

**This is an electronic reprint of the original article.
This reprint *may differ* from the original in pagination and typographic detail.**

Author(s): Waller, Katja; Kujala, Urho; Kaprio, Jaakko; Koskenvuo, Markku; Rantanen, Taina

Title: Effect of physical activity on health in twins: a 30-yr longitudinal study

Year: 2010

Version:

Please cite the original version:

Waller, K., Kujala, U., Kaprio, J., Koskenvuo, M., & Rantanen, T. (2010). Effect of physical activity on health in twins: a 30-yr longitudinal study. *Medicine & Science in Sports & Exercise*, 42 (4), 658-664. doi:10.1249/MSS.0b013e3181bdeea3

All material supplied via JYX is protected by copyright and other intellectual property rights, and duplication or sale of all or part of any of the repository collections is not permitted, except that material may be duplicated by you for your research use or educational purposes in electronic or print form. You must obtain permission for any other use. Electronic or print copies may not be offered, whether for sale or otherwise to anyone who is not an authorised user.

Effect of physical activity on health in twins: a 30-year longitudinal study

Running headline: Physical activity and health in twins

Katja Waller, M.Sc.¹, Urho M. Kujala, M.D., Ph.D.¹, Jaakko Kaprio, M.D., Ph.D.^{2,3,4}, Markku Koskenvuo MD., Ph.D.², Taina Rantanen, Ph.D.^{1,5}

¹ Department of Health Sciences, University of Jyväskylä, Jyväskylä, Finland

² Department of Public Health, University of Helsinki, Helsinki, Finland

³ Department of Mental Health and Alcohol Research, National Public Health Institute, Helsinki, Finland

⁴ Institute for Molecular Medicine, University of Helsinki, Helsinki, Finland

⁵ Finnish Centre for Interdisciplinary Gerontology, University of Jyväskylä, Jyväskylä, Finland

Correspondence to:

Katja Waller, M.Sc

Department of Health Sciences, University of Jyväskylä

P.O.Box 35 (LL227) 40014 Jyväskylä, Finland

Tel work: +358 14 2602075, Tel mobile: +358 44 3685661, Fax: +358 14 2602011

E-mail: katja.waller@jyu.fi

Funding received: This study was supported by the Finnish Ministry of Education, the Juho Vainio Foundation and the University of Jyväskylä. The Finnish Twin Cohort Study is part of the Academy of Finland Centre of Excellence in Complex Disease Genetics.

Abstract

Purpose The aim was to investigate whether persistent leisure-time physical activity, adjusted for genetic liability and childhood experiences, protects against chronic diseases, early signs of disability and loss of life satisfaction.

Methods From 5663 healthy adult twin pairs 146 pairs were identified who were discordant for both intensity and volume of leisure physical activity in 1975 and 1981. Of them, both members of 95 pairs were alive and participated in our follow-up study in 2005 when chronic diseases (such as diabetes, CVD, osteoarthritis), life-satisfaction and disability were assessed by a structured telephone interview. Mean age of the participants was 58 years (range from 47 to 79) in 2005. Paired tests were used in analyses.

Results At end of follow-up the active co-twins had a decreased risk of reporting at least one chronic diseases, while active MZ twins had two or more chronic diseases significantly less often than their inactive co-twins (OR=0.14, p=0.031). Overall, the risk for type 2 diabetes or glucose intolerance (OR=0.09, p=0.022) and elevated blood pressure (OR=0.46, p=0.039) was decreased among the active co-twins. These effects were seen clearly among DZ, but not always among small number of MZ twins. The active co-twins reported greater life satisfaction (p=0.047), and tended to be less likely to be hospitalized (p=0.065). Although, active co-twins had somewhat more sports-related injuries (OR=1.9, p=0.051) than inactive co-twins. Studied disability variables did not differ between the active and inactive co-twins.

Conclusions Physical activity reduces the risk for chronic diseases and helps in maintaining life satisfaction. However, genetic factors may play a role in this association, as some findings emerged more clearly among dizygotic than monozygotic twins discordant for physical activity.

Key words: physical activity, morbidity, chronic disease, follow-up studies, twin study

Introduction

Paragraph number 1 Observational follow-up studies have provided substantial evidence that physical activity plays an important role in the prevention of several chronic diseases, such as cardiovascular disease (CVD), coronary heart disease (CHD) type 2 diabetes and hypertension (19, 23, 29, 36). Although physical activity has many positive outcomes for health, adverse effects include an increased rate of musculoskeletal injuries (11).

Paragraph number 2 Genetic selection can also play a role in accounting for the relationship between physical activity and chronic disease. Physical fitness and the ability to achieve high levels of physical activity have a genetic component (4, 17, 33). The review by Casas et al. (2006) (7) clearly demonstrated that coronary artery disease (CAD) has a genetic component and that different risk factors for CAD have high heritabilities. Significant genetic influences on cholesterol levels, smoking and hypertension have repeatedly been shown (3, 7, 22). Twin studies have shown that age at death from CAD has a strong genetic component, particularly early onset of CAD (27). A genetic predisposition also underlies the increased tendency for weight gain and other metabolic syndrome-related conditions (2, 25). Interestingly, some evidence is now available that inherited biological characteristics make it easier for some individuals to exercise and also favour them with lower morbidity and mortality (15, 17, 20).

Paragraph number 3 Despite recent progress in defining the individual genes underlying the genetic component identified from family and twin studies, known genes account only for a small fraction of the estimated heritabilities for common diseases and physical activity. Thus, twin and family studies still remain a powerful tool for investigating the role of genetic and environmental factors in risk factor – disease relationships. Dizygotic twins (DZ) share half of

their segregating genes, while monozygotic (MZ) pairs are genetically identical. Both kinds of pairs nearly always have the same childhood environment. By studying outcomes in twin pairs discordant for an exposure, such as physical activity, the possible confounding role of genetic and early childhood experiences can be controlled for.

Paragraph number 4 We followed the Finnish Twin Cohort for 30 years to study the associations between physical activity, chronic diseases, life satisfaction and preclinical disability in healthy twin pairs discordant for leisure-time physical activity. Given the current knowledge of both positive and negative effects of physical activity on some conditions we were interested in gaining an overview of the whole spectrum of health-related conditions. The aim of the study was to see whether baseline physical activity protects broadly from morbidity assessed using wide range of diseases and associated measures.

Methods

Participants

Paragraph number 5 The Finnish Twin Cohort consists of all same-sex twin pairs born in Finland before 1958 with both co-twins alive in 1967 (12). Figure 1 shows the flow of the participants. For the present study, the initial inclusion criteria were employment in 1981 and complete questionnaire data on leisure physical activity in 1975 and 1981. The subjects were aged from 24 to 60 years on January 1, 1982 (n=17,968 individuals). All pairs in which at least one co-twin did not respond to the questionnaires, had died or had a chronic disease, except hypertension, by the end of 1982 were excluded (12, 17). The healthy cohort comprised 5663 same sex twin pairs (17). Determination of zygosity was based on an accurate and validated questionnaire method (32).

Paragraph number 6 For this study, 146 same-sex twin pairs were selected who were discordant for leisure-time physical activity both for participation in vigorous activity and volume of activity in 1975 and 1981. The final study sample at the 2005 follow-up comprised 111 twin pairs, as only those pairs were included in which both twins were still alive (24 co-twins from 146 pairs, 16 inactive and 8 active, had died by end of 2004 (unpublished data: Waller K, Kujala UM, Rantanen T, Kauppinen M, Silventoinen K, Koskenvuo M, Kaprio J. Physical activity, morbidity and mortality in twins: a 22-year prospective follow-up. Under review 2009)). In addition, we required that both were known to be living in Finland and spoke Finnish as their mother tongue, which resulted in the exclusion of 12 pairs. An attempt was made to contact all 222 subjects. Of these 203 subjects (95 complete pairs, 54 female) took part in the interview as one died during the interview period and 18 did not participate. The mean age of the subjects was 58 years (range 47 to 79) at interview.

Assessment of exposure variables

Paragraph number 7 The questionnaires in 1975 and 1981 included identical questions on weight, height, physical activity, occupation, alcohol use, smoking and physician-diagnosed diseases. Among the twin pairs whose addresses could be identified (93.5 percent of subjects) the response rate was 87.6 percent in 1975 and the re-response rate was 90.7 percent in 1981.

Paragraph number 8 Physical activity habits elicited by identical questions in 1975 and 1981 were used as the main exposure in the present study. This information is considered to be valid on the basis of earlier studies (13, 14, 19). Participation in vigorous physical activity was assessed by following question: Is your physical activity during leisure-time about as strenuous on average as: 1) walking 2) alternately walking and jogging 3) jogging (light run) 4) running. Those who chose alternative 2, 3 or 4 were classified as participating in vigorous activity. Assessment of leisure activity volume (MET index) was based on a series of structured questions (14, 19) on leisure physical activity (monthly frequency, mean duration and mean intensity of physical activity sessions) and physical activity during commuting to and from work. The index was calculated by assigning a multiple of resting metabolic rate (MET score) to each activity and by calculating the total volume of activity, using formula: intensity x duration x frequency (19). The MET index was expressed as the sum-score of leisure MET hours per day. Those subjects whose volume of activity was ≥ 2 MET hours/day (corresponding to about 30 min walking per day) and participated in vigorous activity (alternatives 2, 3 or 4), were classified as physically active. This had to be true at both time-points (1975 and 1981) and their co-twin had to be inactive at both time-points. Figure 2 shows the MET indices for active and inactive co-twins in 1975 and 1981.

The MET index was validated in a previous study (35) by comparing the questions used for calculating MET index to a 12-month detailed physical activity questionnaire conducted by telephone interview. The intraclass correlation (ICC) between these two was relatively high: The ICC between the MET index 2005 (same as the original questions used in 1975 and 1981) and the detailed 12-month physical activity MET index was 0.68 ($p < 0.001$) for leisure-time physical activity and 0.93 ($p < 0.001$) for work journey.

Follow-up assessment and outcomes

Paragraph number 9 In 2005, after being sent an invitation letter and giving their informed consent to participate in the study, subjects were interviewed by telephone. The study was approved by the ethics committee of the University of Jyväskylä. All outcome assessments (interview and data entry) were carried out by researchers blinded to the subjects' baseline status. Two experienced and trained interviewers interviewed each twin in a pair at random. The average duration of the interview was 50 minutes and included questions on physical activity habits, functional limitations, use of medications and occurrence of chronic diseases.

Paragraph number 10 The follow-up interview included a four-question dyspnea scale concerning whether the subject became breathless during walking and performing daily tasks (31). This scale has 5 response categories (range: 0; no breathlessness to 4: breathless during daily tasks). A four-question scale on life satisfaction (LS) yielded a sum score ranging between 4-20, with an increasing score indicating a decrease in life satisfaction (16). The life satisfaction scale correlates well ($r > 0.6$) with depressiveness on the Beck Depression Inventory (16).

Paragraph number 11 Subjects were asked if they had specific physician-diagnosed diseases. For example: “Has your doctor ever told you that you have rheumatoid arthritis?”.

Information about individually asked diseases can be found from the results section.

Glucose intolerance and type 2 diabetes were assessed in the interview with a question: Has your doctor told you that you have diabetes? Responses were classified as no, yes (type 2 diabetes) or no, but has been diagnosed as having elevated blood glucose (impaired glucose tolerance or impaired fasting glycaemia). The latter were classified as having prediabetes. Subjects were also asked whether they had specific musculoskeletal diseases or conditions (rheumatoid arthritis, osteoarthritis (knee, hip or other), sports-related injuries, sciatica and tension neck). Finally, the presence of other physician-diagnosed diseases was assessed with an open question: “Do you have any other physician-diagnosed diseases?”.

Paragraph number 12 Recent hospitalisations were investigated with the question “How many days have you spent in hospital during the last 3 years?” Only inpatient visits were counted.

Paragraph number 13 Mobility was assessed with 6-12 questions ranging from preclinical mobility limitations, such as task modification, to frank disability and inability (24, 26). This scale is reliable (κ coefficient between 0.47 – 1.00) (24) and it has been validated against objective measurements of muscle power and walking speed (26).

Statistical Analysis

Paragraph number 14 As we were studying occurrence of diseases among twin pairs discordant for physical activity all the statistical analyses were based on pairwise tests. To compare differences in outcome measurements between the inactive and active co-twins

paired samples t-test, McNemar's test and conditional logistic regression were used. The level of significance was set at $p < 0.05$ and all the p-values reported are two-sided. Data were analyzed with SPSS 14.0 or Stata 9.0.

Results

Paragraph number 15 Table 1 shows the baseline characteristics for 95 pairs. In 1975 a slightly higher proportion of the active co-twins were single and a slightly higher proportion of the inactive co-twins were married. Baseline characteristics show that the inactive subjects smoked or had smoked more than their active co-twins. The active co-twins reported greater life satisfaction at baseline. No other differences were seen between inactive and active co-twins at baseline.

Paragraph number 16 The active co-twins remained more satisfied with their life at the end of follow-up: mean life satisfaction (LS) was 6.5 for the active co-twins and 7.1 for inactive co-twins (paired t-test $p=0.047$). Rather similar results were obtained for dizygotic (6.4 vs. 6.9, $p=0.12$) and monozygotic (6.8 vs. 7.9, $p=0.24$) pairs. Inactive co-twins had a tendency towards dyspnea at follow up when compared with their active co-twins ($p=0.067$), more so in DZ ($p=0.10$) than in MZ pairs ($p=1.00$).

Paragraph number 17 The results for physician-diagnosed diseases in inactive and active co-twins are shown in table 2. Among monozygotic twin pairs the active co-twins had a reduced risk of having at least 2 chronic diseases, (with the exception of hypertension), as 1 active MZ and 7 inactive MZ co-twins had 2 or more chronic diseases (OR=0.14, $p=0.031$), although the difference was not significant when MZ and DZ pairs were taken together (OR=0.54, $p=0.19$). No differences were seen in the cumulative incidence of diagnosed hypertension between the inactive and active co-twins, when studying new cases of hypertension since 1975. Overall, the active co-twins had a decreased risk for elevated blood pressure (OR=0.46, $p=0.039$; DZ OR=0.44, 95 % CI 0.19 – 1.02; MZ OR=0.5, 95 % CI 0.09 – 2.73). The active

co-twins also had a decreased risk for type 2 diabetes or prediabetes (OR=0.09, $p=0.022$; DZ OR=0.1, 95 % CI 0.01 – 0.78; MZ no difference). Although statistically non-significant, the active twins showed a lower prevalence of type 2 diabetes, any pulmonary disease and other physician-diagnosed diseases.

Paragraph number 18 We observed some differences in selected musculoskeletal problems between the inactive and active co-twins (Table 3). The active co-twins had a marginally non-significant increased risk for at least one sports-related injury (OR=1.9, $p=0.051$) compared to their inactive co-twins, the finding being more salient in DZ pairs (OR=2.2, 95 % CI 1.07 - 4.45) than in MZ pairs (OR=1, 95 % CI 0.25 – 4.0). For individual sports-related injuries the active co-twins again had a statistically non-significant increased risk for getting an ankle ligament injury (OR=1.8, $p=0.14$; DZ OR=2.17, 95 % CI 0.82 – 5.70; MZ OR=1.3, 95 % CI 0.34 – 4.66). The risk for conditions other than knee or hip osteoarthritis and sciatica did not differ between active and inactive twins (table 3).

Paragraph number 19 Out of 95 pairs, 23 inactive and 13 active co-twins had been hospitalised within last 3 years prior to the interview for a total of 171 and 95 nights respectively. On average, the inactive co-twins spent 1.8 nights and the active co-twins 1 night (paired t-test $p=0.16$) in hospital during that period. The active co-twins had non-significant decreased risk for having been hospitalised (OR=0.47, $p=0.065$) did not differ by zygosity (DZ OR=0.54, 95 % CI 0.22 - 1.35; MZ OR=0.33, 95 % CI 0.07 – 1.65).

Paragraph number 20 The results of the preclinical disability analyses did not reach statistical significance between inactive and active co-twins. However, there was a tendency for the inactive co-twins to have more difficulties and to report more task modification in daily

activities compared to their active co-twins. For example active co-twins were less likely to have made changes in walking for 2 kilometres (OR=0.53, 95 % CI 0.22 – 1.35, p=0.19).

Discussion

Paragraph number 21 Our 30-year longitudinal follow-up study on twins discordant for physical activity found greater life satisfaction among the active than inactive co-twins. The inactive co-twins reported breathlessness more often than their active co-twins. Abnormalities in glucose metabolism (diabetes or prediabetes) and elevated blood pressure were less common among the active co-twins. The active co-twins had also been hospitalised less often and for shorter times. In contrast, the active co-twins showed a tendency to having more sports-related injuries at follow-up than their inactive co-twins.

Paragraph number 22 In line with our results similar effects of physical activity on a number of different diseases, for instance diabetes/prediabetes and hypertension, has been reported in previous studies (5, 29, 36). Although we did not find a difference in reported diagnoses of depression between inactive and active co-twins in our study the active co-twins reported greater life satisfaction. In their review in 2001 Rejeski and Mihalko (30) found a lack of consistency in the results of previous studies on physical activity and life satisfaction in older adults with only some studies reporting positive effects.

Paragraph number 23 When studying differences between inactive and active subjects it would be reasonable to expect differences to be seen first in fitness and body fatness. In the present study we documented a trend to higher frequency of breathlessness during specific daily tasks in the inactive compared to active co-twins. In our earlier study we documented an

association between long-term physical activity and lower weight gain in our twin sample (35). Next, a difference is usually seen in insulin sensitivity, as in the present study; where a difference was seen in DZ but not MZ pairs, suggesting a possible gene-physical activity interaction, such as documented for the FTO gene (1) for physical activity in BMI and glucose metabolism parameters. In our earlier study, among the same cohort, we found that discordance pattern in physical activity had continued for 30 years in a subgroup of 42 pairs (35). That study showed that adulthood physical activity habits are often maintained for a long period of time, and thus it is possible that the continuation of physical activity habits partly explains the difference in the occurrence of chronic diseases in the present study.

Paragraph number 24 As expected, the active co-twins seem to have more musculoskeletal problems and sports related injuries. Hootman et al. (11) studied subjects who participated in recreational sports and found that 25% of their subjects had sustained a musculoskeletal injury within the 12 months preceding the survey. Over 83 % of these injuries were physical activity-related and 66% were located in the lower extremities. Although in our study active co-twins had slightly more injuries, the number of injuries in real life could have been even higher as only injuries that had been diagnosed by a physician were included in our study. It is very likely that only the more severe sports-related/musculoskeletal injuries were reported to a physician and therefore excluding less severe injuries from our study.

Paragraph number 25 No differences were seen in the amount of hip or knee osteoarthritis between the inactive and active co-twins. Although, former athletes have higher incidence rates of osteoarthritis in the lower limb compared to controls (8, 34), this relationship has not been confirmed among recreationally physically active people (10, 29). Our active co-twins

were not high-level athletes and therefore the intensity and duration of their activity may not have been high enough to cause them significantly more osteoarthritis.

Paragraph number 26 The need of hospital care can be seen as a summary measure of the impact of morbidity on different diseases and injuries. The findings that physically active members of the twins pairs tended to need hospital care less often and for a shorter duration than their inactive co-twins agrees with earlier analyses of larger cohorts (18) and studies of former athletes (21). Although no overall effect was observed on the preclinical disability scale, there was a tendency for inactive co-twins to have more difficulties and to report more task modification in daily activities. It seems that the benefits of a physically active lifestyle are higher than the adverse effects.

Study strengths and limitations

Paragraph number 27 The strengths of our study were a very long follow-up period and twin study design. We partly controlled for genetic factors and childhood environment by studying twin pairs comprehensively selected from the large Finnish Twin Cohort. Despite the fact that we started with a large population based twin cohort the number of twin pairs discordant for physical activity was relatively small. The small sample size is a limitation especially when studying diseases as outcomes. The reason for finding a low number of twin pairs discordant for disease could be either due to diseases occurring in both co-twins for genetic reasons or to having a relatively young and healthy study cohort at baseline (mean age of subjects was 28.5 years in 1975). Due to the small numbers we were not able to adjust the results of analyses with known covariates. The study design adjusts for gender, age and shared familial factors, and it is known that twins show similarity in their health habits more often than do unrelated

subjects. We did adjust most conditions for smoking (results not shown), but this did not change our results.

Paragraph number 28 A further study limitation is that the medical information was self-reported rather than based on data gathered from medical registers or subjects' formal medical notes. However studies have shown that agreement between self reported medical history and medical records is generally good, especially with respect to well-known chronic diseases (9, 28). Recall bias due to subjects not remembering all their diseases is an issue if the recall is different between active and inactive twins; active subjects may have a better memory for injuries and musculoskeletal disorders as these would have affected an important part of their life more than in the case of inactive subjects, thus biasing our risk estimates upwards. Also, subjects with severe dementia and subjects who had died did not participate. In DZ pairs, but not in MZ pairs, a higher number of inactive than active members of twin pairs had died before the end of our follow-up (unpublished data: Waller K et al. Physical activity, morbidity and mortality in twins: a 22-year prospective follow-up. Under review 2009). Although, another study limitation was self-reported physical activity data at baseline, these type physical activity questions have been commonly used in the epidemiological studies. In a study by Kujala et al. (19), the same physical activity questions predicted morbidity and mortality in a fashion consistent with other studies using somewhat different measures providing external validation to the questions.

Paragraph number 29 The ideal study method would have been to study the occurrence of diseases in a large number of monozygotic pairs discordant for physical activity. However, as the sample size was small and only few diseases were present it is not possible to draw separate conclusions for monozygotic twins. Therefore we cannot totally exclude the effect of

genetic selection bias on some of the results. The evidence on whether genetic selection explains, for example, the association between high physical activity and low mortality is conflicting. In a study among Swedish twins, in which no exclusion criteria regarding baseline diseases were imposed, genetic selection did not explain this association (6) whereas in a study of healthy twins from the Finnish Twin Cohort (17) genetic selection partially explained the association.

Conclusion

Paragraph number 30 Our longitudinal twin pair study found that the benefits of a physically active lifestyle outweigh the adverse effects even after taking familial effects into account. Physical activity reduces the risk for chronic diseases and helps in maintaining life satisfaction. However, genetic factors may play a role in explaining some of the association between disease occurrence and physical activity, as some of the findings were more salient among dizygotic than monozygotic twin pairs discordant for physical activity.

Acknowledgements

Financial support: This study was supported by the Finnish Ministry of Education, the Juho Vainio Foundation and the University of Jyväskylä. The Finnish Twin Cohort Study is part of the Academy of Finland Centre of Excellence in Complex Disease Genetics.

The results of the present study do not constitute endorsement by ACSM.

Conflict of Interest Statement

The authors have no potential conflicts of interest related to the funding.

References

1. Andreasen CH, KL Stender-Petersen, MS Mogensen, et al. Low physical activity accentuates the effect of the FTO rs9939609 polymorphism on body fat accumulation. *Diabetes*. 2008; 57(1):95-101.
2. Barroso I. Genetics of Type 2 diabetes. *Diabet Med*. 2005; 22(5):517-35.
3. Batra V, AA Patkar, WH Berrettini, SP Weinstein, FT Leone. The genetic determinants of smoking. *Chest*. 2003; 123(5):1730-9.
4. Bouchard C, FT Dionne, JA Simoneau, MR Boulay. Genetics of aerobic and anaerobic performances. *Exerc Sport Sci Rev*. 1992; 20:27-58.
5. Brown WJ, NW Burton, PJ Rowan. Updating the evidence on physical activity and health in women. *Am J Prev Med*. 2007; 33(5):404-11.
6. Carlsson S, T Andersson, P Lichtenstein, K Michaelsson, A Ahlbom. Physical Activity and Mortality: Is the Association Explained by Genetic Selection? *Am J Epidemiol*. 2007; 166:255-9.
7. Casas JP, J Cooper, GJ Miller, AD Hingorani, SE Humphries. Investigating the genetic determinants of cardiovascular disease using candidate genes and meta-analysis of association studies. *Ann Hum Genet*. 2006; 70(Pt 2):145-69.
8. Conaghan PG. Update on osteoarthritis part 1: current concepts and the relation to exercise. *Br J Sports Med*. 2002; 36(5):330-3.
9. Haapanen N, S Miilunpalo, M Pasanen, P Oja, I Vuori. Agreement between questionnaire data and medical records of chronic diseases in middle-aged and elderly Finnish men and women. *Am J Epidemiol*. 1997; 145(8):762-9.
10. Hart LE, DA Haaland, DA Baribeau, IM Mukovozov, TF Sabljic. The relationship between exercise and osteoarthritis in the elderly. *Clin J Sport Med*. 2008; 18(6):508-21.

11. Hootman JM, CA Macera, BE Ainsworth, CL Addy, M Martin, SN Blair. Epidemiology of musculoskeletal injuries among sedentary and physically active adults. *Med Sci Sports Exerc.* 2002; 34(5):838-44.
12. Kaprio J, M Koskenvuo. Genetic and environmental factors in complex diseases: the older Finnish Twin Cohort. *Twin Res.* 2002; 5(5):358-65.
13. Kaprio J, M Koskenvuo, H Langinvainio, K Romanov, S Sarna, RJ Rose. Genetic influences on use and abuse of alcohol: a study of 5638 adult Finnish twin brothers. *Alcohol Clin Exp Res.* 1987; 11(4):349-56.
14. Kaprio J, S Sarna, M Koskenvuo, I Rantasalo. *The Finnish Twin Registry: baseline characteristics. Section II. History of symptoms and illnesses, use of drugs, physical characteristics, smoking, alcohol and physical activity.* Helsinki: University of Helsinki, Department of Public Health; 1978. pp **120-122.**
15. Karjalainen J, H Tikkanen, M Hernelahti, UM Kujala. Muscle fiber-type distribution predicts weight gain and unfavorable left ventricular geometry: a 19 year follow-up study. *BMC Cardiovasc Disord.* 2006; 6(1):2.
16. Koivumaa-Honkanen H, R Honkanen, M Koskenvuo, H Viinamaki, J Kaprio. Life dissatisfaction as a predictor of fatal injury in a 20-year follow-up. *Acta Psychiatr Scand.* 2002; 105(6):444-50.
17. Kujala UM, J Kaprio, M Koskenvuo. Modifiable risk factors as predictors of all-cause mortality: the roles of genetics and childhood environment. *Am J Epidemiol.* 2002; 156(11):985-93.
18. Kujala UM, J Kaprio, S Sarna, M Koskenvuo. Future hospital care in a population-based series of twin pairs discordant for physical activity behavior. *Am J Public Health.* 1999; 89(12):1869-72.

19. Kujala UM, J Kaprio, S Sarna, M Koskenvuo. Relationship of leisure-time physical activity and mortality: the Finnish twin cohort. *JAMA*. 1998; 279(6):440-4.
20. Kujala UM, P Marti, J Kaprio, M Hernelahti, H Tikkanen, S Sarna. Occurrence of chronic disease in former top-level athletes. Predominance of benefits, risks or selection effects? *Sports Med*. 2003; 33(8):553-61.
21. Kujala UM, S Sarna, J Kaprio, M Koskenvuo. Hospital care in later life among former world-class Finnish athletes. *JAMA*. 1996; 276(3):216-20.
22. Kupper N, G Willemsen, H Riese, D Posthuma, DI Boomsma, EJ de Geus. Heritability of daytime ambulatory blood pressure in an extended twin design. *Hypertension*. 2005; 45(1):80-5.
23. LaMonte MJ, SN Blair, TS Church. Physical activity and diabetes prevention. *J Appl Physiol*. 2005; 99(3):1205-13.
24. Leinonen R, E Heikkinen, M Hirvensalo, et al. Customer-oriented counseling for physical activity in older people: study protocol and selected baseline results of a randomized-controlled trial (ISRCTN 07330512). *Scand J Med Sci Sports*. 2007; 17(2):156-64.
25. Loos RJ, C Bouchard. Obesity--is it a genetic disorder? *J Intern Med*. 2003; 254(5):401-25.
26. Mänty M, A Heinonen, R Leinonen, et al. Construct and predictive validity of a self-reported measure of preclinical mobility limitation. *Arch Phys Med Rehabil*. 2007; 88(9):1108-13.
27. Marenberg ME, N Risch, LF Berkman, B Floderus, U de Faire. Genetic susceptibility to death from coronary heart disease in a study of twins. *N Engl J Med*. 1994; 330(15):1041-6.
28. Okura Y, LH Urban, DW Mahoney, SJ Jacobsen, RJ Rodeheffer. Agreement between self-report questionnaires and medical record data was substantial for diabetes, hypertension,

- myocardial infarction and stroke but not for heart failure. *J Clin Epidemiol.* 2004; 57(10):1096-103.
29. Physical Activity Guidelines Advisory Committee. *Physical Activity Guidelines Advisory Committee Report, 2008.* Washington, DC: U.S. Department of Health and Human Services; 2008, **pp.G2;4-12, G3;9-15.**
30. Rejeski WJ, SL Mihalko. Physical activity and quality of life in older adults. *J Gerontol A Biol Sci Med Sci.* 2001; 56 Spec No 2:23-35.
31. Rose GA, H Blackburn. Cardiovascular survey methods. *Monogr Ser World Health Organ.* 1968; 56:1-188.
32. Sarna S, J Kaprio, P Sistonen, M Koskenvuo. Diagnosis of twin zygosity by mailed questionnaire. *Hum Hered.* 1978; 28(4):241-54.
33. Stubbe JH, DI Boomsma, EJ De Geus. Sports participation during adolescence: a shift from environmental to genetic factors. *Med Sci Sports Exerc.* 2005; 37(4):563-70.
34. Vignon E, JP Valat, M Rossignol, et al. Osteoarthritis of the knee and hip and activity: a systematic international review and synthesis (OASIS). *Joint Bone Spine.* 2006; 73(4):442-55.
35. Waller K, J Kaprio, UM Kujala. Associations between long-term physical activity, waist circumference and weight gain: a 30-year longitudinal twin study. *Int J Obes.* 2008; 32:353-61.
36. Warburton DE, CW Nicol, SS Bredin. Health benefits of physical activity: the evidence. *CMAJ.* 2006; 174(6):801-9.

Figure legends

Figure 1. Flow chart of participants.

Figure 2. Leisure-time MET indices for 146 comprehensively selected twin pairs discordant for both intensity and volume of physical activity in 1975 and 1981. Similar results were seen for male, female, monozygotic and dizygotic pairs.

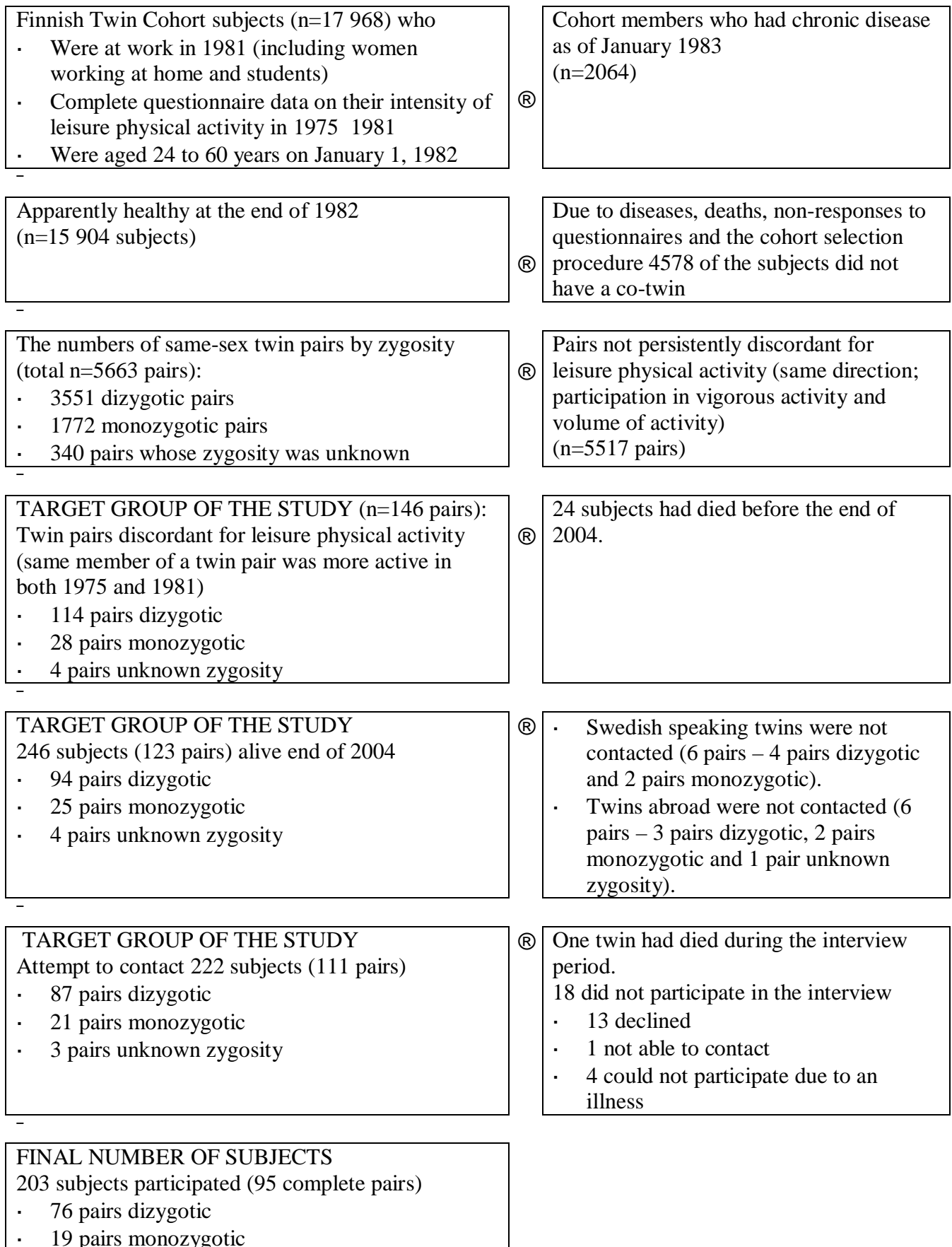


Figure 1.

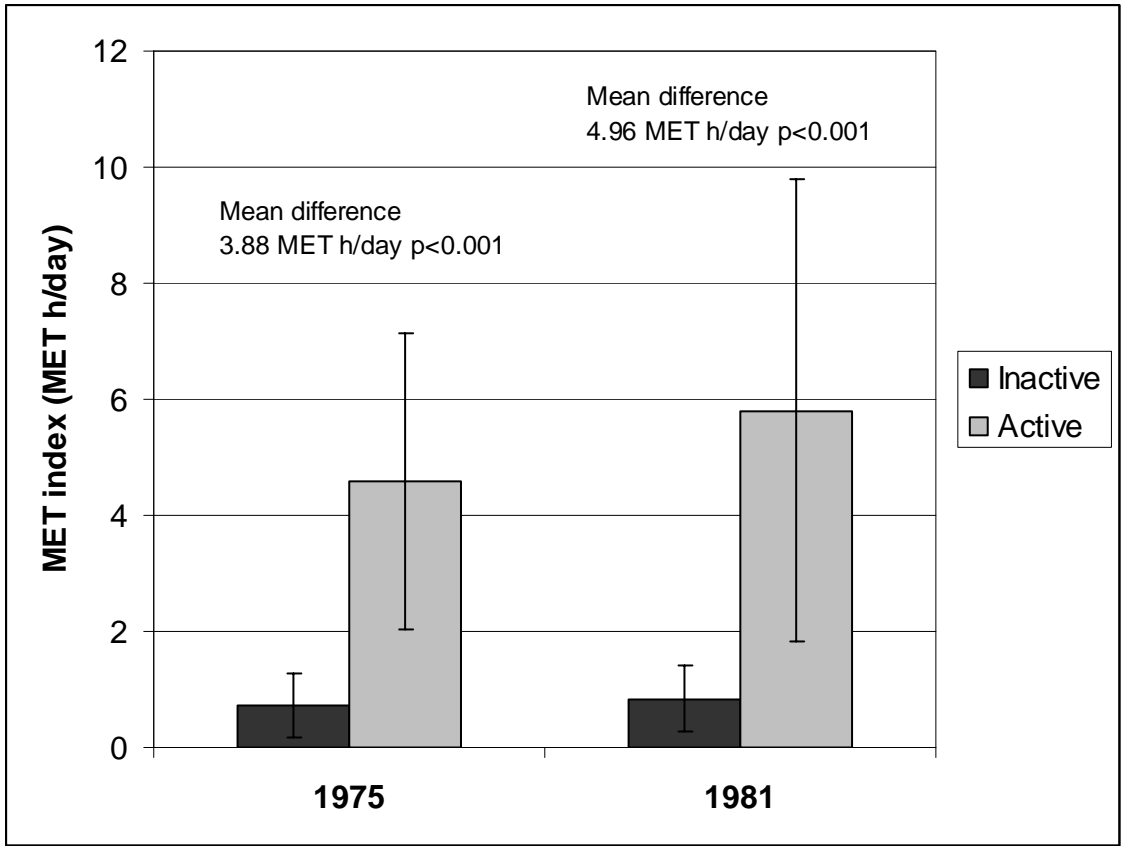


Figure 2.

Table 1. 1975 baseline characteristics for 95 twin pairs. *

Characteristics	Inactive	Active	p-value
Age (Mean ± SD)	28.5 ± 6.9	28.5 ± 6.9	
Height (Mean ± SD)	169.2 ± 8.4	169.5 ± 8.1	0.53
Weight (Mean ± SD)	63.2 ± 12.1	63.7 ± 10.2	0.65
BMI (Mean ± SD)	22.0 ± 2.8	22.1 ± 2.3	0.66
Ever regular smoker (N, %)	51 (53.7%)	43 (45.3%)	0.22
Pack-years smoked (Mean ± SD)	3.1 ± 4.8	1.9 ± 3.4	0.008
Alcohol grams/day (Mean ± SD)	7.2 ± 14.4	7.6 ± 11.8	0.74
Diagnosed hypertension (N, %)	7 (7.4%)	5 (5.3%)	0.75
Life satisfaction (Mean ± SD) †	8.8 ± 2.5	8.0 ± 2.7	0.026
Marital status (N, %)			0.027
Single	28 (29.5%)	41 (43.2%)	
Married	62 (65.3%)	52 (54.7%)	
Divorced	5 (5.3%)	2 (2.1%)	
Work-related physical activity in 1975 (N, %)			0.19
Sedentary	28 (29.8%)	33 (34.7%)	
Standing or walking at work	14 (14.9%)	20 (21.1%)	
Light manual labour	46 (48.9%)	39 (41.1%)	
Heavy manual labour	6 (6.4%)	3 (3.2%)	
Social class (N, %)			0.26
Upper white-collar	6 (6.3%)	8 (8.4%)	
Clerical work	28 (29.5%)	25 (26.3%)	
Skilled workers	33 (34.7%)	39 (41.1%)	
Unskilled workers	7 (7.4%)	8 (8.4%)	
Farmer	14 (14.7%)	2 (2.1%)	
Other (Students, conscript, retired, unknown)	7 (7.4%)	13 (13.7)	
MET index ‡	0.71 ± 0.54	4.23 ± 2.23	<0.001

* Plus-minus values are means ± SD.

† The life satisfaction index was a four-question scale with sum score ranging between 4-20, with an increasing score indicating a decrease in life satisfaction.

‡ MET index includes leisure-time physical activity and work journey activity

Table 2. Chronic and other physician diagnosed diseases for 95 pairs

Disease	Inactive N (%)	Active N (%)	OR	95 % CI	p- value
At least 1 chronic disease *	41 (43.2 %)	41 (43.2 %)	1.00	0.56 – 1.78	1.00
At least 2 chronic diseases *	25 (26.3 %)	19 (20.0 %)	0.7	0.35 – 1.39	0.31
At least 1 chronic diseases * except hypertension	45 (47.4 %)	42 (44.2 %)	0.88	0.49 – 1.57	0.66
At least 2 chronic diseases * except hypertension	15 (15.8 %)	9 (9.5 %)	0.54	0.21 – 1.35	0.19
Prediabetes	7 (7.4%)	1 (1.1%)	0.14	0.02 – 1.16	0.07
Type 2 diabetes	7 (7.4%)	3 (3.2%)	0.2	0.02 – 1.71	0.14
Type 2 diabetes or prediabetes	14 (14.7%)	4 (4.2%)	0.09	0.01 – 0.70	0.022
Cardiovascular disease *	5 (5.3%)	7 (7.4%)	1.67	0.40 – 6.97	0.48
CHD including MI	4 (4.2%)	5 (5.3%)	1.5	0.25 - 8.98	0.66
Stroke or intermittent claudication	1 (1.1%)	2 (2.1%)	2	0.18 – 2.06	0.57
Cardiac failure	0	2 (2.1%)			
BP medication in 2005 †	18 (21.4%)	19 (22.6%)	1.09	0.48 – 2.47	0.84
Elevated BP or BP medication in 2005 †	43 (51.2%)	31 (36.9%)	0.46	0.22 – 0.96	0.039
Pulmonary disease *	8 (8.4%)	3 (3.2%)	0.33	0.09 – 1.23	0.099
Asthma	7 (7.4%)	2 (2.1%)	0.29	0.06 – 1.38	0.12
COPD	1 (1.1%)	0			
Chronic bronchitis	2 (2.1%)	2 (2.1%)	1		1
Gastric ulcer	6 (6.3%)	6 (6.3%)	1		1
Depression	9 (9.5%)	9 (9.5%)	1		1
Other physician diagnosed chronic disease ‡	30 (31.6%)	21 (22.1%)	0.57	0.28 – 1.16	0.12

* At least one of the following listed below

† New cases since 1975, If person had hypertension by questionnaire or medication for hypertension in 1975 they were excluded from the analyses, 84 pairs included in the analyses

‡ Includes diseases such as cancer 8 individuals (of which breast cancer 4), different allergies 7, osteoporosis 5, thyroid gland problem 5, eye problems 5 (glaucoma 3), migraine 3.

BP = blood pressure

Table 3. Selected musculoskeletal problems for 95 pairs

Disease	Inactive N (%)	Active N (%)	OR	95 % CI	p- value
Arthritis *	22 (23.2%)	27 (28.4%)	1.38	0.68 – 2.83	0.37
Rheumatoid arthritis	1 (1.1%)	4 (4.2%)	4	0.45 – 35.79	0.22
Osteoarthritis *	22 (23.2%)	25 (26.3%)	1.21	0.60 – 2.46	0.59
Hip osteoarthritis	5 (5.3%)	4 (4.2%)	0.75	0.17 – 3.35	0.71
Knee osteoarthritis	10 (10.5%)	11 (11.6%)	1.13	0.43 – 2.92	0.81
Any other osteoarthritis †	10 (10.5%)	17 (17.9%)	2.17	0.82 – 5.70	0.12
Sciatica	29 (30.5%)	22 (23.2%)	0.68	0.35 – 1.31	0.25
Tension neck	11 (11.6%)	9 (9.5%)	0.78	0.29 – 2.09	0.62
Injuries typical for athletes *	29 (30.5%)	42 (44.2%)	1.87	0.997 – 3.49	0.051
Acute injuries	24 (25.3%)	31 (32.6%)	1.44	0.76 – 2.72	0.27
Tendon rupture (achilles or other)	6 (6.3%)	5 (5.3%)	0.8	0.22 – 2.98	0.74
Achilles tendon	2 (2.1%)	2 (2.1%)	1		1
Other tendon	4 (4.2%)	3 (3.2%)	0.67	0.11 – 4.00	0.66
Knee or ankle injury	20 (21.1%)	30 (31.6%)	1.77	0.90 – 3.49	0.10
Knee meniscus	5 (5.3%)	8 (8.4%)	1.75	0.51 - 5.98	0.37
Knee ligament	5 (5.3%)	5 (5.3%)	1		1
Ankle ligament	13 (13.7%)	21 (22.1%)	1.8	0.83 – 3.90	0.14
Stress injury/ Tendonitis (achilles or other)	10 (10.5%)	17 (17.9%)	1.88	0.80 – 4.42	0.15
Achilles tendon inflammation	4 (4.2%)	6 (6.3%)	1.5	0.42 - 5.32	0.53
Other tendon inflammation	7 (7.4%)	12 (12.6%)	1.83	0.68 – 4.96	0.23

* At least one of the following listed below

† The other osteoarthritis includes osteoarthritis in hand (15 individuals), shoulder 6, neck 6, back 4, toes 3 and wrists 1