twin Register,[12] these registries mostly cover twins born earlier in this century according to published reports. For example, the Danish Twin Register[6,8] has been established on the basis of information from parish registers and the register comprises the birth cohorts 1870–1930.

The unavailability of hospital records, the changing criteria for the diagnosis and classification of many diseases, and the many twins unaccessible because of death make the above-mentioned registries less suitable for studies of diseases which manifest early in life. Today, research into disease causation will often require detailed clinical data for assessment of diagnosis and classification, as well as access to biological samples (DNA, serum, tissue specimens).

In 1990, we decided to establish a population-based register of young Danish twins in order to investigate the genetic contribution of insulin-dependent diabetes mellitus and provide a tool for future research into the interaction between genes and environment in various diseases and traits. We here report the establishment and basic characteristics of this new Danish twin register, together with an analysis of the secular trend in twinning rates, based on established zygosity diagnosis.

MATERIALS AND METHODS

The Danish Civil Registration System

We decided to utilize the Danish Civil Registration System (CRS), which was established in 1968, to ascertain twins. In Denmark every newborn baby and every new inhabitant is assigned a unique 10-digit identification number at birth or when reporting name and address to the national registration office, which is compulsory. The first six digits indicate the person's date of birth (day-month-year), the following three digits represent a serial number to distinguish between people born on the same day, and the last digit is a checking number for coding and furthermore indicates the sex, i.e. women being assigned an even and men an odd number, respectively.

From the start in 1968 the CRS registered all living Danish inhabitants and connected family members by means of the address. As a rule, this link was erased when the child reached 18 years, got married or moved away from home, and this turned out in many ways to be impractical. After 1978 children were instead linked to the mothers' identification number and this connection will be maintained for the future. The CRS has succeeded in having all children born from 1968 and forwards linked to the biological or adoptive mother. They are now 'working their way backwards' through the earlier birth cohorts trying to connect families by means of the national registration offices and parish registers and re-establish hidden links between families (personal communication – CRS).

Use of the Civil Registration System in this Study

In 1991, when this study commenced, the CRS offered to identify twins born after 1952, by means of the mother. The system was programmed to identify all women who in the period 1 January 1953 to 31 December 1982 had given birth to more than one child on the same day (+/– one day in order to find twins born on either side of midnight). The cutoff was chosen at 1982, because we wanted the twins to be old enough to participate in the decision as to whether they were to participate in this and future studies. These children were then identified and their name, address, birth data, civil registration number and vital status sent to us.

Additional Sources of Twins

It turned out that the CRS had not been able to identify nearly all twins from the period 1 January 1953 to 31 December 1968 and especially the birth cohorts 1953–1960 (incl.) were poorly covered. We decided to ascertain as many twins as possible from two alternative sources which were available from earlier studies at the Genetic Epidemiology Research Unit. These two alternative sources were not computerized and data had to be sought manually.

One source comprised a register of twins who had appeared before a Conscript Board, which all male Danish citizens have to do before their 20th birthday. Since 1948 all conscripts have been asked if they are twins and, if so, to fill in a short questionnaire to be sent to the Genetic Epidemiology Research Unit. This source provided several male–male (MM) and OS pairs.

Another source comprised some old data lists of same-sex (SS) twins born between 1943 and 1968 and living in the Copenhagen area in 1969. These twins had been identified as part of a study of febrile convulsions.[13] We used this additional source for twin pairs born between 1 January 1953 and 31 December 1960. A few twin pairs were enrolled after self-referral, as a consequence of publicity for the study.

Questionnaire Study

All twins who were alive and resident in Denmark (including Greenland) on 1 March 1991 were sent a one-side questionnaire in which they were asked about the

TABLE 1 *Questions of similarity used in questionnaire study in the new Danish Twin Register*

Are/were you and your twin as like as	☐ Two peas in a pod ☐ Ordinary sibling ☐ Not at all ☐ Do not remember
Are/were you mistaken by family and friends	☐ Yes ☐ No ☐ Do not remember
Are/were you mistaken by teachers and schoolmates	☐ Yes ☐ No ☐ Do not remember
Do/did you have the same eye and hair colour	☐ Yes ☐ No ☐ Do not remember

presence of diabetes, willingness to take part in other questionnaire studies, and some questions on similarity and mistaken identity. They were also asked about their co-twin's name and address. One reminder was sent to non-responders.

Zygosity Diagnosis

Zygosity was based on the questions on similarity (Table 1), which is a well-established procedure in questionnaire studies.[14] Based on the answers to these questions the zygosity was established as MZ or DZ. It has earlier been shown that being as like as 'two peas in a pod' will classify most MZ correctly.[15] All twins answering yes to this question, to at least one of the questions of being mistaken and to having same eye and hair colour were classified as MZ. Twins answering yes to being as alike as ordinary siblings, to both questions of being mistaken and to having same eye and hair colour were also classified as MZ. The rest were classified as DZ and all inconsistent answers, or disagreeing answers between co-twins implied classification as being of unknown zygosity (UZ). The validity of this method has earlier been shown to be more than 90% for all ages.[8,15–17] In twin pairs where only one co-twin responded, the zygosity was based on this one answer which is regarded as a reliable method.[15]

Reference Source

The validity of the ascertainment of twins was assessed from the Danish vital statistics where the annual number of births in Denmark is recorded. It is compulsory for midwives to report all births, including stillbirths, to Danmarks Statistik (the National Bureau of Statistics), which publishes yearly reports of the complete numbers of births in Denmark, including twin births.

Statistical Methods

Chi-square tests were used to analyse non-responders versus responders, for sex, zygosity- and age-distribution. The possible linear trends in twinning rates were analysed by means of a χ^2 test for linear trend in proportions considering the twin births as the proportion of all births. The twin register does not approach completeness until 1968, and the tests for trend are therefore done for the twin pairs born during the period 1968–1982 only.

Ethical Consideration

This study was evaluated and approved by the Central Scientific-Ethical Committee of Denmark. Furthermore, approval was obtained from the Danish Data Protection Agency.

RESULTS

Ascertainment of the Twin Material

In all, 20 928 twin pairs, 169 triplets and four quadruplets were ascertained. The triplets and quadruplets will not be considered further in this report. Furthermore, it appeared from the subsequent questionnaire information that 40 presumed twin pairs were in fact not twins and had to be excluded. This was due to administrative problems: people who live abroad temporarily, but are registered in CRS as emigrated are assigned a new identification number upon return to Denmark and thus have two; children of refugees or immigrants with missing birth certificates sometimes have been assigned the same birth date; adopted children with identical birth dates also seem to be twins. The final number of twin pairs is listed according to ascertainment source in Table 2. According to the Danish vital statistics, 24 188 pairs of twins were born during the period of ascertainment in our study. With adjustment for twin pairs born outside Denmark our material comprises 20 203 pairs, corresponding to a mean ascertainment probability of 83.5% (Table 3). The estimated completeness of the study material increases from about 59% for birth cohorts in 1953–1957 to more than 95% for the birth cohorts after 1967.

The sex distribution in the total register is 21 744 (52.1%) males, 20 022 (47.9%) females and 14 of unknown sex (dead very shortly after birth). This distribution corresponds with 6720 OS pairs, 7506 male–male (MM) pairs and 6657 female–female (FF) pairs. The expected distribution, by applying Weinberg's rule,[3] should comprise 7443 MZ and 13 440 DZ twin pairs.

TABLE 2 *Summary of the study material comprising the new Danish Twin Register*

Year	Principal source	Supplementary sources			Total
	Civil Registration System	Conscript register	Copenhagen twin study	Volunteers	
1953–1957	2236	389	280	82	2987
1958–1962	3662	47	25	13	3747
1963–1967	4146	0	0	4	4150
1968–1972	3658	0	0	0	3658
1973–1977	3376	0	0	0	3376
1978–1982	2969	0	0	1	2970
1953–1982	20 047	436	305	100	20 888

TABLE 3 *Validation of identification procedure used in the new Danish Twin Register. Based on identified twin pairs born in Denmark and thereby included in the Vital Statistics*

Year	Identified	Vital Statistics	Coverage (identified/ vital statistics in %)
1953–1957	2933	4996	58.7
1958–1962	3657	4649	78.7
1963–1967	4021	4687	85.8
1968–1972	3536	3666	96.5
1973–1977	3232	3309	97.7
1978–1982	2824	2881	98.0
1953–1982	20 203	24 188	83.5

Response to the Questionnaire Study

Of the total number of twin individuals (n = 41 776), 1574 were dead, 1394 had emigrated and 193 had a protected address. Further, 109 were impossible to trace. Among the remaining 38 506 individuals, 35 528 responded to the questionnaire (92.3% after one reminder). The responders represented 19 180 twin pairs, of which 16 348 pairs comprised both partners.

The distribution of the responding pairs according to zygosity classification is shown in Table 4. The proportion of SS pairs is larger than expected based on the OS pairs. Application of Weinberg's rule,[3] ignoring UZ pairs, shows a statistically highly significant deviation from the expected distribution (χ^2, 1d.f. = 165.8, $P < 0.0001$), with a relatively low proportion of MZ pairs and a relatively high proportion of SS pairs.

There were only 8% non-responders in this study (Table 5). In comparison with the responders this group

TABLE 4 *Distribution of zygosity among responders to questionnaire in the new Danish Twin Register*

	Monozygotic pairs	Dizygotic pairs		Unknown zygosity pairs	Total no. of pairs
		Same sex	Opposite sex		
Both twins potentially available	5108 (28.5) [96.3]	6565 (36.6) [95.7]	5760 (32.1) [92.2]	493 (2.8) [64.0]	17 926 (100.0) [93.5]
One twin dead	82 (10.7) [1.6]	136 (17.7) [2.0]	299 (39.1) [4.8]	250 (32.5) [32.4]	768 (100.0) [4.0]
One twin emigrated	114 (23.4) [2.1]	160 (32.9) [2.3]	185 (38.0) [3.0]	28 (5.7) [3.6]	487 (100.0) [2.5]
Total	5304 (27.6) [100.0]	6861 (35.8) [100.0]	6244 (32.6) [100.0]	771 (4.0) [100.0]	19 180 (100.0) [100.0]

() = % of row total.
[] = % of column total.

TABLE 5 *Characteristics of individual non-responders versus responders*

	Non-responders	%	Responders	%
Sex (male/female)	2012/966	(67.6/32.4)	17 905/17 623	(50.9/49.1)
Zygosity				
Monozygotic	268	(8.9)	10 144	(28.6)
Dizygotic same sex	549	(18.4)	12 877	(36.2)
Dizygotic opposite sex	695	(23.3)	11 310	(31.8)
Unknown zygosity	1466[a]	(49.4)	1197	(3.4)
Total	2978	(100.0)	35 528	(100.0)
Age distribution				
9–13	340	(11.4)	5091	(14.4)
14–18	492	(16.5)	5673	(16.0)
19–23	530	(17.9)	6004	(17.0)
24–28	674	(22.6)	7121	(20.0)
29–33	519	(17.4)	6510	(18.3)
34–38	423	(14.2)	5129	(14.3)
Total	2978	(100.0)	35 528	(100.0)

[a] Included all non-responders where no information on zygosity is available.

comprises more men than women (χ^2, 1d.f. = 323.54, $P < 0.0001$), fewer MZ and more DZ-OS pairs (χ^2, 2d.f. = 143.56, $P < 0.0001$). The age distribution is slightly different (χ^2, 5d.f. = 28.77, $P < 0.0001$), but this significance is possibly due to the very large number of people and not to a real biological difference. It is known from other twin studies that women and MZ pairs are better responders,[6,18] but due to the low proportion of non-responders, this bias is possibly not a serious one. The group of non-responders also comprise more twins where one partner is dead or has emigrated, possibly due to a feeling in the twins that their answer was worthless without that of the twin partner.

Of the responders 3.9% were unwilling to participate in other studies. This group was also characterized by more men (χ^2, 1d.f. = 95.27, $P < 0.0001$) and fewer MZ (χ^2, 1d.f. = 373.27, $P < 0.0001$) than among those willing to participate in other studies.

Twinning Rates According to Zygosity

Figure 1 shows the trends in live-birth rates and twinning rates as reported in official Danish vital statistics for the period 1953–1982 (incl.). Both the overall twinning rate and the live-birth rate have declined gradually. Figure 2 shows the estimated twinning rates

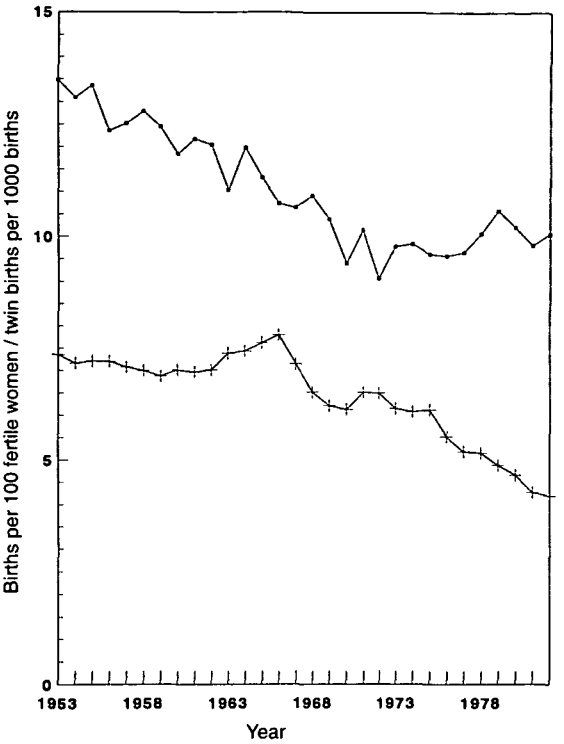
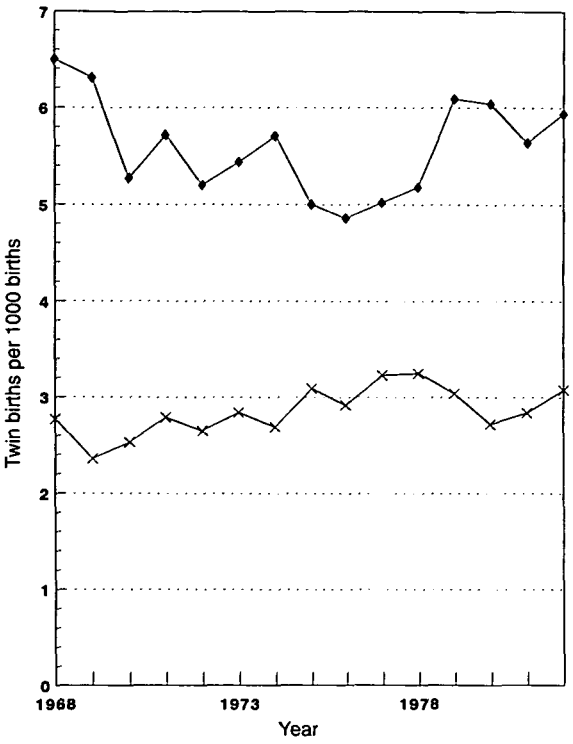


FIGURE 1 *Birth and twinning rates in Denmark 1953–1982 (incl.) based on vital statistics*

according to zygosity. Because of the deficit in our study material for birth cohorts before 1968 (Table 3), we have restricted our analysis to twins born during the period 1968–1982 (incl.). Whereas the MZ twinning rate increased gradually and statistically significantly (χ^2 for linear trend, 1d.f. = 8.40, $P < 0.005$), the DZ twinning rate (sex composition not considered) showed no consistent trend. The DZ twinning rate has been further studied by separation according to sex composition (Figure 3). This analysis showed a significant decline in the DZ-OS twinning rate (χ^2 for linear trend, 1d.f. = 14.355, $P < 0.001$) and no consistent trend in the DZ-SS twinning rate (χ^2 for linear trend, 1d.f. = 3.131, $P > 0.05$).

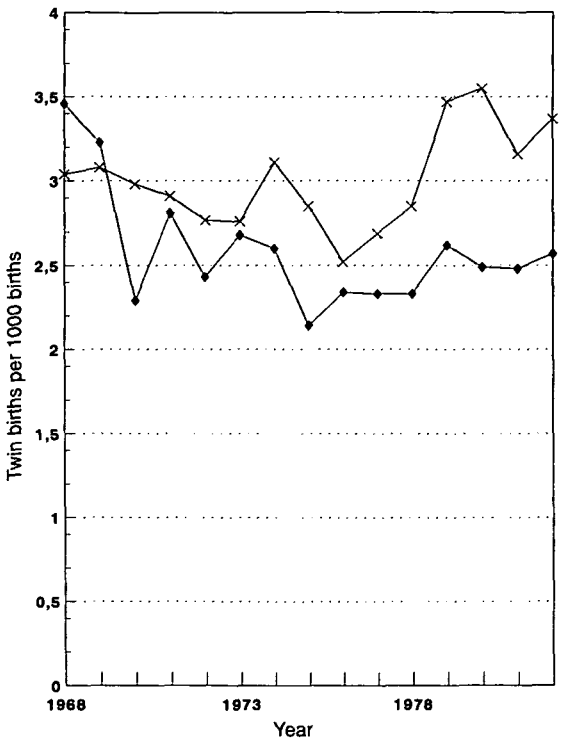
DISCUSSION

This twin register has been compiled from administrative population registries, and not from registries based on health status. Therefore, biases caused by selection according to health status and self-referral have been avoided. Furthermore, the Danish population



× *Monozygotic rate*, ◆ Dizygotic rate

FIGURE 2 *Estimated twinning rates by zygosity in Denmark 1968–1982 (incl.)*



× *Dizygotic same-sexed rate*, ◆ Dizygotic opposite-sexed rate

FIGURE 3 *Estimated dizygotic twinning rates in Denmark 1968–1982 (incl.)*

registration system is generally believed to be complete and of high validity. Nevertheless, the cohorts 1953–1967 (incl.) possibly represent to a certain degree survivors of the first years of life.

The lesser degree of ascertainment of twins born in the period 1953–1967, and especially 1953–1959, has several explanations. Some of the deficit is no doubt related to incomplete information in the CRS on family structure, emigration and mortality for the population born before 1968. It has been possible to overcome these biases only partly by the use of the supplementary ascertainment sources (Table 2).

Early deaths in twins represent probably a major reason for the deficit in our study material for the period 1953–1967. The CRS was established in 1968, which means that twin pairs being separated before this year were not included. Furthermore, the official vital statistics depend on information from midwives who report all births, regardless of outcome, anonymously. The CRS data on origins of births come from all parishes that are informed about the birth by the parents and the maternity ward/midwife. The parish thereafter reports the births to the local branch of the national registration office, who then report on-line to CRS where the child is given an identification number. Stillborn children are not reported to the CRS or assigned a unique identification number, but children alive at birth, even if only for a short time, are. Furthermore, in some periods these children have not been given personal identification numbers for emotional reasons. However, this practice has now been terminated (personal communication by the parish clerk, St Ansgar's parish, Odense). Twin pairs where one or both are stillborn might therefore be registered in the vital statistics as a twin pair, while the CRS have had no possibility to register or connect them. The death of twins is only reported on an individual basis in the vital statistics, without possibilities of linking twin partners.

If it is assumed that twins born during the period 1953–1967 experienced a mortality rate equal to that of 1968 we may have missed dead twins representing about 10% of the twins born in that period. This is probably an underestimate because of the decline in perinatal

mortality of twins during this period.[19–24] The young Finnish cohort[12] and our twin register represent the only updated population-based materials of young twins published. These are also the only registries which in principle are following the twins from birth. In the young Finnish cohort, the distribution according to zygosity has been estimated by Weinberg's rule, and to our knowledge no study has reported any contact with these twins. The completeness of the young part of the Finnish twin register is 83.1% and 96.5% for the birth cohorts 1958–1973 and 1974–1986, respectively.[12] These figures are very similar to those estimated for our study material (Table 3).

Our study has demonstrated that although the twinning rate in general is decreasing, the MZ rate is increasing and that behind fluctuations in the DZ twinning rate may be found a decrease in the OS rate. It should be kept in mind though, that the zygosity determination by questionnaire, feasible as it is for studies of this size, may affect the patterns of zygosity, although the frequency of misclassification is usually of the order 5%. It has been shown previously that the questionnaire method is sufficiently accurate for the ages 6 months to 6 years[17] and for ages ⩾33 years.[8,15,16] There is no reason to suspect that it should not be so in the age group 9–23 years, which are the ages used for our analysis of twinning rates. The most certain zygosity-specific twinning rates are those of the OS-DZ twins and if changes in the SS-DZ and MZ twinning rates are due to misclassification, we have at least made a conservative estimate of these changes. Improvement in maternal care since the 1960s is possible affecting the outcome of twin pregnancies and thereby the MZ twinning rate, which is not dependent on the age or previous number of pregnancies of the mother. Possibly, calendar time trends in maternal age might be the explanatory factor in describing the fluctuating DZ twinning rate, but reported studies have found inconsistent conclusions as to the effect of maternal age.[24–31]

Other studies have proposed that the widespread use of oral contraceptives (OC) may explain the trends in the twinning rates.[32] The use of ovulation induction and in vitro fertilization is known to induce both MZ and DZ twinning pregnancies.[32] It is unknown whether these practices have had any noticeable effect on the reported twinning rates. Through record linkage with other Danish registries, such as the Register of Births, the Register of Causes of Deaths and the Register of Congenital Malformations, data on the parents' age and work, on the circumstances of birth and causes of death will be available for future research in the biological aspects of the twinning phenomenon.

The observed distribution of MZ, SS-DZ and OS-DZ pairs deviated from that expected by Weinberg's rule. We have no immediate explanation for the discrepancy. The time trends in the zygosity-specific twinning rates indicate that estimation of distribution by zygosity according to Weinberg's rule will yield different results for different time periods. Therefore, application of Weinberg's rule should be interpreted with caution.

We conclude that we have established a material of approximately 20 000 Danish twin pairs, representative for the birth cohorts 1953–1967 and almost complete for the birth cohorts 1968–1982. As many as 92% of the twins responded, and of these more than 96% have declared their willingness to contribute to further research. Therefore, our twin register constitutes a unique resource for future research in twins.

ACKNOWLEDGEMENTS

This study has been supported by The Danish Diabetes Association; The Clinical Research Institute, Odense University Hospital; The Danish Medical Association Research Fund; Poul & Erna Sehested Hansens Foundation; Fonden til Lægevidenskabens Fremme; Nordic Insulin Foundation Committee; Overlægerådets Legatudvalg, Odense University Hospital; P Carl Petersens Foundation; Novo's Foundation Committee. We wish to thank Dr Niels Holm for allowing us to use the manual registers at the Danish Twin Register as secondary data sources and Mrs Elise Beck-Nielsen for excellent secretarial assistance.

REFERENCES

[1] Galton F. *Inquiries into Human Faculty and its Development.* London: J M Dent & Co., 1883.

[2] Little J, Thompson B. Descriptive epidemiology. In: MacGillivray I, Campbell D M, Thompson B (eds). *Twinning and Twins.* Chichester: John Wiley & Sons, 1988, pp. 37–66.

[3] Weinberg W. Beiträge zur Physiologie und Pathologie der Mehrlingsgeburten beim Menschen. *Archiv für die gesamte Physiologie des Menschen und der Tiere* 1902; **88:** 346–430.

[4] James W H. Is Weinberg's differential rule valid? *Acta Genet Med Gemellol Roma* 1979; **28:** 69–71.

[5] Bryan E M. The role of twins in epidemiologic studies. *Paediatr Perinat Epidemiol* 1992; **6:** 460–64.

[6] Harvald B, Hauge M. Hereditary factors elucidated by twin studies. In: Neel J V, Shaw M W, Schull W J (eds). *Genetics and the Epidemiology of Chronic Diseases.* Washington DC: US Department of Health, Education and Welfare. Public Health Service Publication no. 1163, 1965, pp. 61–76.

[7] Nance W E. The value of population-based twin registries for genetic and epidemiologic research. In: Banbury Report 4. *Cancer Incidence in Defined Populations.* Cold Spring Harbour Laboratory, 1980, pp. 215–32.

[8] Hauge M. The Danish twin register. In: Mednick S A, Baert A E, Bachmann B P (eds). *Prospective Longitudinal Research.*

An Empirical Basis for the Primary Prevention of Psychological Disorders. Oxford: Oxford University Press, 1981, pp. 217–21.

[9] Kaprio J, Sarna S, Koskenvuo M *et al*. The Finnish Twin Registry. Formation and compilation, questionnaire study, zygosity determination procedures, and research program. In: Nance W E (ed.). *Twin Research*. Proceedings of the second international congress of twin studies. Part B. Biology and epidemiology. New York: Alan R Liss, 1978, pp. 179–84.

[10] Kringlen E. Norwegian Twin Registers. In: Nance W E (ed.). *Twin Research*. Proceedings of the second international congress of twin studies. Part B. Biology and epidemiology. New York: Alan R Liss, 1978, pp. 185–87.

[11] Cederlöf R, Lorich U. The Swedish Twin Registry. In: Nance W E (ed.). *Twin Research*. Proceedings of the second international congress of twin studies. Part B. Biology and epidemiology. New York: Alan R Liss, 1978, pp. 189–95.

[12] Kaprio J, Koskenvuo M, Rose R J. Population-based twin registries: Illustrative applications in genetic epidemiology and behavioral genetics from the Finnish twin cohort study. *Acta Genet Med Gemellol Roma* 1990; **39:** 427–39.

[13] Schiöttz-Christensen E. Computer selection of twin pairs. *Acta Genet Med Gemellol Roma* 1970; **19:** 341–43.

[14] Gedda L. World Health Organization. The use of twins in epidemiological studies. Report of the WHO Meeting of Investigators on Methodology of Twin Studies. *Acta Genet Med Gemellol Roma* 1966; **15:** 109–28.

[15] Magnus P, Berg K, Nance W. Predicting zygosity in Norwegian twin pairs born 1915–1960. *Clin Genet* 1983; **24:** 103–12.

[16] Cederlöf R, Friberg L, Jonsson E *et al*. Studies on the similarity diagnosis in twins with the aid of mailed questionnaire. *Acta Genet Stat Med* 1961; **11:** 338–62.

[17] Bønnelykke B, Hauge M, Holm N, Kristoffersen K, Gurtler H. Evaluation of zygosity diagnosis in twin pairs below age seven by means of mailed questionnaire. *Acta Genet Med Gemellol Roma* 1989; **38:** 305–13.

[18] Friedman G D, Lewis A M. The Kaiser-Permanente Twin Registry. In: Nance W E (ed.). *Twin Research*. Proceedings of the second international congress of twin studies. Part B. Biology and epidemiology. New York: Alan R Liss, 1978, pp. 173–77.

[19] Botting B J, Davies I M, Macfarlane A J. Recent trends in the incidence of multiple births and associated mortality. *Arch Dis Child* 1987; **62:** 941–50.

[20] Puissant F, Leroy F. A reappraisal of perinatal mortality factors in twins. *Acta Genet Med Gemellol Roma* 1982; **31:** 213–19.

[21] Moreault L, Marcoux S, Fabia J *et al*. Time trends in characteristics and outcome of twin pregnancies. *Acta Genet Med Gemellol Roma* 1991; **40:** 181–92.

[22] Hartikainen Sorri A L, Rantakallio P, Sipila P. Changes in prognosis of twin births over 20 years. *Ann Med* 1990; **22:** 131–35.

[23] Lumme R H, Saarikoski S V. Perinatal deaths in twin pregnancy: a 22-year review. *Acta Genet Med Gemellol Roma* 1988; **37:** 47–54.

[24] Campbell D M, MacGillivray I. Outcome of twin pregnancies. In: MacGillivray I, Campbell D M, Thompson B (eds). *Twinning and Twins*. Chichester: John Wiley & Sons, 1988, pp. 179–202.

[25] Hogberg U, Wall S. Secular trends of twinning rate in Sweden. *J Biosoc Sci* 1992; **24:** 487–96.

[26] Rachootin P, Olsen J. Secular changes in the twinning rate in Denmark 1931 to 1977. *Scand J Soc Med* 1980; **8:** 89–94.

[27] Mosteller M, Townsend J I, Corey L A *et al*. Twinning rates in Virginia: secular trends and the effects of maternal age and parity. *Prog Clin Biol Res* 1981; **69A:** 57–69.

[28] MacGillivray I. The probable explanation for the falling twinning rate in Scotland. *Prog Clin Biol Res* 1981; **69A:** 15–19.

[29] Orlebeke J F, Eriksson A W, Boomsma D *et al*. Changes in the DZ unlike/like sex ratio in The Netherlands. *Acta Genet Med Gemellol Roma* 1991; **40:** 319–23.

[30] Elwood J M. Changes in the twinning rate in Canada 1926–70. *Br J Prev Soc Med* 1973; **27:** 236–41.

[31] Brackenridge C J. The secular variation of Australian twin births over fifty years. *Ann Hum Biol* 1977; **4:** 559–64.

[32] Campbell D M. Aetiology of twinning. In: MacGillivray I, Campbell D M, Thompson B (eds). *Twinning and Twins*. Chichester: John Wiley & Sons, 1988, pp. 27–36.

(Revised version received December 1994)