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# The Swedish Young Male Twins Register: A Resource for Studying Risk Factors for Cardiovascular Disease and Insulin Resistance

Finn Rasmussen<sup>1,2</sup> and Malin Johansson-Kark<sup>2</sup>

<sup>1</sup>Division of Epidemiology, Norrbacka, Karolinska University Hospital, SE-171 76 Stockholm, Sweden

<sup>2</sup>Division of Epidemiology, Institute of Environmental Medicine, Karolinska Institute, SE-171 76 Stockholm, Sweden

A new Swedish twin register was created in 1998. All male twins born in Sweden 1973–1979 were identified in the Swedish Medical Birth Register. 3566 twins (1783 pairs) who were alive and residents of Sweden in 1997 were included in the new register. Data on birthweight, birthlength, gestational age, and so forth, were obtained from the Medical Birth Register. Record linkage was effected with the Military Service Conscription Register for the years 1991–1999. Anthropometrical data and information on blood pressure were obtained from this latter source. In 1998 a questionnaire was mailed to all twins in the register. Questions were posed about zygosity, socioeconomic conditions, lifestyle factors (physical activity, smoking habits, etc.), body shape and body size. Complete responses were obtained from 2654 twins (1327 pairs). In 2002 the cohort is being followed-up by a more extensive mailed questionnaire. Data will be collected about socioeconomic conditions, lifestyle, eating behaviour (TFEQ), body size and body shape. In the next few years genomic DNA will also be collected from buccal mucosa (using brush techniques).

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Twin research has a long tradition in Sweden. A population-based twin register was initiated in Sweden as early as in the late 1950s (Cederlöf et al., 1961). During the following decades generations of researchers have contributed to the maintenance and development of this important resource for genetic epidemiologic research. A task force under the auspices of the National Research Council in Sweden has recently evaluated this large “old” twin register (Smedby et al., 2000). In general terms, the evaluation was positive and the reviewers agreed that the register should continue to receive substantial funding. Most, but not all, research conducted on this “old” twin register has addressed health problems and diseases in people of middle age or older.

The current authors set up a new, smaller and more focused twin register in 1997. The driving force behind it was strong research interest in behavioural and biological risk factors for cardiovascular disease and insulin resistance among young adults in Sweden. One objective is to test the fetal-origins hypothesis in a twin population. Up to now, the authors have published a paper on the relation between fetal growth and systolic blood pressure (Johansson-Kark et al., 2002) and another on the relationship between fetal growth and body mass index in young adulthood

(Johansson & Rasmussen, 2001). A second objective of the new twin register is to study behavioural and biological risk factors for insulin resistance. As described in greater detail below, a new survey of the twin cohort will be conducted in 2002. In a long-term perspective, the overall goal of the new register is to study the importance of behavioural, environmental and genetic factors in the pathogenesis of the metabolic syndrome (hypertension, insulin resistance, overweight, dyslipidemia) and coronary heart disease.

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## Components of the Young Male Twins Register

Over the last decade it has become increasingly difficult to obtain a high response rate in surveys of the general Swedish population. As a consequence, it is becoming more important to combine information from existing registers with specific information collected ad-hoc using questionnaires, telephone interviews, and/or clinical examinations.

### Identification of the Twin Cohort in the Medical Birth Register

As a first step in the creation of the present twin register, all male twins born in Sweden 1973 to 1979 were identified in the Swedish Medical Birth Register (MBR). The register covers over 99% of all births in Sweden (Cnattingius et al., 1990). 3936 male twins (1968 pairs) were identified in the MBR. Of these 3936 twins, 10 had died during the previous three years (1994–1997), and 251 did not have an identifiable address in Sweden. In late 1997, record linkage was effected with Sweden’s Register of the Total Population. This register, which is intended to include all individuals in Sweden with a residence permit, made it possible to identify all 1783 complete male twin pairs (3566 twins), born 1973 to 1979, of which both members were alive in 1997.

Values on the following variables were obtained from the MBR: date of birth, birth order, birthweight, birthlength, gestational age, mother’s parity, mother’s age, ICD diagnoses for maternal diseases in pregnancy or at birth,

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*Address for correspondence: Finn Rasmussen, Associate Professor, Division of Epidemiology, Norrbacka, Karolinska University Hospital, SE-171 76 Stockholm, Sweden. Email: finn.rasmussen@imm.ki.se*

and ICD diagnoses for any diseases among offspring. Information on stillbirths and perinatal deaths in the cohort was obtained from the MBR and Sweden's Cause of Death Register. Unfortunately, no reliable information is available on chorionicity in the MBR (Derom et al., 2001).

It has recently been shown that so-called "vanishing" of a co-twin in early pregnancy may be common (Pharaoh & Adi, 2000). But during 1973 to 1980 no ultrasound examinations were performed routinely, and vanishing twins would never have been detected. Thus, there may be surviving co-twins of vanishing twins among singletons in the MBR.

#### **Military Service Conscription Register**

In 1997 record linkage was effected with Sweden's Military Service Conscription Register (MSCR). The MSCR has nationwide coverage, and conscription data were obtained for the years 1991–1999. From the conscription examinations, performed at 18 years of age, data were obtained on height, weight, systolic blood pressure, diastolic blood pressure, muscle strength (a weighted mean for arm flexion, knee extension and handgrip), working capacity (as measured by cycle-ergometer test), and aerobic capacity. Among the 3566 twins, 55 (from 40 pairs) decided against being entered into the twin register. Data on height and weight were available in the MSCR for 3052 (88%) of the 3486 remaining twins. Information on systolic blood pressure was available for 3080 (88%) of the 3486 twins.

In Sweden military-service conscription examination is compulsory for all young men, and failure to turn up has legal consequences. A certificate issued by a physician stating a relevant severe diagnosis is required for any individual to be allowed to miss this examination. All young men are required to participate, even though some may not be enlisted for military service later on due to a severe chronic disease or disability.

#### **Mailed Questionnaire in 1998**

A questionnaire was mailed to 3566 twins (1783 pairs) in 1998. The questionnaire included items about zygosity, birthweight, birth order, chronic diseases and handicaps, use of prescription drugs, smoking habits, use of snuff (Swedish moist snuff), height, weight, perceived body size, diabetes among parents or grand parents diagnosed after age 40, occupation and educational level, occupational physical activity, physical activity during leisure time, amount of time spent at different levels of physical activity during leisure time, amount of time spent watching television, and social support (both emotional and practical). Twins who had not responded after two reminders were approached for interview by telephone.

Of the 3566 twins, 2806 (79%) responded to the questionnaire. Among all 1783 twin pairs, full sets of responses were obtained from 1327 (74%) complete twin pairs. Most twins responded to the questionnaire, but information was collected by telephone interview in the case of 313 individuals. Fifty-five twins from 40 pairs refrained from taking part in this cohort study. Fifty-seven twins could not be traced. One twin died in 1998, after the questionnaire had been mailed, and the co-twin did not reply. No reply was obtained from the remaining 646 twins.

#### **Zygosity**

The items on zygosity in the questionnaire have been widely used in twin research (Cederlöf et al., 1961; Pedersen & Lichtenstein, 2000), and were based on self-reports of a) degree of similarity in childhood, and b) difficulties teachers may have had in distinguishing between twins in school. The pairs where both twins reported "as like as two peas in a pod", and that teachers "always or nearly always" had problems in distinguishing between them were categorized as monozygotic (MZ). The pairs where both twins responded "no more alike than siblings in general" to the first question, and "seldom" or "never or almost never" to the second question were categorized as dizygotic (DZ). All remaining pairs were regarded as of uncertain zygosity (XZ). In 1998 no DNA was available for classification of twins as MZ or DZ. Included in the register are 888 MZ twins, 1118 DZ twins and finally 1480 XZ twins. Among the 1480 XZ twins there are 680 twins who did not answer the questionnaire in 1998.

#### **Data-Linkage Errors**

In Sweden, when an infant is a few weeks old, the Swedish civil-registration authorities assign a unique personal identification number to him or her. There is evidence that, for some twin pairs, this process leads to so-called "cross-over", meaning that the medical birth record of one twin in a pair is incorrectly allocated to the co-twin. Since linkage between the MBR and any other Swedish register (e.g., MSCR) is based on personal identification number, there is possibility of misclassification, and thereby underestimation of the strength of any statistical association found. The possible extent of cross-over was assessed by examining self-reported birthweight in relation to the birthweight reported in the MBR. Further details on the cross-over misclassification problem and how it can be taken into account are available elsewhere (Johansson & Rasmussen, 2001; Johansson-Kark et al., 2002). For the majority of twin pairs, consistency of information suggests that cross-over did not occur. However, in 59 twin pairs there was strong evidence of cross-over. For these 118 individuals, assumed cross-over was corrected by reassignment of birth-registry information on any one twin to its co-twin. In the cases of 671 twin pairs other inconsistencies between self-reported information and that from the MBR were identified. These 671 twin pairs were excluded from analyses in the two papers addressing the fetal-origins hypothesis based on the MBR and the MSCR (Johansson & Rasmussen, 2001; Johansson-Kark et al., 2002). It should be noted that cross-over misclassification is only a problem when the MBR is linked to another Swedish register (with personal identification number as header).

#### **Mailed Questionnaire in 2002**

The study population for this survey was delimited as follows. In principle, all twins eligible for the survey of 1998 were regarded as eligible for that of 2002. In 1998, 55 twins from 40 pairs refrained from taking part in the cohort study. In 1998, these 40 pairs had been excluded from any further investigation. There was also an exclusion of six pairs of twins due to severe handicap and inability in

answering the questionnaire in 1998. Twelve pairs with the death of one twin between 1998 and 2002 were also excluded. Thirty-five individuals had emigrated to another country and these were not included. Current mailing addresses were searched for the remaining 3415 numbers of twins. Six twins could not be traced. Accordingly, 3409 twins were eligible for the survey conducted in 2002.

The questionnaire to be used in 2002 is more extensive than that employed in 1998. Items include family type, education, occupation, and social network. Further questions are posed on lifestyle factors, (physical activity, eating habits, smoking, taking snuff (Swedish moist snuff), alcohol consumption, etc., and eating behaviours. Some of the questions from 1998 will be repeated in 2002, but many others are new. The questionnaire incorporates the Three Factor Eating Questionnaire (TFEQ; Karlsson et al., 2000), and also the Baecke questionnaire on physical activity (Philippaerts et al., 1999). Twins will also be requested to report their height, weight, and waist circumference. Perceived body size and shape are measured using nine outline drawings, illustrating "extremely thin" to "very fat" male sizes (Rand et al., 1997).

### Determination of Zygosity by Analysis of DNA

As part of the survey conducted in 2002, all twins will be invited to participate in a test of zygosity based on molecular genetics. DNA will be extracted from buccal mucosa cells (collected using brushes). Clearly, many of the 740 pairs of undetermined zygosity according to the survey of 1998 will be classified as MZ or DZ after DNA has been analyzed.

### Future Research Orientations and Forms of Collaboration

Several studies focusing on physical activity, perceived body shape and body size, eating habits, and eating behaviours are in progress. One study specifically focuses on associations between eating behaviour and longitudinal increase in body weight and BMI. Research on the heritability of eating behaviour is also in progress. Twin researchers could benefit from more international collaboration, and the principal investigator (FR) welcomes

inquiries from colleagues potentially interested in data from the Swedish Young Male Twins Register.

### References

- Cederlöf, R., Friberg, L., Jonsson, E., & Kaij, L. (1961). Studies on similarity diagnosis in twins with the aid of mailed questionnaires. *Acta Geneticae Medicae et Gemellologiae*, *11*, 338–362.
- Cnattingius, S., Ericson, A., Gunnarskog, J., & Kallén, B. (1990). A quality study of a medical birth register. *Scandinavian Journal of Social Medicine*, *18*, 143–148.
- Derom, R., Bryan, E., Derom, C., Keith, L., & Vlietinck, R. (2001). Twins, chorionicity and zygosity. *Twin Research*, *4*, 134–136.
- Johansson, M., & Rasmussen, F. (2001). Birthweight and body mass index in young adulthood. The Swedish young male twins study. *Twin Research*, *4*, 400–405.
- Johansson-Kark, M., Rasmussen, F., De Stavola, B., & Leon, D. A. (2002). Fetal growth and systolic blood pressure in young adulthood: The Swedish young male twins study. *Paediatric & Perinatal Epidemiology*, *16*, 200–209.
- Karlsson, J., Persson, L-O., Sjöström, L., & Sullivan, M. (2000). Psychometric properties of factor structure of the three-factor Eating Questionnaire (TFEQ) in obese men and women. Results from the Swedish Obese Subjects (SOS) study. *International Journal of Obesity*, *4*, 1715–1725.
- Pedersen, N., & Lichtenstein, P. (2000). The Swedish twin registry: A presentation. In B. Smedby, I. Lundberg, & T. I. A. Sørensen (Eds.), *Scientific evaluation of the Swedish twin registry*. Stockholm: Gotab.
- Pharaoh, P. O., & Adi, Y. (2000). Consequences of in-utero death in a twin pregnancy. *Lancet*, *355*, 1597–1602.
- Philippaerts, R. M., Westerterp, K. R., & Lefevre, J. (1999). Doubly labelled water validation of three physical activity questionnaires. *International Journal of Sports and Medicine*, *20*, 284–289.
- Rand, C. S. W., Resnick, J. L., & Seldman, R. S. (1997). Assessment of socially acceptable body sizes by university students. *Obesity Research*, *5*, 425–429.
- Smedby, B., Lundberg, L., & Sørensen, T. I. A. (Eds.). *Scientific evaluation of the Swedish twin registry*. Stockholm: Gotab. (FRN report 2000:10.)