
The Swedish Young Male Twins Study: A Resource for Longitudinal Research on Risk Factors for Obesity and Cardiovascular Diseases

Finn Rasmussen,^{1,2} Malin Kark,^{1,2} Sanna Tholin,² Nina Karnehed,¹ and Per Tynelius²

¹ Child and Adolescent Public Health Epidemiology Group, Department of Public Health Sciences, Karolinska Institute, Norrbacka, Sweden

² Division of Epidemiology, Stockholm Center of Public Health, Sweden

The Swedish Young Male Twins Study is a population-based longitudinal twin study founded in 1997 through record-linkages of several national registers. Details on pregnancy and birth were obtained from the Swedish Medical Birth Register and used to identify 3566 male twins (1783 pairs) born in Sweden between 1973 and 1979 and resident in Sweden in 1997. A record-linkage was made between the Medical Birth Register and the Military Service Conscription Register for the years 1991 to 1999, providing information on body weight, height, blood pressure, muscle strength, cognitive ability of these twins at age 18 and 19 years. In 1998, 2002 and 2005 to 2006, the twins were surveyed on their zygosity, socioeconomic status, lifestyle factors (such as eating habits, physical activity, smoking habits, use of alcohol etc), height and weight. In 2002, additional information was collected on perceived body shape and size, and eating behavior, according to the Three-Factor Eating Questionnaire. In 2003, DNA via buccal mucosa was collected from a subset of the twins. Recent research using the Swedish Young Male Twins datasets has explored the relationships between fetal growth, body size and blood pressure in young adulthood, genetic and environmental contributions to eating behavior and physical activity, and relationships between diet and physical activity patterns with longitudinal changes in body mass index and attained waist circumference.

Research on Swedish twins has been conducted since the late 1950s when a population-based twin register was created for the first time (Cederlöf et al., 1961). Generations of twin researchers have contributed to the maintenance and development of the Swedish Twin Register, which is now one of the largest in the world. The Swedish Young Male Twins Study, initiated in 1997, is a separate, smaller and more focused information source (Rasmussen & Johansson-Kark, 2002). The long-term goal of this longitudinal twin study is to enable research on genetic and environ-

mental influences on behavioral and biological risk factors for blood pressure, obesity, type 2 diabetes and cardiovascular diseases. The most recent research from this population-based twin cohort has explored relationships of fetal growth with body size and blood pressure in young adulthood (Johansson & Rasmussen, 2001; Johansson-Kark et al., 2002), genetic and environmental contributions to eating behavior (Tholin et al., 2005), and influences of physical activity, diet and gene-environment interactions on longitudinal changes in body mass index (BMI) and attained waist circumference (Karnehed et al., 2006). Other recent papers have focused on genetic factors in physical activity (Eriksson et al., 2006), and longitudinal changes in BMI and attained body fatness (Silventoinen et al., 2006).

Linkage of Information Sources

When the cohort study was initiated in 1997 the foundation was a linkage of several national registers in addition to a mailed survey conducted in 1998. As described below this information source has been extended by surveys conducted in 2002 and 2005 to 2006, longitudinal growth data from childhood and, for a subset, DNA samples. These information sources are linked by the unique personal identification number assigned to all Swedish citizens.

Identification of the Twin Cohort in the Medical Birth Register

As a first step in the creation of the cohort study, all male twins born in Sweden between 1973 and 1979 were identified in the Swedish Medical Birth Register (MBR). The MBR covers more than 99% of all births in Sweden (Cnattingius et al., 1990). In 1997, 3936 male twins (1968 pairs) were identified in the MBR.

Received 2 July, 2006; accepted 15 August, 2006.

Address for correspondence: Finn Rasmussen, Child and Adolescent Public Health Epidemiology Group, Department of Public Health Sciences, Karolinska Institute, Norrbacka SE-171 76 Stockholm, Sweden. E-mail: finn.rasmussen@ki.se

Some of the variables obtained from the MBR were: date of birth, birth order, birthweight, birth length, gestational age, Apgar score, head circumference, mother's parity, mother's age, *International Classification of Diseases* (ICD) diagnoses for maternal diseases in pregnancy or at birth, and ICD diagnoses for diseases among the offspring at birth (see Appendix A). In addition, information on stillbirths and perinatal deaths in the cohort was obtained from the MBR and Sweden's Cause of Death Register.

In 1997, record linkage with Sweden's Register of the Total Population, a record of all individuals with permission to stay permanently in Sweden was carried out. Matching information from this register with the MBR made it possible to identify 1783 complete male twin pairs (3566 twins), born between 1973 and 1979, both of whom were resident in the country in 1997.

Military Service Conscription Register

Record linkage with Sweden's Military Service Conscription Register (MSCR) was carried out. The MSCR has nationwide coverage, and conscription data have been obtained for the years 1991 to 1999. From the conscription examinations, performed at 18 and 19 years of age, data were obtained on date and place of conscription, height, weight, systolic blood pressure, diastolic blood pressure, muscle strength, submaximal work capacity, estimated aerobic fitness, cognitive ability (IQ) as assessed by a general intelligence test, and ICD diagnoses for all diseases identified or reported at the conscription examination (see Appendix B). The intelligence test comprised four basic tests (i) a logic/general intelligence test, (ii) a verbal test assessing the subject's ability to detect synonyms, (iii) a test of visuospatial/geometric perception, and, (iv) a test of technical/mechanical skills with mathematics/physics problems (Carlstedt, 2000; David et al., 1997). The raw scores from these tests have been transformed to stanine scores by the staff at the National Conscription Board on a yearly basis (Carlstedt, 2000). During the years 1991 to 1999 the conscription examination was compulsory and a certificate issued by a physician stating the medical reasons was required for exemption from this examination. However, due to a change of method, IQ is available only for a subset of twins (510 complete pairs) who conscripted before 1995.

Mailed Questionnaire in 1998

A questionnaire was mailed to the 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, height, weight, perceived body size, diabetes diagnosed after the age of 40 among parents or grandparents, occupation, educational level, physical activity at work and 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; see Appendix C). Twins who had not responded after two reminders were approached for interview by telephone.

Of the 3566 twins, 2810 (79%) responded to the questionnaire. Full sets of responses were obtained from 1331 (75%) complete pairs. Most twins responded to the questionnaire, but information was collected by telephone interview in the case of 313 individuals. There were 55 twins from 39 pairs that refrained from taking part in this cohort study. One twin died in 1998, after the questionnaire had been mailed, and the co-twin did not reply. These 40 pairs were excluded from any further investigation. Fifty-six twins could not be traced. No reply was obtained from 644 twins.

Mailed Questionnaire in 2002

In principle, all twins eligible for the survey in 1998 were also regarded as eligible for that in 2002 with the following exceptions and for the 40 pairs described in the previous section. Six pairs of twins were excluded, due to severe handicap and consequent inability to respond to the 1998 questionnaire. Twelve pairs, where one twin in the pair had died between 1998 and 2002 were also excluded. Thirty-five twins had emigrated and were also excluded. Some twins who could be traced in 2002 but not in 1998 were included. In 2002 mailing addresses were sought for 3415 twins and only six of these individuals could not be traced. Accordingly, 3409 twins were approached in the questionnaire survey conducted in 2002.

The questionnaire employed in 2002 was more extensive than that in 1998. Items included were family type, education, occupation, and social network. Further questions were posed on perceived general health, chronic diseases, use of prescribed drugs, physical activity, eating habits, eating behaviors, smoking habits, use of snuff, and alcohol consumption (see Appendix D). Some of the questions from 1998 were repeated in 2002, but many others were new. The questionnaire incorporated the Three-Factor Eating Questionnaire (Karlsson et al., 2000), and also the Baecke questionnaire on physical activity (Philippaerts et al., 1999). The Baecke instrument contains four dimensions of physical activity: (i) physical activity at work, (ii) sport during leisure time, (iii) physical activity during leisure time excluding sport, and (iv) total physical activity. The validity of the Baecke questionnaire has been confirmed by comparison with energy expenditure measured by double-labelled water which is the 'gold standard' method (Philippaerts et al., 1999). Twins were also requested to report their height and weight and to measure their waist circumference by a tape measure included in the mail package. Perceived body size and shape were also rated using nine silhouette drawings showing very thin to very fat body shapes (Rand et al., 1997).

Finally, the twins were asked to give the investigators written informed consent to collect data on height and weight from archived child-health-centre records

and school-health records (see next section). Of the 3409 eligible twins, 2169 (64%) responded to the questionnaire after two reminders or via telephone interviews. Responses were obtained from 950 complete pairs. In all, 836 complete pairs participated in both 1998 and 2002.

Data on Childhood Growth

Growth data had been recorded routinely by trained nurses or physicians as part of health check-ups at public child health centers from birth to 6 years of age and after that in annual health care examinations at school to age 16 to 17 years. There were 1870 twins who responded to the questionnaire in 2002 and gave us permission to collect information about height and weight from their growth records. For these twins municipal and county council archives all over Sweden were contacted for information about growth data. Because of the national school system in Sweden, nearly all children in these birth cohorts were enrolled in public schools and thus attended the public school health services. We were able to locate archived records from child health centers and/or school health services for 1196 (64%) of the 1870 twins. For some individuals we were able to locate growth data from child health centers but not from school health services and vice versa. Records including at least five measurement points with height and weight between birth and age 16 years were found for 1151 twins (62%) of the 1870 twins.

Web-Based Questionnaire or Telephone Interview in 2005/2006

In 2005 the twins were invited to answer a web-based questionnaire survey conducted in collaboration with the Swedish Twin Register. Nonrespondents were followed-up by three written reminders. Thereafter nonrespondents were approached by telephone and invited to participate in a telephone interview. In May 2006, interviews were still conducted and the final response rate and number of complete pairs were unknown.

This third survey was extensive and covered a subset of all variables including: socioeconomic status (SES) (statuses) and demographic variables (education, occupation and employment, and marital status), frequency of contacts with the co-twin, perceived general health, lifestyle factors (smoking habits, use of snuff, alcohol consumption, and physical activity), sleep patterns, psychological and psychiatric symptoms (anxiety, depression, perfectionism, neuroticism and extraversion, dieting, body weight fluctuations, preoccupation with body size and shape, and eating disturbance) and self-reported height and body weight (see Appendix E).

Determination of Zygosity

The items on zygosity in the questionnaires of 1998 have been widely used in twin research (Cederlöf et al., 1961; Pedersen & Lichtenstein, 2000), and were based on self-reports of (i) degree of similarity in childhood and (ii) difficulties teachers have had in distinguishing between twins in school. The pairs where both twins reported themselves to be 'as like two peas in a pod', and

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 undetermined zygosity. As part of the survey conducted in 2002, all twins of undetermined zygosity, according to the data collected in 1998, were requested to respond once more to the same questions about zygosity. In 2003, those who remained of undetermined zygosity were invited to undergo a DNA test. Scope mouthwash solution (Procter & Gamble) was mailed to the twins and DNA was purified from buccal cells in the returned samples (Heath et al., 2001). Zygosity was determined by 16 highly polymorphic microsatellite markers from Weberset 6. A pair was considered MZ if concordant for all 16 markers and DZ if they differed in one or more marker. However, no twin pairs differed in only one marker. Of the 140 twin pairs of undetermined zygosity, all 114 pairs that completed the test could be classified as either MZ or DZ. Remaining DNA is stored in the biobank at the Karolinska Institute.

Linkage to Population and Housing Censuses

In a record-linkage scheduled to 2007, information on parental SES during childhood will be extracted from Statistics Sweden's Population and Housing censuses of 1970 to 1990 and own adult SES data from the Longitudinal Database on Education, Income and Employment of 2005. Parental SES data during childhood will include the parents' marital status and employment, educational level, income and type of housing. Data on own adult SES will include marital status, educational level, and income.

Papers from the Swedish Young Male Twins Study

Two early papers explored the fetal-origins hypothesis. In the first paper the association of birthweight with BMI at age 18 years was studied by mixed linear models among 400 MZ and 284 DZ pairs of twins (Johansson & Rasmussen, 2001). The results revealed a weak positive within-pair effect of birthweight on BMI at the age of 18 among the MZ pairs of twins. No between-pairs effect of birthweight on BMI was observed for the MZ twin pairs. The within-pair effect observed among the MZ twin pairs persisted after various adjustments. While these results did not contradict the notion that growth in utero may have effects on BMI in adulthood, they did not support the fetal-origins hypothesis. In the second paper relationships between fetal growth and systolic blood pressure were studied among 384 MZ and 269 DZ pairs of twins (Johansson-Kark et al., 2002). No within-pair effect of birthweight on systolic blood pressure was found for either MZ or DZ twin pairs. For the between-pair effect there was a weak negative association for the MZ twin pairs. These results provided little support for the fetal-origins hypothesis.

In a study including 326 DZ and 456 MZ pairs of twins, we intended to disentangle genetic and environmental influences on eating behavior which was assessed by the Three-Factor Eating Questionnaire (Tholin et al., 2005). The result showed strong genetic influences on eating behaviors. Heritability was found to be 59% for cognitive restraint, 60% for emotional eating, and 45% for uncontrolled eating (Tholin et al., 2005).

The contribution of genetic factors to physical activity was further investigated in another study including 1022 pairs of twins (Eriksson et al., 2006). Information on physical activity was obtained from the questionnaires of 1998 and 2002. Heritability was estimated to 49% for total physical activity and the other dimensions of physical activity showed genetic contributions between 40% and 65%. Nonshared environmental factors were important, whereas shared environmental factors did not contribute to physical activity behaviors. The authors also explored possible violation of the equal environment assumption in relation to physical activity from empirical and simulated data, but found no support for any such violation.

We have also conducted a collaborative study on the influences of physical activity, diet and gene-environment interactions on 4-year changes in BMI and attained waist circumference (Karnehed et al., 2006). The results indicated that people with a sedentary lifestyle combined with genetic susceptibility to obesity had a greater 4-year increase in weight than those with no genetic susceptibility. Similarly, associations between low fiber intake in diet and weight gain were more pronounced among those with genetic susceptibility to obesity.

Previous studies have shown that BMI in childhood and adolescence is associated with BMI in adulthood, but it is not known how genetic and environmental factors contribute to these associations (Silventoinen et al., 2006). We studied the correlations of BMI at 18 years of age with BMI from birth to 17 years of age in a Swedish longitudinal cohort of 231 MZ and 144 DZ male twin pairs. The trait correlation of BMI at age 18 was highest with BMI at age 17 and it decreased steadily to age one. A major part of these correlations was because of common genetic factors, but also unshared environmental correlations were found. The correlation between BMI at age 18 and at birth was weak and was solely due to unshared environmental factors. Our results suggest that there is a persistent environmental component, not shared by a twin pair, affecting BMI at age one, or even at birth, which contribute to BMI in early adulthood. A challenge of future research is to identify environmental factors affecting BMI through the growth period independently or in interaction with genetic factors.

Future Research and External Access to Data

Many hypotheses may be explored and tested on this longitudinal dataset. It would for example be interesting to explore whether IQ is associated with behavioral risk factors for type 2 diabetes, obesity and

coronary heart disease. Besides genetic determinants, IQ also seems to be associated with parental SES and childhood environmental factors. IQ may be an intermediate factor between parental SES and own behavioral risk factors. Whilst cognition is, in part, genetically determined, there has recently been a suggestion that growth in fetal life and growth during early childhood — both indices of nutrition — may also play an important role. The effects of these and other potential correlates (e.g., gestational age, size at birth, growth during infancy, SES and educational background of the parents) can be examined in relation to cognition using twin data. The Swedish Young Male Twins Study is open for researchers with new research questions.

Acknowledgments

Grants received from the Swedish Council for Working Life and Social Research (contract number 2002–0623) and the Swedish Council for Research (contract 40186801) are greatly appreciated.

References

- Carlstedt, B. (2000). *Cognitive abilities: Aspects of structure, process and measurement*. Doctoral dissertation, Acta Universitatis Gothoburgensis.
- 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., & Källen, B. (1990). A quality study of a medical birth registry. *Scandinavian Journal of Social Medicine*, 18, 143–148.
- David, A. S., Malmberg, A., Brandt, L., Allebeck, P., & Lewis, G. (1997). IQ and risk for schizophrenia: A population-based cohort study. *Psychological Medicine*, 27, 1311–1323.
- Eriksson, M., Rasmussen, F., & Tynelius, P. (2006). Genetic factors in physical activity and the equal environment assumption — The Swedish young male twins study. *Behavior Genetics*, 36, 238–247.
- Heath, E. M., Morken, N. W., Campbell, K. A., Tkach, D., Boyd, E. A., & Strom, D. A. (2001). Use of buccal cells collected in mouthwash as a source of DNA for clinical testing. *Archives of Pathology and Laboratory Medicine*, 125, 127–133.
- 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 and 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*, 24, 1715–1725.
- Karnehed, N., Tynelius, P., Heitmann, B., & Rasmussen, F. (2006). Physical activity, diet, and gene-environment interactions in relation to body mass index and waist circumference. The Swedish Young Male Twins Study. *Public Health Nutrition*, 9, 851–858.
- Pedersen, N., & Lichtenstein, P. (2000). *Scientific evaluation of the Swedish Twin Registry* (Report. No. 2000-10). Stockholm, Sweden: Swedish Council for Planning and Coordination of Research.
- Philippaerts, R. M., Westerterp, K. R., & Lefevre, J. (1999). Doubly labeled water validation of three physical activity questionnaires. *International Journal of Sports Medicine*, 20, 284–289.
- Rand, C. S., Resnick, J. L., & Seldman, R. S. (1997). Assessment of socially acceptable body sizes by university students. *Obesity Research*, 5, 425–429.
- Rasmussen, F., & Johansson-Kark, M. (2002). The Swedish Young Male Twins Register: A resource for studying risk factors for cardiovascular disease and insulin resistance. *Twin Research*, 5, 433–435.
- Silventoinen, K., Pietilainen, K., Tynelius, P., Sørensen, T., Kaprio, J., & Rasmussen, F. (2006). Genetic and environmental factors in growth in body mass index from birth to age 18: The Swedish Young Male Twins Study. Manuscript submitted for publication.
- Tholin, S., Rasmussen, F., Tynelius, P., & Karlsson, J. (2005). Genetic and environmental influences on eating behavior: The Swedish Young Male Twins Study. *American Journal of Clinical Nutrition*, 81, 564–569.

Appendix A

Data From the Swedish Medical Birth Register

Maternal place of residence at delivery (county, municipality, and parish)
 Delivery hospital
 Family type
 Mother's country of birth
 Previous pregnancies (spontaneous abortions, stillbirths, live births)
 ICD diagnoses for maternal diseases in pregnancy
 Date of last menstrual period
 Diseases at first visit to antenatal clinic
 Date of admission to delivery unit
 Mother's delivery diagnoses (ICD)
 Assisted delivery (caesarean section, vacuum extraction, other)
 Type of analgesia and/or anaesthesia during delivery
 Date and time of birth
 Gestational age
 Birthweight
 Birth length
 Head circumference
 Multiple births, including number
 Apgar scores at 1, 5, 10 minutes
 Infant diagnoses (ICD)
 Stillborn/live born
 Date of death offspring, underlying causes of death (ICD)

Appendix B

Data From the Swedish Military Service Conscription Register

Place of residence at time of conscription examination (county, municipality, parish)

Conscription office

Conscription date

Measured height

Measured weight

Systolic blood pressure

Diastolic blood pressure

Diseases at conscription examination (ICD)

Driver's license

Visual acuity

Colour vision

Hearing capacity (audiometry)

Muscle strength (a weighted mean of arm flexion, knee extension and handgrip)

Work capacity (measured by cycle-ergometer test)

Aerobic capacity

Intelligence tests: (i) a logic/general intelligence test, (ii) a verbal test assessing the subject's ability to detect synonyms, (iii) a test of visuospatial/geometric perception, (iv) a technical/mechanical skills test with mathematical/physics problems

Reading and writing difficulties

Handedness

Appendix C

Mailed Questionnaire in 1998

Questions about zygosity

Educational level

Current occupation and/or ongoing studies

Perceived general health

Chronic diseases and handicaps

Use of prescription drugs

Height (self-reported)

Weight (self-reported)

Weight history (self-reported)

Diabetes diagnoses among parents and grandparents after age 40

Occupational physical activity

Leisure-time physical activity

Time spent on light, moderate and vigorous physical activity (hours per week)

Amount of time spent in front of television/video/computer

Smoking habits

Use of snuff

Access to emotional support in case of personal problems or crises

Access to practical support from someone outside the household in case of illness

Appendix D
Mailed Questionnaire in 2002

Questions about zygosity
Contact frequency with twin brother
Educational level
Marital status and cohabitation
Housing
Current occupation and/or ongoing studies
Perceived general health
Chronic diseases and handicaps
Use of prescription drugs
Height (self-reported)
Weight (self-reported)
Waist circumference (self-measured by tape)
Perceived body size according to silhouette drawings
Ideal body size according to silhouette drawings
Occupational physical activity (as in 1998)
Leisure-time physical activity (as in 1998)
Baecke questionnaire of habitual physical activity
Habitual sleeping time
Three-Factor Eating Questionnaire, revised 21-item version
Breakfast habits
Food frequency questions
Type and amount of spread used on bread
Smoking habits
Use of snuff
Alcohol habits

Appendix E
Web-Based Questionnaire in 2005

Marital status and cohabitation
Education
Occupation and employment
Sleep pattern
Perceived general health
Height (self-reported)
Weight (self-reported)
Weight fluctuations
Physical activity
Food frequency questions
Smoking habits
Use of snuff
Alcohol consumption
Eating disorders
Generalized anxiety
Perfectionism
Depression
Neuroticism and extraversion